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Development of a Novel Validated Tool for Predicting Patient Adherence to Prescribed Medication

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Abstract

Patient nonadherence to medication harms patient outcomes and raises costs via wasted and unnecessary treatment (Osterberg and Blaschke, 2005). However, current adherence measures are far from optimal (Vitolins et al., 2000), and adherence enhancing interventions rarely successful (Haynes et al., 2008). This may be a reflection of inadequate patient targeting and adherence measurement. This thesis describes the development of questionnaires intended to be clinically useful by predicting patient risk of nonadherence. A scoping review with meta-analysis was undertaken to identify predictors objectively shown to be associated with nonadherence. Any pre-existing questionnaires to measure the selected predictors were identified via literature review. Pre-existing questionnaires incorporated were the Beliefs about Medicines Questionnaire (Horne et al., 1999), Perceived Stress Scale (Cohen et al., 1983), Patient Health Questionnaire (Kunik et al., 2007), and the Patient-Doctor Relationship Questionnaire (Van der Feltz-Cornelis et al., 2004). Novel items were developed to measure patient demographics, health literacy, mental health, risky health behaviours, beliefs about medicines, self-efficacy , social support, and access to medicines. These scales were incorporated into two novel questionnaires. The Patient and Lifestyle Scale (PALS), and the Wellbeing and Medications Scale (WAMS). A feasibility study was conducted with 16 patients at a GP surgery to identify limitations in research design and perform preliminary psychometric assessment. Issues with participant identification were highlighted, however, indications were that PALS and WAMS could be used to predict self-reported and prospective refill adherence. A practitioner focus group appraised the clinical utility of the questionnaires whilst acceptability and validity were assessed via six participant interviews. The PALS and WAMS were perceived to be potentially clinically useful and most items were considered acceptable. Findings also indicated that mental distress is associated with nonadherence and that long term adherence may depend more upon integrating medicines into every day habits than rational cost-benefits appraisals.

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Chapter 1 – Introduction

1.1 General Introduction

It is estimated that between 25% and 50% of all patients diagnosed with a chronic disease do not take their medication as prescribed (Sackett and Snow, 1979, DiMatteo, 2004c). This is a significant issue for the NHS, which dispensed 886 million prescriptions in 2009 at a cost of over £8.5 billion (NHS Information Centre, 2010). If a quarter of those medicines are not taken, this represents a significant waste of public resources and a high cost to public health. The UK's Department of Health (2008) costs the number of unused and unwanted medications that are returned to pharmacies at approximately £100 million per year, while NICE (National Institute for Clinical Excellence, 2009) report that between 0.3 and 1.2% of hospital admissions are directly related to patients not taking their medicine as prescribed, at a further cost of between £36 million to £196 million per year to the NHS. Osterberg and Blaschke (2005) estimate the cost of unnecessary admissions to hospital in the US caused by patients not taking medicines as prescribed to be approximately $100 billion per year, while Hovstadius and Petersson (2011) report that in Sweden over €1 billion are spent on medicines that are never taken.

With such huge financial pressures attached to a major public health concern, the question of how and why patients do not take their medicines as prescribed has become a vast field of research. Despite the number of articles concerning whether patients take medication as prescribed now stretching into the tens of thousands (Martin et al., 2005), there is remarkably little cohesion in the field, and consequently, progress has been poor (Nunes et al., 2009). There is no definitive measure employed, nor a coherent picture of the key variables. Even the words used to describe the problem remain debated. Patient compliance, adherence, and concordance are used, often without definition or with due sensitivity given to their specific meanings. This lack of coherence further fragments an intricate and complicated research problem (Vermeire et al., 2001, Kyngäs et al., 2000).

1.2 Compliance, Adherence, and Concordance

1.2.1 Compliance

The two most common terms used to describe patients following the recommendations of health professionals are 'adherence' and 'compliance'. Haynes et al.(1979) defined compliance as 'the extent to which a person's behavior [sic] (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice'. This definition assumes that the more patient behaviour coincides with medical advice then the 'better behaved' the patient(RPSGB and Merck Sharp & Dohme, 1997). Words such as 'comply' or 'obey' can be perceived as reducing patients to 'passive followers of doctors' instructions (Stimson, 1974). Haynes et al.(1979) did stipulate that compliance is an appropriate response only where a diagnosis is correct, the treatment prescribed is effective, and where the patient has provided informed consent, however, others have not been so careful with the use of the term(Trostle, 1988). For example, one study defined 'compliance' as completing a treatment regime in a clinical trial whether or not doctors had advised participants to stop taking the medicines (Glynne-Jones et al., 2008).

Although 'compliance' is still frequently used in the literature, it has been largely replaced by the term 'adherence' which is considered less authoritarian (Sawyer and Aroni, 2003).

1.2.2 Adherence

Adherence is most commonly defined as 'the extent to which a person's behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider' (World Health Organisation, 2003). This definition emphasises the requirement of agreement, reflecting a trend towards seeing the patient as a partner in a therapeutic alliance (Kyngäs et al., 2000).

The WHO definition of adherence does not fully articulate what is meant by a "nonadherent" patient. It would not make sense to label a patient who misses one dose of their medication at no cost to their health as nonadherent (Horne, 2000). Many

authors take the approach of dichotomising adherence into patients taking a sufficient proportion of their medicines to receive therapeutic benefit and those that are not (Chapman, 2004). For example, researchers investigating antiretroviral medications usually indicate that those taking less than 95% of their medications are nonadherent, because when adherence is below this proportion of medicines taken the benefits of antiretrovirals become dubious (Atkinson and Petrozzino, 2009). However, this method requires each medication regimen to have a different cut off for adherence. For example, Sackett and Snow (1979) report that only 30% of a prophylactic penicillin regime was required to offer protection from rheumatic fever, while 80% of an antihypertensive medication regimen must be taken before therapeutic benefit is conferred. When the required dose for each medication is not known it may be unproductive to stigmatise patients with the 'nonadherent' label when their behaviour may cause them no harm (Steiner and Earnest, 2000). It may be more appropriate to report mean proportions of medicines taken across all participants instead of reporting proportions of adherent versus nonadherent individuals (Horne, 2000). This would more accurately reflect the true rates of adherence and provide more accurate measurement. This would also remove an element of judgement placed upon the patient. However, judgements about adherence rates could only be performed at the population level which may lack clinical utility. Most authors define adherence rates in terms of proportions of adherent individuals (DiMatteo, 2004c). They also tend to do so using Sackett and Snow's 80% cut off (Peterson et al., 2007).

1.2.3 Concordance

The traditional 'paternalistic' model of medicine defines the practitioner as an expert and the patient is expected to comply with their advice based on superior knowledge (Britten and Weiss, 2004, Charles et al., 1997). However, the priorities of patients may not be the same as the priorities of healthcare providers. Medical professionals' priorities are to eradicate or prevent illness, while patients' are more concerned with maintaining normal functioning (Pollock, 2005). Patients often cease to take medication once they feel better and this could be due to the medicines lowering quality of life via side effects and forced routines, more than they confer benefits by offering an improvement in health (Miller, 1997). The concordance movement was initiated to encourage acknowledgement that

patients health beliefs could be internally valid and consistent yet contrary to that of the health care provider (Marinker, 2004). Concordance aims to promote a therapeutic alliance with patients 'in which the most important determinations are agreed to be those that are made by the patient'(RPSGB and Merck Sharp & Dohme, 1997). Because concordance describes an approach to consultations it is improper to use the term as a synonym for adherence (Cushing and Metcalfe, 2007).

1.3 Measurement of adherence

An accurate measure of adherence is necessary in order to identify which patients are nonadherent and to quantify the effects of any intervention (Insull Jr., 1984). However, there is no universally accepted 'gold standard' of adherence measurement. All measures have strengths and weaknesses in terms of practicality, accuracy, and acceptability (Vitolins et al., 2000).

All attempts to measure adherence to medication will be susceptible to three types of bias unless covert measurement is used, which may not always be an ethically appropriate option. Reactivity bias refers to the phenomenon whereby observing behaviour, changes the behaviour that is being observed (Horne, 2000). White coat adherence refers to adherence improving in the period shortly before patients visit health professionals (Schwartz and Quigley, 2008, Rudd, 1998). Pygmalion effects refer to the phenomenon where researcher expectations may generate a self-fulfilling prophecy. For example, patients' adherence may be improved when they are receiving an intervention to improve adherence because they receive preferential treatment to patients not receiving an intervention. Patients with a good relationship with their doctor may also receive a higher standard of treatment than those with lower quality relationships (Chapman, 2004).

Measures of adherence may also differ in terms of their sensitivity and specificity. A measure of adherence is sensitive if it is able to correctly identify nonadherent patients and specific if it identifies only nonadherent patients as nonadherent. This can vary by measurement type. For example, when patients self-report as nonadherent this is usually accurate, but self-reports often incorrectly identify nonadherent patients as adherent (Farmer, 1999). In contrast, electronic monitoring devices are more likely to incorrectly label an adherent patient as nonadherent. Because of these various differences between the methods of measurement, DiMatteo (2004c) found significant differences in adherence rates reported by different measurement types.

1.3.1 Direct measurement of adherence

The most obvious way of measuring adherence is to observe patients taking their medicines. However, this is impractical in the out-patient setting where the administration of medicine is under a greater degree of patient control (DiMatteo, 2004c). Even in closely monitored clinical trials and in-patient settings, direct patient observation is imperfect, with some patients feigning adherence and removing medication from their mouths when no longer observed (Farmer, 1999).

A more common direct measurement of patient adherence is to take a blood sample from a patient and detect whether the medicine or one of its metabolites is present in the blood (Horne, 2000). The primary advantage to this method is high sensitivity (Farmer, 1999). However, due to individual variability in metabolism it is not possible to quantify how adherent a patient has been via this method (Mattson and Friedman, 1984, Kettler et al., 2002). For this reason direct measurement of adherence is particularly sensitive to white coat adherence because patients only need to take pills immediately before measurement to give the impression of adherence (Horne, 2000, Chapman, 2004, Cramer et al., 1989).

It is also extremely difficult to directly measure metabolites of many medicines (Gordis, 1979). One way to circumvent this issue is to develop a marker which can be added to the medicine preparation. Unfortunately developing an adequate marker is both expensive and difficult. An ideal marker must be chemically inert, pharmacologically inactive, non-toxic, and must not accumulate in the body, with a half-life suitable for accurate detection but not so long that the test loses its sensitivity (Insull Jr., 1984).

Further problems with using direct methods are that they are expensive, requiring collection, storage, and testing of blood samples, and they are also ethically dubious. Direct measurements are often uncomfortable and invasive for patients (Horne, 2000). Direct measurement of adherence is only practical for single-dose therapies, where administration of medication is intermittent, or when patients are hospitalised (Vermeire et al., 2001, Gordis, 1979).

1.3.2 Indirect measures of adherence

1.3.2.1 Pill Counts

One of the most popular methods of assessing adherence rates has been to determine how many pills patients have in their possession compared to how many they would have if they had perfect adherence. At least until the development of electronic monitoring systems, pill counts were considered the reference standard for all other adherence measures (Farmer, 1999). The measure is simple, requiring no advanced technology (Horne, 2000) and pill counts can also be adapted to other preparation modes by weighing powder or liquid preparations (Farmer, 1999). However, pill counts have a tendency to overestimate adherence because pills may be taken incorrectly, given to other people, moved to a different container, removed from the bottle and dropped, or lost prior to ingestion (Gordis, 1979). There is also no indication of the pattern of nonadherence a patient may display (Farmer, 1999). A patient may have missed occasional doses due to lapses of memory, or they may have taken a medicine holiday, or else they may have taken medication only in periods leading up to medical assessment (Gordis, 1979, Cramer et al., 1989). Doses may also be deliberately dumped where patients are aware their medication is being monitored (Gordis, 1979, Horne, 2000, Osterberg and Blaschke, 2005, Farmer, 1999, Vitolins et al., 2000, Rudd et al., 1989, Pullar et al., 1989). This measure is also dependent upon patients remembering to bring pill bottles for assessment which may increase reactivity biases (Vitolins et al., 2000, Haynes et al., 1980). Pill bottles can also be mislaid, confounding results (Cramer et al., 1989). Unannounced pill counts might generate more accurate estimates of adherence (Horne, 2000, Pullar et al., 1989, Farmer, 1999, Haynes et al., 1980).

1.3.2.2 Prescription refill rates

Refill rates estimate adherence based upon either how much time patients had medication available to them or else estimating nonadherence based upon how many

days patients did not have access to medication (Steiner and Prochazka, 1997). Prescription refills are easy to quantify by various methods. This can make them adaptable, as they can measure total adherence rates over a whole regimen, or else provide a picture of the pattern of adherence over a long period of time if regular measurement intervals are used (Steiner and Prochazka, 1997). For example, if there is one large gap evident this may imply the patient had taken a medication holiday. Conversely persistent small delays may imply occasional missed doses. One of the major benefits of refill rates is that they allow a measure of adherence that can be taken without patient knowledge, sidestepping the problems of reactivity (Vitolins et al., 2000, Balkrishnan and Jayawant, 2007). The low cost of the measure also makes it a very popular method when dealing with large populations or for lengthy longitudinal studies (Van Wijk et al., 2006).

However, refill rates do have significant limitations. There is a lack of consistency in measurement which can make refill rates difficult to interpret (Van Wijk et al., 2006). Refill rates are also an abstract measure of adherence because they measure acquisition of medication rather than its consumption (Feinstein, 1979, Steiner and Prochazka, 1997). Refill adherence give the maximum possible adherence a patient could have displayed (Sherman et al., 2000), and consequently offer high specificity but poor sensitivity (Steiner and Prochazka, 1997). Furthermore, when medicines are not prescribed in regular short intervals it can be difficult to describe the different patterns of nonadherence displayed by patients (Balkrishnan and Jayawant, 2007). Refill rates can be compromised if patients are able to acquire medicines from alternate sources to those in a study or from multiple pharmacies (Vitolins et al., 2000, Balkrishnan and Jayawant, 2007). A final problem is that it can be difficult to determine whether changes in patients medication behaviour are due to nonadherence or a change in the medical advice they have been given (Van Wijk et al., 2006).

1.3.2.3 Electronic monitoring devices

Electronic monitors work by recording the time and date of each opening of a medicine container (Cramer et al., 1989). Records can also be transmitted remotely to prevent data loss (Sajatovic et al., 2010). Electronically monitoring adherence offers the possibility of

collecting the exact pattern of adherence participants exhibit (Cramer et al., 1989). Andrejak et al. (2000) used electronic monitors to compare two antihypertensive medicines, and although the proportion of medicines taken for each was comparable, use of electronic monitors was able to show how one medicine was more readily taken on schedule than another. Moreover, it can be seen whether a patient regularly misses a specific dose, misses doses sporadically, or has taken a longer break from medication (Farmer, 1999). No other method of adherence assessment allows an accurate assessment of this type of data, which can differentiate between dose and schedule adherence (Waterhouse et al., 1993, Smith et al., 2010). Some modern monitors can also offer extra clinical utility as adherence aids, capable of reminding participants to take their medicines (Haberer et al., 2012).

Despite these strengths there are significant limitations with electronic monitoring devices. As with pill counts, actual ingestion of the medication once the pill box has been opened cannot be proven (Ingerski et al., 2011). Martin et al. (2007) found that 60% of participants in their sample required data to be deleted because they had opened the bottle for reasons other than to take a dose. For this reason electronically recorded data frequently gives lower adherence rates than alternative adherence measures (Liu et al., 2001, Smith et al., 2010, Byerly et al., 2005). Some devices can partially correct for this by asking participants if they have opened the device to take a dose or not (Sajatovic et al., 2010), and it has been demonstrated that pill counts correlate more strongly with electronic monitoring when this adjustment is made (Haberer et al., 2012). However, these adjustments do not account for patients who are intentionally nonadherent and opening the box only to dump the dose, although some inhaler monitors can note multiple uses in a short period of time to identify dumped doses (Ingerski et al., 2011). Data loss can and does happen, with malfunction rates ranging from 5 to 20% for bottle cap monitors and 8 to 21% for inhaler monitors (Ingerski et al., 2011). Wu et al. (2008) lost data from 13 patients in their sample because the monitor hardware or software malfunctioned, or because the patients lost or damaged the device. The bulk of the devices can cause problems for patients with some preferring to remove more than one dose per opening in order to move medication into more portable or less conspicuous packaging (Sajatovic et al., 2010). Smith et al. (2010) had one participant that opened their monitoring device only once per week to place medicine into a pill box. This resulted in their being classified as nonadherent by electronic device but 100% adherent via pill

count and self-report. Wetzels et al. (2006) found that there was almost no agreement between electronic monitoring of adherence and refill data. The primary cause of this was the very high adherence of patients over the 2 month period of electronic monitoring versus the arguably more natural behaviour of patients over the 12 month duration assessed by medication refill data. These difficulties mean that electronic monitoring can underestimate adherence when patients swap pill boxes (Liu et al., 2001) or overestimate adherence when measurement is over the short term (Wetzels et al., 2006). Often, a choice has to be made regarding which prescribed medication is electronically monitored due to the prohibitive costs of providing each patient with multiple monitoring devices (Sajatovic et al., 2010). These costs also prohibit their use in many naturalistic studies and practice settings, and limit their deployment primarily to clinical trials (Horne et al., 2005). Many current devices are also difficult to conceal, and so an explanation must be given to patients as to why their medication container appears different to normal if adherence is to be measured covertly (Waterhouse et al., 1993). The constant visual reminder of observation from electronic devices can exaggerate the reactivity biases and keep adherence rates artificially high for long periods of time (Chui et al., 2003).

The wealth of data provided by electronic monitors makes them an attractive option when the resources are in place to allow their use. However, the limitations should not be underestimated and claims that they mark the gold standard of adherence measurement are premature (Smith et al., 2010).

1.3.2.4 Therapeutic outcome

A final objective measure of adherence is the use of therapeutic outcomes as an indication of adherence. This is dependent on a close relationship between adherence and outcome being true (Horne, 2000). This can be the case for some medicines, for example Cramer et al. (1989) could directly attribute epileptic episodes to missed doses of medication. However, while good adherence is associated with clinical outcome (DiMatteo et al., 2002), it does not logically follow that a good outcome must be the result of good adherence; nor is it true that other factors besides adherence do not affect outcome (Gordis, 1979). Clinical outcome is, therefore, a very abstract measure of adherence, and it would be highly judgemental to assume a poor outcome was due to

nonadherence on behalf of the patient. Balkrishnan and Jayawant (2007) also argue that the level of medication adherence required to maintain normal blood glucose levels in a patient with diabetes may be very different to the level of adherence below which patients may suffer negative consequences. The choice of therapeutic outcome measured may therefore have a significant impact upon how patients are classified.

1.3.2.5 Physician estimates of adherence

In the clinical setting physicians must determine whether or not treatment non-response is due to treatment failure or nonadherence. However, physician estimates barely differ from chance (Gordis, 1979, Paterson et al., 2000). Byerly et al. (2005) found that physicians failed to correctly identify a single nonadherent patient as assessed by electronic monitoring. This could result in patients being removed from or denied potentially effective therapy or being prescribed stronger doses than required (Paterson et al., 2002). It is therefore imperative that physicians are able to gather information from their patients that will improve the accuracy of judgements of nonadherence to ensure treatment decisions are appropriate.

1.3.2.6 Patient self-reports of adherence

Questionnaires, interviews and diaries can be used to obtain a subjective assessment of adherence directly from patients. Self-reports are inexpensive because they do not require any advanced technology, and they are generally easy to process (Vitolins et al., 2000). However, the subjectivity of self-report measures makes absolute adherence rates impossible to calculate. Guénette et al. (2005) argue that self-reports can only adequately identify nonadherence and not adherence, because the authenticity of high self-reported adherence cannot be verified. Furthermore Wu et al. (2008) found that objectively rated adherence via electronic monitoring was related to health outcome, whereas patient self-reported adherence was not.

Recall biases prevent accurate quantification of self-report measures (Chung et al., 2008). Patients will be better able to recall recent events, making self-reports of adherence over

a short time period more accurate than more global assessments of adherence (Oppenheim, 1992). However, asking about adherence over the last couple of days makes it hard to determine a pattern of adherence behaviour (Paterson et al., 2002). Horne (2000) also argues that patients are more likely to remember positive events than negative events, such as not taking medication. Mental health and emotions are also known to influence memory and bias recall. For example, depressed patients are more likely to recall negative events and so may be more likely to self-report nonadherence (Payne and Corrigan, 2007).

1.3.2.7 Adherence diaries

Medication taking diaries are an uncommon method of adherence measurement. Diaries take longer to process than questionnaires and are highly susceptible to reactivity biases because patients must fill them in after each medication dosing event which may enhance adherence. Furthermore they are an additional behaviour patients may be intentionally or unintentionally non-adherent to (Horne, 2000). If a patient forgets to take their medication they may also be more likely forget to fill in their diary to note the omission. However, diaries are reported to correlate better to objective measures of adherence than do interviews (Garber et al., 2004).

1.3.2.8 Interviews

All self-reports are subject to patients wishing to present themselves in the best possible way (Furnham and Henderson, 1982). Being in the same room as a clinician or researcher heightens the motivation of the participant to appear socially desirable (Richman et al., 1999). Haynes et al. (1980) found that interviews overestimated clinically measured adherence by 17%. It has been argued that interviews can feel like an “interrogation” to participants, exaggerating any self-presentation bias (Myers and Branthwaite, 1992, Farmer, 1999). Poor wording can make self-presentation biases even stronger. Myers and Branthwaite (1992) included questions such as ‘When you took the tablets, did you take the proper number each time, or did you vary it at all?’ which makes any deviation the patient may have made from the prescription ‘improper’. Non-judgemental phrasing and

having interviews administered by a third party not involved with the patients care can reduce self-presentation biases (Horne, 2000, Morisky et al., 1986b, Morisky et al., 2008, Paterson et al., 2002).

The primary advantage of interviews over questionnaires is the ability to clarify ambiguities for participants and to ensure constant reporting. Participants have been reported to prefer someone on hand to clarify questionnaire items (Chesney et al., 2000). Furthermore interviews can offer a richness of data impossible by any other method (Cox, 2003, Kelly et al., 2008). Haynes et al. (1980) found that while interviews had poor sensitivity and exaggerated patient adherence, they provide very high specificity. Patients who are willing to admit to nonadherence may also be those most suitable for intervention (Gordis, 1979).

1.3.2.9 Questionnaires

Questionnaires are the most common form of patient self-report and share many weaknesses of interviews including social desirability and recall biases (Furnham and Henderson, 1982, Farmer, 1999). The process of completing a questionnaire may also make patients reflect upon their adherence and change their behaviour (Chesney et al., 2000). There have been a number of attempts to measure adherence via questionnaire, however all have significant weaknesses (Lavsa et al., 2011).

1.3.2.9.1 Morisky et al. adherence scales (1986b, 2008)

The most commonly employed self-report tool was developed by Morisky et al. (Morisky et al., 1986b). Despite its widespread usage, this scale has a number of substantial flaws. Although validated on over 400 patients, the sample was 91% black and 70% female, which is not representative of the population with hypertension (Roger et al., 2012). There are documented racial differences in adherence behaviour (Shenolikar et al., 2006, Williams et al., 2007a, Gerber et al., 2010) and therefore the tool may not be generalisable. Furthermore, there are only four questions offered to explain nonadherence, each with only a ‘yes’ or ‘no’ response. This type of assessment produces classification errors, and patients on the borderline are encouraged to opt for the socially

desirable response (Koschack et al., 2010). This approach also reduces reliability as it dichotomises a continuous variable (Gabriel and Violato, 2010). This led to a skewed distribution, with 43% of participants reporting perfect adherence behaviour (Morisky et al., 1986b), when this is an unrealistic target for most patients. Morisky et al. also validated the scale according only to therapeutic outcome, which is a poor indicator of adherence behaviour. There are further questions surrounding the psychometrics of this scale. The internal reliability of the scale is reported as 'relatively high' with a Cronbach's alpha of 0.61, when the conventional cut off for acceptable internal reliability is an alpha of above 0.7 or 0.8 (Bland and Altman, 1997, Oppenheim, 1992). Koschack et al. (2010) found particularly poor internal consistency for the Morisky scale with Cronbach's alpha only 0.25.

The Morisky adherence scale has been updated with the addition of four additional items (Morisky et al., 2008), however the assessment of this scale retained a number of significant problems. The primary criterion for validity was the assessment of the size of the correlation between the new eight item and the previous four item version of the same questionnaire. Although the wording of all items was changed, it remained very similar to that used in the original scale and so covariance between the two scales is very likely. Therapeutic outcome was again used to assess validity. Finally, the sample in the update retained many of the problems that impacted upon generalisability in the prior study with 77% being black, 51% not having attended college and 26% being married, and 54% having an income below $5,000.

Kim et al. (2000) developed the "Hill-Bone" scale by adapting the Morisky scale into a new adherence measure specific to hypertension by including more items pertaining to lifestyle modifications. Kripalani et al. (2009) then adapted the "Hill-Bone" scale to develop the "Adherence to Refills and Medications Scale" (ARMS) in order to make it generalisable to other chronic conditions and to simplify the wording for patients with low literacy. This was done via cognitive interviewing with 10 patients, and by assessing the literacy of the scale. It was found that the scale had reasonable internal consistency ($\alpha = 0.81$). The scale had an average reading level that would be suitable for a reader with an 8^{th} grade reading level in the US (age 13-14) which is above the capacity of the average adult in the UK (Williams, 2003). Methodologically the ARMS scale has a number of strengths. The scale was compared to multiple measures of adherence and measures of

outcome. However, correlations with refill adherence were relatively low, and evidence for an association with outcome was weak. Further, sampling problems were again evident with 91% of the sample in the study African American and 45% having inadequate literacy.

1.3.2.9.2 Svarstad et al. "Brief Medication Questionnaire" (1999)

Svarstad et al. reported that seven of the eight questionnaires developed before the Brief Medication Questionnaire had a sensitivity of below 60%. Ben et al. (2012) compared the Brief Medication Questionnaire to the Morisky scale and found sensitivity and specificity of 77% and 58% for the Brief Medication Questionnaire as opposed to 61% and 36% for the Morisky scale. Svarstad also claimed that the questions used in other questionnaires were often vague or insensitive. Respondents were rarely asked to recall events over a specific time period or else were asked to recall behaviour over an unrealistically long period of time. For the purpose of validation adherence was measured using a MEMS cap which is an advance over the therapeutic outcome used by Morisky. The scale attempts to identify different types of nonadherent behaviour, such as sporadic forgetting versus repeated and persistent nonadherence. Despite these theoretical strengths, there are significant weaknesses in the development of the questionnaire. Ambiguousness was not eliminated from the questionnaire. The item "Do your medications bother you in any way" is intended to assess patient concerns about medications regarding their side effects or long term risks. However, there are a number of ways the question could be interpreted which do not deal with beliefs about the impact of the medicines upon their body. However the main weaknesses of this study lie in the small sample size they were able to obtain, and the short prospective follow up period. Most results presented are based on 20 participants that were observed using MEMS for a period of one month. This provided the authors with a sample that had a limited amount of variability in adherence behaviour and this made it impossible to assess sections on their questionnaire which examined practical barriers to adherence such as accessing a new supply, opening bottles, or reading labels. Consequently these items have not been validated. Another consequence is the risk of sampling bias which is not acknowledged by the authors. They report that their section for screening aspects of the drug regimen that may impact on adherence had a sensitivity of 80% while their beliefs about medicines section had a

sensitivity of 100%. However, these sensitivities are based on observations from only five nonadherent participants. The results are not presented as a pilot or feasibility study and no further validation of this questionnaire has taken place. The scale has also been said to be difficult to score at the point of care (Lavsa et al., 2011).

1.3.2.9.3 Chesney et al "Adult Aids Clinical Trial Group Adherence Instrument" (AACTG) (2000)

The AACTG was developed specifically for HIV rather than chronic illnesses in general; however it is covered here because of its widespread use. In common with most adherence questionnaires the AACTG lacks any theoretical underpinning and the content is based upon a limited review of the literature, with only three cited works. The scale is not validated against any other adherence measure, and all but two of the scales used for construct validity were non-validated tools developed by the authors. Offering participants a list of reasons for skipping a dose could provide useful information for intervention, although incorporating an "other" option might have improved the scale. Their sample was also predominantly middle class and white which limits generalizability.

1.3.2.9.4 George et al. "Beliefs and Behaviour Questionnaire" (BBQ), (2006)

The items on the BBQ were generated based on a series of 28 in-depth interviews which were thematically analysed using the model of adherence behaviour proposed by Becker and Maiman (1975). The questionnaire was validated against the Medication Adherence Rating Scale (MARS Cummings et al., 1982). However, no reference for the validity of this comparison scale is provided because there is no paper which describes the construction and validity of the MARS tool. Further, correlations between the MARS and BBQ on items that directly assessed behaviours associated with adherence and nonadherence were small (Spearman's Rho = 0.09, and 0.40 respectively). The items on nonadherence also demonstrated poor internal consistency with $\alpha = 0.59$. The value is presented as acceptable because Cronbach's Alpha represents the lower bound of reliability and so "high values of alpha are informative and reassuring while low values are ambiguous" (George et al., 2006, p. 57). While this argument is true it does not sufficiently explain the reasons they were unable to achieve a more reassuring value for Alpha.

1.3.2.9.5 Hahn et al. "ASK-20 Adherence Barrier Survey" (2008)

The aim of ASK-20 was to develop a scale for clinical use that would identify specific barriers to adherence for patients in chronic illness. It sought to build on the Morisky and Brief Medication Questionnaire scales. The Morisky scale was perceived to screen adherence but not identify causes of nonadherence, while the Brief Medication Questionnaire was perceived to assess beliefs about medicines but not practical barriers. Items were generated from a literature review, but the methods for this are not described. The content validity piloting of the scale is comprehensive with a large number of patients and medical practitioners consulted. However, the study suffers from having the items included based heavily on subjective assessments of worth. Further, the authors chose a 12 factor solution because it fit their a priori assumptions best, however the information required to assess the suitability of this solution versus others is not presented. The origin of a 12 factor solution is also not fully described and is at odds with the initial statement that 16 topic areas were being assessed. Further questions about the validity of the scale are raised by relying on a web sample where patients were asked to provide their own diagnosis with no confirmation as to the accuracy of this provided by a physician. The internet deployment also specified that participants had to answer every question on the scale which meant that useful information regarding how acceptable participants found individual items could not be gathered as only complete case analysis was possible.

1.3.2.9.6 McHorney (2009) and McHorney et al. (2009) "The Adherence Estimator"

The adherence estimator measures concerns about taking medicines, the perceived necessity of taking medicines, and the affordability of medicines to assign patients as being at high, medium or low level risk of nonadherence. The scale is brief and easy to score having just three items. It was also validated on much larger samples than any other adherence tool. However there are some issues with the development of this questionnaire. A number of predictors seemed to perform better than medication affordability in identifying nonadherers. These include patient knowledge, proneness to side effects, trust in physician, participation in consultations, and perceived value of

supplementary medication. The consequence of this is that information that might be useful in predicting adherence is left out of the eventual scale. Coupled with the high rate of error associated with single item tests of a variable (Epstein, 1979, Shaughnessy et al., 2009) this results in a situation where the maximum and minimum possible adherence refill scores were found for participants at all levels of risk in the validation trial, and a specificity of just 49%.

1.3.2.9.7 Indirect self-reports of adherence

An alternative to directly measuring adherence is to measure beliefs that have been shown to correlate with adherence. Avoiding direct questioning can reduce self-presentation biases and because medication taking is not directly assessed recall biases are no longer an issue. Two examples of this approach are the 'Satisfaction with Information about Medicine Scale (SIMS)' (Horne et al., 2001) and the 'Beliefs about Medication Questionnaire (BMQ)' (Horne et al., 1999).Questionnaires of this type can be used to assess patients' perspectives of aspects of their care which may affect outcomes, including their adherence to medication. For example, the SIMS seeks to explore how the patient feels about the quality of information provision regarding their medication, while the BMQ explores how far patients perceptions about medicine in general and their own prescribed medication in particular may impact upon medication usage.

1.4 Typology of nonadherence

There are many ways that nonadherent behaviour can be expressed, and an even greater number of causes of such behaviour. Nonetheless, nonadherence can be categorised as primary or secondary. Nonadherence can then be further split into unintentional and intentional nonadherence.

1.4.1 Primary nonadherence

Patients are described as displaying primary nonadherence when they fail to fill their prescription. It can be thought of as the most severe form of nonadherence as the patient fails to follow any of their prescribed regime (Jackevicius et al., 2008). However, primary nonadherence has not been extensively studied. In part this is due to the difficulty of knowing what prescriptions are dispensed by practitioners when these are not filled by patients; it is much easier to track medication use after a prescription has been filled (Williams et al., 2007b). There are many possible causes of primary nonadherence. Many prescriptions can be more affordably purchased by patients over-the-counter (Jones and Britten, 1998) and difficulty affording or justifying the cost of prescriptions is an often cited cause of primary nonadherence (Wamala et al., 2007, Beardon et al., 1993, Jones and Britten, 1998, Stavropoulou, 2011, Kennedy and Morgan, 2006). Lack of concordance has been cited as a factor in primary nonadherence (Storm et al., 2008). How much patients respect the prescriber may also have some impact. Beardon et al. (1993) found higher primary nonadherence rates when patients had consultations with trainee versus more experienced doctors. Primary nonadherence is also more likely for medications perceived to be less essential to patients. For example, non-cardiac versus cardiac medication (Jackevicius et al., 2008), patients with mild asthmatic symptoms versus those with severe or frequent symptoms (Williams et al., 2007b) and contraceptive prescriptions (Beardon et al., 1993). However, Storm et al. (2008) found that the adherence rates were not different for emergency versus non-emergency patients in a dermatology clinic, and the only difference was in the haste prescriptions were filled. Younger age has also tended to be shown to be associated with lower primary adherence (Williams et al., 2007b, Beardon et al., 1993), although this may be partly accounted for

by younger females receiving prescriptions for contraceptives. Younger patients are also more likely to present with less serious disease states (Beardon et al., 1993).

1.4.2 Secondary Nonadherence

Secondary nonadherence refers to the patient deviating from the prescribed medication regimen once in possession of the medication. The extent of secondary nonadherence can range from a patient not taking any of their medicine, to missing only a single dose, or not taking their medication on time (Osterberg and Blaschke, 2005). Consequently 'secondary nonadherence' covers a wide range of behaviours with an extensive number of possible causes, causing some authors to question whether the term adherence has any real relevance at all (e.g. Steiner and Earnest, 2000). Because adherence covers a range of possible behaviours it is difficult to identify a standard set of causes. One way to simplify this task has been to split adherence into unintentional or accidental nonadherence and intentional nonadherence.

1.4.3 Unintentional nonadherence

Unintentional nonadherence refers to occasions where patients are incapable of adhering to their medicine regimen. The most commonly cited reasons for unintentional nonadherence are forgetting to take doses, misunderstanding or misreading the instructions, or physical impairments preventing access to the medication (Horne, 2001). Gordis (1979) argues that the term 'medication error' is more appropriate to prevent stigmatising patients as nonadherent or noncompliant when they are unable to comply. Nonetheless, unintentional nonadherence is a significant problem. When participants in studies are asked to give reasons for their nonadherence, factors such as forgetting, being too busy, or experiencing a change in their daily routines are those most frequently cited implying unintentional factors responsible for a significant proportion of nonadherent behaviour (Atkins and Fallowfield, 2006).

One proposed cause of unintentional nonadherence is complexity of the medicine regimen. The larger the number of pills to be taken, and the more rigid the conditions

under which they must be taken, the more potential there is for a patient to make a mistake, the more likely they are to forget some aspect of their treatment, and the greater an adjustment they must make to their normal routines (Horne et al., 2005). It has been found that there is an inverse relationship between adherence and complexity of the medication regimen (Claxton et al., 2001, Connor et al., 2004). van Dulmen et al. (2007) performed a review of the systematic reviews into interventions to increase adherence to medication and found that medicine regimens demanding fewer doses are associated with better adherence than those requiring more frequent doses. Developing medicines with longer dosing intervals, combining different medicines into a single dose, and which have fewer conditions for effective action may help to reduce nonadherence of this type (Connor et al., 2004).

Providing patients accurate and consistent information which can be both understood and remembered is integral to a patient's ability to comply with their medicine (Ley, 1988). However, beyond the basic requirement of allowing patients to know how to take their medicine, information provision has not been found to be a strong predictor of adherence behaviour. Peterson et al. (2003) conducted a meta-analysis that found that behavioural interventions to improve adherence, such as providing blister packs or reminder notes, offer small but reliable improvements to adherence while educational interventions had a far less reliable positive impact. Furthermore, studies have often failed to be able to ascribe the direction of causality in this relationship. It cannot be easily ascertained whether nonadherent patients are less interested in their treatment and so seek less information, or whether that those with less information become more nonadherent (Horne et al., 2005).

The costs of medication may also be barrier to secondary adherence. The poor are disproportionately affected by adherence barriers (World Health Organisation, 2003). In chronic illness many patients will have repeat prescriptions and this will often come at a significant direct cost to patients. Patients may also expect further indirect costs from having to travel to and from hospitals or pharmacies to collect their medicines. Schafheutle (2003) argues that the cost of medication remains a problem in the UK, which uses a flat prescription charge rather than the co-payments and insurance systems adopted elsewhere. While 85% of medications are provided free of charge, around half the population are not exempt from paying the prescription charge (Bradley et al., 1998).

Schafheutle et al. (2002) identified patients not filling prescriptions or purchasing cheaper alternatives, patients also took less of their medication than prescribed to make it last longer due to their inability to afford their prescriptions.

Forgetting to take medicine is the most heavily cited cause of unintentional nonadherence by practitioners, researchers and patients themselves. Estimates of the extent to which forgetting impacts nonadherence are biased by patients reporting that they forgot to take medication when they chose not to take them, believing this a more socially desirable way to allow their doctors to know they have not taken all of their medicine (Atkins and Fallowfield, 2006). Nonetheless, forgetting to take a dose would appear to be the most common single cause of nonadherence, accounting for approximately 30% of non-adherent cases (Osterberg and Blaschke, 2005). Haynes et al. (2008) find that while a number of interventions can improve adherence and boost recall, such as telephoning patients or offering medicines counselling, the effect is rarely large, tends to lack longevity, and rarely has a significant impact on treatment outcome.

1.4.4 Intentional nonadherence

The focus upon unintentional nonadherence reflects the perception of patients as passive recipients of health advice, when they are more properly perceived as active decision makers (Horne, 2000). However there is still a wide literature which seeks to identify what factors influence the decision to not take medicines. It is commonly assumed that behaviours are based upon individuals' beliefs about those behaviours, and there are a number of theories for how the relationship between beliefs and behaviour can be modelled (Lehane and McCarthy, 2007).

1.4.4.1 Health Belief Model

A common explanatory framework for adherence behaviour is the Health Belief Model (HBM). The HBM assumes that patients make a rational choice about whether to engage in a specific behaviour (Chisolm et al., 2010). These rational decisions are based upon patients weighing up the costs and benefits of a health intervention based upon the

perceived threat of the health concern, versus the perceived effectiveness of the medical intervention (Munro et al., 2007). The perceived threats are based upon an assessment of how susceptible to illness the patient is, and how severe the consequences of illness will be; while the perceived effectiveness of intervention is based upon the perceived benefits of the intervention versus the barriers that are in place to obtaining those benefits (Janz and Becker, 1984).

Evidence for the efficacy of using the HBM to predict adherence via meta-analysis has indicated that there are significant but small relationships between variables in the model and adherence behaviours (Harrison et al., 1992). Moreover, estimates of the variance accounted for by the HBM are also typically around 20% for the full model (Olsen et al., 2008) and range between 0.01% – 9% for individual constructs (Harrison et al., 1992). Due to the small magnitude of relationships between HBM constructs and adherence individual studies have often failed to identify the existence of these relationships. Instead situational factors such as social support or ability to perform behaviour are found to have greater influence upon adherence. For example, Cummings et al. (1982) explored the size of the relationship between variables in the HBM and medication adherence in 116 haemodialysis patients. The study identified a positive relationship between all variables in the HBM and adherence as measured via serum phosphorus and potassium levels recorded in medical charts. However, the only relationship reaching statistical significance was that between lower perceived efficacy for adherence and actual measured adherence. It was proposed that the influence of health beliefs was largely overwhelmed by variance in situational factors that impact upon decision making. On these grounds, the HBM has been criticised for being too simple. It does not allow the variables in the model to interact with one another, and it is assumed that threat and effectiveness beliefs directly affect health behaviours (Munro et al., 2007). The model is not considered to be comprehensive, neglecting the role of social influence and overstating the role of rationality in decision making; many activities are engaged in habitually, not consciously deliberated each time (Munro et al., 2007). Additionally, one study found that HBM constructs were correlated with adherence during treatment but not before treatment was initiated (Taylor, 1979). This suggests that health beliefs develop alongside experience with treatment rather than determine treatment behaviours themselves. It has also been observed that once adherence ceases to occur there are no observable changes in health beliefs (Becker et al., 1978) which undermines

the causal attributions specified in the model. For these reason it is argued that the HBM is a better model for one off behaviours such as health screening than for long term adherence to therapy (Horne, 2000).

1.4.4.2 Theory of Reasoned Action

Some weaknesses in the HBM are accounted for in the Theory of Reason Action (TRA, Fishbein and Ajzen, 1975). The TRA shared the cost benefits assessment of the HBM and proposed that this assessment determines an individual's attitude toward engaging in a specific behaviour. However, the TRA has two additional elements to improve predictive power. The TRA accounts for the HBM's problem of having beliefs about specific behaviours directly relate to the enactment of that behaviour. In the TRA, attitudes impact upon the intention to engage in behaviour rather than upon behaviour directly. This helps to account for the often small observed relationship between attitudes about a behaviour and the overt performance of that behaviour (Fishbein and Ajzen, 1975). This is done by accounting for the role of social norms, which are seen as an additional influence upon intentions to perform behaviours. Social norms are thought to consist of the perception of what significant others think about a behaviour, and the amount of motivation to conform with the norms of those significant others (Fishbein and Ajzen, 1975).

Utilisation of the TRA has been rare in adherence research and when utilised has been found to more strongly predict behaviours other than medication adherence. Syrjälä et al. (2002) used the TRA to predict tooth brushing and adherence to medication in 149 diabetic patients and found that attitudes but not subjective norms were significantly related to self-reported adherence to diabetes medication. In contrast subjective norms and attitudes were both highly indicative of whether or not tooth brushing was adhered to. Miller et al. (1992) used path analysis with 56 newly diagnosed patients with hypertension and although the TRA was able to predict adherence to smoking cessation and prescribed diet, no significant relationships between variables in the TRA and adherence medication was identified. Despite these weaknesses the TRA may still represent an advance over the HBM. Ried and Christensen (1988) directly compared the explanatory power of the HBM and the TRA in predicting self-reported adherence to

medication for urinary tract infections. They recruited 113 participants from both a university health centre and pharmacies represented by a single Health Maintenance Organisation presenting with a prescription for trimethoprim 160 mg/sulfamethoxazole 800 mg. Participants were interviewed via telephone 10 days after the prescription was dispensed. Reid and Christensen found that HBM variables could only explain 10% of the variance in adherence to the antibiotic regimen, however combining the HBM with the TRA was able to explain 29% of variance in the same behaviour. However despite this additional explanatory power, the TRA is limited by its ability to explain only volitional behaviour (Fishbein and Ajzen, 1975) and may not predict adherence behaviour as well as it does other behaviour. To account for the fact that the enactment of behaviour is not always under an individual's control once an intention has been formed, the TRA was extended into the Theory of Planned Behaviour (TPB, Ajzen, 1991).

1.4.4.3 Theory of Planned Behaviour

The TPB builds upon the TRA by incorporating the concept of self-efficacy from social learning theory. Social learning theory stipulates that behaviour is based upon past experiences and observation of others, which influences beliefs about the outcome of specific behaviours (Bandura, 1991, Munro et al., 2007). Moreover, past experience and observation also impacts upon an individual's perception of how capable they are of carrying out a specific behaviour, which has been termed "self-efficacy" (Bandura, 1991, Bandura, 1994). The TPB incorporates self-efficacy under the variable "perceived behavioural control". Perceived behavioural control is composed of self-efficacy and controllability which is the extent to which performance of the task is under the volitional control of the individual (Ajzen, 2002). Perceived behavioural control is thought to impact upon the intention to perform behaviour in the same way as social norms and attitudes. However, it is also said to directly impact upon behaviour and help to bridge the gap between intention and overt behaviour (Ajzen, 2001, Ajzen, 2002).

Like the TRA, the TPB has rarely been utilised in the medication adherence literature and the evidence that does exist does not provide strong support for its utilisation as a theoretical framework to guide the development of an adherence questionnaire. One review (Burns, 2009) identified only two prior articles that have directly applied the TPB

to medication taking. Farmer et al. (2006) utilised the MARS adherence questionnaire as part of a self-report questionnaire which aimed to measure the correlations between TPB constructs and adherence intentions and behaviour. The questionnaire was posted to patients with diabetes aged over 40 taking oral hypoglycaemic medication but not insulin. Their analysis showed that for their 121 respondents beliefs about medicines were correlated with adherence intentions and behaviours, but evidence for correlations with social norms and perceived control variables with outcomes were more limited. Russell et al. (2003) utilised the TPB as a framework in a series of 16 qualitative interviews with adult renal transplant recipients and found that patients form attitudes based upon the comparative utility and disutility of competing behavioural options, that family support was a key facilitator of adherence, and that steps were taken by patients to enhance perceived behavioural control. However, as a qualitative study utilising the TPB as a framework no direct inferences regarding the ability to the TPB to predict actual behaviour can be derived from this study. An additional study omitted by the Burns review found that the TPB predicted 41% of the variance in intention to adhere to immunosuppressant therapy in renal transplant patients. However, intentions regarding adherence explained only 10% of the variance in adherence behaviour (Chisholm et al., 2007). In contrast 23% of behaviour could be explained by past adherence behaviour again reinforcing the role of situational factors over beliefs about medicines alone in predicting adherence behaviours.

Despite a lack of applications directly to adherence, the TPB has been used extensively elsewhere. A meta-analysis of the TPB incorporating 185 studies found broad support for the capability of the theory to predict behaviour and intentions with variance accounted for of 27% and 39% respectively (Armitage and Conner, 2001). Similarly, a meta-analysis of prior meta-analyses of the TPB indicated that the TPB could account for between 35% to 50% of variation in intentions and 26% to 35% of variance in actual behaviours (Sutton, 2007). However, these studies also identified areas of weakness in the theory, in particular the weakness of the relationships identified between social norms and intentions in many papers. However, the lack of influence of social norms may be a facet of the culture in which most studies are carried out rather than a weakness of theory. The literature relating adherence to the TPB encompasses studies exclusively conducted in western industrialised nations in the US and Europe which comprise of more individualist cultures. Individualist cultures are characterised by societies in which individuals are

expected to look after themselves and their immediate families. Conversely collectivist cultures are typified by societies in which there exist strong cohesive in groups which exchange protection for unthinking loyalty (Hofstede, 1997). The role of social norms has been identified as being more powerful in more collectivist than individualist cultures (Aleassa et al., 2011). Regardless of the appropriateness or otherwise of the social norms variable, the TPB has been criticised for not taking sufficient account of affective influences on decision making and assuming behaviour is rationally determined (Mullen et al., 1987). It is also assumed that cognitive processes determine behaviour, and does not allow for behaviour to affect cognitive processes (Weinstein, 2007). The brain must interpret behaviour as well as cause it, and it often interprets behaviour in such a way as to reduce cognitive dissonance (Weinstein, 2007). An additional concern is that the TPB does not offer formal guidance upon the design of interventions but only targets which beliefs are thought to be of importance (Bratby, 2008). For this reason an extensive review of behaviour change interventions designed using the TPB found that most studies had not fully incorporated the theory into their design and were mostly standard educational interventions with little or no measurable change in behaviour being the most common outcome (Hardeman et al., 2002). Because the TPB does not offer a clear theoretical guide for designing interventions and does not have a firm empirical track record for predicting adherence behaviour it may not be a strong candidate on which to base any attempt to predict adherence.

1.4.4.4 The self-regulatory model of adherence

The SRM attempts to produce a framework for adherence which marries the findings from modelling approaches such as the HBM and TPB with cognitive and affective processes (Leventhal et al., 1992). The theory suggests illness is understood by patients producing a framework of their illness based upon its cause, its effects, how long it lasts, and what can be done to cure or control it (Reynolds, 2003, Weinman et al., 1996). Like the HBM the model accounts for rational decision making, and like the TPB influences upon perceptions are permitted to come from the individual and their wider socio-cultural context. However, the theory gives a far more prevalent role to affective processes via the "parallel response framework"(Leventhal et al., 1992). The parallel response framework proposes a largely separate cognitive and affective response to

stimuli, with both proposing partially independent coping strategies. Coping strategies are then appraised based upon their outcomes, which have a direct influence upon the stimuli that are put forward for reappraisal. While the two systems are proposed as separate, they are allowed to interact. The inclusion of affective processing is a major advance over previous models of health behaviour because it provides an explanation for irrational responses to illness, such as patients not taking medicines they know will help in the long term (Horne, 2000).

The SRM is a far more comprehensive model of adherence than the current alternatives, but is unwieldy for facilitating the design of interventions (Munro et al., 2007). The strength of the SRM is that it puts forth an argument for complex interventions which incorporate education to moderate cognitive decision making, skill provision to facilitate coping, and affective support to manage patients expectations and coping strategies for the difficulty and duration of treatment (Reynolds, 2003). However, a review of studies purportedly utilising the SRM for self-monitoring of therapy identified that few studies actually use the constructs of the SRM to guide their design but instead focus broadly on illness or medication beliefs (Breland et al., 2013). One study that did utilise the SRM to design a simple intervention was the use of text messages targeted to combat specific illness beliefs thought to undermine adherence (Petrie et al., 2012). Patients with asthma that self-identified as non-adherent between 16 – 45 years of age (n = 216) were recruited via flyers dispensed with asthma preventer medication alongside e-mails sent to members of a marketing website. This study demonstrated that this simple SRM based intervention might help to maintain adherence, with mean self-reported adherence remaining broadly similar to baseline in the intervention group. Baseline adherence was 56.5% and averaged 57.8% over the course of the study. In comparison, a control group that received no text messages experienced a drop in adherence over the nine months follow up with baseline adherence estimated to be 54% and averaging 43.2% over the full study period. However, these conclusions are compromised by a very high dropout rate (32%), which is not controlled for statistically. Such a high attrition rate raises doubts about the acceptability of the intervention. Moreover, adherence was not improved by the intervention, which may indicate the text messages served as reminders and not as belief modifiers. Therefore it is impossible even in this relatively simple case to be able to ascribe with confidence the effect upon adherence to the health beliefs proposed by the SRM. Furthermore, meta-analysis of 15 studies utilising the SRM found that only

perceptions regarding whether the illness can be controlled or cured was associated with adherence and other self-care behaviours (r = 0.12). Correlations for beliefs about consequences, identity, and timeline ranged from -0.01 to 0.01 (Hagger and Orbell, 2003). As a consequence there is not currently a strong empirical argument for utilising the SRM as a basis for the design of a questionnaire to identify patients at risk of non-adherence despite its appeal as a coherent and comprehensive theoretical model.

1.4.4.5 The proximal-distal model of adherence

The weaknesses of behavioural models to inform the design of a tool to predict adherence can be illustrated using the proximal-distal model of adherence which is presented in figure 1.1. The model proposes that the more specific a skill, belief, or experience is for adherence then the greater the association between the two variables will be, and with more distal causes of adherence feeding into the more proximal (McHorney, 2009). This model was utilised in the design of the Adherence Estimator questionnaire (see section 1.2.3.9.6). However, if this questionnaire identified a patient as being at risk of nonadherence it is not clear what a clinician could do to intervene because there are no indications of the causes of the beliefs that put patients at risk of nonadherence in the tool or in the model. The only specification given in the model is that weaker correlates of adherence partially contribute to the stronger correlates of adherence. These associations are also assumed to be causal, when evidence for the model is based entirely upon correlational research. A criticism common to all models apart from the SRM (Weinstein, 2007). A structural equation modelling study has been performed to determine whether more distal causes of adherence are associated with more proximal causes of adherence(McHorney et al., 2012). This study utilised an online sample of 1072 chronic disease patients and did demonstrate links between patient characteristics and distal adherence beliefs, and distal beliefs with proximal adherence beliefs. However, this paper does not explore the relationships between beliefs and actual adherence behaviour so the predictive power of the model is unclear. On these grounds it is difficult to see how the theory can inform the design of an intervention to improve adherence or provide an underlying theory upon which to design a questionnaire.

Figure 1.1 The proximal-distal model of adherence. Adapted from McHorney (2009)

A clinically useful tool for adherence needs to measure beliefs about medicines and illness, as well as specific barriers to enacting behaviour, in order to accurately predict whether or not a patient will be adherent to their medication. It also needs to measure the variables that determine those beliefs and barriers so that clinicians are able to identify specific targets for intervention tailored for individual patients. There has been a vast amount of speculation as to what variables might be associated with adherence to medication but no consensus (Lehane and McCarthy, 2007, Arbuthnott and Sharpe, 2009).

1.5 Summary and statement of aims

Given the prevalence of nonadherence and its health and financial implications, it is essential that practitioners are able to identify which patients are at risk of nonadherence, and identify the causes of nonadherence for individual patients so that adjustments can be made to optimise treatment acceptability and outcomes. However, current methods of measurement are suboptimal. In particular physicians' own estimates of nonadherence are particularly inaccurate. Moreover there is no current single questionnaire which synthesises the various proposed correlates of adherence behaviour into a single brief instrument.

1.6 Aims and objectives of the thesis

The aim of this thesis is to develop a new tool which will predict the likelihood of nonadherence to medication and help clinicians to identify patient specific interventions to mitigate specific risk factors for nonadherence. The questionnaire will do this by avoiding direct questioning of adherence, and instead measuring correlates of adherence which have been empirically shown so be related to the behaviour.

The objectives are to:

Chapter 2

- Identify variables objectively shown via meta-analysis to correlate with nonadherence to medication

Chapter 3

- Perform a literature review of best practice in questionnaire design to develop a new tool to predict nonadherence to medication

Chapter 4

- Perform a feasibility study of the proposed research to appraise the new adherence tool, and perform preliminary psychometric assessments

Chapter 5

- Perform a qualitative assessment with clinicians and patients to determine the clinical utility and acceptability of the new tool; and to provide a comprehensive assessment of its validity

Chapter 6

- Assess the performance of the new questionnaire by synthesising the results of chapters 4 and 5 and discuss the contribution of the thesis to the wider adherence literature

Chapter 2 – Identification of the indicators of adherence

2.1 Introduction

Over 200 correlates and indicators of adherence behaviour have been studied in the literature (Lehane and McCarthy, 2007, Arbuthnott and Sharpe, 2009). Focussing on indicators with a demonstrable relationship to adherence contributes to brevity and thus increased acceptability of the resulting adherence questionnaire (Marshall, 2005). Thus a literature review of the indicators of adherence was undertaken to identify those with sufficient evidence to support inclusion in the new questionnaire.

2.1.1 Narrative Reviews of the adherence literature

There are a number of narrative reviews of the adherence literature (Vlasnik et al., 2005, Sawyer and Aroni, 2003, Kettler et al., 2002, Lakatos, 2009, Lehane and McCarthy, 2007, Horne, 2006, Osterberg and Blaschke, 2005, Vermeire et al., 2001). However, the broad scope of these reviews restricts the depth of the coverage provided for specific issues, such as identifying indicators of adherence behaviour. Vermeire (2001), Horne (2006) and Lehane and McCarthy (2007) provide a more thorough consideration of possible indicators however these articles remain susceptible to a number of known biases that can impact upon the selection and presentation of evidence in narrative reviews.

The biases associated with narrative reviews are summarised below. “Preference bias” describes the propensity for authors to design an investigation so that their preferred outcome is likely to be found (Wilholt, 2009). For example, authors may omit poor quality studies that counter the authors proposed view, but include studies that support this view (Stanley, 2001). “Availability bias” refers to the ease with which associations are brought to mind being used as a heuristic to ascertain their likelihood (Shanteau, 1989, Tversky and Kahneman, 1973). “Cognitive Dissonance” refers to discomfort that is felt when information inconsistent with what we already believe is presented (Festinger, 1957). “Selective exposure” refers to seeking information congruent with what is already believed and avoiding contrary evidence to avoid cognitive dissonance (Hart et al., 2009, Wason, 1960). “Confirmation bias” refers to the tendency to both seek and misperceive

or misremember incongruent information in a manner that supports prior beliefs (Oswald and Grosjean, 2004, Smith et al., 2008, Smith et al., 2007). The inevitable introduction of these biases mean that narrative reviews cannot be replicated, and their results cannot be independently verified (Easley et al., 2000, Hemingway and Brereton, 2009).

2.1.2 Systematic Review and meta-analysis

2.1.2.1 Fundamentals of systematic review and meta-analysis

The aim is to produce an objective list of the most relevant and highest quality literature from a comprehensive list of primary sources in order to answer a specific research question (Higgins and Green, 2006, Akers et al., 2009). The procedures adopted enforce transparency and rigour via an explicit and reproducible method (Hemingway and Brereton, 2009). The process by which articles are identified, included or excluded in the review, processed, and conclusions drawn are all presented alongside summaries of data. This ensures that all conclusions must be grounded in the data identified, and limits the extent to which the prior beliefs and assumptions of a researcher can influence interpretations of that data.

Where possible, mathematically combining the results of different studies into a single effect size via meta-analysis (Hunter and Schmidt, 2004) offers additional power to find real but rare events or effects (Green et al., 2006). Furthermore, the larger sample size allows for a more accurate approximation of the population effect size (Sutton et al., 2000). However, it is rare that there is a single invariant population effect size that all samples measure in research involving humans (Schmidt et al., 2009). The use of different definitions, variables, cut-offs, and scales when measuring phenomena can introduce further between study differences beyond random error (Higgins and Green, 2006). It is therefore often more appropriate to adopt a random effects model which does not assume an identical population effect size, as opposed to a fixed effects model which does (Hunter and Schmidt, 2000, Raudenbush, 2009).

Systematic reviews can take teams of specialists months or years to complete. When time is at a premium alternative options are to complete a Rapid Evidence Assessment (REA,

Akers et al., 2009) or scoping review (Hetrick et al., 2010, Levac et al., 2010). REA's are designed to take two to six months to complete, and prioritise achieving a broad overview of the available literature over an in depth analysis of a single hypothesis (REA Methods, 2009). The aim in an REA or scoping study is to achieve conceptual breadth of available studies rather than to identify all available studies.

2.1.2.2 Prior attempts to meta-analyse the adherence literature

Despite these difficulties there have been attempts to meta-analyse the adherence literature. Atkinson and Petrozzino (2009) tried to reduce between study differences by including only studies regarding HIV and excluding all studies that did not measure the relationships between indicator variables and adherence in terms of odds ratios or hazard ratios. Focussing on only a single disease, however, significantly reduces generalisability because adherence rates differ between different diseases (DiMatteo, 2004c, Claxton et al., 2001). Furthermore, including studies which use only two of the available effect size measures excludes a large number of relevant studies.

DiMatteo et al. have conducted a series of meta-analyses into specific indicators of adherence (DiMatteo et al., 2000, DiMatteo et al., 2002, DiMatteo, 2004b, DiMatteo, 2004c, DiMatteo et al., 2007). However, these analyses confound their results by incorporating adherence to medicines, diet, and exercise into a single estimate of effect despite also finding that adherence rates differ between these different types of therapy (DiMatteo, 2004c). Therefore the estimated relationships are unlikely to be accurate for medication adherence alone.

Drotar and Bonner (2009), Karamanidou et al. (2008) and Jindel et al. (2003) used the approach of comparing the number of statistically significant results for or against a relationship between an indicator and adherence. However, this method has poor statistical rigour (Stanley, 2001, Borenstein et al., 2009, Bushman and Wang, 2009, Greenland, 1987). Furthermore, a tally of p-values does not aggregate the individual samples as meta-analysis should; consequently there is no increase in power or ability to detect small but true effects. Publication bias, where studies are more likely to be published if they find a significant result, and outcome bias, where significant results are more likely to be reported within studies, may also skew conclusions (Palmer, 2000, Egger

et al., 1997, Gøtzsche, 1987, Nieminen et al., 2007). Together these biases make it more likely that vote counting procedures will suggest that variables are associated with adherence when the strength of evidence is weak.

2.1.2.3 Additional biases in Systematic Reviews and Meta-analysis

Systematic reviews limit, but do not remove bias (Egger et al., 1997). Song et al. (2010) published a comprehensive review of all the dissemination biases that may impact upon the review process.

2.1.2.3.2 Time lag bias

"Time lag bias" occurs where significant results take longer to be published than non-significant results (Song et al., 2010). It is recommended that systematic reviews are regularly updated to ensure effect sizes remain accurate and that risk of publication bias is assessed whenever a review is undertaken (Higgins and Green, 2006). Stern and Simes (1997) also recommend limiting studies to those started before a certain date to allow all studies undertaken during a specific time frame an opportunity to be published.

2.1.2.3.3 Grey literature bias

"Grey literature bias" refers to the tendency for unpublished or non-peer reviewed articles and those published by non-commercial organisations to have lower effect sizes than peer reviewed journal articles (Song et al., 2010). There is rarely a difference in the scientific quality of published versus unpublished or non-peer reviewed studies (Conn et al., 2003). The higher effect size in peer reviewed articles reflects the preferences of journals to publish findings with a larger impact. Including grey literature can reduce bias in an analysis but because unpublished articles are difficult to retrieve, time constraints can often render this impossible.

2.1.2.3.4 Database indexing bias

"Database indexing bias" refers to the fact that different electronic databases have different content and often systematically differ from each other (Song et al., 2010).

Systematic reviews should therefore search more than one database (Higgins and Green, 2006, Critical Reviews Advisory Group, 1996, Akers et al., 2009).

2.1.2.3.5 Data-extraction bias

"Data-extraction bias" refers to differentially extracting information from, or applying exclusion or quality assessment criteria differently to, studies that support the authors own views (Petticrew and Roberts, 2006). Similarly, authors may be biased for or against specific authors or institutions. Blinding reviewers by blanking out author information can help reduce this bias, and it is recommended that more than one author be involved in data extraction to limit individual author bias (Critical Reviews Advisory Group, 1996, Higgins and Green, 2006, Handoll and Smith, 2004, Akers et al., 2009). It is also possible to validate the extraction process by having the data extraction checked by another person, or by another independent reviewer performing the same data extraction for comparison.

2.1.2.4 Control of bias in systematic reviews

A number of techniques are available to limit or control for bias in meta-analyses. Duval and Tweedie's (2000) Trim and Fill method is used to correct effect size estimates for papers missing due to publication bias. The 'fail safe' number can provide an estimate of the robustness of the meta-analysis findings by calculating the number of studies of no effect that would need to be identified before the findings of the meta-analysis were nullified (Palmer, 2000). It is also possible to estimate whether or not bias is present in studies via regression (Egger et al., 1997). However, these techniques require access to specialist software.

Including low quality studies in a systematic review can introduce bias (Chalmers et al., 1981) and so it can be advantageous to assess study quality (Akers et al., 2009). However, standardised checklists of study quality have been criticised for being arbitrary and failing to take sufficient account of the context in which research takes place (Juni et al., 1999, Greenland, 1994). An alternative to checklists is to use meta-regression with coded indices for different methodological criteria to determine the level of influence methodological factors had upon results (Greenland, 1994, Stanley, 2001, Shapiro, 1994,

Stroup et al., 2000). However, in a scoping study where the aim is to collate and summarise areas of research it is not always appropriate or feasible to exclude or rank studies according to quality (Hetrick et al., 2010). However it can be useful to collect and quantify some measures of study quality to provide context to results.

2.1.3 The need for meta-analysis

Despite the difficulties associated with meta-analysis, this approach offers the best method available for evaluating relative strength of evidence for indicators of adherence objectively. By sacrificing sensitivity for higher specificity, a large number of indicators can be compared in a relatively short time. The costs of this approach in terms of comprehensiveness can be weighed against the value of achieving comprehensive conceptual breadth within a feasible timeframe.

2.1.4 The scope of the proposed meta-analysis

The nature of the relationships between adherence and indicator variables is not uniform across all populations. Patients on hospital wards, in prisons, on military bases, and in care homes might have their medication regimens enforced upon them (DiMatteo, 2004c). Children may also face different constraints and freedoms regarding their medication taking than independent adults (DiMatteo, 2004a, DiMatteo, 2004c, Wrubel et al., 2005, Landier, 2011). In addition, patients on a medication regime targeted towards treating a mental illness may be expected to face separate and specific challenges to their adherence to those faced by the mentally healthy population (Yen et al., 2005). Furthermore, there may be a greater need for coercive practices when dealing with mentally ill patients (Jaeger and Rossler, 2010). Consequently these populations were excluded from the analysis. It has also been argued that the inclusion of small studies with sample sizes below 100 has been found to introduce bias into meta-analysis (Nüesch et al., 2010). However a greater concern can be a possible lack of statistical power. Turner et al. (2013) examined existing Cochrane reviews and re-examined the data excluding underpowered studies. They identified that where adequately powered studies were available, excluding studies of smaller sample sizes can provide more accurate estimates of effect size with less heterogeneity. However, they also identified that the vast majority of studies are underpowered, with 70% of meta-analyses including only underpowered

studies, and 34% of meta-analyses themselves being underpowered. Given the relatively shallow search strategy adopted it was determined that a lack of power was a greater concern than was rising heterogeneity and so studies with small sample sizes are not excluded. However, studies with sample sizes below 10 were excluded in order to narrow the search away from articles extremely unlikely to include quantifiable data such as qualitative investigations and case studies (DiMatteo, 2004c).

2.1.5 Objectives

The objectives of the systematic review were to:

- Identify the correlates of adherence to medicines identified in the literature.
- Estimate the size of relationships between identified indicators of adherence via meta-analysis.
- Use estimates of effect size to evaluate the strength of evidence for a relationship between identified indicators and adherence.
- Evaluate the extent of heterogeneity in effect size estimates to determine the reliability of the identified relationship between an indicator and adherence (Sutton et al., 2000).

2.2 Methods

2.2.1 Population

- Adult patients (aged 18 or over). Samples with a small minority (< 5%) of patients under this age were not excluded.
- Diagnosed with a chronic illness (condition typically lasting longer than 6 months).
- Prescribed medicinal therapy.

2.2.2 Exclusion Criteria

- Patients with institutional controls over medicine taking (such as prisoners, drug or alcohol dependent patients, and military personnel).
- Medication regimes designed to treat mental illness. Non-institutionalised patients diagnosed with a mental illness or substance dependency in addition to other chronic conditions were not excluded. Such patients would be found in a normal population of chronic disease sufferers, and so it would be inappropriate to discount data from these sources.
- Studies of sample sizes below 10, to avoid case studies (DiMatteo, 2004c).
- Non-English language studies.
- Investigations on non-human samples.

2.2.3 Outcomes

- Effect size measures for the magnitude of association between adherence and another variable.
- Estimates of heterogeneity in the effect size estimate for the magnitude of association between adherence and another variable.

2.2.4 Study design

2.2.4.1 Search criteria

The aim of scoping reviews is to cover the conceptual breadth of a topic, and not to achieve the full depth of literature coverage expected in a systematic review (Gough et al., 2012). Therefore in order to balance the competing requirements of depth of coverage with plausible research aims the search was limited to studies that dealt explicitly with indicators and correlates of medication adherence by limiting the search to articles that included such terms in their titles (see point 2 below). Additionally, the search focussed upon patients that were nonadherent to their medicines rather than those that had ceased to take them altogether. For this reason the term "persistence" was not included in the search. However given the lack of consistency in the use of terms it is acknowledged that this may result in relevant articles not being included in the search (Vrijens et al., 2012). The search was conducted on 26.04.2010. The full search protocol was:

- The databases Medline, Embase and PsychInfo were searched using the following terms in the title, abstract, subject headings, heading word, or original title:
    - "patient complian* or patient adheren* or patient nonadheren* or patient noncomplian* or patient non-adheren* or patient non-complian* or patient non adheren* or patient non complian*" and "medic*"
- To limit search results to those that dealt explicitly with indicators and correlates of medication adherence, the following terms were specified in the title field of articles.
    - "predic* or influ* or determ* or caus* or correla*or associat*".
- No limits were placed upon publication date.

Retrieved studies were saved to a dedicated Endnote Library to identify any duplicated citations. Titles and abstracts of the remaining articles were then examined for relevance. Full texts of potentially relevant articles were then acquired before being assessed against the inclusion and exclusion criteria. Where full texts were not available, authors were contacted with a request for the article. Due to a lack of funding, articles which could not be retrieved in this manner were excluded from the analysis. All data was extracted, coded and analysed by a single researcher. However, a practice run of 10 randomly selected studies was performed with the results discussed with the principle supervisor and a research collaborator who was a specialist in meta-analysis. This stage was

performed in order to modify the extraction sheet and procedures in order to ensure they would meet study aims.

2.2.4.2 Effect size extraction

All data were extracted only from published material. For purposes of this analysis, the original study author's own definitions of adherence were used. Adherence rates were also recorded where available.

Where authors reported univariate and multivariate effect sizes, the univariate effect size was preferred. This limited the impact of different multivariate models impacting upon effect size estimates (Atkinson and Petrozzino, 2009).

Effect sizes were recorded as either Pearson's correlation coefficients (r) or as Odds Ratios (OR). Pearson's r was the preferred metric. Adherence behaviour occurs on a continuum, and r represents the relationship between continuous variables in a robust way. The Odds Ratio was employed when the indicator of adherence was a categorical variable or when a majority of studies in the analysis had used the OR. Metrics were converted by Comprehensive Meta-Analysis (Borenstein et al., 2010).

Where effect sizes were not reported directly as OR or as r, they were calculated via contingency tables, reports of mean differences, or the results of statistical tests. Where authors presented significance levels rather than exact p-values, the significance level was recorded and treated as if it were the exact p for the purposes of analysis (DiMatteo, 2004c). This is a conservative method which underestimates the true significance level, but reduces the probability of a Type 1 error (Borenstein et al., 2009). To account for significance values and effect sizes that were not reported or reported only as not significant, sensitivity analysis was performed. The analysis was run once where non-significant or unreported results were omitted and a second time with all unreported or non-significant values assumed to be $r = 0$. If this second analysis changed the statistical significance of the association, the new effect size and significance test were reported (Hönekopp and Watson, 2011, DiMatteo et al., 2007, DeCoster, 2009).

2.2.4.3 Statistical analysis

2.2.4.3.1 Effect size estimation

Each indicator identified in the literature was coded to link together identical and similar indicators for analysis, and to separate dissimilar indicators (Sharpe, 1997). Indicators were assigned codes as they emerged. Indicators within each category were then sorted so that only indicators sufficiently similar to each other were combined. Because HIV requires high adherence to a regimen more complicated than for most other illnesses (Atkinson and Petrozzino, 2009), subgroup analysis was performed with HIV studies also examined in isolation. These are reported only where a difference was found in effect size estimates. Meta-analyses were not performed when less than three identified studies could have an effect size calculated for synthesis, or when indicator variables were too variable for combination. In this case whether or not any direction of effect could be discerned from individual study results is reported.

Random effects meta-analysis was employed with all effect size estimates presented alongside confidence intervals and p-values.

Where studies reported multiple measures for the same outcome, data were amalgamated by using the mean scores for this outcome. This prevented bias from including information from the same sample more than once (Gleser and Olkin, 2009). Amalgamation was not considered appropriate where the differences in outcome between measures were large. When this occurred the study sample was excluded to prevent author preference biasing results.

All effect sizes are presented so that OR's greater than 1 and positive values for r indicate a variable is associated with greater adherence.

2.2.4.3.2 Heterogeneity analysis and Meta-regression variable coding

The I^2 statistic was used to quantify the extent of heterogeneity in analyses. This variable expresses the percentage of variation in a meta-analysis which can be attributed to differences between studies as opposed to random error around a single effect size (Borenstein et al., 2009).

2.2.4.3.3 Descriptors of studies

Data were recorded to describe the population of studies in terms of year and place of publication, type of study design, how and whether adherence was defined in the study, how and if adherence was dichotomised, the method of adherence measurement, whether self-reported adherence utilised an existing measure or not, the duration of adherence measurement, and the disease studied. These findings are summarised in appendix A. None of these indicators were utilised for ranking or rating of study quality. This data is collected and presented only to characterise the type of evidence available in terms of study designs utilised. This helps to place presented results in the context of the methods employed (Hetrick et al., 2010). For example, a lack of experimental studies and RCTs makes attributions of causality inappropriate in the identified body of research.

2.2.4.3.4 Expanded results

An expanded table of results providing more detail into the outcomes of analysis is presented in appendix B for studies analysed via the correlation coefficient and appendix C for studies analysed via the odds ratio. In addition to the results presented in the main text, these appendices presents median, minimum, and maximum effect sizes within meta-analyses for all variables, a significance test to identify whether heterogeneity is statistically significant or not within the analysis, and estimates of standard error and tau for comparison of within and between study error. Appendix D lists the studies included in each meta-analysis along with individual effect size estimate and presents a bibliography for these studies.

2.3 Results

Figure 2.1 summarises the flow of article inclusion and exclusion. A total of 97 articles could not be obtained, and 317 articles failed to fulfil inclusion criteria or else met exclusion criteria. A total of 198 articles met all inclusion criteria (10.44%). The reasons for exclusion during full text review are indicated in figure 2.1. Other than a lack of relevance and inability to acquire a full text, the primary cause of exclusion was articles providing insufficient data to calculate an effect size. Of the 198 articles which had data extracted, 53 contained indicators which could not be combined with those from other studies and so analyses are based upon a final sample of 145 studies. Included studies had a median (Quartiles) sample size of 288 (121, 708) with a minimum sample size of 28 and a maximum of 1,888,682.

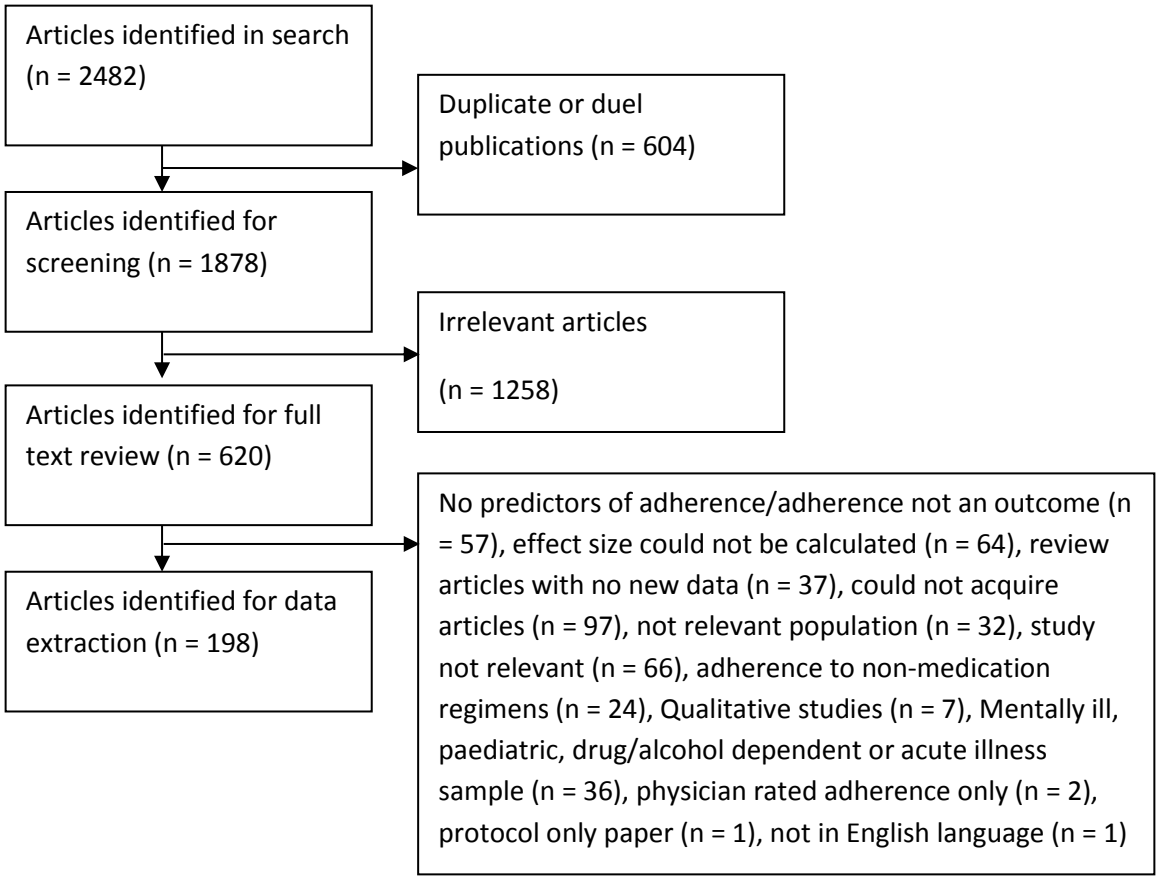


Figure 2.1 Flow of articles included in review

For all articles that dichotomised adherence as a proportion of medicines taken (k = 124), the median (Quartiles) per cent of patients rated as adherent was 67.28% (52.5%, 80.85%), with a range of 10% to 98.53%.

