Journal of Affective Disorders 382 (2025) 462–470

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Research paper

A qualitative investigation of the modifiable determinants of medication adherence in bipolar disorder (BD): Views of patients and their family and friends

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ARTICLE INFO

Keywords:
Adherence
Bipolar disorder
Theoretical domains framework
Barriers and facilitators
Behavioural medicine

ABSTRACT

Background: Medication nonadherence in bipolar disorder (BD) can lead to adverse outcomes including relapse, hospitalisation and suicidility. Adherence research traditionally excludes mental health populations and their family and friends, contributing to inequity between physical and mental health. We used behavioural science to characterise modifiable adherence determinants in BD from the perspectives of patients and their family and friends.

Method: Between April-June 2020, we conducted two focus groups and 26 interviews with adults with BD and their family and friends. We explored modifiable adherence determinants which were mapped to the Theoretical Domains Framework (TDF), followed by a thematic analysis and prioritisation of determinants.

Results: Sixty-three (including 13 new) adherence determinants, mapped to nine TDF domains, were prioritised. Four themes of adherence determinants emerged: the medication itself; practicalities; how patients perceive themselves, their illness, and treatments; and collaboration between patients, their family and friends, and healthcare professionals. Nine prioritised TDF domains were: 'Environmental context and resources', 'Intentions', 'Emotion', 'Social Influences', 'Goals', 'Memory, attention and decision processes', 'Beliefs about consequences', 'Knowledge' and 'Social/professional role and identity'. Respective examples include side effects, treatment preferences, fear of not being 'myself', relationships with healthcare team, medication affecting life goals, forgetfulness, beliefs about negative consequences, not knowing the risk of stopping medication, and involvement in treatment decisions.

Conclusion: Targeting antecedents of forgetfulness as well as newly identified determinants linked to 'Emotion' and 'Intentions', may improve adherence. Mapping adherence determinants to TDF domains provides a framework for designing personalised adherence interventions by selecting appropriate behaviour change techniques.

1. Background

Bipolar Disorder (BD) is a recurrent mental health condition characterised by mood swings, significant change in energy level and ability to function. It is associated with significant socioeconomic burden and high risk of disability and mortality (Bobo et al., 2011; Dembek et al., 2023; Vázquez et al., 2015). Medication remains the mainstay of BD treatment, however an estimated 40 % of patients do not take their medication as prescribed (Chakrabarti, 2017; Lingam and Scott, 2002; Vargas-Huicochea et al., 2014). This medication non-adherence leads to relapse, hospitalisation, functional impairment and suicidality and decreased likelihood of achieving remission and recovery (Gonzalez-Pinto et al., 2006; Hong et al., 2011; Jawad et al., 2018; Keck et al., 1998; Lingam and Scott, 2002; Velligan et al., 2009; Vieta and Colom, 2024). Additionally, medication nonadherence leads to increased social and healthcare costs (Bagalman et al., 2010; Dembek et al., 2023; Jawad

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https://doi.org/10.1016/j.jad.2025.04.149
Received 2 January 2025; Received in revised form 22 April 2025; Accepted 23 April 2025

et al., 2018; Velligan et al., 2009).

Medication taking is a complex health behaviour influenced by various modifiable and non-modifiable adherence determinants (MacDonald, 2017; Velligan et al., 2009; Youn et al., 2022). While adherence determinants such as age and gender are non-modifiable, others such as a patient's knowledge about how to take their medication are modifiable and are thus potential intervention targets (Allemann et al., 2016; Prajapati et al., 2021). The UK Medical Research Council highlights the critical role of theory in developing interventions and offers a structured approach that integrates theoretical perspectives to enhance intervention effectiveness (Skivington et al., 2021).

Addressing medication non-adherence requires patients to change established patterns of behaviour. The application of behaviour change theory to identify and understand determinants of the behaviour permits the development of interventions that target the underlying behavioural mechanisms. The Theoretical Domains Framework (TDF) is a synthesis of 33 behaviour change theories comprising 14 domains (Knowledge, Skills, Social/ Professional Role and Identity, Beliefs about Capabilities, Optimism, Beliefs about Consequences, Reinforcement, Intentions, Goals, Memory, Attention and Decision Processes, Environmental Context and Resources, Social Influences, Emotion and Behavioural Regulation) that determine behaviour (Atkins et al., 2017). The TDF has been applied to guide the exploration of modifiable determinants of medication adherence for treating physical health conditions (Easthall et al., 2019). The domains of the TDF have been linked to evidence-based behaviour change techniques (BCTs), which are the active ingredients of behaviour change interventions (Michie et al., 2021). Therefore, mapping modifiable determinants to the TDF domains offers an evidence-based, theory-informed framework to guide medication adherence intervention development.

Our 2021 systematic review underpinned by the TDF reported a range of modifiable determinants of medication adherence in BD (Prajapati et al., 2021). The review highlighted the absence of views of patients' family and friends on modifiable determinants of adherence (Prajapati et al., 2021). This is a significant knowledge gap because family and friends can play an important role in supporting medication adherence in mental health (Deane et al., 2018).

This study aimed to explore the relevance and importance of literature-reported modifiable determinants of medication adherence as perceived by patients with BD, their family and friends, and identify any new determinants.

2. Method

2.1. Ethical approval

Ethical and governance approvals were obtained from Cambridgeshire and Hertfordshire Research Ethics Committee (Reference:19/EE/0288) and United Kingdom Health Research Authority (IRAS project ID:261687), respectively.

Informed consent was obtained from all the participants

2.2. Design

We employed a qualitative descriptive methodology to explore modifiable adherence determinants in BD. We conducted semi-structured focus groups and interviews with patients with BD and their family and friends. Discussions were guided by the **TDF** (Atkins et al., 2017) **and adherence determinants identified in our systematic review (Prajapati et al.,** 2021)**. The study findings were reported according to** the consolidated criteria for reporting qualitative research (COREQ) checklist (Tong et al., 2007) – see supplementary file I.

2.3. Settings, eligibility criteria and recruitment

Potential participants were identified and recruited from community mental health services in Norfolk and Suffolk counties in England – see supplementary file II for the recruitment process. Study posters and information for recruitment were displayed in communal areas of mental health Recovery College, Outpatient clinic, and MIND charity office. Outpatient clinic staff shared study details with potential participants. Additionally, the study was advertised through our organization's weekly bulletin and on social media platform X. Patients aged ≥18 years, with a diagnosis of BD and prescribed at least one medication for BD were eligible. Family and friends of eligible patients aged ≥18 years were also eligible. We used maximum variation, purposive sampling (Palinkas et al., 2015) using a screening survey (see supplementary file III) to include a wide range of demographic characteristics such as age, duration of BD, paying for prescription and number of BD medication prescribed. Participants were offered a shopping voucher (£10/h) for participation.

2.4. Data collection

We offered participants the choice of a focus group or individual interview, and either face-to-face, telephone (interview only) or online.

Evidence suggests that over 80 % of themes were discoverable within two to three focus groups, and 90 % within three to six (Guest et al., 2017). We planned to undertake two focus groups with patients, two with families and friends, and up to eight interviews with either participant group. Given the extensive list of adherence determinants already identified in our systematic review (Prajapati et al., 2021) this sample size was deemed sufficient to explore the relevance and importance of these determinants while also identifying any new determinants. We developed a topic guide for focus group and interviews (see supplementary file IV) in partnership with our stakeholder group (containing patients and their family members, healthcare professionals, and behavioural medicine experts). The topic guide was based on our systematic review (Prajapati et al., 2021), which identified literature reported modifiable adherence determinants in BD, and the TDF to which these determinants were mapped. To ensure it was patient-centred and aligned with study aim, we refined it through consultation with a stakeholder group. The topic guide was piloted with six colleagues. Feedback from the pilot, including enhancements to the icebreaker, prompt questions, and flow of conversation, was incorporated into the final topic guide.

Participants were provided with an information pack (see supplementary file V and VI) to familiarise themselves with the literature reported modifiable determinants that we planned to discuss at the focus groups and interviews.

To minimise participant burden of discussing all literature-reported determinants, the determinants were divided into Group 1 and 2, each comprising determinants mapped to nine different TDF domains with four domains (Skills, Reinforcement, Optimism, Behavioural Regulation) overlapping in each group. Sixteen participants were allocated to discuss Group 1 determinants and 18 participants to Group 2 determinants. See supplementary file VII for more details on which TDF domains were allocated for each group and rationale behind it.