2.3.1 Patient Demographics

The results of meta-analyses exploring the evidence for links between adherence and categorical demographic variables are presented in table 2.1 where the results were analysed using the odds ratio. Therefore factors which such as age or income which are better presented as correlations are not included in the table. In general there was no evidence for associations between patient demographics and adherence behaviour. Furthermore, all analyses displayed high heterogeneity. However, being employed was found to be associated with improved adherence to medication.

Indicator	k	n	OR	Lower CI	Upper CI	p	I^2
Sex (Female vs. male)	68	2167404	0.988	0.933	1.045	0.665	84.059
Education (as level of education increases)	48	48321	1.144	0.942	1.389	0.176	87.224
Education (college education vs. none)	25	42361	1.150	0.861	1.537	0.345	89.579
Employment (yes vs. no)	**15**	**5661**	**1.315**	**1.006**	**1.719**	**0.045**	**72.422**
Health insurance (Yes vs. No)	7	3118	1.080	0.693	1.685	0.734	64.313

Items in bold show a statistically significant association with adherence at $\alpha = 0.05$.
Items in italics show a statistically significant association at $\alpha = 0.1$.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.

Table 2.1 Relationship to adherence between demographic characteristics

A weak positive correlation was associated between age and adherence, k = 83, n = 2,079,337, r (95% CI) = 0.057 (0.037, 0.078), $R^2 = 0.003$, $p < 0.001$, $I^2 = 98.485$. There was no indication that income had any relationship with adherence, k= 19, n = 7657, r (95% CI) = 0.006 (-0.051, 0.063), $R^2 < 0.001$, p = 0.835, $I^2 = 69.057$. Classification of samples into high or low sociodemographic groupings was rare (k = 3) and the methods of those studies too variable to draw conclusions. Only three studies examined the effects of having children on adherence, and they indicated that having children was associated with improved adherence (Moralejo et al., 2006, Corless et al., 2005), and that having more children correlated with improved adherence (Corless et al., 2005, Golin et al., 2002). Sexuality was investigated by three studies in HIV regimens. All were small samples with a combined n of 343, and there was a lack of evidence for any effect, OR (95% CI) = 1.404 (0.538, 3.662), p = 0.488, $I^2 = 59.578$.

2.3.2 Patient Race

The relationships between race and adherence are represented in table 2.2. Despite large sample sizes and a tendency for white participants to have higher adherence, this effect was not statistically significant at $\alpha = 0.05$. However, comparisons of white patients to non-white patients as a whole, and to ethnic minorities that were neither black nor Hispanic did achieve significance at $\alpha = 0.1$. Black patients were shown to be less adherent than other ethnic minority patients.

Indicator	k	n	OR	Lower CI	Upper CI	p	I^2
Black / Other races	**6**	**40263**	**0.601**	**0.464**	**0.777**	**<0.001**	**42.771**
White / black	*13*	*1954297*	*1.432*	*0.956*	*2.143*	*0.081*	*99.118*
White / Hispanic	6	1892707	1.121	0.789	1.593	0.522	80.418
White / non-white	*12*	*6901*	*1.376*	*0.942*	*2.008*	*0.098*	*81.371*
White / other	9	1947200	1.204	0.831	1.745	0.327	98.901

Items in bold show a statistically significant association with adherence at $\alpha = 0.05$.
Items in italics show a statistically significant association at $\alpha = 0.1$.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.

Table 2.2 Relationship between adherence and race

2.3.3 Adherence to non-medication regimens

It was not possible to meta-analyse adherence to appointments or to exercise because too few studies were identified. Any identified associations were weak (Stanton, 1987, Bane et al., 2006, Trivedi et al., 2008). Four studies explored the relationship between adherence to medications and to diet (n = 1881) and those that were more adherent to diet regimens were also more adherent to their medication regimens, r (95% CI) = 0.187 (0.034, 0.332), $R^2 = 0.035$, p = 0.017, $I^2 = 86.473$.

2.3.4 Medication regimen

Table 2.3 represents the results of meta-analyses utilising ORs which explored relationships between adherence and characteristics of patients medication regimen. Differences in medication regimen were not related to adherence. One exception to this

was a higher number of unique medications for HIV patients. Longer duration of a medication regimen was associated with lower adherence, k = 12, n = 20806, r (95% CI) = -0.062 (-0.116, -0.007), R^2 = 0.003, p = 0.027, I^2 = 97.344. The number of pills taken throughout the day was not associated with adherence, k = 11, n = 4482, r (95% CI) = 0.034 (-0.033, 0.100), R^2 = 0.001, p = 0.318, I^2 = 59.524. It was not possible to combine studies comparing weekly to daily regimens because effect sizes could not be calculated for studies that were sufficiently similar to combine, nor could any direction of effect be discerned. Patients that had experienced a change in medication regimen may have lower adherence (Parruti et al., 2006, Lam et al., 2007, Deschamps et al., 2004), but it was not possible to calculate an effect size for these studies.

Indicator	k	n	OR	Lower CI	Upper CI	p	I^2
Number of co-medications	4	24204	1.002	0.790	1.271	0.987	91.885
Fewer different types of pills per day	14	180468	0.984	0.695	1.395	0.929	99.5
Fewer different types of pills per day for HIV	**5**	**1504**	**1.888**	**1.300**	**2.740**	**0.001**	**44.103**
Fewer different types of pills per day for non-HIV	9	178964	0.738	0.485	1.122	0.155	99.686
Complexity of regimen (e.g. monotherapy vs. combination /pills per dose)	8	4435	0.857	0.508	1.444	0.562	88.71

Items in bold show a statistically significant association with adherence at α = 0.05.
Items in italics show a statistically significant association at α = 0.1.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.

Table 2.3 Relationship between adherence and medication regimen factors

2.3.5 Use of memory aids

A total of 6 studies (n = 2419) examined the use of memory aids. These were associated with higher levels of adherence, OR (95% CI) = 1.971 (1.463, 2.656), p < 0.001, I^2 = 35.597.

2.3.6 Barriers to adherence

Where studies explored practical or perceived barriers to adherence without further specification, it was found that patients that reported a greater number of barriers were less adherent than those facing fewer obstacles, k = 8, n = 2941, r (95% CI) = -0.253 (-0.356, -0.142), R^2 = 0.064, p < 0.001, I^2 = 84.489. Patients reporting good access to

medical care were more likely to be adherent, k = 4, n = 912, OR (95% CI) = 2.323 (1.659, 3.253), p < 0.001, I^2< 0.001. Ease of access to medication was also associated with better adherence, k = 3, n = 688, OR (95% CI) = 2.333 (1.445, 3.765) p = 0.001, I^2< 0.001.

2.3.7 Costs of treatment

There were 10 studies (n = 55,800) that investigated the effects of cost of medicines upon adherence. A significant difference whereby higher costs were associated with lower adherence was identified, OR (95% CI) = 0.760 (0.654, 0.884), p < 0.001, I^2 = 92.529. There was no significant relationship found between the total cost of medical treatment and adherence, k =4, n = 23,013 OR (95% CI) = 1.250 (0.826, 1.891), p = 0.292, I^2 = 90.279.

2.3.8 Comorbidity

All analyses exploring the relationship between comorbidity and adherence are shown in table 2.4. The presence of hypertension was found to have a small but statistically significant relationship with adherence. Three studies also examined five respiratory conditions (Ho et al., 2008, Diette et al., 1999, Balkrishnan and Christensen, 2000), however these studies were not sufficiently similar to combine. There were no clear indications of the direction of any effect.

Indicator	k	n	OR	Lower CI	Upper CI	p	I^2
Comorbidity	19	2047198	0.987	0.821	1.186	0.885	98.530
Dyslipidaemia	3	19852	1.027	0.762	1.384	0.861	84.105
Liver Disease	3	6015	0.758	0.343	1.675	0.493	43.740
Hypertension	**6**	**91860**	**1.081**	**1.002**	**1.165**	**0.045**	**72.301**
Other cardiovascular conditions	6	89450	1.119	0.965	1.297	0.136	89.496
Diabetes	10	74563	0.988	0.930	1.050	0.692	53.442
Stroke	4	43097	1.072	0.960	1.196	0.215	55.578
Myocardial infarction	4	48287	1.058	0.959	1.167	0.264	34.747
Heart Failure	*5*	*79940*	*1.106*	*0.993*	*1.232*	*0.067*	*67.986*

Items in bold show a statistically significant association with adherence at α = 0.05.
Items in italics show a statistically significant association at α = 0.1.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.

Table 2.4 Relationships between adherence and comorbidity

2.3.9 Disease severity and outcomes

The relationship between indicators of disease severity and outcome with adherence as measured via ORs are presented in table 2.5. In most cases any relationship between disease severity and outcomes with adherence was weak and not statistically significant. However, HIV patients were more likely to be hospitalised when adherence was low. The correlation between symptom severity and adherence was not statistically significant, k = 15, n = 8460, r (95% CI) = -0.019 (-0.046, 0.008), p = 0.163, I^2 = 73.726. The duration a patient had presented with a particular illness was not significantly associated with adherence, k = 21, n = 15608, r (95% CI) = -0.008 (-0.052, 0.037), p = 0.731, I^2 = 66.788.

Indicator	k	n	OR	Lower CI	Upper CI	p	I^2
CD4 Count	15	9775	0.980	0.820	1.171	0.822	76.470
HIV RNA	15	9811	1.072	0.839	1.369	0.578	83.159
HIV Status (More severe/AIDS vs. less severe/no AIDS)	11	2768	1.028	0.760	1.390	0.860	51.645
Systolic BP	5	2025	0.949	0.640	1.408	0.795	76.937
Diastolic BP	5	2025	1.137	0.738	1.751	0.561	80.687
Fewer/No symptoms	6	6016	1.400	0.915	2.144	0.121	87.157
No GP/Outpatient visit	11	180297	0.919	0.825	1.023	0.123	94.425
Fewer/No Hospitalisation	13	84332	1.090	0.921	1.289	0.317	94.361
Fewer/No Hospitalisation - HIV	**4**	**1099**	**1.861**	**1.383**	**2.504**	**<0.001**	**12.670**
Fewer/No Hospitalisation - non-HIV	9	83233	0.956	0.802	1.140	0.619	95.569
Fewer/No Emergency department visits	4	40056	1.032	0.811	1.313	0.796	95.243

Items in bold show a statistically significant association with adherence at α = 0.05.
Items in italics show a statistically significant association at α = 0.1.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.

Table 2.5 Relationship between adherence and measures of disease severity and outcome

2.3.10 Quality of life and patient wellbeing

Table 2.6 presents the estimates of association between measures of quality of life and adherence to medication. Higher patient quality of life was associated with better adherence. However, sub-group analyses showed that the statistical significance of these effects was primarily due to the strength of these relationships in HIV patients. General measures of patient mental wellbeing were not associated with adherence behaviour.

Additionally, all but two studies in this sample were cross sectional making causal inferences impossible.

Indicator	k	n	OR	Lower CI	Upper CI	p	I^2
General QOL measures	**15**	**5379**	**0.102**	**0.043**	**0.161**	**0.001**	**65.53**
General QOL measures, HIV only	**6**	**1129**	**0.178**	**0.115**	**0.240**	**<0.001**	**<0.001**
General QOL measures, non-HIV only	9	4250	0.061	-0.017	0.139	0.127	72.278
Physical functioning	**18**	**15175**	**0.075**	**0.007**	**0.142**	**0.030**	**81.106**
Physical functioning, HIV only.	**8**	**1721**	**0.175**	**0.034**	**0.310**	**0.015**	**85.172**
Physical functioning, non-HIV only.	10	13454	0.012	-0.052	0.075	0.175	67.134
Mental wellbeing	7	1942	0.056	-0.014	0.126	0.115	50.743

Items in bold show a statistically significant association with adherence at $\alpha = 0.05$.
Items in italics show a statistically significant association at $\alpha = 0.1$.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.

Table 2.6 Relationships between adherence and measures of patient quality of life

2.3.11 Side effects of treatment

Side effects of treatment were found to be negatively associated with treatment adherence. Presence of side effects versus their perceived absence was shown to predict lower adherence, k = 11, n = 4161, OR (95% CI) = 0.402 (0.193, 0.837), p = 0.015, I^2 = 95.231. The number of side effects experienced was associated with lower adherence, k = 5, n = 1394, r (95% CI) = -0.168 (-0.290, -0.040), p = 0.010, I^2 = 86.355. The severity of experienced side effects was also associated with lower adherence, k = 5, n = 3672, r (95% CI) = -0.222 (-0.261, -0.182), p < 0.001, I^2 = 2.329.

2.3.12 Health beliefs

It was not possible to meta-analyse outcome expectations because the measures were too inconsistent. Perceived susceptibility to disease was not found to be a significant indicator, k = 4, n = 988, r (95% CI) = -0.004 (-0.232, 0.225), p = 0.975, I^2 = 89.265. Higher self-efficacy was associated with higher adherence, k =21, n = 9047, r (95% CI) = 0.273 (0.202, 0.342), R^2 = 0.075, p < 0.001, I^2 = 83.854.

2.3.13 Patient beliefs regarding their medication

Correlations between patient's beliefs about medicines and adherence are presented in table 2.7. Positive beliefs were associated with greater adherence. However, the evidence was far less strong regarding any effect of negative beliefs regarding medication.

Indicator	k	n	r	Lower CI	Upper CI	p	R^2	I^2
Satisfaction with medicines	**5**	**1872**	**0.245**	**0.118**	**0.364**	**<0.001**	**0.060**	**82.975**
Positive belief regarding medicine	**6**	**3207**	**0.153**	**0.100**	**0.205**	**<0.001**	**0.023**	**39.898**
BMQ Necessity	**4**	**622**	**0.286**	**0.136**	**0.423**	**<0.001**	**0.082**	**69.812**
BMQ Concerns	3	622	-0.041	-0.152	0.072	0.481	0.002	46.197

Items in bold show a statistically significant association with adherence at α = 0.05.
Items in italics show a statistically significant association at α = 0.1.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.
BMQ refers to the Beliefs about Medicines Questionnaire (Horne et al., 1999).

Table 2.7 Relationship between adherence and patient beliefs about medication

Belief in the effectiveness of medicine was associated with better adherence, k = 6, n = 1607, OR (95% CI) = 2.244 (1.121, 4.492) p = 0.022, I^2 = 80.295. Studies using scales other than the Beliefs about Medicines Questionnaire (Horne et al., 1999) to measure patient concerns about medication were too varied in design to combine, and also varied in terms of outcome so no indications for direction of effect could be determined (Carr et al., 2006, Bardel et al., 2007, Mann et al., 2007, Mann et al., 2009). Two studies examined the role of the BMQ General harms scale and the BMQ General overuse scale, and greater concerns were associated with lowered adherence (Menckeberg et al., 2008, Gauchet et al., 2007). A further two studies examined the role of the perceived importance of medication on adherence behaviour (Bardel et al., 2007, Mann et al., 2007) and both found a positive association.

2.3.14 Patient knowledge and education

Patients having better knowledge of their medication, illness and their general health literacy are all associated with improved medication adherence. Knowledge of medication was assessed by 10 studies (n = 6208) with a correlation of r (95% CI) = 0.084 (0.080, 0.261), R^2 = 0.007, p < 0.001, I^2 = 80.362, while knowledge of a patients illness was

assessed by eight studies (n = 2945) with an OR (95% CI) of 2.486 (1.551, 3.983) p < 0.001, I^2 = 86.850. Health literacy was assessed by four studies (n = 2062) finding a positive relationship with adherence with r (95% CI) = 0.193 (0.069, 0.311), R^2 = 0.037, p = 0.002, I^2 = 74.525.

2.3.15 Risky health behaviours

The relationships between patients' engagement in risky health behaviours are presented in table 2.8. Patients engaging in risky health behaviours were more likely to be nonadherent. Studies investigating the use of complementary medicines were not similar and so were not meta-analysed. Evidence for any association between adherence and complementary medicine was not consistent in the individual studies (Ng et al., 2004, Murri et al., 2009, Liu et al., 2007). Similarly, it was not possible to combine studies investigating the impact of Body Mass Index (BMI) upon adherence. However, where the direction of the association between BMI could be discerned and calculated, the indications were toward larger BMI being associated with lower adherence (Shah et al., 2007, Janson et al., 2008). Only two studies examined the relationship between adherence and exercise, and both suggested that more exercise was associated with lower adherence (Shah et al., 2007, Irvine et al., 1999).

Indicator	k	n	OR	Lower CI	Upper CI	p	I^2
Smoking Yes/More vs. No/Less)	**15**	**151636**	**0.708**	**0.630**	**0.796**	**<0.001**	**42.910**
Alcohol use	**11**	**4449**	**0.657**	**0.534**	**0.809**	**<0.001**	**<0.001**
Problem alcohol use	**7**	**10351**	**0.471**	**0.352**	**0.629**	**<0.001**	**21.130**
Drug use	**11**	**2862**	**0.516**	**0.401**	**0.665**	**<0.001**	**41.318**

Items in bold show a statistically significant association with adherence at α = 0.05.
Items in italics show a statistically significant association at α = 0.1.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.

Table 2.8 Relationship between adherence and health behaviours

2.3.16 Relationship with medication provider

The associations between measures of patient-provider relationship and adherence are presented in table 2.9. Having a good relationship with healthcare providers predicts higher adherence. Furthermore, receiving care from a family physician or GP is associated

with higher adherence than is care received from other medical personnel, k = 5, n = 25153, OR (95% CI) = 0.820 (0.730, 0.922), p = 0.001, I^2 = 43.408.

Indicator	k	n	r	Lower CI	Upper CI	p	R^2	I^2
Satisfaction with care	**9**	**3336**	**0.131**	**0.045**	**0.216**	**0.003**	**0.017**	**85.445**
Trust in physician	**8**	**7263**	**0.164**	**0.117**	**0.210**	**<0.001**	**0.027**	**68.152**
Good communication / Relationship with Physician	**13**	**8592**	**0.100**	**0.057**	**0.142**	**<0.001**	**0.010**	**53.401**

Items in bold show a statistically significant association with adherence at α = 0.05.
Items in italics show a statistically significant association at α = 0.1.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.

Table 2.9 Relationships between adherence and provider relationship factors

2.3.17 Social support

Social support was directly measured by 22 studies (n = 6641) with more social support associated with higher medication adherence, r (95% CI) = 0.138, (0.080, 0.195), R^2 = 0.019, p < 0.001, I^2 = 75.349. The value of the subjective norms of patients significant others was investigated by four studies and five samples, however an effect size could not be calculated. Nonetheless, all five samples indicated that the support of significant others improved adherence (Holstad et al., 2006, Brus et al., 1999, Barclay et al., 2007, Bane et al., 2006). The benefit of being married or living with a long term partner was assessed by 19 studies (n = 9799) and adherence was higher in patients with such a relationship, OR (95% CI) = 1.267 (1.077, 1.491) p = 0.004, I^2 = 59.026. Patients that received help taking their medicines was investigated by five studies (n = 2682) and was found to produce a statistically significant boost to adherence, OR (95% CI) = 1.752 (1.159, 2.649), p = 0.008, I^2 = 47.713.

2.3.18 Patient affect

The relationships between measures of mental distress and adherence are presented in table 2.10. Hostility was not found to be associated with adherence behaviour. Hope may help patients adhere to their medications, but the evidence is scant with only two studies investigating this (Van Servellen et al., 2002, Treadaway et al., 2009).

Indicator	k	n	r	Lower CI	Upper CI	p	R^2	I^2
Anxiety	**11**	**1375**	**-0.163**	**-0.250**	**-0.073**	**<0.001**	**0.027**	**59.343**
Stress	**12**	**3423**	**-0.162**	**-0.229**	**-0.094**	**0.001**	**0.026**	**80.008**
Distress	**6**	**885**	**-0.167**	**-0.246**	**-0.086**	**<0.001**	**0.028**	**48.881**
Hostility	3	671	-0.158	-0.415	0.121	0.266	0.025	91.592

Items in bold show a statistically significant association with adherence at $\alpha = 0.05$.
Items in italics show a statistically significant association at $\alpha = 0.1$.
k refers to the number of studies in the meta-analysis
n refers to the pooled sample size.

Table 2.10 Relationship between adherence and patient affect

2.3.19 Patient mental health

Mental health summary scores, with higher scores suggesting better mental health, correlated positively with improved adherence behaviour, k = 6, n = 4154, r (95% CI) = 0.153 (0.102, 0.204), $R^2 = 0.023$, $p < 0.001$, $I^2 = 50.741$. Furthermore, patients with a past or current psychiatric diagnosis were significantly less adherent than those without such a diagnosis, k = 8, n = 16849, OR (95% CI) = 0.531, (0.356, 0.791), p = 0.002, $I^2 = 76.590$. Depression was a significant risk factor for nonadherence, k =39, n = 95192, r (95% CI) = -0.100, (-0.127, -0.073), $R^2 = 0.010$, $p < 0.001$, $I^2 = 76.664$. Anxiety disorders were investigated by three studies (Tucker et al., 2003, Woods et al., 2009, Cluley and Cochrane, 2001) which could not be combined, but all indicated a negative relationship to adherence. Similarly, only one study (n = 5548) looked into the effect of psychosis (Ye et al., 2007). Adherence was found to be lower when psychosis was present (54.70% vs. 64.50%) but this difference was not statistically significant (p = 0.135).

2.3.20 Cognitive ability

While measures of general cognitive ability were too varied to combine, it could be determined that the onset of dementia or cognitive decline in old age was associated with lowered adherence, k = 8, n = 49596, OR (95% CI) = 0.839 (0.741, 0.949), p = 0.005, $I^2 < 0.001$. Strength of memory in the general population was also associated with better adherence, k = 4, n = 441, r (95% CI) = 0.181 (0.006, 0.345) $R^2 = 0.033$, p = 0.043, $I^2 = 65.992$.

2.3.21 Personality variables

A wide variety of personality measures are used in the literature which resulted in very few variables having a sufficient number of studies available for meta-analysis. In particular it was noted that only two studies were identified which employed the Big 5 or OCEAN model of adherence with one of these Evangelista et al. (2001), only utilising the Neuroticism dimention indicating greater neurotisism was associated with lower adherence in their sample of 82 patients with heart failure. Christensen and Smith (1995) utilised all five dimesions of the OCEAN model but only identified a positive relationship between greater conscientiousness and adherence in a sample of 72 renal transplant patients. Only variables examining the importance of locus of control, and of coping style could be combined. There were five studies and six samples that examined the relationship between adherence and an internal locus of control, however only three of these studies could have an effect size calculated for them to indicate a non-significant positive correlation between the two variables, n = 485, r (95% CI) = 0.131 (-0.071, 0.323), R^2 = 0.017, p = 0.203, I2 = 77.246. The three samples that could not be combined also indicate a positive relationship between the two variables (Barclay et al., 2007, Molassiotis et al., 2002). A chance locus of control measure could not be synthesised. Barclay et al. (2007) identified a statistically significant relationship with poor adherence and a chance locus of control (t = 1.96, p = 0.05). Lynam et al. (2009), and Frazier et al. (1994) also identified negative associations between a greater chance locus of control and lower adherence (r = -0.11 and r = -0.15 respectively). Two measures from one sample in Lynam at al. (2009) and one from Frazier et al. (1994) examined the role of powerful others locus of control and found no evidence of any effect, with r's ranging from -0.03 to 0.06.

The benefits of adopting an active coping style was investigated by four studies (n = 536) but no strong evidence of an effect was found, r (95% CI) = -0.032 (-0.134, 0.071), R^2 = 0.001, p = 0.071, I2 = 62.510. Adoption of avoidant coping strategies was examined by just two studies (Frazier et al., 1994, Deschamps et al., 2004) and both indicated that such strategies were associated with lower adherence.

2.4 Discussion

2.4.1 Indicators of adherence to medication

In common with previous reviews of the literature, the proportion of patients adhering to their medication varied greatly between studies (DiMatteo, 2004c, Vermeire et al., 2001). However the overall estimate of approximately one third of patients not taking medications as prescribed underlines the importance of being able to identify and offer appropriate interventions to this large group of patients. The study has also identified which indicators of adherence can be objectively shown to be related to adherence.

2.4.1.1 The role of health and healthcare

Measures of disease severity were not associated with adherence which agrees with findings of DiMatteo et al. (2007). It was also demonstrated that most outcomes were not highly correlated with adherence. This finding is in partial agreement with DiMatteo et al. (2002). Although this study reported a 26% benefit to outcomes from adherence, the identified benefits were larger for non-medication regimens, and also in 'soft' non-disease specific patient orientated outcomes such as experience of pain, weight gain or hospitalization, than in 'hard' disease specific outcomes such as blood pressure, cholesterol levels, or CD4 counts. One explanation for the lack of association between adherence and outcome is the variable dichotomisation of adherence when the therapeutic effect of adherence above or below specific values is unknown. Patients may be being asked to take more medicines than is required for therapeutic benefit. Consequently, prescribers should approach each individual patient as a therapeutic experiment and modify regimens to find the optimal dose for individual patients, rather than assume the average effect from randomised controlled trials will necessarily apply (Healy, 2004).

Patients' access to medical care and to medicines has been shown to impact upon adherence. This validates efforts to introduce schemes that enhance patient access to care. These include pharmacist domiciliary visiting (Bhattacharya et al., 2008), NHS walk-in centres (Jackson et al., 2005), and the NHS direct helpline (Knowles et al., 2002,

O'Cathain et al., 2005). Furthermore, access to care in UK pharmacies has been criticised, and could benefit from regulation which ensures pharmacies are located in such a way as to ensure access for remote communities (Lluch and Kanavos, 2010). Personal barriers to medication taking were also shown to predict up to 6% of adherence behaviour. Intervening to identify and remove individual patient's barriers could therefore enhance adherence (Krousel-Wood et al., 2009, Horne, 2006). Interventions may include reducing regimen complexity (Catz et al., 2000), the use of memory aids (Fogarty et al., 2002), and discussing the affordability of medicines and the availability of schemes that may help patients to afford them (Schafheutle et al., 2002). While the overall cost of healthcare was not found to predict adherence, the cost of medicine was an indicator. The affordability of medicine to those on a low income in the NHS is important to ensure the patient has access to required medication.

Complexity of the drug regimen was not a significant predictor of adherence. Iskedjian et al. (2002) and Bangalore et al. (2007) did find increased regimen complexity to be associated with lower medication adherence in prior meta-analyses with a similar number of studies identified here ($k = 8$, and $k = 9$ respectively). Failure to replicate these results may be due to varied cut points being used to indicate higher or lower complexity with this being less controlled for in the current study with different measures of complexity more broadly grouped so as to maintain statistical power. The relationship between adherence and regimen complexity may not be linear (Patel and David, 2004, Demyttenaere, 2003), which would also lower the likelihood of the current analyses identifying a relationship.

It was demonstrated that the longer a patient is prescribed a regimen then the more likely they are to become nonadherent. It is common for the proportion of patients categorised as adherent to fall sharply in the first 6 months, with a more gradual decline after this period (Chapman et al., 2005, Chapman, 2004). Encouraging adherence during this critical early period of adjustment may prove important and the reasons why patients become less likely to become nonadherent after 6 months explored.

The current analysis did not find that comorbidity was a reliable indicator of adherence. Prior research has found that patients with more than one condition experience more side effects and dislike having to take multiple medicines (Williams et al., 2008). However, Schüz et al. (2011) also performed a longitudinal study that did not find a significant

association between the number of illnesses or prescribed medications and adherence in an older population. Comorbidty may only impact adherence when patients have a high disease or medication burden.

Comorbidity is also an important indicator of adherence when patients have concurrent or prior mental health issues, or for those displaying symptoms of cognitive decline and dementia. The studies included in the review strongly indicate that patients with mental health difficulties are less likely to be able to adhere to their medication. Patients with comorbid mental health difficulties should be considered at greater risk of nonadherence (Demyttenaere, 2003). However, even in mentally health patients' tests of memory were suggested to be indicative of ability to adhere to medication. This corroborates prior research which has found patients executive functioning and prospective memory to be associated with medication adherence (Zartman, 2006, McNally et al., 2010, Insel et al., 2006). Therefore the importance of cognitive abilities even in mentally healthy populations should not be discounted.

2.4.1.2 Patient experience, beliefs, and knowledge about medicines

Patients experiencing side effects from their medicines are less adherent to them. This can be seen as a rational response of patients to preserve their quality of life (Gay et al., 2011, Johnson et al., 2005). Qualitative studies show that many patients do not like taking medicines as they are seen as toxic or unnatural (Britten, 1994, Benson and Britten, 2002), and an inability to cope with adverse effects have been cited as the primary reason for nonadherence by patients in focus groups (Golub et al., 2006). Such beliefs, coupled with experience of side effects, will encourage patients to become nonadherent either by reducing their doses or stopping altogether. Factor analysis of doctors' prescribing decisions shows that they do consider side effects of various competing drugs when prescribing (Monteiro et al., 2010). However, individual risk factors in patients are often overlooked (Scheiman and Hindley, 2010). Appropriate and minimal prescribing to optimise patient benefit and minimise the costs of medication taking should be sought, with medication reviews using validated criteria to identify inappropriate or over prescribing implemented to reduce potential harm to patients (e.g. STOPP and START criteria, O'Mahony et al., 2010).

Moreover it was demonstrated that actual negative experiences were consistently associated with nonadherence while concerns about medicines were not. An economic framework can be used to investigate these trade-offs (Elliott et al., 2008). Adherence is lower in asymptomatic conditions (DiMatteo et al., 2002), possibly because patients may believe they are only ill when symptoms flair up (Svensson et al., 2000). Here medicines may induce side effects whilst not offering any obvious health improvement to the patient, increasing the likelihood of a rational but potentially harmful decision to not adhere to medicine (Iskedjian et al., 2002). Patients positive beliefs in the necessity of medicines were shown to be associated with adherece and this may help to offset some of the negative impact of side effects from medicine.

Patient knowledge of their medicines and illness, as well as health literacy, were shown to be associated with greater adherence. Reviews appraising the impact of increasing patient knowledge upon adherence indicate that such interventions are of benefit, but are not sufficient (Haynes et al., 1996, Weinman, 1990). Patients seek information about their medicines, and application of simple tools to measure patient satisfaction with information received may prevent lack of knowledge damaging patient adherence (Horne et al., 2001).

2.4.1.3 Key relationships

In support of previous literature, patient relationships with healthcare providers and prescribers was identified as important for promoting adherence (Bultman and Svarstad, 2000). The personal qualities of physician may be a key determinant of adherence (Sencan et al., 2011). Prior reviews of the literature have found that open, friendly, and collaborative consultations are associated with better adherence (Banning, 2008, Arbuthnott and Sharpe, 2009). What constitutes a good consultation will be sensitive to context and individual, and what is good practice with one patient may alienate another (Penn et al., 2011). Consequently, practitioners need to be sensitive to the needs and barriers of individuals in order to enhance adherence (Broers et al., 2005, Ong et al., 1995, DiMatteo, 2003).

The current investigation has also emphasised the importance of a patient's support network outside of the healthcare setting, including the benefits of being married or in a

long term relationship. This is in agreement with a prior meta-analysis (DiMatteo, 2004b). Improving a patient's social support is difficult. While patient disclosure of illness has been shown to improve adherence, it has also been linked to patients facing social stigma and isolation (Burstein et al., 2011). Careful analysis of how and when it is of benefit to patients to disclose their illness offers potential for maximising gains and limiting risks (Chaudoir et al., 2011).

2.4.1.4 Individual differences and adherence

Stress, anxiety, and distress were all found to explain largely the same amount of variability in the adherence relationship, and the different constructs will co-vary to some degree. The variables are also likely to co-vary with the relationship between adherence and depression (Mineka et al., 1998). Although causality is difficult to determine, negative affect in patients should be treated as both an indicator of adherence and a target for interventions. Intervening to combat negative emotional states in subclinical samples can prevent the onset of more severe psychiatric comorbidity (Lovibond and Lovibond, 1995). The negative relationship between medication adherence and anxiety found here contradicts a previous meta-analysis of this issue (DiMatteo et al., 2000). However, DiMatteo et al.(2000) did not sperate adherence to medication regimens and other therapeutic behaviours such as diet and exercise and the correlations closest to zero in their analysis were for non-medication regimens.

There was a scaricity of studies available for exploring any association between personality and adherence. Horne argues against the use of personality variable to inform adherence research because personality is not amenable to change and so is of limited use for informing the design of interventions (Horne, 2001), and because correlations between adherence and personality tend to be small (Horne, 2000). Correlations between personality variables and most behaviours tend to be small, however they benefit from being consistent across an individual's lifespan (Nettle, 2007). Furthermore, Christensen argues that much of the debate surrounding the personality literature in adherence stems from failing to acknowledge the importance of context and interaction effects with other variables (Christensen, 2000). This does not mean that personality traits are not potentially useful indicators. Patients of different personalities may respond to medical

interventions differently and this should be investigated, particularly in reference to communication with prescribers. Therefore it is argued that specific review of the influence of personality, and in particular the OCEAN model of personality, is warrented. A large study investigating the relationship between the OCEAN model dimentions and personality in 749 Swedish chronic disease patients has already suggested that studies with adequate power to cope with the anticipated small relationships expected in personality research can successfully identify such relationships (Axelsson et al., 2011). In particular this study found that it is the interation of personality traits that are most important. For example, while conscientiousness is usually associated with greater adherence, where higher conscientiousness is coupled with high neuroticism lower adherence was identified. However, further research exploring the causes and implications of these relationships is necessary before they can be utilised to help predict adherence.

An internal locus of control is associated with the belief that an individual's actions impact upon outcomes, and evidence suggets that such beliefs are associated with greater adherence to medicines. Conversely, patients with a chance locus of control, indicating a more fatalistic outlook, may be negatively associated with adherence. A lack of belief in the power of personal actions could contribute to lowered motivation to adhere to a medication regimen (Lynam et al., 2009, Frazier et al., 1994, McDonald-Miszczak et al., 2000). Lynam et al and Frazier et al. also failed to find any effect for the influence of the powerful others locus of control. It may be expected that any effect of this trait may be expected to be mediated by the positions of that individual's social group.

Active coping styles tend to be found amongst patients with a belief in the importance of their actions, while passive coping strategies are analogous to the fatalistic chance locus of control. Evidence was scarce for any effect of an active coping style. This may be because prior research has indicated that it is not the prevailing coping style of the patients in isolation that is important, but how appropriate that style is to a particular patient's circumstances (Christensen, 2000, Wiebe and Christensen, 1996). The two available studies suggest avoidant coping styles may be associated with lower adherence (Frazier et al., 1994, Deschamps et al., 2004), but there is a need for more research on this issue that addresses the problem of interaction effects.

2.4.1.5 Patient demographics

In common with prior research, few patient demographics were related to adherence (Horne, 2000, Falagas et al., 2008), despite some assertions to the contrary (Bezie et al., 2006).

Older patients have a tendency towards superior adherence supporting previous research (Kripalani et al., 2010, Atkins and Fallowfield, 2006). The reasons why patients of a younger age may be less adherent has not yet been fully elucidated. Older patients may be more experienced with taking medicine (Kripalani et al., 2010), more concerned with or cautious about their health (Leventhal and Crouch, 1997), may be more accepting of illness and thus more capable of normalising medication taking (McDonald-Miszczak et al., 2000, Gooberman-Hill et al., 2003, Kondryn et al., 2011, Kondryn et al., 2009). Alternatively older patients may be more conscientious (Soto et al., 2010) which has been shown to be correlated with adherence (O'Cleirigh et al., 2007) and engagement in other health behaviours (Terracciano et al., 2008).

The current results do identify differences between races in adherence behaviour. White patients were more adherent than other races, and black patients were less adherent than other races. Almost all studies that used race as an indicator were based in the USA, with only four exceptions limiting how far findings should be generalised to other nations. The causes of racial difference in adherence are most likely environmental factors. Gerber et al. (2010) indicate covariance between race and greater depression, lowered social support, lower health literacy, and poorer relationships with providers. Each of these factors has been identified as a correlate of adherence in this analysis. The difference between races is apparently larger for white-black than for white-Hispanic. Comparing the experience of the three races directly could identify the barriers patients of different races have adhering to medicine.

Being employed was found to be a significant indicator of higher adherence; however, there is very little discussion as to why this should be the case in the extant literature. Employment may offer greater structure to the day facilitating the taking of medication. Employed patients may also be experiencing less severe disease than those unable to work, and it has been demonstrated that adherence is lower for the most severely ill patients (DiMatteo et al., 2007).

2.4.2 Limitations of the collected literature and implications for findings

The majority of articles collected were published in the last 5 years. This reflects that where it was impossible to source articles via current library subscriptions, it was easier to contact authors of more recent articles and they may be more willing to share recent publications. It also reflects more thorough cataloguing of recent articles in electronic databases. Similarly a wide number of disease states were studied, and each may influence patient behaviour differently. A number of different definitions of adherence were employed, with a majority of studies not providing any definition at all, and a number of different cut points for the percentage of pills required to be taken for a patient to be categorised as adherent were used. Furthermore, a number of different measures were used for both adherence and indicators of adherence, and measures were taken over a wide variety of time periods. These differences between study methods and sample populations will contribute to heterogeneity in the presented results and should be born in mind. The vast majority of presented studies were also observational, and the majority of these were cross-sectional. This makes causal inferences difficult to ascribe, and it may be the case that the relationship between indicators may not be unidirectional.

2.4.3 Limitations of analysis and implications for future research

The series of meta-analyses and evidence syntheses presented are wide ranging in scope, generated a number of hypotheses for further work, and revealed areas where the evidence base is currently weak. However, the wide scope of the project forced a more shallow review of individual indicators than would be possible with a series of individual systematic reviews. In particular the search string failed to identify a significant proportion of the literature exploring health beliefs and beliefs about medications which limits the conclusions that could be drawn upon these topics. However, the relative utility of these beliefs was reviewed in chapter 1. In the absence of such reviews for most indicators of adherence, the results presented provide the most comprehensive assessment of the strength of evidence for the many indicators of adherence currently available.

Heterogeneity in analyses was often very high, a factor present in other meta-analyses of the adherence literature (Shi et al., 2010, Demonceau et al., 2013). Included literature were primarily observational studies from a wide variety of different nations using different tools in patients of varied disease states, whilst the quality of included studies was not controlled for. All of these factors may have contributed to the high heterogeneity identified and introduced some risk of bias (Simpson et al., 2006, Sutton et al., 2000, Yang et al., 2010, Egger et al., 1998). Use of the robust random effects model helped to limit the impact of heterogeneity but the precision of estimates will be reduced as a consequence of these factors.

2.4.4 Conclusion

This analysis has identified where the strength of evidence for a relationship between indicators and adherence is strongest, such as the experience of side effects, patient affect, mental health, and the relationships between patients, practitioners, and social support considered more broadly. The analyses further indicate which areas require greater research before any firm conclusions can be drawn, such as personality, the complexity of regimen, and the importance of patient concerns about medicine. A final consideration is that the R^2 estimates were for most variables very low, highlighting that adherence is a complicated behaviour and interventions which target only a single facet are unlikely to be successful (Haynes et al., 2008, Haynes et al., 1996). Further, despite the large number of indicators examined in this analysis, much of the variation in adherence behaviour remains unexplained. It is clear that despite decades of research, much remains unknown regarding why patients do or do not take their medications as prescribed.

Chapter 3 –Questionnaire development

3.1 Introduction

The meta-analyses of chapter 2 were used to identify variables that have been empirically shown to be associated with adherence. This chapter describes the process of developing a questionnaire to measure these variables in order estimate how at risk a patient is for nonadherence to medication whilst utilising the best evidence available to optimise reliability, validity, and acceptability.

3.1.1 Reliability

Kerlinger (1973) identifies three key facets of reliability; reproducibility of results on multiple administrations, accuracy of captured information, and the amount of error found in measurement. In any effort to measure an attribute numerous sources of error may be present such as the mood or health of a participant upon a given day, the manner a questionnaire is delivered, the instructions given to participants, or the weather (Nunnally, 1978). Similarly, questions which can be interpreted in different ways might elicit different responses from different participants or from the same participant on different occasions (de Vaus, 1995). Steps to reduce the impact of error includes the use of standard instructions which can be understood by all participants, piloting questions to ensure their meaning is clear and the way to respond is properly understood, or ordering questions so as to not confuse participants.

3.1.2 Validity

There are three primary categories of validity: content validity, criterion validity and construct validity (Kerlinger, 1973, Nunnally, 1978, Cronbach and Meehl, 1955).

3.1.2.1 Content validity

Face validity is determined by discussing the items generated for the questionnaire with individuals representative of the target population to ensure items are appropriate, inoffensive, and mean the same thing to participants as they do to the researchers (Rosenthal and Rosnow, 2008, Oppenheim, 1992, Hardesty and Bearden, 2004, Alumran et al., 2012). Content validity is then established by ensuring questionnaire items are comprehensive and representative of the construct under consideration via consultation with experts in a research field (Oppenheim, 1992, Huang et al., 2006, Beckstead, 2009, Cronbach and Meehl, 1955, Kerlinger, 1973).

3.1.2.2 Criterion validity

Criterion validity refers to comparing a new questionnaire to one or more external variables believed to measure the attribute under study (Kerlinger, 1973). Criterion validity is often split into predictive validity and concurrent validity. Predictive validity is ability to predict behaviour external to the measurement itself (Nunnally, 1978). For example, a questionnaire which purports to measure willingness to take medication should predict how medication is actually taken. When phenomena cannot be measured directly or no good measure of the phenomena exist concurrent validity may be established instead, which involves correlating scores on a new questionnaire with validated measures on the same topic (Oppenheim, 1992, Nunnally, 1978).

3.1.2.3 Construct validity

Construct validity refers to how well a test measures the theoretical construct it is assumed to measure (Oppenheim, 1992, Shaughnessy et al., 2009). Looking at patterns of convergence and divergence is one way to assess construct validity (Kerlinger, 1973). Most commonly this is performed via factor analysis which identifies which items on a questionnaire correlate most strongly with each other and so are most likely to be measuring a single underlying construct. Factor analysis is most properly employed to confirm patterns of convergence and divergence that were predicted from theory, but analyses may be exploratory to help inform the development of theory (Nunnally, 1978).

3.1.3 Questionnaire construction

Item wording, item ordering, how participants are asked to respond to items plus questionnaire design and layout can influence questionnaire validity and reliability.

3.1.3.1 Question wording

The key principals involved in the formation of a questionnaire item are:

- To avoid jargon, leading questions, and ambiguity or multiple meanings (Oppenheim, 1992, Williams, 2003, Meadows, 2003, Murray, 1999, McColl et al., 2001, de Vaus, 1995)
- To ensure a conversational tone to build rapport with the participant (Edwards, 2010).
- To minimise the cognitive burden required of participants (Groves et al., 2004).

Murray (1999) recommends that items should be comprehensible for those at the lower end of the educational background of the target population and not the average level to ensure most respondents will be able to comprehend questionnaire items. Edwards (2010) recommends the use of a metric such as the Flesch reading ease score to test for readability. The average reading age in the UK is approximately 12 years (Williams, 2003) and so questions and instructions should be comprehensible at this reading level at a maximum. Adhering to these principles helps to maintain acceptability to participants and the accuracy of responses.

3.1.3.2 Question ordering

It is widely agreed that easy and interesting questions should be placed early in the questionnaire while more difficult and sensitive questions should be later, and items on a single topic should as far as possible be grouped together (Oppenheim, 1992, Murray, 1999, Rattray and Jones, 2007, Meadows, 2003, McColl et al., 2001, Edwards, 2010). In contrast there is less agreement regarding the optimal positioning of demographic

questions. It has been argued that demographic questions ease participants into a questionnaire (Murray, 1999), but others argue that demographic questions can be boring or threatening and should be placed at the end of a questionnaire (Sudman and Bradburn, 1982, Oppenheim, 1992, de Vaus, 1995, Stone, 1993). However, it is argued that ordering is less important in postal questionnaires where many participants read the entire questionnaire prior to completion (McColl et al., 2001).

3.1.3.3 Participant responses

There are two basic types of questionnaire item: those that aim to elicit participants' attitudes to specific concepts or current feelings, and questions which seek factual information.

3.1.3.3.1 Attitude items

There are a number of possible ways in which participant attitude can be measured. Some of the most powerful scales are those based upon Thurstone's law of comparative judgement (Thurstone, 1927). The utility of this type of scale is that each of the items used to gauge attitude are designed to be equally spread across a bipolar attitude dimension. Having items that are equally spread across an attitude dimension allows for a greater approximation of normality permitting the use of more powerful statistical analyses. However, items on a Thurstone scale are all dichotomous, which means that a large number of items are required to measure each attitude or belief. A second attitude measurement technique is the Guttman or scalogram scale (Oppenheim, 1992). Scalogram analysis employs a series of agree-disagree statements of increasing extremity to order participants by attitude. The underlying assumption is that participants that agree to items higher in the scale will also agree to all items lower in the scale, and will not agree with statements higher in the scale than their first item of disagreement (Rattray and Jones, 2007). However, this ranking is ordinal, which limits the use of powerful statistical methods. Further, the binary response set requires a number of questions per attitude to determine participants' ranking on the attitude spectrum reliably (Schooler, 1968).

Likert scaling is the most popular attitude measuring technique, and they offer an approximation of a Thurstone scales whilst being less laborious to produce (Oppenheim, 1992). Participants rate where they lie on an attitude dimension for a number of related items. Likert scaling has been shown to have the best correlations with actual behaviour of the various attitude measurement techniques (Foddy, 1993). Furthermore, having a greater number of response options per item increases the sensitivity of individual items in terms of placing participants' attitudes accurately upon a dimension. This accuracy can be increased by having a greater number of response options or by having a greater number of items addressing the attitude of interest.

A controversy in the use of Likert scales is whether or not to include a mid-point on the scale which can represent the lack of an opinion, or ambivalence. Some authors argue that including a mid-point allows participants to tick the middle box rather than invest the effort required to make a decision (McColl et al., 2001, Edwards, 2010). There is also evidence that participants interpret the mid-point as the 'typical' response and use it as a reference for their own position (Tourangeau et al., 2004, Schwarz, 1990). Others claim that providing a mid-point can reflect genuine ambivalence on the part of participants (Murray, 1999, Wandzilak et al., 1987, Schuman and Presser, 1996). Rattary and Jones (2007) argue that excluding the mid-point irritates participants and may increase non-response. Furthermore, omitting the mid-point can force participants to make a meaningless choice when participants are uncertain which can affect the conclusions made from a study (Bishop et al., 1982). Consequently, forcing participants that genuinely have no opinion or lack the information required to make a sensible choice to make a choice could lead to erroneous conclusions (Sudman and Bradburn, 1982).

Visual analogue scales contrast to the "discrete" scales discussed above by asking participants to place how they feel on a 10cm line (Williams, 2003, Reips and Funke, 2008). The line may or may not be separated into Likert style sections which guide participants as to where on the line different strengths of attitude lie. This true continuous measurement better allows the proper use of parametric statistics. However, on a Visual Analogue Scale each score must be measured manually to see how far along the continuum it is which takes far longer than checking which of five boxes has been ticked. As a consequence, visual analogue scales are laborious to measure without

computer assistance (Reips and Funke, 2008) and thus inappropriate for use beyond the research setting.

3.1.3.3.2 Factual items

The design of questions seeking accurate and honest responses to factual questions follows many of the guidelines already described. The questions should be short, simple to understand, unambiguous, and easy for participants to process. The additional requirements are to not over burden participants' long term memory and to ensure multiple choice questions are as comprehensive as possible (Oppenheim, 1992).

3.1.3.4 Presentation of the Questionnaire

The design and layout of a questionnaire is an important aspect of development (Oppenheim, 1992). Smith (1995) demonstrated how small errors in design led to misleading conclusions for a number of studies. For example, boxes that were out of line with their responses were considered confusing by participants and ignored, as were questions that were too cramped together. Despite the demonstrated importance of design McColl et al. (2001) note that very little empirical evidence is available to guide questionnaire design.

3.1.3.4.1 Use of space

The need for white space has been emphasised as it makes questionnaires seem less intimidating, confusing, and difficult (Sudman and Bradburn, 1982). McColl et al. (2001) cite evidence by Layne and Thompson (1981) indicating that a cluttered one page questionnaire garnered a lower response rate than the same content appearing over three pages. Subar et al. (2001) also showed that a questionnaire that was designed to optimise the cognitive ease of completion attained a similar response rate to a far shorter questionnaire. Whilst maximising white space between sections and questions is advantageous, questions should ideally not be spread over two pages. This has been

shown to make questionnaires more difficult for participants to complete (Murray, 1999, Meadows, 2003).

3.1.3.4.2 Typeface

It is advised that a minimum of a 10-point font is used (McColl et al., 2001) or a 12-point font where participants may be of older age (Edwards, 2010). Guidance regarding the type of font to be used is scarce. However, it is recommended that typeface should have a distinct separation between characters. For example, 'rn' may be mistaken for 'm' in some typefaces (McColl et al., 2001). Although it is claimed that sans serif fonts are better for readers with dyslexia (e.g. British Dyslexia Association, UXMovement, Hobo-web, Evett and Brown, 2005), no literature supporting this claim was identified.

3.1.3.4.3 Use of colour

The use of colour in questionnaires has not been widely researched (Edwards, 2010, Edwards et al., 2002, McColl et al., 2001). Edwards et al. (2002) identified one study which found that the use of coloured ink improved response rates. A further eight studies indicated non-white questionnaires may produce slightly higher response rates. However this effect did not reach statistical significance. Prior opinion stresses the importance of being consistent in presentation (Groves et al., 2004) and including an eye catching front cover to arouse interest (Sudman and Bradburn, 1982).

3.1.4 Principles guiding questionnaire development

The aim is to produce a questionnaire that will be easy for participants to complete, for practitioners and researchers to assess, and which accurately predicts which patients are more likely to be nonadherent to their medications. As far as was possible existing measures were used in favour of developing new items. This decision was made for two reasons. The first was to reduce the time required to develop the questionnaire (Boynton and Greenhalgh, 2004, Williams, 2003). The second was that using existing scales allows for the direct comparison of scores on the questionnaire to those found in other studies

(Boynton and Greenhalgh, 2004, Edwards, 2010). Using scales familiar to practitioners and researchers should also help with interpretation of scores. To improve acceptability, where available scales came in long and short versions the shorter version was preferred. It has been demonstrated that practitioners prefer short questionnaires because they save time when making decisions (Spitzer et al., 1999). It was considered that the increased measurement error from a shorter scale was an acceptable trade off to maximise the acceptability and clinical utility of the questionnaires (Edwards, 2010).

3.2 Methods

3.2.1 Indicator selection

The meta-analyses of chapter 2 were performed to provide an objective assessment of what indicators of adherence should be measured in the questionnaire. The first criterion for inclusion was a statistically significant result from meta-analysis. The second was a larger than negligible effect size estimate from meta-analysis. Negligible effect sizes were defined as those with a correlation between r = -0.05 to 0.05 or Odds Ratios between OR = 0.80 – 1.20, as these values approximate to effect sizes of Cohen's $d \approx 0.1$. Calculations to establish equivalence in effect sizes were performed using the formulae detailed by Borenstein et al. (2009) and Durlak (2009).

3.2.2 Identification of existing questionnaire items

A literature review was conducted to identify and evaluate existing questionnaires. Questionnaires were identified via the studies in the meta-analyses of Chapter 2 and by searching the PubMed, Web of Knowledge, and ScienceDirect databases. Any questionnaires that were identified also had their references explored to identify additional questionnaires. The 'cited by' lists available in some electronic databases such as Web of Knowledge were also examined to see if questionnaires had been updated, or if new questionnaires had been developed on the same topics. In addition, specific searches for review articles were also conducted as a way to quickly identify a number of scales in a specific topic area. Keyword searches were also conducted in both Google and Google Scholar for each topic area. Each identified scale was then checked for suitability according to length, appropriateness to the current population, evidence for reliability, validity, and acceptability, and whether the questionnaire was available to be used either via permission from the copyright holder or because they were in the public domain. Whether work was in the public domain or not the original authors of questionnaires were contacted wherever possible to seek approval for including their work in the PALS or WAMS. Approval was also obtained prior to making any adjustments to existing questionnaires.

3.2.3 Face validity

Testing of face validity was performed using a convenience sample of friends and lay colleagues of the research team. The aim was to ask people of different ages, educational levels, and nationalities to read the questionnaire and to make comments upon it. Volunteers were contacted both in person and by e-mail. Where volunteers were able to be spoken to in person, this was embellished by talking with them about each of the questions, what they thought they meant and if there were any response options that should be made available to them. Five volunteers took part exclusively by e-mail, and four discussed the questionnaires in person. The four participants that took part in person discussed multiple drafts of the questionnaire up to and including the final draft. E-mail participants were contacted once at the end of September 2009, and again at the end of October 2009 with three respondents in the first instance and two respondents in the second. Participants were presented with the following instructions:

“If you could I would like you to tell me:

1. How long did it take you to complete each questionnaire?
2. Did the questions make sense to you?
3. Are they the sort of things you would expect to be asked, or be happy to answer in the situations described above?
4. Could you understand what each of the questions was asking you to do?
5. Could you understand how you should respond to each of the questions?
6. Did you find any of the questions to be too personal or inappropriate? Would you be uncomfortable answering any of them bearing in mind the questions may be seen by researchers and by medical staff?
7. Did you spot any mistakes? For example, typos, repeated words, incorrect punctuation, or poor grammar that may have escaped our eyes?

Finally, because we're looking for a range of people from different backgrounds and of different ages, if you are comfortable doing so it would be very useful for us to be able to

get this information from your parents or other older family members. But neither you nor they should not feel under any pressure to do this."

Face validity was to be further expanded upon in a full qualitative appraisal following preliminary assessment of the questionnaire in a genuine clinical sample in order to have any refined questionnaire based upon the experiences of participants that have actually completed the questionnaire in a real world setting (see chapter 5).

3.2.4 Content validity

Content validity was provided by a consultant hospital pharmacist with an interest in adherence, and a GP based in a surgery near York. They were invited to comment upon question appropriateness, response appropriateness, questionnaire length, potential utility of the scale, and comprehensiveness of the tools. This is a relatively superficial assessment of content validity, but as with face validity a more complete assessment was planned with clinical staff that had utilised the designed questionnaire in order to optimise clinical utility (see chapter 5).

3.2.5 Reading comprehension

The comprehension of questionnaire instructions and items was assessed during face and content validity testing. This was augmented by collecting Flesch-Kinkaid grade levels for each section on the questionnaire (Kripalani et al., 2009).

3.3 Results and discussion

3.3.1 Summary of questionnaire content

Content validity assessment suggested that clinical utility and could be improved if the questionnaire was split into two. One questionnaire would comprise indicators that change only slowly over time, while another would comprise indicators which may change more readily. The intention was that the former questionnaire would only need to be completed rarely; once every few years or when welcoming a new patient to a clinic. The second questionnaire would be used more routinely in patient follow up to assess how the patient is coping with their medicines in the current context of their life situation. This division would reduce the burden of questionnaire completion on healthcare professionals by ensuring that only information that genuinely required regular monitoring was regularly collected. An additional benefit would be that patients would be required to complete two shorter questionnaires rather than one long questionnaire which should improve acceptability to patients (Chipperfield and Steel, 2011). It was decided that the questionnaire which measures more static indicators of adherence would be called the Patient And Lifestyle Scale (PALS – Appendix E). The questionnaire which measures more transient indicators of adherence was called the Wellbeing And Medications Scale (WAMS - Appendix F).

3.3.2 Indicator selection

Indicators which met the inclusion criteria are detailed alongside indicator of the relevant items on the PALS and WAMS scales and the location of the discussion regarding the development of these items within this chapter in table 3.1.

Indicator	Chapter section	PALS item(s)*	WAMS item(s)
Sex#	3.3.3.1	1	NA
Employment	3.3.3.1	2	NA
Marital status	3.3.3.6	3	NA
Age	3.3.3.1	4	NA
Health literacy	3.3.3.2	5	NA
Beliefs about medicine	3.3.3.3	6-13	NA
Mental health	3.3.3.4	14	NA
Alcohol consumption	3.3.3.4	15	NA
Smoking habits	3.3.3.4	16	NA
Stress	3.3.3.5	NA	1-4
Depression	3.3.3.5	14	5-6
Anxiety	3.3.3.5	NA	7-9
Side effects of medication	3.3.3.6	NA	10-11
Positive beliefs about medicines	3.3.3.6	NA	12-14
Self-efficacy	3.3.3.6	NA	15-17
Social support	3.3.3.6	NA	17-20
Access to medications	3.3.3.6	NA	21
Relationship to provider	3.3.3.7	NA	22-30

* PALS questionnaire also includes items 6-13 which comprise the BMQ General Beliefs sub-scale. This scale was not selected because of a large evidence base in the meta-analysis but because the established strength of the BMQ scale. See section 3.4.5 below.
#Item not statistically associated with adherence, but included as a filler question to aid flow of questionnaire.

Table 3.1 Indicators included in the final questionnaires

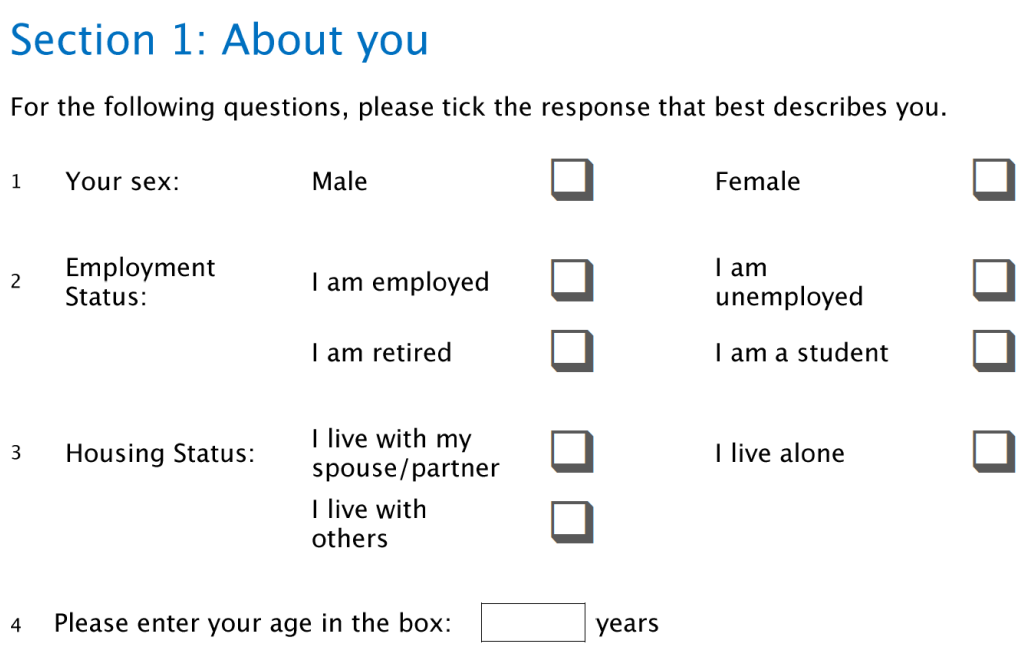
3.3.3 Question item identification and generation

3.3.3.1 Demographics

Few demographic indicators were associated with adherence to medications. The exceptions were age and current employment. Current employment can be assessed with a simple yes versus no question. However, a complication would be patients that do not easily fit this dichotomy such as those that are retired or students. Face validity testing highlighted that the option of being a student was not on initial drafts of the scale and so was added to the questionnaire. To satisfy the need for these response options with a lack of evidence surrounding them, patients who identify as being either retired or a student will not have their employment status contribute to a prediction of adherence. Age has been demonstrated to be associated to adherence; however it could not be

determined accurately how large this relationship is. Consequently age will not be used to predict adherence until a more precise estimate of this variable on the weighting of adherence prediction can be achieved. Age, as well as sex, will be assessed in the questionnaire but will act only as filler questions. This should aid the flow of the questionnaire as well as providing an expected and non-threatening introduction to the scale (Williams, 2003).

Early drafts of the questionnaire complied with the majority of the literature which argues for placing demographic information near the end of the questionnaire. However, after face validity testing it became clear that some participants were confused to find this information near the end of the questionnaire rather than at the beginning. Consequently the decision was made to split the demographic information into two sections. The less sensitive information such as the patient's age, sex, and occupational status was moved to the start of the questionnaire and the more sensitive questions regarding patient's mental health, smoking and drinking habits remained at the end of the questionnaire. It was deemed that these questions were sufficiently different to the basic demographic information to make their separation seem natural to participants. The demographic section of PALS is illustrated in figure 3.1.



Section 1: About you

For the following questions, please tick the response that best describes you.

1	Your sex:	Male	☐	Female	☐
2	Employment Status:	I am employed	☐	I am unemployed	☐
		I am retired	☐	I am a student	☐
3	Housing Status:	I live with my spouse/partner	☐	I live alone	☐
		I live with others	☐		

4 Please enter your age in the box: ☐ years

Figure 3.1 An illustration of the demographics section of the PALS questionnaire

3.3.3.2 Health Literacy

Health literacy is defined as "the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions" (Committee on Health Literacy, 2004). Health literacy is an important concept that has been associated with patient outcomes (Wallace, 2010). Pleasant and McKinney (2011) argue that most health literacy scales have not undergone rigorous psychometric testing and that new tools are urgently required. Nonetheless, existing health literacy tools were reviewed.

NHS Wales (Puntoni and Aylward, 2010) published a report which identified three measures assessing health literacy: the Rapid Assessment of Adult Literacy in Medicine (REALM-S, Davis et al., 1993), the Test of Functional Health Literacy in Adults (TOFHLA, Parker et al., 1995), and the Newest Vital Sign (NVS, Weiss et al., 2005). However, the NVS was deemed inappropriate for current needs because it asks patients questions about a nutrition label, and it was thought that this would lack face validity. The NVS is also not yet validated in the UK (Puntoni and Aylward, 2010). The REALM-S requires an interview and so is not appropriate to current needs, while the TOFHLA is too long for current use with over 40 questions. A new tool to screen health literacy with only three items has recently been developed (McNaughton et al., 2011). However, at present the exact contents of this tool are not in the public domain, and it is not yet validated as a self-report measure. Chew et al. found that single questions regarding health literacy can provide adequate screening (Chew et al., 2004, Morris et al., 2006). Consequently, their best performing question that was most relevant to the current population was adapted. "How often do you need to have someone help you when you read instructions, pamphlets or other written material from your doctor or pharmacy" (Morris et al., 2006) was adapted to "How often do you have someone help you to understand medical information?" with the additional clarification moved to the introduction of the health literacy section of the questionnaire. This section of the PALS is illustrated in figure 3.2.

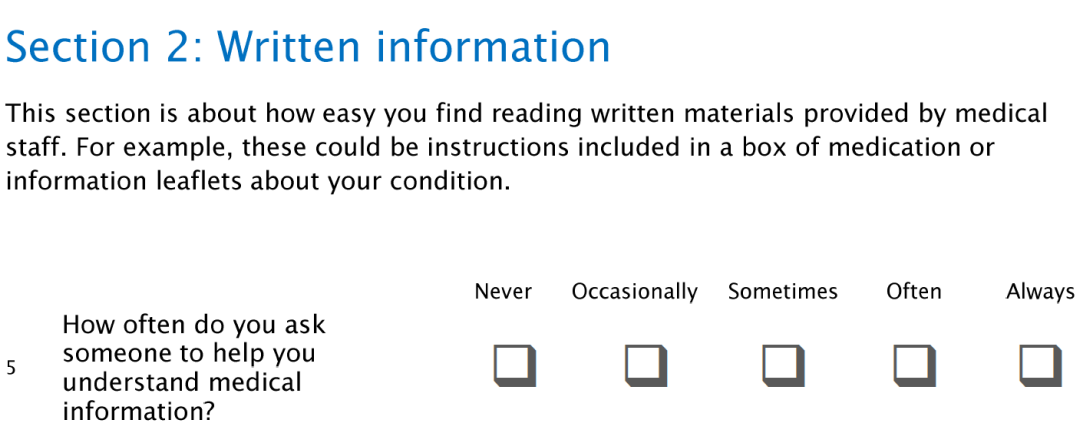
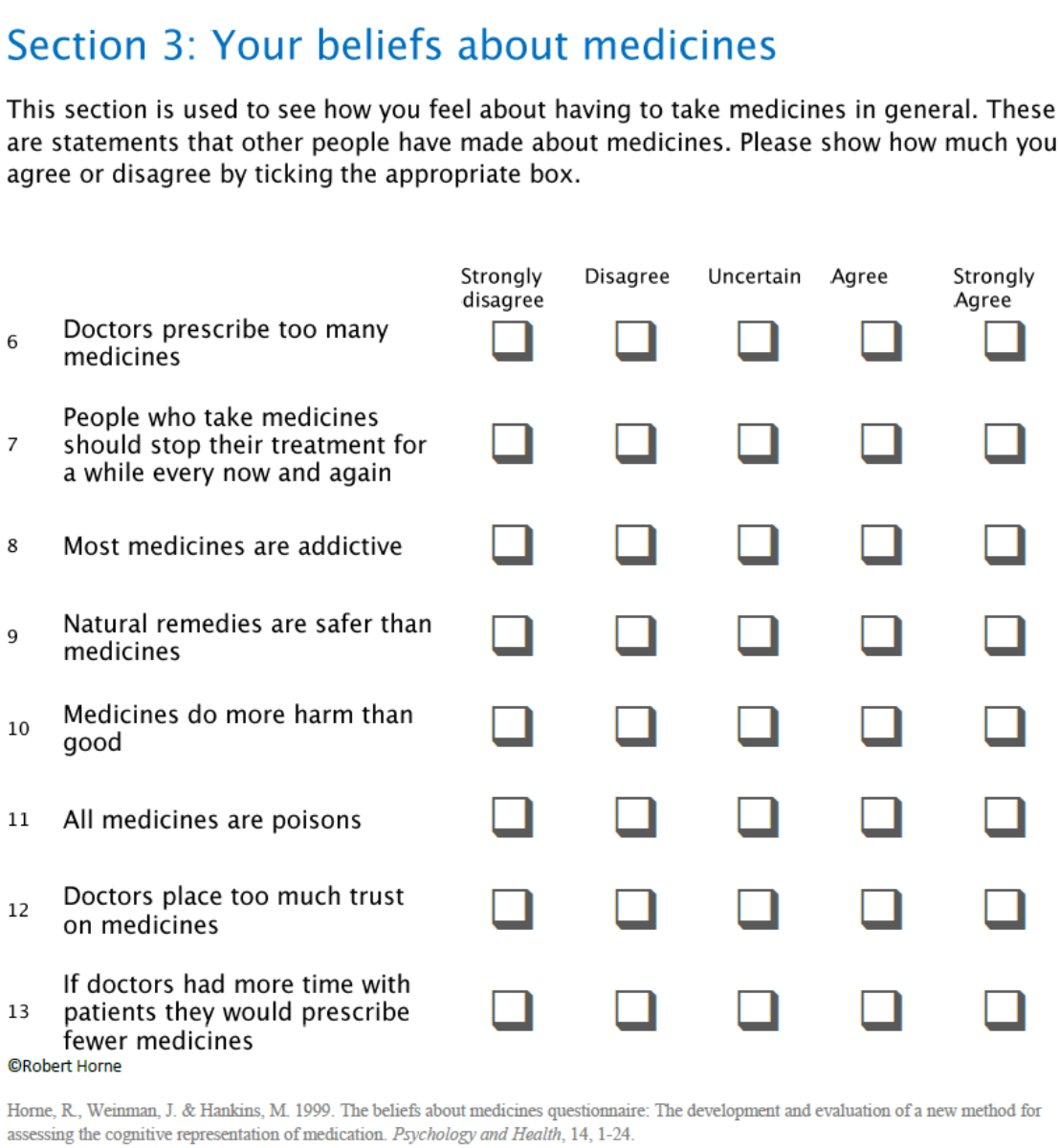


Figure 3.2 An illustration of the health literacy section of the PALS questionnaire

3.3.3.3 Patients beliefs about medicines in general

The BMQ general subscale, which examines patients' concerns about medicines as a category rather than considering a specific medicine a patient is taking, was incorporated. The meta-analyses did not identify enough studies to properly assess the utility of the subscale and so a subjective assessment of its importance to adherence prediction was made. The BMQ general has been associated with adherence and patient outcomes in a number of studies outside the current meta-analysis (Mårdby et al., 2007, Saks et al., 2012, Bermingham et al., 2011, Bautista and Jain, 2011, Horne et al., 1999). The questionnaire can also give practitioners and researchers valuable information about the type of nonadherence a patient is displaying because high scores on the questionnaire are associated with unintentional but not intentional nonadherence (Schüz et al., 2011). For this reason, it was judged that the evidence defending the use of the scale was adequate for it to be incorporated into the tool. The presentation of the BMQ general questionnaire is illustrated in figure 3.3.



Section 3: Your beliefs about medicines

This section is used to see how you feel about having to take medicines in general. These are statements that other people have made about medicines. Please show how much you agree or disagree by ticking the appropriate box.

		Strongly disagree	Disagree	Uncertain	Agree	Strongly Agree
6	Doctors prescribe too many medicines	☐	☐	☐	☐	☐
7	People who take medicines should stop their treatment for a while every now and again	☐	☐	☐	☐	☐
8	Most medicines are addictive	☐	☐	☐	☐	☐
9	Natural remedies are safer than medicines	☐	☐	☐	☐	☐
10	Medicines do more harm than good	☐	☐	☐	☐	☐
11	All medicines are poisons	☐	☐	☐	☐	☐
12	Doctors place too much trust on medicines	☐	☐	☐	☐	☐
13	If doctors had more time with patients they would prescribe fewer medicines	☐	☐	☐	☐	☐

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Horne, R., Weinman, J. & Hankins, M. 1999. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*, 14, 1-24.

Figure 3.3 An illustration of the presentation of the BMQ general questionnaire on the PALS questionnaire

3.3.3.4 Mental health and risky health behaviours

Questions addressing participants' mental health and engagement in risky health behaviours were considered sensitive and so were presented together at the end of the PALS questionnaire. The items developed are presented in figure 3.4.

3.3.3.4.1 Mental health

The evidence for the effects of mental illnesses other than depression on adherence was scant in the meta-analysis. Nonetheless the direction of the relationship between the two variables was clear. However, when identifying mental illness as an indicator of nonadherence it was decided to ask about depression and other mental illness separately to reflect the different levels of confidence associated with each. This will allow the relative contributions of each question to be assessed and prevent the less well known association between mental illness and nonadherence confounding the results of the question regarding depression. The sensitivity of these questions is acknowledged and so to limit the capacity for this item to reduce response rates participants will be offered the right to indicate that they prefer to not say whether or not they have had a diagnosis of a mental illness.

3.3.3.4.2 Risky health behaviours

Meta-analysis indicated that patients that engage in healthy lifestyle behaviours were also more likely to be adhering to their medication and vice versa. This phenomenon is known as the healthy adherer effect (Silverman and Gold, 2011). The factors shown by meta-analysis to be associated with lower medication adherence were taking illegal drugs, drinking alcohol, and smoking tobacco.

Questioning patients about illegal drug use poses unique challenges. Patients might be unwilling to discuss engaging in illegal activities. Confidentiality can also be hard to assure for such patients when any researcher or medical staff may be forced to reveal responses under a court order. There are some “dejeopardizing” techniques available to limit the impacts of these problems (Lee, 1993). However, these techniques all rely upon making it impossible to identify whether an individual’s response is genuine or else which individual provided the response. These techniques are appropriate where inferences are made at the level of the sample or population, but are useless for a questionnaire intended to inform clinical decision making for individual patients.

There are many questionnaires in existence to elicit information about patients’ smoking and drinking habits, and many are produced on an ad-hoc basis (e.g. Magid et al., 2009, Reed et al., 2007). Others use a combination of ad-hoc measures and validated tools (e.g.

Peters et al., 2011). Peters et al. developed their own measure for smoking and marijuana use, but used the Daily Drinking Questionnaire (DDQ, Collins et al., 1985) to gauge participants' drinking habits. However, the compositions of these questionnaires are similar. They attempt to assess the frequency of engagement in the activity, and the extent to which the behaviour is carried out when engaged in. Consequently the question about drinking was split into two separate questions. The first asked how often a patient drank alcohol; the second asked how much a patient drank when they drank alcohol. A similar approach was adopted for the smoking question. These items were based on the approach taken for a health survey for England conducted by the NHS (Craig and Hirani, 2010). However, face validity piloting indicated that this split made the question regarding smoking more difficult. Further, the medical professionals consulted during piloting indicated that the questions could be simplified for participants while offering useful information to the practitioners via a single question format. Considering the views of the face validity sample and the consulted medical practitioners it was decided to instead ask respondents to indicate how many comparable units of alcohol they have in a week, and how many cigarettes they smoke per day. They will also be given the option to indicate that they do not drink alcohol or smoke.

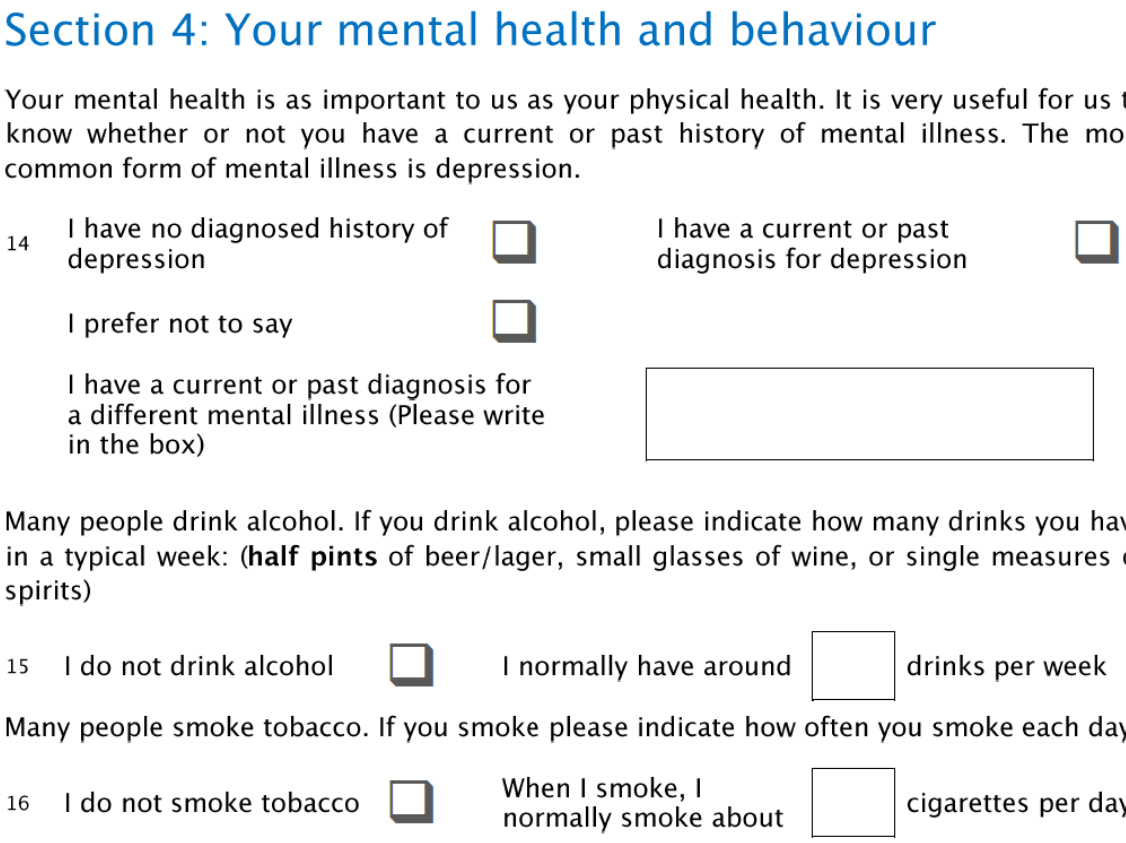


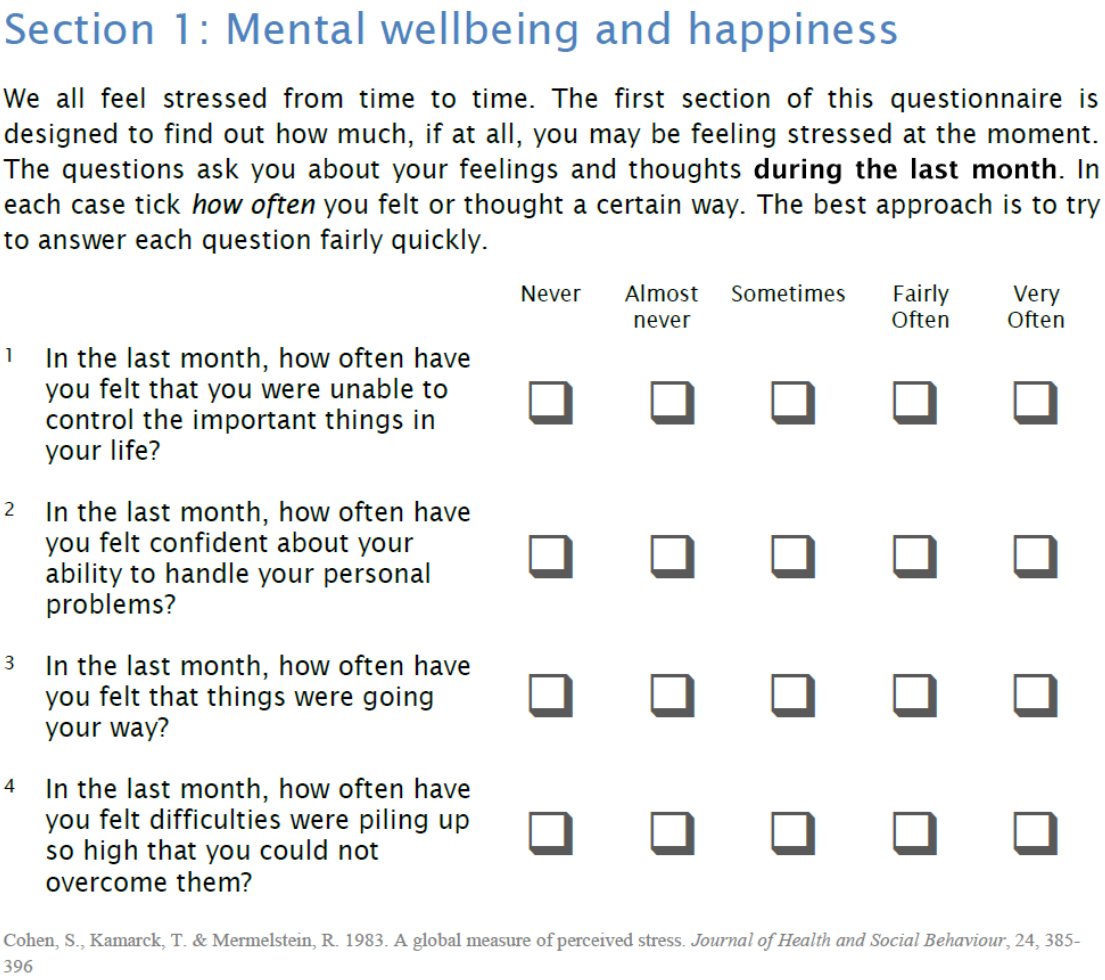
Figure 3.4 An illustration of the item addressing mental illness diagnoses on the PALS questionnaire

3.3.3.5 Mental wellbeing

3.3.3.5.1 Stress

There are a number of widely used measures of stress. The Holmes and Rahe Social Readjustment Rating Scale (1967) tallies the number of stressful life events experienced over the past 6 months. The greater the number of stressful life events, then the greater the likelihood the individual will become ill. This scale was rejected because with 43 separate items it was considered too burdensome for patients to complete. A widely used scale in the studies in the meta-analyses and elsewhere is the Perceived Stress Scale (PSS, Cohen et al., 1983). The scale comes in three versions with 14, 10 and 4 items. Although the four item version loses some internal consistency with Cohen's α dropping from 0.78 to 0.60 from the 10 to four item version (Johnston et al., 1995), the PSS retains validity by having much the same correlation with health related variables as the two larger scales

(Leung et al., 2010). Given the space constraints present the four item version of the PSS was deemed to be the most appropriate measure of stress available. The PSS-4 is shown as presented on the WAMS questionnaire in figure 3.5.



Section 1: Mental wellbeing and happiness

We all feel stressed from time to time. The first section of this questionnaire is designed to find out how much, if at all, you may be feeling stressed at the moment. The questions ask you about your feelings and thoughts **during the last month**. In each case tick ***how often*** you felt or thought a certain way. The best approach is to try to answer each question fairly quickly.

		Never	Almost never	Sometimes	Fairly Often	Very Often
1	In the last month, how often have you felt that you were unable to control the important things in your life?	☐	☐	☐	☐	☐
2	In the last month, how often have you felt confident about your ability to handle your personal problems?	☐	☐	☐	☐	☐
3	In the last month, how often have you felt that things were going your way?	☐	☐	☐	☐	☐
4	In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	☐	☐	☐	☐	☐

Cohen, S., Kamarck, T. & Mermelstein, R. 1983. A global measure of perceived stress. *Journal of Health and Social Behaviour*, 24, 385-396

Figure 3.5 An illustration of the PSS-4 as presented on the WAMS questionnaire

3.3.3.5.2 Anxiety and depression

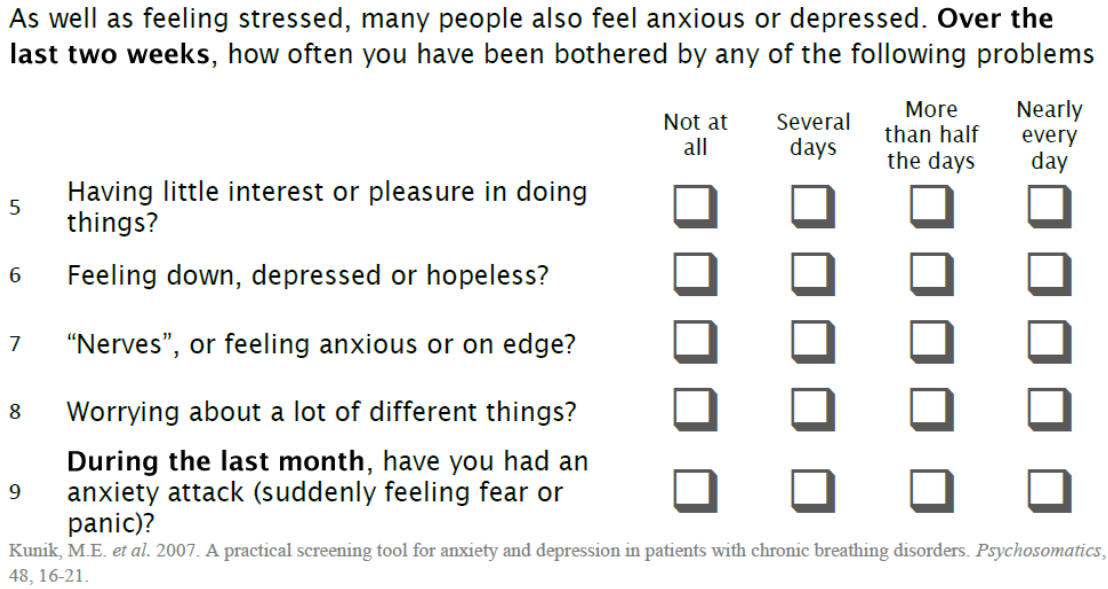
The Profile of Mood States (POMS) questionnaire which was used by some of the investigations found via the meta-analyses was rejected for being too long with 65 separate items in the full scale and 30 items in the short scale (McNair et al., 1989). For similar reasons, the Symptom Check List – 90 was rejected for taking up to 15 minutes to complete. Furthermore, neither scale was freely available for public use.

The three scales most often used in clinical practice are Beck's Depression Inventory (BDI, Beck et al., 1961), the Hospital Anxiety and Depression Scale (HADS, Zigmond and Snaith, 1983) and the Patient Health Questionnaire (PHQ, Spitzer et al., 1999). The BDI is a 21 item questionnaire, which has seen extensive usage and possesses a strong psychometric profile (Beck et al., 1988). However, Beck's scale examines both the physical and psychological symptoms of depression. This means that when administered to patients with a chronic illness the results of the BDI are confounded by symptoms of illness being falsely ascribed to depression (Moore et al., 1998). There is a 4 item version of the BDI developed for use in primary care which seeks to avoid the potential confound with physical symptoms of other diseases (Steer et al., 1999), however, like all versions of the BDI it is not available for public use.

The HADS scale is a 14 item instrument with a large body of research to support its validity (Bjelland et al., 2002). It was also developed with use in chronically ill patients in mind and so avoids the issue of confounding physical symptoms of illness with physical symptoms of depression (Herrmann, 1997). However, it is not available for public use.

The PHQ is available for public use, and was developed for use in primary care and so avoids confounding physical and depressive symptoms (Kroenke et al., 2001). A further advantage of the PHQ over the HADS lies in its shorter format, taking only three minutes to complete versus HADS five minutes. Furthermore, a short 5 item version of the PHQ is available to further reduce patient burden (Kunik et al., 2007). This version is composed of a two item depression screen (Whooley et al., 1997), and three item anxiety screen. The demonstrated clinical usefulness, shortness of the scale, and freedom of usage made the PHQ the most appropriate validated tool to incorporate into the new questionnaire. However, the 5 item scale was modified slightly. To return the PHQ-5 to a format more akin to the PHQ-9 and to detect more current feelings of depression and anxiety the time frame patients are asked to consider when indicating how they feel has been returned to two weeks rather than a month. Furthermore to attempt to detect a greater range of anxiety levels besides that indicating pathology, the response set has been modified from a dichotomous 'yes/no' response to the four point scale of the PHQ-9 which concerns how often particular emotional states have been expressed from 'not at all' to 'nearly

every day'. The PHQ-5 as adapted is utilised as the second part of section 1 on the WAMS scale and is presented in figure 3.6.



As well as feeling stressed, many people also feel anxious or depressed. **Over the last two weeks**, how often you have been bothered by any of the following problems

		Not at all	Several days	More than half the days	Nearly every day
5	Having little interest or pleasure in doing things?	☐	☐	☐	☐
6	Feeling down, depressed or hopeless?	☐	☐	☐	☐
7	"Nerves", or feeling anxious or on edge?	☐	☐	☐	☐
8	Worrying about a lot of different things?	☐	☐	☐	☐
9	**During the last month**, have you had an anxiety attack (suddenly feeling fear or panic)?	☐	☐	☐	☐

Kunik, M.E. *et al.* 2007. A practical screening tool for anxiety and depression in patients with chronic breathing disorders. *Psychosomatics*, 48, 16-21.

Figure 3.6 An illustration of the PHQ-5 as presented on the WAMS questionnaire

3.3.3.6 Patient adjustment to medications

A number of indicators identified via meta-analysis as being associated with adherence were related to patients' ability to integrate their medicines into their lives. These variables were patients' experiences of side effects and positive beliefs about medicines, self-efficacy for medicines, social support, and the ease with which patients could access their medications. The development of these items is discussed below and the section on WAMS comprised of these constructs is presented in figure 3.7.

3.3.3.6.1 Patient beliefs about and experiences with medicines

In line with the work of Horne et al. (1999) it was found that important indicators of medication adherence were patients beliefs in the importance of their medicines for health maintenance and a positive experience of their medication versus the negative impacts of their medicines such as the experience of side-effects. The Beliefs about Medicines Questionnaire (BMQ) is one scale which assesses patient's beliefs about their

medicines specifically and their beliefs about medicines as a category generally (Horne and Weinman, 1999, Horne et al., 1999). However, the evidence found via meta-analysis was only able to identify positive beliefs and experiences with medicines as being an indicator of adherence behaviour. Evidence regarding more long term and abstract concerns patients have about their medicines was not as strong as that found by Horne et al. (1999). The evidence was much stronger for the importance of side-effects (Watson et al., 2012). Given that the BMQ specific concerns subscale has only one question about side-effects it did not seem appropriate to use this scale. The decision to not use the BMQ concerns scale precluded the possibility of using the necessity subscale as the author of the scale stipulates that the two must be used in combination. Unique questions were consequently developed to assess how necessary and important patients felt their medicines were for maintaining their quality of life both now and in the future. In line with the results of the meta-analyses the questions concerning patients concerns about their medicines focussed upon the somatic experience of side effects and the extent to which medications negatively impacted upon their quality of life. Conversely, the questions regarding the necessity of medicines also focussed upon the extent to which medicines had improved or protected patients' daily living standards.

3.3.3.6.2 Self-efficacy

Self-efficacy refers to an individual's beliefs about their ability to perform successfully and can be conceptualised as a person's perceived ability to cope with challenges in general or with regard to specific tasks (Bandura, 1994). As well as the more direct links between self-efficacy and adherence demonstrated by the current meta-analyses, there are also links between self-efficacy and health behaviours which may themselves be related to adherence such as smoking, eating well, or participating in health screening programs (Schwarzer and Fuchs, 1995). Furthermore, self-efficacy has links to both mental wellbeing and successful social relationships (Bandura, 1994). It is a fundamental variable in many of the socio-cognitive models that have been employed to explain adherence behaviour including the Transtheoretical Model (Prochaska et al., 1992), the Theory of Planned Behaviour as 'perceived behavioural control' (Ajzen, 2002), and the Health Belief Model as 'barriers to taking action' (Rosenstock, 1966). It is important patients believe they can successfully complete or maintain their treatment if they are to become

motivated to engage with their therapy. This belief in their ability to succeed must itself be maintained for the continued successful implementation of treatment. Consequently, self-efficacy could be a key underlying construct for the initiation and maintenance of adherence.

There are a number of self-efficacy scales available, some specific to adherence behaviour. However, some of these scales suffer from being specific to one condition or overlong, such as the 35 item Self-Efficacy for Diabetes Scale (Grossman et al., 1987). The 13 item revised Medication Adherence Self-Efficacy Scale' (MASES, Fernandez et al., 2008) has only been validated in hypertensive patients, and so was not considered broad enough in scope for inclusion. The best candidate for inclusion was the Medication Understanding and use Self-Efficacy Scale (MUSE, Cameron et al., 2010). This is a revised version of the Communication and Attitudinal Self-Efficacy Scale (CASE, Wolf et al., 2005). The advantages held by the revised scale were a reduced item pool of 8 questions, and greater generalisability. The CASE instrument was cancer specific while MUSE was developed with primary care chronic illness patients. However, there are two primary difficulties with incorporating any existing self-efficacy measure into the current tool. The first is that self-efficacy is highly variable between particular tasks. The same person may feel they have no difficulty remembering to take their medicines or organising their medicines around their day, but feel as though they would find it very difficult to cope with the side effects of treatment. The consequence of this is that measures of self-efficacy must cover a wide range of possible behaviours. However, when a scale is designed to assess a wide number of indicators of non-adherence, self-efficacy will be a covariate in a great number of these indicators. Consequently, this will produce a number of repeated or redundant items and introduce issues of dependency between items which will also impact upon discriminant validity. One option to circumvent this problem was to incorporate a general self-efficacy scale such as the "Generalized Self-efficacy Scale" (Schwarzer and Jerusalem, 1995). However, this would require additional items evaluating the self-efficacy of specific behaviours which are not covered in the scale (Schwarzer and Jerusalem, 1995). Therefore, it was decided to instead develop questions that directly measure self-efficacy where there were not significant overlaps with other indicators that are included in the questionnaire. In particular with patient's ability to remember to take their medicine and to cope with the number of medicines they must take.

3.3.3.6.3 Social support

There are three key aspects to social support, each of which may have distinct and separate relationships to distress alleviation (Barrera, 1986). The first is an individual's social integration which refers to number and density of the interconnectedness between an individual's relationships (Barrera, 1986). The second is perceived social support which refers to an individual's interpretation of the availability and adequacy of their support network. The final construct is enacted support which refers to the actual behaviours of the support network when called upon. The three types of social support are all independently correlated with physical and mental health, but are not necessarily well correlated with each other. They may also have distinct causal relationships to health and behaviours including adherence (Bloom, 1990). Although it is recommended that the ideal social support questionnaire should measure all of these facets (Stansfeld and Marmot, 1992), most existing measures address only one of the three constructs. Furthermore, these scales tend to be appropriate only to a specific population, and generally comprise too many items to be feasible for use in the current tool (Cohen et al., 2000). More general measures of social support also tend to be overly long for present purposes. For example, the Short Form Social Support Questionnaire (SSQ6, Sarason et al., 1987) comprises only six questions. However, each question requires the participant to recall all the people in their life that can provide a certain type of support, and then rate how satisfied they are with this help. Similarly, the Significant Others Scale (SOS, Power et al., 1988) requires participants to rate the frequency of two types of emotional and two types of practical support for their seven closest relationships. Both of these scales would require a significant cognitive burden and ten minutes or more to complete. This would not be appropriate within a multi scale questionnaire. Similarly the social support scale developed for the Medical Outcomes Survey had 19 items making it too long for the current questionnaires (Sherbourne and Stewart, 1991). The 23 item Social Support for Transactions scale (Suurmeijer et al., 1995) was also excluded for being too long, despite being shown to have validity across a number of European nations.

It was decided that new items would need to be developed to assess social support. The aim was to create a scale covering the major facets of social support whilst remaining brief by drawing inspiration from existing scales. In particular the Short Scale of Social

Support (SSS, Funch et al., 1986). This scale has 17 items in total but it has shorter sections which individually measure family attitudes and behaviours. It was decided to remove the specific role of the family in giving support, and to adapt items such as "My family will listen to me if I want to discuss my weight problem/pain/illness" to be more general in terms of where the support comes from. This helps to make the new items more applicable to a wider range of patients and illnesses.

Four items were developed. The item "I am concerned about how others will react if I tell them what medicines I take" assesses whether or not a patients significant others are supportive of the patients particular medicine requirements. The item "I have people I can talk to about my illness" assesses the availability of support, while "I can count on my family and friends to help me deal with my illness" assesses the perceived efficacy of that support. It is difficult to assess enacted support directly in a self-report measure, since any assertion of help can only be that which is noticed and available to the memory of the participant (Barrera, 1986). Consequently, the item "There are people who will help me with my medicines if needed" was developed to assess any practical support that patients perceive is available to them. This only demands the participant be able to recall that people have in the past been generally available to offer help when required.

The simplest measure of social support identified was whether or not the patient was married or in a significant relationship. After face validity testing, it was suggested that the question be further split into those that live with their partner, those that live alone, and those that live with others to account for a wider variety of housing statuses.

3.3.3.6.4 Access to medications

One of the most significant barriers patients may face is being able to get their medicine supply, either because of cost or obstacles to accessing their supplier (Wamala et al., 2007). Initial drafts of the questionnaire focussed upon the cost of medicine because this was suggested to be a stronger indicator of adherence based upon a greater number of studies in the meta-analyses. However, the importance of cost is liable to fluctuate heavily between both individuals and healthcare systems. Upon consultation with medical staff to discuss content validity of the questionnaire, it was felt that in some contexts it might be expected that no patients would have to pay for their medicines and

that any question about costs may prove either confusing or else not provide much information. Consequently it was decided to produce a question which focussed upon patient's access to their medication, and how difficult it was for them to acquire a new supply of their medicine when needed. The question developed was "I find it hard or inconvenient to get my supply of medicine".

Section 2: Adjusting to your medicines

Thinking about your medicine and your condition, please show how much you agree or disagree with each statement by ticking the appropriate box.

		Strongly disagree	Disagree	Uncertain	Agree	Strongly Agree
10	I think my medicines are giving me side effects	☐	☐	☐	☐	☐
11	If my medicines are making me feel worse than my illness, I think it makes sense to stop taking it for a while	☐	☐	☐	☐	☐
12	I think my medicines make me feel better than I would without them	☐	☐	☐	☐	☐
13	I think my illness would be worse without my medicines	☐	☐	☐	☐	☐
14	I think my medicines help to keep me feeling as healthy as possible	☐	☐	☐	☐	☐
15	I find it hard to remember to take all of my medicines each day	☐	☐	☐	☐	☐
16	I think I can cope with the number of medicines I am prescribed at the moment	☐	☐	☐	☐	☐
17	I am concerned about how others will react if I tell them what medicines I take	☐	☐	☐	☐	☐
18	There are people who will help me with my medicines if needed	☐	☐	☐	☐	☐
19	I have people I can talk to about my illness	☐	☐	☐	☐	☐
20	I can count on my family and friends to help me deal with my illness	☐	☐	☐	☐	☐
21	I find it hard or inconvenient to get my supply of medicine	☐	☐	☐	☐	☐

Figure 3.7 An illustration of the items addressing patient adjustment to medicines as presented on the WAMS questionnaire

3.3.3.7 Provider relationships

The current model for chronic condition management is to facilitate patient self-care with guidance from the patient's family doctor, who acts to also facilitate any movement between primary and secondary care (Black et al., 2004). Consequently, it was decided that the patient-GP relationship would prove most useful for the prediction of adherence.

A review exists of questionnaires which are designed to be completed by patients to evaluate their experiences with their physicians (Evans et al., 2007). However, while this study identified six potential questionnaires each was deemed too long for inclusion in the current questionnaires, with the shortest scale having 18 items. Also excluded for being too long were the 55 item Patient Satisfaction Questionnaire (Ware Jr et al., 1983, Hagedoorn et al., 2003), and the 18 item short form of the Patient Satisfaction Questionnaire developed by RAND Health (Marshall et al., 1994). Also rejected was the Medical Interview Satisfaction Scale which has 21 items and is focussed heavily on single interactions (Meakin and Weinman, 2002). The Patient Involvement in Discussions (PID, Makoul et al., 1995) has only four items but was deemed to focus too heavily on the level of concordance in patient-physician interactions rather than on the relationship between the two parties. Furthermore, despite being heavily cited, this has yet to be formally validated against another measure of patient-doctor communication. A number of other tools also focus heavily on patient satisfaction with single interactions, rather than assessing the patient's relationship with their physician. Examples include the consultation satisfaction questionnaire (Poulton, 1996), and the 11 item Patient Satisfaction Scale recommended by the Royal College of General Practitioners during GP training (Royal College of General Practitioners).

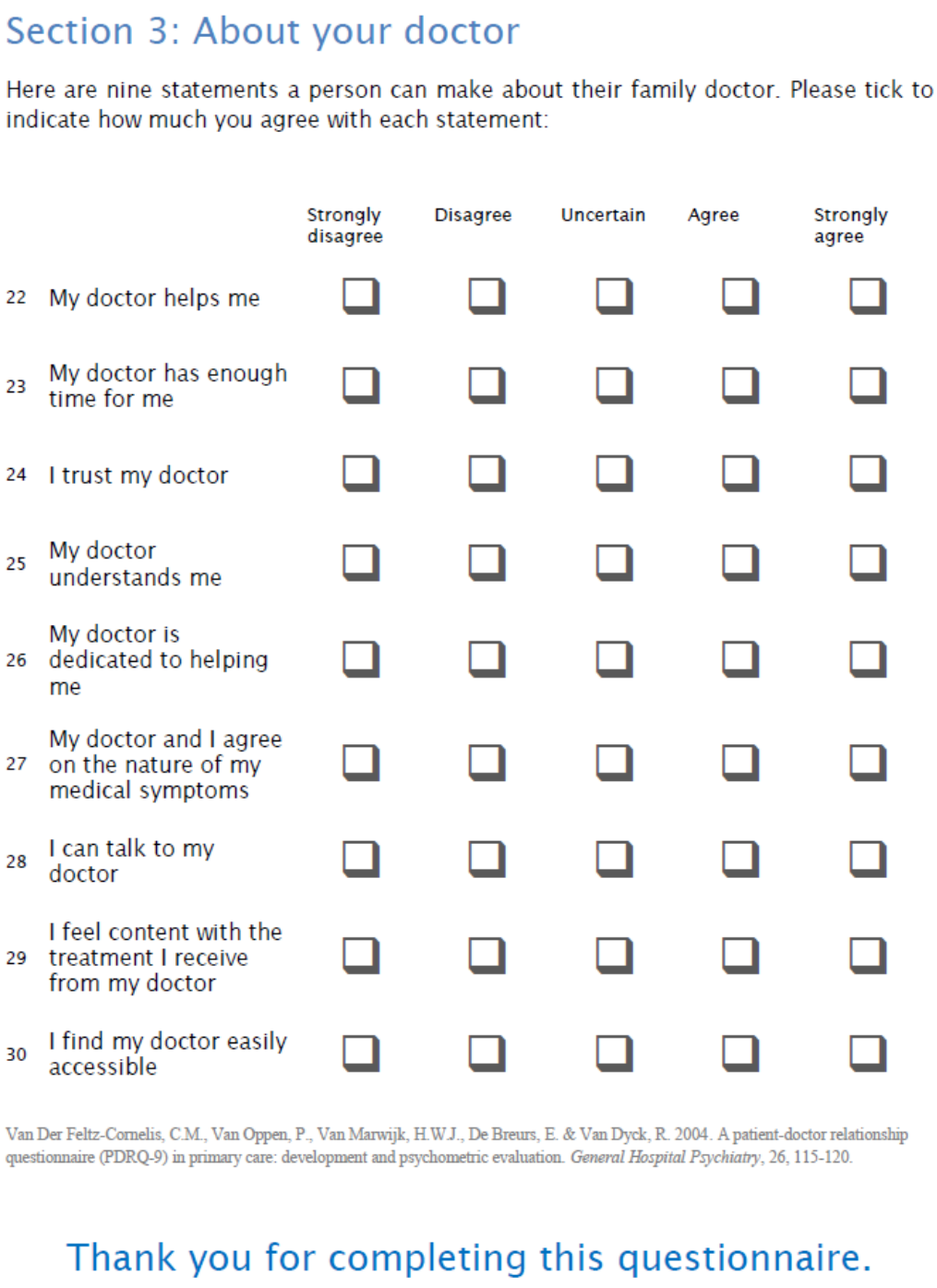
A more viable alternative was the Wake Forest Physician Trust Scale (Hall et al., 2002). This scale focusses on the level of trust in the physician-patient relationship which was shown to be the strongest indicator within the realm of the provider relationship in the meta-analyses of chapter 2. Initial drafts of the questionnaire included this scale after contact with the authors revealed a short four item version of the scale (Dugan et al., 2005). However, testing for face validity and acceptability of the questionnaire indicated that some felt uncomfortable completing the questions on the scale. Consequently, an alternative scale was selected which had greater acceptability. This was the Patient-Doctor Relationship Questionnaire (PDRQ-9, Van der Feltz-Cornelis et al., 2004). This

questionnaire is more comprehensive than the Wake Forest scale and has good internal consistency with a Cronbach's alpha of 0.94. However, there were concerns over the ambiguity of some of the items and the response scale. Consequently some adaptations were made. The original scale has a five-point response of statements being 'not at all appropriate', 'somewhat appropriate', 'appropriate', 'mostly appropriate' or 'totally appropriate'. It was felt that it was unclear whether something that was 'mostly appropriate' was more appropriate than something described only as 'appropriate'. It was considered that couching the response in terms of level of agreement with the statements made the response more straightforward for participants. One of the questions on this scale was also modified. The original item 'I feel content with my primary care provider's treatment' was considered to be ambiguous. Consequently it was modified to 'I feel content with the treatment I receive from my doctor'. This also highlights a final change made to this scale. To aid clarity and to keep the focus on the patient's GP's, the use of the phrase 'primary care provider' was replaced with the word 'doctor'. The adapted PDRQ-9 is shown as presented on the WAMS in figure 3.8.

3.3.4 Questionnaire design and layout

Content validity testing indicated a preference on behalf of the medical staff using the PALS or WAMS for the questions to be worded such that high scores would always be associated with worse adherence for both individual items and subscales. I.e. all questions should be either positively or negatively worded. It was felt that this would make the scales very easy to interpret in a busy clinical environment. However, face validity testing with this question style in place indicated that only having negatively worded items made some of the questions hard to interpret. Furthermore, it is claimed that mixing both positively and negatively worded questions in a scale minimises the risk of participants responding the same way to each of the questions (Rattray and Jones, 2007). Altering the wording and scoring of existing scales would also negate their current validity. Furthermore, it was felt that it was more important to have a questionnaire that was easy to complete for participants than it was to have one that was easy to score (Murray, 1999). A further concession to this preference was to use a tick-box approach over asking participants to circle numbers. It has been found that asking participants to circle numbers can affect their perception of the scale (Tourangeau et al., 2004) even if

this format makes data entry simpler (McColl et al., 2001). Questions were numbered because this has been shown to help guide participants more easily through the questionnaire (Murray, 1999).



Section 3: About your doctor

Here are nine statements a person can make about their family doctor. Please tick to indicate how much you agree with each statement:

		Strongly disagree	Disagree	Uncertain	Agree	Strongly agree
22	My doctor helps me	☐	☐	☐	☐	☐
23	My doctor has enough time for me	☐	☐	☐	☐	☐
24	I trust my doctor	☐	☐	☐	☐	☐
25	My doctor understands me	☐	☐	☐	☐	☐
26	My doctor is dedicated to helping me	☐	☐	☐	☐	☐
27	My doctor and I agree on the nature of my medical symptoms	☐	☐	☐	☐	☐
28	I can talk to my doctor	☐	☐	☐	☐	☐
29	I feel content with the treatment I receive from my doctor	☐	☐	☐	☐	☐
30	I find my doctor easily accessible	☐	☐	☐	☐	☐

Van Der Feltz-Cornelis, C.M., Van Oppen, P., Van Marwijk, H.W.J., De Breurs, E. & Van Dyck, R. 2004. A patient-doctor relationship questionnaire (PDRQ-9) in primary care: development and psychometric evaluation. *General Hospital Psychiatry*, 26, 115-120.

Thank you for completing this questionnaire.

Figure 3.8 An illustration of the PDRQ-9 as presented on the WAMS questionnaire

After piloting for face validity no significant issues were found with the design of the questionnaire. However, some found the original tick boxes used to be imposing. To counteract this, the ink colour was changed from black to a lighter grey and this softened the appearance of the boxes adequately. The questionnaires also feature a cover page which details the basic instructions and length of the questionnaire. The cover page incorporates the University of East Anglia logo and leaves space to include any collaborating organisation's logo (e.g. the NHS). The colour scheme was based around the blue of the UEA logo to maintain consistency and to develop a use of colour that would be presentable in greyscale. Evidence for serif fonts being more difficult for readers with dyslexia is not strong, however, in the absence of evidence to the contrary a sans serif typeface was utilised. A 12 point size typeface with a large x height was employed to ensure legibility (Edwards, 2010, Bix et al., 2003). It was also ensured that space remained to thank participants for their time (Stone, 1993, Sudman and Bradburn, 1982, Meadows, 2003, Murray, 1999). The front cover of the PALS as utilised in the project described in chapter 4 is shown in figure 3.9 to illustrate how the questionnaire can be adapted to particular needs. This version of the front cover incorporates the NHS logo, a section for participant reference numbers to be recorded, and a description of a self-report of adherence added to the PALS used for validation purposes.

3.3.5 Reading comprehension

The Flesch-Kincaid reading score for all sections of both PALS and WAMS is presented in table 3.2. While some sections are above the target level of grade 8, face and content validity testing revealed no problems with comprehension of the questions or instructions. The high scores may also be an artefact of the topic at hand and the requirement to use polysyllabic words such as "medication".

3.3.6 Questionnaire scoring

The full scoring guide for both the PALS and WAMS is provided as Appendix G. Many of the principles underlying the scoring strategy are based on the Quality of Life in Epilepsy

scoring manual (Vickrey et al., 1993), which also requires the combination of multiple sections of a questionnaire into a single summary score.

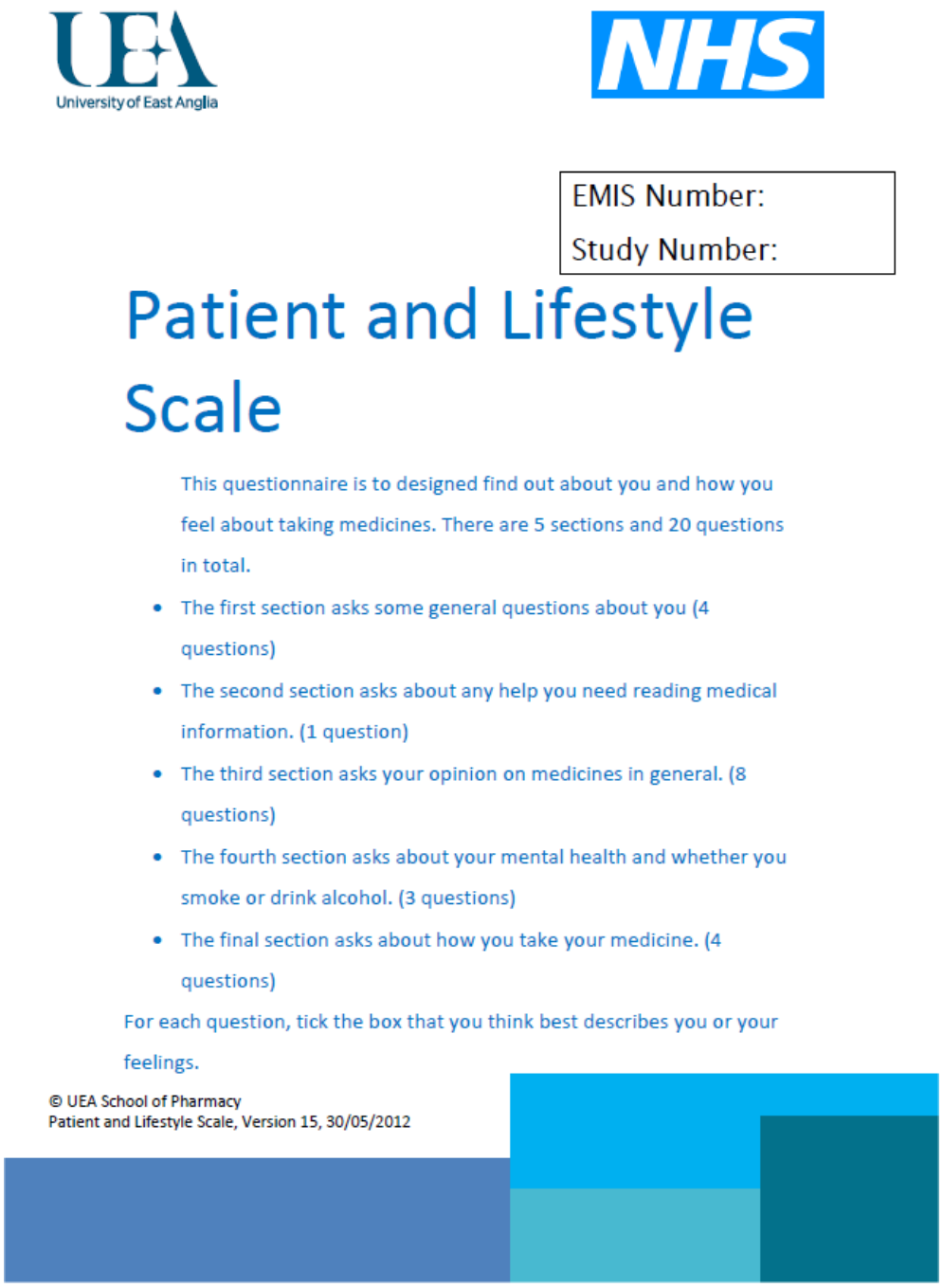


Figure 3.9 Front cover of the PALS questionnaire as utilised in the project described in chapter 4.

Questionnaire	Section	Flesch-Kincaid Score
PALS	Introduction	7.0
	1. Demographics	5.8
	2. Health Literacy	12.0
	3. BMQ General subscale	7.6
	4. Mental health and health behaviours	6.4
	Full scale	9.4
WAMS	Introduction	7.3
	1. Mental wellbeing	6.2
	2. PAMS	12.8
	3. PDRQ-9	7.7
	Full Scale	10.3

Table 3.2 Flesch-Kincaid reading grade for questionnaire sections

How the questionnaires would be scored was guided by what the medical practitioners consulted stated they would like to derive from the questionnaires. The practitioners stated that they wanted a tool that made decision making easy. They wanted to know which patients were at risk of nonadherence. Having identified which patients were at risk they wanted to know why those patients were at risk. The simplest way to achieve this aim is to produce a summary score at the end of the questionnaire which would indicate which patients were likely to be at risk of nonadherence. Providing a summary score for each subscale in the questionnaire allows for a similarly simple estimate to be made for the relative position of each participant for each indicator of adherence. To further ease the clarity of the decision-making process, it was decided to convert all raw scores on the scale into a percentage. It was felt that using a percentage value would make it easier for those using the scales to conceptualise scores. Although this aids understanding, it should be noted that the use of the percentage mark is purely arbitrary.

In addition to user-friendliness, a second factor determining how the scales would be scored was the limitations of the meta-analytic procedures that were employed in designing the tools. The meta-analyses described in chapter 2 helped determine which

indicators of adherence were important. However, they were not very successful in terms of providing accurate point estimates for the true relationship between individual indicators and adherence. Consequently, any attempt to weight individual items of subscale impact upon the results would be highly dubious. Instead, it will be assumed that all indicators have an equal impact upon adherence. Once data from a sufficiently large sample have been collected using the final questionnaire, regression analyses could be employed to weight the subscales according to their beta-weights.

In order to give items equal weight, scores were based on the number of possible responses. A 5 point Likert scale was divided into scores of 0, 25, 50, 75, and 100 to represent the available points. A four point scale was allocated values of 0, 33, 67, and 100, while dichotomous variables take values of 0 and 100. Two questions where the format did not quite fit this operation were the items concerning drinking and smoking where participants fill in an empty box and do not select from a range of alternatives. Here the scaling is revealed only to the individual responsible for data entry. To inform the cut points to be used the current advice from the NHS was employed. The NHS choices website (NHS, 2011) stated at the time of development that the upper limit of alcohol intake for a man should be 4 units no more than 5 times a week. This would give a maximum of 20 units per week. This was used as the upper limit and above this the maximum a score of 100% would be given. A total of 6 categories were used for this scale. Not drinking was scored as 0, 1-5 drinks was scored as 20%, 6-10 drinks was scored as 40%, 11-15 drinks as 60%, 16-20 drinks as 80%, and 21+ drinks as 100%. A similar approach was used for smoking. The NHS does not offer guidelines on an upper limit of acceptable smoking, however, there is a dichotomy made between light and heavy smokers. Heavy smokers are defined as those that smoke more than 20 cigarettes a day (NHS Clinical Knowledge Summaries, 2011). Smoking was split at the same cut points as alcohol to make data processing simpler. I.e. Not smoking was scored as 0, 1-5 cigarettes was scored as 20%, 6-10 cigarettes was scored as 40%, 11-15 cigarettes as 60%, 16-20 cigarettes as 80%, and 21+ cigarettes as 100%.

To prevent subscales with more items having a higher weighting on outcome each subscale has the sum of the scores on the scale divided by the number of responses on that scale while omitting any items that are left blank or as ‘prefer not to say’. I.e. if all items on the PSS-4 are completed the sum of the scores for the four items would be

divided by four, and by three if a participant had omitted one item. This ensures that each scale is given equal weighting in the questionnaire by taking an average score across the answered questions.

To calculate summary scores for the PALS, WAMS and total scores on both scales the scores for each subscales should be summed, and then divided by the number of subscales completed either on the WAMS, PALS, or both together. This will give a final score out of 100 to allow for the comparison of individuals on either the two tools separately or in combination by taking an average score across subscales.

3.3.7 Conclusion

This chapter has detailed the efforts taken to ensure the questionnaire developed has the greatest chance of identifying patients as being at risk of nonadherence to their medicines. It has shown how the results of the meta-analyses in chapter 2 were utilised to identify the constructs that were required in the final questionnaire. It has indicated how these constructs had been measured using short pre-validated scales where possible. Where this was not possible new scales were developed which aimed to balance accuracy of measurement with patient acceptability and the brevity required by healthcare practitioners. This process resulted in preparation of two separate questionnaires. One questionnaire which measures slow changing and static indicators of adherence (PALS), and one which measure more changeable indicators of adherence (WAMS). Chapter 4 details the quantitative assessment of these new tools based upon a sample of patients with hypertension.

Chapter 4 – Piloting with preliminary psychometric evaluation of the PALS and WAMS questionnaires

4.1 Introduction

Chapter 3 charted the development of two new questionnaires to predict adherence to medication. The Patient And Lifestyle Scale (PALS) which measures stable risk factors for nonadherence, and the Wellbeing And Medications Scale (WAMS) which measures risk factors that may change over a short time. The questionnaires were pre-tested on lay members of the public and shown to medical professionals to ensure face and content validity in chapter 3. This chapter is a feasibility study to appraise the proposed methods for assessing the psychometric properties of the PALS and WAMS whilst performing a preliminary assessment of those psychometric properties.

4.1.1 The importance of piloting questionnaires

Piloting of new questionnaires ensures that flaws in research and questionnaire design are identified before a large number of people complete the questionnaire (de Vaus, 1995). This is particularly important for questionnaires designed for clinical populations to prevent wasting practitioner and patient time.

Pilot studies are defined as a small version of a final study which seeks to ensure all aspects of the study work in harmony with one another. In contrast a feasibility study is performed to assess whether or not a study design is fit for purpose, and to estimate parameters needed to design the main study. These include measures of central tendency and spread for measures or outcomes, attrition rates, response rates, and the number of eligible participants (Arain et al., 2010, NETSCC, 2013, Thabane et al., 2010). Because the PALS and WAMS are in an early stage of development with no quantitative information about their acceptability, utility, or accuracy it was determined that it would be most useful to characterise the current investigation as a feasibility study.

4.1.2 Statistical inference in feasibility studies

The small sample sizes generally associated with feasibility studies result in p-values unlikely to be significant except where effect sizes are very large (Cohen, 1992). Estimates of effect size can be inaccurate in small samples due to sampling error and extreme effects are also more common (Field, 2009). However, preliminary estimates of the relative effect sizes of the items, subsections, PALS scores, WAMS scores, and outcomes can be made (Bender and Lange, 2001). de Vaus (1995) identifies further analyses that can be performed during a feasibility study on a small number of participants:

1. Variation – If all respondents give the same answer the item will not add useful information.
2. Meaning – Are there any indications that the respondents have misunderstood any questions, and can all responses be interpreted by the researcher?
3. Scalability – Do all items on a scale contribute to scores on that scale? Items on the same scale should correlate with each other. If they do not then they can be said to not properly form part of the same scale.
4. Non-response – If a number of participants skip an item this can be an indication that items are not acceptable for some reason.

4.1.3 Objectives

The objectives of the current study are informed by those presented by van Teijlingen and Hundly (2001) for feasibility studies. The objectives are to:

• Estimate the participant identification and consent rate

• Assess the acceptability of PALS and WAMS to participants

• Assess the feasibility of clinical data acquisition

• Estimate variability in outcomes to help determine the sample size for a definitive study

• Provide an early indication of the psychometric properties of PALS and WAMS

• Assess the proposed data analysis techniques

4.2 Methods

4.2.1 Setting

Collection of data from patient participant medical records took place at Elvington Medical Practice which has been certified as a research ready practice by the Royal College of General Practitioners. This is a rural dispensing GP practice near York in a moderately affluent area. The surgery has a list size of approximately 7000 individuals (NHS Information Centre, 2011).

4.2.2 Sample selection

Patients with a diagnosis of hypertension were selected because testing in multiple populations would increase the number of variables exogenous to the questionnaire that could impact upon outcomes. Hypertension was selected as the condition of choice because it is monitored by GP surgeries for the Quality and Outcomes Framework (QOF) which means GP surgeries should have comparatively complete and accurate patient records (National Institute for Clinical Excellence, 2012), and it is a very common condition so should offer a reasonable sample size for pilot testing (Chockalingam et al., 2006). A final rationale for this choice was that the PALS and WAMS were validated against the Morisky adherence scale, and this scale was originally validated in a hypertensive population (Morisky et al., 1986a).

4.2.2.1 Participant identification

All patients on Elvington Medical Practice's hypertension register who had not attended an annual hypertension review within the previous nine months were posted a request to attend for review plus the study documentation.

4.2.2.2 Inclusion criteria

- Current prescription for medication for the treatment of hypertension.
- No record of a hypertension review in the nine months before study commencement.

4.2.2.3 Exclusion Criteria

- Under 18 years of age.
- Considered by the healthcare team to be unable to provide written informed consent.
- Housebound or considered by the healthcare team to be too physically or mentally unwell to undertake the research.
- Unable to read or speak English fluently.

4.2.3 Sample size

No formal sample size calculation was performed however, it was estimated that approximately 200 patients would be eligible for inclusion. Previous studies employing similar methodology obtained response rates between 24% to 60% (Moshkovska et al., 2011, Lynch et al., 2011, Neame and Hammond, 2005, Desborough et al., 2008, Quine et al., 2012). This would give a final sample size of between 48 and 120 participants.

4.2.4 Outcomes

To meet the objectives described in the introduction, the following outcomes were estimated:

- Appraisal of research methods:
    - Identification rate

- Participation rate
- Attrition rate
- Feedback from patients who elected to not participate in the study

- Preliminary psychometric evaluation of PALS and WAMS
  - Score distributions on questionnaire sub-scales
  - Internal consistency estimates for questionnaire sub-scales
  - Summary score distributions for PALS + WAMS.
  - Summary score distributions for the combined PALS + WAMS
  - Correlations between sub-scales, PALS, WAMS, combined PALS + WAMS, blood pressure control, adherence measured using hypertension medication refill over the previous 12 months and the Morisky scale
  - Correlations between sub-scales, PALS, WAMS, combined PALS + WAMS, blood pressure control, adherence measured using hypertension medication refill over the three months subsequent to questionnaire postage and the Morisky scale

4.2.5 Study Procedures

4.2.5.1 Participant consent and confidentiality

Written, informed consent was sought for completion of the PALS and WAMS, access by a researcher to patient medical records to identify their previous two blood pressure readings and examination of their history of prescription refills. Participants were informed that the medical practice may use the information in PALS to update their records regarding smoking and drinking behaviours. Participants were informed that practitioners would not see their responses to the WAMS questionnaire and so the WAMS was returned by post to the surgery in a different coloured envelope to the PALS to prevent inadvertent opening by surgery staff and to reassure patients.

Participants who did not return a questionnaire were sent a postcard requesting their reasons for choosing to not participate (Appendix H). This card was fully anonymous with no way to identify individual responders.

4.2.5.2 Questionnaire completion

Participants completed the questionnaires in their own homes, and returned them either to Elvington Medical Practice when they attended for their hypertension review or in a reply paid envelope. Questionnaires were returned to the medical practice rather than researcher for two reasons:

1. The questionnaires are intended for use in primary care by practitioners and therefore returning the questionnaires to the practice offers a more accurate estimate of how acceptable the questionnaires are to patients in a clinical setting. There is conflicting evidence as to whether or not response rates differ when questionnaires are returned to GP practices or researchers (Desborough et al., 2008, Smith et al., 1985).

2. The data regarding patients' drinking and smoking habits are routinely collected and recorded by the surgery using a variety of strategies. The questionnaire data provided an efficient means for this data to be collected by the surgery and so contributed to their Quality Outcomes Framework reporting. This contribution acted as an incentive for the surgery to take part in the research and provided a realistic evaluation of the response rate to requests for potentially sensitive information by GP surgeries.

4.2.5.2.1 PALS completion

On 23rd August 2012 all eligible patients were posted an invitation to hypertension review at the surgery which notified the participant of the study (appendix I), and included a copy of the PALS questionnaire (appendix E), the study information sheet (appendix J), consent form (appendix K), an interview information sheet (appendix L), an interview consent form (appendix M) and a pre-paid envelope. Patients wishing to participate then presented completed forms when attending for hypertension review or posted them to the surgery. Returned questionnaires were then posted to the research team by the surgery. The available population was lower than expected so ethical approval was obtained for distribution of the questionnaires to a second cohort of patients that had become eligible for inclusion after the study commenced. These were posted on the 25th September 2012. The range of scores for all items, subscales and the full PALS scale ranges from 0 to 100.

4.2.5.2.2 WAMS completion and follow up

Four weeks after the initial posting, the WAMS questionnaire (appendix F) was sent to all respondents completing the PALS for return in a pre-paid envelope. Responders were also sent an information sheet reminding them of what they needed to do to take part in the study (appendix N). To all non-responders of PALS, a follow up pack was posted. This included a follow up information sheet (appendix O), consent form, PALS and WAMS questionnaires, the interview information sheet and consent form, and a pre-paid envelope for return. Returned questionnaires were collected from the surgery by a member of the research team. The range of scores for all items, subscales and the full WAMS scale ranges from 0 to 100.

4.2.5.3 Measurement of adherence

In order to collect information on self-reported adherence the PALS questionnaire contained the Morisky adherence scale. As noted in chapter 1, there is at present no gold standard self-reported measure of adherence. In the absence of such a measure the Morisky adherence scale was utilised to determine the validity of the PALS and WAMS questionnaires. While the Morisky adherence scale has a number of limitations including questions regarding the sample and criteria upon which it was validated, and reports of low internal consistency, it is nonetheless the scale is the most widely used in adherence research. To mitigate against these weaknesses the PALS and WAMS are also validated against an objective measure of adherence. The Morisky scale has four questions appraising whether or not participants engage in nonadherent behaviours (Morisky et al., 1986a). Thus the scale provides scores ranging from 0-4 with 0 indicating perfect adherence and 4 indicating multiple reasons for nonadherence. The four questions on the measure are:

1. Do you ever forget to take your medicines?
2. Are you careless at times about taking your medicines?
3. When you feel better do you sometimes stop taking your medicines?
4. Sometimes if you feel worse when taking your medicines, do you stop taking them?

To mitigate against the weaknesses of the Morisky scale the PALS and WAMS are also validated against an objective measure of adherence. Medical records were accessed to determine the rate of medication refills over one year pre and three months post questionnaire completion. Patients at Elvington medical practice are provided prescriptions at 28 day intervals. Therefore prospective follow up for all patients included three refill events for the purposes of calculating nonadherence. Where participants were prescribed multiple medications, a day was considered covered by medication only where their full medical regimen was available to them. Medication availability was counted from the prescription collected prior to commencement of the study, up until the end date giving a "Medication Refill Adherence" score or MRA. This method was preferred over the Proportion of Days Covered (PDC) or Medication Possession ratio (MPR) because the PDC does not take account of excess medication which can lead to an underestimate of medication adherence, while the MPR is poorly defined and can be calculated in a number of ways (Hess et al., 2006). The MRA score was estimated according to the following formula:

$$MRA = \frac{Cumulative\ days\ of\ medication\ collected\ by\ patient}{Total\ number\ of\ days\ medication\ prescribed}$$

4.2.5.4 Blood pressure measurements

Medical records were accessed to obtain participants' previous two blood pressure readings. This ensured all participants had one blood pressure reading from the prospective follow up period and one from the year retrospectively monitored.

4.2.6 Data Analysis

The recruitment and dropout rates of participants were calculated alongside 95% confidence intervals to provide an estimate of plausible population response rates. Subscale, PALS, WAMS, and PALS + WAMS scores were described in terms of medians and quartiles or means and standard deviations as appropriate. The analyses presented differ for existing subscales and those developed for the PALS and WAMS. For newly developed items and subscales internal consistency was described via Cronbach's alpha, and scales

were retested with each item removed from the scale to identify any items that negatively impact upon consistency of the scales. Furthermore, inter-item correlations were performed for questionnaire subscales. This information is presented in appendix P. Measures of correlation were undertaken to examine the relationship between questionnaire items, total and subscale scores, adherence behaviour, and patient outcomes. For previously validated scales incorporated into the PALS and WAMS only the correlations between total subscale scores, PALS, WAMS, PALS+WAMS and the three measures of adherence are presented.

Due to the lack of a gold standard adherence measure (Paterson et al., 2002, Smith et al., 2010, Vitolins et al., 2000, Wetzels et al., 2006) the new scales were compared to multiple measures of adherence to aid triangulation (Paterson et al., 2002). Correlations between subjective and objective measures of adherence were corrected such that a negative correlation always indicated that higher scores on PALS or WAMS were associated with lower adherence. This had the effect of reversing the scoring of the Morisky questionnaire, with scores now ranging from 0-4 with 4 indicating perfect adherence. This correction was performed by reversing the sign of correlations performed on raw scores and so the results presented in appendix Q are the inverse of those reported in the main thesis. Blood pressure was dichotomised as controlled or uncontrolled at 140/90mmHg (NHS, 2011). Given that most comparisons involved ordinal data correlations are presented as Spearman's Rho. Rho was also employed where ordinal or skewed data were correlated with a dichotomous variable because it was considered that this was more appropriate than the use of the point biserial coefficient, given that the non-dichotomous variable was ordinal (Nunnally, 1978). Where two dichotomous outcomes were compared the Phi coefficient was employed (Rosenthal and Rosnow, 2008). As a further concession to the small sample size acceptable adherence was defined as 100% adherence via medication refills and not the more commonly used 80%. Results are discussed in terms of their theoretical plausibility and the strength of evidence gathered in this study and the existing literature and not in terms of their statistical significance (Bender and Lange, 2001).

To further explore data and ensure interesting facets of the data were not hidden in summary statistics, the relationship between continuous subscale scores and adherence measures were examined using scatter plots, and ordinal or categorical subscale scores

and adherence measures were examined with boxplots. These are presented in appendix Q.

Area Under the Curve analyses were performed to assess the predictive validity of the questionnaires. However, the small sample sizes obtained lacked the power to make any such analysis sufficiently accurate (Hanley and McNeil, 1982). As a consequence these analyses are not reported, but are presented in appendix R.

Factor analysis was planned to estimate discriminant validity, however this would be inappropriate in a small sample. As a consequence, an alternative method of assessing construct validity was employed through analysing only bivariate relationships. Bivariate correlations between all subscales were produced. Correlations between individual subscales and estimates of adherence should be stronger than with other subscales in the PALS and WAMS. The correlations with adherence indicate that the variable makes a meaningful contribution to an estimate of adherence. The lack of correlation with other subscales in the PALS and WAMS indicates that there is not excessive collinearity between variables (Campbell and Fiske, 1959).

4.3 Results

4.3.1 Response rates and procedure evaluation

Initial screening identified 74 participants listed as having hypertension which was much lower than anticipated. This reduction occurred because an administrative delay in the approval of Research Governance shifted the start date of the study from before to after the Quality and Outcomes Framework data submission deadline for Elvington. The majority of outstanding reviews for patients with hypertension had therefore been completed prior to study initiation. Furthermore, while screening participants for exclusion criteria, 17 (22.97%) were identified as incorrectly labelled with hypertension in the surgery records. Figure 4.1 illustrates the sample size at each stage of recruitment and analysis. Of the 13 participants that completed the PALS, two opted to not complete the WAMS giving an attrition rate (95% CIs) of 15.38% (0.01%, 34.99%).

Of 56 patients that did not respond to the research invitation, 15 (26.79%) returned a postcard which detailed their reasons for not taking part. These are highlighted in Figure 4.2. Participants were given a free text box in which to include any additional reasons for non-participation which are presented in table 4.1. One of the non-responding patients also inadvertently returned a non-response form for a different study run by the University of York.

Of those returning questionnaires, nine (69 ± 25.14%) returned the PALS by post rather than in person at the surgery while 11 (78.57 ± 21.49%) returned the WAMS by post. All 13 participants who completed the PALS scale also completed the Morisky adherence scale. Morisky scores cannot be compared with WAMS for those participants that chose to complete that scale but not the PALS. Therefore comparisons between PALS and Morisky is for n = 13 participants, while for WAMS and the combined PALS and WAMS scale and Morisky it is n = 11. Retrospective refill data was available for eight participants, with one of the 11 participants that completed both scales not sufficiently completing the consent form, and two other participants refusing to allow their medical records be examined should the research be audited by the ethics committee. Consequently their data was not accessed. Blood pressure measurements were only available for seven participants. When accessing medical records it was discovered that one participant in

the sample was taking medication appropriate for hypertension but not because of hypertension. As a consequence they were excluded from this analysis.

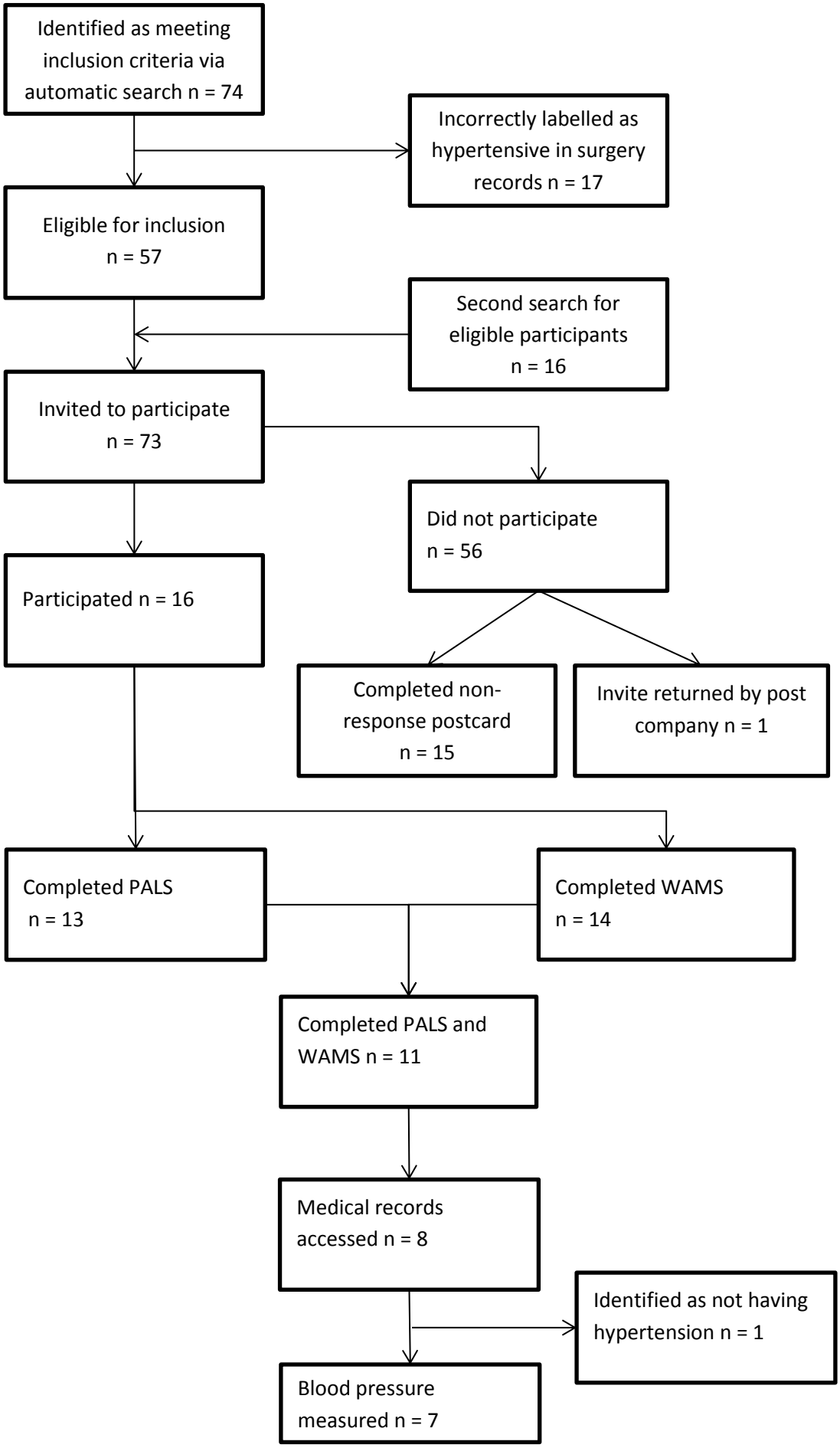


Figure 4.1 Flow diagram of study recruitment and participation

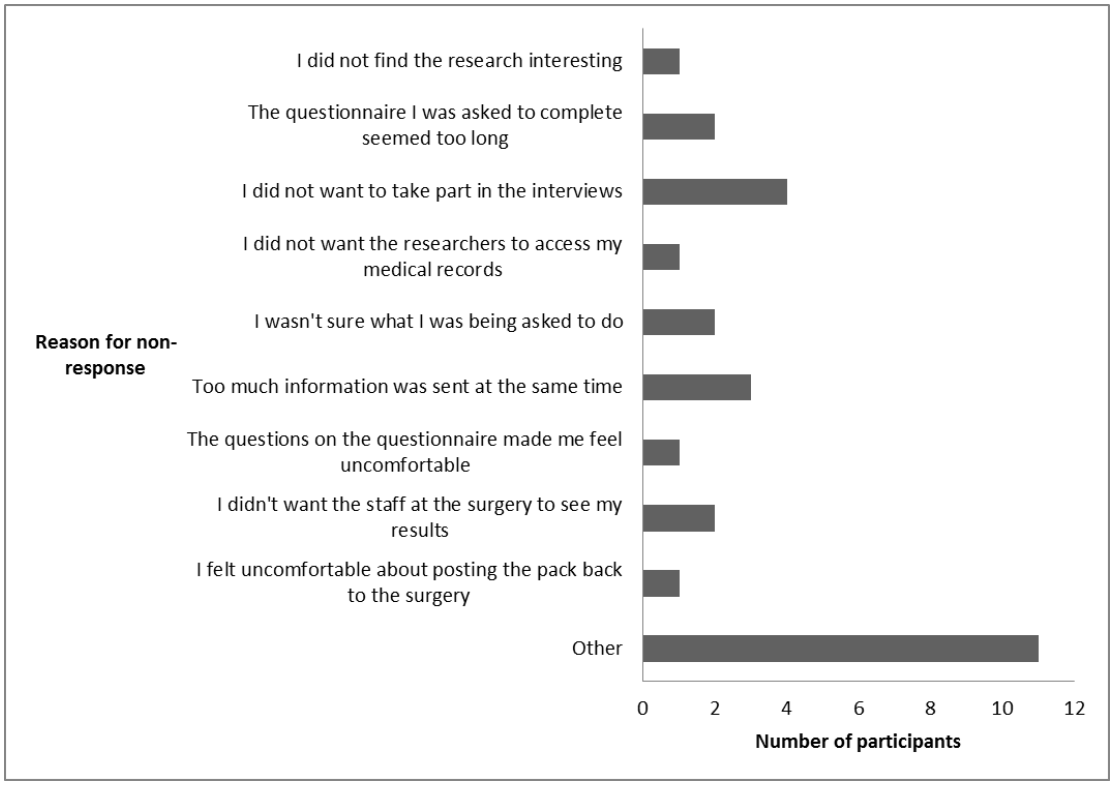


Figure 4.2 Reasons for non-response to the questionnaire submitted by participants

4.3.2 Participant demographics

The demographics of the sample can only be described for patients that completed the PALS questionnaire (n = 13). These participants had a mean (sd) age of 62.31 (9.68) years and are further described in table 4.2. The median (minimum, maximum) period of time between study commencement and previous blood pressure measurement was 351 (301, 400) days. Of seven participants, five (71.43 ± 33.47%) had controlled blood pressure pre questionnaire completion. The median (minimum, maximum) period of time between study commencement and the post questionnaire blood pressure measurement was 18 (12, 89) days. Of seven participants, five (71.43 ± 33.47%) had controlled blood pressure, with two participants becoming controlled since the previous measurement and two becoming uncontrolled.

Response category	Response number	Reason given
Time or organisation	2	"Lack of time"
	4	"I put it on one side and forgot about it"
	6	"I'm sorry, the forms got mislaid"
	7	"On Jan 4th I begin a world cruise and will not be back in England until the end of April 2013. Because of my long absence I did not think that my input would help your very worthwhile study"
	15	"The pack was misplaced"
Total responses:	***5***	
Errors or confusion	1	"Something wrong, I agree to take part with Elvington's ideas"
	3	"Am not on medication for hypertension"
	13	"I did not receive this literature"
Total responses:	***3***	
Dissatisfaction or anger with research	8	"Felt that GP has all our records and the survey was wasting NHS money! Sorry."
	12	"I don't want to continuously be pestered by questionnaires"
	14	"I DID NOT WANT TO TAKE PART!"
Total responses:	***3***	

Table 4.1 Participant volunteered reasons for non-participation

Characteristic		Frequency (N = 13)	Per cent	Lower CI	Upper CI
Sex	Male	8	61.5	35.1	88.0
Employment	Employed	7	53.9	26.8	81.0
	Unemployed	1	7.7	0	22.2
	Retired	4	30.8	5.7	55.9
	Missing	1*	7.7	0	22.2
Housing status	Lives with partner	8	61.5	35.1	88.0
	Lives alone	2	15.4	0	35.0
	Lives with others	2	15.4	0	35.0
	Missing	1	7.7	0	22.2
Drinks alcohol	Yes	13	100		
Smokes tobacco	No	12	92.3	77.8	100
	Missing	1	7.7	0	22.2

*Participant wrote on the form that they were disabled.

Table 4.2 Participant demographics

4.3.2 Medication adherence

In this sample, Morisky had a Cronbach's alpha of 0.60. The median (quartiles) score on the Morisky adherence measure was 0 (0, 1.5) with seven participants (53.8 ± 27.10%) reporting perfect adherence. Three participants reported one reason for adherence, two reported two reasons for nonadherence and only one participant reported three reasons for nonadherence. Reasons for nonadherence given via Morisky are presented in figure 4.3. According to participant medication refills, five participants (62.5 ± 33.55%) were 100% adherent in the year prior to study commencement, and three participants (37.5 ± 33.55%) were 100% adherent in the three months after study commencement. Distributions of participants' refill adherence over the study period are shown in figure 4.4. Seven of eight participants who self-identified as adherent via the Morisky scale were 100% adherent with both prospective and retrospective refills (87.5 ± 22.92%). Participants who were adherent in the year before the study start date remained adherent in the three months follow up on six of eight occasions (75 ± 30.01%).

Evidence for a correlation between adherence and blood pressure was stronger for measurements of refill adherence retrospectively and prospectively in the year before study commencement (Rho = -0.656, p = 0.109, Rho = -0.523, p = 0.228 respectively) than for current blood pressure (Rho = 0.164, p = 0.725, Rho = 0.087, p = 0.852). This was also true for Morisky with Rho = 0.529, p = 0.222 for blood pressure in the past year and no correlation identified with current adherence (Rho = 0, p = 1).

4.3.2 Description of full scales

The distribution of the scores on the PALS, WAMS, and all subsections are presented in Appendix S. The PALS scale was approximately normally distributed with a mean (sd) score of 26.19 (11.64). The WAMS scale was positively skewed and had a median (quartiles) score of 21.35 (16.90, 43.62). Combining PALS and WAMS into a single summary score also produced a positively skewed distribution with a median (quartiles) score of 24.10 (20.30, 26.99).

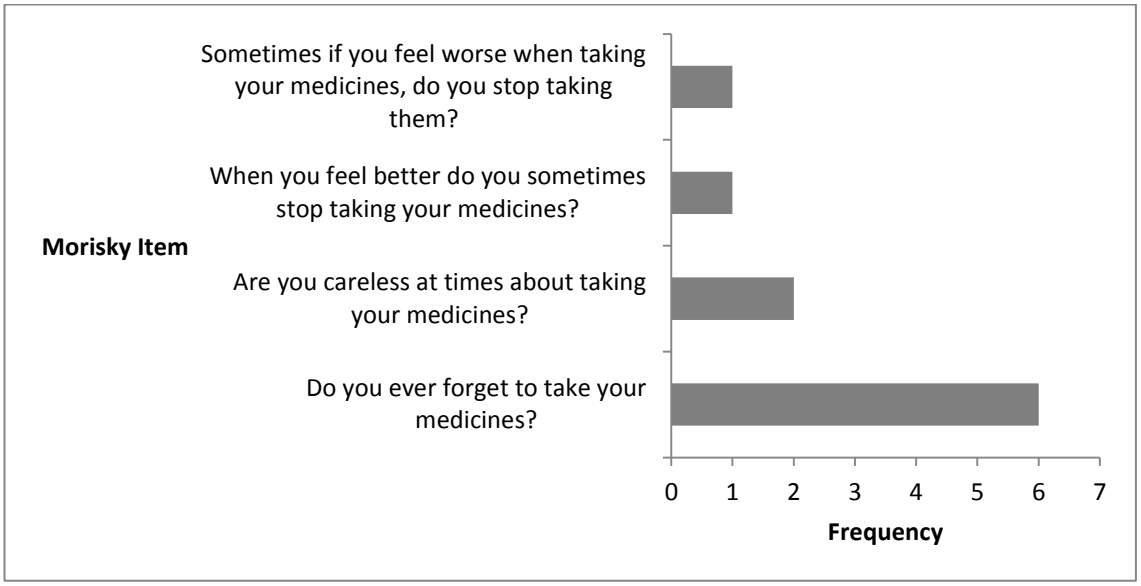


Figure 4.3 Reasons for nonadherence to the medications identified by the Morisky adherence tool

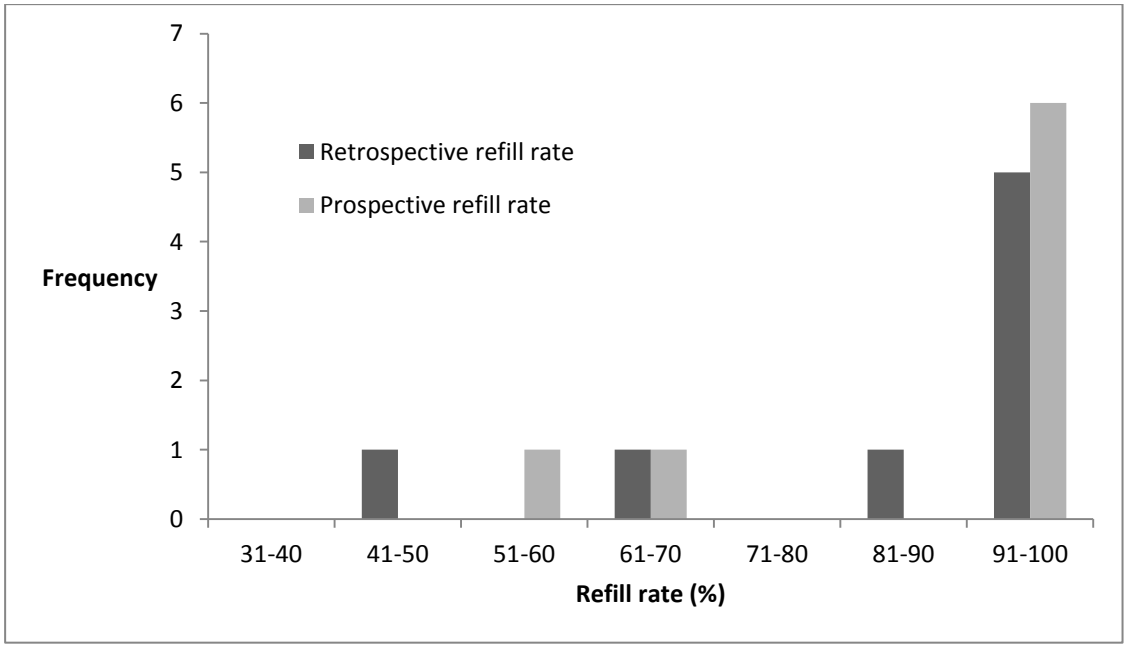


Figure 4.4 Distribution of participant refill rates during the study period

4.3.3 Predictive validity of the PALS, WAMS and combined scales

The correlations between questionnaire summary scores and measures of adherence and blood pressure are presented in table 4.3. The questionnaires have a stronger relationship with self-reported and prospective refill adherence than they do with retrospective refill adherence. Similarly the scales are more strongly correlated with current blood pressure than previous blood pressure.

Questionnaire	**Validity measure**									
	Morisky (n = 13 PALS, 11 WAMS/ combined)*		**Retrospective Refill (n = 8)**		**Prospective Refill (n = 8)**		**Retrospective Blood Pressure (n =7)**		**Prospective Blood Pressure (n = 7)**	
	Rho	p	Rho	p	Rho	p	Rho	p	Rho	p
PALS	-0.241	0.427	0.146	0.729	**-0.518**	0.188	0.158	0.735	*-0.474*	0.282
WAMS	**-0.520**	0.101	0.146	0.729	*-0.300*	0.470	*0.316*	0.490	*0.316*	0.490
Combined	*-0.391*	0.234	0.122	0.774	*-0.464*	0.267	0.158	0.735	-0.158	0.735

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**

Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.3 Correlations between questionnaire summary scores and outcomes for adherence and blood pressure

4.3.4 Sub-scale and item analyses

4.3.4.1 Demographics

One participant did not tick any of the available boxes to indicate their employment status but instead wrote in that they were disabled. Only one participant indicated that they were unemployed making comparison between unemployed and employed participants impossible. Instead this participant was combined with four retired participants and one participant identified as disabled to create a separate comparison between those working (n =7) and those not working or unable to work (n =6). Participants that indicated that they lived with others but not a romantic partner were treated as missing data, because no evidence for a relationship between this living arrangement and adherence was identified in chapter 2. An additional participant also omitted this question reducing the sample size from 13 to 10 for this variable. One participant indicated that they both lived with a spouse and with others. This participant

was treated in the analyses as if they had indicated that they live with their romantic partner.

4.3.4.1.1 Demographics and medication adherence

The correlations between participant demographics and measures of medication adherence are presented in table 4.4. There was a moderate correlation between being male and self-reported nonadherence. There was no strong evidence for a correlation between employment and adherence. There was a large correlation between not living with a romantic partner and retrospective and prospective adherence. However, these correlations are heavily influenced by a lack of variability in that only two participants in the sample live alone and both have 100% refill adherence both retrospectively and prospectively. There was also a large correlation indicating older participants were more likely to have greater prospective refill adherence.

Demographic	**Measure of adherence**					
	Morisky (n = 13)		**Retrospective Refill (n = 8)**		**Prospective refill (n = 8)**	
	Rho	p	Rho	p	Rho	p
Sex	*0.463*	0.111	0.173	0.682	0.194	0.646
Employment	0.249	0.413	0.224	0.595	0.125	0.768
Housing status (n = 10)	*0.398*	0.254	**0.656**	0.109	**0.587**	0.126
Age	0.275	0.364	0.220	0.601	**0.546**	0.162

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.4 Correlations between three measures of adherence and participant demographics

4.3.4.1.2 Demographics and blood pressure

There was also no evidence for a correlation between previous blood pressure control and sex (Phi = 0.091, p = 0.809). All three female participants had controlled blood pressure during the prospective collection period which resulted in a moderate non-statistically significant relationship between the two variables (Phi = 0.548, p = 0.147). There was no indication of a relationship between employment and past controlled blood pressure or current controlled blood pressure (for both Phi = -0.091, p = 0.809). There

was no evidence for a correlation between housing status and past or current blood pressure control (for both Phi = -0.250, p = 0.540). Increased age was statistically significantly associated with having uncontrolled blood pressure prior to questionnaire completion (Rho = -0.791, p = 0.034) but there was no evidence for a correlation with current blood pressure control (Rho = -0.400, p = 0.374).

4.3.4.1.3 Demographics and PALS, WAMS and combined summary scores

Table 4.5 presents the correlations between demographic variables and scale summary scores. There was a small non-statistically significant relationship indicating males scored more highly on the PALS and PALS + WAMS score. No relationship was identified between sex and scores on WAMS. Being employed was moderately correlated with a lower score on PALS. Living with a romantic partner was correlated with higher scores on PALS, WAMS, and to a lesser extent the combined PALS + WAMS total indicating a greater risk for nonadherence. There was a moderate correlation between age and the combined PALS + WAMS score.

Demographic	**Scale Summary Score**					
	PALS (n = 13)		**WAMS (n = 11)**		**Combined (n = 11)**	
	Rho	p	Rho	p	Rho	p
Sex	-0.254	0.403	0	1	-0.258	0.443
Employment	*0.330*	0.270	-0.173	0.611	0.115	0.735
Housing status (n = 10)	**0.611**	*0.061*	**0.725**	**0.001**	*0.311*	0.416
Age	0.116	0.706	-0.137	0.689	*-0.401*	0.222

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**

Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.5 Correlations between PALS, WAMS and combined scale scores and participant demographics

4.3.4.2 Health literacy

The sample displayed a range of ability with regard to health literacy (Appendix S). There was a moderate and statistically significant relationship indicating that lower health literacy was associated with lower self-reported adherence (Rho = -0.615, p = 0.025).

There were also statistically significant relationships indicating that lower literacy was associated with lower refill adherence both retrospectively (Rho = -0.872, p = 0.005) and prospectively (Rho = -0.860, p = 0.006). There was weak evidence to suggest blood pressure may be less likely to be controlled when health literacy is good (Rho = 0.683, p = 0.091). However, this was not evident for current blood pressure (Rho = -0.400, p = 0.374). The item did not correlate with scores on PALS (Rho = 0.242, p = 0.425), WAMS (Rho = 0.275, p = 0.413), or the combined scales (Rho = 0.034, p = 0.921).

4.3.4.3 BMQ Overuse scale

One participant omitted the item "Doctors prescribe too many medicines". The scale did not correlate with self-reported adherence (Rho = -0.086, p = 0.780) or retrospective adherence (Rho = -0.075, p = 0.859). The correlation identified for prospective adherence was moderate but not statistically significant (Rho = -0.394, p = 0.334). There was no indication that the BMQ Overuse scale was correlated with blood pressure retrospectively (Rho = -0.242, p = 0.602) or prospectively (Rho = -0.081, p = 0.684).BMQ Overuse scores was also not statistically significantly related to PALS summary scores (Rho = 0.376, p = 0.205), WAMS summary scores (Rho = -0.203, p = 0.580) or the combined PALS + WAMS summary scores (Rho = 0.295, p = 0.379).