AP and SS or DB facilitated focus group discussions and AP conducted all interviews; all were audio-recorded.

2.5. Analysis

Audio recordings were transcribed verbatim and anonymised by a professional transcriber. The transcripts were imported into NVivo 12 (Lumivero., 2024) for analysis. A 'best fit' framework approach (Carroll et al., 2013) with the TDF as an a priori framework was used to analyse the data in three phases:

2.5.1. Phase I: Extracting and mapping adherence determinants to TDF domains or 'Others'

The coding of data was an integral part of the analytical process and it involved:

- Initial Coding: AP conducted the initial coding by identifying and extracting modifiable adherence determinants and coding them to relevant TDF domains or 'Others' category if they did not map to any specific TDF domain. New adherence determinants not reported in our systematic review (Prajapati et al., 2021) were labelled as 'New'.
- Review and Validation: Another reviewer (AD, DB, or SS) independently reviewed the coding to ensure reliability and validity in the coding process. Discrepancies were resolved through discussion and referral to a third reviewer for arbitration if necessary.

2.5.2. Phase II: Thematic analysis

The development of themes followed a structured and iterative approach using thematic analysis within the 'best fit' framework approach (Carroll et al., 2013) involving three steps:

1. Indexing: Modifiable adherence determinants were indexed according to their mapping to TDF domains, organising data into preliminary categories.
2. Charting: Indexed data were rearranged into charts, facilitating visualisation and comparison within and across different TDF domains.
3. Interpretation and Theme Generation: Initial themes were developed from the charted data and refined through discussions with experienced researchers (AD, DB, SS) and stakeholders, ensuring accurate representation of adherence determinants in BD.

2.5.3. Phase III: Prioritisation of modifiable adherence determinants

Adherence determinants were prioritised according to the following criteria:

- Direct causal relationship reported between the determinant and adherence (e.g., 'fear of side effects from Lithium stopped me from taking them in the first place')
- Sense of the strength of determinant to influence adherence (e.g., 'I feel very strongly that I would not have stopped my medication if I had been alerted to the risk of stopping medication')
- Strength of corroboration (e.g., not being listened to as a barrier to adherence reported by most participants with no disagreement)

3. Results

A total of 34 participants (24 patients with BD and 10 family and friends) participated in the study. Data were collected via two semi-structured focus groups and 26 interviews, conducted online or by phone due to COVID-19 restrictions.

All participants were white, British or European, aged between 22 and 76, and mostly women. See Table 1 for participant details.

Table 1
Demographic and other characteristics of participants.

Description	Interview Participants				Focus Group Participants	
	Patients		Family & Friend		Patients	
	Group 1 (N = 8)	Group 2 (*N* = 8)	Group 1 (*N* = 5)	Group 2 (N = 5)	Group 1 (*N* = 3)	Group 2 (N = 5)
Age range	28 to 66	28 to 76	22 to 62	22 to 62	29 to 66	26 to 49
Gender						
Male	2	2	1	1	0	0
Female	6	6	4	4	3	5
No. of Medications, Range (Median)	1 to 5 (3)	1 to 10 (3.5)	NA	NA	2 to 3 (3)	1 to 7 (5)
How often do you miss taking a prescribed medicine?						
Rarely	6	4	0	0	3	1
Sometimes	1	2	0	0	0	3
NA	1	2	5	5	0	1
Pay for prescriptions?			NA	NA		
Yes	6	2			0	0
No	2	6			3	5
How long have you had bipolar disorder? Range (Median years)	<1 year to 37 years (22.5)	<1 year to 55 years (14. 5)	NA	NA	2 to 20 years (12)	2 to 14 years (6)
How often do you need somebody to help you with reading instructions or other written material from your doctor or pharmacy?			NA	NA		
Sometimes	3	5			1	2
Rarely	1	1			1	1
Never	4	2			1	2
Relationship with patient	NA	NA	Mothers, Wives, Brothers and friends		NA	NA

3.1. Phase I: Mapping adherence determinants to TDF domains or 'Others'

As shown in Table 2, eighty-five adherence determinants were extracted from focus group and interviews transcripts, 25 of which were new (labelled "New"). Some facilitators are the antonym of barriers, such as beliefs about the positive effects of medication being a facilitator whereas beliefs about negative effects of medication being a barrier. In other cases, facilitators are described as a solution to overcome the barrier. For example, forgetfulness is presented as a barrier whilst putting medication in a common visible place to help remember as a facilitator.

3.2. Phase II: Thematic analysis

No new adherence determinants were identified from the fifth (family and friends group) to the eighth (patients group) interviews. We generated four themes representing the modifiable determinants of medication adherence in BD: I) The medication itself, II) The practicalities, III) How patients perceive themselves, their illness, and their treatments, and IV) Working collaboratively.

3.2.1. I. The medication itself

The characteristics of the medication itself were voiced by most participants as a key determinant of adherence. Both *actual experience and patients' perception of medication effectiveness* were prominent determinants of adherence.

We found that *the severity of side effects and their impact on individual patients*, rather than simply side effects per se, determined whether adherence was compromised. For example, one patient described how he continued taking his medication for bipolar depression despite it causing chronic diarrhoea. In contrast, another patient explained that she stopped taking her mood stabiliser as it made her feel emotionless. In

Table 2
All identified modifiable adherence determinants in bipolar disorder, categorized by themes and mapped to TDF domains.

Facilitators ($n = 33$ total, 26 prioritised)	Barriers ($n = 52$ total, 37 prioritised)	TDF Domains ($n = 9$)
Theme 1: The Medication itself		
Acceptable formulation	Unacceptable formulations	Environmental context and resources
Not having to pay (e.g., >65 or other exemptions) or ways to minimise the cost of medication (e.g., NHS prepayment certificate) (New)	Cost of medication or pill organiser	
Effective medication (Medication working/ helping)	Medication not working/ helping	
	Pill burden / Higher number of prescribed medications	
	Higher dose frequency	
	Experience of side effects	
	Medication sedative effects interfering with life/job	Goals
	Medication reducing quality of life (New)	
Decision to take medications if the benefit outweighs negative effects (New)		Memory, attention and decision processes
Belief that medication is/ will be helpful	Belief that It is unhealthy or unnatural to take medication	Beliefs about consequences
Belief about Positive effect of medication, e.g., will keep me out of hospital	Belief that Mental health medications are harmful	
	Belief about Negative effects of medication, e.g., felt less creative, numb	
Belief that not taking medication would lead to relapse or hospitalisation	*Beliefs that medications make it harder to get well in the long term (New)*	
Understanding the reason behind why to take medications	Not knowing the why medications were prescribed	Knowledge
Good understanding of how the medication works (New)	Not knowing the risks of stopping the medication	
Learning through experience that stopping medications is not a good idea (New)	Not understanding Prescriber's direction	
	Fear of addiction to medication	Emotion
	Fear of side effects of medication	
	Fear that the medication might alter personality, identity ('Not being myself)	
	Seeing other people having side effects (New)	Social influences
Theme 2: The practicalities		
Having a job/routine that does not prevent taking medications	Irregular (or change of) daily routine or work schedule	Environmental context and resources
Being able to maintain a routine of medication taking	Not having a daily regular routine / Chaotic lifestyle	
Provision of online ordering and delivery of prescription and medications (New)		
Provision of pill organiser (New)	Difficulty accessing health service	
Provision of easily accessible medicine information service (New)	*Running out of medications and not being able to get them quickly (New)*	
Provision specific warnings related to the risk of stopping medications (New)		
Help to remember (putting medications in a visible place)	Forgetfulness	Memory, attention and decision processes
	Laziness/Carelessness	
Not having to remember (e.g., CPN visits to inject)	Difficulty remembering	
Family member reminding to take medications (e.g., text messages reminders)		Social Influences
Theme 3: How patients perceive themselves and their world		
	Not accepting the need for treatment	Intentions
	Denial of illness or diagnosis/lack of insight into the illness	
	Denying illness severity	
	Wanting to use different treatment	
	Not wanting to take medications/chemicals (New)	
	Wanting to get a little bit manic	
Fear of getting unwell, relapse or hospitalisation (New)	Fed up with taking medications	Emotion
Fear of being sectioned or enforced medication	Feeling bothered that mood was controlled by medication	
	Medication as an unwelcome reminder of the illness (New)	
Not Feeling stigmatised (I'm not ashamed)	Feeling stigmatised and wanting to conceal illness/ medication	Social Influences
	Cultural opposition	
	Reading (online, books) about negative things about medications (New)	
	Strong dysfunctional belief that nobody wants to take medication as a barrier (New)	
Medication being the top of the priority	Medication not being a priority	Goals
Having a goal to be stable in mood (New)		
	Seeing oneself as not wanting to be controlled by medications (New)	Social/professional role and identity
Identifies as someone who takes medication religiously (New)	*Patient seeing their role in self-adjusting the dose as the medication is not working as expected*	
Medications taking embedded in routine (just like brushing your teeth or putting on clothes) (New)	*Finding it hard to bring oneself to take medications (New)*	
	Identify as strong person but taking medications is seen a weakness (New)	
Having a good understanding of bipolar disorder	*Not knowing about bipolar disorder*	Knowledge
Theme 4: Working collaboratively		
Facilitators	Barriers	TDF Domains
Being involved in the decision about treatment choices and options	Not being involved in the decision about treatment choices and options	Social/professional role and identity
Patient inherently trusting professionals (New)	Prescriber not listening / lacks empathy	