4.3.4.4 BMQ General Harm scale

One participant indicated that they found two items on the scale difficult to answer by underlining the word "Most" in "Most medicines are addictive" and "All" in "All medicines are poisons". The BMQ General Harm scale was not statistically significantly associated with adherence as measures by Morisky (Rho = 0.147, p = 0.632), retrospective medication refills (Rho = -0.264, p = 0.527), or prospective medication refills (Rho = -0.394, p = 0.334). There was no evidence to suggest a correlation between BMQ General Harm scores and past blood pressure measurements (Rho = 0, p = 1), or current blood pressure (Rho = 0.164, p = 0.725). The BMQ General Harm scale was also not associated

with summary scores for PALS (Rho = 0.165, p = 0.590), WAMS (Rho = -0.210, p = 0.536), or the PALS + WAMS (Rho = 0.219, p = 0.517).

4.3.4.5 Mental Health

The sample contained two patients diagnosed with depression, and one participant wrote that they "possibly" have depression next to this option. It was assumed that this participant had not been diagnosed and so they were treated as not having a mental health diagnosis. No participants indicated having a diagnosis for any other mental illness. One participant did not respond to this question. Consequently analyses are based on the 12 participants that responded to the depression question.

There was no evidence found to indicate that the two patients with depression scored any differently on self-reported nonadherence (Rho = -0.070, p – 0.829), nor was there any indication that depression affected retrospective refill rates (Rho = 0.258, p = 0.537) or prospective refill rates (Rho = 0.289, p = 0.488). There was no identified association between a depression diagnosis and past or current blood pressure control (Rho = -0.300, p = 0.427, and Rho = 0.400, p = 0.290 respectively). There was no correlation between having depression and total scores for PALS (Rho = 0.389, p = 0.211), WAMS (Rho = 0.149, p = 0.662) or the combined total (Rho = 0.075, p =0.828).

4.3.4.6 Health behaviours – Smoking and drinking.

No participants indicated that they smoked, and so no analyses could be run on this variable. The amount of alcohol drunk per week was positively skewed, with most participants drinking a little or not at all, but with three participants (23.08%) drinking more than the NHS recommended maximum (appendix S). A moderate relationship between drinking and self-reported adherence was found (Rho = -0.433, p = 0.139), but the evidence was weak for a relationship between retrospective refill adherence (Rho = -0.050, p = 0.906) or prospective refill adherence (Rho = -0.280, p = 0.503). While there was no identified correlation between drinking and past blood pressure control (Rho = 0.406, p = 0.366) there was evidence to suggest that the more participants drank then the

greater the likelihood of not having controlled blood pressure in the present (Rho = -0.813, p = 0.026). There was no indication that the amount participants drank per week correlated with scores on PALS (Rho =0.243, p = 0.424), WAMS (Rho = 0.270, p = 0.422) or the combined total (Rho = 0.163, p = 0.632).

4.3.4.7 Perceived Stress Scale (PSS-4)

Scores on the PSS-4 correlated fairly strongly with self-reported (Rho = -0.720, p = 0.012) and prospective adherence (Rho = -0.878, p = 0.004), but there was little evidence for a correlation with retrospective adherence (Rho = -0.245, p = 0.558). Evidence was not found to suggest that stress was associated with blood pressure control in the past year (Rho = 0.558, p = 0.193) or currently (Rho = -0.319, p = 0.485). The PSS-4 also correlated with total PALS (0.616, p = 0.044), WAMS (Rho = 0.760, p = 0.002), and combined scale scores (Rho = 0.639, p = 0.034).

4.3.4.8 PHQ Depression items

There was reasonable evidence to suggest the scale correlated with self-reported nonadherence (Rho = -0.671, p = 0.024). Evidence for a correlation with refill adherence was weaker, particularly for retrospective refill adherence (Rho = 0.208, p = 0.208). Prospective refill adherence displayed a moderate but not statistically significant correlation (Rho = -0.375, p = 0.360). There was no evidence to suggest a correlation between blood pressure control from participants previous (Rho = 0.394, p = 0.381) or current (Rho = -0.197, p = 0.672) blood pressure readings. The PHQ depression scale items were significantly correlated with scores on WAMS (Rho = 0.846, p = 0.001) and the combined PALS + WAMS (Rho = 0.748, p = 0.008), but there was no evidence the items were correlated with scores on PALS (Rho = 0.484, p = 0.131).

4.3.4.9 PHQ Anxiety items

There was evidence for a correlation between anxiety and self-reported nonadherence (Rho = -0.695, p = 0.018), but not for a relationship with retrospective or prospective refill adherence (Rho = 0.127, p = 0.765 and Rho = -0.425, p = 0.294 respectively). There was no evidence to suggest that anxiety scores were related to previous or current blood pressure readings (Rho = 0.529, p = 0.222 and Rho = -0.176, p = 0.705 respectively). PHQ – Anxiety items showed evidence for a correlation between summary scores for WAMS (Rho = 0.877, p < 0.001) and the PALS + WAMS (Rho = 0.621, p = 0.041). However, there was no evidence of a relationship between PHQ Anxiety items and PALS scores (Rho = 0.249, p = 0.461).

4.3.4.10 Medication Concerns scale

One participant did not respond to any item on the Patient Adjustment to Medication (PAMS) scale which comprises patient concerns about medicines, beliefs in medication necessity, self-efficacy for medicines, social support, and access to medications. Consequently the sample size is reduced by one in the following section until the end of 4.3.4.14. This reduction does not affect the refill rate calculations as the participant omitting this section did not give consent for their medical records to be accessed.

The two items that comprise the medications concerns scale had only modest inter-item reliability (Cronbach's α = 0.621). The scale was normally distributed (Appendix S) with a mean (sd) of 50.00 (26.02). Correlations between the medications concerns scale and measures of adherence are presented in table 4.6. Scores on this scale were not found to be related to self-reported adherence or refill behaviour. However, there was some evidence that the highest scorers were also more likely to self-report non-adherence which may indicate a non-linear relationship between concerns and adherence (Appendix Q). There was no evidence found to correlate medication concerns with past blood pressure (Rho = 0, p = 1). Evidence for a correlation with current blood pressure was not strong (Rho = 0.497, p = 0.256). Scale scores were related to total WAMS scores but were not related to PALS or combined scores. All correlations between the medication concerns scale and summary scores are presented in table 4.7.

Medication Concerns Item	Measure of adherence					
	Morisky (n = 10)		**Retrospective Refill (n = 8)**		**Prospective refill (n = 8)**	
	Rho	p	Rho	p	Rho	p
I think my medicines are giving me side effects	*-0.389*	0.266	0.088	0.836	-0.070	0.869
If my medicines are making me feel worse than my illness, I think it makes sense to stop taking it for a while	-0.075	0.838	**0.570**	0.140	0.170	0.688
Medication Concerns	-0.245	0.496	0.214	0.611	0.183	0.665

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**

Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.6 Correlations between three measures of adherence and the medication concerns scale

Medication Concerns Item	Scale Summary Score					
	PALS (n = 10)		**WAMS (n = 13)**		**Combined (n = 10)**	
	Rho	p	Rho	p	Rho	p
I think my medicines are giving me side effects	-0.277	0.439	**0.529**	*0.063*	-0.094	0.795
If my medicines are making me feel worse than my illness, I think it makes sense to stop taking it for a while	-0.119	0.744	**0.614**	**0.018**	0.163	0.654
Medication Concerns	-0.179	0.621	**0.616**	**0.025**	0	1

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**

Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.7 Correlations between PALS, WAMS and combined scale scores and the medication concerns scale

4.3.4.11 Medication Necessity scale

In addition to the participant that omitted the entire PAMS scale, an additional participant omitted the item "I think my medicines help to keep me feeling as healthy as possible" reducing the sample size to 12 for this question. The three items in this scale displayed good internal reliability with a Cronbach's α of 0.890. The scale was normally distributed (appendix S) with a mean (sd) of 25.00 (18.94). Correlations between items on the medication necessity scale and measures of adherence are presented in table 4.8. There was no evidence that medicine concerns were associated with refill adherence in

this sample. However, as with medication concerns there was an indication that those that see their medicines as least necessary were more likely to self-report being non-adherent which may indicate a non-linear relationship between necessity and adherence (Appendix Q). No strong evidence was found to indicate that medication concerns are correlated with controlled blood pressure retrospectively (Rho = -0.479, p = 0.277) or prospectively (Rho = 0.558, p = 0.193). Correlations between scale summary scores and items on the medication necessity scale are presented in table 4.9. Scores on the necessity scale were significantly related to scores on WAMS but not with PALS or the combined scales.

Medication Necessity Item	**Measure of adherence**					
	Morisky (n = 10)		**Retrospective Refill (n = 8)**		**Prospective refill (n = 8)**	
	Rho	p	Rho	p	Rho	p
I think my medicines make me feel better than I would without them	-0.208	0.563	**0.510**	0.196	0.102	0.809
I think my illness would be worse without my medicines	*-0.440*	0.193	0.224	0.595	0.125	0.768
I think my medicines help to keep me feeling as healthy as possible	*-0.449*	0.193	0.200	0.634	0	1
Medication Necessity	*-0.319*	0.369	*0.383*	0.349	0.097	0.820

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**

Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.8 Correlations between three measures of adherence and the Medication Necessity scale

Medication Necessity Item	**Scale Summary Score**					
	PALS (n = 10)		**WAMS (n = 13)**		**Combined (n = 10)**	
	Rho	p	Rho	p	Rho	p
I think my medicines make me feel better than I would without them	0.065	0.858	0.575	0.040	0.521	0.123
I think my illness would be worse without my medicines	-0.121	0.740	0.609	0.027	0.107	0.768
I think my medicines help to keep me feeling as healthy as possible	-0.097	0.790	0.575	0.050*	0.065	0.859
Medication Necessity	-0.012	0.973	0.649	0.016	0.275	0.441

* N = 12 for this item

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**

Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.9 Correlations between PALS, WAMS and combined scale scores and the Medication Necessity scale

4.3.4.12 Self-Efficacy scale

The two items on the self-efficacy scale did not correlate well with each other (Rho = 0.314, p = 0.296) and so have very poor inter-item reliability (Chronbach's α = 0.299). The scale was positively skewed, but with a relatively wide distributions of scores (appendix S). Correlations between items on the self-efficacy scale and adherence measures are presented in table 4.10. There was reasonable evidence to suggest that the items on the scale were related to self-reported adherence and prospective refill adherence. The evidence was weak with regard to any relationship to retrospective refill adherence. Self-efficacy did not appear to be correlated with blood pressure control in the past year (Rho = 0.080, p = 0.865) or currently (Rho = 0.160, p = 0.733). The correlations between self-efficacy items and scale summary scores are presented in table 4.11. There was evidence to suggest that scores on the scale were related to overall WAMS scores, but this was stronger for the item regarding remembering to take medicine than for the item regarding coping with medication. There was little evidence to suggest the scale was associated with scores on PALS or combined total scores.

Self-Efficacy Item	**Measure of adherence**					
	Morisky (n = 10)		**Retrospective Refill (n = 8)**		**Prospective refill (n = 8)**	
	Rho	p	Rho	p	Rho	p
I find it hard to remember to take all of my medicines each day	**-0.796**	**0.006**	**-0.555**	0.153	**-0.751**	**0.032**
I think I can cope with the number of medicines I am prescribed at the moment	**-0.579**	*0.079*	-0.256	0.540	*-0.459*	0.253
Self-Efficacy	**-0.695**	**0.018**	-0.259	0.535	**-0.607**	0.110

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.10 Correlations between three measures of adherence and the Self-Efficacy scale

Self-Efficacy Item	Scale Summary Score					
	PALS (n = 10)		WAMS (n = 13)		Combined (n = 10)	
	Rho	p	Rho	p	Rho	p
I find it hard to remember to take all of my medicines each day	*0.363*	0.302	**0.618**	**0.024**	*0.363*	0.302
I think I can cope with the number of medicines I am prescribed at the moment	*0.317*	0.372	*0.388*	0.190	*0.414*	0.235
Self-Efficacy	*0.454*	0.188	**0.565**	**0.044**	**0.541**	0.107

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.11 Correlations between PALS, WAMS and combined scale scores and the Self-Efficacy scale

4.3.4.13 Social Support

One participant wrote on their questionnaire that they were unsure of what the phrase "help me" referred to in the item "There are people that will help me with my medications if needed". The four items concerning social support had a Cronbach's α of 0.695. Removing the item "I am concerned about how others will react if I tell them what medicines I take" would improve the inter-item reliability to 0.849. As a consequence the analyses were run with and without this item included in the scale, but since it made no major difference to the results, the results incorporating the full four item full scale are presented here. The scale was approximately normally distributed (Appendix S) with a mean (sd) of 30.29 (20.06). The correlations between items on the social support scale and measures of adherence are shown in table 4.12. There was no strong evidence to suggest a relationship between scores on the scale and measures of adherence. Correlations between social support and blood pressure were identical to those found between self-efficacy and blood pressure with Rho = -0.080, p = 0.865 for previous blood pressure and Rho = 0.160, p = 0.733 for current blood pressure. Correlations between items on the social support scale and scale summary scores are presented in table 4.13. There was evidence to suggest a correlation between higher scores on the social support scale and higher scores elsewhere on WAMS. This was not found for PALS or combined scale scores.

Social Support Item	Measure of adherence					
	Morisky (n = 10)		Retrospective Refill (n = 8)		Prospective refill (n = 8)	
	Rho	p	Rho	p	Rho	p
I am concerned about how others will react if I tell them what medicines I take	-0.263	0.462	0.144	0.734	0.044	0.918
There are people who will help me with my medicines if needed	**-0.548**	0.101	-0.118	0.781	**0.512**	0.195
I have people I can talk to about my illness	-0.046	0.899	**0.553**	0.155	0.177	0.675
I can count on my family and friends to help me deal with my illness	-0.012	0.973	*0.493*	0.214	0.016	0.970
Social Support	-0.183	0.614	*0.491*	0.217	0.110	0.796

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.12 Correlations between three measures of adherence and the Social Support scale

Social Support Item	Scale Summary Score					
	PALS (n = 10)		WAMS (n = 13)		Combined (n = 10)	
	Rho	p	Rho	p	Rho	p
I am concerned about how others will react if I tell them what medicines I take	-0.007	0.986	*0.411*	0.162	0.243	0.499
There are people who will help me with my medicines if needed	**0.610**	*0.061*	**0.684**	**0.010**	*0.400*	0.252
I have people I can talk to about my illness	*0.395*	0.259	**0.652**	**0.016**	*0.395*	0.259
I can count on my family and friends to help me deal with my illness	*0.390*	0.266	**0.599**	**0.031**	**0.629**	*0.051*
Social Support	*0.422*	0.224	**0.752**	**0.003**	**0.563**	*0.090*

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at α = 0.1 are in *italics,* correlations significant at α = 0.05 are in **bold**

Table 4.13 Correlations between PALS, WAMS and combined scale scores and the Social Support scale

4.3.4.14 Access to Medications

The item assessing patient's ease of access to a new supply of medicines indicated that most participants have little or no difficulty with this (Appendix S). The item was statistically significantly correlated with self-reported adherence (n = 10, Rho = 0.739, p = 0.015) but not with retrospective refill (Rho = -0.264, p = 0.528) or prospective refill adherence (Rho = -0.471, p = 0.238). No evidence was found to link blood pressure control to access to medications in the past year (Rho = 0.088, p = 0.851) or currently

(Rho = 0.529, p = 0.222). There was evidence to suggest the scale was associated with overall WAMS scores (n = 13, Rho = 0.785, p = 0.001) but not PALS (n = 10, Rho = 0, p = 1) or the combined totals (n = 10, Rho = 0.098, p = 0.788).

4.3.4.15 Patient-Doctor Relationship Questionnaire (PDRQ-9)

One participant wrote on their questionnaire that their responses on this scale depended upon which doctor they were thinking about. Scores on individual items and consequently the final scale were skewed with few participants criticising their doctor (Appendix S). Evidence was weak for a correlation between self-reported nonadherence and higher scores on the PDRQ-9 (Rho = -0.490, p =0.126), but no evidence was found for a relationship between the PDRQ-9 and retrospective or prospective refill adherence (Rho = -0.02, p = 0.977 and Rho = -0.206, p = 0.625 respectively). There may be an indication of a non-linear relationship where the relationship between self-reported nonadherence and doctor relationships become more important when relationships are especially poor (Appendix Q). There was no relationship identified between the relationship participants had with their doctor and past or current blood pressure control (Rho = 0.316, p = 0.490 and Rho = 0.474, p = 0.282 respectively). There was little evidence to suggest scores on the PDRQ-9 items were correlated with total scores on the PALS (Rho = -0.142, p = 0.678), WAMS (Rho = 0.498, p = 0.070), or combined scales (Rho = -0.009, p = 0.979).

4.3.5 Discriminant validity

As described in section 4.2.6 discriminant validity was assessed by comparing the bivariate relationships between subscales with estimates of adherence and each other. Correlations between individual subscales should be stronger with estimates of adherence than with any other subscale if it is to be concluded that the subscale is contributing unique variance over and above that provided by other subscales. A full table highlighting the correlations between all subscales can be found in Appendix T. Whether or not a person lived with a long term partner correlated more strongly with retrospective refill data than any other measure other than social support, for which it is a proxy. This suggests this variable contributes unique variance to an estimate of risk of nonadherence.

Health literacy correlated more strongly with all three measures of adherence than it did with any other subscale suggesting adequate discriminant validity. The BMQ Overuse scale correlated more strongly with prospective refill rates than any other measure on the scale other than the BMQ General Harm scale which suggests significant overlap between the contributions to an estimate of nonadherence provided by the two BMQ scales. The PSS-4 correlated more strongly with prospective refill rates than any other measure, but correlated more strongly with the PHQ Depression and Anxiety subscales than the Morisky or retrospective refill measures of adherence. Similarly, the PHQ-Depression subscale correlated most strongly with the Morisky measure of adherence. However the PHQ-Depression scale correlated more strongly with PHQ Anxiety scale and the PSS-4 than with retrospective or prospective adherence. This suggests significant overlap in the variance explained by the three mental wellbeing scales. Access to medications correlated more strongly with self-reported adherence than with any other variables. No other scales demonstrated sufficient discriminant validity according to the criteria of Campbell and Fiske (1959).

When the scales considered are restricted to those with a Rho > 0.5 with at least one measure of adherence as an arbitrary indication of having sufficient convergent validity, then all scales other than depression have a greater correlation with at least one measure of adherence than they do with any other scale. Table 4.14 illustrates these correlations.

	PALS/WAMS Subscale						**Measure of adherence - Rho**		
	Housing Status	**Health literacy**	**PSS-4**	**PHQ-D**	**PHQ-A**	**Self-Efficacy**	**Morisky**	**Retro-spective Refill**	**Pro-spective Refill**
Housing Status	1	-0.467	0.106	0.283	0.184	0.321	0.398	**0.656**	0.394
Health literacy	-	1	0.493	0.112	0.066	0.491	*-0.615*	**-0.872**	*-0.860*
PSS-4	-	-	1	0.813	0.760	0.534	-0.720	-0.245	**0.878**
PHQ-D	-	-		1	**0.865**	0.343	-0.671	0.208	-0.375
PHQ-A	-	-	-	-	1	0.307	-0.684	0.127	-0.425
Self-Efficacy	-	-	-	-	-	1	**-0.627**	-0.259	*-0.607*

* Items in **bold** identify the strongest correlation for a subscale; items in *italics* indicate a correlation with adherence stronger than with any other subscale.

Table 4.14 Discriminant validity of the subscales comprising the PALS and WAMS tools

4.4 Discussion

4.4.1 Main findings

4.4.1.1 Development of the research method

Targeting patients with hypertension appears to have been appropriate as triangulation of adherence, and clinical outcome data has been achieved. The available population was, however, smaller than expected at the start of the study. This was largely due to the host surgery actively inviting patients for hypertension review immediately prior to study implementation. Furthermore, over a fifth of the patients listed as having hypertension in the surgery's database did not have hypertension. This substantially impaired the ability of the designed study to meet a number of the studies aims. In particular the sample size was inappropriate for psychometric testing and so all conclusions must be discussed with the strength of evidence available in this study borne in mind. If a larger multisite study were to take place ethical approval could be sought for a clinically trained member of the research team to assess whether or not a participant is eligible and appropriate for inclusion across all sites to ensure consistency and to minimise the impact of record errors and variations in interpretation of the inclusion criteria across different surgeries.

Items within the questionnaires may have affected response rates which would also partially account for participation in this study approximating the lower bound estimated prior to study initiation. It was expected that some participants might object to questions regarding their mental health, smoking, drinking and relationship with their provider. Asking sensitive questions can impact upon both item and total response rates (Dillman et al., 1993). Ideally the acceptability of these sections would be assessed via the use of alternate forms of the questionnaire. This would allow a direct comparison of how much each section impacted upon acceptability to be made. However, there were too many comparisons for this to be feasible. Instead it was decided to include the sensitive items and measure total acceptability of the questionnaire, with a qualitative assessment of the acceptability of these sections with patients and practitioners that had experience with the questionnaires (chapter 5). Responses from non-participants indicate that at least some participants were uncomfortable with the questions they were being asked,

sending the questionnaires back to the surgery, and with staff at the surgery seeing their responses. Removing or rewording these sections in collaboration with the relevant population may improve acceptability.

The responses provided by non-responders to the survey also indicate that some participants may have been over-burdened with requests to participate in research. The questionnaire was split into two sections, PALS and WAMS, in order to reduce respondent burden (Chipperfield and Steel, 2011). However, this may be counterproductive when respondent burden comes from the number of questionnaires administered rather than the length of a single questionnaire. Although only two participants that completed the PALS did not go on to complete the WAMS this represented 15% of the current sample. Response rates from a single questionnaire versus a split PALS and WAMS could assess whether or not respondent fatigue affected scores or acceptability. An alternative approach to avoid over-burdening participants is to exclude participants that have taken part in research in the last year. However with a small available population it was considered unwise to further restrict the potential sample.

Participant non-response postcards indicated additional procedural problems. Streamlining the process to make it easier for participants to take part, and modifying the instructions to enhance ease of understanding may be achieved through lay review of study documents and procedures. Some participants indicated that they did not take part in the study because they did not want to take part in the interviews. The instructions stated that participation in the main study did not obligate participation in interviews; however some participants may not be comfortable taking part in only one element. An alternative design might have been to inform participants that interviews are taking place at the end of the study and if they were interested in taking part they could tick a box on the consent form. Information could then be sent out separately only to those that were interested. Some participants also felt that the research was not interesting or that the questionnaire was too long. This reinforces the importance of keeping respondent burden to a minimum so as to minimise the costs of taking part (Chipperfield and Steel, 2011). It was also clear that a number of participants forgot about the questionnaire or else lost the forms. A more thorough follow up procedure may limit the impact of participant forgetfulness (Edwards et al., 2002).

A final factor that lowered the sample size was that some participants refused permission for their data to be audited by the ethics committee or for researchers to access their medical records. The ethics committee's standard wording for this section of the consent form was used. Previous literature has indicated that patients and practitioners consider medical records to be highly private (Goodwin et al., 2002, Shaw et al., 2011). However a qualitative study exploring the specific problem of researcher access to medical records would be valuable.

A final methodological consideration was the return of questionnaires by post versus in person. Most participants returned their questionnaire by post, but a significant proportion decided to return questionnaires by hand. This was true even for the WAMS which contained instructions only on how to return the questionnaire by post. This indicates that participants appreciate a number of alternative methods for questionnaire return that best suit their needs. Offering a number of different modes of administration might also improve response rates and acceptability.

4.4.1.2 The central role of mental health and wellbeing

In line with work based upon the findings of chapter 2 (Watson et al., 2011), a relationship between stress and mental wellbeing and adherence was demonstrated in this study. It is not clear whether stress impacts directly upon adherence, whether it influences other mediating variables, or what the direction of causality is between adherence and distress. Nonetheless mental distress is an indicator of nonadherence and should be dealt with when recognised to prevent worsening mental health (Lovibond and Lovibond, 1995) which may have a detrimental impact upon both adherence and clinical outcome (DiMatteo et al., 2000).

4.4.1.3 The role of beliefs about medicines

The importance of patient beliefs about medicines in adherence has been emphasised in the literature and has received some endorsement in this study. The medication necessity scale had a moderate association with self-reported adherence, and there was an indication that patients reporting multiple types of nonadherence were less likely to rate

their medicines as necessary. Evidence for a correlation between patients' concerns about their medicines and adherence was weak in this study as it has been in others (Carr et al., 2006, Bardel et al., 2007, Mann et al., 2007, Mann et al., 2009). However, there was an indication that patients reporting multiple types of nonadherence had the highest concern about medicines scores.

In contrast to previous studies (Horne et al., 1999, Mahler et al., 2012, Mårdby et al., 2007, Saks et al., 2012), evidence for a correlation between the BMQ General subscales and adherence was weak in this study. However, correlations between the BMQ General subscale and adherence have tended to be low. Mahler et al. (2012) found all correlations between BMQ subscales and adherence to be below a Rho of 0.3. In the validation study for the BMQ correlations between the General Harm and Overuse scale were even lower (Rho = -0.19 and Rho = -0.06 respectively). It is unlikely that a sample of the size available for this study would identify a relationship between adherence and the BMQ general scales.

4.4.1.4 Health literacy and adherence

The item assessing health literacy correlated with all three measures of adherence. A recent systematic review failed to find consistent evidence for the importance of health literacy in adherence (Loke et al., 2012). However, the conclusion of this review was that there was a lack of robust studies rather than that there is no association between health literacy and adherence. Moreover, no meta-analyses could be performed to properly quantify the estimated relationships between health literacy and adherence in the studies they identified. Consequently whether or not health literacy is associated with medication adherence remains an open question which should be explored further.

4.4.2 Prediction of nonadherence

The PALS and WAMS are designed to predict which patients are likely to be at risk of being nonadherent to medicines. The PALS and WAMS have been shown to have moderate to large correlations with self-reported adherence and prospective adherence

over three months. Although not statistically significant due to the small sample size, these correlations indicate that the questionnaires may perform well at predicting adherence over the short term. Correlations with longer term retrospective adherence were lower. This reflects that the strongest indicators of adherence are those most proximal to the behaviour (McHorney, 2009), and these are more changeable and context specific. However, the questionnaires aim to go beyond achieving a strong correlation with adherence and identify specific causes of nonadherence and targets for intervention. Therefore items with a small correlation with adherence may still be useful for practitioners so long as they are correlated with more proximal causes of nonadherence and present a clinically useful target for intervention. The clinical utility of questionnaire sections is appraised in chapter 5.

4.4.3 Correlation with patient outcomes

The study identified that measures of adherence and blood pressure correlated more strongly with past rather than current blood pressure. The relationship between medication adherence and patient outcome is unclear, with some analyses finding a stronger relationship between the two variables than others (DiMatteo et al., 2002, Simpson et al., 2006). For less serious disease adherence to medication can be associated with worse health outcomes (DiMatteo et al., 2007). The current sample had the most severely ill patients screened out which might explain the lack of association between adherence and current outcome. An alternative explanation is that participation in the study introduced reactivity effects and adherence improved for participants before current blood pressure was taken. The number of patients displaying perfect adherence increased by two after the study began. Reduced variation in outcome in a small sample could explain the lack of relationship identified.

It was hypothesised that the PALS and WAMS might have a stronger correlation with patient outcome than traditional adherence measures because it contains sub-scales that might also correlate with patient outcomes such as mental wellbeing and health literacy. However few correlations were identified. One possible cause for the lack of identified relationships is that only seven participants could have their blood pressure measured. This provides extremely low power for any analysis. Despite this lack of power, age,

drinking alcohol and health literacy were associated with uncontrolled blood pressure. The relationship between age and blood pressure is well established and age is the primary indicator for hypertension (Baksi et al., 2009). There is also a documented independent effect of drinking on blood pressure (Klatsky et al., 1977). Drinking is acknowledged as one of the most important causes of resistant hypertension alongside nonadherence to therapy (Mancia et al., 2007). It has also been demonstrated via meta-analysis that reducing alcohol intake directly reduces blood pressure (Xin et al., 2001). In contrast health literacy has not been associated reliably with blood pressure control in the past (Pignone et al., 2005, DeWalt and Hink, 2009) nor was the evidence for a relationship strong in the current investigation. Given the strength of evidence available and the lack of an underpinning theoretical argument to support the direction of the effect it is impossible to rule out chance and sampling error as the cause of the negative correlation found between health literacy and controlled blood pressure.

4.4.4 Interpretation of subscale performance

4.4.4.1 Recommendations for PALS

4.4.4.1.1 Patient demographics: "About you"

Absence of a relationship between sex and adherence was expected as none was identified via meta-analysis. The meta-analysis did identify a small relationship between age and nonadherence however the current sample was far too small to show a significant effect. There is no reason to suggest changing or removing these items from the questionnaires at this stage. One participant had to write in that they were disabled and so did not fit into any of the pre-specified criteria for the item regarding employment. Adding this option alongside an "other, please specify" box could solve this problem. Housing status did not correlate strongly with adherence, but only two participants did not live with their romantic partner restricting the power to detect any association between the variables. The item should be tested in a larger sample. This item may also be too ambiguous as currently worded. One participant indicated that they live with

others and their romantic partner, and if an individual lives with their spouse and their children it would not be clear how they should respond. The item should be modified whilst still maintaining the focus on spousal support which has been shown to be the strongest form of social support available (Johnson, 1983). This could be done by asking only whether or not the patient lives with a long term romantic partner.

4.4.4.1.2 Health literacy: "Written information"

The health literacy item correlated well with all measures of adherence. However, the item did not correlate strongly with summary scores for the PALS and WAMS. However many items on PALS had poor correlations with adherence. The lack of correlation with WAMS scores may be due to the high covariance between high scoring items on the WAMS such as depression, anxiety, and stress. The discriminant validity analysis indicated that health literacy correlated moderately with the PSS-4 correlations but less strongly with the PHQ anxiety and depression scales. This might indicate that health literacy explains a significant amount of unique variation in adherence behaviour otherwise not assessed in the WAMS. Therefore this item should be retained in future versions of the scale.

4.4.4.1.3 BMQ General subscale: "Your beliefs about medicines"

Correlations between the items on the BMQ and adherence were low in this and other studies and are likely to have weak predictive power (Mahler et al., 2012, Horne et al., 1999). However, the BMQ general scale offers insight to the general beliefs patients have about treatment. While such beliefs are difficult to change and therefore not generally a suitable target for interventions, distal beliefs can inform practitioners of the perspectives of their patients and facilitate consultations (Porteous et al., 2010).

4.4.4.1.4 Mental health and risky behaviours: "Your mental health and behaviour"

Only two participants in this sample were diagnosed with depression, and no other mental illness was present. This lack of variation makes proper assessment of the importance of this variable impossible to determine in this sample. Nonetheless, the

importance of mental wellbeing was reinforced in this study via the PSS-4 and PHQ tools. However, there will be significant overlap between a diagnosis for depression and scores on the PHQ and PSS which might suggest this item will add little unique information. Additional problems were identified by participants writing freehand on the questionnaire. One wrote that they were "possibly" depressed indicating that they were worried that their concerns would be overlooked because they lacked a formal diagnosis. Another emphasised the word "past" in the phrase "I have a current or past diagnosis for depression" which may indicates that they do not want to be judged according to historical events. Given these issues omitting the item on diagnosis of a mental health problem is recommended.

No participants reported smoking in this sample. There is a strong link between smoking and hypertension (Virdis et al., 2010) and it is unlikely that a sample with no smokers is representative of the surgery's hypertension population. A wider range of alcohol consumption behaviours was reported. However, it remains possible that a number of heavier drinkers elected to not participate rather than send this sensitive information to the doctor. There is evidence to suggest that both patients (Simmons et al., 2009, Ulbricht et al., 2011) and doctors (Noordman et al., 2010, Mules et al., 2012) are uncomfortable discussing lifestyle behaviours with each other. Consequently the accuracy of this information in patients' medical records is poor (Thiru et al., 2003). However, both smoking and drinking were shown to be correlated with adherence in chapter 2, and this study has also demonstrated a relationship between alcohol consumption and blood pressure. Given these arguments the reasons why participants may have been unwilling to complete these items should be explored (chapter 5) and a decision on whether to include smoking and drinking information withheld until after this stage.

4.4.4.2 Recommendations for WAMS

4.4.4.2.1 Patient affect: "Mental wellbeing and happiness"

The items in the mental wellbeing section may correlate highly with each other. The amount of collinearity can be assessed in a study with a larger sample size. If collinearity is excessive options would be to include only the scale which adds most information, or else is most acceptable to participants. Another option is be to employ factor analysis with rotation to identify whether or not three independent factors emerge representing stress, anxiety, and depression. If one factor were to emerge, indicating the tests are measuring a single underlying variable, then the items which loaded most heavily upon this factor could be used to form a new short measure of mental distress.

4.4.4.2.2 Patient concerns about medicines

The medication concerns scale had modest inter-item reliability. This would suggest an expansion of this scale might be necessary (Nunnally, 1978). Further modifications are recommended. The conditional from the item "If my medicines are making me feel worse than my illness, I think it makes sense to stop taking it for a while" should be removed. The current wording makes this question impossible to answer for participants that have not experienced their medicine making them feel worse than their illness. The item is also a fairly direct question about adherence. The PALS and WAMS aimed to avoid direct assessment of adherence to avoid social desirability biases. This item might be replaced by questions that collect information about experiences taking their medicines less directly. For example "I think my medicines make me feel worse than my illness".

4.4.4.2.3 Perceived necessity of medications

The medication necessity scale had good internal consistency, and there was an indication that in a larger sample a statistically significant relationship with self-reported adherence may have been identified. Given the strength of evidence for the importance of medication necessity in prior literature (Byer and Myers, 2000, Gauchet et al., 2007, Menckeberg et al., 2008, Bardel et al., 2007, Schneider et al., 2004, Horne and Weinman, 1999, Horne et al., 1999) and the otherwise desirable psychometric properties of the scale it should be retained in its present form for trial in a larger sample which can more accurately estimate the importance of the scale in predicting adherence.

4.4.4.2.4 Self-efficacy for medicines

There was some evidence to suggest the items on the self-efficacy scale were related to adherence, however there was no strong indication that the items were related to each other. Item 15, "I find it hard to remember to take my medicines each day", may be too direct an assessment of adherence and may not properly assess self-efficacy. A revision such as "I am confident I can take all of my medicines each day" might remove these problems. It might also be useful to expand the self-efficacy scale in order to improve the internal consistency of the scale.

4.4.4.2.5 Social support

The social support scale did not have a strong relationship with adherence with the exception of the item "There are people who will help me with my medicines if needed" which had a Rho > 0.5 with both self-reported and prospective refill adherence. This was also the only item on the questionnaire that directly assessed social support with regard to medicines and not the illness. Revising the items "I have people I can talk to about my illness" and "I can count on my friends and family to help me deal with my illness" to items that focus upon the relationship participants have with their medicines and not their illness is recommended. Despite this weakness the scale was internally consistent with the exception of the item "I am concerned about how others will react if I tell them what medicines I take". This item might refer more to social stigma associated with the participant's illness and not the support they receive. This item did not correlate well with adherence independently of the other items in the social support scale and so should be removed.

4.4.4.2.6 Access to medications

The item assessing the impact of access to a new supply of medications was associated with self-reported adherence, and total scores on the WAMS scale. The item may also serve as an important indicator to a medical professional that a participant has a specific problem that needs to be addressed. The item should be retained in any future scale.

4.4.4.2.7 Provider relationship: "About your doctor"

One participant wrote on the questionnaire that their answers would vary depending upon the particular doctor they were seeing indicating that respondents may be unclear as to how to answer the questionnaire as currently worded. One solution could be to change the wording of the questionnaire to be more explicit that the scale seeks information about the practitioner that is most involved with their care for a particular course of medications. Responses on the scale also indicated that almost all participants considered themselves to have a good relationship with their doctor. This lack of variation will have contributed to the very high internal consistency of the scale. The high scores might reflect that the patients that did not think highly of their doctor did not respond, which might have in part accounted for the low response rate. Despite this, a number of items on the scale did correlate with self-reported adherence in particular. The scale should be removed from the study if it can be demonstrated that its inclusion has a significant impact upon response rates.

4.4.5 Limitations of the adherence measures used

All available measures of adherence have demonstrable flaws (Vitolins et al., 2000). While the weaknesses of the methods employed are acknowledged it is also considered that they were optimal given the constraints in place for this study. The Morisky scale has numerous flaws including a low internal consistency (Morisky et al., 1986a), which was also identified in this sample. Similarly there are known flaws with the use of refill rates, with the strongest criticism being that it is not a direct measure of medication taking behaviour. Pill counts or electronic monitoring of medication taking provide a more direct estimate of medication taking but the resources were not in place to utilise such an approach. Moreover, the use of refill rates significantly reduces the likelihood of reactivity effects artificially increasing adherence rates in the sample, particularly when follow up is over a short period (Vitolins et al., 2000). As a consequence, in the absence of a superior existing scale for the self-report of non-adherence it was determined that the best option was to utilise the Morisky scale and use refill rates as an objective measure of adherence.

4.4.6 Conclusion

Several opportunities to improve the design of the PALS and WAMS questionnaires and their psychometric testing have been identified. The research methodology is further explored qualitatively in chapter 5. Despite the small sample size, some indications for the relative utility of different sections on the PALS and WAMS are identified. However, it is clear that refinements in design are necessary in order to optimise response rate. Further, tentative evidence has been found for the relationship between mental wellbeing, patient medication beliefs, and health literacy in adherence.

Chapter 5 – Qualitative appraisal of the PALS and WAMS

5.1 Introduction

5.1.1 Study Rationale

Chapter 4 detailed the quantitative assessment of the PALS and WAMS questionnaires by estimating the ability of the new questionnaires to predict prospective and retrospective adherence. In the absence of a widely accepted gold standard measure to validate against, achieving a non-zero correlation with another imperfect measure of adherence is insufficient evidence of validity. Qualitative techniques provide insight into the meaning behind question responses and so may illuminate how the indicators of adherence are related to each other and adherence. Further, exploring participant understanding of items can highlight where questions need to be reworded to correct for ambiguity (Morgan, 1997, Morgan, 1996, Huston and Hobson, 2008, Krueger and Casey, 2000). Moreover, it has not yet been appraised how useful medical professionals will find PALS and WAMS or whether or not they would be able to use the responses to inform decision making with patients. To provide insight into these questions a qualitative study is necessary.

5.1.2 Aims and Objective

The aims of this qualitative section of the project were to:

1. Assess the validity of participant responses to the PALS and WAMS
2. Improve the design and content of the PALS and WAMS
3. Improve the design of the quantitative study of the PALS and WAMS for future testing of the questionnaires

The objectives are to:

- Examine the agreement and contradiction between participants attitudes and behaviours as expressed via interview versus those expressed via postal questionnaire
- Explore participant feelings about taking part in the research
- Identify strategies to increase questionnaire response rates
- Explore participant understanding of items and instructions in the questionnaires
- Explore participant understanding of instructions for taking part in the research
- Explore whether practitioners consider subsections of the questionnaires useful and relevant for intervening to improve medication adherence
- Identify better ways of conducting research with GP practices so as to minimise cost and time disruptions

5.1.3 Method selection

Focus groups can be employed after the development of an initial corpus of questions to help develop questions that are worded in a way that is meaningful to the target group (Alquati Bisol et al., 2008). The advantage of a focus group over traditional face validity piloting is the ability for a compromise to be reached regarding wording that is appropriate to representatives of the target population during the group, rather than the researcher having to amalgamate disparate views after a number of individual sessions. Participants in a focus group tend to talk in a manner appropriate to the norms of the group rather than in a way that expresses private views (Morgan, 1997, Wight, 1994). This makes focus groups useful for understanding how a peer group understands a topic by analysing naturalistic talk between peers (Wilkinson, 2008, Michell, 1999, Wilkinson, 2004). Further, disagreements in a group can lead to further elaboration of accounts, particularly when group members are known to each other (Wilkinson, 2004). However, minority positions or the views of those with less power in a group may be crowded out or suppressed (Michell, 1999). Moreover, the group interaction can lead to the changing of held views and so using focus groups to establish current views is not recommended (Barbour, 2008). When individual accounts of behaviour are desired, one-to-one interviews are the preferred choice because focus groups can quickly become disjointed and informative narratives lost (Barbour, 2008).

Focus groups can also be useful for bringing together a group which has multiple objectives. For example, O'Donnell et al. (2007) utilised focus groups of GPs in the UK and the US after they had used a new method of comparing diagnoses between UK and US doctors in order to appraise the tool and the proposed research methodology. The method allowed for assessment of comprehensibility of the individual questions and identification of ways to facilitate conducting research with physicians based upon their experiences in the study simultaneously.

A common method of qualitative validation of questionnaires is cognitive interviewing (Ericsson and Simon, 1993, Hernandez et al., 2011). There are two versions of cognitive interview, "think aloud" and "verbal probing" (Willis, 1999, Willis, 2005). "Think aloud" involves asking participants to verbalise their thought processes as they go through each item in order to gain insight into what the question might mean to participants and identify any problems that may arise when participants are asked to respond to each item. "Verbal probing" involves direct questioning of participants to gather this information. The process is very time consuming so often very few interviews are conducted which can lead to inappropriate generalisations being made about the adequacy of an item based upon an opinion or thought process that may be very rare (Dillman et al., 2009).

An alternative to cognitive interviewing is the use of semi-structured interviews. Mallinson (2002) used individual interviews to appraise the SF-36 Health Status Questionnaire instead of cognitive interviewing to avoid changing how participants would normally complete the questionnaire. Their analysis identified a number of problems with the questions in the SF-36. The problems identified in the scale included asking about multiple behaviours in a single question, asking questions about distance in absolute terms such as how many miles they can walk which mean little to respondents, and asking about a number of behaviours which may not be important or relevant to participants with no option to opt out. A key finding of this study was the importance of relativism. Participants respond to questions based upon the context of their lives. If a respondent indicates that they are "stressed" this may reflect how well the participant feels they are coping compared to others in their own situation rather than provide a population level ranking of stress. Such an assessment might reflect very different absolute levels of stress in populations with a different illness, age, or prognosis. Including

qualitative validation of questionnaire responses can therefore provide a rich understanding of what responses actually mean and thus appraise validity at a deeper level of meaning than correlation with external measures (Mason, 2002, Fern, 2001).

This study would require the use of both focus groups and semi-structured interviews in order to meet the dual aims of identifying the needs of practitioners for the questionnaires, and corroborating questionnaire responses with individual testimony.

5.1.4 Focus groups

5.1.4.1 Sampling strategy and selection of group members

Sample selection should ensure that information which is representative of the biases and perspectives inherent in the target population is gathered (Morgan, 1997). The goal is to identify "information rich sources" that can provide depth of information on a topic (Krueger and Casey, 2000). Segmenting all participants into individual groups that are similar ensures that the research project covers the relevant population while minimising the difficulty of conducting individual groups (Fern, 2001, Krueger and Casey, 2000, Morgan, 1997). The number of groups required to answer a research question therefore varies between studies, with one important factor being the diversity of the population under study (Morgan, 1997, Krueger and Casey, 2000).

The present study is interested in research active practitioners who have a need to assess adherence in their patients. Ideally a number of practitioners practicing in different socio-demographic areas and both the primary and secondary care setting would be consulted to ensure as wide as possible acceptability for the tool. However, at this early stage in the development of the questionnaire it is more appropriate to focus on the population most frequently reviewing patient adherence; it would be inappropriate to use the time of a large number of health practitioners.

The PALS and WAMS questionnaires were designed with the assumption that in the UK, care for chronic illness is primarily the responsibility of the patient's GP (Black et al., 2004). However, it is not uncommon for nurses to take an active role in management of

chronic conditions (Bonsall and Cheater, 2008). Including GPs and nurses in the same focus group lowers group homogeneity and introduces differences in social ranking. This can make it more difficult for the researcher to identify differences between the views of the two groups as group processes tend to lead toward consensus (Finch and Lewis, 2003). However, the PALS and WAMS may be used in multidisciplinary teams and so it was considered that having the nurses in the same group might encourage the GPs to consider viewpoints other than their own and enable a compromise between the needs of two groups to be reached (Barbour, 2008).

Conducting research with pre-existing groups can make participants more willing to challenge views that are expressed during a focus group (Rabiee, 2004). However, shared assumptions may not be expressed which can lead to biases in the data that remain unknown to the researcher if they cannot be elicited (Finch and Lewis, 2003, Morgan, 1997). Moreover, in a pre-existing group dominance hierarchies will be set before the group begins and so it is difficult for a moderator to influence these in a one off discussion (Finch and Lewis, 2003).

5.1.4.2 Location and Environment of focus groups

The location and internal ambiance of the room can impact upon data generated during a focus group (Fern, 2001). For pre-existing groups using a location at which the group normally meets reduces the likelihood of participants not attending and helps the group feel more comfortable and willing to share (Finch and Lewis, 2003). Provision of refreshments before the group discussion can help to put participants at ease, become acquainted, and provide the researcher with an opportunity to identify participants who might require encouragement to take part or else need to be limited from dominating the discussion (Krueger and Casey, 2000). Participants can then be positioned in the focus group seating so that more reticent participants are closer to the moderator to encourage their discussion and the more dominating members opposite the researcher so their contributions can be more readily managed (Morgan, 1997).

5.4.1.3 Management of the group and moderating style

Having an experienced moderator with interviewing and people management skills is important for creating the atmosphere and type of talk required to generate the type of data that a particular study desires (Wilkinson, 2008). Moderating can be either flexible or directive (Fern, 2001, Morgan, 1997, Finch and Lewis, 2003). Flexible groups allow the participants to take more control of the conversation with the moderator making less frequent interjections. Directive groups are required when the topics to be discussed are relatively fixed. Flexible groups allow the topics of greater interest and importance to the group to be identified and prioritised within the discussion, but can lead to some relevant topics either being passed over or omitted from the discussion. A directed approach allows the moderator to ensure all relevant topics are covered (Morgan, 1997).

5.1.5 Individual interviews

5.1.5.1 Sampling strategy

In common with focus group research, the aim in interview research is to create a purposive sample which is capable of fully illustrating the phenomena of interest (Ritchie et al., 2003a). Theoretical sampling is one robust method for achieving this within a grounded theory approach (Mason, 2002). Theoretical sampling is an iterative process where cases that might disconfirm the proposed process or explanations for phenomena are sought. Sampling continues until a reasonable explanation of the phenomena of interest can be generated and substantial data for amending the proposed theory is not obtained from further interviews (Mason, 2002, Charmaz, 2008).

Heterogeneous sampling seeks to achieve the same aims as theoretical sampling but is less intensive (Ritchie et al., 2003a). Heterogeneous sampling seeks a diverse range of participants to maximise the likelihood of having disconfirming cases when sampling is not iterative, and is useful for identifying themes that cut across a diverse population. Homogenous sampling samples a number of similar cases and is useful for exploring specific phenomena in depth. Extreme case sampling can be used to explore rare or unusual cases. Intensity sampling is similar to extreme case sampling but focuses on cases

especially representative of the phenomenon of interest rather than unusual ones. Typical case sampling focusses on average cases. Stratified sampling merges different approaches by seeking different groups of relatively homogenous membership in order to contrast the different groups more fully.

5.1.5.2 Location and Environment of the interviews

The location of interviews can produce different types of data. For example, participants interviewed in their place of work tend to respond as employees in accordance with company policy, feel less empowered, and worry more about giving "the right answers" compared with participants interviewed in their homes. Anderson and Jones (2009) found that when children were interviewed in their classrooms they see adults as authority figures and were more relaxed and open when interviews were conducted in the school storage cupboard. The location of the interview should be one participants are comfortable with and one in which the feel empowered. Giving participants the option to choose where interviews are conducted is one way to achieve this (Anderson and Jones, 2009, Elwood and Martin, 2000).

5.1.5.3 Interviewing conduct

The context and conduct of the interview is a key determinant of what is said. Knowledge is therefore constructed during the interview not extracted from it (Holstein and Gubrium, 2004). Talking about specific experiences can help ensure that data more accurately reflect how participants think, feel and act in the context of interest (Mason, 2002). Probing responses to explore the reasons provided can also reveal contradictions in reasoning or the cause of any context-dependent differences in behaviour and attitude. Conducting an interview that fulfils these criteria requires an interviewer to listen, process what is being said, identify how or whether it fits with the research aims, ensure coverage of the intended material and that interesting data are followed up (Legard et al., 2003).

5.1.6 Validity of analyses

Investigating the same topic in different ways gives access to different levels of meaning (Mason, 2002). Triangulation of data from different methodologies (e.g. survey and interview) and perspectives (e.g. patients and practitioners) can provide a more thorough understanding of how questionnaires are perceived and can utilised most effectively. However, responses from focus groups, interviews, or surveys cannot be added together to produce an "overall truth" (Silverman, 2005). Deviations between responses in interview versus questionnaire might be expected in a different context where ideas are considered in a new light, or the meaning of questions reconsidered after further deliberation. Consequently corroboration between survey and interview responses allows an evaluation of how well the questions elicit the experiences and perceptions of participants in a meaningful way.

A further requirement for validity in qualitative research is a transparent process of analysis demonstrating the development of analyses from initial thought to the final presented themes (Yardley, 2008). Comparison of analysis decisions between more than one researcher and participant feedback further enhance validity (Yardley, 2008).

A final method to improve upon the validity of any analysis is constant comparative analysis (Mason, 2002, Yardley, 2008, Lewis and Ritchie, 2003). Researchers should seek to identify, present, and explain evidence that seems to disconfirm the current theory (Mason, 2002).

5.1.7 Qualitative data analysis

Qualitative data analysis can attempt to access different levels of meaning which can inform what type of analysis is employed (Mason, 2002). A useful starting point can be to revisit the study's epistemological position (Braun and Clarke, 2006). Essentialist epistemologies assume a straightforward relationship between meaning and language. In contrast more constructionist epistemologies tend to see the meanings themselves as socially produced and reproduced. Therefore studies which employ the former views may focus more upon what is said while studies with the latter assumption may be more interested in analysing why what was said was said (Braun and Clarke, 2006). A second

decision to make is whether the study seeks a rich description of the full data set or else a detailed account of an individual phenomena (Braun and Clarke, 2006). A related question is whether or not to engage in "content" or "ethnographic" analysis (Silverman, 2005). Procedures that are closer to the content approach seek to systematically cover all data to identify what topics are mentioned and how often. Ethnographic approaches are more interpretive and therefore more selective in terms of what data are analysed. Ethnographic approaches address how and why topics are discussed. An allied question is whether analysis is at the semantic or latent level (Braun and Clarke, 2006). Semantic analyses move from a purely descriptive account to interpreting the meaning behind what is said, but analyses are firmly based upon the actual words of participants. Latent analyses seek to identify underlying ideas and assumptions that give rise to what participants have said. A final question posed by Braun and Clarke (2006) is whether analysis are inductive, or theoretical. Inductive analyses are "bottom up" with theory is generated from the data. Theoretical analyses have prior assumptions about what the underlying will be. As a result the aim in this kind of analysis is to assess how well the data fit the theory. However, even in a theoretical analysis it is expected that the data will challenge prior theory and some "bottom up" analysis will take place.

Where study aims require constructionist, interpretive, and latent analysis the most appropriate methods are observer participation, or phenomenological analysis (Mason, 2002, Smith and Osborn, 2008, Silverman, 2005). Thematic, content, and framework analysis approaches are more appropriate when studies require essentialist, descriptive, and semantic analyses. Content analysis is more appropriate where results are highly descriptive and less interpretation of meaning is required (Silverman, 2005). Thematic analysis should be preferred when some interpretation is required and analyses are predominantly inductive (Braun and Clarke, 2006). Framework analysis is most appropriate when analyses are mostly descriptive and theoretically based, but some inductive and interpretive analysis is required (Ritchie and Spencer, 1994, Ritchie et al., 2003c, Rabiee, 2004).

The components of a valid qualitative analysis centre on transparency in the decisions made with regard to choice of method, sampling, and analysis. The assumptions made by the researcher at each stage should be made explicit and be open to external scrutiny.

5.2. Methods

5.2.1 Practitioner focus group study procedures

5.2.1.1 Participant identification and sample selection

All practitioners at Elvington medical practice were invited by the local collaborator to attend one focus group as part of the regular weekly lunchtime meeting. Written, informed consent was sought from practitioners for focus group participation and audio recording. Upon being invited to participate all practitioners were given electronic and physical copies of the two questionnaires to look over before the focus group session took place.

5.2.1.2 Setting

The focus group was conducted in a meeting room at Elvington medical practice.

5.2.1.3 Interview conduct

The focus group was moderated by the principal investigator and the primary supervisor acted as assistant moderator.

5.2.2 Participant interview study procedures

5.2.2.1 Participant identification

All participants who were invited to take part in the trial described in chapter 4 were concurrently asked to provide consent to take part in an interview. Consequently, the identification, inclusion and exclusion criteria are identical to those specified in Chapter 4.

5.2.2.2 Sample selection

Heterogeneous purposive sampling was utilised to ensure a comprehensive range of views and to allow for disconfirming cases to be included (Ritchie et al., 2003b). Participant selection was to maximise variability in terms of adherence to medication, employment, beliefs about medicines, mental wellbeing, social support, relationship with practitioners, and sex.

5.2.2.3 Participant consent

Written, informed consent was sought from participants for interviews to be audio recorded and discussions held about the participant experience of study involvement and to explore perception and understanding of the adherence questionnaires. Participants that consented to take part but were not selected for interview, or else consented to take part but not to have the audio of the interview recorded were sent a letter informing them that they would not be required for the study.

5.2.2.4 Setting

Participants were given a choice of being interviewed in their own home or at Elvington Medical Practice.

5.2.2.5 Interview conduct

Interviews were directive in that the interviewer steered discussion towards topics that appeared upon the questionnaire, and discussing the process of taking part in the research. However, interviewee's were given freedom to introduce new topics, change the order in which topics were introduced, or stray from the current topic in order for participant priorities or topics missing from the questionnaire or interview guide to be elucidated (Morgan, 1997).

5.2.3 Plan of analysis for the practitioner focus group and participant interviews

Data analysis was based upon Framework analysis as described by Ritchie and Spencer (1994), Ritchie et al. (2003c), and Rabiee (2004).

5.2.3.1 Topic Guide development

Topic guides were developed for the practitioner focus group and patient interviews (Appendix U, and Appendix V respectively). The focus group was more directed than the interviews in order to ensure all relevant topics were covered within the allotted hour. This is reflected in a more prescriptive topic guide, which follows a comparatively rigid order. In contrast, the interview topic guide had few specifically worded prompts (Arthur and Nazroo, 2003). More sensitive questions are also located toward the end of interviews. This placement allows for a rapport to be built between interviewer and interviewee before these topics are broached (Smith and Osborn, 2008). It also allows for these topics to be introduced by the interviewee at a time they are comfortable bringing them up without the interviewer having to force the topics into the conversation (Arthur and Nazroo, 2003).

The aims of the focus group topic schedule were to begin with a discussion regarding the use of questionnaires in regular practice, to consider good and bad features of tools in general and then the specific tools. The questions placed at the end were about how best to engage practitioners and GP practices in research were asked as these questions were

considered less fundamental to the study aims. In contrast, exploring the experience of taking part in research was the first item on the interview schedule. It was thought that as a non-personal topic this would be the least sensitive topic to be discussed.

5.2.3.2 Development of an initial framework

Initial frameworks were developed from the results of the meta-analyses described in chapter 2 and qualitative studies of influences upon adherence (Benson and Britten, 2002, Marshall et al., 2012, Britten, 1994). The interview framework therefore resembled the sections identified on the questionnaire. The addition of themes taken from qualitative studies allowed for comparison of items which may correlate with adherence but may not be the primary drivers of adherence. Fewer directly applicable studies were identified to inform the design of the focus group framework. However, the work of O'Donnell et al. (2007) which also examined practitioner assessments of a newly developed tool and how best to include practitioners in research was influential. The initial framework developed for the practitioner focus group is shown in table 5.1. The initial framework for the patient interviews is shown in table 5.2.

Theme	Subtheme
1. Perception of questionnaire tools	
1.1	Influence on decision making
1.2	Impact upon consultations (time, rapport, structure)
1.3	Influence on relationship with the patient (understanding and knowledge of patient)
2. Design of questionnaire tools	
2.1	Wording
2.2	Length
2.3	Scoring and interpretation
3. Ethical considerations	
3.1	Dealing with sensitive questions
3.2	Managing difficult responses (e.g. mental illness screening and dislike of practitioners)
4. Patient adherence	
4.1	Identification
4.2	Causes
4.3	Management
5. *Participation in research* (O'Donnell et al., 2007)	
5.1	Incentives
5.2	Barriers
5.3	Logistics

*Themes in italics taken from research articles (cited)

Table 5.1 Initial thematic framework for the practitioner focus group

Theme	Subtheme
1. Patient factors	
	1.1 Demographic
	1.2 Normalising of medicine/illness
	1.3 *Stress and anxiety* (Marshall et al., 2012)
2. Perception of medicines	
	2.1 Aspects of the drug regimen
	2.2 Perceptions of side effects
	2.3 *Positive aspects of the medicine* (Benson and Britten, 2002)
	2.4 *Reservations about medicines* (Benson and Britten, 2002)
3. Perception of illness	
	3.1 Causes of illness/exacerbating factors
	3.2 Perception and impact of symptoms
	3.3 Impact and role of any comorbid conditions
	3.4 Perception of general health and wellbeing
4. Access to health care	
	4.1 Obtaining a new supply
	4.2 Paying for medication
	4.3 Getting a consultation
	4.4 Dealing with problems
	4.5 Literacy and understanding
5. Social factors	
	5.1 Practical help
	5.2 Emotional support
	5.3 Role of romantic partners
	5.4 Giving and receiving advice
6. Relationship with health care providers	
	6.1 Relationship to individuals
	6.2 Relationship to the surgery
	6.3 Trust
	6.4 Time
	6.5 Empathy
7. Participation in research	
	7.1 Perceived benefits of participation
	7.2 Perceived risks of participation
	7.3 Barriers to participation
8. Recurrent themes/meta classifications (Ritchie et al., 2003a)	
	8.1 Trust – In researcher, practitioner, drug companies and support group
	8.2 Normalisation – of medicine and illness
	8.3 Motivations – to take pills, to participate, to see doctor

*Themes in italics taken from research articles (cited)

Table 5.2 Initial thematic framework for the participant interviews

5.2.3.3 Data familiarisation

To aid in data familiarisation, the focus group and interviews were transcribed verbatim by the principal investigator (Gorecki et al., 2012, Braun and Clarke, 2006, Wilkinson, 2008, Lewis and Ritchie, 2003). Non-verbal cues and speech patterns that might be

considered important for interpretation by the principal investigator or assistant moderator in the practitioner focus group were also included (Charmaz, 2008).

5.2.3.4 Indexing the data

For participant interviews, indexing was initiated on a transcript felt to be rich in data by the principal investigator. Where data did not fit adequately within an existing theme Rabiee (2004) was followed:

The theme was modified to better fit or a new theme was developed. Where the data were not considered useful for achieving the study aims it was not coded. The revised framework was then used to index a second transcript and further changes were made as required. The revised framework was then reapplied to the first transcript to ensure the data fit the new framework. When all the data considered relevant to the study aims could be coded the process was repeated for the third transcript and so on until a framework was developed that was capable of classifying all relevant data present in all transcripts.

For the practitioner focus group the initial framework was adapted to fit the data according to the same principles outlined above. Indexing was carried out independently by two researchers (SW with either MA or DB) with disagreements resolved via discussion.

5.2.3.5 Synthesising and charting the data

Data were grouped by participant and charted using NVivo VS. 10 software. For both interview and focus group data this permitted the analysis of frequency, and intensity with which ideas were expressed to be analysed (Rabiee, 2004). Themes that did not contain sufficient meaningful data were discarded, and their contents either moved to alternative themes or else removed from analysis. Where overlaps between different themes were identified the possible reasons for these were explored (Ritchie et al., 2003c). Synthesis of data was performed by one researcher (SW) with a second (DB) applying the revised frameworks to transcripts independently to ensure robustness.

Issues identified during checking were referred to the first researcher (SW) who re-examined the developed framework for subsequent checking. This procedure was followed iteratively until both researchers were satisfied that the developed thematic framework was sufficient to summarise the findings of the study.

5.2.3.6 Data description and interpretation

The final stage of analysis was to present and interpret the responses of participants in the context of the present study. Where possible, underlying explanations for the views presented were proposed (Ritchie et al., 2003c). Inferences will be based upon the recurring conjunction of ideas or else by comparing the accounts of participants that do not make an observation with those that do (Ritchie et al., 2003c). Additional explanations will be sought via comparison with the existing literature. As with previous stages all analyses were performed with input from multiple researchers to ensure the presented analyses are trustworthy. The interpretations offered by SW were checked with reference to the source material by DB, and additional independent reviewing by FP highlighted any areas where assumptions were being made in reporting or where the interpretations offered were not suitably transparent.

5.2.3.7 Validity assurance

Survey, focus group, and interview data were triangulated so that inconsistencies in participant testimony could be highlighted for discussion whilst ensuring that the interpretations offered for participants' testimony were internally consistent with the multiple sources of evidence gathered (Mason, 2002). Additionally, regular meetings were held as described above between the primary researcher and supervisors to ensure that interpretations were grounded in the data and not the presupposed ideas of an individual researcher (Yardley, 2008, Mason, 2002). The trustworthiness of the results was further ensured by maintaining intermediate copies of data files and thematic frameworks as the work progressed (Yardley, 2008).

5.3 Results

5.3.1 Practitioner Focus group

5.3.1.1 Focus group composition and management

Seven practitioners consented to participate in the focus group. At the beginning of the session practitioners were asked whether or not they had looked over the questionnaires prior to the session. They had not and so physical copies of the questionnaires were distributed and practitioners looked over these whilst the investigators prepared the session and equipment. Practitioners were also encouraged to refer to these during the session. The sample comprised of two nurses and five GPs including a trainee GP and a partner in the practice (table 5.3).

Participant Code	Role in Surgery	Sex
1	Practice Nurse	Female
2	Partner	Male
3	GP Registrar	Male
4	GP	Female
5	Practice Nurse	Female
6	GP	Female
7	GP	Female
SW	Moderator	Male
DB	Assistant Moderator	Female

Table 5.3 Focus Group participant demographics

There was no evidence that the nurses tended to defer to the doctors. Although P1 was the least active participant in the discussion, P5 was one of the most active. The greater seniority of P2 as a partner in the practice did impact upon group discussions; his perceived rank permitted him to give views counter to the group consensus and this often opened up new ideas to debate. However, his rank also led to his views rarely being challenged. On the one occasion where his views were challenged he conceded the point. The willingness of participant (P4) to challenge him may indicate that deference was based more upon respect than hierarchy. The willingness of the junior GP (P3) to express

sometimes contrary opinions also bears witness to this claim. With the exception of P2 all participants appeared to have equal status.

5.3.1.2 Construction of themes from the practitioner focus group

Whilst coding, new themes were developed that could not be represented with the initial framework presented in table 5.1. This resulted in two additional primary themes and the number of subthemes increased from 14 to 22. This expanded framework is presented in Appendix W. After overlaps and links between different themes were identified and examined, it was judged that data could be adequately described and interpreted using seven themes but a condensed set of 10 subthemes. Table 5.4 illustrates the final set of themes and subthemes.

Theme	Subtheme
1. Perception of questionnaire tools	
	1.1 Influence of questionnaires upon the process and outcomes of consultations
	1.2 Motivations for use of tools
2. Design of questionnaire tools	
	2.1 Ease of use and administration
3. Areas for improvement in current tools	
	3.1 Omissions
	3.2 Ambiguities
	3.3 Ethical considerations
4. Patient adherence	
	4.1 Causes
	4.2 Management of non-adherence
5. Participation in research	
	5.1 Incentives
	5.2 Barriers
6. Perception of patients	
7. Practitioner Professional autonomy	

Table 5.4 Final framework of practitioner focus group themes

5.3.1.2.1 Perception of questionnaire tools.

Participants were concerned that introducing questionnaires during a consultation could stop the flow of the conversation. The view that paper forms can act as a barrier between

patients and practitioners was expressed by a majority of GPs (P2, P3, P4 and P7). The following quote in response to a question asking about the impact of questionnaires on the timing of consultations demonstrates the stresses the use of questionnaires during a consultation can impose on GPs:

> *"It's just another pressure, our consultation times are between ten and twelve minutes and I think it's already pressured and sometimes you can ask the patient to fill it in while you're there but that is time consuming, you could ask them to bring it back I guess, but with the PHQs the pressures to get it done at the first assessment."* (P2)

This GP expresses the discomfort he experiences with trying to balance the need to give time to a patient, his own obligations to complete a time consuming questionnaire, and the additional pressure of trying to keep the consultation within a reasonable total time. P7 was also concerned that relying on questionnaires to guide consultations might lead to practitioners not asking questions that might be on the questionnaire in a context appropriate manner, or else not asking questions that are not on the questionnaire.

However, it was stated by P2, P5, and P7 that patients completing questionnaires before the consultation could allow for better discussions. One nurse (P5) stated that rather than being a block to communication is was possible to use questionnaires to generate a more effective consultation:

> *"…sometimes with questionnaires its better using or reading them in advance as well so you can, rather than use it as a barrier, there's a piece of paper as a barrier, you can use the questions as prompts to speak to the patient afterwards or when they come in the consultation"* (P5)

P2 and P4 said the potential utility of questionnaires was maximised when patients are unknown to the doctors, or when it was known that patients were nonadherent and the aim of the consultation was to address specific problems. This view was also expressed by P4 who had been the most critical of questionnaires up to this point in the discussion, finding them "intrusive" even when completed before the consultation. However, the assumption that the doctors knew their regular patients well enough to derive no benefit from questionnaires was questioned by P2 who mentioned the capacity for patients to surprise doctors or to change their beliefs based upon their background or new

information e.g. from newspapers. He suggests that the BMQ general subscale could provide valuable information to inform a consultation and the type of patient education necessary. P7 also stated that an additional benefit of the questionnaire might be the opportunity for patients to express views that they may feel uncomfortable mentioning in person. The dissent of the authoritative P2 appeared to be the point in conversation at which it became acceptable to question the capabilities of practitioners to get all of the relevant information from patients.

The practitioners were sceptical of the probability of patients returning questionnaires. However, P2 stated that having to complete a questionnaire for the Quality and Outcomes Framework (QOF) can serve as a motivator for the surgery to dispense questionnaires and encourage patients to respond. The practitioners had individual strategies for collecting and uploading data making a trade-off between ensuring a response and maximising time in a consultation. One nurse (P5) said that she asks her patients to complete questionnaires in the consultation and enters the information into the patients' medical records immediately to ensure the information is captured. Two doctors (P2 and P3) said they also used to do this but no longer did because it took up too much consultation time. It was widely acknowledged by the group that since information on anxiety and depression had to be collected routinely for patients with chronic illness it would be economical to incorporate this into a questionnaire that addressed a larger number of issues such as PALS or WAMS. The group came to accept the utility of this approach after their initial reluctance to collect information on anxiety and depression after P2 legitimised considering whether there were benefits to collecting information on mental wellbeing.

5.3.1.2.2 Design of Questionnaire tools

Time was mentioned throughout the discussion as a vital consideration for the practitioners. One aspect of this was a desire for questionnaires that are easy to score (P2), and with no free text for participants to complete (P1). One participant (P2) twice brought up the possibility of utilising technology to both deliver and collect information. There was a feeling that a useful questionnaire would make it simple to categorise respondents into adherers and non-adherers using a summary score. In particular it was felt it would be useful to be able to differentiate patients requiring a simple solution such

as the provision of a dosett box from those requiring motivational and behavioural interventions to influence intentional non-adherence. There was initial reluctance from the practitioners to consider having scores which differentiated patients further regarding specific reasons for nonadherence; however, P2 mentioned some ways this could lead to greater time economy. This eventually led to group wide agreement that more detailed information on the causes of nonadherence would be useful:

> *"Although I could see the problem group, if we can call them that, having diametrically opposite reasons for that, like [P1] said some people can't swallow tablets, some can't get to surgery, em, believe that all medicines are poisonous, you know it's completely different reasons and so you'd approach these completely different so if you could categorise those without too many categories, what your core reason is then it helps you know how to deal with them…"* (P2)

The practitioners as a group agreed that they would be happy to score the questionnaire as it is currently, although one practitioner (P6) would have preferred there to not be a middle option on the Likert scales on the questionnaires.

5.3.1.2.3 Areas for Improvement in the current tools

The practitioners noted the lack of questions regarding the cost of medicines, whether or not patients had a stockpile of medicines at home, and whether patients were having difficulties swallowing their pills. The lack of a section concerning cost was of particular concern to P4:

> *"The other thing this questionnaire doesn't address is cost of medicines. We certainly see patients who are on multiple medications [some umms of agreement from P5] who don't qualify for various benefits and they'll only take one or two or none of the medicines you prescribe, they literally can't afford them."* (P4)

Another area of importance unrepresented in the questionnaire was the possibility of over adherence and patients self-treating inappropriately:

> *"…we're reviewing all of our patients on thyroxine because of [unintelligible] anyway I found two patients that have been buying additional thyroxin on the internet."* (P6)

Another perceived omission was related to access to medications. Two practitioners (P3 and P7) were concerned that the 'occupation question' did not take into account working hours which can make it difficult for some patients to collect their medicines. A final omission of the tool was the capacity for it to be completed by someone other than the patient themselves. One practitioner (P3) noted that often patients don't necessarily have much awareness of what medicines they are taking or why and it is their partner that ensures adherence.

The practitioners found some aspects of the questionnaire to be ambiguous:

> "*21 on the, "I find it hard to get my supply of medicine" on section 2, the bottom of section 2. I don't know if you're just getting at the sort of place that they go to wherever they pick it up or the frequency with which they have to pick it up?"* (P2)
>
> *"So that's perhaps not as clear as it could be?"* (SW)
>
> *"Yeah, "do you find it frustrating to collect it monthly or about twice, six times a year" or whatever. That could be an issue. We are supposed to, as a quality measure, supply monthly quantities. Which implies someone on a long term treatment has to visit the surgery or the chemist twelve times a year and I wonder sometimes if that was me, how frustrating that would be. Would it actually be a barrier to being reliable and compliant?"* (P2)

These practitioners express frustration that they are unable to exercise their judgement regarding whether or not to allow patients to collect more than a month's supply or not, particularly when they think this may reduce patient adherence.

A second area of ambiguity concerned which doctor would be implicated if a patient indicated that they had a poor relationship with their doctor. Patient's often do not see the same doctor. Moreover, patients often see a practice nurse for routine check-ups. Consequently it was said that the questionnaire could be improved by disambiguating which doctor was referred to on the PDRQ-9, and by better representing nurse involvement.

The most critical problems perceived with the questionnaires were those that dealt with possible ethical failings:

"With the mental health scoring system, you're doing a two week window aren't you with the depression anxiety screening tool, aren't you endangering the fact you're going to get a lot of positives with the two week window that aren't actually, you wouldn't ever give them officially depression or anxiety?" (P3)

…

"That puts you in a can of worms. You don't do anything about it and next week they kill themselves. It doesn't look good." (P6)

There is a perceived risk that having a two week window for screening anxiety and depression may identify a number of healthy participants as potentially having mental illness. This will result in wasted time for practitioners. An additional concern was the culpability that might be placed upon the practice if they failed to follow up on a patient that scored highly on this scale. However, P2 later points out that they are required to collect this information anyway.

Some GPs (P3, P4 and P7) also said that the section assessing the doctor-patient relationship may make some patients uncomfortable. It was said that a "prefer not to say" option might ameliorate these concerns. An additional problem was how practitioners might respond to this information:

"What about information in the relationship you have with the patient or the patient has with you? Would you necessarily want to know if they don't like you very much? Would that impact on your relationship with the patient?" (SW)

[long pause]

"If I think it's useful." (P5)

"Difficult when people say they see different doctors. You don't know which doctor they mean when they make a comment then. You don't always see, I mean, most people try and see the same doctor most of the time but that doesn't happen for all sorts of reasons." (P4)

The long pause at the beginning of this exchange suggested discomfort on the part of the practitioners answering this question. The initial response of P5 does not directly address

the question and the response of P4 could be interpreted as defensive. The section is perceived by the practitioners as potentially threatening to both patients and themselves.

5.3.1.2.4 Patient adherence

The practitioners as a group acknowledged the importance of patient beliefs about medicines upon adherence. P2 initiated a discussion regarding the importance of understanding the patient's perspective and potential biases towards their medication. He argues that applying a single uniform strategy to all patients will not necessarily lead to adherence:

> *"I think these sorts of things are highlighted in a modern medical curriculum which is far more based upon patients expectations and ideas, not just about the condition they've got …if they haven't gained that understanding where the patients coming from with that perspective we're not going to progress with treatment full stop."* (P2)

An educational approach to help patients balance the costs and benefits of medicine was also highlighted as a method by which adherence could be encouraged by P5.

The cost of treatment and access to medicines were also considered as potential causes of nonadherence. P4 stated that there was not always a solution that could be implemented by practitioners to remedy some access problems including the limitations of rural transport and not being able to prescribe more than one month's medication at a time. Therefore collecting this information would not necessarily be useful from a clinical perspective.

5.3.1.2.5 Participation in research

P2 and P7 emphasised that they would like to see some potential for benefit of participation in research for their patient population. P4 advised that it was best to approach a partner in the surgery because they could unilaterally introduce basic research, and where research was more complicated they would still have the greater say in the decision. The potential for a personal incentive was brought up jokingly by P2:

"Any other thoughts on how to get you excited, interested or?" (SW)

"Early retirement possibly?" (P2)

[laugher]

Following this exchange P4 and P1 joined in with jokes about receiving personal incentives, but when directly asked if they would prefer researchers to offer more personal gifts P4 quickly shut down the suggestion with the support of the group. This indicated that the group saw personal incentives as improper and not an approach that should be employed.

The importance of time was again mentioned in terms of providing a barrier to participation in research by P2, P7 and P4. Staff time was considered a valuable resource and there was a desire for researchers to implement systems that would minimise time burdens and to compensate surgeries monetarily for the cost of staff time, postage or other analogous costs.

5.3.1.2.6 Perception of patients

An issue not mentioned frequently by any individual but brought up separately by P2, P3, and P7 was the issue of trusting patients to return questionnaires. In all cases the lack of trust was based upon experience of having difficulty getting responses from patients. As a potential solution the doctors note that they currently send two follow up letters to patients if no response is obtained and after that they receive a phone call.

5.3.1.2.7 Professional Autonomy

An underlying theme that reoccurred during many discussions was distaste for anything that impinged upon the autonomy of the GPs in the group. Reluctance towards questionnaire tools was heavily influenced by a perception that they get in the way of the assumed superiority of doctors to identify problems and find solutions for patients within consultations. There was a similar hostility towards the inability to dispense medicines in larger quantities to patients. The group was only willing to consider that questionnaires

might assist the doctors in making a decision or getting to know a patient after their most senior member (P2) opened up that possibility.

5.3.2 Participant Interviews

5.3.2.1 Profile of participants and their interviews

Only six participants consented for interview so all were invited. However, one participant withdrew from the project. This left a convenience sample of five participants. Table 5.5 presents the demographic characteristics of the sample alongside their scores on the PALS and WAMS questionnaire, measures of medication adherence, and medical outcome.

Participant ID	Sex	Age	PALS Score	WAMS Score	Morisky*	Retrospective Refill Rate (% collected)	Prospective Refill Rate (% collected)	Blood pressure controlled
PA	Female	68	30.9	19.3	0	100	100	Yes
PB	Male	59	32.1	8.6	1	43.3	69.6	No
PC	Male	71	22.7	15.3	0	100	100	Yes
PD	Male	84	21.5	19.1	1	63.3	100	NA[#]
PE	Female	49	22.1	23.8	1	81.4	97.8	Yes

*Morisky scores range from 0-4 with higher scores indicating a greater number of reasons for non-adherence.

[#] Participant was taking medication that reduces blood pressure, but was not diagnosed with hypertension.

Table 5.5 Interview participant demographics, adherence and blood pressure outcomes

Two participants had no indications of nonadherence (PA and PC), two participants were intermittently nonadherent (PD and PE), and one participant consistently nonadherent (PB). The consistently nonadherent participant was the only individual in the sample that did not have controlled blood pressure. Participants in the sample tended to be more nervous and eager to please the interviewer, or else more defensive when interviewed in

their own home. A brief profile of each participant and interview is contained within appendix Y.

5.3.2.2 Construction of themes from participant interviews

During the process of analysis the theme "Patient factors" was removed. There was insufficient evidence for any relevance of demographic factors. The "stress and anxiety" subtheme was moved into the "Perception of illness" theme because discussion was primarily in relation to the relationship between stress and the symptoms of hypertension. The remaining elements of the theme "Patient factors" were subthemes that were brought up by participants in a number of contexts and so are considered recurrent themes and have been moved accordingly (Ritchie et al., 2003b). The framework prior to synthesis is presented in appendix X. The final framework is presented in table 5.6.