(*continued on next page*)

Table 2 (*continued*)

Facilitators (*n* = 33 total, 26 prioritised)	Barriers (*n* = 52 total, 37 prioritised)	TDF Domains (*n* = 9)
Good relationship with prescriber	Poor relationship with the prescriber	Social Influences
Personal support from the healthcare service provider	Lack of personal support from HCPs	
Support from family and friends to take medication	Opposition from family or friends or other HCPs	
	Lack of real choice provided by prescriber other than medications (New)	
Positive and optimistic communication from HCPs.	*Poor communication (lack of info, unclear info, not asking for the patient about treatment, lack of communication between different HCPs) from HCPs*	

(Note: New = New determinant identified in this study, Black text = prioritised, Italicised text = Not prioritised, HCP = Healthcare Professionals)
(Total determinants identified = 85 [33 facilitators and 52 barriers as shown below], Determinants Prioritised = 63 [26 facilitators and 37 barriers])

both cases, patients felt their medication was helping their mental health but adherence was based on *their own harm-benefit evaluation*, a new determinant.

Side effects were described to have a greater negative impact on medication adherence by patients compared to family and friends.

In the absence of side effects experienced, *fear and worry about potential side effects* was a reported barrier to adherence.

“The only fly in the ointment is knowing about the side effects….it takes away all your courage to take the medication.” 66-year-old female patient.

Moreover, *emotions such as worry of medication changing personality (fear of not being ‘myself’)* is mentioned by most patients as an important barrier to adherence.

Most participants expressed an *overarching positive or negative attitude toward their medication* which in turn affected their adherence. Participants who believed that *medication is or will be helpful in keeping them well* took their medication regularly. Whilst others who viewed *medications as unnatural, unhealthy or harmful* often stopped or skipped their medication.

Lack of knowledge about the risk of stopping medication led some patients to stop their medication.

“There isn’t enough said about the risk of stopping……when I stopped it before…I wasn’t fully warned of the consequences…. I feel very strongly that I would not have stopped my mood stabiliser if I had been alerted to the risks.” 66-year-old female patient.

We also discovered that the effect of *number of medications and medication formulation* on adherence was more nuanced than previously thought. Most participants mentioned that patient’s acceptance and preference of *number of medications or formulation* is more important than the absolute number of medications or formulation. For example, many patients preferred oral medication, yet others preferred monthly injections as it relieves them from the burden of daily medication. Many patients also suggested a new determinant that *free or subsidised medication* through the UK National Health Service helped them take their medication without any financial worries.

3.2.2. II. The practicalities

Participants described how life practicalities affected their adherence. The most frequently described adherence determinant under this theme was *forgetfulness.* Practicalities such as *medication dose being in the middle of the day* or *changes in routine such as holidays or unusual work shifts* exacerbated *forgetfulness*.

The underlying reason for the forgetfulness differed individually; for some, it was driven by the conflicting demand; for others, it was due to cognitive impairment such as impaired memory or attention; and some forgot because taking medication was not a priority.

“…. I am awful in the morning um… I get up and feed my cats. I do everything else, but my meds get forgotten.” 26-year-old female patient.

While many patients mentioned *difficulty remembering to take medications* as a barrier to adherence, some had a *system to make it easier to remember*, e.g., *placing medication on the bedside table.* Many participants reported *a pill organiser* as being very helpful for taking medication. This new determinant, *provision of pill organiser* provided a routine (and ability to check if a dose had been taken) for some and for others, reduced the burden of sorting medications, such as popping out pills.

Patients’ families and friends played a significant role in supporting medication adherence by addressing *forgetfulness.* A mother, who lived 30 miles away, explained how she ordered her daughter’s medication, sorted them out in a pill organiser and reminded her to take medication regularly. Family and friends perceived their role in supporting medication adherence as more important than patients perceived the role of their family and friends.

Many participants described (and most agreed) some new practical facilitators such as *provision of online ordering of medication and delivery service.* Another new barrier many participants highlighted was *the difficulty in accessing quick advice about medication.*

“I’ve done that all the time, self-adjust ……. trouble is you have to wait three weeks to see your doctor so um I thought that’s ages …….. because three weeks you can be in a totally different, so I did adjust [medication dose] mine.” 56-year-old female patient.

3.2.3. III. How patients perceive themselves, their illness and their treatments

Patients’ perception of themselves, BD and its treatment influenced medication adherence.

Patients who did not accept a bipolar diagnosis, who lacked insight into the illness, who denied the need for medication, and patients who felt bothered that their mood was being controlled by medication were more likely to be non-adherent. Similarly, many patients who *were fed up taking medication* often stopped or skipped their medication.

“My son did not want to take medication because he says that he wasn’t ill, there’s nothing wrong with him, doctors got it wrong he said.” Mother of a son with BD.

Some patients intentionally stopped medication because they *do not want to take chemicals.* All patients who *preferred non-medicinal treatment* were often non-adherent.

“I wanted a natural answer really. So, I took things like starflower oil and different things……so I did take natural supplements and different things.” 56 years old female patient.

Some patients described how they *feel ashamed or embarrassed* (e.g., collecting medication), while others expressed that they don’t feel any *stigma. Patients who felt stigmatised and wanted to conceal their illness/medication* had poor adherence.

Some patients described how strongly they were influenced by what they *hear or read online* e.g., *reading negative stories about medication* leading to stopping their medication. Some patients did not take their medication because *they saw themselves as someone who does not want to be controlled by medication.* Family and friends with similar views discouraged patients from taking their medication.

Fear of getting unwell, relapse or hospitalisation or being sectioned if they don’t take their medication, was noted by all patients who reported good adherence. This view was strongly supported by patients’ family and friends too.

“I’m too scared to not take my medication and end up hospitalised again…I just take it because I’m just fearful that if I don’t take it what will happen.” 24 years old female patient.

Most patients who *set medication taking as a priority* had good medication adherence and vice versa.

3.2.4. IV. Working collaboratively

Patients, their family and friends and healthcare professionals working together facilitated medication adherence and vice versa. Working collaboratively was primarily described in terms of *patients' involvement in their treatment decisions, availability of personal support, the relationship between patients and healthcare professionals.*

Whether patients are being offered treatment choices and whether treatment decisions were made in partnership with patients influenced medication adherence. Participants differed on how much involvement they wanted but feeling that medication being imposed upon them was a clear barrier.

"…in my experience, you don't get a lot of involvement in how you're treated … you're not really treated as a person with an opinion or any rights…it does make you feel like it's something that's been imposed upon." 54-year-old male patient.

"When he was in the hospital, they decided and said he needs to go on antipsychotic injection. He was just absolutely horrified, he said, 'I never consented to this' and the way at that meeting, they almost had a smirk about it saying, 'you don't consent to this'." Mother of a son with BD.

This patient took the matter to the mental health tribunal and won, so he did not go on the antipsychotic injection.

Some patients complained that there was *a lack of real choice apart from medication* to manage their BD. They suggested that healthcare professionals need to work with patients and offer broader treatment options based on their preferences.

Personal support was described as *psychological support, such as providing assurances about medication and practical support, such as sorting out medication. Personal support* facilitated medication adherence and vice versa.

Lack of personal support from healthcare professionals, making patients feel like the "system doesn't give a toss", discouraged patients from taking their medications.

Participants explained how the *relationship between patients and healthcare professionals* was very important for medication adherence. Making patients feel listened to, understood and treating them like an equal partner in the treatment is critical for a good relationship which facilitated adherence and vice versa.