5.3.2.2.1 Perception of medicines

Both of the participants with perfect adherence (PA and PC) stressed the importance of routine in their lives. These two participants also did not express that they found having to take medicines an imposition on their life. In contrast PB, PD and PE did. The next most adherent participant, PD, had no problem taking his morning medicines because "you have a routine", but was more likely to forget his medicine in the evening because "You're not thinking about medicines" and he found taking them at a certain time of day "restrictive". PB and PE seemed to actively resist incorporating medicines into their lives. PB did not like being dependent upon medicines, whether for a headache or hypertension. PE said she wants to have her medicines "whenever I choose to take it". She does not want an external power such as her medicines or doctor decide when she will do things.

Participants considered the positive and negative aspects of their medications. PA and PC seemed to have regular reminders for the benefits of taking their medicines. PA has friends that have had strokes and she said she wants to avoid a stroke herself. For PC the reminder was calling his medicines his "stay alive pills". In contrast PD and do not

emphasise the good health they enjoy because of their medicines but instead stress the more negative view that they would be worse without them:

> *"Well the only positive, if you want to call it a positive, is that I know that without it I can't do what, things I like doing, and probably without it my health would deteriorate. So it's an indirect positive isn't it if that makes sense."* (PB)

PB expresses the freedom provided by taking his medicines as an "indirect" benefit of his medicines. He has a negative view of his medicines impinging upon his independence which he tolerates only because they confer a net benefit to that independence via the alleviation of symptoms.

A contrast can be made between PB and PC in the way they talk about the potential unknown side effects of medicines. PC talks about thalidomide as an example of when drug companies and doctors got it wrong and prescribed medicines that did lasting harm. But he has faith that doctors and drug manufacturers get it right most of the time because "some bright guys have had a look at it." For PB the assumption was that medical advice changes all the time and he was concerned that in ten years the drugs he takes now may have been found to have a detrimental effect.

PA, PD and PE all stated that they would not stop their medicine without the permission of a doctor, with PA considering this "immoral". PA and PD said they would stop taking medicines that made them feel ill until they could see a doctor. However, PE described an experience where she kept taking her medicine until she could see a doctor even when it was making her feel ill and causing her hair to fall out. PC argued it acceptable to stop taking a medicine that makes you feel ill and that he would mention it at a routine visit to the doctor but not make a special appointment.

Theme	Subtheme
1. Perception of medicines	
	1.1 Aspects of the drug regimen
	1.2 Perception of side effects
	1.3 Positive aspects of the medicine
2. Perception of Illness	
	2.1 Role of stress as an exacerbating factor
	2.2 Perception and impact of symptoms
3. Access to healthcare	
	3.1 Obtaining a new supply
	3.2 Paying for medication
	3.3 Getting a consultation
	3.4 Literacy and understanding
4. Social Factors	
	4.1 Practical help
	4.2 Emotional Support
	4.3 Role of romantic partners
	4.4 Giving and receiving advice
5. Relationship with health care providers	
	5.1 Doctor-Patient relationship
	5.2 Trust
	5.3 Time
	5.4 Empathy and rapport
6. Participation in research	
	6.1 Perceived benefits of participation
	6.2 Perceived threats from participation
	6.3 Understanding questions and instructions
7. Recurrent themes	
	7.1 Normalisation
	7.2 Emotive responses versus rationalisations
	7.3 Social desirability
	7.4 Desire for independence v4
	7.5 Desire for information

Table 5.6 Final framework of participant interview themes

5.3.2.2.2 Perception of illness

The role of stress as an exacerbating and causal factor in hypertension was expressed by participants PB, PC, and PE. For all three participants stress was considered a potential cause of their hypertension. PB and PE both said that stress exacerbates their symptoms.

PB and PE also use the experience of symptoms as a reminder to take their medication. PA and PC do not experience symptoms of hypertension.

5.3.2.2.3 Access to healthcare

The highly adherent PA had not taken her pills at all in the week of the interview because a road closure had made getting to the surgery very difficult. PB has to travel to a different village to collect his medicines and this is something he "just has to get used to". Collecting medicines was a greater irritant for PE because she does not have a local pharmacy and considers traveling to the surgery every month to collect her prescription an unreasonable expense of time and money. She did not understand why medicines could not be posted to her or why they could not dispense more than a month's medication. Some participants expressed difficulty in getting a consultation. PE is frustrated that there is a local surgery branch that is rarely open to her. PB was frustrated because he needs to travel a lot for work so getting an appointment would require taking a day off.

The cost of medicines was seen as a potential barrier to adherence by participants. PA and PD do not have to pay for medicines but expressed concern for the potential for cost to be prohibitive for others. PB does not have a problem affording his medicines. PE was irritated by having to pay for medicine. She felt that as someone that has paid taxes she should be rewarded for that with free medication.

Participants PB and PC had no difficulty understanding written instructions. Participant PE did not discuss literacy. PA and PD expressed that they sometimes found patient information leaflets difficult to understand. PA found the language in them too technical and wished they'd "call salt salt". PD expressed that he did not seek clarification if he didn't understand the information sheet.

5.3.2.2.4 Social factors

Participants did not discuss receiving much practical help regarding their adherence. However, PA did talk about being concerned about getting her medicines if she did become ill because she is far from the surgery and her neighbour that used to help her in

this situation had moved away. She also talked about her own experiences giving help to an individual that had large stockpiles of medicines at home.

The most adherent participants, PA and PC, discussed how they remain socially active. PC said his group of friends provide a direct coping mechanism for illness and the process of aging. He talks about how whenever anyone is having a problem with illness or their medicines someone else in the group has probably had the problem before and can offer advice. He mentions multiple times about the groups use of humour to remove the anxiety from health problems. For PA engaging in varied social activities seems to be about maintaining a healthy lifestyle rather than a way of coping with new health problems. If others bring up medicines she'll talk about them but she would rather "take them and forget about them" than discuss them at length with others. In contrast PB talks about only being open with his wife, sister, best friend and preferred doctor, PD relies only upon his wife for support, and PE makes no mention of any support she receives outside of work.

All three married participants emphasised the importance of their spouses in coping with their illnesses. For PB his wife made a number of crucial interventions, first making him go to the doctor to get diagnosed with hypertension, and second making him go to the doctor after having a brain haemorrhage. PB and PD shared a reluctance to seek support from those outside of their marriage. PC, who did receive support from a wider circle of friends, still considered his wife to be the single most important source of support.

Participants PE and PC expressed how useful they found sharing their own experiences with others. PE seems to get satisfaction from directing people at work to the doctor if they have been feeling ill in ways that she recognises as similar to her experiences with hypertension. She finds it "cathartic" to help people in this way. This was important for PC too. He is particularly keen to talk to people about stress after his own experience of a "breakdown".

5.3.2.2.5 Relationship to health care providers

Participants had good relationships with at least one GP at the surgery. Particularly important aspects of the doctor-patient relationship were perceived to be trust, not feeling rushed during consultations, and the empathy displayed by their doctor. PA

discussed the changing role of the doctor. She prefers that doctors more approachable now, but misses having a relationship with a single doctor. PB and PE reported mostly seeing one doctor they felt they had a particularly good affinity with. The other three participants had preferred doctors but were willing to see any of the doctors. Some participants completed the PDRQ-9 considering the surgery as a whole (PA, PD) and some considering a specific doctor (PB, PE).

Participants PA and PD said that honesty from practitioners is essential. They wanted doctors to tell them what is wrong, what action they propose and why. For PD it was especially important that he felt like he had "a right to veto" any decision about his healthcare. PA, PB and PD all expressed the view that they were unlikely to remain registered with a GP surgery they did not like. PB also stated that if he didn't like his doctor he wouldn't have completed the questionnaire and PC said the PDRQ-9 might worry some patients.

Trust in practitioners was very high in this sample. The participants' trust in practitioners contrasted with their lack of trust in drug companies, with all five participants describing the primary purpose of patient information leaflets as "covering the back" of the drug companies in case someone were to get side effects. The participants also trusted the doctor over other information sources to know whether what they experienced was a side effect or not. PE expressed this most strongly:

> *"…I put my trust in the doctor. I think well if he says I've got to be on this then I trust his instincts to be right, I think he's the one that's qualified to know whether I'm feeling bad or not as the case may be so I leave all the trust with him."* (PE)

Here PE goes as far as to say the doctor is better qualified than she is to determine whether or not she feels bad. PD assumed his doctor will know he is experiencing side effects such as impotency without him having to tell them. Doctors were also trusted by participants over friends (PA), and the internet (PC and PE).

5.3.2.2.6 Participation in research

A common reason for participation was a desire to help the surgery or a particular doctor (PB, PD and PE). The desire to help was also present for PA who participated partly because it was a student project. PD commented that the research was interesting to

him, which was why he took part despite getting a lot of questionnaires. The opportunity to take part in research that might help others was important for PC. PB also liked the idea of helping others but admitted his motive was more selfish in terms of hoping it would be possible to stop taking medicine. A desire to contribute to improving the NHS was a motivation for PA and PD, particularly PA who considers the waste of medicines to be a waste of money that could be spent elsewhere.

For participant PC a key reason for taking part was that the process of taking part in the study and completing the questionnaire looked easy. PA and PB also said that it did not take long to complete the questionnaires. PA and PD commented that they did not find completion of questions that did not apply to them intrusive or a waste of time. PE said the questions were "very very straightforward" and "you'd have to be an idiot not to be able to answer them".

However, some problems regarding the interpretation of questions and instructions were identified. PB has longstanding concerns about side effects that do not become known until a drug has been used for a long time, and so he was unsure about how to answer the questions on side effects because he thought it was likely that he may have side effects he doesn't know about. A second problem was that while PD had no problems with the individual questions, he and his wife completed it together as a single person. This means that the responses represent a compromise of views and not his individual opinions. PE struggled to answer the question about her average weekly alcohol intake because she said her drinking habits vary from having almost no alcohol one week to three bottles of wine the next. PC said the BMQ items were difficult to answer because they were too sweeping. I.e. "Most medicines are addictive" and "All medicines are poisons" were interpreted as 'yes' 'no' answers which he did not have the relevant expertise to answer.

Some sections of the questionnaire were perceived as threatening. PC thought some might be "frightened off" by the questions on the PDRQ-9, particularly if completed face to face. PA expressed a preference for completing the smoking and drinking questions in person rather than on a questionnaire, and PC thought that people might omit or lie on this section. PC was the only participant to have any other concerns. He thought that the option to "prefer not to say" should be the first option available to participants as when placed at the end of the question it would feel like a "yes" rather than a refusal to

respond. PC also agreed with P3 from the practitioner focus group that 2 weeks would be an insufficient period of time to identify people having difficulties with mental health.

5.3.2.2.7 Recurrent themes

One theme that underpinned much of the interviews were patients' ability to "normalise" or accept their change in every day circumstances as a result of being prescribed medication or receiving a diagnosis. The participants who accepted hypertension and taking medicines most readily (PA and PC) were also the most adherent. Participants PB and PE were least adherent and most actively resisted accepting medicines as part of everyday life:

> *"…because I remember I was only like 41 I think when I started on blood pressure tablets and I kept thinking I was far too young to be on blood pressure tablets, so yeah I was toying with that quite a lot in the early days, but no not now. It's something you have to adapt to very easily and you know it's the difference between you live or die, so it's a case of you just take it."* (PE)

Here PE expresses her initial reluctance to be diagnosed with hypertension and be required to take tablets, but then expresses that she quickly adapted because of the perceived necessity of her medication. Participant PD becomes frustrated at having to take medicines about once per month. PB expressed similar feelings saying that taking medicines doesn't bother him "ninety per cent of the time". In contrast, PA she says you "just take them and forget about them". The process of normalisation goes beyond just medication adherence, with PC using his group of friends to adapt to illness. He talks about having to get used to getting older and accepting that you are no longer "fireproof". Another expression of this tendency is PD's normalisation of his side effects. His medicines make him dizzy every day and he has become accustomed to the loss of sexual function even though this was initially troubling.

A related tendency was for participants to respond emotionally in the first instance then to engage in an active decision making process. Few participants responded favourably to having to take medicines in the first instance, but considered the advantages and decided to take their medicines. PA and PC had methods of supporting a regular reappraisal of the

benefits of taking medicine via knowing people that had experienced strokes, discussing experiences with friends, or calling medicines “stay alive pills”.

A theme that was present in the interviews of PA, PD, PE and especially PB was a desire to maintain independence. For PA, PD and PE this was expressed in terms of doctors explaining fully what they were advising and why. PE refuses to set alarm clocks or keep medicines next to the bedside because she does not want to feel restricted by her medicines even though she suggests that these techniques might help her to remember her medicines. The independence theme largely defined the interview with PB. He aims to balance the benefits from his medicines with not feeling he is dependent upon them. Despite this PB continues to take propranolol even though both he and his doctor consider this to have a nominal effect and to be primarily only for reassurance.

The desire for information was a common theme; PA, PD, and PE wanted their doctors to fully explain the reasons for any recommendations. PA said that information exchange was a way to build rapport between doctor and patient. Participants also sought information about their illness from other sources, such as their friends, patient information leaflets, and the internet. However, none of these sources were trusted to the same extent as the doctor.

A final theme that could impact upon the interpretation of data from both questionnaire and interview was the differing extents to which participants tried to present themselves in a socially desirable light. In most of the interviews instances of this were fleeting and unlikely to have impacted heavily upon the results. For example, PA felt compelled to go and fetch a glass to show how much alcohol she drank to assure the interviewer that she did not drink to excess. For PB there might be a suggestion that he felt uncomfortable talking about his nonadherence because he claimed in the interview to be “98%” adherent when this would appear impossible from his medication refills. The desire to be seen as helpful was a persistent theme in the interview with PE both when discussing her participation in the research and when discussing how she enjoys referring co-workers to the doctor when they describe symptoms similar to her own.

5.3.2.3 Triangulating participant survey and interview data

Participant demographic data collected via PALS is assumed to be correct, except in the case of PE who had split up with her partner between completing the survey and conducting the interview. All other sections of PALS and WAMS have their responses cross referenced with interview testimony.

5.3.2.3.1 Health literacy

Participant PA indicated that she sometimes struggled to understand medical terminology in interview, but indicated that she never needed to ask for help on the PALS. PB also indicated that he had no difficulty understanding patient information leaflets contained with his medication in interview, but indicated that he often had to ask for help reading medical information on PALS. The difficulty PD reported in understanding literature was detected on the health literacy screen. No other participants mentioned any difficulties and none were reported on the PALS.

5.3.2.3.2 BMQ-General subscale

The BMQ general subscale validates PA's opinion that skipping medicines is immoral, where she strongly disagrees that people should stop their treatment every now and again. However, she otherwise portrays a largely negative view of medicines. However, four responses indicate "uncertain" rather than actual negative views. Uncertainty was also expressed by PB. Otherwise participant responses on the BMQ accurately represented the generally positive views expressed by PC, PD and PE and the more negative views of PB.

5.3.2.3.3 Mental health and behaviour

Only PC reported ever having had a past diagnosis of mental illness, which was corroborated during interview. No participants gave any indications during interview that the volume of alcohol consumed reported upon the PALS was inaccurate.

5.3.2.3.4 Morisky Adherence Scale

Participants PB, PD and PE did report forgetting to take medicines in interview and this was identified by Morisky. PA and PC identified as perfectly adherent on Morisky. Pc confirmed he always takes his medicines. PA did report sometimes skipping evening doses but this was rare and in the context of her perfect refill rate adherence this not being identified by Morisky seems reasonable.

5.3.2.3.5 Mental wellbeing and happiness

PA and PC did not describe experiences of stress during interview or on the PSS-4 or PHQ-5. The stress described at work as well as the breakup of her marriage was reflected in the responses on the PSS-4 and PHQ-5 provided by PE. However, PD expressed some concern about the health of his wife and the severity of his condition during interview which was not reflected on the PSS-4. PD also stated during interview that he felt these items did not apply to him. However he ticked “never” for all items, when for two items this indicated a greater amount of stress. PB indicated that he experiences stress during interview, though the only item which indicates a significant amount of difficulty on the PSS-4 or PHQ-9 for this participant was the question “In the last month, how often have you felt things were going your way” to which PB replied “never”.

5.3.2.3.6 Patient concerns about medications

Participants PC, and PD were adequately represented by the concerns scale. Participant PE contradicts herself by saying she has no side effects in interview, but indicated that she was uncertain on the questionnaire. Participant PA indicated that she was uncertain if she should stop taking medicine when she has side effects. From interview this uncertainty may be caused because she thinks it is only sensible to stop if you intend to see the doctor to solve the problem. Participant PB indicated that he disagreed that he was experiencing side effects, but during interview expressed concerns about the long term effects of medicines.

5.3.2.3.7 Medication necessity

All participants indicated that they found their medications to be necessary via WAMS. These sentiments were expressed during interview.

5.3.2.3.8 Self-efficacy

The scale accounted for the occasional forgetting by participants and that they all expressed an ability to cope with taking their medicines during interview. Only PA gave counter intuitive responses in this scale by indicating that she could not cope with her medicines when no such difficulties were reported during interview, and she has very high adherence.

5.3.2.3.9 Social support

All participants indicated that they had good social support via WAMS, and this was also indicated during interviews. The exception may be PE who made no mention of social contacts outside of the workplace but her survey results are confounded by the breakup of her marriage. However, while PB and PD receive social support from a very small network in comparison to PA and PC. The size of the social support network is not well accounted for on the current questionnaire. PA indicated that she is concerned how others will react if they knew what medicines she took. This concern was not clearly articulated during interview, although she did say she preferred to not talk about her medicines.

5.3.2.3.10 Access to medications

The difficulty PE had getting her medicine was reported on the WAMS. However, the occasional difficulties PA had obtaining her medicines were not identified, though this may be due to the rarity of those events. The minor difficulties expressed by the remaining participants in collecting medicines were represented on the questionnaire.

5.3.2.3.11 Provider relationship

All participants indicated that they had a good relationship with at least their preferred doctor at the surgery and this was reflected on the WAMS. PC scores “agree” for all items on the PDRQ-9 and this may reflect his opinion that the quality of the doctors at the surgery is variable but generally good, and so he has avoided extreme scores. PE expressed her mixed opinion of the doctors in the surgery by indicating “uncertain” for the first item on the scale, with a note to say “Depends on which doctor” and then marked her scores so as to indicate the remainder of her responses were applicable to her preferred doctor only.

5.3.2.3.12 Triangulation summary

Overall the PALS and WAMS accurately reflected the perceptions of participants as expressed during interview. However, the PSS may not be sufficiently comprehensive, and participants understanding of side effects and how these should be managed may be more nuanced than can be detected upon a questionnaire. These findings stress that while the PALS and WAMS may be useful for identifying areas of concern for patient adherence they should be used to guide but not replace physician consultations.

5.4 Discussion

5.4.1 Incorporating questionnaires into clinical practice

The findings of this study indicate that doctors and patients see value in a questionnaire that can be used to improve adherence, and that participant views were predominantly accurately represented by the questionnaire. However, there was reticence on the part of doctors to incorporate questionnaires into routine practice. Questionnaires are perceived to stunt consultations, be time consuming, and be inferior to professional judgement. The best methods to combat these perceptions were to have a method of delivery pre-consultation that required minimal staff time in the practice and which allowed a questionnaire to guide a consultation rather than dominate it. Scoring and interpretation should be simple to indicate clear solutions. Items which address patient forgetting, dysphasia, stockpiling, and prescription augmentation via OTC medicines or the internet were seen as important problems that could easily be fixed if practitioners were aware of them. However, only forgetting is currently assessed on the current questionnaire. Mandatory collection of data for QOF assessment was a key motivation for practitioners to complete questionnaires. This validates the strategy of incorporating items already required for QOF assessment in order to increase uptake of the questionnaire and to make collection of this data simpler for GP surgeries.

5.4.2 Beliefs about medicines and adherence

The beliefs measured on the BMQ general scale were seen as relevant and useful for informing a consultation with a patient. Benson and Britten (2002) conducted a qualitative study of nonadherence to anti-hypertensive medicines and identified general negative beliefs about medicines as being important. However, they did not have the capability in their study to compare participant testimony with actual adherence behaviour or with responses on a questionnaire. In this sample it was shown that the general negative beliefs about medicines expressed by PA did not result in nonadherence. However, her interview and responses on WAMS indicated few concerns with her antihypertensive medicines specifically. Adherence to medications can fluctuate within

individuals depending upon medication (Krigsman et al., 2007). This indicates that more direct beliefs about specific medicines are more important for predicting adherence than general beliefs (McHorney, 2009, McHorney et al., 2012). The experiences of PA support these prior findings.

A finding that has been identified in the qualitative and quantitative literature is the importance of perceptions about the costs and benefits of taking medicines (e.g. Benson and Britten, 2002, Horne et al., 1999, McHorney, 2009, Pound et al., 2005). The current sample demonstrated that most participants would rather not take their medicines but had decided that taking them was sufficiently important to overcome this dislike. This decision took place rapidly after the initial prescription was made, and occurred for all participants whether they were adherent or not. However, it has been suggested that adherent patients are more likely to take their medications for granted, and that only patients that are opposed to taking medicine need to continue to consider the costs and benefits of their medicine (Britten, 1994). This study replicated this finding but has been able to demonstrate that patients that incorporate medicines into their daily routine did have higher adherence than those that continue to resist having to take medicines. Therefore, an initial assessment of necessities and concerns may be essential for the initiation of adherence but continued deliberation of the costs and benefits may have a detrimental impact.

As well as taking their medicines for granted, the two most adherent participants received frequent reminders about the benefits of adherence. Participant PA had frequent exposure to the negative effects of stroke, and PC talked positively about his pills frequently with friends. These experiences may serve to motivate continued adherence via easing the recall of the benefits of hypertension medications (Tversky and Kahneman, 1973, Chen and Chaiken, 1999). The interaction between affective and heuristic cognition versus deliberate thought should be explored more thoroughly in future studies of adherence.

5.4.3 Stress, adherence and hypertension

The experience of symptoms and stress were very closely associated for the less adherent participants PB and PE, with both participants using the experience of symptoms as a

reminder to take medication. This belief has been shown to be widely held despite the relationship between the experience of stress and raised blood pressure being weak (Marshall et al., 2012). This could lead to patients taking hypertension medication to alleviate stress instead of addressing the underlying stressor which could have a direct detrimental impact upon physical health and generate predispositions toward unhealthy behaviours (Steptoe, 1991). An additional concern with patients associating their illness with felt symptoms is that research in asthma has indicated that the belief that a disease is only present when symptoms are felt is associated with lower adherence (Halm et al., 2006). Thus relying on symptom expression to maintain adherence could lower patient outcomes.

5.4.4 Patient information

The importance of information provision to patients was also highlighted. Individual patients have differing requirements for how much information they desire, and meeting those requirements may improve adherence (Weinman, 1990, Horne et al., 2001). Provision of information was the primary means by which the practitioners in this sample sought to improve adherence. Despite this, there are currently no items on the questionnaire which assess how well patients feel they have adequate information to make an informed choice about taking their medicine.

5.4.5 Questionnaire refinement

Both the practitioners and one participant had concerns about using a two week window to assess anxiety and depression. It was perceived that this would produce false positives which could waste practitioner time. However, while the PHQ-5 uses a month long screening period, the PHQ-9 recommended by the NHS for QOF uses a two week window (NHS Information Centre, 2012). A two week duration of symptoms is also required for a diagnosis of depression according to the DSM-IV (American Psychiatric Association, 2000). One way to ameliorate the controversy and facilitate using QOF questionnaires to improve questionnaire uptake would be to incorporate the full PHQ-9. This may appear

more familiar to doctors, and the extra items will reduce the likelihood of false positives by making extreme scores less likely.

Only the item “In the last month, how often have you felt things were going your way” on the PSS-4 was able to represent the stress described by PB. This might reflect the importance of feeling in control to this participant. The other three items on the PSS all address participant’s ability to control or deal with problems they face. PB may respond that he is in control because he perceives of himself as someone that is in control, but it is only when asked whether that perceived control is producing positive results that the experience of stress is identified.

The PDRQ-9 measured aspects of the doctor-patient relationship considered important by participants, however, both practitioners and patients were uncomfortable with this section of WAMS. There was also a mix of responding styles between patients with some rating an individual doctor and some the surgery overall. The scale as modified also does not sufficiently take into account the role of nurses in chronic illness management. This discomfort on the part of participants may partially explain the low response rate for the questionnaire. Participants also said that they would not stay at a doctor they did not like, and some chose to respond based upon an individual doctor they did like if they did not approve of all GPs at the surgery. The ambiguities in interpretation, the potential effect upon response rate, and the discomfort with the information expressed by practitioners suggest this scale should be omitted from future version of WAMS.

The items addressing smoking and drinking were perceived as likely to reduce response rates and produce false or inaccurate information. However, smoking and drinking behaviours are reliable indicators of adherence and also serve as a motivation for the uptake of the questionnaire in primary care because they are required for QOF assessment. Therefore, comparing the response rate of WAMS with the section removed and with a “prefer not to say” option is advocated.

Participants had difficulty interpreting some questions on the BMQ-General scale. Participants used the “uncertain” option frequently and one participant stated they did not consider themselves qualified to answer the questions. However, the practitioners stressed that this section would be useful for informing consultations with patients. Consequently negotiating rewording with the authors of the scale to improve the wording

of items or else developing a new scale which seeks to assess similar content is recommended.

The section on access to medicines could be expanded. Cost of medicines was identified as a potential cause of non-adherence by both practitioners and patients. Participant PE also indicated that willingness to pay may be a separate factor to ability to pay. It was suggested that difficulty in getting access to a new supply of medicines should be considered separately to difficulty with the frequency of requiring a new supply of medicines. However, there was also reluctance on the part of the practitioners to identify problems that they could not solve. Expanding the access section beyond cost may not be productive, and individual access problems can be discussed in consultation.

Routine was shown to be extremely important to participants. It could be useful to add items regarding whether participants have a routine and whether or not they find taking medicines restricts their freedom.

Participant PA indicated that the current item regarding health literacy may confound social support and health literacy. This participant lived alone and this might have been a factor in their stating that they "never" have help reading health materials when during interview she stated she finds PILs difficult to read.

The item "If my medicines are making me feel worse than my illness, I think it makes sense to stop taking it for a while" is ambiguous. This question as phrased does not make it clear whether or not a patient should agree or disagree to this statement if they think they should stop if medicines feel worse but only if they then plan to seek a consultation to discuss this with their doctor.

Participants PB and PC expressed concerns regarding the long term effects of medicines. The concerns scale could be expanded to consider these beliefs as well as the felt experience of side effects.

Having both positively and negatively worded items caused confusion for some participants. PD said during interview that the section on stress did not apply to him, but scored maximally at risk for nonadherence for the negatively worded items on the PSS-4 which might indicate that he had ticked the wrong box. Similarly PA is very adherent and gave no indications during interview of struggling with her medicines but ticked the box to indicate that she could not cope with the number of medicines she has to take on

WAMS. The most likely explanation is that the switch from positive to negative wording confused her. Outside of pre-validated scales, it might be advantageous to reword questions to be all positively or negatively worded to reduce the probability of respondents making errors of this kind.

5.4.6 Opportunities for further study

The role of social network size on adherence requires further study. All participants received emotional support from at least one other individual, or from colleagues at work. One proposed mechanism for this relationship is that higher social engagement increases self-efficacy (Berkman et al., 2000). Regular social activity, particularly in the elderly has been shown to increase self-efficacy and promote engagement in healthy activities. The comments from the adherent patients within this study suggest plausible mechanisms for this increase in self-efficacy. Participant PC's friends would often discuss their problems in order to reduce how threatening they seemed. The use of humour seemed especially important and could be explored further. Participant PA did not like to discuss her illness. However, her regular activities may give her an identity other than as a "sick person". A phenomenological study has indicated that not defining yourself by your disease can lead to acceptance and improved adherence (Tilden et al., 2005). This hypothesis requires further study.

Practitioners liked the idea of using technology to deliver questionnaires in order to improve response rates and automate data collection. The evidence is not strong that the use of technology would increase response rates, with e-mailed questionnaires having especially low response rates (Sheehan, 2001). However, the difference in response rates between mail and e-mail surveys may be reducing (Shih and Fan, 2009), and additional options for deployment such as smartphones are being developed (Millar and Dillman, 2012). The advantages and disadvantages of utilising these technologies require continued study.

The reluctance of participant PB, who had a strong dislike of taking and relying on medicines, to stop taking a medication he and his doctor acknowledged was having no effect upon his health. This represents a waste of NHS money and an unneeded restriction upon the patient's routine. The endowment effect refers to the tendency for

individuals to place greater value on properties that they own than they would ascribe to the same property if they did not own it (Thaler, 1980). This loss aversion could explain the choice to keep taking medicine even taking medicine is generally resisted. No prior studies into this effect have been identified.

5.4.7 Limitations

The primary limitation of this study was the low consent rate which enforced a convenience sampling method. Participants are therefore unlikely to be representative of the wider population. Additionally, deliberately selecting a heterogeneous sample to ensure conceptual breadth was not possible. However, the sample was heterogeneous in terms of adherence, age, social support, and beliefs about medicines. Only mental wellbeing and relationship to providers were mostly homogenous in the sample so the lack of deliberate sampling may not impact heavily upon the conclusions that were reached. However, the sample had very little heterogeneity in social class, and issues of access to medicines in terms of cost and transport may be very different to those experienced in urban populations.

When participants were interviewed in their own home they tended to be more prone to presenting themselves in a socially desirable light. This effect was particularly pronounced in the two female participants. This may be related to the discomfort participants in interview feel when interviewed in their own home, and a third, neutral location may have reduced the impact of self-presentation biases (Elwood and Martin, 2000).

Regarding the practitioner focus group a particular limitation was that the practitioners had not read the questionnaires before the session as instructed. This meant that the flow of the focus group was impacted due to a lack of familiarity with the materials required for the session. As a consequence practitioners were required to frequently refer to the written material rather than engage freely in discussion about it. In itself that the questionnaires were not read is a useful result in terms of highlighting the premium healthcare practitioners place upon their time and their reluctance to engage in non-essential tasks. Nonetheless the session was able to meet the objectives of exploring practitioner perceptions of the questionnaires clinical utility, patient acceptability and optimising practitioner time for research.

5.4.8 Conclusion

This chapter has built upon the quantitative assessment of the PALS and WAMS in chapter 4 and presented additional opportunities to improve the tools for future use. Methods for increasing the probability of GPs incorporating the questionnaire into regular practice have been identified. Potentially important omissions, confounds, and ambiguities in current questions have also been highlighted. Importantly, the qualitative treatment has provided a richer understanding of how the indicators identified via meta-analysis in chapter 2 such as stress and beliefs about medicines interact with patients' experiences of illness and medicines to influence adherence.

Chapter 6 – General Discussion

6.1 The necessity of the current work

Chapter 1 highlighted the need for a new clinically useful measure of nonadherence. Physicians predominantly overestimate the probability that their patients are adherent and so may fail to attribute treatment failure to nonadherence, an additional and greater concern is that physicians may underestimate adherence and so not prescribe potentially valuable therapy (Paterson et al., 2000). Existing measures for nonadherence are not adequate for improving the accuracy of physician estimates. The scales overestimate adherence by asking direct questions about adherence which introduces social desirability biases (Guénette et al., 2005, Paterson et al., 2002). Moreover, existing scales either lack clinical utility by failing to identify targets for intervention to improve nonadherence (Morisky et al., 1986a, McHorney, 2009), or else have significant psychometric weaknesses such as sections that have not been validated (Svarstad et al., 1999), poor internal consistency and criterion validity (George et al., 2006), or have ambiguous structure due to an incomprehensive description of test construction (Hahn et al., 2008). The stated aim of this thesis was therefore to develop a new tool which could predict the likelihood of nonadherence to medication and help clinicians to identify patient specific interventions to mitigate risk factors for nonadherence.

6.2 Identified indicators of adherence

A barrier to achieving the aims of the thesis was that existing models of adherence fail to identify the antecedents of the beliefs that contribute to adherence behaviour; and knowledge of these is required in order to inform interventions (Weinstein, 2007). Moreover the models often explain only a small proportion of adherence behaviour and so cannot be said to be comprehensive (Chisolm et al., 2010). In order to develop a new questionnaire, the indicators of adherence were therefore identified via a quantitative review. By searching for all indicators of adherence with a demonstrable relationship with adherence and not only those with the strongest relationships both proximal and more

distal variables could be identified. This helps to ensure that the questionnaire was comprehensive and able to inform clinical decisions.

This review revealed that the adherence literature is vast and poorly coordinated. The majority of identified studies did not define adherence, over a third did not provide information regarding how they divided participants into adherers and nonadherers, and most developed their own measure of adherence particular to the individual study. The lack of consistency and quality of medication adherence measurement made providing any accurate assessment of the size of the relationship between any indicator and adherence challenging. There is therefore a desperate need for consistency of definitions, methods, and measurement in adherence research (Vermeire et al., 2001, Kyngäs et al., 2000). In an attempt to foster greater consistency across the adherence literature, the discrepancies in definition prevalent in the current literature have been quantified and a standardised taxonomy of adherence proposed (Vrijens et al., 2012).

Despite the lack of coherence in the literature, a number of indicators were reliably associated with adherence. These included patients' engagement in risky health behaviours, quality of life and mental wellbeing, beliefs about medicines, self-efficacy, barriers to medicine taking and acquisition, social support, the relationship patients have with their healthcare providers, and health literacy. It was also considered that these variables may be amenable to intervention. Previous reviews have identified that education about the benefits of medicine, reducing the difficulty of taking medicines, using peer or family support, stress management, and skill building or routine management can all help to improve adherence (Demonceau et al., 2013, Haynes et al., 2008). This suggests that the identified factors could have clinical utility as well as the property of being able to identify patients at risk of nonadherence. Therefore it was decided that the new adherence questionnaire should measure these variables.

6.3 Incorporating identified indicators into an adherence measure

Practitioner consultation to optimise clinical utility identified that brevity is of paramount importance both to reduce the burden placed upon patients, but also to facilitate rapid decision making (Spitzer et al., 1999). The use of existing scales was also perceived as likely to improve acceptability to GPs and the use of previously validated scales also

streamlines the questionnaire development process. As a consequence, two new questionnaires were composed, where possible comprising of existing scales which measured the constructs identified as associated with adherence. Splitting the questionnaire into two sections was expected to reduce the burden of questionnaire administration for both patients and medical personnel and therefore allow the new questionnaires to optimise comprehensiveness with pragmatism (Chipperfield and Steel, 2011).

6.4 Quantitative appraisal of the PALS and WAMS

Despite a small sample size it was possible to discern some aspects of the questionnaire which had associations with adherence. Health literacy was an indicator of both refill and self-reported adherence. If health literacy is considered a proxy for a patient's ability to seek and comprehend information about their illness and medicines, then the cause of the strong association identified could be related to the study participants having above average adherence. It has been demonstrated that patients are more likely to seek information that confirm prior hypotheses, and are not generally able to develop searches that would also present information for alternative hypotheses (Kayhan, 2013). Thus patients with high health literacy may be more able to seek information that reinforces their own positive view about medicines. This could account for the more variable association between health literacy and adherence identified elsewhere (Loke et al., 2012) because for samples which incorporate patients with a more negative view of medicines or illness, health literacy may promote identification of information that reinforces nonadherence.

Stress, anxiety and depression were also identified as predicting self-reported and prospective adherence. It has been proposed that depression may negatively impact upon adherence because belief in the positive efficacy of treatment is diminished (DiMatteo et al., 2000). It is plausible that subclinical mental distress has a similar impact upon adherence. Measuring how stressed, anxious, or depressed patients are could be interpreted as estimating the extent of negative bias introduced into appraisal of medicines through the affective stream of the parallel response framework (Leventhal et al., 1992). This hypothesis is supported by the finding that that general stress, but not

disease specific stress, mediated adolescent adherence to diabetes medication (Farrell et al., 2004). Disease specific stress may augment the cognitive perception of the necessity for one's medicine while general stress and a lower quality of life may inhibit the perception of benefit from medicine (DiMatteo et al., 2000, Farrell et al., 2004). One of the core benefits of medicinal therapy for patients is the restoration of quality of life (Erlen and Mellors, 1999), and so optimising patient quality of life would bring the aims of practitioners and the aims of patients closer together (Pollock, 2005). Regular monitoring and early intervention to prevent deterioration of patient mental health has been advocated (Watson et al., 2011).

6.5 Qualitative appraisal of PALS and WAMS

In chapter 5 a group of practitioners were consulted to appraise the clinical utility of the scale. Practitioners stated that they thought the key to improving adherence was to educate their patients about the benefits of their medicines. However, all interviewed patients stated that they felt that the benefits of their medicines outweighed the costs whether they were adherent or not. Recent evidence from a meta-analysis has suggested that the benefits of cognitive interventions to improve adherence become smaller as the duration of the study increases (Demonceau et al., 2013). Similarly, Haynes et al. (2008) found that interventions to increase adherence were more successful for short term treatments than for chronic conditions. These findings suggest that cognitive appraisals may be more important soon after initiation of a new medicine. This could explain why the perceived importance of a medicine has been shown to be critical for primary adherence (Jackevicius et al., 2008, Williams et al., 2007b, Beardon et al., 1993), and why the rate at which patients become nonadherent is much more rapid in the first six months of therapy (Chapman, 2004). Moreover, a study directly comparing the importance of habit versus appraisal for long term adherence found habit to be the stronger indicator, particularly for long term adherence (Phillips et al., In press). However, all patients will continue to hold positive and negative beliefs about medicines, and these beliefs will both cause and be caused by behaviour (Weinstein, 2007). Therefore patients with high adherence will report that medicine is necessary despite their concerns, while nonadherent patients may report side effects and concerns more strongly than a belief in the importance of medicine. However, these appraisals may not represent an everyday

decision making process so much as one provoked by a researcher, doctor, or in the case of one participant, a newspaper. These findings highlight the need for regular monitoring of patient perceptions of medicines, but also the necessity of investigating beyond patients beliefs about medicines and exploring their ability to incorporate medicines into their everyday life.

The importance of social support in adherence was also highlighted. In particular the key role relationship partners play in offering direct practical and emotional support to improve adherence which for some individuals they might be the only source of support available. However prior research has indicated that a wider network of social support offers greater benefits for adherence (DiMatteo, 2004b).The various ways in which social support can help improve adherence were described in chapter 5. For one participant their support network provided a distraction that prevented them feeling defined by their illness, which has been tentatively linked to improved adherence (Tilden et al., 2005). For another, the role of the support network was to provide direct reassurance and information, and help to maintain an optimistic outlook (Berkman et al., 2000). Thus the role of social support for two adherent individuals appeared very different. There has also been evidence to suggest social support does not have a universally beneficial effect upon adherence. Warner et al. (2013) performed a longitudinal study of the effect of social support upon adherence in older individuals and found that general social support had no effect upon adherence while medication specific social support had a negative effect upon later medication adherence. The study also found evidence that the cause of medication specific social support lowering adherence could be explained by social conflict. This proposes that unwanted social support that reduces an individual's sense of autonomy may have a negative impact upon adherence. This account would fit with the resistance of some participants to receive support from outside their marriage and unwillingness to talk to others about their medical condition. However the present analyses were not designed to answer this specific question. Focussed qualitative studies exploring the ways in which patients utilise social support to manage their medicines and illness may identify the ways in which wanted and unwanted social support is sought and managed which could help to develop theory which could facilitate the design of group interventions involving a wider support network to improve adherence.

Interviews with patients also highlighted that modern healthcare is characterised by a lack of continuity in care; with patients receiving treatment from multiple GPs and nurses as part of chronic illness management. The quality of relationship between patients and different healthcare practitioners is also variable. Adherence is related to both the quality of the relationship patients have with their practitioners, and congruence between patient and practitioners interpretations of illness and treatment (Leventhal et al., 1992, Arbuthnott and Sharpe, 2009). Evidence from chapter 5 indicated that the disclosures made to practitioners may differ depending upon the quality of the doctor-patient relationship. Therefore, in a multi-personnel, multi-disciplinary healthcare framework, standardisation of information retrieval via objective measures such as the PALS and WAMS could help to ensure quality of care for all patients.

Participants and practitioners alike discussed the importance of honesty from medical practitioners when discussing the impacts of diagnoses and treatments with patients. However, there was a perceived reluctance on the part of participants to talk about some topic with their doctors. It was thought that some patients might lie to their doctors about their smoking and drinking habits, and disclosing information to the GP was one reason for non-participation amongst those invited to complete the PALS and WAMS. It is suggested patients are uncomfortable talking about unhealthy behaviours because they are wary of being stigmatised by their doctors, particularly in older patients (Simmons et al., 2009). Moreover doctors are also reluctant to discuss these topics with patients (Mules et al., 2012, Noordman et al., 2010). Therefore for doctors to be able to learn about behaviours patients may be reluctant to discuss, such as smoking, drinking, or nonadherence, they need to be able to foster non-judgemental relationships with their patients. In particular the qualitative study found that some participants were only comfortable discussing their health with a preferred doctor. Thus participants expressed a desire to have a genuine relationship with their medical practitioners based upon trust. This is one motive for the concordance initiative (Marinker, 2004). While it has been questioned whether all patients desire a concordance model of health care (Kettunen et al., 2001, Levinson et al., 2005), fostering relationships with patients where doctors are not seen to pass judgement may promote greater disclosure on the part of patients.

6.6 Future development of the questionnaire

An important first step in any future development of the PALS and WAMS is negotiation with copyright owners of the utilised scales to extend permissions for use beyond the current investigation. This is a particularly pressing concern should future development seek to profit financially from any use of the PALS and WAMS. Some questionnaire authors may prefer to have their work kept in the public domain while others may prefer to retain the right to control when and by whom their questionnaire is utilised, and these different positions will need to be consolidated before the scales are utilised further.

A weakness of the appraisal of the PALS and WAMS was that a sample size suitable for full psychometric testing was not obtained. While the intention of chapter 4 was primarily to identify potential weaknesses in the research method and ensure feasibility, and while other questionnaires have been successfully implemented having been tested on similarly small samples (Svarstad et al., 1999), the small sample size obtained severely restricted the confidence with which statements regarding the performance of PALS and WAMS could be made. Before further refinement of the PALS and WAMS is undertaken there therefore needs to be revisions made to the proposed testing methods.

The first recommendation is to significantly expand the extent of face and content validity testing. Chapters 4 and 5 both identified some unease on the part of participants to complete sections of the questionnaire, as well as instances in which questions where there were possible ambiguities in interpretation. This included items on the BMQ general scale and the PDRQ-9. Therefore it would appear worthwhile to engage in cognitive interviewing of the full PALS and WAMS scales with both patients and health care workers in order to fully explore the different potential meanings of items with participants (Ericsson and Simon, 1993, Hernandez et al., 2011, Willis, 1999, Willis, 2005). Any required changes to existing scales could be negotiated with existing authors.

Having determined acceptability and comprehensibility via this step there would be considerably less risk in trialling the revised questionnaire on a larger sample size. Testing at multiple sites should negate the risk of procedural problems at any one site having an overly significant impact upon total sample size while also allowing for greater claims of generalisability. Similarly, it could be advantageous to test the PALS and WAMS in illnesses beyond hypertension to establish validity across disease states as was performed during the validation of the BMQ questionnaires (Horne et al., 1999). This approach is

preferred to the use of the internet to achieve a wide sample as utilised by (Hahn et al., 2008) because it better represents the clinical situation in which the questionnaires would be deployed, and it permits the collection of patient outcome data.

In addition to general recommendations for the future design of the scales, the findings of chapters 4 and 5 have also highlighted action that could be applied to specific subscales.

6.6.1 Patient demographics: "About you"

Employment status should be expanded to account for patients unable to work because of disability. Similarly, not all possible living arrangements are accounted for and this item should be reworded so that it asks only whether or not a patient lives with their romantic partner.

6.6.2 Health Literacy: "Written information"

This item predicted adherence well, however chapter 5 indicated that the current item "How often do you ask someone to help you understand medical information?" may be difficult to answer if a person has nobody to ask for help. It is also acknowledged that given the small sample it remains plausible that health literacy may have different relationships with adherence depending upon patient health beliefs and so the factor would not remain so strongly predictive if tested in a more diverse sample. However, given the strong performance of this question for predicting nonadherence thus far, it is recommended that no changes should be made at this stage.

6.6.3 BMQ-General subscale: "Your beliefs about medicines"

Practitioners thought that the content of the BMQ would be useful with regard to planning a consultation with a patient. However, the BMQ should be tested via cognitive interviewing to identify how participants understand the items on the scale (Willis, 2005).

If significant problems are identified a new set of questions should be developed, or the current BMQ reworded with the consent or collaboration of the original authors.

6.6.4 Mental health and risky behaviours: "Your mental health and behaviour"

The item on mental health should be removed. The omission of risk behaviours might negatively impact upon the ability of the tool to predict adherence. However, this section may have lowered response rate in chapter 4. Consequently the impact of including and excluding this section on acceptability and adherence prediction should be directly measured.

6.6.5 Patient affect: "Mental wellbeing and happiness"

The PSS-4 and PHQ were used to measure stress, anxiety, and depression, and the tools should both be retained for future iterations of the questionnaire. However, the extent of the collinearity between the three constructs should be estimated. The two week window for responses on the PHQ also caused some concern for practitioners and one of the patients. To remedy these concerns swapping the PHQ-5 for the PHQ-9 as currently utilised for QOF is recommended.

6.6.6 Patient Adjustment to Medications Scale: "Adjusting to your medicines"

6.6.6.1 Concerns about medicines

The item "If my medicines are making me feel worse than my illness, I think it makes sense to stop taking it for a while" contains a conditional which should be removed. The item also asks about whether patients think they should do something, not how they actually behave which may lower accuracy (Mason, 2002). The item also asks about

adherence in a direct way which the questionnaire aims to avoid. In chapter 4 the alternative “I think my medicines make me feel worse than my illness” was suggested. Chapter 5 also indicated that the scale should be expanded to include items which consider long term concerns about the effects of medicines beyond perceived side effects.

6.6.6.2 Medication necessity

No immediate problems were identified with the medication necessity scale. However, based upon the experiences of participants interviewed in chapter 5 the scale could be expanded in scope to cover the extent to which medicines are integrated into the everyday life of patients, and not just how necessary they are deemed to be.

6.6.6.3 Self-efficacy

The items on this scale did not appear to be measuring a unitary construct. It was suggested that the question “I find it hard to remember to take my medicines each day” may be too direct an assessment of unintentional nonadherence and could be made to measure self-efficacy by changing the wording to “I am confident I can take all of my medicines each day”. However, the practitioners expressed a desire for items on the questionnaire which identified unintentional nonadherence behaviours that could be fixed with simple interventions. An alternative to expanding the self-efficacy scale is to use this section to instead determine whether patients think they find the number of medicines they take overwhelming or difficult to remember, in which case a pill box could be used to help with adherence (Petersen et al., 2007). Additional items could identify difficulties caused by dysphasia, the stockpiling of medicines, or the augmentation of prescriptions via OTC or internet purchases.

6.6.6.4 Social support

This item "I am concerned about how others will react if I tell them what medicines I take" measures social stigma of illness and not social support and should be removed. Chapter 5 indicated that there may be an important role for social network size in adherence. The social stigma item could be replaced with a question which gave an indication of the number of people in a patient's social circle. Further the scale should focus more upon support received pertinent to taking medication, and not dealing with illness. This more direct relationship may improve the ability of the section to predict nonadherence.

6.6.6.5 Access to medication

The single item in the scale predicted adherence successfully. However, practitioners felt that there were important aspects of access that were not covered. Practitioners and patients were concerned about the cost of medicines. However further expansion of the scale beyond cost risks exposing doctors to an expectation that they can change access problems beyond their control.

6.6.7 Provider relationship: "About your doctor"

Scores on the PDRQ-9 were heavily skewed toward indicating a good relationship with doctors limiting how much information is provided by this scale. Further, given the possible impact upon response rates and the potential difficulties the responses on the questionnaire may create for the doctor patient relationship it should be excluded outright from future versions of the questionnaire. This does not indicate that the patient-practitioner relationship is not considered to be important, the evidence presented has reinforced that it is a factor of high importance for medication adherence. The recommendation to remove the section only reflects the belief that this questionnaire is not the correct forum in which to explore patient-practitioner relationships.

6.7 Final conclusions

The objective of the thesis was to develop and pilot a novel clinically useful questionnaire which would help clinicians to identify patients at risk of nonadherence and help to inform tailored interventions to augment adherence. The result was the production of the PALS and WAMS questionnaires. Preliminary psychometric evaluation and qualitative validity assessment has indicated that while the PALS and WAMS could make a meaningful contribution to clinical management of adherence, further development of the questionnaires is required. Some subjects within the PALS and WAMS may be considered too sensitive for measurement via a clinical tool, such as smoking, drinking, mental health, and assessment of the patient-practitioner relationship. Further, some scales required expansion in order to improve internal consistency and clinical decision making, such as the self-efficacy scale and assessment of barriers to taking medicines. However, in the main both the PALS and WAMS were seen by clinicians and patients as potentially useful, and easy to understand.

Appendices

Appendix A – Description of studies included in meta-analyses

	Number of Studies	Per cent of Sample
Year published		
1981-1990	3	1.52
1991-2000	18	9.09
2001-2005	59	29.80
2005-2010	118	59.60
Total	**198**	**100**
Study Type		
RCT	6	3.03
Cross-sectional	95	47.98
Prospective cohort	46	23.23
Retrospective cohort	45	22.73
Before-After	4	2.02
Case-Control	2	1.01
Total	**198**	**100**
Definition of adherence		
Haynes (1979)	13	6.57
WHO (2003)	6	3.03
Studies own	38	19.19
Other	5	2.53
None	136	68.69
Total	**198**	**100**
Cut point for % pills required to be adherent		
0-79%	7	3.54
80-89%	42	21.21
90-94%	14	7.07
95-99%	18	9.09
100%	20	10.10
Unclear/Not stated	70	35.35
Not dichotomised	27	13.64
Total	**198**	**100**
Method of adherence measurement		
Direct (E.g. Blood sample)	4	2.02
Questionnaire	48	9.09

Interview	60	30.30
Refill rate	47	23.74
Pill Count	12	6.06
Electronic device	13	6.57
Multiple	10	5.05
Unclear/Not stated	4	2.02
Total	**198**	**100**
Questionnaire/Interview tools used to measure adherence		
Morisky	18	16.98
AACTG	10	9.43
Other	13	12.26
Studies own	65	61.32
Total	**106**	**100**
Adherence assessment period		
0-1 week	29	14.65
> 1 week – 1 month	29	14.65
> 1 month – 6 months	37	18.69
> 6 months – 1 year	30	15.15
> 1 Year	21	10.61
Unclear	52	26.26
Total	**198**	**100**
Disease State		
HIV	64	32.32
Hypertension	26	13.13
Other cardiovascular illness	21	10.61
Diabetes Type 1	1	0.51
Diabetes Type 2	13	6.57
Diabetes (Type not specified)	2	1.01
Osteoporosis	8	4.04
Cancers	6	3.03
Asthma	12	2.53
Renal illness	5	2.53
Arthritis	5	2.53
Tuberculosis	5	2.53

Multiple Sclerosis	4	2.02
Sleep Apnoea	3	1.52
Glaucoma	2	1.01
Cerebrovascular disease	1	0.51
Dermatological conditions	1	0.51
Inflammatory Bowel Disease	1	0.51
Migrane	1	0.51
Parkinson's	1	0.51
Epilepsy	1	0.51
Multiple/Unclear	15	5.56
Total	**198**	**100**

Appendix B - Expanded table of meta-analysis results, variables expressed via the correlation coefficient

Indicator	k	n	Median r	Minimum r	Maximum r	R[1]	R[2]	Lower C.I.	Upper C.I.	p	Q[2]	d.f.[3]	Q-p[4]	I[2]	S.E.[5]	Tau[6]
Demographics																
Increasing age	83	2079337	0·06	-0·21	0·51	0·06	<0·01	0·04	0·08	<0·001	5022·31	82	<0·001	98·37	0·01	0·08
Income	19	7657	-0·04	-0·31	0·3	0·01	<0·01	-0·05	0·06	0·208	58·17	18	<0·001	69·06	0·01	<0·01
Adherence behaviours																
Adherence to diet	4	1881	0·21	0·03	0·37	0·19	0·03	0·03	0·33	0·017	22·18	3	<0·001	86·47	0·02	0·14
Affect																
Anxiety	11	1375	-0·20	-0·48	0·16	-0·16	0·03	-0·25	-0·07	<0·001	24·60	10	0·006	59·34	0·01	0·11
Stress	12	3423	-0·17	-0·4	-0·03	-0·16	0·03	-0·23	-0·09	0·001	55·02	11	<0·001	80·01	0·01	0·10
Distress	6	885	-0·18	-0·35	-0·07	-0·17	0·03	-0·25	-0·09	<0·001	9·78	5	0·082	48·88	0·01	0·07
Hostility	3	671	-0·16	-0·35	0·04	-0·16	0·02	-0·42	0·12	0·266	23·79	2	0·001	91·59	0·07	0·24
Beliefs about medicines																
Satisfaction with medicines	5	1872	0·29	0·1	0·4	0·25	0·06	0·12	0·36	<0·001	23·50	4	0·001	82·98	0·02	0·13
Positive belief regarding medicine	6	3207	0·16	0·11	0·32	0·15	0·02	0·10	0·21	<0·001	8·32	5	0·139	39·90	<0·01	0·04
BMQ Necessity	4	622	0·34	0·11	0·44	0·29	0·08	0·14	0·42	<0·001	9·94	3	0·019	69·81	0·02	0·13
BMQ Concerns	3	622	-0·02	-0·13	0·05	-0·04	<0·01	-0·15	0·07	0·481	3·72	2	0·156	46·20	0·01	0·07
Fewer concerns (Including BMQ)	7	2783	0·13	-0·09	0·32	0·09	0·01	-0·04	0·22	0·151	39·374	6	<0·001	84·90	0·02	0·15
Knowledge																
Knowledge of medication	10	6208	0·18	-0·03	0·56	0·08	0·01	0·08	0·26	<0·001	45·83	9	<0·001	80·36	0·01	0·13
Health Literacy	4	2062	0·24	0·07	0·29	0·19	0·04	0·07	0·31	0·002	11·78	3	0·008	74·53	0·01	0·12

Appendix B - Expanded table of meta-analysis results, variables expressed via the correlation coefficient

Regimen																
Frequency pills per day	11	4482	0·014	-0·4	0·21	0·03	<0·01	-0·03	0·10	0·318	24·71	10	0·006	59·52	0·01	0·08
Longer time on regimen	12	20806	-0·08	-0·21	0·45	-0·06	<0·01	-0·12	-0·01	0·027	414·17	11	<0·001	97·34	0·01	0·07
Social Support																
Social support	22	6641	0·16	-0·2	0·61	0·14	0·02	0·08	0·20	<0·001	109·53	27	<0·001	75·35	0·01	0·13
Costs																
Cost of Medicines	10	55800	-0·08	-0·35	0·03	-0·08	0·01	-0·11	-0·04	<0·001	119·45	9	<0·001	92·47	<0·01	0·06
Total costs of treatment	4	23013	0·09	-0·13	0·18	0·06	<0·01	-0·05	0·16	0·302	30·66	3	<0·001	90·22	0·01	0·10
Provider Relationship																
Satisfaction with care	9	3336	0·17	-0·08	0·61	0·13	0·02	0·05	0·22	0·003	54·96	8	<0·001	85·45	0·01	0·11
Trust in physician	8	7263	0·19	0·1	0·31	0·16	0·03	0·12	0·21	<0·001	21·98	7	0·003	68·15	<0·01	0·05
Good communication/Relationship with Physician	13	8592	0·09	-0·13	0·35	0·10	0·01	0·06	0·14	<0·001	25·75	12	0·012	53·40	<0·01	0·05
Disease Severity																
Symptom severity	15	8460	-0·02	-0·25	0·15	-0·02	<0·01	-0·05	0·01	0·163	53·29	14	<0·001	73·73	<0·01	0·03
Duration of disease	21	15608	-0·01	-0·24	0·27	-0·01	<0·01	-0·05	0·04	0·731	60·22	20	<0·001	66·79	<0·01	0·08
Side effects																
Number of side effects	5	1394	-0·16	-0·3	-0·02	-0·17	0·03	-0·29	-0·04	0·010	29·32	4	<0·001	86·36	0·02	0·13

Appendix B - Expanded table of meta-analysis results, variables expressed via the correlation coefficient

Severity of side effects	5	3672	-0·27	-0·31	-0·2	-0·22	0·05	-0·26	-0·18	<0·001	4·11	4	0·392	2·63	<0·01	0·01
Disease Beliefs																
Susceptibility to disease	4	988	0·09	-0·07	0·49	<-0·01	<0·01	-0·23	0·23	0·975	27·95	3	<0·001	89·27	0·08	0·22
Barriers to medication																
General Barriers	8	2941	-0·28	-0·53	-0·06	-0·25	0·06	-0·36	-0·14	<0·001	45·04	7	<0·001	84·46	0·02	0·14
Good access to medical care	4	912	0·23	0·02	0·26	0·20	0·04	0·09	0·29	<0·001	4·73	3	0·193	36·53	0·01	0·06
Good access to medication	3	688	0·15	0·14	0·38	0·20	0·04	0·07	0·32	0·004	3·77	2	0·152	46·94	0·02	0·08
Mental Health																
Mental health summary scores	6	4154	0·17	-0·01	0·22	0·15	0·02	0·10	0·20	<0·001	10·15	5	0·071	50·74	<0·01	0·05
Depression	39	95192	-0·12	-0·56	0·31	-0·10	0·01	-0·13	-0·07	<0·001	162·84	38	<0·001	76·66	<0·01	0·06
Cognitive ability																
Good memory	4	441	0·14	-0·01	0·42	0·18	0·03	0·01	0·35	0·043	8·82	3	0·032	65·99	0·03	0·15
Social cognition																
Self-efficacy/Perceived behavioural control	21	9047	0·26	-0·02	0·64	0·27	0·07	0·20	0·34	<0·001	123·87	20	<0·001	83·85	0·01	0·15
Quality of Life/Wellbeing																
General QOL measures	15	5379	0·12	-0·26	0·25	0·10	0·01	0·04	0·16	0·001	40·62	14	<0·001	65·53	0·01	0·09

Appendix B - Expanded table of meta-analysis results, variables expressed via the correlation coefficient

General QOL measures, HIV only	6	1129	0·20	0·05	-0·26	0·18	0·03	0·12	0·24	<0·001	3·50	4	0·624	<0·01	0·01	<0·01
General QOL measures, non-HIV only	9	4250	0·09	-0·26	0·23	0·06	<0·01	-0·02	0·14	0·127	28·86	8	<0·001	72·28	0·01	0·10
Physical functioning	18	15175	0·10	-0·27	0·59	0·08	0·01	0·01	0·14	0·030	89·98	17	0·001	81·11	0·01	0·12
Physical functioning, HIV only.	8	1721	0·14	-0·2	0·59	0·18	0·03	0·03	0·31	0·015	47·21	7	<0·001	85·17	0·03	0·19
Physical functioning, non-HIV only.	10	13454	0·04	-0·27	0·18	0·01	<0·01	-0·05	0·08	0·175	27·38	8	0·001	67·13	0·01	0·08
Mental wellbeing	7	1942	0·06	-0·08	0·15	0·06	<0·01	-0·01	0·13	0·115	12·18	6	0·058	50·74	0·01	0·07
Personality																
Locus of control																
Internal LOC	3	485	0·07	-0·01	0·41	0·13	0·02	-0·07	0·32	0·203	8·79	2	0·012	77·25	0·03	0·16
Coping style																
Active	4	536	-0·04	-0·31	0·1	-0·03	<0·01	-0·13	0·07	0·554	8·00	3	0·146	62·51	0·01	0·08

Appendix C - Expanded table of meta-analysis results, variables expressed via the Odds Ratio

Indicator	k	n	Median OR	Minimum OR	Maximum OR	OR[1]	Lower C.I.	Upper C.I.	p	Q[2]	d.f.[3]	Q-p[4]	I^2	S.E.[5]	Tau[6]
Demographics															
Black vs Other races	6	40263	0.51	0.43	0.96	0.60	0.46	0.78	<0.001	8.74	5	0.120	42.77	0.07	0.20
White vs black	13	1954297	1.46	0.20	4.38	1.43	0.96	2.14	0.081	1360.30	12	<0.001	99.12	0.55	0.69
White vs. Hispanic	6	1892707	1.38	0.13	3.43	1.12	0.79	1.59	0.522	25.53	5	<0.001	80.42	0.13	0.35
White vs non-white	12	6901	1.74	0.30	5.00	1.38	0.94	2.01	0.098	59.05	11	<0.001	81.37	0.22	0.54
White vs other	9	1947200	1.16	0.18	2.33	1.20	0.83	1.75	0.327	728.02	8	<0.001	98.90	0.28	0.48
Sex (Female vs male)	68	2167404	1.00	0.36	3.82	0.99	0.93	1.05	0.665	420.30	67	<0.001	84.06	0.02	0.15
Education (all)	48	48321	1.15	0.19	10.60	1.14	0.94	1.39	0.176	367.87	47	<0.001	87.22	0.15	0.59
Education (college education vs none)	25	42361	1.18	0.23	10.60	1.15	0.86	1.54	0.345	230.30	24	<0.001	89.58	0.24	0.65
Employment (yes vs no)	14	5661	1.12	0.41	4.33	1.32	1.01	1.72	0.045	47.14	13	<0.001	72.42	0.11	0.41
Health insurance (Yes vs No)	7	3118	1.12	0.25	2.40	1.08	0.69	1.69	0.734	16.81	6	<0.001	64.31	0.21	0.47
Health behaviours															
Smoking Yes/More vs No/Less)	15	151636	0.67	0.32	1.40	0.71	0.63	0.80	<0.001	24.52	14	0.040	42.91	0.02	0.12
Alcohol use	11	4449	0.77	0.36	0.99	0.66	0.53	0.81	<0.001	7.23	10	0.704	<0.01	0.57	<0.01
Problem alcohol use	7	10351	0.64	0.30	0.86	0.47	0.35	0.63	<0.001	7.61	6	0.268	21.13	0.09	0.18
Drug use	11	2862	0.48	0.14	0.92	0.52	0.40	0.67	<0.001	17.04	10	0.073	41.32	0.08	0.26
Complementary medicine use	3	2334	0.59	0.35	1.26	0.68	0.34	1.34	0.261	23.30	2	<0.001	91.42	0.40	0.56
Beliefs about medicines															
Effectiveness	6	1607	2.70	0.77	5.18	2.24	1.12	4.49	0.022	25.37	5	<0.001	80.30	0.50	0.73
Fewer Concerns about medication (independent of BMQ)	4	2161	2.04	0.69	3.40	1.68	0.75	3.79	0.208	29.90	3	<0.001	89.97	0.66	0.75
Fewer concerns (Including BMQ)	7	2783	1.61	0.69	3.40	1.41	0.88	2.25	0.158	37.43	6	<0.001	83.97	0.26	0.56
Knowledge															
Knowledge of illness	8	2945	3.04	1.15	7.89	2.49	1.55	3.98	<0.001	53.23	7	<0.001	86.85	0.31	0.59
Regimen															
Number of co-medications	4	24204	1.05	0.78	1.25	1.00	0.79	1.27	0.987	36.97	3	<0.001	91.89	0.06	0.22

Appendix C - Expanded table of meta-analysis results, variables expressed via the Odds Ratio

Different types of medicines per day for condition	14	180468	1.04	0.16	3.43	0.98	0.70	1.40	0.929	2599.52	13	<0.001	99.50	0.32	0.63
Fewer different types of medicines per day for HIV	5	1504	1.89	1.12	3.43	1.89	1.30	2.74	0.001	7.16	4	0.128	44.10	0.13	0.28
Fewer different types of medicines per day for non-HIV	9	178964	0.94	0.16	1.34	0.74	0.49	1.12	0.155	2551.13	8	<0.001	99.69	0.32	0.63
Complexity of regimen	8	4435	0.97	0.30	3.39	0.86	0.51	1.44	0.562	62.00	7	<0.001	88.71	0.35	0.66
Increasing number of pills per day, require 90% pills to be adherent	4	2293	0.60	0.57	1.32	1.58	1.18	2.13	0.002	2.23	3	0.526	<0.01	0.08	<0.01
Social Support															
Married/Living together	19	9799	1.30	0.80	2.10	1.27	1.08	1.49	0.004	43.93	18	0.001	59.03	0.04	0.25
Help taking meds	5	2682	1.73	1.06	3.78	1.75	1.16	2.65	0.008	7.65	4	0.105	47.71	0.15	0.31
Costs															
Cost of Medicines	10	55800	0.76	0.18	1.10	0.76	0.65	0.88	<0.001	120.47	9	<0.001	92.53	0.04	0.21
Total costs of treatment	4	23013	1.39	0.63	2.16	1.25	0.83	1.89	0.292	30.86	3	<0.001	90.28	0.17	0.39
Provider Relationship															
Under GP's care	5	25153	0.83	0.70	1.30	0.82	0.73	0.92	0.001	7.07	4	0.132	43.41	0.01	0.08
Disease Severity															
CD4 Count	15	9775	0.97	0.33	3.44	0.98	0.82	1.17	0.822	59.50	14	<0.001	76.47	0.06	0.23
HIV RNA	15	9811	1.04	0.38	3.25	1.07	0.84	1.37	0.578	83.13	14	<0.001	83.16	0.14	0.37
HIV Status (More severe/AIDS vs less severe/no AIDS)	11	2768	1.17	0.35	3.70	1.03	0.76	1.39	0.860	20.68	10	0.023	51.65	0.11	0.34
Systolic BP	5	2025	1.11	0.41	1.55	0.95	0.64	1.41	0.795	17.34	4	0.002	76.94	0.15	0.37
Diastolic BP	5	2025	1.42	0.18	1.80	1.14	0.74	1.75	0.561	20.71	4	<0.001	80.69	0.18	0.42
Fewer/No symptoms	6	6016	1.33	0.85	3.00	1.40	0.92	2.14	0.121	38.93	5	0.001	87.16	0.21	0.48
No GP/Outpatient visit	11	180297	1.01	0.38	1.16	0.92	0.83	1.02	0.123	179.38	10	<0.001	94.43	0.02	0.16
Fewer/No Hospitilisation	13	84332	1.05	0.64	4.05	1.09	0.92	1.29	0.317	212.82	12	<0.001	94.36	0.05	0.26
Fewer/No Hospitilisation - HIV	4	1099	1.89	1.31	3.69	1.86	1.38	2.50	<0.001	3.44	3	0.329	12.67	0.08	0.11
Fewer/No Hospitilisation - non-HIV	9	83233	1.00	0.64	4.05	0.96	0.80	1.14	0.619	180.54	8	<0.001	95.57	0.04	0.24
Fewer/No Emergency department visits	4	40056	1.04	0.68	2.13	1.03	0.81	1.31	0.796	63.07	3	<0.001	95.24	0.06	0.22
Side effects															

Appendix C - Expanded table of meta-analysis results, variables expressed via the Odds Ratio

presence of side effects	11	4161	0.48	0.10	1.19	0.40	0.19	0.84	0.015	209.67	10	<0.001	95.23	0.94	1.17
Comorbidity															
Comorbidity	19	2047198	1.04	0.51	3.12	0.99	0.82	1.19	0.885	1224.17	18	<0.001	98.53	0.12	0.36
Dyslipedemia	3	19852	1.07	0.73	1.28	1.03	0.76	1.38	0.861	12.58	2	0.002	84.11	0.07	0.24
Liver Disease	3	6015	0.63	0.21	1.54	0.76	0.34	1.68	0.493	3.56	2	0.169	43.74	0.53	0.47
Hypertension	6	91860	1.11	0.90	1.30	1.08	1.00	1.17	0.045	18.05	5	0.003	72.30	0.01	0.08
Other cardiovascular conditions	6	89450	1.15	0.80	1.57	1.12	0.97	1.30	0.136	47.60	5	<0.001	89.50	0.02	0.17
Diabetes	10	74563	1.01	0.78	1.24	0.99	0.93	1.05	0.692	19.33	9	0.023	53.44	0.00	0.06
Stroke	4	43097	1.06	0.97	1.32	1.07	0.96	1.20	0.215	6.75	3	0.080	55.58	0.01	0.08
Myocardial infarction	4	48287	1.04	0.90	1.22	1.06	0.96	1.17	0.264	4.60	3	0.204	34.75	0.01	0.06
Heart Failure	5	79940	1.16	0.97	1.34	1.11	0.99	1.23	0.067	12.50	4	0.014	67.99	0.01	0.10
Barriers to medication															
Good access to medical care	4	912	2.38	1.13	3.20	2.32	1.66	3.25	<0.001	2.71	3	0.439	<0.01	0.10	<0.01
Good access to medication	3	688	2.17	1.73	4.56	2.33	1.45	3.47	0.001	2.66	2	0.265	24.71	0.18	0.21
Mental Health															
Presence/History of psychiatric conditions	8	16849	0.57	0.07	1.01	0.53	0.36	0.79	0.002	29.90	7	<0.001	76.59	0.20	0.42
Cognitive ability															
General cognitive ability															
Dementia/Cognitive decline	8	49596	0.82	0.50	0.95	0.84	0.74	0.95	0.005	4.59	7	0.710	<0.01	0.02	<0.01
Use of a memory aid															
Use of a memory aid	6	2419	1.86	1.46	4.22	1.97	1.46	2.66	<0.001	7.76	5	0.170	35.60	0.09	0.22

Appendix D – List of references for meta-analyses

This appendix provides additional details regarding the meta-analyses of chapter 2. Author names, study publication dates and country of origin, sample sizes and individual point estimates for the relationship with adherence are presented. Analyses are presented in the order they appear in the thesis. References for all analyses are provided at the end of the appendix.

Section 1 – Demographics

Sex (female vs male):					
Author	Year	Country	n	OR Estimate	r Estimate
Amfilochiou et al.	2009	Greece	98	3.06	0.25
Balkrishnan and Christensen	2000	USA	1595	0.84	-0.05
Benner et al.	2004	USA	19422	0.9	-0.03
Benner et al.	2005	USA	9510	0.96	-0.01
Benner et al.	2009	USA	5759	0.8	-0.06
Bosley, Fosbury and Cochrane	1995	UK	72	0.57	-0.15
Carlucci et al.	2008	Zambia	409	1.01	0
Chan et al.	2010	USA	14257	0.87	-0.04
Chapman et al.	2005	USA	8406	0.85	-0.04
Cluley and Cochrane	2001	UK	66	0.58	-0.15
Cohen et al.	1998	Australia	1611	1.43	0.1
Curtis et al.	2009	USA	101038	1.25	0.06
Darkow et al.	2007	USA	267	0.51	-0.18
Deschamps et al.	2004	Belgium	43	1.79	0.12
Diette et al.	1999	USA	4235	1.4	0.09
Dosse et al.	2009	Brazil	68	1.09	0.02
Ferguson et al.	2002	USA	149	1.1	0.02
Frazier, Davis-Ali and Dahl	1994	USA	246	1.8	0.16
Garcia et al.	2006	Brazil	182	1.16	0.04
Gardner et al.	2008	USA	325	0.83	-0.03
Gauchet, Tarquinio and Fischer	2007	France	127	2.26	0.18
Gazmarian et al.	2006	USA	1549	0.99	0
Gebo, Keruly and Moore	2003	USA	196	0.6	-0.13
Gifford et al.	2000	USA	133	0.6	-0.13
Godin et al.	2005	Canada	376	0.36	-0.27
Gregoire et al.	2006	Canada	509	1.24	0.06
Hashmi et al.	2007	Pakistan	438	0.93	-0.02
Heath et al.	2002	Canada	638	0.62	-0.06
Ho et al.	2008	USA	13596	0.87	-0.04
Hovinga et al.	2008	USA	408	1.57	0.12
Ickovics et al.	2002	USA	93	3.6	0.33
Irvine et al.	1999	Canada	341	0.74	-0.06
Janson et al.	2008	USA	113	1.02	0

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Jindal et al.	2009	USA	32757	1.1	0.03
Jose et al.	2007	India	506	0.84	-0.04
Kaissi and Parchman	2009	USA	618	1.27	0.06
Kaplan et al.	2004	USA	578	1.25	0.06
Lam, Lu, and Leung	2007	Hong Kong	209	1.74	0.15
Mesfin et al.	2009	Ethiopia	237	1.33	0.08
Miura et al.	2000	Japan	325	0.86	-0.04
Moralejo et al.	2006	Spain	143	0.7	-0.09
Murri et al.	2009	Italy	296	1.3	0.07
Nachega et al.	2006	South Africa	6288	1.23	0.05
Nguyen et al.	2009	USA	235	0.82	-0.06
Nichol et al.	2009	USA	5943	1.09	0.02
Nieuwkerk et al.	2001	Netherlands	160	1.4	0.09
Olthoff et al.	2009	Netherlands	153	1.19	0.05
Parruti et al.	2006	Italy	171	1.16	0.04
Pinheiro et al.	2002	Brazil	195	1.67	0.14
Pinsky et al.	2009	USA	11027	1.08	0.02
Royal et al.	2009	USA	350	1.62	0.12
Sarna et al.	2008	India	310	0.8	-0.04
Schultz et al.	2005	USA	21239	0.67	-0.11
Shah et al.	2007	USA	708	1	0
Shea et al.	1992	USA	202	2.22	0.21
Shuter and Bernstein	2008	USA	64	1.41	0.09
Treadaway et al.	2009	USA	798	0.94	-0.01
Trividi et al.	2008	USA	636	0.96	-0.01
Ulfvarson et al.	2007	Sweden	200	0.74	-0.08
van den Bemt et al.	2009	Netherlands	228	0.92	-0.02
Van Servellen et al.	2002	USA	182	0.53	-0.17
Walker et al.	2006	USA	1,020	0.78	-0.06
Woods et al.	2009	USA	79	3.82	0.26
Wu et al.	2008	USA	134	1.89	0.17
Wu et al.	2010	USA	592	0.78	-0.07
Yang et al.	2009	USA	1,888,682	0.92	-0.02
Ye et al.	2007	USA	5548	0.83	-0.05
Youssef and Moubarak	2002	Egypt	316	0.66	-0.11

Education (More vs less):					
Author	Year	Country	n	OR Estimate	r estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	0.93	-0.02
Brus et al.	1999	Netherlands	55	3.59	0.33
Burge et al.	2005	USA	150	0.58	-0.15
Carlucci et al.	2008	Zambia	409	1.28	0.07
Catz et al.	2001	USA	84	0.32	-0.3

Appendix D – List of references for meta-analyses

Evangelista et al.	2001	USA	82	0.19	-0.42
Garcia et al.	2006	Brazil	182	0.68	-0.1
Gauchet, Tarquinio and Fischer	2007	France	127	1.18	0.04
Gazmarian et al.	2006	USA	1549	3.03	0.22
Gifford et al.	2000	USA	133	0.76	-0.08
Gordillo et al.	1999	Spain	366	0.47	-0.14
Gregoire et al.	2006	Canada	509	0.97	-0.01
Hashmi et al.	2007	Pakistan	438	1.35	0.08
Heath et al.	2002	Canada	638	0.46	-0.19
Hovinga et al.	2008	USA	408	1.29	0.06
Ickovics et al.	2002	USA	93	1.22	0.05
Irvine et al.	1999	Canada	341	7.56	0.48
Janson et al.	2008	USA	113	3.04	0.28
Jindal et al.	2009	USA	32757	0.96	-0.01
Kalichman et al.	2008	USA	145	10.6	0.54
Kleeberger et al.	2001	USA	539	0.81	-0.05
Lam, Lu, and Leung	2007	Hong Kong	209	2	0.17
Liu et al.	2007	USA	807	6.9	0.47
Mann et al.	2007	USA	71	0.58	-0.13
Mizuno et al.	2008	Japan	121	1.39	0.06
Moralejo et al.	2006	Spain	143	0.34	-0.26
Murri et al.	2009	Italy	296	2.17	0.21
Nguyen et al.	2009	USA	235	0.83	-0.05
Olthoff et al.	2009	Netherlands	153	1.12	0.02
Pinheiro et al.	2002	Brazil	195	1.62	0.11
Royal et al.	2009	USA	350	1.24	0.06
Saounatsou et al.	2001	Greece	40	0.45	-0.21
Sarna et al.	2008	India	310	0.74	-0.08
Schneider et al.	2004	USA	554	2.33	0.17
Shea et al.	1992	USA	202	1.1	0.02
Shuter and Bernstein	2008	USA	64	1.63	0.1
Sleath et al.	2009	USA	141	0.75	-0.08
Treadaway et al.	2009	USA	798	2.61	0.21
Ulfvarson et al.	2007	Sweden	200	0.95	-0.01
van den Bemt	2009	Netherlands	228	2.36	0.23
Van Servellen	2002	USA	182	2.78	0.27
Wagner et al.	2002	USA	40	0.41	-0.24
Walker et al.	2006	USA	1,020	0.5	-0.19
Woods et al.	2009	USA	79	0.23	-0.32
Wu et al.	2008	USA	134	0.97	-0.01
Yahaya et al.	2009	Malaysia	52	1.34	0.08
Youssef and Moubarak	2002	Egypt	316	1.27	0.07
Zafran et al.	2005	Israel	857	1.19	0.04

Appendix D – List of references for meta-analyses

Education (college vs. no college):					
Author	Year	Country	n	OR Estimate	r Estimate
Carlucci et al.	2008	Zambia	409	1.24	0.06
Gauchet, Tarquinio and Fischer	2007	France	127	1.18	0.04
Gazmarian et al.	2006	USA	1549	1.29	0.06
Gifford et al.	2000	USA	133	7.56	0.48
Golin et al.	2002	USA	117	2.33	0.17
Gordillo et al.	1999	Spain	366	1.62	0.11
Gregoire et al.	2006	Canada	509	1.28	0.07
Hashmi et al.	2007	Pakistan	438	1.12	0.02
Hovinga et al.	2008	USA	408	0.97	-0.01
Ickovics et al.	2002	USA	93	0.5	-0.19
Irvine et al.	1999	Canada	341	0.95	-0.01
Janson et al.	2008	USA	113	0.47	-0.14
Jindal et al.	2009	USA	32757	0.46	-0.19
Kaplan et al.	2004	USA	578	0.45	-0.21
Kleeberger et al.	2001	USA	539	1.27	0.07
Liu et al.	2007	USA	807	0.75	-0.08
Mann et al.	2007	USA	71	0.34	-0.26
Mizuno et al.	2008	Japan	121	10.6	0.54
Moralejo et al.	2006	Spain	143	1.39	0.06
Royal et al.	2009	USA	350	0.68	-0.1
Sarna et al.	2008	India	310	3.04	0.28
Shuter and Bernstein	2008	USA	64	0.23	-0.32
Treadaway et al.	2009	USA	798	1.1	0.02
Ulfvarson et al.	2007	Sweden	200	1.63	0.1
Walker et al.	2006	USA	1,020	1.19	0.04

Employment (yes vs no):					
Author	Year	Country	n	OR Estimate	r Estimate
Frazier, Davis-Ali and Dahl	1994	USA	246	1.12	0.03
Gordillo et al.	1999	Spain	366	1.98	0.17
Heath et al.	2002	Canada	638	2.16	0.21
Kleeberger et al.	2001	USA	539	1.01	0
Liu et al.	2007	USA	807	1.12	0.03
Moralejo et al.	2006	Spain	143	0.66	-0.11
Nguyen et al.	2009	USA	235	4.33	0.31
Parruti et al.	2006	Italy	171	1.13	0.03
Sarna et al.	2008	India	310	2.44	0.18
Shea et al.	1992	USA	202	0.41	-0.22
Singh et al.	1996	USA	46	3.29	0.29
Treadaway et al.	2009	USA	798	1.11	0.03

Van Servellen et al.	2002	USA	182	0.8	-0.06
Zafran et al.	2005	Israel	857	1.95	0.12

Health insurance (yes vs no):					
Author	Year	Country	n	OR estimate	r Estimate
Gifford et al.	2000	USA	133	0.25	-0.35
Gregoire et al.	2006	Canada	509	1.12	0.02
Kaplan et al.	2004	USA	578	2.4	0.23
Kleeberger et al.	2001	USA	539	0.85	-0.02
Liu et al.	2007	USA	807	0.9	-0.03
Royal	2009	USA	350	1.83	0.09
Shea et al.	1992	USA	202	1.61	0.11

Age:					
Author	Year	Country	n	OR Estimate	r Estimate
Amfilochiou et al.	2009	Greece	98	4.02	0.36
Barclay et al.	2007	USA	185	4.12	0.32
Bosley, Fosbury and Cochrane	1995	UK	72	1.6	0.13
Brus et al.	1999	Netherlands	55	1.34	0.08
Burge et al.	2005	USA	150	2.02	0.19
Carr, Thompson and Cooper	2006	UK	533	1	0
Catz et al.	2001	USA	84	1.04	0.01
Chan et al.	2010	USA	14257	1.69	0.14
Chapman et al.	2008	USA	4052	0.92	-0.02
Cox	2009	USA	378	1.7	0.14
Darkow et al.	2007	USA	267	1.14	0.04
deJong et al.	2004	USA	168	0.64	-0.12
Deschamps et al.	2004	Belgium	43	1.6	0.13
Diette et al.	1999	USA	4235	1.48	0.09
Esposito et al.	2009	USA	37408	0.59	-0.14
Evangelista et al.	2001	USA	82	5.97	0.44
Frazier, Davis-Ali and Dahl	1994	USA	246	1.94	0.18
French et al.	2005	USA	590	0.65	-0.12
Garcia et al.	2006	Brazil	182	1	0
Gardner et al.	2008	USA	325	1.1	0.03
Gauchet, Tarquinio and Fischer	2007	France	127	1.51	0.11
Gazmarian et al.	2006	USA	1549	1.04	0.01
Golin et al.	2002	USA	117	2.02	0.19
Gordillo et al.	1999	Spain	366	1.21	0.04
Gregoire et al.	2006	Canada	509	1.17	0.04
Hashmi et al.	2007	Pakistan	438	1.64	0.11
Ho et al.	2008	USA	13596	1.28	0.06
Hovinga et al.	2008	USA	408	1.11	0.03

Appendix D – List of references for meta-analyses

Ickovics et al.	2002	USA	93	2.1	0.2
Irvine et al.	1999	Canada	341	1.22	0.04
Janson et al.	2008	USA	113	1.6	0.11
Jindal et al.	2009	USA	32757	2.5	0.12
Jose et al.	2007	India	506	0.81	-0.06
Kaissi and Parchman	2009	USA	618	1.06	0.02
Kalichman et al.	2008	USA	145	1	0
Kiortsis et al.	2000	France	193	2.77	0.22
Kleeberger et al.	2001	USA	539	1.07	0.02
Lacasse et al.	2005	Canada	124	1.05	0.01
Lam, Lu, and Leung	2007	Hong Kong	209	1.63	0.13
Larizza et al.	2006	Australia	24	8.59	0.51
Luszczynska, Sarkar, and Knoll	2007	India	104	1.49	0.11
Mann et al.	2007	USA	71	6.98	0.4
Mellins et al.	2003	USA	97	1.2	0.05
Mesfin et al.	2009	Ethiopia	237	0.56	-0.16
Miura et al.	2000	Japan	325	2.41	0.2
Moralejo et al.	2006	Spain	143	1.59	0.12
Murri et al.	2009	Italy	296	1	0
Nachega et al.	2006	South Africa	6288	1.19	0.03
Nichol et al.	2009	USA	5943	1.04	0.01
Nieuwkerk et al.	2001	Netherlands	160	0.45	-0.21
Olthoff et al.	2009	Netherlands	153	3.32	0.31
Pamboukian et al.	2008	USA	80	1.8	0.16
Parruti et al.	2006	Italy	171	0.58	-0.13
Penning-van Beest	2008	Netherlands	8822	0.97	-0.01
Pinheiro et al.	2002	Brazil	195	0.77	-0.05
Pinsky et al.	2009	USA	11027	1.21	0.04
Rosen et al.	2003	USA	79	3.26	0.31
Royal et al.	2009	USA	350	2.59	0.24
Sarna et al.	2008	India	310	0.95	-0.01
Schneider et al.	2004	USA	554	1.73	0.15
Schultz et al.	2005	USA	21239	1.58	0.12
Shah et al.	2007	USA	708	1.53	0.12
Shaya et al.	2009	USA	568	1.36	0.06
Shea et al.	1992	USA	202	2.22	0.21
Shuter and Bernstein	2008	USA	64	0.59	-0.14
Singh et al.	1996	USA	46	0.58	-0.14
Sleath et al.	2009	USA	141	0.99	0
Sullivan et al.	2007	USA	5,887	1.15	0.03
Treadaway et al.	2009	USA	798	1.46	0.1
Trividi et al.	2008	USA	636	1.61	0.13
Tuldra et al.	2000	Netherlands	116	6.16	0.45

Appendix D – List of references for meta-analyses

Ulfvarson et al.	2007	Sweden	200	1.06	0.01
van den Bemt et al.	2009	Netherlands	228	1.44	0.1
Van Servellen et al.	2002	USA	182	0.69	-0.1
Wagner	2002	USA	180	4.65	0.39
Walker et al.	2006	USA	1,020	1.03	0.01
Wilson et al.	1986	USA	184	0.69	-0.1
Woods et al.	2009	USA	79	1.44	0.1
Wu et al.	2008	USA	134	1.45	0.1
Wu et al.	2010	USA	592	1.19	0.05
Yang et al.	2009	USA	1,888,682	2.06	0.13
Ye et al.	2007	USA	5548	1.23	0.06
Youssef and Moubarak	2002	Egypt	316	0.77	-0.06

Income:					
Author	Year	Country	n	OR Estimate	r Estimate
Barclay et al.	2007	USA	45	3.13	0.3
Bardel, Wallander and Svardsudd	2007	Sweden	1406	0.8	-0.06
Frazier, Davis-Ali and Dahl	1994	USA	246	1.94	0.18
Garcia et al.	2006	Brazil	182	1.12	0.03
Gebo, Keruly and Moore	2003	USA	196	2.21	0.21
Gregoire et al.	2006	Canada	509	1.07	0.02
Hashmi et al.	2007	Pakistan	438	0.96	-0.01
Hovinga et al.	2008	USA	408	0.69	-0.1
Ickovics et al.	2002	USA	93	0.48	-0.2
Janson et al.	2008	USA	113	0.45	-0.18
Kleeberger et al.	2001	USA	539	1.87	0.16
Liu et al.	2007	USA	807	0.81	-0.06
Nguyen et al.	2009	USA	235	1.44	0.1
Pinheiro et al.	2002	Brazil	195	0.75	-0.06
Van Servellen et al.	2002	USA	182	0.83	-0.05
Walker et al.	2006	USA	1,020	1.63	0.12
Wu et al.	2008	USA	134	0.88	-0.04
Yahaya et al.	2009	Malaysia	52	0.31	-0.31
Zafran et al.	2005	Israel	857	0.7	-0.08

Sociodemographic status:					
Author	Year	Country	n	OR Estimate	r Estimate
Bosley, Fosbury and Cochrane	1995	UK	72	NA	NA
Parruti et al.	2006	Italy	171	NA	NA
Sarna et al.	2008	India	310	NA	NA

Effects of having children:					
Author	Year	Country	n	OR Estimate	r Estimate

Moralejo et al.	2006	Spain	143	NA	NA
Corless et al.	2005	USA	165	NA	NA
Golin et al.	2002	USA	117	NA	NA

Sexuality (homosexual vs heterosexual):					
Author	Year	Country	n	OR Estimate	r Estimate
Barclay et al.	2007	USA	45	3.42	0.32
Gauchet, Tarquinio and Fischer	2007	France	127	0.69	-0.1
Parruti et al.	2006	Italy	171	1.44	0.09

Section 2 – Race

Black vs Other races:					
Author	Year	Country	n	OR Estimate	r estimate
Gebo, Keruly and Moore	2003	USA	196	0.48	-0.17
Gifford et al.	2000	USA	133	0.46	-0.2
Jindal et al.	2009	USA	32757	0.54	-0.15
Kleeberger et al.	2001	USA	539	0.43	-0.14
Nachega et al.	2006	South Africa	6288	0.92	-0.01
Royal et al.	2009	USA	350	0.96	-0.01

White vs black:					
Author	Year	Country	n	OR Estimate	r estimate
Deschamps et al.	2004	Belgium	43	1.64	0.09
Esposito et al.	2009	USA	37408	4.38	0.36
Ferguson et al.	2002	USA	149	0.61	-0.13
Gazmarian et al.	2006	USA	1549	1.83	0.11
Kaplan et al.	2004	USA	578	0.2	-0.4
Liu et al.	2007	USA	807	0.59	-0.14
Nachega et al.	2006	South Africa	6288	1.14	0.01
Nguyen et al.	2009	USA	235	4	0.36
Nichol et al.	2009	USA	5943	1.52	0.09
Pinsky et al.	2009	USA	11027	1.42	0.09
Shaya et al.	2009	USA	568	2.31	0.2
Walker et al.	2006	USA	1,020	1.4	0.08
Yang et al.	2009	USA	1,888,682	1.46	0.08

White vs Hispanic:					
Author	Year	Country	n	OR Estimate	r estimate
Gazmarian et al.	2006	USA	1549	1.40	0.06
Kaplan et al.	2004	USA	578	0.13	-0.50
Liu et al.	2007	USA	807	0.71	-0.09
Mann et al.	2007	USA	71	3.43	0.31
Walker et al.	2006	USA	1,020	1.51	0.09

Yang et al.	2009	USA	1,888,682	1.37	0.05

White vs. non-white:					
Author	Year	Country	n	OR Estimate	r estimate
Diette et al.	1999	USA	4235	2.06	0.14
Frazier, Davis-Ali and Dahl	1994	USA	246	0.78	-0.07
Gardner et al.	2008	USA	325	0.95	-0.02
Hovinga et al.	2008	USA	408	0.69	-0.08
Janson et al.	2008	USA	113	2.03	0.18
Moralejo et al.	2006	Spain	143	0.33	-0.13
Rosenbaum et al.	2005	USA	465	2.39	0.17
Shuter and Bernstein	2008	USA	64	5	0.41
Singh et al.	1996	USA	46	2.33	0.22
Sleath et al.	2009	USA	141	0.3	-0.31
Trividi et al.	2008	USA	636	2.77	0.27
Woods et al.	2009	USA	79	1.44	0.1

White vs other:					
Author	Year	Country	n	OR Estimate	r estimate
Esposito et al.	2009	USA	37408	2.1	0.18
Gazmarian et al.	2006	USA	1549	2.33	0.06
Heath et al.	2002	Canada	638	1.68	0.11
Kaplan et al.	2004	USA	578	0.18	-0.43
Liu et al.	2007	USA	807	0.48	-0.2
Nichol et al.	2009	USA	5943	1.16	0.04
Pinsky et al.	2009	USA	11027	1.37	0.08
Shaya et al.	2009	USA	568	1	0
Yang et al.	2009	USA	1,888,682	0.98	0

Part 3 – Adherence to non-medication regimens

Exercise:					
Author	Year	Country	n	OR Estimate	r Estimate
Trividi et al.	2008	USA	636	NA	NA

Appointments:					
Author	Year	Country	n	OR Estimate	r Estimate
Stanton	1987	USA	50	NA	NA
Bane, Hughes and McElnay	2006	UK	139	NA	NA

Diet:					
Author	Year	Country	n total	OR Estimate	r Estimate
Christensen and Smith	1995	USA	72	4.24	0.37

Trividi et al.	2008	USA	636	1.34	0.08
Youssef and Moubarak	2002	Egypt	316	4.92	0.33
Zafran et al.	2005	Israel	857	1.14	0.03

Part 4 – Medication regimen

Number of co-medications:					
Author	Year	Country	n	OR Estimate	r Estimate
Carr, Thompson and Cooper	2006	UK	533	1.01	0
Chan et al.	2010	USA	14257	1.1	0.02
Penning-van Beest	2008	Netherlands	8822	0.78	-0.07
Wu et al.	2010	USA	592	1.25	0.06

Fewer different types of pills:					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	1.34	0.08
Benner et al.	2004	USA	19422	0.97	-0.01
Benner et al.	2005	USA	9510	0.94	-0.02
Benner et al.	2009	USA	5759	0.91	-0.03
Catz et al.	2001	USA	84	1.39	0.09
Chapman et al.	2008	USA	4052	0.56	-0.16
Curtis et al.	2009	USA	101038	0.95	-0.01
Esposito et al.	2009	USA	37408	0.16	-0.4
French et al.	2005	USA	590	1.89	0.17
Golin et al.	2002	USA	117	1.12	0.03
Jones et al.	2003	USA	174	3.43	0.32
Kleeberger et al.	2001	USA	539	1.99	0.16
Sleath et al.	2009	USA	141	0.53	-0.17
van den Bemt	2009	Netherlands	228	1.34	0.08

Complexity of regimen:					
Author	Year	Country	n	OR Estimate	r Estimate
Gauchet, Tarquinio and Fischer	2007	France	127	3.39	0.18
Gazmarian et al.	2006	USA	1549	1.31	0.07
Hashmi et al.	2007	Pakistan	438	2.32	0.23
Lam, Lu, and Leung	2007	Hong Kong	209	0.3	-0.31
Larizza et al.	2006	Australia	24	1.61	0.13
Morisky et al.	2008	USA	1367	0.55	-0.16
Olthoff et al.	2009	Netherlands	153	0.3	-0.23
Shaya	2009	USA	568	0.62	-0.12

Duration of medication regimen:					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	1.07	0.02

Benner et al.	2005	USA	9510	0.61	-0.14
Chapman et al.	2005	USA	8406	0.87	-0.04
Garcia et al.	2006	Brazil	182	0.5	-0.18
Golin et al.	2002	USA	117	0.67	-0.11
Holstad et al.	2006	USA	120	0.46	-0.21
Miura et al.	2000	Japan	325	0.75	-0.06
Pinheiro et al.	2002	Brazil	195	0.7	-0.09
Saounatsou et al.	2001	Greece	40	6.11	0.45
Sarna et al.	2008	India	310	1.31	0.07
Tuldra et al.	2000	Netherlands	116	0.59	-0.14
Woods et al.	2009	USA	79	0.91	-0.03

Pills per day:					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	0.71	-0.09
Cohen et al.	1998	Australia	1611	0.58	-0.15
Gifford et al.	2000	USA	133	2.22	0.21
Golin et al.	2002	USA	117	1.29	0.07
Gregoire et al.	2006	Canada	509	1.5	0.11
Larizza et al.	2006	Australia	24	0.21	-0.4
Murri et al.	2009	Italy	296	1.05	0.01
Parruti et al.	2006	Italy	171	1.32	0.07
Pinheiro et al.	2002	Brazil	195	0.57	-0.15
Wu et al.	2008	USA	134	1.18	0.05
Youssef and Moubarak	2002	Egypt	316	0.62	-0.13

Daily vs weekly regimens:					
Author	Year	Country	n	OR Estimate	r Estimate
Curtis et al.	2009	USA	101038	NA	NA
Carr, Thompson and Cooper	2006	UK	533	NA	NA
Penning-van Beest	2008	Netherlands	8822	NA	NA
Downey et al.	2006	USA	10566	NA	NA

Regimen changes:					
Author	Year	Country	n	OR Estimate	r Estimate
Deschamps et al.	2004	Belgium	43	NA	NA
Lam, Lu, and Leung	2007	Hong Kong	209	NA	NA
Parruti et al.	2006	Italy	171	NA	NA

Part 5 – Memory Aides

Memory Aides:					
Author	Year	Country	n	OR Estimate	r Estimate
Amberbir et al.	2008	Ethiopia	383	3.29	0.31

Golin et al.	2002	USA	117	1.78	0.16
Gregoire et al.	2006	Canada	509	1.46	0.07
Lam, Lum, and Leung	2007	Hong Kong	209	1.95	0.17
Walker et al.	2006	USA	1,020	1.57	0.12
Wang and Wu	2007	China	181	4.22	0.32

Part 6 – Barriers to medication

General barriers:					
Author	Year	Country	n	OR Estimate	r Estimate
Brus et al.	1999	Netherlands	55	0.32	-0.3
Carr, Thompson and Cooper	2006	UK	533	0.81	-0.06
Holstad et al.	2006	USA	120	0.27	-0.34
Kuzuyaet al.	2008	Japan	1772	0.59	-0.14
Molassiotis et al.	2002	Hong Kong	136	0.14	-0.47
Sleath et al.	2009	USA	141	0.75	-0.08
Stanton	1987	USA	50	0.1	-0.53
Wu et al.	2008	USA	134	0.38	-0.26

Access to medical care:					
Author	Year	Country	n	OR Estimate	r Estimate
Mesfin et al.	2009	Ethiopia	237	3.2	0.26
Moralejo et al.	2006	Spain	143	1.13	0.02
Royal et al.	2009	USA	350	2.11	0.2
Van Servellen	2002	USA	182	2.66	0.26

Access to medicines:					
Author	Year	Country	n	OR Estimate	r Estimate
Gifford et al.	2000	USA	133	4.56	0.38
Golin et al.	2002	USA	117	1.73	0.15
Hashmi et al.	2007	Pakistan	438	2.17	0.14

Part 7 – Costs of treatment

Cost of medication:					
Author	Year	Country	n	OR Estimate	r Estimate
Berger et al.	2009	USA	2023	0.76	-0.08
Chan et al.	2010	USA	14257	0.71	-0.09
Diette et al.	1999	USA	4235	1.1	0.03
Gardner et al.	2008	USA	325	0.46	-0.18
Hashmi et al.	2007	Pakistan	438	0.6	-0.14
Nachega et al.	2010	South Africa	6833	0.83	-0.05
Sarna et al.	2008	India	310	0.18	-0.35
Schultz et al.	2005	USA	21239	1	0
Wu et al.	2010	USA	592	0.75	-0.08

Ye et al.	2007	USA	5548	0.85	-0.04

Cost of medical treatment:

Author	Year	Country	n	OR Estimate	r Estimate
Gardner et al.	2008	USA	325	2.16	0.18
Schultz et al.	2005	USA	21239	1.4	0.09
Wu et al.	2010	USA	592	0.63	-0.13
Zafran et al.	2005	Israel	857	1.38	0.09

Part 8 – Comorbidity

Comorbidity measures:					
Author	Year	Country	n	OR Estimate	r Estimate
Chan et al.	2010	USA	14257	1.02	0.01
Corless et al.	2005	USA	165	2.06	0.2
Curtis et al.	2009	USA	101038	0.89	-0.03
Gregoire et al.	2006	Canada	509	1.13	0.03
Hashmi et al.	2007	Pakistan	438	1.1	0.03
Mann et al.	2007	USA	71	3.12	0.26
Pamboukian et al.	2008	USA	80	0.58	-0.15
Parruti et al.	2006	Italy	171	1.14	0.04
Pinsky et al.	2009	USA	11027	1.13	0.02
Schultz et al.	2005	USA	21239	1.43	0.1
Shah et al.	2007	USA	708	1.15	0.04
Shaya e al.	2009	USA	568	0.8	-0.06
Treadaway et al.	2009	USA	798	1.31	0.07
Wu et al.	2008	USA	134	0.51	-0.18
Wu et al.	2010	USA	592	0.77	-0.07
Yang et al.	2009	USA	1,888,682	0.68	-0.1
Ye et al.	2007	USA	5548	0.82	-0.04
Youssef and Moubarak	2002	Egypt	316	1.04	0.01
Zafran et al.	2005	Israel	857	0.67	-0.1

Dysplipedemia:

Author	Year	Country	n	OR Estimate	r Estimate
Ho et al.	2008	USA	13596	1.07	0.01
Shah et al.	2007	USA	708	0.73	-0.09
Ye et al.	2007	USA	5548	1.28	0.07

Liver disease:					
Author	Year	Country	n	OR Estimate	r Estimate
Murri et al.	2009	Italy	296	0.63	-0.13
Parruti et al.	2006	Italy	171	1.54	0.11
Ye et al.	2007	USA	5548	0.21	-0.02

Appendix D – List of references for meta-analyses

Hypertension:					
Author	Year	Country	n	OR Estimate	r Estimate
Benner et al.	2004	USA	19422	1.13	0.03
Benner et al.	2005	USA	9510	1.03	0.01
Ho et al.	2008	USA	13596	1.1	0.02
Jindel et al.	2009	USA	32757	1.13	0.03
Pinsky et al.	2009	USA	11027	1.3	0.06
Ye et al.	2007	USA	5548	0.9	-0.03

Other cardiovascular conditions:					
Author	Year	Country	n	OR Estimate	r Estimate
Benner et al.	2004	USA	19422	1.28	0.07
Benner et al.	2005	USA	9510	1.16	0.04
Benner et al.	2009	USA	5759	0.8	-0.06
Chapman et al.	2005	USA	8406	1.15	0.04
Ho et al.	2008	USA	13596	0.96	-0.01
Jindel et al.	2009	USA	32757	1.57	0.06

Diabetes:					
Author	Year	Country	n	OR Estimate	r Estimate
Benner et al.	2004	USA	19422	1.02	0.01
Benner et al.	2005	USA	9510	1.08	0.02
Benner et al.	2009	USA	5759	1.08	0.02
Chapman et al.	2005	USA	8406	0.99	0
Frazier, Davis-Ali and Dahl	1994	USA	246	1.24	0.06
Ho et al.	2008	USA	13596	1	0
Irvine et al.	1999	Canada	341	0.78	-0.05
Pinsky et al.	2009	USA	11027	0.8	-0.06
Shah et al.	2007	USA	708	1.12	0.02
Ye et al.	2007	USA	5548	0.84	-0.04

Stroke:					
Author	Year	Country	n	OR Estimate	r Estimate
Benner et al.	2004	USA	19422	1.01	0
Benner et al.	2005	USA	9510	0.97	-0.01
Benner et al.	2009	USA	5759	1.32	0.08
Chapman et al.	2005	USA	8406	1.1	0.03

Myocardial Infarction:					
Author	Year	Country	n	OR Estimate	r Estimate
Benner et al.	2004	USA	19422	1.22	0.05

Benner et al.	2005	USA	9510	1.02	0.01
Benner et al.	2009	USA	5759	0.9	-0.03
Ho et al.	2008	USA	13596	1.05	0.01

Heart Failure:					
Author	Year	Country	n	OR Estimate	r Estimate
Benner et al.	2004	USA	19422	0.97	-0.01
Benner et al.	2009	USA	5759	1.34	0.08
Chapman et al.	2005	USA	8406	1.22	0.05
Ho et al.	2008	USA	13596	1	0
Jindel et al.	2009	USA	32757	1.16	0.03

Respiratory conditions:					
Author	Year	Country	n	OR Estimate	r Estimate
Balkrishnan and Christensen	2000	USA	1595	NA	NA
Balkrishnan and Christensen	2000	USA	1595	NA	NA
Diette et al.	1999	USA	4235	NA	NA
Diette et al.	1999	USA	4235	NA	NA
Ho et al.	2008	USA	13596	NA	NA

Part 9 – Disease severity and outcomes

CD4 Count:					
Author	Year	Country	n	OR Estimate	r estimate
Gardner et al.	2008	USA	325	2.04	0.19
Gebo, Keruly and Moore	2003	USA	196	0.97	-0.01
Gifford et al.	2000	USA	133	0.33	-0.29
Golin et al.	2002	USA	117	0.72	-0.09
Gordillo et al.	1999	Spain	366	0.75	-0.08
Ickovics et al.	2002	USA	93	2.5	0.24
Kleeberger et al.	2001	USA	539	0.61	-0.13
Liu et al.	2007	USA	807	0.89	-0.03
Mellins et al.	2003	USA	97	1.43	0.1
Murri et al.	2009	Italy	296	1.01	0
Nachega et al.	2006	South Africa	6288	0.97	-0.01
Sarna et al.	2008	India	310	3.44	0.26
Shuter and Bernstein	2008	USA	64	0.48	-0.2
Singh et al.	1996	USA	46	1.11	0.03
Wang et al.	2009	China	98	0.37	-0.26

HIV RNA:					
Author	Year	Country	n	OR Estimate	r Estimate
Cruess et al.	2007	USA	116	2.02	0.19
deJong et al.	2004	USA	168	0.5	-0.19

Appendix D – List of references for meta-analyses

Gauchet, Tarquinio and Fischer	2007	France	127	0.61	-0.14
Gifford et al.	2000	USA	133	0.41	-0.23
Golin et al.	2002	USA	117	1.04	0.01
Heath et al.	2002	Canada	638	3.19	0.25
Ickovics et al.	2002	USA	93	1.9	0.17
Jones et al.	2003	USA	174	0.38	-0.26
Kleeberger et al.	2001	USA	539	1.18	0.05
Liu et al.	2007	USA	807	1.45	0.1
Mellins et al.	2003	USA	97	1.09	0.02
Murri et al.	2009	Italy	296	3.25	0.31
Nachega et al.	2006	South Africa	6288	1	0
Nieuwkerk	2001	Netherlands	160	0.7	-0.1
Townsend et al.	2007	USA	58	0.69	-0.1

HIV Status (AIDS vs Non-AIDS):					
Author	Year	Country	n	OR Estimate	r Estimate
Carlucci et al.	2008	Zambia	409	0.75	-0.07
deJong et al.	2004	USA	168	0.63	-0.12
Deschamps et al.	2004	Belgium	43	0.84	-0.04
Gifford et al.	2000	USA	133	0.35	-0.27
Kleeberger et al.	2001	USA	539	0.74	-0.07
Liu et al.	2007	USA	807	1.37	0.09
Nieuwkerk et al.	2001	Netherlands	160	1.43	0.1
Parruti et al.	2006	Italy	171	1.17	0.04
Pinheiro et al.	2002	Brazil	195	1.27	0.06
Shuter and Bernstein	2008	USA	64	2.1	0.19
Woods et al.	2009	USA	79	3.7	0.3

Systolic BP:					
Author	Year	Country	n	OR Estimate	r Estimate
Hashmi et al.	2007	Pakistan	438	1.17	0.03
Kiortsis et al.	2000	France	193	0.41	-0.19
Shah et al.	2007	USA	708	1.11	0.03
Stanton	1987	USA	50	0.43	-0.22
Trividi et al.	2008	USA	636	1.55	0.12

Diastolic BP:					
Author	Year	Country	n	OR Estimate	r Estimate
Hashmi et al.	2007	Pakistan	438	1.17	0.03
Kiortsis et al.	2000	France	193	0.41	-0.19
Shah et al.	2007	USA	708	1.11	0.03
Stanton	1987	USA	50	0.43	-0.22
Trividi et al.	2008	USA	636	1.55	0.12

Appendix D – List of references for meta-analyses

Fewer/no symptoms vs more/any symptoms:					
Author	Year	Country	n	OR Estimate	r Estimate
Diette et al.	1999	USA	4235	0.91	-0.03
Gregoire et al.	2006	Canada	509	0.91	-0.02
Hovinga et al.	2008	USA	408	3	0.29
Kalichman et al.	2008	USA	145	1.75	0.13
Kleeberger et al.	2001	USA	539	0.85	-0.04
Wagner	2002	USA	180	2.55	0.25

GP Outpatient visits (fewer vs more):					
Author	Year	Country	n	OR Estimate	r Estimate
Benner et al.	2004	USA	19422	1.03	0.01
Benner et al.	2005	USA	9510	1.04	0.01
Chan et al.	2010	USA	14257	1.01	0
Chapman et al.	2005	USA	8406	1.16	0.04
Curtis et al.	2009	USA	101038	0.9	-0.03
Diette et al.	1999	USA	4235	0.52	-0.15
Gardner et al.	2008	USA	325	1.15	0.03
Kaissi and Parchman	2009	USA	618	1.05	0.01
Kleeberger et al.	2001	USA	539	0.38	-0.12
Schultz et al.	2005	USA	21239	0.78	-0.07
Shah et al.	2007	USA	708	1	0

Hospitalisations (fewer vs more):					
Author	Year	Country	n	OR Estimate	r Estimate
Benner et al.	2004	USA	19422	0.98	-0.01
Benner et al.	2005	USA	9510	1.04	0.01
Benner et al.	2009	USA	5759	1.18	0.04
Chan et al.	2010	USA	14257	1	0
Chapman et al	2005	USA	8406	1.05	0.01
Diette et al.	1999	USA	4235	0.7	-0.06
Gardner et al.	2008	USA	325	2.1	0.18
Gordillo et al.	1999	Spain	366	1.67	0.14
Miura et al.	2000	Japan	325	0.82	-0.06
Pamboukian et al.	2008	USA	80	4.05	0.36
Sarna et al.	2008	India	310	1.31	0.06
Schultz et al.	2005	USA	21239	0.64	-0.11
Wang et al.	2009	China	98	3.69	0.3

Emergency department visits (fewer vs more):					
Author	Year	Country	n	OR Estimate	r Estimate
Chan et al.	2010	USA	14257	1.18	0.04

Diette et al.	1999	USA	4235	0.68	-0.06
Gardner et al.	2008	USA	325	2.13	0.18
Schultz et al.	2005	USA	21239	0.9	-0.03

Symptom severity:					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	0.94	-0.02
Brus et al.	1999	Netherlands	55	1.39	0.09
Carr, Thompson and Cooper	2006	UK	533	1.12	0.03
Diette et al.	1999	USA	4235	1.21	0.05
Dobkin, Sita and Sewitch	2006	Canada	121	0.97	-0.01
Gifford et al.	2000	USA	133	0.65	-0.11
Holstad et al.	2006	USA	120	0.8	-0.06
Janson et al.	2008	USA	113	0.7	-0.1
Liang et al.	2008	Taiwan	92	0.65	-0.12
Nguyen et al.	2009	USA	235	1.05	0.01
Reynolds	2004	USA	384	0.39	-0.25
Sewitch et al.	2004	Canada	127	0.95	-0.01
Wagner	2002	USA	180	1.73	0.15
Wu et al.	2010	USA	592	0.76	-0.08
Wu et al.	2008	USA	134	0.54	-0.17

Duration of disease:					
Author	Year	Country	n	OR Estimate	r Estimate
Bosley, Fosbury and Cochrane	1995	UK	72	0.43	-0.23
Catz et al.	2001	USA	84	0.58	-0.15
Corless et al.	2005	USA	165	0.63	-0.13
French et al.	2005	USA	590	0.4	-0.24
Golin et al.	2002	USA	117	1.39	0.09
Gregoire et al.	2006	Canada	509	0.93	-0.02
Holstad et al.	2006	USA	120	2.77	0.27
Kalichman et al.	2008	USA	145	1.51	0.1
Linde et al.	2008	Sweden	174	1.12	0.03
Mellins et al.	2003	USA	97	0.9	-0.03
Mizuno et al.	2008	Japan	121	0.73	-0.08
Nguyen et al.	2009	USA	235	0.5	-0.19
Olthoff et al.	2009	Netherlands	153	0.86	-0.04
Pinsky et al.	2009	USA	11027	1.04	0.01
Sarna et al.	2008	India	310	0.95	-0.01
Sewitch et al.	2004	Canada	127	1.02	0.01
Sleath et al.	2009	USA	141	1.19	0.05
Treadaway et al.	2009	USA	798	1.49	0.11
van den Bemt	2009	Netherlands	228	2.18	0.21

Woods et al.	2009	USA	79	0.56	-0.15
Youssef and Moubarak	2002	Egypt	316	0.95	-0.01

Part 10 – Quality of life and patient wellbeing

General QOL scores:					
Author	Year	Country	n	OR Estimate	r Estimate
Burge et al.	2005	USA	150	0.38	-0.26
Cote, Farris and Feeny	2003	Canada	199	1.54	0.12
deJong et al.	2004	USA	168	1.22	0.05
Gifford et al.	2000	USA	133	2.52	0.24
Gregoire et al.	2006	Canada	509	0.86	-0.04
Holstad et al.	2006	USA	120	2.1	0.2
Janson et al.	2008	USA	113	1.15	0.03
Kaplan et al.	2004	USA	578	1.8	0.16
Moralejo et al.	2006	Spain	143	1.57	0.12
Nguyen et al.	2009	USA	235	1.94	0.18
Reynolds	2004	USA	384	2.02	0.19
Ulfvarson et al.	2007	Sweden	200	2.68	0.23
van den Bemt	2009	Netherlands	228	1.16	0.04
Wang and Wu	2007	China	181	3.2	0.25
Williams et al.	2009	USA	2,038	1.39	0.09

Physical functioning:					
Author	Year	Country	n	OR Estimate	r Estimate
Brus et al.	1999	Netherlands	55	1.94	0.18
Burge et al.	2005	USA	150	0.36	-0.27
Catz et al.	2001	USA	84	2.55	0.25
Cote, Farris and Feeny	2003	Canada	100	0.78	-0.07
Cote, Farris and Feeny	2003	Canada	199	1.45	0.1
Cote, Farris and Feeny	2003	Canada	365	1.4	0.09
Golin et al.	2002	USA	117	1.34	0.08
Hovinga et al.	2008	USA	408	1.18	0.04
Janson et al.	2008	USA	113	0.83	-0.05
Luszczynska, Sarkar, and Knoll	2007	India	104	14.17	0.59
Martinez et al.	2008	Mexico	239	0.66	-0.09
Molassiotis et al.	2002	Hong Kong	136	0.48	-0.2
Murri et al.	2009	Italy	296	1.64	0.14
Pinsky et al.	2009	USA	11027	1.15	0.02
Reynolds	2004	USA	384	1.73	0.15
Schneider et al.	2004	USA	554	1.55	0.12
Singh et al.	1996	USA	46	2.71	0.26
Treadaway et al.	2009	USA	798	1.49	0.11

Appendix D – List of references for meta-analyses

Mental wellbeing:					
Author	Year	Country	n	OR Estimate	r Estimate
Cote, Farris and Feeny	2003	Canada	100	0.82	-0.06
Cote, Farris and Feeny	2003	Canada	199	1.62	0.13
Cote, Farris and Feeny	2003	Canada	365	1.23	0.06
Golin et al.	2002	USA	117	0.78	-0.07
Lacasse et al.	2005	Canada	124	0.74	-0.08
Martinez et al.	2008	Mexico	239	1.53	0.09
Treadaway et al.	2009	USA	798	1.74	0.15

Part 11 – Side effects

Presence of side effects (any vs none):					
Author	Year	Country	n	OR Estimate	r Estimate
Carr, Thompson and Cooper	2006	UK	533	1.19	0.05
Gauchet, Tarquinio and Fischer	2007	France	127	0.58	-0.13
Gregoire et al.	2006	Canada	509	1	0
Hashmi et al.	2007	Pakistan	438	0.48	-0.15
Ickovics et al.	2002	USA	93	0.17	-0.44
Kaplan et al.	2004	USA	578	0.33	-0.29
Lam, Lu, and Leung	2007	Hong Kong	209	0.52	-0.16
Moralejo et al.	2006	Spain	143	0.45	-0.16
Pinheiro et al.	2002	Brazil	195	0.58	-0.15
Walker et al.	2006	USA	1,020	0.1	-0.53
Youssef and Moubarak	2002	Egypt	316	0.12	-0.21

Number of side effects:					
Author	Year	Country	n	OR Estimate	r Estimate
Burge et al.	2005	USA	150	0.41	-0.24
Trividi et al.	2008	USA	636	0.93	-0.02
van den Bemt	2009	Netherlands	228	0.56	-0.16
Vytrisalova et al.	2008	Czech Republic	200	0.55	-0.16
Wagner	2002	USA	180	0.32	-0.3

Severity of side effects:					
Author	Year	Country	n	OR Estimate	r Estimate
Catz et al.	2000	USA	72	0.3	-0.25
Heath et al.	2002	Canada	638	0.3	-0.31
Kaplan et al.	2004	USA	578	0.3	-0.31
Pollack et al.	2010	USA	2074	0.48	-0.2
Sarna et al.	2008	India	310	0.19	-0.27

Part 12 – Health beliefs

Appendix D – List of references for meta-analyses

Outcome expectations:					
Author	Year	Country	n	OR Estimate	r Estimate
Brus et al.	1999	Netherlands	55	NA	NA
Hashmi et al.	2007	Pakistan	438	NA	NA
Mann et al.	2007	USA	71	NA	NA
Pinheiro et al.	2002	Brazil	195	NA	NA

Susceptibility to disease:					
Author	Year	Country	n	OR Estimate	r Estimate
Deschamps et al.	2004	Belgium	43	2.37	0.23
Gregoire et al.	2006	Canada	509	1.69	0.14
Holstad et al.	2006	USA	120	0.83	-0.05
Youssef and Moubarak	2002	Egypt	316	0.35	-0.25

Self-efficacy:					
Author	Year	Country	n	OR Estimate	r Estimate
Bane, Hughes and McElnay	2006	UK	139	16.31	0.53
Brus et al.	1999	Netherlands	55	13.23	0.58
Burge et al.	2005	USA	150	5.83	0.44
Catz et al.	2000	USA	72	6.31	0.36
Gifford et al.	2000	USA	133	6.96	0.47
Godin et al.	2005	Canada	376	1.68	0.14
Golin et al.	2002	USA	117	1.2	0.05
Holstad et al.	2006	USA	120	1.73	0.15
Ickovics et al.	2002	USA	93	2.2	0.21
Liang et al.	2008	Taiwan	92	2.27	0.22
Luszczynska, Sarkar, and Knoll	2007	India	104	5.63	0.43
Lynam et al.	2009	USA	189	2.36	0.23
Mann et al.	2009	USA	151	2.7	0.26
Mellins et al.	2003	USA	97	0.93	-0.02
Molassiotis et al.	2002	Hong Kong	136	4.65	0.39
Mosen et al.	2007	USA	4108	2.65	0.26
Pinheiro et al.	2002	Brazil	195	3.47	0.32
Reynolds et al.	2004	USA	384	2.55	0.25
Tuldra et al.	2000	Netherlands	116	21	0.64
Van Servellen	2002	USA	182	1.16	0.04
Williams et al.	2009	USA	2,038	1.47	0.11

Part 13 – Beliefs about medication

Satisfaction with medicines:					
Author	Year	Country	n	OR Estimate	r Estimate
Carr, Thompson and Cooper	2006	UK	533	1.49	0.1
Deschamps et al.	2004	Belgium	43	3.12	0.29

Garcia et al.	2006	Brazil	182	5.15	0.4
Treadaway et al.	2009	USA	798	3.51	0.14
Youssef and Moubarak	2002	Egypt	316	4.27	0.33

Positive beliefs about medicines:					
Author	Year	Country	n	OR Estimate	r Eestimate
Gauchet, Tarquinio and Fischer	2007	France	127	3.92	0.32
Gebo, Keruly and Moore	2003	USA	196	1.96	0.18
Godin et al.	2005	Canada	376	1.56	0.12
Holstad et al.	2006	USA	120	2.55	0.25
Royal et al.	2009	USA	350	2.04	0.15
Williams et al.	2009	USA	2,038	1.49	0.11

BMQ Necessity:					
Author	Year	Country	n	OR Estimate	r Estimate
Byer and Myers	2000	UK	34	5.91	0.44
Gauchet, Tarquinio and Fischer	2007	France	127	3.26	0.31
Menckeberg et al.	2008	Netherlands	233	4.05	0.36
van den Bemt	2009	Netherlands	228	1.49	0.11

BMQ Concerns:					
Author	Year	Country	n	OR Estimate	r Estimate
Byer and Myers	2000	UK	34	1	0
Gauchet, Tarquinio and Fischer	2007	France	127	0.86	-0.04
Menckeberg et al.	2008	Netherlands	233	0.62	-0.13
van den Bemt	2009	Netherlands	228	1.2	0.05

Effectiveness of medication:					
Author	Year	Country	n	OR Estimate	r Estimate
Gregoire et al.	2006	Canada	509	0.77	-0.07
Hashmi et al.	2007	Pakistan	438	3.31	0.22
Moralejo et al.	2006	Spain	143	2.09	0.07
Murri et al.	2009	Italy	296	1.75	0.15
Wagner et al.	2002	USA	40	4.05	0.36
Wang and Wu	2007	China	181	5.18	0.27

Concerns about medicines (Non-BMQ):					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	NA	NA
Carr, Thompson and Cooper	2006	UK	533	NA	NA
Mann et al.	2007	USA	71	NA	NA
Mann et al.	2009	USA	151	NA	NA

BMQ General scale:					
Author	Year	Country	n	OR Estimate	r Estimate
Gauchet, Tarquinio and Fischer	2007	France	127	NA	NA
Menckeberg et al.	2008	Netherlands	233	NA	NA

Perceived importance of medicines:					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	NA	NA
Mann et al.	2007	USA	71	NA	NA

Part 14 – Patient knowledge and education

Knowledge of medicines:					
Author	Year	Country	n	OR Estimate	r Estimate
Burge et al.	2005	USA	150	2.12	0.2
Jackevicius, Li and Tu	2008	Canada	4591	1.23	0.05
Miura et al.	2000	Japan	325	2.56	0.25
Sarna et al.	2008	India	310	1.84	0.17
Stanton	1987	USA	50	11.52	0.56
Ulfvarson et al.	2007	Sweden	200	0.91	-0.03
van den Bemt	2009	Netherlands	228	1.12	0.03
Wagner	2002	USA	180	2.66	0.26
Wagner et al.	2002	USA	40	3.88	0.35
Wu et al.	2008	USA	134	1.27	0.07

Knowledge of illness:					
Author	Year	Country	n	OR Estimate	r Estimate
Gifford et al.	2000	USA	133	3.48	0.32
Miura et al.	2000	Japan	325	1.81	0.16
Moralejo et al.	2006	Spain	143	4.03	0.2
Morisky et al.	2008	USA	1367	1.15	0.04
Murri et al.	2009	Italy	296	2.6	0.25
Wang and Wu	2007	China	181	7.89	0.48
Wilson	1986	USA	184	4.44	0.38
Youssef and Moubarak	2002	Egypt	316	1.22	0.05

Health literacy:					
Author	Year	Country	n	OR Estimate	r Estimate
DeMasi et al.	2001	USA and Puerto Rico	194	2.36	0.23
Gazmarian et al.	2006	USA	1549	1.3	0.07
Jones et al.	2003	USA	174	2.55	0.25
Kalichman et al.	2008	USA	145	2.99	0.29

Part 15: Risky health Behaviours

Smoking (more vs less/none):					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	0.94	-0.02
Boulet et al.	2008	Canada	107	0.32	-0.24
Curtis et al.	2009	USA	101038	0.67	-0.11
Gebo, Keruly and Moore	2003	USA	196	0.82	-0.05
Ho et al.	2008	USA	13596	0.77	-0.06
Irvine et al.	1999	Canada	341	0.83	-0.05
Janson et al.	2008	USA	113	1.4	0.08
Jindel et al.	2009	USA	32757	0.63	-0.05
Kiortsis et al.	2000	France	193	0.46	-0.17
Kleeberger et al.	2001	USA	539	0.75	-0.07
Murri et al.	2009	Italy	296	0.41	-0.24
Pamboukian et al.	2008	USA	80	0.53	-0.17
Shah et al.	2007	USA	708	0.89	-0.02
Shea et al.	1992	USA	202	0.4	-0.21
Shuter and Bernstein	2008	USA	64	0.44	-0.14

Alcohol use (more vs less/none):					
Author	Year	Country	n	OR Estimate	r Estimate
Braithwaite et al.	2005	USA	2702	0.67	-0.11
Catz et al.	2001	USA	84	0.36	-0.27
Catz et al.	2000	USA	72	0.89	-0.02
deJong et al.	2004	USA	168	0.51	-0.18
Gebo, Keruly and Moore	2003	USA	196	0.77	-0.07
Ickovics et al.	2002	USA	93	0.91	-0.03
Kalichman et al.	2008	USA	145	0.81	-0.05
Kiortsis et al.	2000	France	193	0.99	0
Molassiotis et al.	2002	Hong Kong	136	0.48	-0.2
Royal	2009	USA	350	0.78	-0.04
Sarna et al.	2008	India	310	0.5	-0.14

Problem alcohol use:					
Author	Year	Country	n	OR Estimate	r Estimate
Braithwaite et al.	2005	USA	2702	0.3	-0.26
Conen et al.	2009	Switzerland	6323	0.4	-0.24
Kleeberger et al.	2001	USA	539	0.64	-0.06
Parruti et al.	2006	Italy	171	0.82	-0.04
Royal et al.	2009	USA	350	0.65	-0.1
Shea et al.	1992	USA	202	0.35	-0.19
Shuter and Bernstein	2008	USA	64	0.86	-0.04

Illegal drug use:					
Author	Year	Country	n	OR Estimate	r Estimate
Barclay et al.	2007	USA	140	0.48	-0.2
deJong et al.	2004	USA	168	0.29	-0.19
Gebo, Keruly and Moore	2003	USA	196	0.36	-0.26
Jones et al.	2003	USA	174	0.39	-0.25
Kleeberger et al.	2001	USA	539	0.92	-0.02
Liu et al.	2007	USA	807	0.57	-0.15
Mellins et al.	2003	USA	97	0.14	-0.48
Moralejo et al.	2006	Spain	143	0.65	-0.09
Royal	2009	USA	350	0.72	-0.09
Shea et al.	1992	USA	202	0.58	-0.1
Singh et al.	1996	USA	46	0.18	-0.41

Complementary medicine use:					
Author	Year	Country	n	OR Estimate	r Estimate
Liu et al.	2007	USA	807	NA	NA
Murri et al.	2009	Italy	296	NA	NA
Ng, Tan and Kua	2004	Singapore	1231	NA	NA

BMI:					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	NA	NA
Carlucci et al.	2008	Zambia	409	NA	NA
Janson et al.	2008	USA	113	NA	NA
Shah et al.	2007	USA	708	NA	NA

Exercise:					
Author	Year	Country	n	OR Estimate	r Estimate
Irvine et al.	1999	Canada	341	NA	NA
Shah et al.	2007	USA	708	NA	NA

Part 16 – Relationship with medication provider

Satisfaction with care:					
Author	Year	Country	n	OR Estimate	r Estimate
Burge et al.	2005	USA	150	2.11	0.2
Golin et al.	2002	USA	117	1.08	0.02
Gregoire et al.	2006	Canada	509	0.73	-0.08
Hashmi et al.	2007	Pakistan	438	3.19	0.21
Larizza et al.	2006	Australia	24	16.2	0.61
Morisky et al.	2008	USA	1367	1.07	0.02

Schneider et al.	2004	USA	554	1.87	0.17
Sewitch et al.	2004	Canada	127	1.8	0.16
Stanton	1987	USA	50	2.69	0.26

Trust in physician:					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	1.43	0.1
Diette et al.	1999	USA	4235	1.57	0.11
Gauchet, Tarquinio and Fischer	2007	France	127	3.26	0.31
Golin et al.	2002	USA	117	2.1	0.2
Hovinga et al.	2008	USA	408	2.46	0.22
Nguyen et al.	2009	USA	235	3.13	0.3
Schneider et al.	2004	USA	554	1.8	0.16
Wang and Wu	2007	China	181	4.93	0.18

Good communication/Relationship with provider:					
Author	Year	Country	n	OR Estimate	r Estimate
Catz et al.	2001	USA	84	2.88	0.28
Diette et al.	1999	USA	4235	1.42	0.09
Hashmi et al.	2007	Pakistan	438	1.52	0.11
Holstad et al.	2006	USA	120	1.39	0.09
Hovinga et al.	2008	USA	408	1.04	0.01
Moralejo et al.	2006	Spain	143	2.09	0.07
Schneider et al.	2004	USA	554	1.87	0.17
Sewitch et al.	2004	Canada	127	1.8	0.16
Stanton	1987	USA	50	3.92	0.35
Van Servellen	2002	USA	182	0.62	-0.13
Williams et al.	2009	USA	2,038	1.31	0.08
Woods et al.	2009	USA	79	2.06	0.19
Wu et al.	2008	USA	134	1.15	0.04

GP care (Yes vs no):					
Author	Year	Country	n	OR Estimate	r Estimate
Chan et al.	2010	USA	14257	0.78	-0.05
Gregoire et al.	2006	Canada	509	1.08	0.01
Penning-van Beest	2008	Netherlands	8822	0.83	-0.05
Shah et al.	2007	USA	708	0.7	-0.1
Zafran et al.	2005	Israel	857	1.3	0.05

Part 17 – Social support

Social support:					
Author	Year	Country	n	OR Estimate	r Estimate
Amberbir et al.	2008	Ethiopia	383	1.82	0.16

Appendix D – List of references for meta-analyses

Brus et al.	1999	Netherlands	55	2.1	0.2
Catz et al.	2001	USA	84	1.58	0.13
Corless et al.	2005	USA	165	1.77	0.16
DeMasi et al.	2001	USA and Puerto Rico	194	1.04	0.01
Dobkin, Sita and Sewitch	2006	Canada	121	2.17	0.21
Frazier, Davis-Ali and Dahl	1994	USA	246	1.04	0.01
Gifford et al.	2000	USA	133	3.94	0.35
Golin et al.	2002	USA	117	0.67	-0.11
Gordillo et al.	1999	Spain	366	2.03	0.17
Gregoire et al.	2006	Canada	509	0.83	-0.05
Hashmi et al.	2007	Pakistan	438	1.83	0.16
Johnell	2005	Sweden	1288	2.2	0.21
Larizza et al.	2006	Australia	24	16.2	0.61
Luszczynska, Sarkar, and Knoll	2007	India	104	4.87	0.4
Molloy et al. A	2008	UK	195	1.23	0.05
Molloy et al. B	2008	UK	262	4.58	0.38
Reynolds et al.	2004	USA	384	1.12	0.03
Van Servellen	2002	USA	182	1.67	0.14
Wagner	2002	USA	180	0.48	-0.2
Wilson et al.	1986	USA	184	1.73	0.15
Wu et al.	2008	USA	134	2.16	0.21

Social norms:					
Author	Year	Country	n	OR Estimate	r Estimate
Bane, Hughes and McElnay	2006	UK	139	NA	NA
Barclay et al.	2007	USA	140	NA	NA
Barclay et al.	2007	USA	45	NA	NA
Brus et al.	1999	Netherlands	55	NA	NA
Holstad et al.	2006	USA	120	NA	NA

Long term relationship (Yes vs no):					
Author	Year	Country	n	OR Estimate	r Estimate
Bardel, Wallander and Svardsudd	2007	Sweden	1406	0.8	-0.06
Deschamps et al.	2004	Belgium	43	2	0.18
Frazier, Davis-Ali and Dahl	1994	USA	246	2.1	0.2
Gauchet, Tarquinio and Fischer	2007	France	127	1.31	0.06
Gazmarian et al.	2006	USA	1549	0.95	-0.02
Hashmi et al.	2007	Pakistan	438	1.2	0.03
Hovinga et al.	2008	USA	408	1.3	0.07
Irvine et al.	1999	Canada	341	1.39	0.08
Kaplan et al.	2004	USA	578	2.1	0.2
Nguyen et al.	2009	USA	235	1.44	0.1

Parruti et al.	2006	Italy	171	1.84	0.16
Shea et al.	1992	USA	202	0.88	-0.03
Treadaway et al.	2009	USA	798	0.87	-0.03
Trividi et al.	2008	USA	636	2.02	0.19
Ulfvarson et al.	2007	Sweden	200	1.22	0.05
van den Bemt	2009	Netherlands	228	1.7	0.11
Walker et al.	2006	USA	1,020	1.28	0.06
Youssef and Moubarak	2002	Egypt	316	1.12	0.03
Zafran et al.	2005	Israel	857	1.21	0.05

Receive help taking medicines (Yes VS No):					
Author	Year	Country	n	OR Estimate	r Estimate
Berger , Hudmon and Liang	2004	USA	516	1.06	0.02
Gifford et al.	2000	USA	133	3.78	0.34
Holstad et al.	2006	USA	120	1.73	0.15
Kuzuya et al.	2008	Japan	1772	2.03	0.14
Sleath et al.	2009	USA	141	1.52	0.11

Part 18 – Patient affect

Anxiety:					
Author	Year	Country	n	OR Estimate	r Estimate
Bosley, Fosbury and Cochrane	1995	UK	72	0.04	-0.48
Catz et al.	2001	USA	84	0.39	-0.25
Cruess et al.	2007	USA	116	1.8	0.16
Deschamps et al.	2004	Belgium	43	0.89	-0.03
Frazier, Davis-Ali and Dahl	1994	USA	246	0.33	-0.29
Moralejo et al.	2006	Spain	143	0.66	-0.08
Singh et al.	1996	USA	46	0.46	-0.2
Van Servellen	2002	USA	182	0.44	-0.22
Wagner	2002	USA	180	0.51	-0.18
Wilson et al.	1986	USA	184	0.78	-0.07
Woods et al.	2009	USA	79	0.33	-0.28

Stress:					
Author	Year	Country	n	OR Estimate	r Estimate
Catz et al.	2001	USA	84	0.36	-0.27
Frazier, Davis-Ali and Dahl	1994	USA	246	0.36	-0.27
French et al.	2005	USA	590	0.59	-0.14
Gifford et al.	2000	USA	133	0.6	-0.13
Golin et al.	2002	USA	117	0.83	-0.05
Ickovics et al.	2002	USA	93	0.53	-0.17
Mellins et al.	2003	USA	97	0.78	-0.07
Morisky et al.	2008	USA	1367	0.91	-0.03

O'Cleirigh, Ironson and Smits	2007	USA	116	0.21	-0.4
Royal et al.	2009	USA	350	0.37	-0.2
Singh et al.	1996	USA	46	0.43	-0.22
Wilson et al.	1986	USA	184	0.56	-0.16

Distress:					
Author	Year	Country	n	OR Estimate	r Estimate
Dobkin, Sita and Sewitch	2006	Canada	121	0.65	-0.12
Irvine et al.	1999	Canada	341	0.75	-0.07
O'Cleirigh, Ironson and Smits	2007	USA	116	0.26	-0.35
Singh et al.	1996	USA	46	0.39	-0.24
Van Servellen	2002	USA	182	0.44	-0.22
Woods et al.	2009	USA	79	0.57	-0.15

Hostility:					
Author	Year	Country	n	OR Estimate	r Estimate
Catz et al.	2001	USA	84	0.56	-0.16
Frazier, Davis-Ali and Dahl	1994	USA	246	0.26	-0.35
Irvine et al.	1999	Canada	341	1.21	0.04

Hope:					
Author	Year	Country	n	OR Estimate	r Estimate
Treadaway et al.	2009	USA	798	NA	NA
Van Servellen	2002	USA	182	NA	NA

Part 19 – Patient mental health

Mental health summary scores:					
Author	Year	Country	n	OR estimate	r Estimate
Hovinga et al.	2008	USA	408	1.98	0.18
Murri et al.	2009	Italy	296	0.98	-0.01
Royal et al.	2009	USA	350	3.03	0.22
Schneider et al.	2004	USA	554	2.1	0.2
Trividi et al.	2008	USA	636	1.8	0.16
Tucker et al.	2003	USA	1,910	1.47	0.11

Psychiatric diagnosis:					
Author	Year	Country	n	OR Estimate	r Estimate
Chan et al.	2010	USA	14257	1.01	0
Cluley and Cochrane	2001	UK	66	0.57	-0.12
Cruess et al.	2007	USA	116	0.6	-0.14
deJong et al.	2004	USA	168	0.35	-0.27
Mellins et al.	2003	USA	97	0.07	-0.59
Parruti et al.	2006	Italy	171	0.57	-0.14

Shuter and Bernstein	2008	USA	64	0.33	-0.24
Tucker et al.	2003	USA	1,910	0.58	-0.12

Depression:					
Author	Year	Country	n	OR Estimate	r Estimate
Amberbir et al.	2008	Ethiopia	383	0.47	-0.2
Benner et al.	2004	USA	19422	1	0
Benner et al.	2009	USA	5759	0.94	-0.02
Bosley, Fosbury and Cochrane	1995	UK	72	1.51	0.1
Catz et al.	2001	USA	84	0.58	-0.15
Catz et al.	2000	USA	72	0.25	-0.28
Chapman et al	2005	USA	8406	0.83	-0.05
Cluley and Cochrane	2001	UK	66	0.05	-0.56
Corless et al.	2005	USA	165	0.35	-0.28
Cruess et al.	2007	USA	116	0.42	-0.23
Frazier, Davis-Ali and Dahl	1994	USA	246	0.53	-0.17
Gifford et al.	2000	USA	133	1.25	0.06
Gonzalez et al.	2008	USA	208	0.93	-0.02
Gordillo et al.	1999	Spain	366	0.56	-0.16
Hashmi et al.	2007	Pakistan	438	0.82	-0.05
Ho et al.	2008	USA	13596	0.81	-0.05
Hovinga et al.	2008	USA	408	0.33	-0.21
Ickovics et al.	2002	USA	93	0.56	-0.16
Irvine et al.	1999	Canada	341	0.97	-0.01
Janson et al.	2008	USA	113	0.84	-0.04
Jindel et al.	2009	USA	32757	0.63	-0.1
Kalichman et al.	2008	USA	145	0.86	-0.04
Kleeberger et al.	2001	USA	539	0.84	-0.04
Liu et al.	2007	USA	807	0.82	-0.05
Molassiotis et al.	2002	Hong Kong	136	0.5	-0.19
Moralejo et al.	2006	Spain	143	0.74	-0.06
Reynolds et al.	2004	USA	384	0.28	-0.33
Royal et al.	2009	USA	350	0.33	-0.22
Sarna et al.	2008	India	310	0.31	-0.3
Shuter and Bernstein	2008	USA	64	0.5	-0.19
Singh et al.	1996	USA	46	0.6	-0.14
Tellez-Zenteno and Cardiel	2002	Mexico	189	3.36	0.31
Treadaway et al.	2009	USA	798	0.63	-0.12
Tucker et al.	2003	USA	1,910	0.89	-0.01
Van Servellen et al.	2002	USA	182	0.56	-0.16
Wilson et al.	1986	USA	184	0.6	-0.14
Woods et al.	2009	USA	79	0.95	-0.02
Wu et al.	2008	USA	134	0.38	-0.26

Ye et al.	2007	USA	5548	0.57	-0.04

Anxiety disorders:					
Author	Year	Country	n	OR Estimate	r Estimate
Cluley and Cochrane	2001	UK	66	NA	NA
Tucker et al.	2003	USA	1,910	NA	NA
Woods et al.	2009	USA	79	NA	NA

Psychosis:					
Author	Year	Country	n	OR Estimate	r Estimate
Ye et al.	2007	USA	5548	NA	NA

Part 20 – Cognitive ability

Measures of cognition:					
Author	Year	Country	n	OR Estimate	r Estimate
Hovinga et al.	2008	USA	408	NA	NA
Rosen et al.	2003	USA	79	NA	NA
Wagner	2002	USA	180	NA	NA
Woods et al.	2009	USA	79	NA	NA

Dementia/cognitive decline:					
Author	Year	Country	n	OR Estimate	r Estimate
Benner et al.	2004	USA	19422	0.72	-0.09
Benner et al.	2009	USA	5759	0.95	-0.01
Chapman et al.	2005	USA	8406	0.89	-0.03
Cruess et al.	2007	USA	116	0.5	-0.19
Gazmarian et al.	2006	USA	1549	0.76	-0.06
Ho et al.	2008	USA	13596	0.93	-0.01
Kleeberger et al.	2001	USA	539	0.83	-0.03
Lam, Lu, and Leung	2007	Hong Kong	209	0.81	-0.06

Strength of memory:					
Author	Year	Country	n	OR Estimate	r Estimate
Bane, Hughes and McElnay	2006	UK	139	0.97	-0.01
Molassiotis et al.	2002	Hong Kong	136	1.94	0.18
Woods et al.	2009	USA	79	1.47	0.1
Woods et al.	2008	USA	87	5.23	0.42

Part 21 – Personality variables

OCEAN model:					
Author	Year	Country	n	OR Estimate	r Estimate
Evangelista et al.	2001	USA	82	NA	NA

Christensen and Smith	1995	USA	72	NA	NA

Locus of control:

Internal:

Author	Year	Country	n	OR Estimate	r Estimate
Frazier, Davis-Ali and Dahl	1994	USA	246	0.96	-0.01
Lynam et al.	2009	USA	189	1.29	0.07
Stanton	1987	USA	50	5.1	0.41

Chance:

Author	Year	Country	n	OR Estimate	r Estimate
Frazier, Davis-Ali and Dahl	1994	USA	246	NA	NA
Lynam et al.	2009	USA	189	NA	NA

Powerful others:

Author	Year	Country	n	OR Estimate	r Estimate
Frazier, Davis-Ali and Dahl	1994	USA	246	NA	NA
Lynam et al.	2009	USA	189	NA	NA

Coping style:

Active:

Author	Year	Country	n	OR Estimate	r Estimate
Frazier, Davis-Ali and Dahl	1994	USA	246	0.75	-0.08
Golin et al.	2002	USA	117	1.44	0.1
Sewitch et al.	2004	Canada	127	1.03	0.01
Singh et al.	1996	USA	46	0.3	-0.31

Avoidant:

Author	Year	Country	n	OR Estimate	r Estimate
Deschamps et al.	2004	Belgium	43	NA	NA
Frazier, Davis-Ali and Dahl	1994	USA	246	NA	NA

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University of East Anglia

NHS

EMIS Number:

Study Number:

Patient and Lifestyle Scale

This questionnaire is to designed find out about you and how you feel about taking medicines. There are 5 sections and 20 questions in total.

- The first section asks some general questions about you (4 questions)
- The second section asks about any help you need reading medical information. (1 question)
- The third section asks your opinion on medicines in general. (8 questions)
- The fourth section asks about your mental health and whether you smoke or drink alcohol. (3 questions)
- The final section asks about how you take your medicine. (4 questions)

For each question, tick the box that you think best describes you or your feelings.

Section 1: About you

For the following questions, please tick the response that best describes you.

1	Your sex:	Male	☐	Female	☐
2	Employment Status:	I am employed	☐	I am unemployed	☐
		I am retired	☐	I am a student	☐
3	Housing Status:	I live with my spouse/partner	☐	I live alone	☐
		I live with others	☐		

4 Please enter your age in the box: ☐ years

Section 2: Written information

This section is about how easy you find reading written materials provided by medical staff. For example, these could be instructions included in a box of medication or information leaflets about your condition.

		Never	Occasionally	Sometimes	Often	Always
5	How often do you ask someone to help you understand medical information?	☐	☐	☐	☐	☐

Section 3: Your beliefs about medicines

This section is used to see how you feel about having to take medicines in general. These are statements that other people have made about medicines. Please show how much you agree or disagree by ticking the appropriate box.

		Strongly disagree	Disagree	Uncertain	Agree	Strongly Agree
6	Doctors prescribe too many medicines	❑	❑	❑	❑	❑
7	People who take medicines should stop their treatment for a while every now and again	❑	❑	❑	❑	❑
8	Most medicines are addictive	❑	❑	❑	❑	❑
9	Natural remedies are safer than medicines	❑	❑	❑	❑	❑
10	Medicines do more harm than good	❑	❑	❑	❑	❑
11	All medicines are poisons	❑	❑	❑	❑	❑
12	Doctors place too much trust on medicines	❑	❑	❑	❑	❑
13	If doctors had more time with patients they would prescribe fewer medicines	❑	❑	❑	❑	❑

Horne, R., Weinman, J. & Hankins, M. 1999. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*, 14, 1-24.

Section 4: Your mental health and behaviour

Your mental health is as important to us as your physical health. It is very useful for us to know whether or not you have a current or past history of mental illness. The most common form of mental illness is depression.

14 I have no diagnosed history of depression ☐ I have a current or past diagnosis for depression ☐

I prefer not to say ☐

I have a current or past diagnosis for a different mental illness (Please write in the box) ☐

Many people drink alcohol. If you drink alcohol, please indicate how many drinks you have in a typical week: (**half pints** of beer/lager, small glasses of wine, or single measures of spirits)

15 I do not drink alcohol ☐ I normally have around ☐ drinks per week

Many people smoke tobacco. If you smoke please indicate how often you smoke each day:

16 I do not smoke tobacco ☐ When I smoke, I normally smoke about ☐ cigarettes per day

Section 5: Using your medicine

Many people cannot always take their medicine according to the label on their medicines or according to what their doctor has said to them. Please indicate whether any of the following statements describe things that you sometimes do with your hypertension medicine.

		Yes	No
17	Do you ever forget to take your medicines?	☐	☐
18	Are you careless at times about taking your medicines?	☐	☐
19	When you feel better do you sometimes stop taking your medicines?	☐	☐
20	Sometimes if you feel worse when taking your medicines, do you stop taking them?	☐	☐

Morisky, D., Green, L., Levine, D. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*, 14, 1-24.

Thank you for completing this questionnaire.

University of East Anglia

NHS

Study Number:

Wellbeing and Medications Scale

This questionnaire is designed to find out how you feel about your illness and your medicines. There are 3 sections in total.

- Section one is about any stress, anxiety or depression you may be experiencing. (9 questions)
- Section two assesses how you feel taking your medicines influences your day to day life. (12 questions)
- Section three assesses your relationship with the doctor that prescribed your medicines. (9 questions)

For each question, tick the box that you think best describes your own feelings.

Section 1: Mental wellbeing and happiness

We all feel stressed from time to time. The first section of this questionnaire is designed to find out how much, if at all, you may be feeling stressed at the moment. The questions ask you about your feelings and thoughts **during the last month**. In each case tick *how often* you felt or thought a certain way. The best approach is to try to answer each question fairly quickly.

		Never	Almost never	Sometimes	Fairly Often	Very Often
1	In the last month, how often have you felt that you were unable to control the important things in your life?	❑	❑	❑	❑	❑
2	In the last month, how often have you felt confident about your ability to handle your personal problems?	❑	❑	❑	❑	❑
3	In the last month, how often have you felt that things were going your way?	❑	❑	❑	❑	❑
4	In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	❑	❑	❑	❑	❑

Cohen, S., Kamarck, T. & Mermelstein, R. 1983. A global measure of perceived stress. *Journal of Health and Social Behaviour*, 24, 385-396

As well as feeling stressed, many people also feel anxious or depressed. **Over the last two weeks**, how often you have been bothered by any of the following problems

		Not at all	Several days	More than half the days	Nearly every day
5	Having little interest or pleasure in doing things?	❑	❑	❑	❑
6	Feeling down, depressed or hopeless?	❑	❑	❑	❑
7	“Nerves”, or feeling anxious or on edge?	❑	❑	❑	❑
8	Worrying about a lot of different things?	❑	❑	❑	❑
9	During the last month, have you had an anxiety attack (suddenly feeling fear or panic)?	❑	❑	❑	❑

Kunik, M.E. *et al.* 2007. A practical screening tool for anxiety and depression in patients with chronic breathing disorders. *Psychosomatics*, 48, 16-21.

Section 2: Adjusting to your medicines

Thinking about your medicine and your condition, please show how much you agree or disagree with each statement by ticking the appropriate box.

		Strongly disagree	Disagree	Uncertain	Agree	Strongly Agree
10	I think my medicines are giving me side effects	❑	❑	❑	❑	❑
11	If my medicines are making me feel worse than my illness, I think it makes sense to stop taking it for a while	❑	❑	❑	❑	❑
12	I think my medicines make me feel better than I would without them	❑	❑	❑	❑	❑
13	I think my illness would be worse without my medicines	❑	❑	❑	❑	❑
14	I think my medicines help to keep me feeling as healthy as possible	❑	❑	❑	❑	❑
15	I find it hard to remember to take all of my medicines each day	❑	❑	❑	❑	❑
16	I think I can cope with the number of medicines I am prescribed at the moment	❑	❑	❑	❑	❑
17	I am concerned about how others will react if I tell them what medicines I take	❑	❑	❑	❑	❑
18	There are people who will help me with my medicines if needed	❑	❑	❑	❑	❑
19	I have people I can talk to about my illness	❑	❑	❑	❑	❑
20	I can count on my family and friends to help me deal with my illness	❑	❑	❑	❑	❑
21	I find it hard or inconvenient to get my supply of medicine	❑	❑	❑	❑	❑

Section 3: About your doctor

Here are nine statements a person can make about their family doctor. Please tick to indicate how much you agree with each statement:

		Strongly disagree	Disagree	Uncertain	Agree	Strongly agree
22	My doctor helps me	❑	❑	❑	❑	❑
23	My doctor has enough time for me	❑	❑	❑	❑	❑
24	I trust my doctor	❑	❑	❑	❑	❑
25	My doctor understands me	❑	❑	❑	❑	❑
26	My doctor is dedicated to helping me	❑	❑	❑	❑	❑
27	My doctor and I agree on the nature of my medical symptoms	❑	❑	❑	❑	❑
28	I can talk to my doctor	❑	❑	❑	❑	❑
29	I feel content with the treatment I receive from my doctor	❑	❑	❑	❑	❑
30	I find my doctor easily accessible	❑	❑	❑	❑	❑

Van Der Feltz-Cornelis, C.M., Van Oppen, P., Van Marwijk, H.W.J., De Breurs, E. & Van Dyck, R. 2004. A patient-doctor relationship questionnaire (PDRQ-9) in primary care: development and psychometric evaluation. *General Hospital Psychiatry*, 26, 115-120.

Thank you for completing this questionnaire.

University of East Anglia

Centre for Medicines Management Research

Scoring Guide for the Patient and Lifestyle Scale, and the Wellbeing and Medication Scale

Section 1: Introduction

The Patient and Lifestyle Scale (PALS) and Wellbeing and Medicines Scale (WAMS) are tools designed to identify patients that may be non-adherent to their prescribed medicinal therapy.

Direct questioning of patients about their adherence behaviour is liable to produce socially desirable responses. PALS and WAMS estimate actual behaviour by examining patient focussed correlates of adherence derived from a series of meta analyses. The PALS targets static or slow changing factors such as a patient's general beliefs about medicines, health literacy, or frequency of participation in risky health behaviours such as drinking or smoking. The WAMS examines aspects of the patient's current context and experience such as whether they are experiencing symptoms of stress or depression, whether they perceive their medicines to be necessary, and how much social support they are receiving for their medicines and condition. The WAMS can therefore be used as a part of the regular monitoring of patients to assess any changes in their circumstances or beliefs that may be associated with adherence to medication.

Item scores are all presented as percentages for ease of comprehension where scores closer to 100 indicate a greater likelihood of non-adherence.

Section 2: PALS Scores

The PALS questionnaire has three sections. The first examines patient's beliefs about medicines in general, the second assesses their health literacy, and the final section seeks to examine the life situation of the patient and their behaviours which may indicate their adherence.

Section 1: About you (Items 1-4)
Aspects of the patient's lifestyle are captured in this section.
Scoring
Each question on this scale has slightly different scoring which is described below. For each item, higher scores indicate a greater likelihood of non-adherence.
Item 1: Your sex – Not scored. There is no documented relationship between adherence and sex. This question exists only to ease patients into the scale with a predictable question.
Item 2: Employment status – 2 point scale. I am employed = 0 and I am unemployed = 100. There is no evidence that those that are retired or students have better or worse adherence. Nonetheless patients may be in this situation. In such situations scores for this item should be omitted from the scale summary.
Item 3: Housing status – Two point scale where I live with my spouse/partner = 0, I live alone = 100 and I live with others is omitted from the scale. It is not known whether or not living with others that are not a spouse or partner is associated with adherence.
Item 4: Age – This item does not contribute to a summary score.

Section 2: Written information (Item 5)
This section comprises a single item to establish health literacy.
Scoring
The item is scored on a 5 point Likert scale where never = 0 and always = 100. Higher scores indicate poorer health literacy.

Section 3: Your beliefs about medicines (Items 6-13)
Patients beliefs about medicines are assessed using the 8 item version of the Beliefs about Medicines Questionnaire (BMQ). This scale comprises two 4 item subscales. The *general-overuse* scale addresses patient's beliefs that doctors place too much trust in medicines and may over depend upon them (Items 6, 9, 12 and 13). The *general-harm* scale assesses beliefs regarding how far patients feel medicines to be intrinsically harmful (Items 7,8, 10 and 11).

Scoring
Scores for agreement fall on a 5 point Likert scale from 0 = strongly disagree to 100 = strongly agree. Higher scores indicate stronger negative beliefs about medicines and their use, which may indicate of a lower likelihood of successfully adhering to medicinal therapy.

Section 4: Your mental health and behaviour
This section considers more sensitive topics about patients mental health and their drinking and smoking habits.

Scoring
Item 14a: Diagnoses of depression – this is a two item scale where no diagnosed history of depression = 0 and a current or past diagnosis of depression = 100. Patients that prefer not to say will necessarily have to have this item omitted from a summary score.
Item 14b: Patients may also state if they have a diagnoses of mental illness other than depression. If participants write any mental illness in this box they score 100. Leaving it blank scores 0. Patients that prefer not to say will necessarily have to have this item omitted from a summary score.
Item 15: Alcohol consumption. Participants are asked to indicate how many drinks of a specified size they have on a typical week. They may indicate that they do not drink. Not drinking = 0, 1-5 drinks = 20, 6-10 drinks = 40, 11-15 drinks = 60, 16-20 drinks = 80, and 21+ drinks = 100.
Item 18: Tobacco consumption. Participants are asked to indicate how many cigarettes they have on a typical day. They may indicate that they do not smoke. Not smoking = 0, 1-5 cigarettes = 20, 6-40 cigarettes = 40, 11-15 cigarettes = 60, 16-20 cigarettes = 80, and 21+ cigarettes = 100.

PALS summary score
Each scale is expressed as a percentage of the maximum possible score. For example, a five point scale has possible scores of 0, 25, 50, 75, and 100 while a 2 point scale would have possible scores of 0 and 100. Add these totals together and then divide by the number of items on each scale to express each scale within the PALS as a percentage total on that particular predictor of adherence. Whilst performing this step, omit any responses that are missing or are marked as 'prefer not to say'. To construct a final summary score add together the scale subtotals and then divide by 7 (the total number of subscales assuming at least some of every scale is completed by the patient) to produce a value between 0 – 100 where scores closer to 100 will indicate a patient scoring high on many different subscales and predicting a higher risk of having low adherence to their medication.

Scoring summary:
Subscale total = Sum of item totals/ Total number of items in subscale completed by patient
PALS total = Sum of subscale totals / Total number of subscales completed by patient

Section 3: WAMS Scores

The WAMS has three sections. The first examines a patient's mental wellbeing, the second assesses their beliefs about their medicines and how they are being incorporated into the patient's life, and the final section seeks to examine the quality of the relationship between the patient and their general practitioner.

Section 1: Mental wellbeing and happiness (Items 1–9)
This section comprises two tools which assess a patient's experience of stress, anxiety, and depressive symptoms.
Stress is assessed via the four item version of the Perceived Stress Scale (PSS). Anxiety and depression are assessed using the five item version of the Patient Health Questionnaire (PHQ). This comprises of two questions which screen for depression (items 5 and 6) and three items which assess anxiety (Items 7 – 9).
Scoring
Items on the PSS are scored on a 5 point Likert scale where never = 0 and very often = 100 for items 1 and 4 and never = 100 and Very often = 0 for items 2 and 3. Higher scores indicate greater stress which is predicted to be associated with lowered adherence. Each item on the PHQ is scored on a 4 point scale where not at all = 0 and nearly every day = 100 where any response of 'yes' indicates a positive screen for depression or anxiety which is associated with lower adherence. This changes the scale of the original measure, but not the relative weights of response.

Section 2: Adjusting to your medicines (Items 10–21)
This section comprises of 5 subscales. Items 10 and 11 assess any concerns patients may have about their medicines. Items 12–14 indicate how necessary and important patients consider their medicine to be for their health. Items 15 and 16 examine patients' self efficacy, and how hard patients consider it to be to take their medicine. Items 17–20 capture aspects of social support that a patient receives while item 21 examines how difficult patients find it to access a supply of their medicines.
Scoring
All subscales are measured on a 5 point Likert scale. Items 10, 11, 15, 16, 17 and 19 are scored such that strongly disagree = 0 and strongly agree = 100. Items 12, 13 14, 18, 20 and 21 are scored such that strongly disagree = 100 and strongly agree = 0.

Section 3: About your doctor (Items 22–30)
This 9 item scale assesses a patient's relationship with their general practitioner.
Scoring
All items in this scale are coded on a five point Likert scale where strongly disagree = 100 and strongly agree = 0. Higher scores predict a greater likelihood of patient non-adherence to therapy.

WAMS summary score
Each scale is expressed as a percentage of the maximum possible score. For example, a five point scale has possible scores of 0, 25, 50, 75, and 100 while a 2 point scale would have possible scores of 0 and 100. Add these totals together and then divide by the number of items on each scale to express each scale within the WAMS as a percentage total on that particular predictor of adherence. Whilst performing this step, omit any responses that are missing. To construct a final summary score add together the scale subtotals and then divide by 9 (the total number of subscales assuming at least some of every scale is completed by the patient) to produce a value between 0 – 100 where scores

closer to 100 will indicate a patient scoring high on many different subscales and predicting a higher risk of having low adherence to their medication.

Scoring summary:
Subscale total = Sum of item totals/ Total number of items in subscale completed by patient
WAMS total = Sum of subscale totals / Total number of subscales completed by patient

Section 4: Combined summary scores

The combined summary score can be completed using the following formula:
Score = [(PALS total score * Number of PALS subscales completed by patient) + (WAMS total score * Number of WAMS subscales completed by patient)] / Total number of PALS and WAMS subscales completed by patient.
For example, if a patient completes all subscales on both PALS and WAMS then take the PALS score and multiply it by 7, then multiply the WAMS score by 9. Divide this total by 16. If a patient indicates that they are retired on the PALS, and refuses or forgets to answer how hard or difficult they find it to access a new supply of medicines on WAMS item 21, then the summary score would be calculated by: [(PALS summary score * 6) + (WAMS summary score * 8)] / 14.
Calculating the score in this way ensures that each subscale is given an equal weighting in providing the overall summary score. Scores work the same as they do for the individual scales with scores ranging from 0-100 and with higher scores indicating a greater risk of non-adherence to medicines.

Section 5: Brief Scoring Guide

Find below versions of the questionnaire with a scoring guide in place of response sets. Below each questionnaire is a summary of how to calculate summary scores.

University of East Anglia

CMMR Centre for Medicines Management Research

Patient and Lifestyle Scale Scoring Guide

This questionnaire is to designed find out about you and how you feel about taking medicines. There are 5 sections and 20 questions in total.

- The first section asks some general questions about you (4 questions)
- The second section asks about any help you need reading medical information. (1 question)
- The third section asks your opinion on medicines in general. (8 questions)
- The fourth section asks about your mental health and whether you smoke or drink alcohol. (3 questions)
- The final section asks about how you take your medicine. (4 questions)

For each question, tick the box that you think best describes you or your feelings.

Section 1: About you

For the following questions, please tick the response that best describes you.

1	Your sex:	Male	NA	Female	NA
2	Employment Status:	I am employed	0	I am unemployed	100
		I am retired	NA	I am a student	NA
3	Housing Status:	I live with my spouse/partner	0	I live alone	100
		I live with others	NA		

4 Please enter your age in the box: NA years

Section 2: Written information

This section is about how easy you find reading written materials provided by medical staff. For example, these could be instructions included in a box of medication or information leaflets about your condition.

		Never	Occasionally	Sometimes	Often	Always
5	How often do you ask someone to help you understand medical information?	0	25	50	75	100

Section 3: Your beliefs about medicines

This section is used to see how you feel about having to take medicines in general. These are statements that other people have made about medicines. Please show how much you agree or disagree by ticking the appropriate box.

		Strongly disagree	Disagree	Uncertain	Agree	Strongly Agree
6	Doctors prescribe too many medicines	0	25	50	75	100
7	People who take medicines should stop their treatment for a while every now and again	0	25	50	75	100
8	Most medicines are addictive	0	25	50	75	100
9	Natural remedies are safer than medicines	0	25	50	75	100
10	Medicines do more harm than good	0	25	50	75	100
11	All medicines are poisons	0	25	50	75	100
12	Doctors place too much trust on medicines	0	25	50	75	100
13	If doctors had more time with patients they would prescribe fewer medicines	0	25	50	75	100

Horne, R., Weinman, J. & Hankins, M. 1999. The beliefs about medicines questionnaire: The development and evaluation of a new method for assessing the cognitive representation of medication. *Psychology and Health*, 14, 1-24.

Section 4: Your mental health and behaviour

Your mental health is as important to us as your physical health. It is very useful for us to know whether or not you have a current or past history of mental illness. The most common form of mental illness is depression.

14	I have no diagnosed history of depression	0	I have a current or past diagnosis for depression	100
	I prefer not to say	NA		
	I have a current or past diagnosis for a different mental illness (Please write in the box)		None = 0 Any = 100	

Many people drink alcohol. If you drink alcohol, please indicate how many drinks you have in a typical week: (half pints of beer/lager, small glasses of wine, or single measures of spirits)

15	I do not drink alcohol	0	I normally have around		drinks per week

1–5 drinks = 20, 6–10 drinks = 40, 11–15 drinks = 60, 16 – 20 drinks = 80, 21+ drinks = 100

Many people smoke tobacco. If you smoke, please indicate how often you smoke:

16	I do not smoke tobacco	0	When I smoke, I normally smoke about		cigarettes per day

1–5 drinks = 20, 6–10 drinks = 40, 11–15 drinks = 60, 16 – 20 drinks = 80, 21+ drinks = 100

PALS Summary of scoring

Scale/Item	Response					Sub-total		Scale Score
Employment								
2	0	100	NA					
							Total Score	_____
Housing Status								
3	0	100	NA					
							Total Score	_____
Health Literacy								
5	0	25	50	75	100			
							Total Score	_____
BMQ-General Overuse								
6	0	25	50	75	100	_____		
9	0	25	50	75	100	_____		
12	0	25	50	75	100	_____		
13	0	25	50	75	100	_____		
					Total Score	_____	Total Score/ No. items completed	_____
BMQ-General Harm								
7	0	25	50	75	100	_____		
8	0	25	50	75	100	_____		
10	0	25	50	75	100	_____		
11	0	25	50	75	100	_____		
					Total Score	_____	Total Score/ No. items completed	_____
Mental Illness								
14a	0	100	NA			_____		
14b	0	100	NA			_____		
					Total Score	_____	Total Score/ No. items completed	_____
Health Behaviours								
15	0	20	40	60	80	100	_____	
16	0	33	67	100			_____	
					Total Score	_____	Total Score/ No. items completed	_____

PALS summary = Sum of scale scores/ Number of scales completed
Note: Items 1 and 4 are omitted from scoring and are not included here.

University of East Anglia

Centre for Medicines Management Research

Wellbeing and Medications Scale Scoring Guide

This questionnaire is designed to find out how you feel about your illness and your medicines. There are 3 sections in total.

- Section one is about any stress, anxiety or depression you may be experiencing. (9 questions)
- Section two assesses how you feel taking your medicines influences your day to day life. (12 questions)
- Section three assesses your relationship with the doctor that prescribed your medicines. (9 questions)

For each question, tick the box that you think best describes your own feelings.

Section 1: Mental wellbeing and happiness

We all feel stressed from time to time. The first section of this questionnaire is designed to find out how much, if at all, you may be feeling stressed at the moment. The questions ask you about your feelings and thoughts **during the last month**. In each case tick *how often* you felt or thought a certain way. The best approach is to try to answer each question fairly quickly.

		Never	Almost never	Sometimes	Fairly Often	Very Often
1	In the last month, how often have you felt that you were unable to control the important things in your life?	0	25	50	75	100
2	In the last month, how often have you felt confident about your ability to handle your personal problems?	100	75	50	25	0
3	In the last month, how often have you felt that things were going your way?	100	75	50	25	0
4	In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	0	25	50	75	100

Cohen, S., Kamarck, T. & Mermelstein, R. 1983. A global measure of perceived stress. *Journal of Health and Social Behaviour*, 24, 385-396

As well as feeling stressed, many people also feel anxious or depressed. **Over the last two weeks**, how often you have been bothered by any of the following problems

		Not at all	Several days	More than half the days	Nearly every day
5	Having little interest or pleasure in doing things?	0	33	67	100
6	Feeling down, depressed or hopeless?	0	33	67	100
7	“Nerves”, or feeling anxious or on edge?	0	33	67	100
8	Worrying about a lot of different things?	0	33	67	100
9	During the last month, have you had an anxiety attack (suddenly feeling fear or panic)?	0	33	67	100

Kunik, M.E. *et al.* 2007. A practical screening tool for anxiety and depression in patients with chronic breathing disorders. *Psychosomatics*, 48, 16-21.

Section 2: Adjusting to your medicines

Thinking about your medicine and your condition, please show how much you agree or disagree with each statement by ticking the appropriate box.

		Strongly disagree	Disagree	Uncertain	Agree	Strongly Agree
10	I think my medicines are giving me side effects	0	25	50	75	100
11	If my medicines are making me feel worse than my illness, I think it makes sense to stop taking it for a while	0	25	50	75	100
12	I think my medicines make me feel better than I would without them	100	75	50	25	0
13	I think my illness would be worse without my medicines	100	75	50	25	0
14	I think my medicines help to keep me feeling as healthy as possible	100	75	50	25	0
15	I find it hard to remember to take all of my medicines each day	0	25	50	75	100
16	I think I can cope with the number of medicines I am prescribed at the moment	100	75	50	25	0
17	I am concerned about how others will react if I tell them what medicines I take	0	25	50	75	100
18	There are people who will help me with my medicines if needed	100	75	50	25	0
19	I have people I can talk to about my illness	100	75	50	25	0
20	I can count on my family and friends to help me deal with my illness	100	75	50	25	0
21	I find it hard or inconvenient to get my supply of medicine	0	25	50	75	100

Section 3: About your doctor

Here are nine statements a person can make about their family doctor. Please tick to indicate how much you agree with each statement:

		Strongly disagree	Disagree	Uncertain	Agree	Strongly agree
22	My doctor helps me	100	75	50	25	0
23	My doctor has enough time for me	100	75	50	25	0
24	I trust my doctor	100	75	50	25	0
25	My doctor understands me	100	75	50	25	0
26	My doctor is dedicated to helping me	100	75	50	25	0
27	My doctor and I agree on the nature of my medical symptoms	100	75	50	25	0
28	I can talk to my doctor	100	75	50	25	0
29	I feel content with the treatment I receive from my doctor	100	75	50	25	0
30	I find my doctor easily accessible	100	75	50	25	0

Van Der Feltz-Cornelis, C.M., Van Oppen, P., Van Marwijk, H.W.J., De Breurs, E. & Van Dyck, R. 2004. A patient-doctor relationship questionnaire (PDRQ-9) in primary care: development and psychometric evaluation. *General Hospital Psychiatry*, 26, 115-120.

Thank you for your time in completing this questionnaire.

WAMS Summary of scoring

Scale/Item			Response			Sub-total		Scale Score
PSS-4								
1	0	25	50	75	100	_____		
2	0	25	50	75	100	_____		
3	0	25	50	75	100	_____		
4	0	25	50	75	100	_____		
					Total Score	_____	Total Score/ No. items completed	_____
PHQ-5 Depression								
5	0	33	67	100		_____		
6	0	33	67	100		_____		
					Total Score	_____	Total Score/ No. items completed	_____
PHQ-5 Anxiety								
7	0	33	67	100		_____		
8	0	33	67	100		_____		
9	0	33	67	100		_____		
					Total Score	_____	Total Score/ No. items completed	_____
Medication concerns								
10	0	25	50	75	100	_____		
11	0	25	50	75	100	_____		
					Total Score	_____	Total Score/ No. items completed	_____
Medication necessity								
12	0	25	50	75	100	_____		
13	0	25	50	75	100	_____		
14	0	25	50	75	100	_____		
					Total Score	_____	Total Score/ No. items completed	_____
Self-efficacy								
15	0	25	50	75	100	_____		
16	0	25	50	75	100	_____		
					Total Score	_____	Total Score/ No. items completed	_____
Social Support								
17	0	25	50	75	100	_____		
18	0	25	50	75	100	_____		
19	0	25	50	75	100	_____		
20	0	25	50	75	100	_____		
					Total Score	_____	Total Score/ No. items completed	_____
Access to Medicine								
21	0	25	50	75	100	_____		
							Total Score	_____
PDRQ-9								
22	0	25	50	75	100	_____		
23	0	25	50	75	100	_____		
24	0	25	50	75	100	_____		
25	0	25	50	75	100	_____		
26	0	25	50	75	100	_____		
27	0	25	50	75	100	_____		
28	0	25	50	75	100	_____		
29	0	25	50	75	100	_____		
30	0	25	50	75	100	_____		
					Total Score	_____	Total Score/ No. items completed	_____

WAMS summary = Sum of scale scores/ Number of scales completed

Appendix H – Participant non-response postcard

Front:

Medication adherence in hypertension – participant nonresponse postcard

Recently you were sent a pack containing an invitation to take part in research run by the University of East Anglia and Elvington Medical Practice. We fully respect your decision to not take part and it will be useful to us when designing future research if you would tell us the reasons why you decided to not take part. Nobody will be able to identify you from your response. If you would like to help us, simply tick the boxes that apply to you overleaf and return this card in the prepaid envelope provided. You do not have to respond to this card if you do not wish.

Back:

Please tick all boxes that apply to you: (☐)

I did not find the research interesting	☐
The questionnaire I was asked to complete seemed too long	☐
I did not want to take part in the interviews	☐
I did not want the researchers to access my medical records	☐
I wasn't sure what I was being asked to do	☐
Too much information was sent at the same time	☐
The questions on the questionnaire made me feel uncomfortable	☐
I didn't want the staff at the surgery to see my results	☐
I felt uncomfortable about posting the pack back to the	☐

Other (please state):

Thank you for helping us to improve our research

ELVINGTON MEDICAL PRACTICE
YORK ROAD
ELVINGTON
YORK
YO41 4DY
Tel: 08450 71 71 70

Fax. 01904 608710

~[Title/Initial/Surname]
~[Patient Address Block]

~[Today...]

Dear ~[Title] ~[Surname]

According to our records you are due a blood pressure review/ blood test/ urine test.

It is recommended that all people with known raised blood pressure either on medication or not should have their blood pressure checked six monthly and have annual blood and urine tests.

Please make an appointment at your usual surgery with our Health Care Assistant.

Elvington Medical Practice is also currently doing some research with the University of East Anglia. If you are interested in taking part all the information you need is included in this pack. You do not have to take part in this research if you do not want to.

Yours sincerely

Practice Nurse

9 What if I change my mind about taking part?

You do not have to take part in this research, and if you decide to take part you may withdraw at any point before the research is completed.

10 Who is organising and funding the research?

The study is being organised by Steven Watson, a PhD student at the University of East Anglia. The study is being supervised by Dr. Debi Bhattacharya, and by Dr. Tim Longmore at Elvington Medical Practice. The study is funded by the university.

11 Who can I contact?

You can contact the lead researcher Steven Watson by telephone or e-mail on 01603 59 1973 or steven.watson@uea.ac.uk. You can also speak to Dr. Tim Longmore from Elvington Medical Practice on 01904 60 8224. If you wish to make a complaint about this research please contact Dr Debi Bhattacharya on 01603 59 33 91, or the Patient Relations Team for North Yorkshire on 0800 06 88 000.

12 Thank you for your time!

If you decide you would like to take part, please keep this information sheet and one copy of the consent form for your own records. Please seal a second signed copy of the consent form in the envelope with the questionnaire you return.

University of East Anglia

NHS

Medication adherence in hypertension

Participant information sheet: Part 1 of 2

We would like to invite you to take part in a questionnaire study conducted by the University of East Anglia and Elvington Medical Practice.

Please read this leaflet carefully before you decide whether or not to take part. Feel free to contact us or to discuss this with others. You can contact us using the details at the end of this form.

If you do not wish to take part, it will not

1 What is the purpose of this study?

This study hopes to find out about how patient beliefs and experiences affect how they take their hypertension medicines.

2 Why have I been chosen to take part in this study?

You are registered at Elvington Medical Practice and are due for a review of your hypertension.

3 What will I have to do?

There are two questionnaires that we would like you to complete. The first questionnaire has been posted to you in this pack. It should take less than 10 minutes to complete. In four weeks we will post a second questionnaire. This should also take less than 10 minutes to complete. We would also like to look at your medical records so that we can see how often you have ordered your prescription for your hypertension medicines, and look at your blood pressure history.

4 What are the disadvantages or risks of taking part?

Some questions may make you feel uncomfortable. You may choose to not respond to these questions if you wish. We may also inform your doctor if your results indicate that you have an undiagnosed condition such as depression.

5 What are the benefits of taking part?

There are no direct benefits to you, but this research may help us to better help patients to take their medicine in the future.

6 How will my confidentiality be assured?

No information that leaves the medical practice will have your name or address on it so that you cannot be recognised. The medical team at Elvington will use the questionnaire in this pack to update their records about whether you smoke or drink. The practice will not use any other information in the questionnaires.

7 How will my data be stored and used?

Your data will be kept in a locked filing cabinet, or on a password protected computer. Your data will be used for research and to update your doctor about how much you drink or smoke. This study is part of an educational thesis, may be published. If you would like a summary of the research contact Steven Watson using the details below. Your individual data will not be identifiable in any report that is published.

8 How do I take part?

Please sign the consent form and then complete the questionnaire. You can then either post or take these forms to Elvington Medical Practice. If you would like to post the forms a pre-paid envelope is provided.

University of East Anglia

NHS

Medication adherence in hypertension – Study consent form

If you would like to take part in this study, please initial each of the boxes. You can only be included in the study if you indicate that you have read and understood the participant information leaflet that was posted to you along with this form.

	Please initial
I confirm that I have read and understand the information sheet entitled "Medication adherence in hypertension - Participant information sheet: Part 1 of 2" for the above study and have had the opportunity to ask questions.	
I understand that my participation is voluntary and that I am free to withdraw at any time without my medical care or legal rights being affected.	
I am willing to allow the research team access to my health care records but understand that strict confidentiality will be maintained.	
I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from regulatory authorities which monitor the quality of research.	
I give permission for individuals from the above mentioned regulatory authorities to have access to my records.	
I will allow my GP to use the information I provide in the "Patient and Lifestyle Scale" questionnaire to update my medical records about how much I smoke or drink.	
I agree to take part in the above study.	

…….....	……/……/……	…….....
Name of participant	Date	Signature

Appendix K - Feasibility study consent form (Text size reduced to fit thesis format)

Please complete both copies of this form. Hand one in to the medical practice in the enclosed envelope with your questionnaires, and keep one copy for your own records.

If you would be interested in taking part in an interview as part of this study, please see the separate information sheets and sign the separate consent forms.

Researcher contact details:

Steven Watson
University of East Anglia
Norwich
Norfolk
NR4 7TJ
Tel: 01603 59 1973
E-Mail: steven.watson@uea.ac.uk

Dr. Tim Longmore
Elvington Medical Practice
York Road
Elvington
York
YO41 4DY
Tel: 01904 60 8224

To make a complaint:

Patient Relations Team
North Yorkshire and York PCT
Freepost NEA 13107
York
North Yorkshire
YO31 7ZX
Tel: 0800 06 88 000

Thank you!

9 What if I change my mind about taking part?

You do not have to take part, and if you decide to take part you may withdraw at any point before the research is completed.

10 Who is organising and funding the research?

The study is being organised by Steven Watson. The study is being supervised by Dr. Debi Bhattacharya, and by Dr. Tim Longmore at Elvington Medical Practice. The study is funded by the university.

11 Who can I contact?

You can contact Steven Watson by telephone or e-mail on 01603 59 1973 or steven.watson@uea.ac.uk. You can also speak to Dr. Tim Longmore. If you wish to make a complaint about this research please contact Dr Debi Bhattacharya on 01603 59 33 91 or the Patient Relations Team for North Yorkshire on 0800 06 88 000.

12 Thank you for your time!

If you decide you would like to take part, please keep this information sheet and one copy of the consent form for your own records.

University of East Anglia

NHS

Medication adherence in hypertension

Participant information sheet: Part 2 of 2

In addition to the main study described in part 1 of this leaflet, we would also like to interview some of our participants. The questionnaires used in this study are still under development so we would like to talk to people that have used them to find out how they found the questionnaires and being part of the study. We think this will really help us to design better questionnaires and a better study to further test them later on.

Please read this leaflet carefully before you decide whether or not to take part. You do not have to take part in this part of the study even if you take part in the main study. Feel fr

1 What is the purpose of this study?

This study hopes to find out what our participants thought about two new questionnaires. We would also like to know what it was like taking part in the study.

2 Why have I been chosen to take part in this study?

You are registered at Elvington Medical Practice and are due for a review of your hypertension.

3 What will I have to do?

The interview will be with Steven Watson, a PhD student at the University of East Anglia. If you agree to be interviewed you may choose to have the interview either in your home or at Elvington Medical Practice. We will discuss the new questionnaires and the study design. At the end of the study, you will be invited to comment on a summary of the results. The interview will last for about an hour, and will be tape recorded to help with our analysis. This recording will be typed on paper after the interview, but we will remove any names or information that might identify you.

4 What are the disadvantages or risks of taking part?

Some questions may make you feel uncomfortable and you do not have to answer these. Some people find taking part in interviews upsetting, and you may stop the interview at any point. If you become upset we will offer you support from your doctor or a neutral party such as the patient relations team. We may inform your doctor if we feel that you have an undiagnosed condition such as depression.

5 What are the benefits of taking part?

There are no direct benefits to you, but this research may help us to help patients to take their medicine in the future.

6 How will my confidentiality be assured?

No information that leaves the medical practice will have your name or address on it so that you cannot be recognised. We may use direct quotes from the interview in study reports but we will make sure that these do not identify you.

7 How will my data be stored and used?

Your data will be kept in a locked filing cabinet, or on a password protected computer. Your data will be used for research. This study is part of an educational thesis, and may be published.

8 How do I take part?

Please sign the consent form and post this back with your "Patient and Lifestyle Scale" questionnaire. At the end of the main study, Steven Watson may contact you to arrange an interview. We may not be able to interview everyone that agrees, and we will let you know if we cannot interview you.

University of East Anglia

NHS

Medication adherence in hypertension – Interview participant consent form

We are conducting some interviews as part of this study to help us to improve the design of the new questionnaires and to improve the quality of future research that we conduct. If you would like to take part in these interviews, please initial each of the boxes. You can only be included in the study if you indicate that you have read and understood the participant information leaflet that was posted to you along with this form.

	Please initial
I confirm that I have read and understand the information sheet entitled "Medication adherence in hypertension – Participant information sheet: Part 2 of 2" for the above study and have had the opportunity to ask questions.	
I understand that my participation is voluntary and that I am free to withdraw at any time without my medical care or legal rights being affected.	
I agree to be contacted and invited to be interviewed as part of this study.	
I agree to have the interview recorded on an audio device.	
I permit the researchers to use direct quotes from the interviews so long as they do not reveal information which could be used to identify me	
I understand that data collected during the study may be looked at by individuals from regulatory authorities which monitor the quality of research.	
I give permission for individuals from the above mentioned regulatory authorities to have access to my records.	

Appendix M – Participant interview consent form (text size reduced to fit thesis format)

Please provide a contact telephone number to arrange an interview:
……..…..

……..….. ……/…../…...
…….
Name of participant Date
Signature

Please complete both copies of this form. Hand one in to the medical practice in the enclosed envelope with your "Patient and Lifestyle Scale" questionnaire, and keep one copy for your own records.

Researcher contact details:

Steven Watson
University of East Anglia
Norwich
Norfolk
NR4 7TJ
Tel: 01603 59 1973
E-Mail: steven.watson@uea.ac.uk

Dr. Tim Longmore
Elvington Medical Practice
York Road
Elvington
York
YO41 4DY
Tel: 01904 60 8224

To make a complaint:

Patient Relations Team
North Yorkshire and York PCT
Freepost NEA 13107
York
North Yorkshire
YO31 7ZX
Tel: 0800 06 88 000

Thank you!

9 What if I have changed my mind about taking part?

You do not have to take part in this research, and if you decide to take part you may withdraw at any point before the research is completed.

10 Who is organising and funding the research?

The study is being organised by Steven Watson, a PhD student at the University of East Anglia. The study is being supervised by Dr. Debi Bhattacharya, and by Dr. Tim Longmore at Elvington Medical Practice. The study is funded by the university.

11 Who can I contact?

You can contact the lead researcher Steven Watson by telephone or e-mail on 01603 59 1973 or steven.watson@uea.ac.uk. You can also speak to Dr. Tim Longmore from Elvington Medical Practice on 01904 60 8224. If you wish to make a complaint about this research please contact Dr Debi Bhattacharya on 01603 59 33 91, or the Patient Relations Team for North Yorkshire on 0800 06 88 000.

12 Thank you for your time!

If you decide you would like to take part, please keep this information sheet for your records.

University of East Anglia

NHS

Medication adherence in hypertension

Participant information sheet

We would like to thank you for taking part in this study. Please read this leaflet carefully to remind yourself of what to do now. If there is anything you would like to ask us feel free to contact us using the details at the end of this form.

You do not have to continue to take part in the study if you do not want to. You may also request to have any information you have given to us so far to be withdrawn by contacting us using the details provided. If you no longer wish to take part, it will not affect the care you receive from your doctor in any way.

1 What is the purpose of this study?

This study hopes to find out about how patient beliefs and experiences affect how they take their hypertension medicines.

2 Why was I been chosen to take part in this study?

You are registered at Elvington Medical Practice and are due for a review of your hypertension.

3 What will I have to do?

You have already completed one questionnaire for us. We would like you to complete a second questionnaire for us. This should not take more than 10 minutes to complete. As a reminder, we would also like to look at your medical records so that we can see how often you have ordered your prescription for your hypertension medicines, and look at your blood pressure history.

4 What are the disadvantages or risks of taking part?

Some questions may make you feel uncomfortable. You may choose to not respond to these questions if you wish. We may also inform your doctor if your results indicate that you have an undiagnosed condition such as depression.

5 What are the benefits of taking part?

There are no direct benefits to you, but this research may help us to better help patients to take their medicine in the future.

6 How will my confidentiality be assured?

No information that leaves the medical practice will have your name or address on it so that you cannot be recognised. The medical team at Elvington will not see your individual responses to this second questionnaire. Only the researchers from the University of East Anglia will see your individual responses.

7 How will my data be stored and used?

Your data will be kept in a locked filing cabinet, or on a password protected computer. Your data will be used for research and to update your doctor about how much you drink or smoke. This study is part of an educational thesis, may be published. If you would like a summary of the research contact Steven Watson using the details below. Your individual data will not be identifiable in any report that is published.

8 How do I take part?

Please complete the enclosed questionnaire. You can then post these forms to Elvington Medical Practice in the pre-paid and addressed envelope provided. The questionnaires will only be seen by a researcher from the University. The staff at Elvington Medical Practice will not see the responses you make to this questionnaire.

8 What if I change my mind about taking part?

You do not have to take part in this research, and if you decide to take part you may withdraw at any point before the research is completed.

9 Who is organising and funding the research?

The study is being organised by Steven Watson, a PhD student at the University of East Anglia. The study is being supervised by Dr. Debi Bhattacharya, and by Dr. Tim Longmore at Elvington Medical Practice. The study is funded by the university.

10 Who can I contact?

You can contact the lead researcher Steven Watson by telephone or e-mail on 01603 59 1973 or steven.watson@uea.ac.uk. You can also speak to Dr. Tim Longmore from Elvington Medical Practice on 01904 60 8224. If you wish to make a complaint about this research please contact Dr Debi Bhattacharya on 01603 59 33 91, or the Patient Relations Team for North Yorkshire on 0800 06 88 000.

11 Thank you for your time!

If you decide you would like to take part, please keep this information sheet and one copy of the consent form for your own records. Please seal a second signed copy of the consent form in the yellow envelope with the questionnaire you return.

University of East Anglia

NHS

Medication adherence in hypertension

Participant information sheet: Part 1 of 2

We would like to offer you a reminder about a questionnaire study conducted by the University of East Anglia and Elvington Medical Practice.

Please read this leaflet carefully before you decide whether or not to take part. Feel free to contact us or to discuss this with others. You can contact us using the details at the end of this form.

If you do not wish to take part, it will not affect the care you receive from your doctor in any way. We will also be running interviews with some of our participants. If you would be interested in taking part in these, please read the second leaflet.

1 What is the purpose of this study?

This study hopes to find out about how patient beliefs and experiences affect how they take their hypertension medicines.

2 Why have I been chosen to take part in this study?

You are registered at Elvington Medical Practice and are due for a review of your hypertension.

3 What will I have to do?

There are two questionnaires that we would like you to complete. Both questionnaires have been posted to you in this pack. It should take less than 20 minutes to complete them both. The two questionnaires are a different colour. This is because Elvington Medical Practice will use information in one questionnaire (Patient and Lifestyle Scale - yellow) to update your records about how much you smoke or drink. They will not see the second questionnaire (Wellbeing and Medications Scale - pink). Once you have completed the questionnaires please seal the yellow questionnaire in the yellow envelope, and the pink questionnaire in the pink envelope. We would also like to look at your medical records so that we can see how often you have ordered your prescription for your hypertension medicines, and look at your blood pressure history.

4 What are the disadvantages or risks of taking part?

Some questions may make you feel uncomfortable. You may choose to not answer these questions. We may also inform your doctor if your results indicate that have an undiagnosed condition such as depression.

5 What are the benefits of taking part?

There are no direct benefits to you, but this research may help us to better help patients to take their medicine in the future.

6 How will my confidentiality be assured?

No information that leaves the medical practice will have your name or address on it so that you cannot be recognised. The medical team at Elvington will use the yellow questionnaire in this pack to update their records about how much you smoke or drink. The medical team at Elvington will not see your individual responses to the pink questionnaire.

7 How will my data be stored and used?

Your data will be kept in a locked filing cabinet, or on a password protected computer. Your data will be used for research and to update your doctor about how much you drink or smoke. This study is part of an educational thesis, may be published. If you would like a summary of the research contact Steven Watson using the details below. Your individual data will not be identifiable in any report that is published.

Appendix P – Subscale Inter-item correlations and Cronbach's alpha with item removed

BMQ Overuse subscale

	Item							
	Doctors prescribe too many medicines		People who take medicines should stop their treatment for a while every now and again		Doctors place too much trust on medicines		If doctors had more time with patients they would prescribe fewer medicines	
Item	Rho	p	Rho	p	Rho	p	Rho	p
Doctors prescribe too many medicines	-	-	*0.444*	0.148	0.617	0.033	*0.345*	0.273
People who take medicines should stop their treatment for a while every now and again			-	-	*0.376*	0.206	-0.120	0.696
Doctors place too much trust on medicines					-	-	*0.386*	0.193
If doctors had more time with patients they would prescribe fewer medicines							-	-

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at $\alpha = 0.1$ are in *italics*, correlations significant at $\alpha = 0.05$ are in **bold**

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Doctors prescribe too many medicines	100.0000	2386.364	.567	.595
People who take medicines should stop their treatment for a while every now and again	112.5000	3011.364	.397	.698
Doctors place too much trust on medicines	104.1667	2481.061	.692	.527
If doctors had more time with patients they would prescribe fewer medicines	83.3333	2878.788	.355	.730

Appendix P – Subscale Inter-item correlations and Cronbach's alpha with item removed

BMQ General Harm subscale

	Item							
	Most medicines are addictive		Natural remedies are safer than medicines		Medicines do more harm than good		All medicines are poisons	
Item	Rho	p	Rho	p	Rho	p	Rho	p
Most medicines are addictive	-	-	0.080	0.796	0.508	*0.076*	*0.348*	0.244
Natural remedies are safer than medicines			-	-	0.153	0.617	0.033	0.915
Medicines do more harm than good					-	-	0.618	0.024
All medicines are poisons							-	-

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at α = 0.1 are in *italics*, correlations significant at α = 0.05 are in **bold**

Item-Total Statistics

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
Most medicines are addictive	111.5385	4022.436	.329	.565
Natural remedies are safer than medicines	101.9231	4214.744	.146	.667
Medicines do more harm than good	113.4615	2564.103	.662	.267
All medicines are poisons	111.5385	2459.936	.445	.479

Appendix P – Subscale Inter-item correlations and Cronbach's alpha with item removed

PSS-4:

	Item							
	In the last month, how often have you felt that you were unable to control the important things in your life?		In the last month, how often have you felt confident about your ability to handle your personal problems?		In the last month, how often have you felt that things were going your way?		In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	
Item	Rho	p	Rho	p	Rho	p	Rho	p
In the last month, how often have you felt that you were unable to control the important things in your life?	-	-	0.936	<0.001	0.664	0.010	0.788	0.001
In the last month, how often have you felt confident about your ability to handle your personal problems?			-	-	*0.461*	*0.097*	0.750	0.002
In the last month, how often have you felt that things were going your way?					-	-	0.594	0.025
In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?							-	-

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at $\alpha = 0.1$ are in *italics*, correlations significant at $\alpha = 0.05$ are in **bold**

Appendix P – Subscale Inter-item correlations and Cronbach's alpha with item removed

PSS-4

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
In the last month, how often have you felt that you were unable to control the important things in your life?	89.2857	4780.220	.916	.791
In the last month, how often have you felt confident about your ability to handle your personal problems?	103.5714	7390.110	.836	.849
In the last month, how often have you felt that things were going your way?	80.3571	7228.709	.564	.921
In the last month, how often have you felt difficulties were piling up so high that you could not overcome them?	101.7857	6198.489	.811	.831

PHQ Depression

Correlation between item "Having little interest or pleasure in doing things?" and "Feeling down, depressed or hopeless?" Rho = 0.910, $p < 0.001$

PHQ Anxiety

	Item					
	"Nerves", or feeling anxious or on edge?		Worrying about a lot of different things?		During the last month, have you had an anxiety attack (suddenly feeling fear or panic)?	
Item	Rho	p	Rho	p	Rho	p
"Nerves", or feeling anxious or on edge?	-	-	0.802	0.001	0.577	0.031
Worrying about a lot of different things?			-	-	0.568	0.034
During the last month, have you had an anxiety attack (suddenly feeling fear or panic)?					-	-

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at $\alpha = 0.1$ are in *italics*, correlations significant at $\alpha = 0.05$ are in **bold**

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
"Nerves", or feeling anxious or on edge?	35.5714	1955.341	.756	.547
Worrying about a lot of different things?	21.2857	951.451	.745	.713
During the last month, have you had an anxiety attack (suddenly feeling fear or panic)?	47.4286	2852.879	.683	.776

Medications concerns

Correlation between item "I think my medicines are giving me side effects" and "If my medicines are making me feel worse than my illness, I think it makes sense to stop taking it for a while" Rho = 0.502, p = 0.080.

Medication necessity

	Item					
	I think my medicines make me feel better than I would without them		I think my illness would be worse without my medicines		I think my medicines help to keep me feeling as healthy as possible	
Item	Rho	p	Rho	p	Rho	p
I think my medicines make me feel better than I would without them	-	-	0.714	0.006	0.800	0.002
I think my illness would be worse without my medicines			-	-	0.833	0.001
I think my medicines help to keep me feeling as healthy as possible					-	-

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at α = 0.1 are in *italics*, correlations significant at α = 0.05 are in **bold**

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
I think my medicines make me feel better than I would without them	39.5833	1302.083	.817	.815
I think my illness would be worse without my medicines	52.0833	1756.629	.694	.927
I think my medicines help to keep me feeling as healthy as possible	45.8333	1117.424	.894	.746

Self-efficacy

Correlation between "I find it hard to remember to take all of my medicines each day" and "I think I can cope with the number of medicines I am prescribed at the moment" Rho = 0.314, p = 0.296.

Social support:

	Item							
	I am concerned about how others will react if I tell them what medicines I take		There are people who will help me with my medicines if needed		I have people I can talk to about my illness		I can count on my family and friends to help me deal with my illness	
Item	Rho	p	Rho	p	Rho	p	Rho	p
I am concerned about how others will react if I tell them what medicines I take	-	-	-0.136	0.658	*0.345*	0.249	0.272	0.369

Appendix P – Subscale Inter-item correlations and Cronbach's alpha with item removed

There are people who will help me with my medicines if needed			-	-	0.707	0.007	0.536	*0.059*
I have people I can talk to about my illness					-	-	0.824	0.001
I can count on my family and friends to help me deal with my illness							-	-

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at $\alpha = 0.1$ are in *italics*, correlations significant at $\alpha = 0.05$ are in **bold**

	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
I am concerned about how others will react if I tell them what medicines I take	98.0769	4839.744	.141	.849
There are people who will help me with my medicines if needed	88.4615	4022.436	.413	.675
I have people I can talk to about my illness	88.4615	3084.936	.840	.374
I can count on my family and friends to help me deal with my illness	88.4615	4022.436	.724	.520

Appendix P – Subscale Inter-item correlations and Cronbach's alpha with item removed

PDRQ-9

	Item																	
	My doctor helps me		My doctor has enough time for me		I trust my doctor		My doctor understands me		My doctor is dedicated to helping me		My doctor and I agree on the nature of my medical symptoms		I can talk to my doctor		I feel content with the treatment I receive from my doctor		I find my doctor easily accessible	
Item	Rho	p	Rho	p	Rho	p	Rho	p	Rho	p	Rho	p	Rho	p	Rho	p	Rho	p
My doctor helps me	-	-	0.671	0.012	0.717	0.004	0.694	0.006	0.702	0.005	0.729	0.003	0.590	0.026	0.876	<0.001	*0.432*	0.123
My doctor has enough time for me			-	-	0.835	<0.001	0.794	0.001	0.511	*0.074*	0.766	0.002	0.592	0.033	0.710	0.007	0.512	*0.074*
I trust my doctor					-	-	0.631	0.016	0.780	0.001	0.690	0.006	*0.468*	*0.092*	0.780	0.001	0.513	*0.061*
My doctor understands me							-	-	*0.448*	0.109	0.653	0.011	*0.460*	*0.098*	0.768	0.001	0.168	0.567
My doctor is dedicated to helping me									-	-	0.820	<0.001	*0.464*	*0.095*	0.801	0.001	*0.497*	*0.070*
My doctor and I agree on the nature of my medical symptoms											-	-	0.688	0.006	0.820	<0.001	0.552	0.041
I can talk to my doctor													-	-	0.692	0.006	0.595	0.025
I feel content with the treatment I receive from my doctor															-	-	*0.497*	*0.070*
I find my doctor easily accessible																	-	-

Moderate (> 0.3) correlations are in *italics*, large (> 0.5) correlations are in **bold**
Correlations significant at $\alpha = 0.1$ are in *italics*, correlations significant at $\alpha = 0.05$ are in **bold**

Appendix P – Subscale Inter-item correlations and Cronbach's alpha with item removed

PDRQ-9

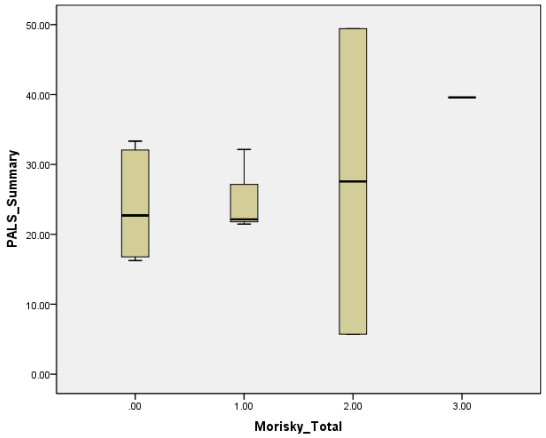
	Scale Mean if Item Deleted	Scale Variance if Item Deleted	Corrected Item-Total Correlation	Cronbach's Alpha if Item Deleted
My doctor helps me	186.5385	16834.936	.866	.943
My doctor has enough time for me	188.4615	17043.269	.889	.941
I trust my doctor	194.2308	17932.692	.868	.942
My doctor understands me	176.9231	17860.577	.779	.947
My doctor is dedicated to helping me	186.5385	17459.936	.850	.943
My doctor and I agree on the nature of my medical symptoms	182.6923	17748.397	.920	.940
I can talk to my doctor	190.3846	19951.923	.612	.954
I feel content with the treatment I receive from my doctor	186.5385	16939.103	.955	.937
I find my doctor easily accessible	184.6154	21097.756	.527	.958

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

Note that correlations with Morisky/Self-reported adherence are the reverse to those presented in the main text because correlations have not been reversed. I.e. higher scores on Morisky represent lower adherence.

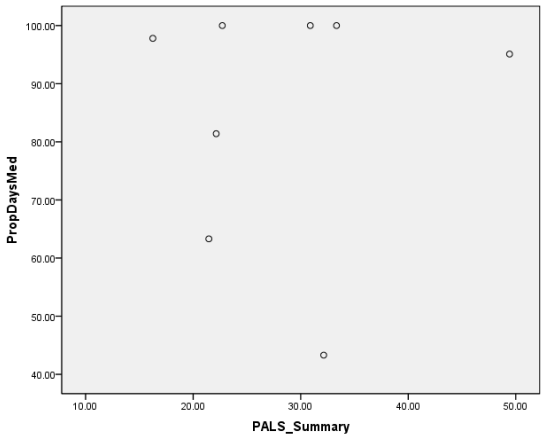
PALS:

With self-reported adherence:



Rho = 0.241, p = 0.427

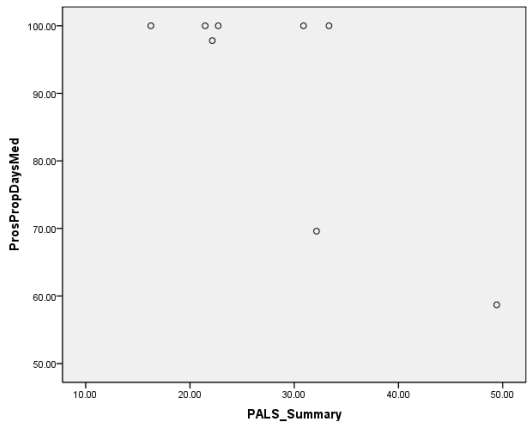
With retrospective refill adherence:



Rho = 0.065, p = 0.879

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

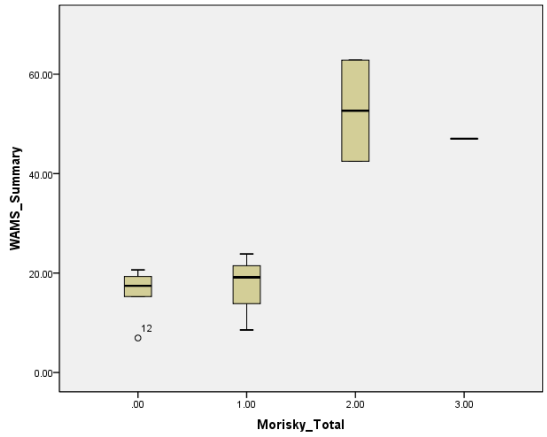
With prospective refill adherence:



Rho = -0.790, p = 0.020

WAMS:

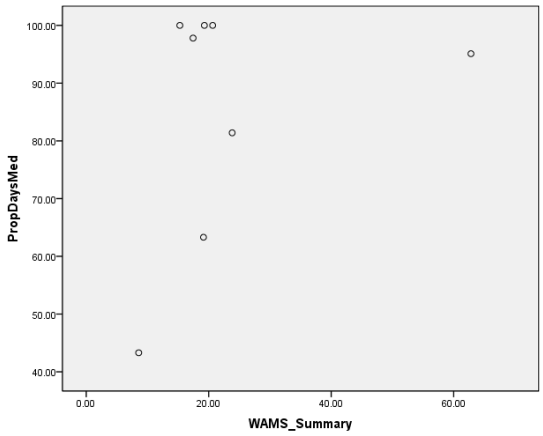
With self-reported adherence:



Rho = 0.520, p = 0.101

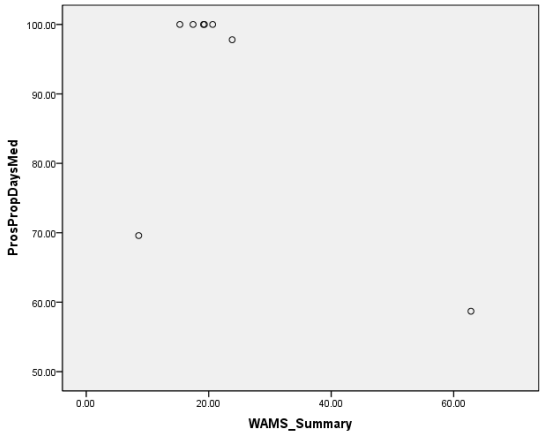
Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With retrospective refill adherence:



Rho = 0.327, p = 0.428

With prospective refill adherence:

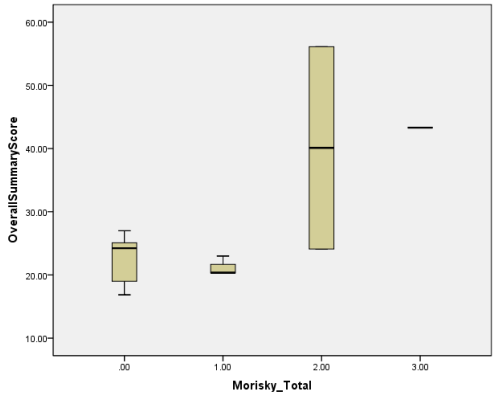


Rho = -0.610, p = 0.109

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

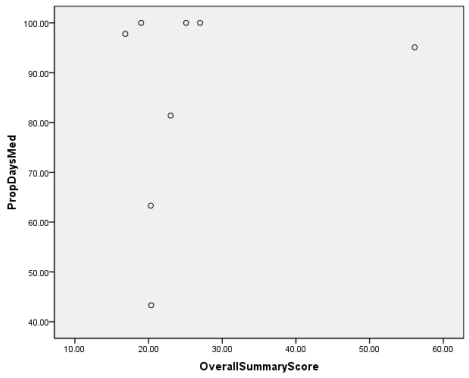
WAMS + PALS:

With self-reported adherence:



Rho = 0.391, p = 0.234

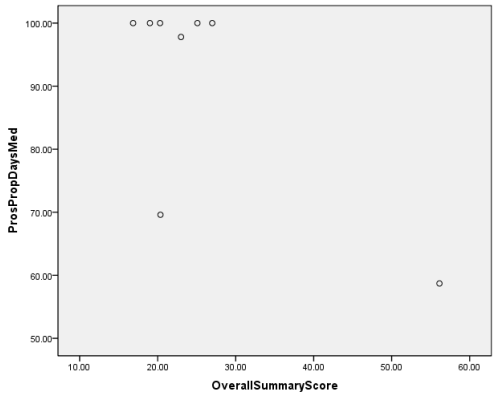
With retrospective refill adherence:



Rho = 0.122, p = 0.774

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

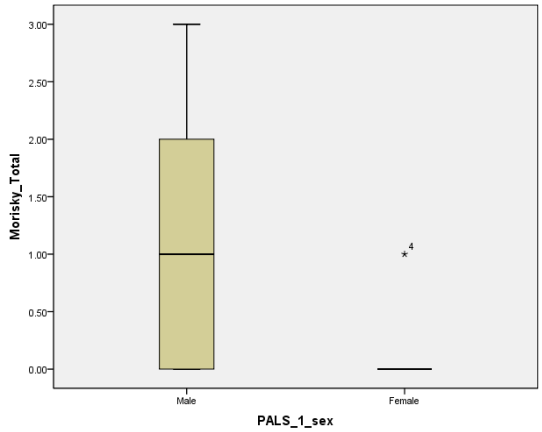
With prospective refill adherence:



Rho = -0.724, p = 0.042

Sex:

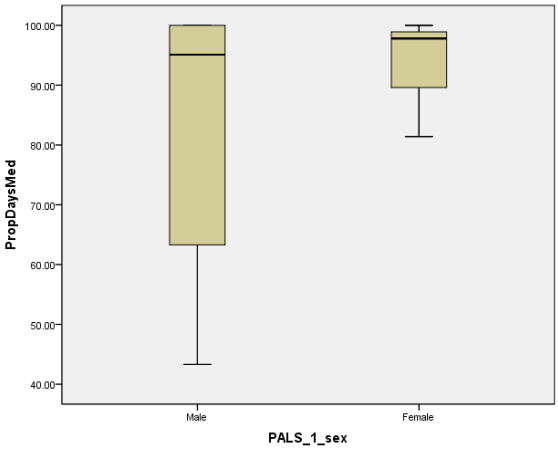
With self-reported adherence:



Rho = -0.463, p =0.111

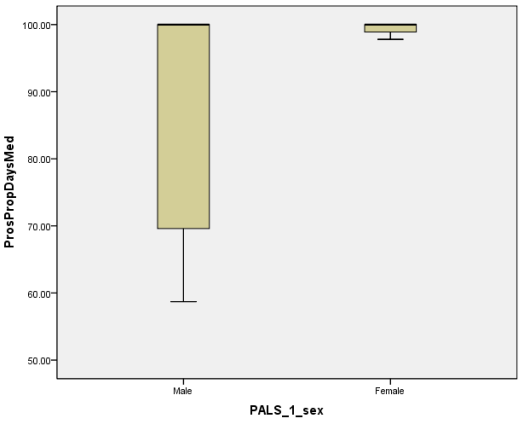
Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With retrospective refill adherence:



Rho = 0.173, p = 0.682

With prospective refill adherence:

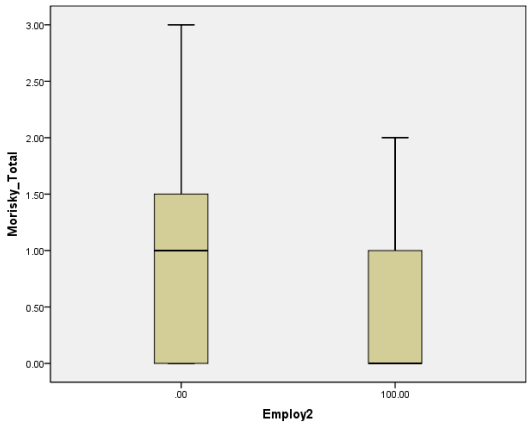


Rho = 0.194, p = 0.646

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

Employment:

With self-reported adherence:



Rho = -0.249, p = 0.413

With retrospective refill adherence:

No unemployed participants consented to give access to medical records

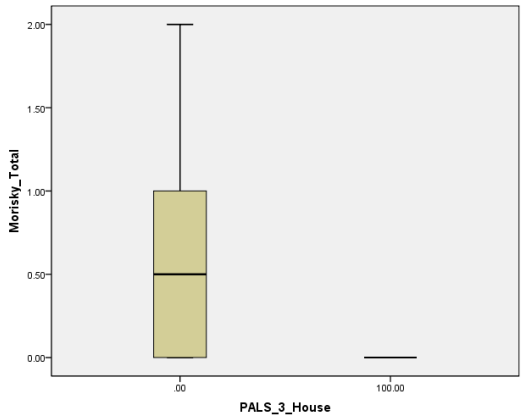
With prospective refill adherence:

No unemployed participants consented to give access to medical records

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

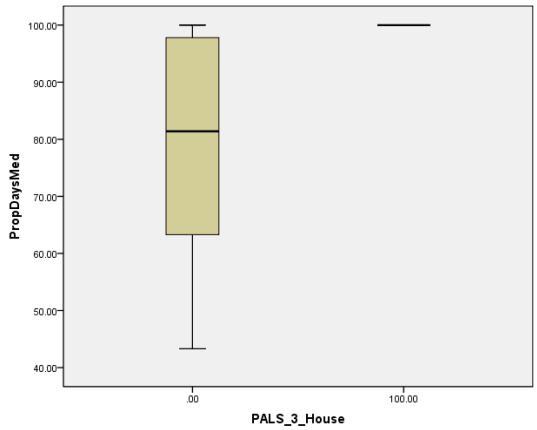
Housing status:

With self-reported adherence:



Rho = -0.398, p = 0.254

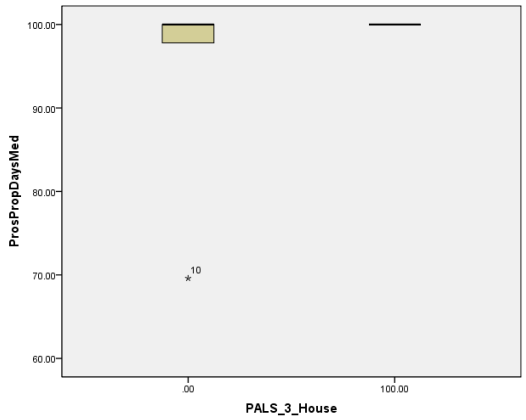
With retrospective refill adherence:



Rho = 0.656, p = 0.109

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

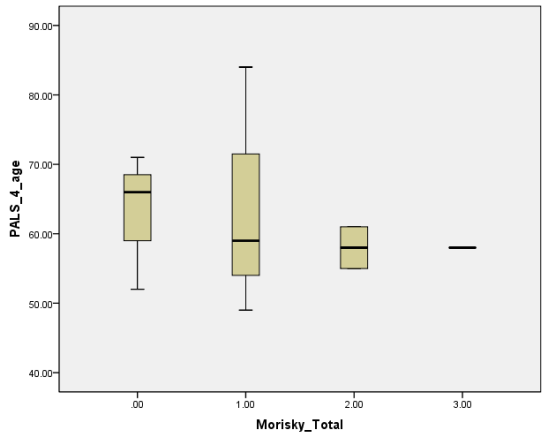
With prospective refill adherence:



Rho = 0.587, p = 0.126

Age:

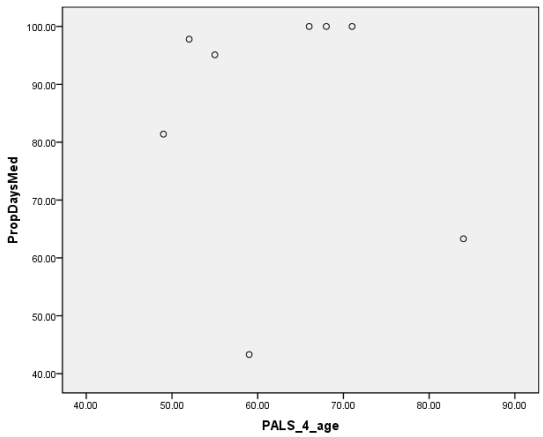
With self-reported adherence:



Rho = -0.275, p = 0.364

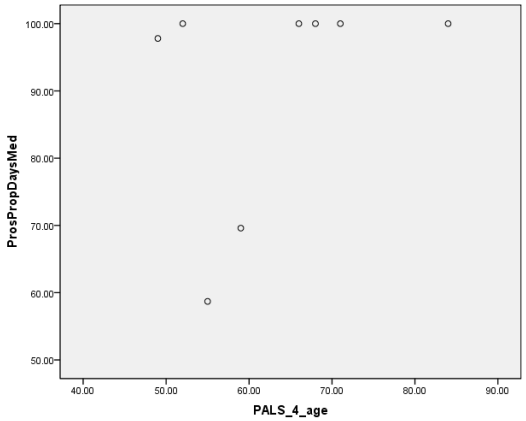
Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With retrospective refill adherence:



Rho = 0.220, p = 0.601

With prospective refill adherence:

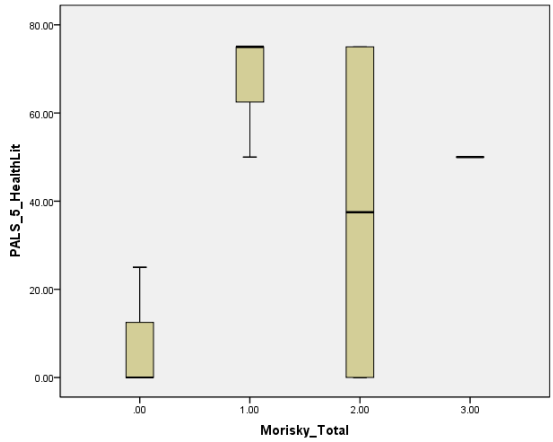


Rho = 0.546, p = 0.162

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

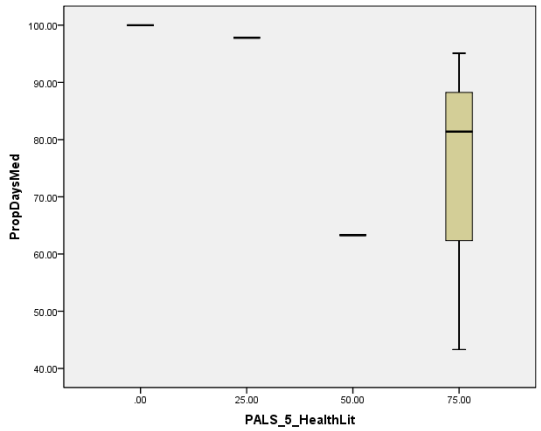
Health Literacy:

With self-reported adherence:



Rho = 0.615, p = 0.025

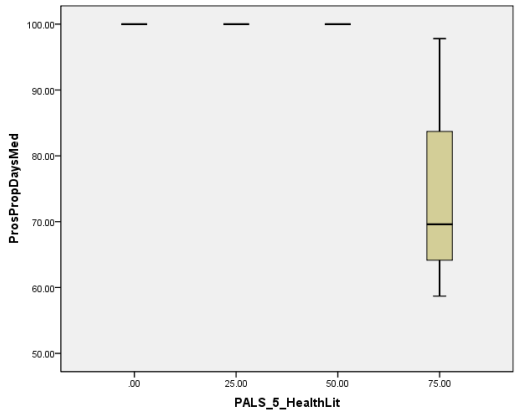
With retrospective refill adherence:



Rho = -0.872, p = 0.005

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

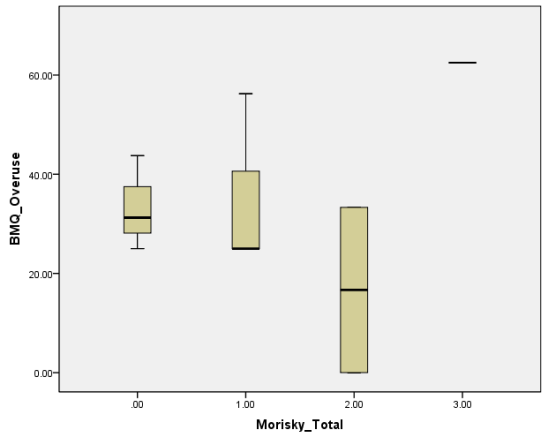
With prospective refill adherence:



Rho = -0.860, p = 0.006

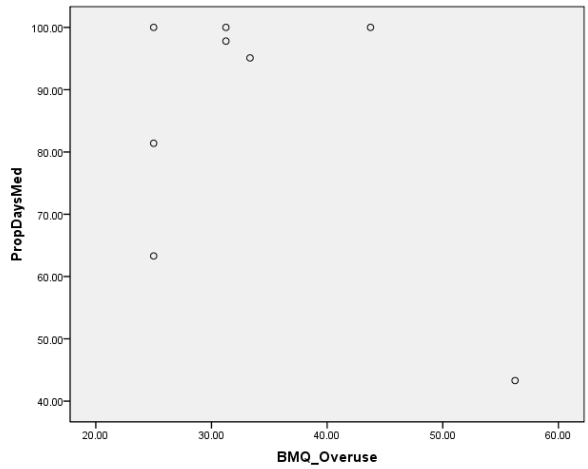
BMQ overuse scale:

With self-reported adherence:



Rho = 0.086, p = 0.780

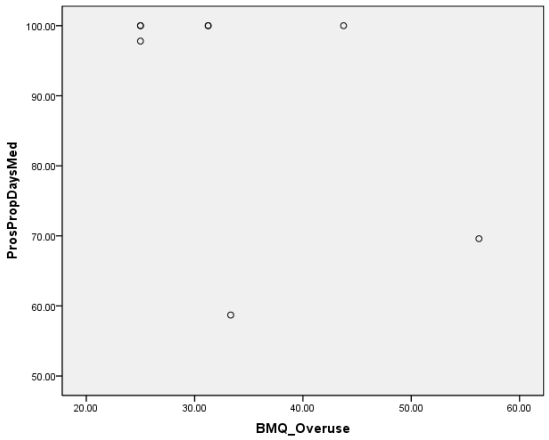
With retrospective refill adherence:



Rho = -0.075, p = 0.859

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With prospective refill adherence:

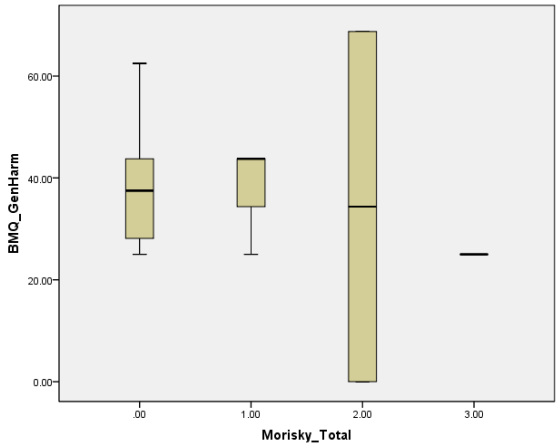


Rho = -0.394, p = 0.334

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

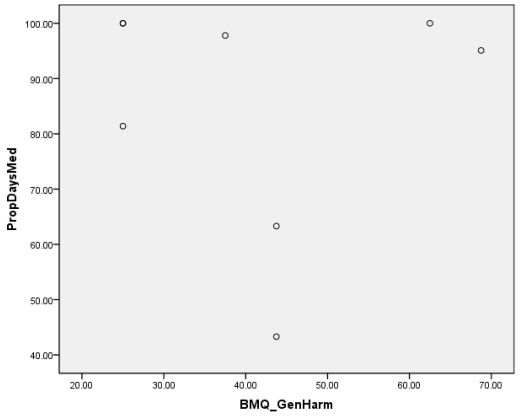
BMQ general harm scale:

With self-reported adherence:



Rho = -0.147, p = 0.632

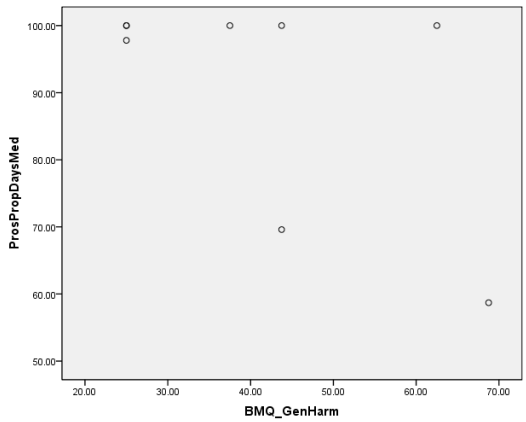
With retrospective refill adherence:



Rho = -0.264, p = 0.527

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

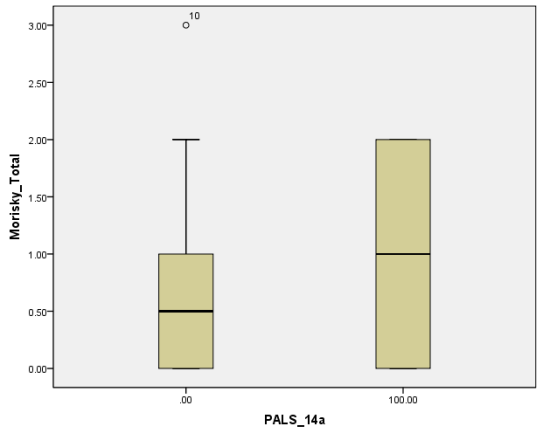
With prospective refill adherence:



Rho = -0.394, p = 0.334

Mental health:

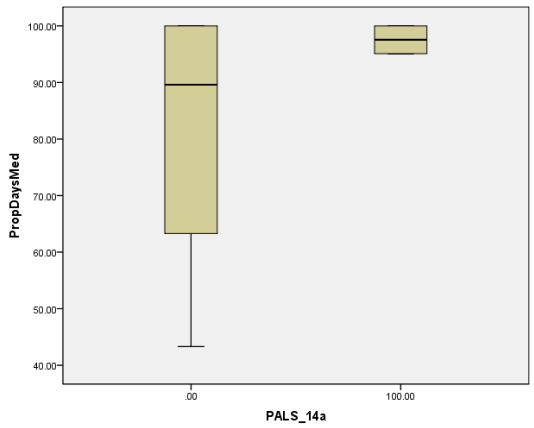
With self-reported adherence:



Rho = 0.070, p = 0.829

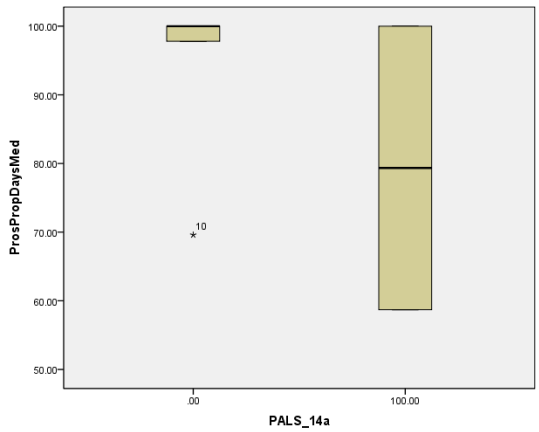
Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With retrospective refill adherence:



Rho = 0.258. p = 0.537

With prospective refill adherence:

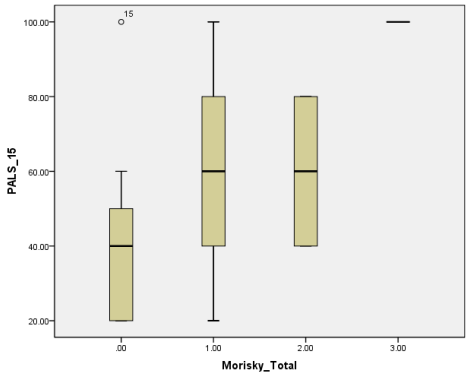


Rho = -0.289 , p = 0.488

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

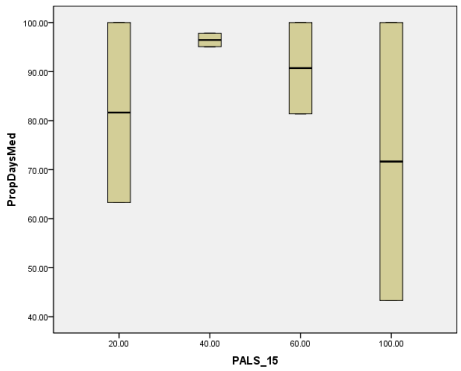
Health behaviour – Drinking alcohol:

With self-reported adherence:



Rho = 0.433, p = 0.139

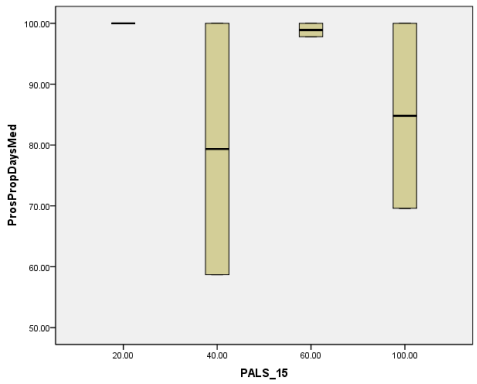
With retrospective refill adherence:



Rho = -0.050, p = 0.906

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

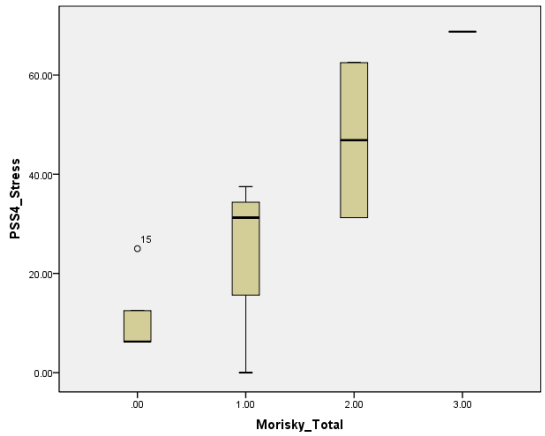
With prospective refill adherence:



Rho = -0.280, p = 0.503

PSS-4:

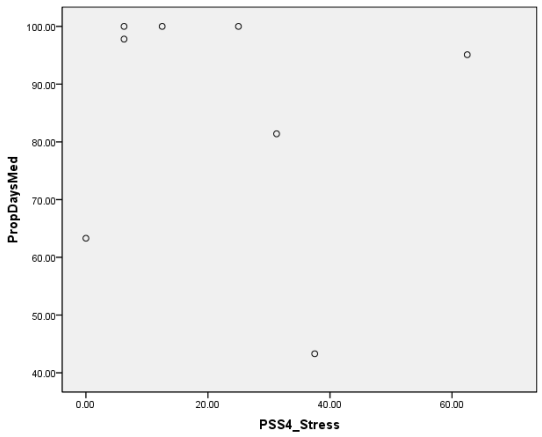
With self-reported adherence:



Rho = 0.720, p = 0.012

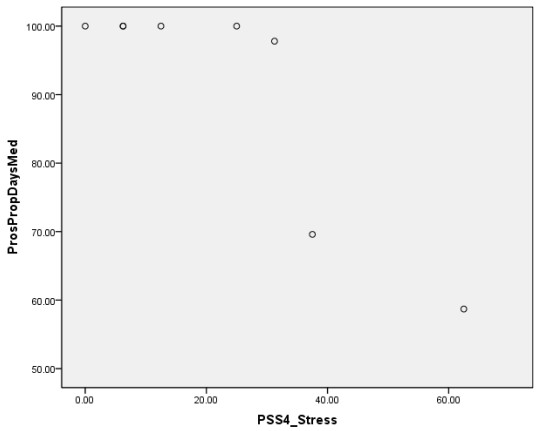
Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With retrospective refill adherence:



Rho = -0.245, p = 0.558

With prospective refill adherence:

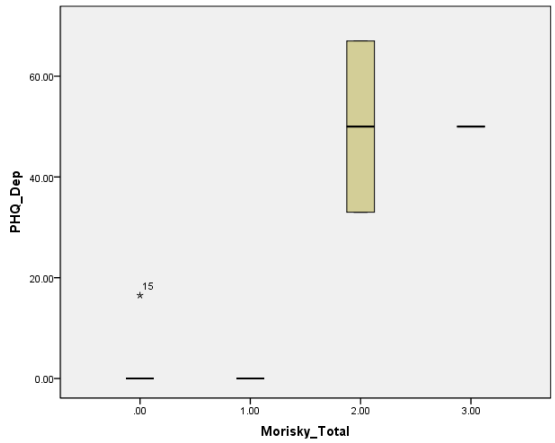


Rho = -0.878, p = 0.004

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

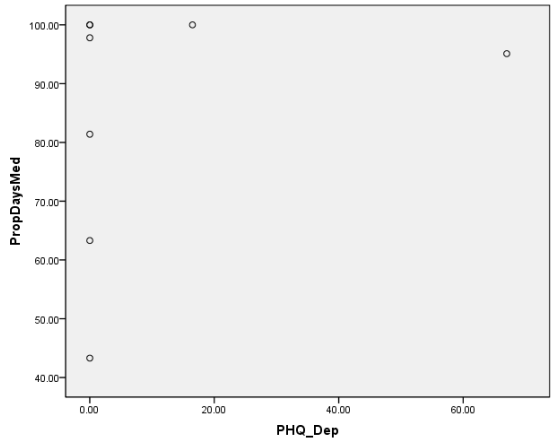
PHQ Depression:

With self-reported adherence:



Rho = 0.671, p = 0.024

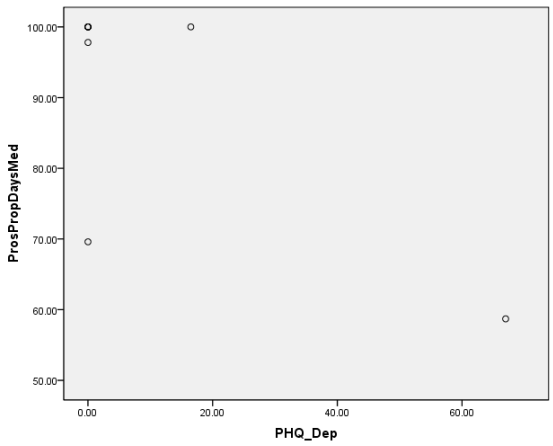
With retrospective refill adherence:



Rho = 0.208, p = 0.622

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

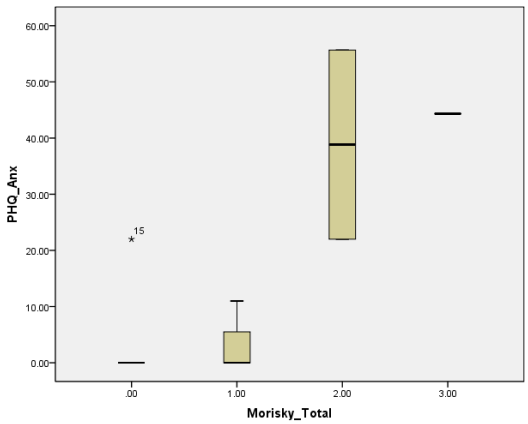
With prospective refill adherence:



Rho = -0.375, p = 0.360

PHQ Anxiety:

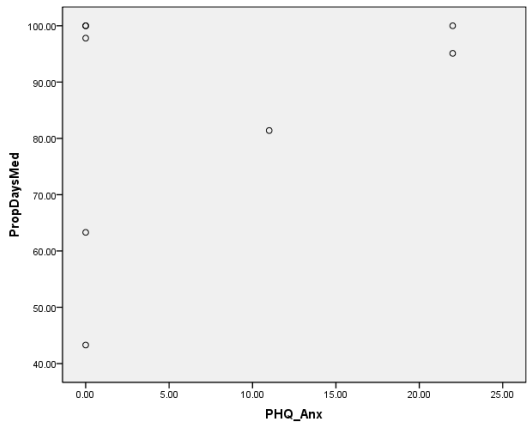
With self-reported adherence:



Rho = 0.695, p = 0.018

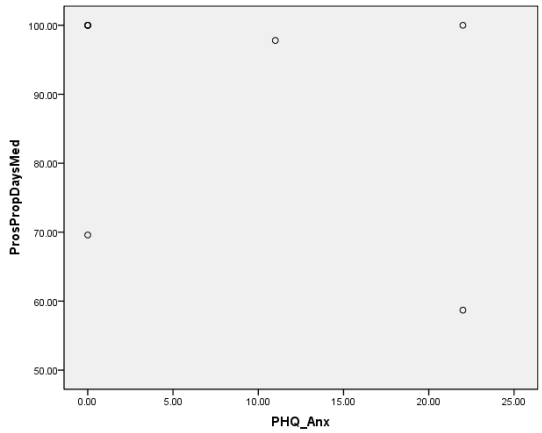
Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With retrospective refill adherence:



Rho = 0.127, p = 0.765

With prospective refill adherence:

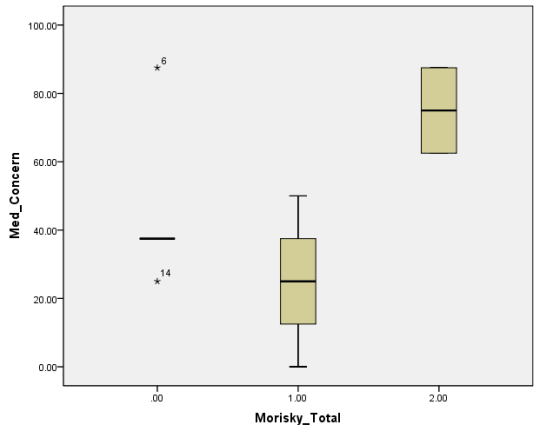


Rho = -0.425, p = 0.294

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

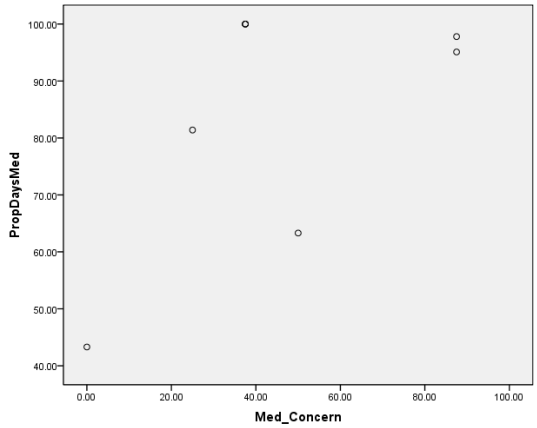
Medication concerns:

With self-reported adherence:



Rho = 0.245, p = 0.496

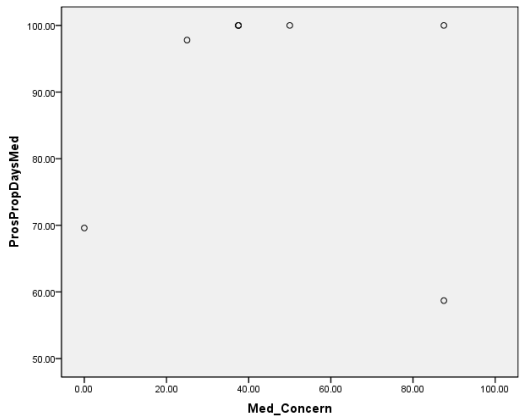
With retrospective refill adherence:



Rho = 0.214, p = 0.611

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

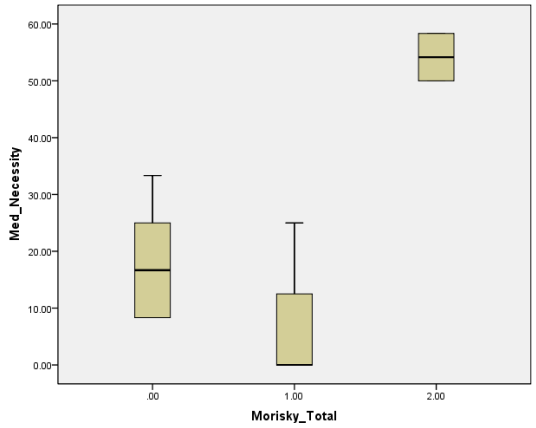
With prospective refill adherence:



Rho = 0.183, p = 0.665

Medications necessity:

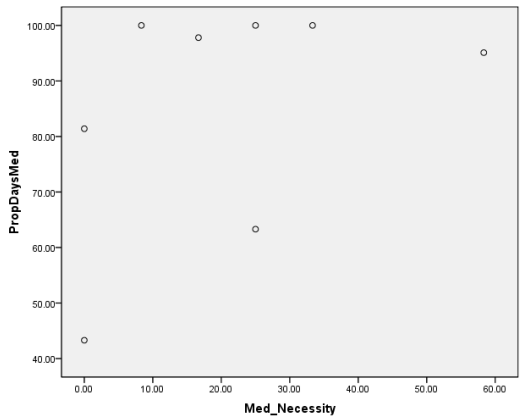
With self-reported adherence:



Rho = 0.319, p = 0.369

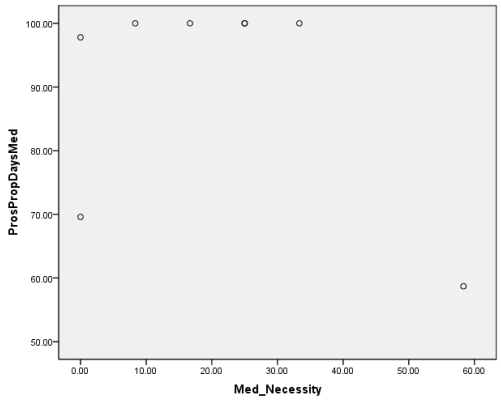
Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With retrospective refill adherence:



Rho = 0.383, p = 0.349

With prospective refill adherence:

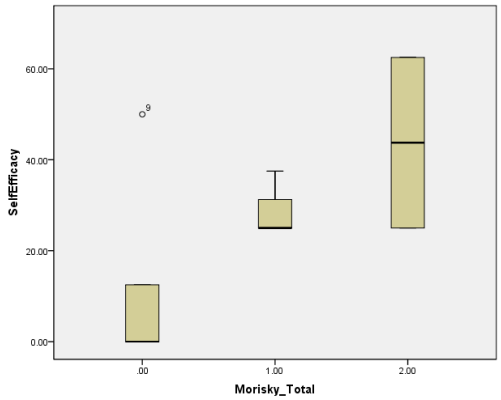


Rho = 0.097, p = 0.820

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

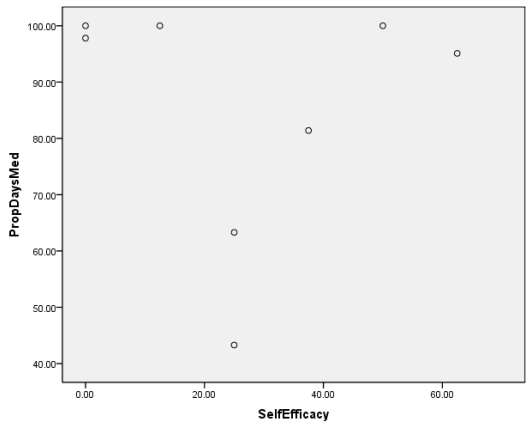
Self-efficacy:

With self-reported adherence:



Rho = 0.695, p = 0.018

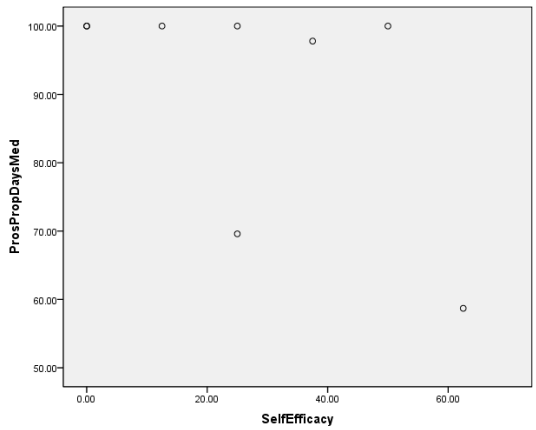
With retrospective refill adherence:



Rho = -0.259, p = 0.535

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

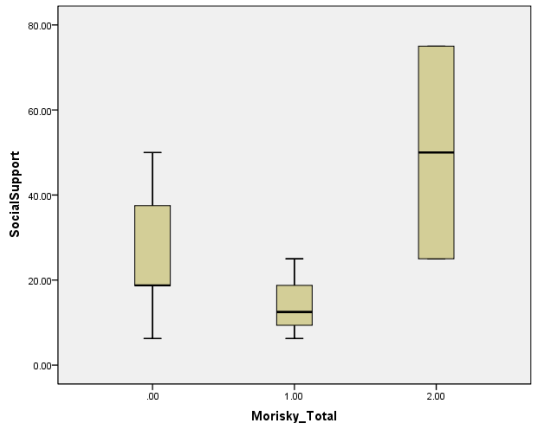
With prospective refill adherence:



Rho = -0.607, p = 0.110

Social support:

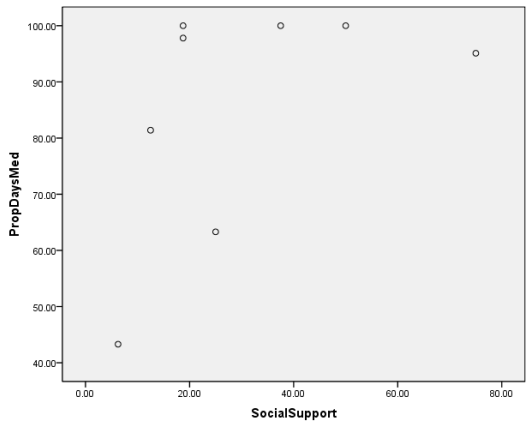
With self-reported adherence:



Rho = 0.183, p = 0.614

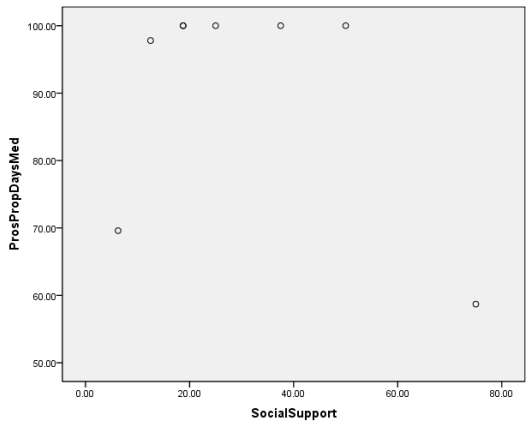
Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With retrospective refill adherence:



Rho = 0.491, p = 0.217

With prospective refill adherence:

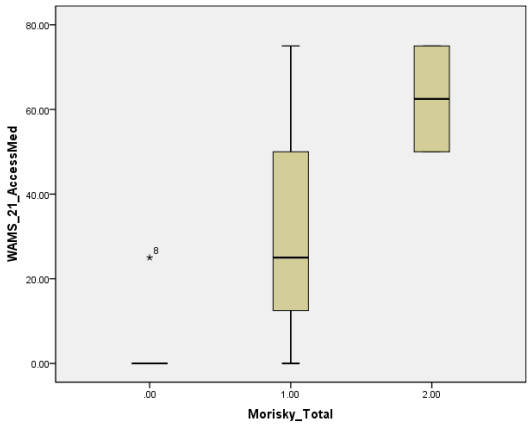


Rho = 0.110, p = 0.796

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

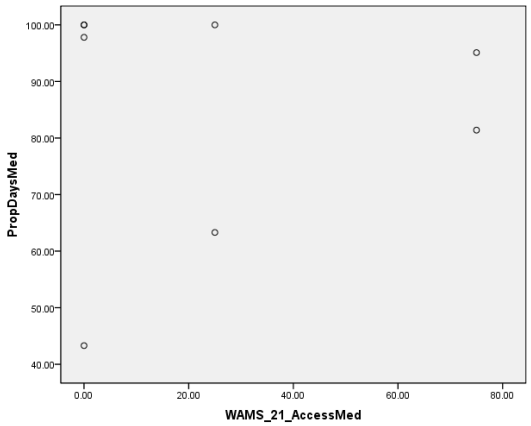
Access to medications:

With self-reported adherence:



Rho = 0.739, p = 0.015

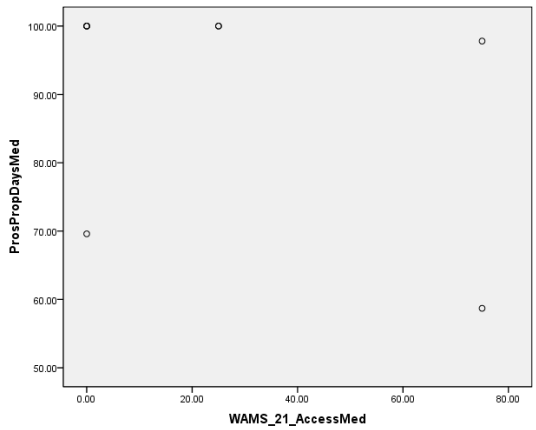
With retrospective refill adherence:



Rho = -0.264, p = 0.528

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

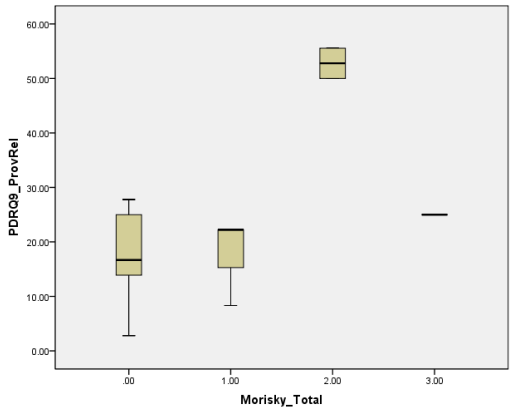
With prospective refill adherence:



Rho = -0.471, p = 0.238

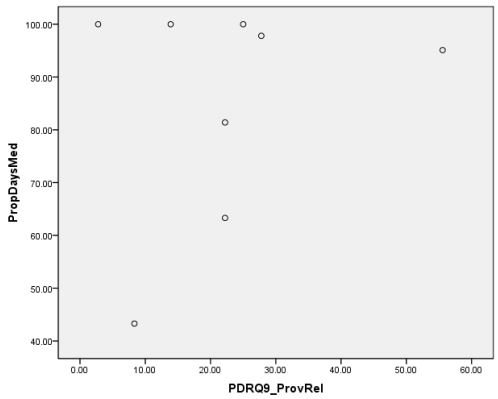
PDRQ-9

With self-reported adherence:



Rho = 0.490, p = 0.126

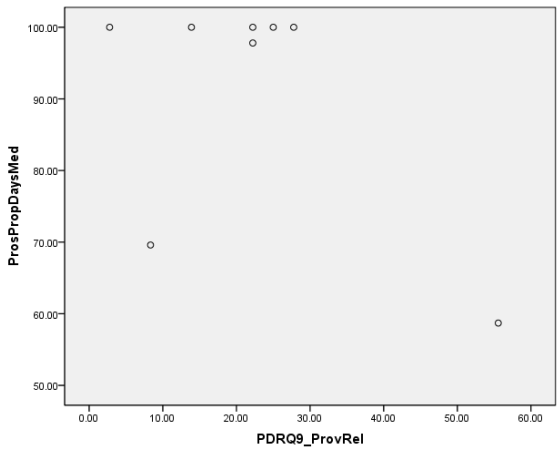
With retrospective refill adherence:



Rho = -0.012, p = 0.977

Appendix Q – Visual representations of correlations between PALS, WAMS, subscales and measures of adherence

With prospective refill adherence:



Rho = -0.206, p = 0.625

Appendix R – Area Under Curve Analysis

ROC curve analyses were performed to illustrate the predictive power of the PALS and WAMS. However, the small sample size made these analyses unlikely to be informative. In the interests of transparency they were performed as planned and the results are presented. However, they were not used to evaluate the questionnaires because of their lack of explanatory power.

Area Under Curve analysis for Morisky Adherence Measure:

Positive state = No reported nonadherence

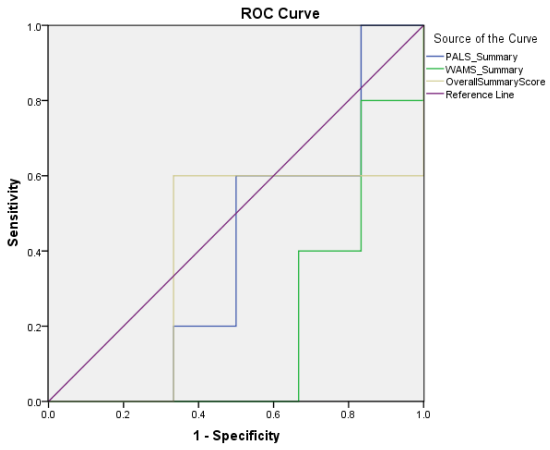
Negative state = Any reported nonadherence

Case Processing Summary

MoriskySplit	Valid N (listwise)
Positive[a]	5
Negative	6
Missing	6

Larger values of the test result variable(s) indicate stronger evidence for a positive actual state.

a. The positive actual state is .00.



Appendix R – Area Under Curve Analysis

Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PALS_Summary	.400	.180	.584	.047	.753
WAMS_Summary	.200	.143	.100	.000	1.000
OverallSummaryScore	.400	.191	.584	.026	.774

a. Under the nonparametric assumption

b. Null hypothesis: true area = 0.5

Appendix R – Area Under Curve Analysis

Coordinates of the Curve

Test Result Variable(s)	Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
PALS_Summary	4.7100	1.000	1.000
	10.9800	1.000	.833
	16.7700	.800	.833
	19.3750	.600	.833
	21.8000	.600	.667
	22.4250	.600	.500
	26.8000	.400	.500
	31.5150	.200	.500
	32.7350	.200	.333
	36.4550	.000	.333
	44.5000	.000	.167
	50.4200	.000	.000
WAMS_Summary	5.9400	1.000	1.000
	7.7500	.800	1.000
	11.9200	.800	.833
	16.3600	.600	.833
	18.2900	.400	.833
	19.2150	.400	.667
	19.9650	.200	.667
	22.2350	.000	.667
	33.1600	.000	.500
	44.7550	.000	.333
	54.9200	.000	.167
	63.8200	.000	.000
OverallSummaryScore	15.8500	1.000	1.000
	17.9250	.800	1.000
	19.6500	.600	1.000
	20.3250	.600	.833
	21.6700	.600	.667
	23.5450	.600	.500
	24.1650	.600	.333
	24.6600	.400	.333
	26.0400	.200	.333
	35.1450	.000	.333
	49.7100	.000	.167

Appendix R – Area Under Curve Analysis

	57.1200	.000	.000

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Area Under Curve analysis for Retrospective Refill adherence:

Positive state = 100% refill adherence

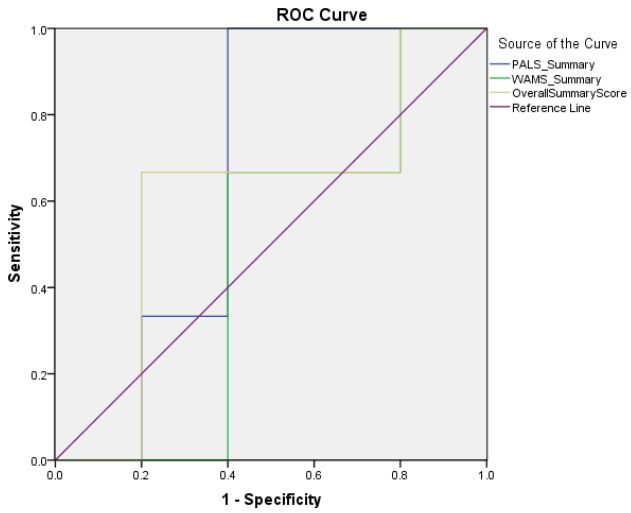
Negative state = <100% refill adherence

Case Processing Summary

PropDaysMed	Valid N (listwise)
Positive[a]	3
Negative	5
Missing	9

Larger values of the test result variable(s) indicate stronger evidence for a positive actual state.

a. The positive actual state is 100.00.



Appendix R – Area Under Curve Analysis

Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PALS_Summary	.667	.202	.456	.000	1.000
WAMS_Summary	.467	.218	.881	.040	.893
OverallSummaryScore	.600	.227	.655	.079	1.000

a. Under the nonparametric assumption

Appendix R – Area Under Curve Analysis

b. Null hypothesis: true area = 0.5

Coordinates of the Curve

Test Result Variable(s)	Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
PALS_Summary	15.2500	1.000	1.000
	18.8550	1.000	.800
	21.8000	1.000	.600
	22.4250	1.000	.400
	26.8000	.667	.400
	31.5150	.333	.400
	32.7350	.333	.200
	41.3750	.000	.200
	50.4200	.000	.000
WAMS_Summary	7.5600	1.000	1.000
	11.9200	1.000	.800
	16.3600	.667	.800
	18.2900	.667	.600
	19.2150	.667	.400
	19.9650	.333	.400
	22.2350	.000	.400
	43.3250	.000	.200
	63.8200	.000	.000
OverallSummaryScore	15.8500	1.000	1.000
	17.9250	1.000	.800
	19.6500	.667	.800
	20.3250	.667	.600
	21.6700	.667	.400
	24.0400	.667	.200
	26.0400	.333	.200
	41.5550	.000	.200
	57.1200	.000	.000

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Area Under Curve analysis for Prospective Refill adherence:

Positive state = 100% refill adherence

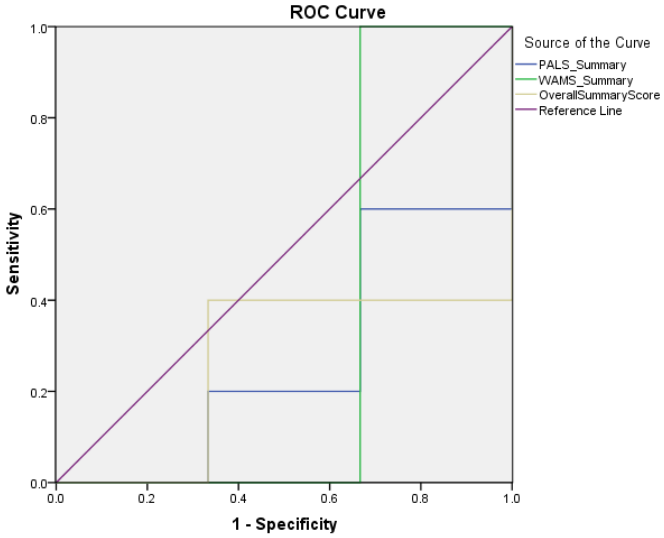
Negative state = <100% refill adherence

Case Processing Summary

ProsPropDaysMed	Valid N (listwise)
Positive[a]	5
Negative	3
Missing	9

Larger values of the test result variable(s) indicate stronger evidence for a positive actual state.

a. The positive actual state is 100.00.



Appendix R – Area Under Curve Analysis

Area Under the Curve

Test Result Variable(s)	Area	Std. Error[a]	Asymptotic Sig.[b]	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
PALS_Summary	.267	.195	.297	.000	1.000
WAMS_Summary	.333	.272	.456	.000	1.000
OverallSummaryScore	.267	.192	.297	.000	1.000

a. Under the nonparametric assumption

Appendix R – Area Under Curve Analysis

b. Null hypothesis: true area = 0.5

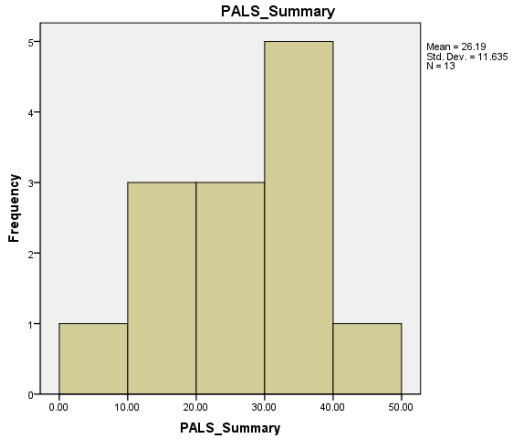
Coordinates of the Curve

Test Result Variable(s)	Positive if Greater Than or Equal To[a]	Sensitivity	1 - Specificity
PALS_Summary	15.2500	1.000	1.000
	18.8550	.800	1.000
	21.8000	.600	1.000
	22.4250	.600	.667
	26.8000	.400	.667
	31.5150	.200	.667
	32.7350	.200	.333
	41.3750	.000	.333
	50.4200	.000	.000
WAMS_Summary	7.5600	1.000	1.000
	11.9200	1.000	.667
	16.3600	.800	.667
	18.2900	.600	.667
	19.2150	.400	.667
	19.9650	.200	.667
	22.2350	.000	.667
	43.3250	.000	.333
	63.8200	.000	.000
OverallSummaryScore	15.8500	1.000	1.000
	17.9250	.800	1.000
	19.6500	.600	1.000
	20.3250	.400	1.000
	21.6700	.400	.667
	24.0400	.400	.333
	26.0400	.200	.333
	41.5550	.000	.333
	57.1200	.000	.000

a. The smallest cutoff value is the minimum observed test value minus 1, and the largest cutoff value is the maximum observed test value plus 1. All the other cutoff values are the averages of two consecutive ordered observed test values.

Appendix S – Distributions of PALS, WAMS and subscales

PALS summary scores:

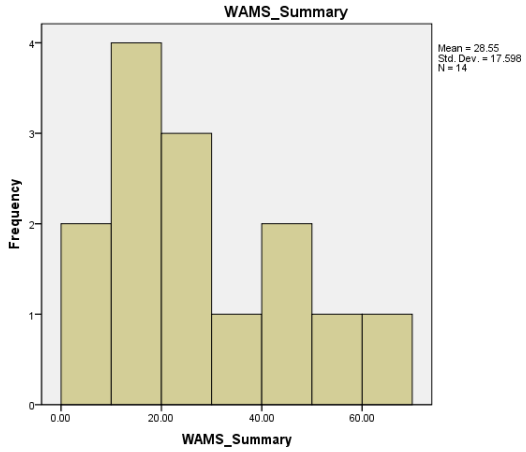


Statistics

PALS_Summary

N	Valid	13
	Missing	4
Skewness		.282
Std. Error of Skewness		.616
Kurtosis		.082
Std. Error of Kurtosis		1.191
Percentiles	25	16.7700
	50	22.7100
	75	33.2900

WAMS summary scores:



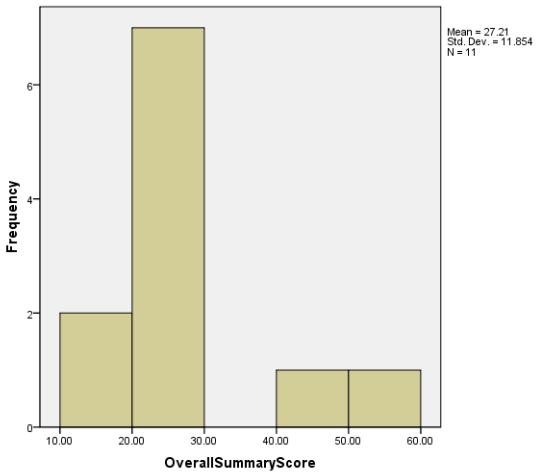
Appendix S – Distributions of PALS, WAMS and subscales

Statistics

WAMS_Summary

N	Valid	14
	Missing	3
Skewness		.768
Std. Error of Skewness		.597
Kurtosis		-.576
Std. Error of Kurtosis		1.154
Percentiles	25	16.9000
	50	21.3500
	75	43.6225

PALS + WAMS summary scores:



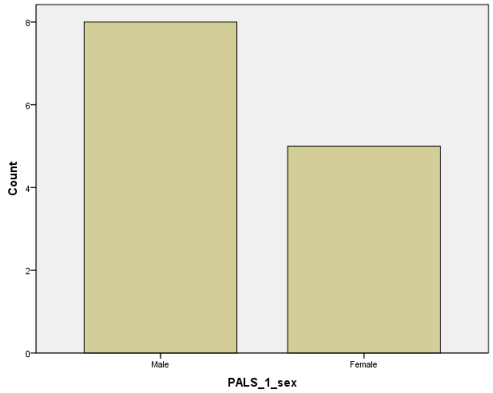
Statistics

OverallSummaryScore

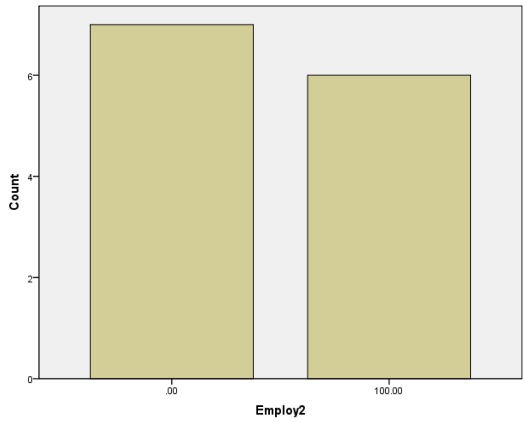
N	Valid	11
	Missing	6
Skewness		1.898
Std. Error of Skewness		.661
Kurtosis		3.137
Std. Error of Kurtosis		1.279
Percentiles	25	20.3000
	50	24.1000
	75	26.9900

Appendix S – Distributions of PALS, WAMS and subscales

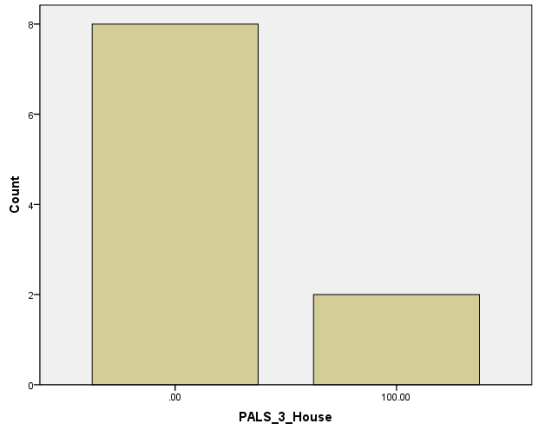
Sex:



Employment:

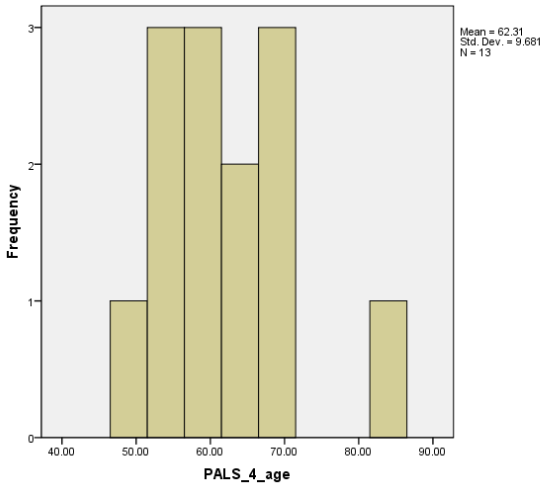


Housing status:



Appendix S – Distributions of PALS, WAMS and subscales

Age:

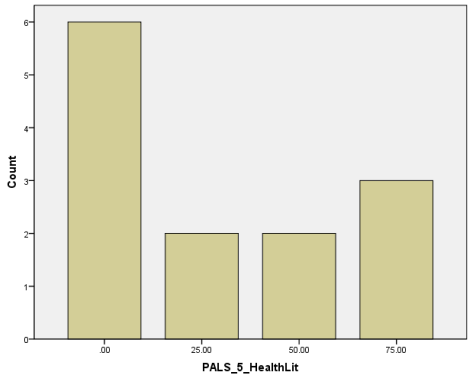


Statistics

OverallSummaryScore

N	Valid	11
	Missing	6
Skewness		1.898
Std. Error of Skewness		.661
Kurtosis		3.137
Std. Error of Kurtosis		1.279
Percentiles	25	20.3000
	50	24.1000
	75	26.9900

Health literacy:



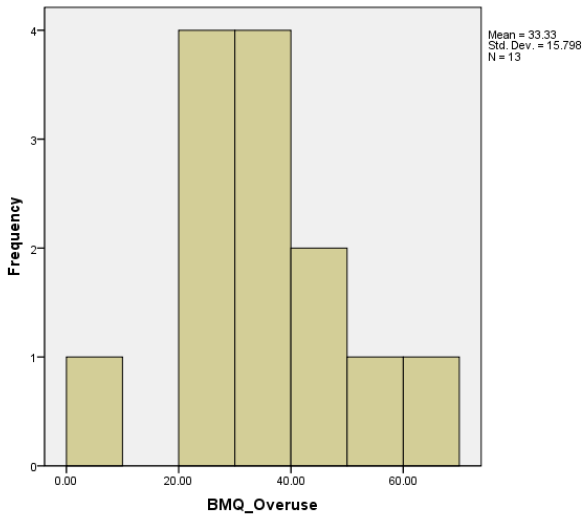
Appendix S – Distributions of PALS, WAMS and subscales

Statistics

PALS_5_HealthLit

N	Valid	13
	Missing	4
Percentiles	25	.0000
	50	25.0000
	75	62.5000

BMQ overuse:



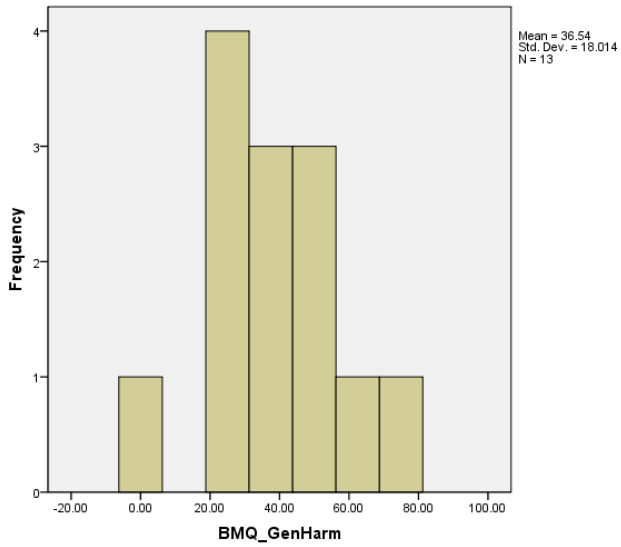
Statistics

BMQ_Overuse

N	Valid	13
	Missing	4
Skewness		-.007
Std. Error of Skewness		.616
Kurtosis		1.113
Std. Error of Kurtosis		1.191
Percentiles	25	25.0000
	50	31.2500
	75	43.7500

Appendix S – Distributions of PALS, WAMS and subscales

BMQ general harm:

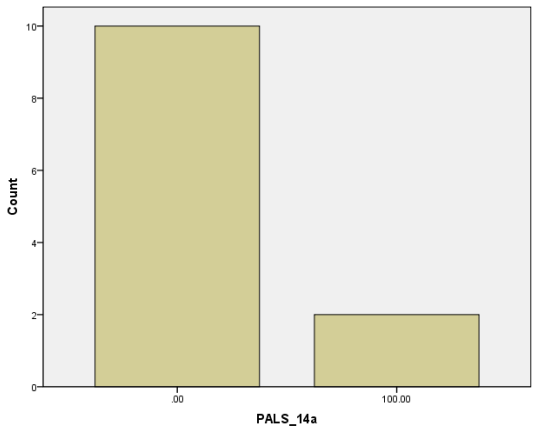


Statistics

BMQ_GenHarm

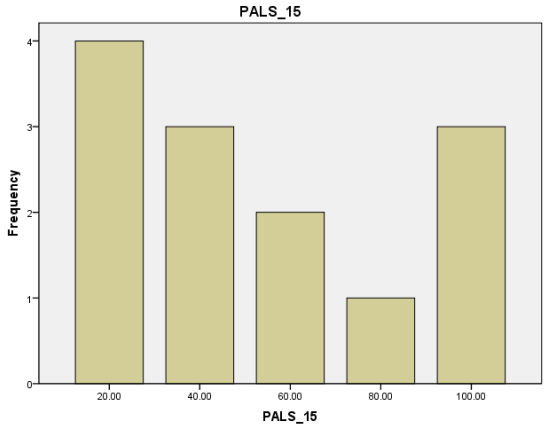
N	Valid	13
	Missing	4
Skewness		-.016
Std. Error of Skewness		.616
Kurtosis		.554
Std. Error of Kurtosis		1.191
Percentiles	25	25.0000
	50	37.5000
	75	46.8750

Mental health:

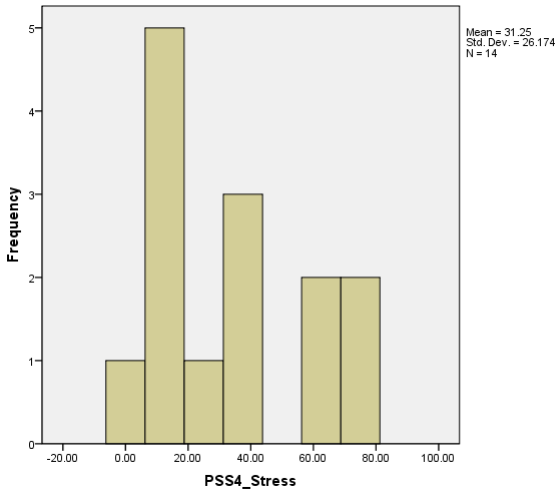


Appendix S – Distributions of PALS, WAMS and subscales

Health behaviour – Drinking alcohol:



PSS-4:



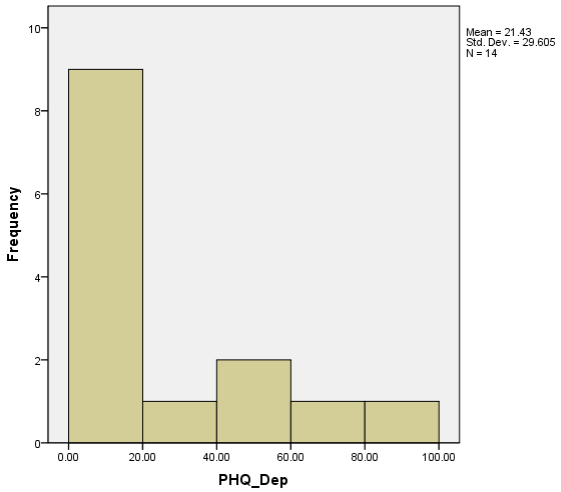
Statistics

PSS4_Stress

N	Valid	14
	Missing	3
Skewness		.535
Std. Error of Skewness		.597
Kurtosis		-1.253
Std. Error of Kurtosis		1.154
Percentiles	25	6.2500
	50	28.1250
	75	62.5000

Appendix S – Distributions of PALS, WAMS and subscales

PHQ Depression:

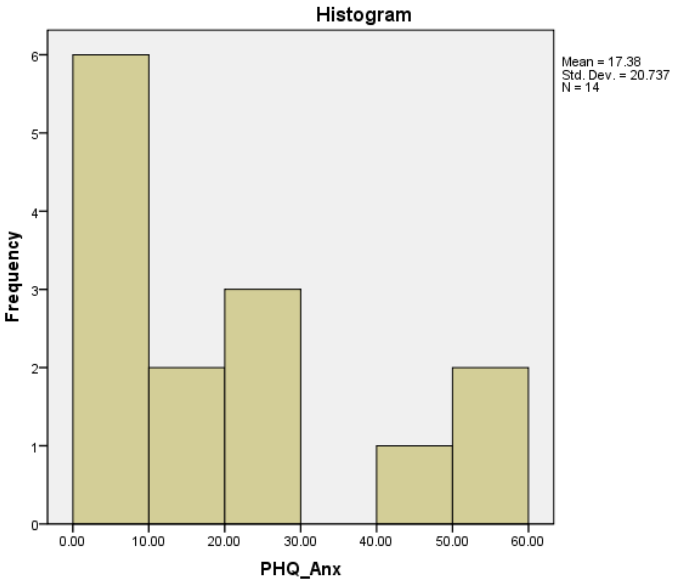


Statistics

PHQ_Dep

N	Valid	14
	Missing	3
Skewness		1.049
Std. Error of Skewness		.597
Kurtosis		-.305
Std. Error of Kurtosis		1.154
Percentiles	25	.0000
	50	.0000
	75	50.0000

PHQ Anxiety:



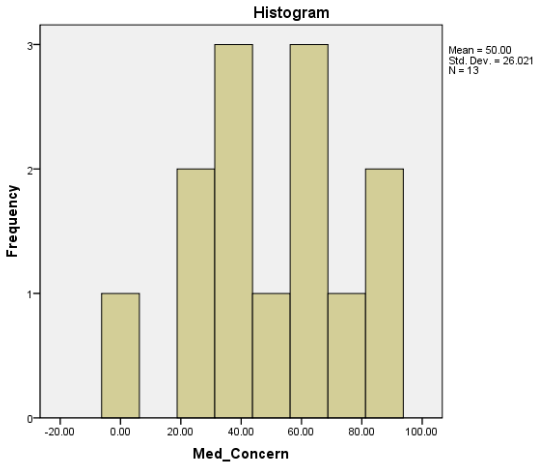
Appendix S – Distributions of PALS, WAMS and subscales

Statistics

PHQ_Anx

N	Valid	14
	Missing	3
Skewness		.993
Std. Error of Skewness		.597
Kurtosis		-.332
Std. Error of Kurtosis		1.154
Percentiles	25	.0000
	50	11.0000
	75	27.5825

Medication concerns:



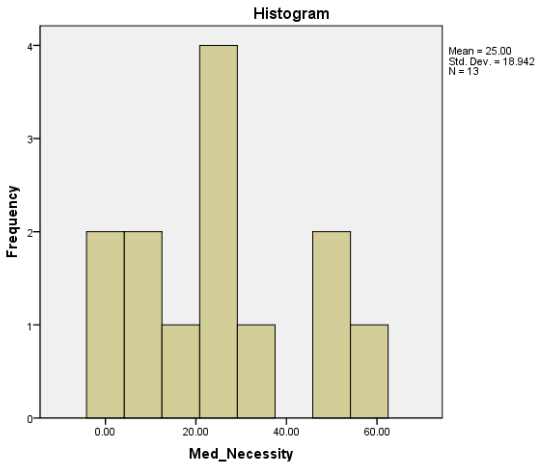
Statistics

Med_Concern

N	Valid	13
	Missing	4
Skewness		-.197
Std. Error of Skewness		.616
Kurtosis		-.462
Std. Error of Kurtosis		1.191
Percentiles	25	31.2500
	50	50.0000
	75	68.7500

Appendix S – Distributions of PALS, WAMS and subscales

Medications necessity:

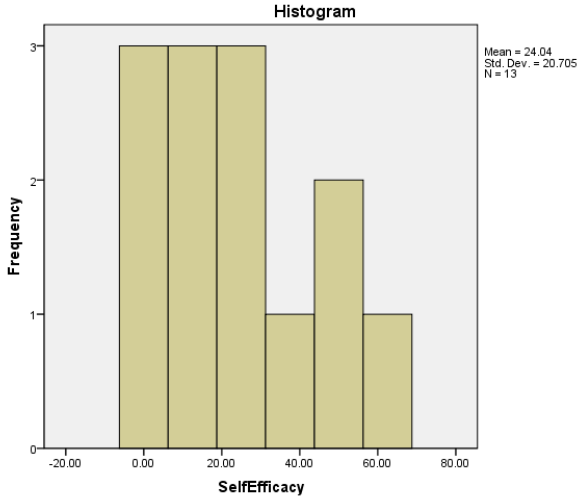


Statistics

Med_Necessity

N	Valid	13
	Missing	4
Skewness		.402
Std. Error of Skewness		.616
Kurtosis		-.756
Std. Error of Kurtosis		1.191
Percentiles	25	8.3300
	50	25.0000
	75	41.6650

Self-efficacy:



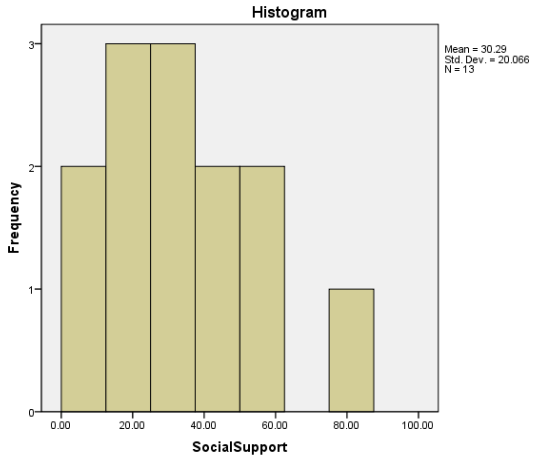
Appendix S – Distributions of PALS, WAMS and subscales

Statistics

SelfEfficacy

N	Valid	13
	Missing	4
Skewness		.533
Std. Error of Skewness		.616
Kurtosis		-.788
Std. Error of Kurtosis		1.191
Percentiles	25	6.2500
	50	25.0000
	75	43.7500

Social support:



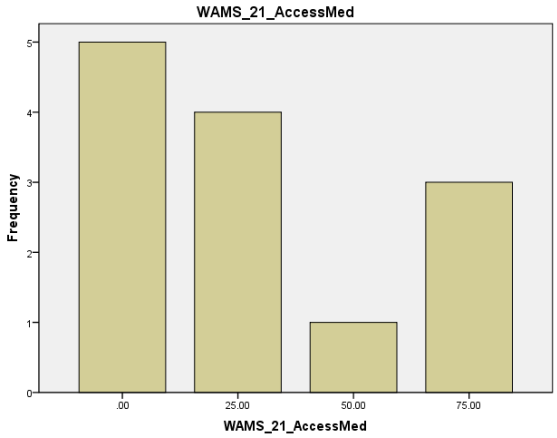
Statistics

SocialSupport

N	Valid	13
	Missing	4
Skewness		.860
Std. Error of Skewness		.616
Kurtosis		.444
Std. Error of Kurtosis		1.191
Percentiles	25	15.6250
	50	25.0000
	75	46.8750

Appendix S – Distributions of PALS, WAMS and subscales

Access to medicines:

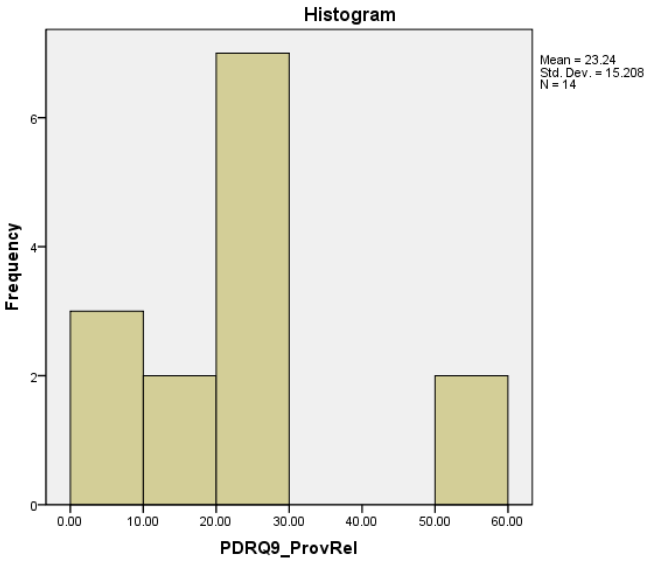


Statistics

WAMS_21_AccessMed

N	Valid	13
	Missing	4
Percentiles	25	.0000
	50	25.0000
	75	62.5000

PDRQ-9:



Appendix S – Distributions of PALS, WAMS and subscales

Statistics

PDRQ9_ProvRel

N	Valid	14
	Missing	3
Skewness		.806
Std. Error of Skewness		.597
Kurtosis		.767
Std. Error of Kurtosis		1.154
Percentiles	25	12.5000
	50	23.6100
	75	27.8675

Appendix T - Discriminant validity of the subscales comprising the PALS and WAMS tools

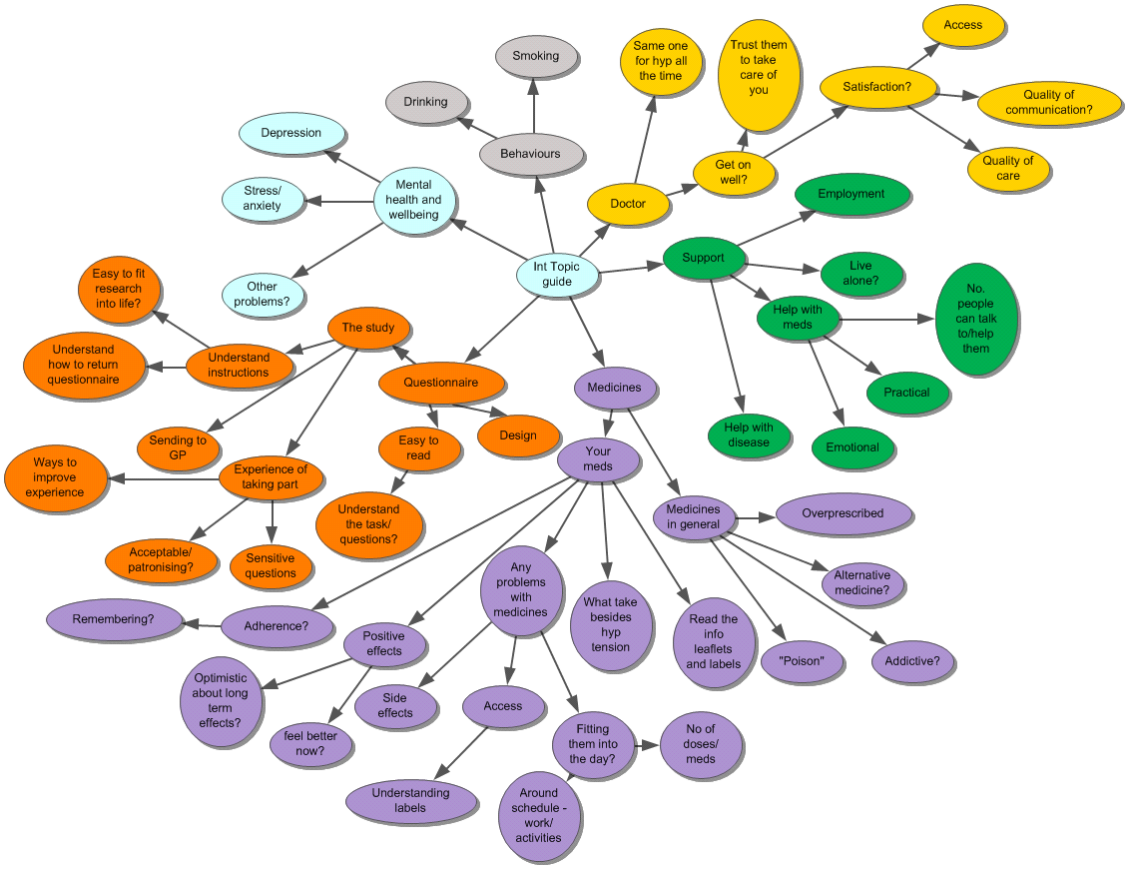
	Employ	Housing Status	Age	Health Literacy	BMQ-Overuse	BMQ-Harm	Mental Health	Alcohol	PSS-4	PHQ-Dep	PHQ-Anxiety	Med Concerns	Med Necessity	Self-Efficacy	Social Support	Access to Meds	PDRQ-9	Morisky	Retro Refill	Pro Refill
Sex	-0.415	0.102	-0.339	-0.045	-0.151	0.064	-0.316	-0.412	-0.163	-0.449	-0.282	0.039	-0.153	0.195	-0.077	-0.082	-0.162	-0.463	0.173	0.194
Employed	1	0.102	0.620	-0.285	-0.211	0.189	0.529	-0.339	-0.409	0.067	-0.158	0.106	0.176	-0.25	0.281	0.075	0.058	-0.249	0.224	0.125
Housing Status	-	1	0.306	-0.467	0.045	0.177	-0.167	0.044	0.106	0.283	0.184	0	0.157	0.321	0.734	-0.456	-0.624	-0.398	0.656	0.394
Age	-	-	1	-0.567	-0.149	0.069	0.13	-0.352	-0.599	-0.285	-0.379	-0.059	0.282	-0.218	0.193	-0.261	-0.389	-0.275	0.220	0.546
Health Literacy	-	-	-	1	0.267	0.24	0.068	0.25	0.493	0.112	0.066	-0.04	-0.245	0.491	-0.146	0.416	0.165	0.615	-0.872	-0.860
BMQ-Overuse	-	-	-	-	1	0.515	0.066	0.071	0.345	0	-0.257	-0.39	-0.162	0.038	-0.315	-0.501	-0.289	0.086	-0.075	-0.394
BMQ-Harm	-	-	-	-	-	1	0.165	-0.604	-0.116	-0.162	-0.51	0.031	0.224	0.385	0.149	-0.195	-0.248	-0.147	-0.264	-0.394
Mental Health	-	-	-	-	-	-	1	-0.033	0.075	0.259	0	0.31	0.483	0.089	0.307	0.467	0.487	0.070	0.258	-0.289
Alcohol	-	-	-	-	-	-	-	1	0.647	0.426	0.562	-0.23	-0.344	-0.083	-0.059	0.05	0.042	0.433	-0.050	-0.280
PSS-4	-	-	-	-	-	-	-	-	1	0.813	0.760	0.225	0.282	0.534	0.471	0.507	0.173	0.720	-0.245	-0.878
PHQ-Depression	-	-	-	-	-	-	-	-	-	1	0.865	0.573	0.609	0.343	0.778	0.538	0.397	0.671	0.208	-0.375
PHQ-Anxiety	-	-	-	-	-	-	-	-	-	-	1	0.465	0.477	0.307	0.647	0.628	0.444	0.684	0.127	-0.425
Medication Concerns	-	-	-	-	-	-	-	-	-	-	-	1	.706	0.071	0.624	0.398	0.653	0.245	0.214	0.183
Medication Necessity	-	-	-	-	-	-	-	-	-	-	-	-	1	0.323	0.696	0.502	0.532	0.319	0.383	0.097
Self-Efficacy	-	-	-	-	-	-	-	-	-	-	-	-	-	1	0.427	0.372	-0.18	0.627	-0.259	-0.607
Social Support	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	0.354	0.205	0.183	0.491	0.110
Access to Medicines	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	0.620	0.739	-0.264	-0.471
PDRQ-9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	0.490	-0.012	-0.206

Items in bold have their strongest correlation with a measure of adherence

Appendix U – Practitioner focus group topic guide

1. For the purposes of the recording, please introduce yourself:
    - What you would like to be called
    - Your current professional role
2. How often do you use questionnaire type tools to help with decision making about individual patients?
    - For example, the PHQ9
3. What features make a good tool?
    - Wording
    - No. Questions
    - Design
    - Scoring
    - Interpretation
4. What is it about bad tools that make them bad?
    - Wording
    - No. Questions
    - Design
    - Scoring
    - Interpretation
    - Admin burden?
5. Given the things we've talked about so far, what were the overall impressions of these two tools?
    - Did the content 'make sense'?
    - Are there any questions are not clearly understood?
    - Are there any questions which may mean different things to different people?
    - Are there any concerns about the content?
        - Anything which you think might upset patients. Anything that might upset the practitioners. Anything which seems ethically dubious?
    - Is there anything that is missing?
    - Does it seem like these tools could be used to help identify non-adherent patients?
    - Does it seem like they could be used to identify other problems with patients?
        - Would you want it to be able to identify other problems? E.g depression/stress.
    - Would they help to make a decision about what to do with a particular patient?
6. What are the best ways to get practitioners involved in research?
    - What sort of things can researchers do to encourage practitioners to take part?
    - What puts people off taking part in research?
    - If we were to run this study again, what could we do to make it easier for the practice?

Appendix V – Participant interview topic guide



Below is the interview guide for patient participants. The questions are coloured to reflect the criteria outlined in the topic map above. These will be used as prompts when necessary to encourage discussion.

First: Run through confidentiality and procedures. Allow them to flick through questionnaire to refamiliarise themselves.

Opening questions:
1: If we can go right to the beginning, you received a letter that told you that you were due to attend for a hypertension review, and telling you about this study. How did you feel as you read that letter?

What were your thoughts before you decided to take part?
Did you decide straight away to take part or did you think about it for a while?
Why did you decide to take part?
How did you feel about taking part in the research?
Is there anything we could have done to make you feel better about taking part?

2: How did you feel when completing the questionnaire?

Were there any sections you'd particularly like to comment on?
Were there any questions you didn't like? (Also ask how felt about knowing doctors would use the questions on smoking and drinking to update their medical records)
Were there any times where you weren't quite sure how to fill it in?
Can you think of anything we could do to make this a better questionnaire?

What could we have done to make it easier to complete?

3: Parts of the questionnaire were asking you about taking your medicines. Tell me, how do you feel about taking them?

How do you find taking them? Is it easy or difficult for you?

(Ask if feel the same or differently about other meds if on any)

4: Do you talk to many people about your hypertension?

Do you talk to them about taking your medicines?

5: How do you feel about talking to your doctor about your hypertension?

Is there anything you'd change about how you get on with your doctor?

6: Overall how would you say you are managing your hypertension?

Would you say you are coping well or not?

Does it have much effect upon your day to day life or not?

7: Is there anything further that you would like to add either about being involved in the study, the questionnaire, or your medicines.

Appendix W – Practitioner focus group framework after coding, prior to synthesis

Theme	Subtheme
1. Perception of questionnaire tools	
	1.1 Influence on decision making
	1.2 Impact upon consultations
	1.3 Influence on relationship with the patient
	1.4 Motivations for use of tools
2. Design of questionnaire tools	
	2.1 Wording of questionnaires
	2.2 Length
	2.3 Scoring and interpretation
	2.4 Mode of administration
	2.5 Patient perspectives
	2.6 Deficiencies of current tools
3. Ethical considerations	
	3.1 Dealing with sensitive questions
	3.2 Managing responses
4. Patient adherence	
	4.1 Identification
	4.2 Causes
	4.3 Management of non-adherence
5. Participation in research	
	5.1 Incentives
	5.2 Barriers
	5.3 Logistics
6. Perception of patients	
	6.1 As patients
	6.2 As participants
7. Practitioner focussed themes	
	7.1 Professional pride
	7.2 Busyness

Appendix X – Participant interview framework after coding, prior to synthesis

Theme	Subtheme
1. Patient factors	
	1.1 Demographic
	1.2 Normalising – Merged with 8.2
	1.3 Stress and anxiety
	1.4 Emotive responses versus rationalisations
	1.5 Social desirability
	1.6 Desire for independence
	1.7 Desire for information
2. Perception of medicines	
	2.1 Aspects of the drug regimen
	2.2 Perception of side effects
	2.3 Positive aspects of the medicine
	2.4 Reservations about medicines
3. Perception of Illness	
	3.1 Causes of illness and exacerbating factors
	3.2 Perception and impact of symptoms
	3.3 Impact and role of comorbid conditions
	3.4 Perception of health and health maintenance renamed
4. Access to healthcare	
	4.1 Obtaining a new supply
	4.2 Paying for medication
	4.3 Getting a consultation
	4.4 Dealing with problems
	4.5 Literacy and understanding
5. Social Factors	
	5.1 Practical help
	5.2 Emotional Support
	5.3 Role of romantic partners
	5.4 Giving and receiving advice
6. Relationship to health care providers	
	6.1 Relationship with individual doctors
	6.2 Relationship to surgeries – suggest merging with 6.1 rename as "The doctor patient relationship"?
	6.3 Trust
	6.4 Time
	6.5 Empathy and rapport
7. Participation in research	
	7.1 Perceived benefits of participation
	7.2 Perceived threats from participation renamed
	7.3 Barriers to participation
	7.4 Understanding Questions and instructions
8. Recurrent themes	
	8.1 Trust
	8.2 Normalisation
	8.3 Motivations
	8.4 Geography
9. Adherence	

Items in bold are changed from initial framework

Appendix Y – Interviewee and interview conduct summaries.

Participant A

This interview was conducted in the participant's home at the end of a quiet cul-de-sac. The interview was very briefly interrupted by post being delivered but this did not faze the participant. The participant was keen to take part and was very talkative, with the interview over running the planned hour by 20 minutes. She seemed to be very motivated to take part in the interview. This motivation seems to have been driven partly by a desire to help a student with their course. Her niece is studying to be a doctor and this seems to have generated a desire to help students more generally. A second motive seemed to be a desire to be helpful mixed with a sense of duty. She feels that she should help whenever she can regardless of whether this was taking part in research or voting. She had a particular fondness for the NHS and showed understanding and concern regarding the consequences of wasting medicines. This desire to please was evident at times during the interview and resulted in the participant remaining slightly nervous throughout although she seemed to enjoy the process. The participant had a weekly routine in which she would engage in a number of social activities, part time work, and household chores throughout the days and weekend. However, this routine was not too rigid and she changed the type of activities she engaged in from time to time. She felt that this routine, which was rigid only in the morning and to an extent in the evening once her day was done, helped her to take her medicines without forgetting.

Participant B

The interview was conducted in the participant's home and his family could be heard talking and cooking in nearby rooms. The door was left open and sometimes people passed by. Despite this lack of privacy the participant was very calm throughout and seemed entirely unperturbed by the possibility of being over heard. Despite this he was a very private man who was unwilling to talk about his condition with anyone other than his wife, sister, and closest friend. This default towards privacy resulted in the participant being reticent to share too much information. His willingness to confide in a only very small number of people also guided his choice of GP. He sought the same GP for appointments "nine times out of ten"

and said he was less open with other doctors. In this context the interview was short at approximately 45 minutes in length and the interview tended to be characterised by short exchanges and more closed questions than would be desired.

Participant C

This interview was conducted in one of the doctor's rooms at Elvington medical practice. The participant approached the interview in a very frank and business-like manner. That is he seemed to enjoy the ability to give constructive feedback and considered himself to be competent to do so given his formerly senior roles. Further, his talk was often about how others may perceive the questionnaire rather than how he himself perceived it. At times the interview reflected a meeting not dissimilar to a student-supervisor meeting. He also demanded some give and take in the conversation, being unwilling to talk without some reciprocation from the interviewer. The setting of the doctor's room may have contributed to the very pragmatic conversation that took place (Elwood and Martin, 2000). The participant seemed very honest and the opportunity to talk frankly about his history of mental health problems was a motivating factor for his participation.

Participant D

This interview also took place in a doctor's room at Elvington surgery. However, unlike with participant C the interview felt did not have the character of a formal meeting and the participant seemed at home in the surroundings. The participant was happy to talk about private matters and voluntarily brought up sexual problems he has as a side effect of drugs after only a moment of hesitation. In particular he seemed to be grateful for an opportunity to talk about the difficulties his wife faces with degenerating sight. Much of this talk was unrelated to the study aims. However the participant was not rushed to change topic given the sensitivity of the issue and his clear desire to talk about it. This interview in particular includes a number of closed questions from the interviewer which limited the ability of the participant to express their own views. The participant does not have hypertension, although this was not known at the time of interview. However, he does take medicines for hypertension and it was felt on the part of the researcher and supervisory team that their

experiences with the survey and of taking medicines meant that their account remained relevant. There did not seem to be any great differences in the testimony of this participant compared to others that could be clearly attributed to their not having hypertension.

Participant E

This participant was conducted in a participant's home whilst decorators were renovating the property. The interview was conducted in a large kitchen and dining space which was often used for the sink by the decorators. The interview was not disturbed although the decorators did enter the room shortly after its conclusion and so conceivably could have done so during the interview. The interruption did not put the participant off their stride in the post interview discussion however, so there is no reason to suspect this potential for interruption changed the interview meaningfully. A phone call that the participant received mid-way through the interview also did not faze the participant, although it did take the interviewer a moment to locate their place in the interview. The impact of this interruption was minimal however, and the conversation resumed its previous flow quickly. This participant seemed somewhat anxious throughout the interview and seemed especially keen to present themselves as an especially open and helpful person. In parallel with PA this anxiousness seemed to be in ensuring they presented themselves well rather than discomfort with the process of interview, the questions or interviewer.

Health Research Authority

NRES Committee East of England - Cambridge East
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18 June 2012

steven.watson@uea.ac.uk

Mr Steven J Watson
Doctoral Student
University of East Anglia
School of Pharmacy
Norwich Research Park
Norfolk NR4 7TJ

Dear Mr Watson

Study title:	**Prediction of current adherence to medication in patients with hypertension**
REC reference:	**12/EE/0203**
Protocol number:	**N/A**

Thank you for your letter of 07 June 2012, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Non-NHS sites

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter		18 April 2012
Evidence of insurance or indemnity - Zurich Municipal		
GP/Consultant Information Sheets - Appendix 3e, phase 1 practitioner	2,	10 April 2012
Interview Schedules/Topic Guides - Appendix 9	v5	30 May 2012
Investigator CV - Steven James Watson		18 April 2012
Letter from Sponsor - UEA		17 April 2012
Letter of invitation to participant - Appendix 6a interview	3,	10 April 2012
Letter of invitation to participant - Appendix 6b interview slots	2,	10 April 2012
Letter of invitation to participant - Appendix 8	v1	01 June 2012
Other: Academic Supervisor CV - Debi Bhattacharya	1	30 March 2012
Other: Appendix 3e Practitioner research notification	3	02 June 2012
Participant Consent Form: Appendix 4a - Main study	Version 11	30 May 2012
Participant Consent Form: Appendix 4b - Patient interview	Version 3	30 May 2012
Participant Consent Form: Appendix 7 - Practitioner focus group	Version 3	30 May 2012
Participant Information Sheet: Appendix 3a, part 1	9	10 April 2012
Participant Information Sheet: Appendix 3b, phase 2	4	10 April 2012
Participant Information Sheet: Appendix 3c, follow up	4	10 April 2012
Participant Information Sheet: Appendix 3d, practitioner participant	4	10 April 2012
Participant Information Sheet: Appendix 5, phase 1	9	10 April 2012
Participant Information Sheet: Appendix 3a - Patient Main Study Part 1	17	03 June 2012

Participant Information Sheet: Appendix 3b - Responders	6	03 June 2012
Participant Information Sheet: Appendix 3c - Nonresponders part 1	7	03 June 2012
Participant Information Sheet: Partitionor focus group part1 main study	16	25 May 2012
Participant Information Sheet: Appendix 5 - Patient interview part 2	13	03 June 2012
Protocol	13	18 April 2012
Questionnaire: PALS, appendix 1	15	03 April 2012
Questionnaire: WAMS, Appendix 2	14	08 February 2012
REC application	Submission code 100149/314898/1/80	18 April 2012
Response to Request for Further Information from Steven Watson		07 June 2012

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

12/EE/0203	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

Dr Daryl Rees
Chair

Email: susan.davies@eoe.nhs.uk

Enclosures: "After ethical review – guidance for researchers" [SL-AR2]

Copy to: Mrs Sue Steel sue.steel@uea.ac.uk
Ms Helen Webster helen.webster@york.nhs.uk

Health Research Authority

NRES Committee East of England - Cambridge East
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05 October 2012

Mr Steven J Watson
Doctoral Student
University of East Anglia
School of Pharmacy
University of East Anglia
Norwich Research Park
NR4 7TJ

Dear Mr Watson

Study title:	**Prediction of current adherence to medication in patients with hypertension**
REC reference:	**12/EE/0203**
Protocol number:	**N/A**
Amendment number:	**Substantial Amendment AM02 IRAS Code: 100149/366008/13/33/15266**
Amendment date:	**21 September 2012**
Amendment Summary:	**Request to follow up Patients not agreeing to fill in questionnaires with a postcard asking for feedback.**

The above amendment was reviewed at the meeting of the Sub-Committee held on 02 October 2012 by email correspondence.

Ethical opinion

None

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Participant Postcard	Version 2	21 September 2012
Protocol	Version 14	21 September 2012

Appendix AA – Ethics committee amendment approval

Notice of Substantial Amendment (non-CTIMPs) : Substantial Amendment AM02 IRAS Code: 100149/366008/13/33/15266		21 September 2012
Covering Letter : From: Steven Watson		21 September 2012

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

12/EE/0203:	**Please quote this number on all correspondence**

Yours sincerely

PP M. Johnson.

Rebekah Lay
Chair

E-mail: melanie.johnson@eoe.nhs.uk

Enclosures: *List of names and professions of members who took part in the review*

Emailed To: Mr Steven J Watson: steven.watson@uea.ac.uk
Ms Helen Webster, : helen.webster@york.nhs.uk
Mrs Sue Steel: sue.steel@uea.ac.uk

Appendix AA – Ethics committee amendment approval

NRES Committee East of England - Cambridge East
Attendance at Sub-Committee of the REC meeting on 02 October 2012
Also in attendance:

Name	*Position (or reason for attending)*
Mrs Rebekah Ley	Assistant Director Medico Legal and Patient Experience
Mrs Alison Wooster	Lay member

Appendix AB – Research and Development approval letter

Dawn.Taylor@nyypct.nhs.uk
Direct Tel: 01845 573863

Reference: PhDStudy

The Hamlet
Hornbeam Park
Harrogate
North Yorkshire
HG2 8RE
Tel: 01845 573863
Fax: 01845 573805
Website: www.northyorkshireandyork.nhs.uk

Steven Watson
School of Pharmacy
University of East Anglia
Norwich Research Park
Norwich
NR4 7TJ

30 July 2012

Dear Steve

Re: **Application for NHS Research Permission**
Project Title: **Medication adherence in hypertension (PhD Study)**

Further to your recent request I am writing to inform you that NHS North Yorkshire and York give research governance permission for the above study.

In accordance with the Trust policy for research governance you are required to inform Dawn Taylor (Head of Corporate Governance) at the Trust of any significant proposed challenges to the original protocol, adverse events or issues of safety. In addition also required will be progress reports and end of study notification.

Wishing you every success with your study.

Yours sincerely

Dawn Taylor
Head of Corporate Governance

Cc: Dr Timothy Longmore
Elvington Medical Centre
York Road
Elvington
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Timothy.Longmore@GP-B82081.NHS.U

Appendix AC – Research and Development amendment approval

NHS

North Yorkshire and York

Our Ref: M-/ZF-SubAmd2

19/11/2012

The Hamlet
Hornbeam Park
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HG2 8RE

Mr Steven J Watson
School of Pharmacy
University of East
Anglia Norwich
Research Park NR4
7TJ

Dear Mr Steven J Watson

Re: Substantial Amendment 2 Approval Letter

--

Study Title: Prediction of current adherence to medication in patients with hypertension Local R&D No: 178

REC No: 121EE10203

Thank you for informing myself of the notification of a substantial amendment and the favourable ethical opinion for the above study. The receipt of the necessary documents has been attained by the PCT.

Further to your recent request I am writing to inform you that NHS North Yorkshire & York give research governance approval for the above study.

In accordance with NHS North Yorkshire & York policy for research governance you are required to inform Dr Marie Girdham (Research Governance Manager) at the trust of any further significant proposed challenges to the original protocol adverse events or issues of safety. In addition Dr Marie Girdham will also require progress reports and end of study notification.

Marie's contact details are as follows:

Dr Marie Girdham
Research Governance Manager
NHS North Lincolnshire
Health Place
Wrawby Road
Brigg
North Lincolnshire
DN20 8GS

Tel: 01652 251000 E: **marie.girdham (nhs.net**

R&D Facilitator contact Email & Telephone details:

Tel: 01652 251134 **E: zowie.fusseNanhs.net**

Wishing you every success with your

study. Yours sincerely

Dawn Taylor

Head of Corporate Governance

Appendix AD – Conference abstract 1

This abstract was submitted to the Health Services Research and Pharmacy Practice conference (HSRPP - 2011) where it won first prize in the poster abstract competition.

Title: Systematic review and meta-analysis shows stress is negatively associated with adherence to medication

Watson S, Bhattacharya D, Wood J, Smith J, Adams M, Song F.

School of Pharmacy, University of East Anglia, Earlham Road, Norwich, nr4 7tj, United Kingdom

Email: steven.watson@uea.ac.uk

Background: Chronic illnesses are most commonly managed with prescribed medications. Such illnesses are associated with prolonged periods of physical and psychological stress. Prescribed medications may exacerbate stress if side-effects are experienced, or by reducing patient's perceived control[1]. This may reduce a patient's capacity or willingness to adhere to their medication[2]. This study provides a meta-analysis addressing the hypothesis that stress impairs patient adherence to medication. This study did not require ethical approval.

Method: Articles were considered relevant if they were published in English and allowed a correlation between stress and medication adherence to be calculated. Articles were identified as part of a larger meta-analysis of adherence predictors by searching Medline, Embase and PsychInfo using the Ovid interface on the 26/04/2010. Variations of the terms "patient adherence" and "patient compliance" were searched alongside "medic*" and "predic* or influ* or determ* or caus* or correla* or associat*" to limit the search to articles examining correlates of medication adherence. No limits were placed on date of publication or study design. Excluded were studies from a mentally ill, institutionalised or paediatric population. Random effects meta-analysis was employed to estimate the size of the relationship between stress and adherence. Results are presented as Pearson's coefficients with 95% confidence intervals. Calculations were performed using Comprehensive Meta-Analysis[3]. Quality assessment criteria were collected for post-hoc testing according to study methodology and the validity and reliability of the measures of adherence and stress employed. Potential reporting bias was explored by visual analysis of a funnel plot[4].

Results: In total, 2007 articles were identified. Searching study abstracts identified 48 articles potentially relevant to the stress hypothesis. Full publications revealed 27 irrelevant articles, and 13 providing inadequate information to calculate an effect size. Inclusion criteria were met by eight studies providing a total sample size of 2603 participants. The mean proportion of adherent patients was 69% based on six studies. Experience of stress was negatively associated with adherence ($r = -0.248$, 95% CI = -0.297, -0.197, $p < 0.001$). The analysis was not significantly heterogeneous (Cochran's $Q = 9.309$, $p = 0.231$). The sample of studies used was too small to analyse the impact of study factors or possible covariates using meta-regression[5]. Lack of reporting for reliability and validity data prohibited further quality analysis. A funnel plot and the high number of studies not fully reporting the stress and adherence relationship may suggest an outcome bias in reporting.

Discussion: Stress is a manageable condition[6] that has a direct impact on health outcomes, and has further damaging implications by lowering adherence to medication. It is therefore essential that healthcare professionals maintain an awareness of patient mental wellbeing and given that a number of treatments for stress exist, offer appropriate interventions[6]. The poor methodological consistency of studies is problematic and reflects a lack of validated measures; however, the low heterogeneity of this meta-analysis increases confidence in the findings. Covariance between stress and other adherence predictors was not addressed; nor was it identified whether the observed non-adherence was intentional or not. These shortfalls will be addressed by a larger meta-analysis examining the relationships between many more predictors of adherence.

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Appendix AD – Conference abstract 1

Schmid CH, *et al*. Meta-regression detected associations between heterogeneous treatment effects and study-level, but not patient-level, factors. *J Clin Epidemiol.* 2004; 57(7): 683-697

Richardson KM, Rothstein HR. Effects of occupational stress management intervention programs: a meta-analysis. *J Occup Health Psychol.* 2008; 13(1): 69-93.

Appendix AE – Conference abstract 2

This abstract was submitted to the Health Services Research and Pharmacy Practice conference (HSRPP - 2012) where it was accepted as an oral presentation

Title: The impact of treatment side-effects upon medication adherence.

Watson S, Bhattacharya D, Wood J, Smith J, Adams M, Song F.

School of Pharmacy, University of East Anglia, Earlham Road, Norwich, nr4 7tj, United Kingdom

Email: steven.watson@uea.ac.uk

Background: Patient non-adherence to prescribed medication therapy is associated with lower treatment efficacy[1] and experience of side-effects is an often cited reason for non-adherence[2]. Meta-analytic treatment of this hypothesis is currently lacking. This study provides evidence for the size of the relationship between patient experience of side-effects and non-adherence to medication. This study did not require ethical approval.

Method: Articles were considered relevant if they were published in English, and provided measures for which an effect size of the relationship between adherence and experience of side-effects could be calculated. Articles were identified as part of a larger meta-analysis of adherence predictors by searching Medline, Embase and PsychInfo using the Ovid interface on the 26/04/2010. Variations of the terms “patient adherence” and “patient compliance” were searched alongside “medic*” and “predic* or influ* or determ* or caus* or correla* or associat*” to limit the search to articles examining correlates of medication adherence. No limits were placed on date of publication or study design. Excluded were studies from a mentally ill, institutionalised or paediatric population. Random effects meta-analysis was employed to estimate the size of the odds ratio (OR) and 95% confidence interval between the presence or absence of side-effects and the proportion of adherent patients, as well as the Pearson’s correlation coefficients (r) between adherence behaviour and the number and severity of side-effects. Quality assessment criteria were collected for post-hoc testing according to study methodology via the meta-regression procedures of Lipsey and Wilson[3]. Potential reporting bias was explored by visual analysis of a funnel plot.

Results: In total, 1878 unique articles were identified. Only studies with sufficiently similar definitions of patient experience of side-effects were incorporated into meta-analyses. Full inclusion criteria were met for 11 articles examining the effects of the presence versus absence of side-effects upon adherence (n = 4161), five articles examining the effect of the number of side-effects upon adherence (n = 1394), and a further five articles examining the severity of side-

effects upon adherence (n = 3672). The presence of side-effects was associated with reduced adherence, OR (95% CI) = 0.40 (0.19, 0.84), p = 0.02. As the number of experienced side-effects increased, adherence decreased, r (95% CI) = -0.17 (-0.29, -0.04), p = 0.01. Similarly, more severe side-effects were associated with lowered adherence, r (95% CI) = -0.22 (-0.26, -0.18), p <0.01. Heterogeneity analysis identified no significant impacts upon effect size estimates from indicators of study quality, although study quality was low. There were no indications of bias in outcome displayed by funnel plots.

Discussion:

Recent national UK guidance to facilitate medication adherence recommended the discussion of side-effects with patients at the point of prescribing in order to allow patients to make an informed choice about their therapy[4]. The findings of this meta-analysis further highlight the relevance of side-effects to medication adherence and therefore the importance of these discussions occurring between healthcare professionals and patients.

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