A 66-year-old lady described how her homeopath's view contradicted with mental healthcare professionals and often discouraged medications which led her to stop her medication. Some patients wanted to reduce the dose, but healthcare professionals were not interested in their views. This led some patients to self-adjust the dose.

3.3. Phase III: Prioritisation of modifiable adherence determinants

We prioritised 63 adherence determinants: 50 from our previous systematic review (Prajapati et al., 2021) and 13 new ones identified in this study. These determinants were mapped to nine TDF domains: 'Environmental Context and Resources', 'Intentions', 'Emotion', 'Social Influences', 'Goals', 'Memory, Attention and Decision Processes', 'Beliefs about Consequences', 'Knowledge', and 'Social/Professional Role and Identity'. The full list of these prioritised determinants is presented in Table 2. Ten determinants identified in our systematic review (Prajapati et al., 2021) were not prioritised, such as, laziness/carelessness, wanting to get manic, understanding of BD. Some of the new prioritised determinants were facilitators of previously reported barriers. For example, cost of medication was previously reported barrier to adherence whereas ways to minimise the cost (e.g., using pre-payment certificate) was identified as new facilitator of adherence. Other new prioritised determinants include patient making decision based on their own risk benefit analysis, provision of online ordering and delivery of prescription and medications, reading negative things about medications, fear of getting unwell and so on.

There were few gender differences in reported adherence determinants. Notably, female participants emphasized certain barriers more frequently than males: a perceived lack of healthcare support, concerns about not being heard, greater disruption of daily life due to medication side effects (e.g., sedation impacting work), and a stronger preference for non-medicinal treatments like natural supplements or lifestyle changes. This may be due to a low number of male participants. However, these differences did not diminish the overall overlap in adherence determinants across genders. Most adherence determinants described by the patients, their families, and friends overlapped; discrepancies are highlighted in the relevant themes.

Table 2 presents result of all 3 phases of analysis including the details of all determinants both new (labelled as "New") and literature reported, and both prioritised and not prioritised.

4. Discussion

Through mapping prioritised determinants to the TDF, this study provides a framework of 63 prioritised modifiable adherence determinants covering nine TDF domains. The framework includes modifiable determinants of medication adherence not previously reported for BD, including those associated with TDF domains 'Emotion' (e.g., Fear of getting unwell, relapse or hospitalisation), 'Intentions' (e.g., not wanting to take chemicals), and 'Social influences' (e.g. reading negative things about mental health medication). The study also provides deeper understanding of previously reported determinants such as side effects (actual or anticipatory), number of medication and formulation. Moreover, the study identifies novel antecedents of forgetfulness, a significant barrier to medication adherence. The framework may be linked via the TDF mechanisms of action to relevant BCTs. This guides clinicians to deliver theory and evidence-based strategies to address non-adherence.

This study adopted a novel approach by investigating not only barriers but also facilitators of medication adherence through a behavioural science lens. This enabled the identification of several new determinants and a deeper understanding of previously reported determinants.

4.1. Complex interplay between medication characteristics, patient perceptions and medication adherence

Our study sheds light on inconsistencies in the literature regarding how medication characteristics, such as side effects, efficacy, and pill burden, affect adherence. While some studies find these factors significantly affect adherence, other report little or no effect (Arvilommi et al., 2014; Baldessarini et al., 2008; De las Cuevas et al., 2014; Lingam and Scott, 2002). Our findings highlight the complex relationship between medication characteristics and patients' perceived medication value for their overall wellbeing, as reflected in two TDF domains: 'Environmental context and resources' (e.g., medication type or regimen) and 'Memory, attention, and decision processes' (e.g., patient decision process), being the key drivers of adherence. Mapping these determinants helps establish whether adherence barriers are best addressed by modifying external factors, such as changing medications, or internal factors, like managing unrealistic expectations. Furthermore, if the patient's concern is about outcomes from taking their medication (TDF Domain 'Beliefs about consequences') then BCTs such as 'Pharmacological Support' or 'Pros and Cons' may be more effective (The UCL Centre for Behaviour Change, 2024).

Similarly, although *the experience of side effects is* a commonly reported barrier (Chakrabarti, 2017; Johnson et al., 2007; MacDonald, 2017; Prajapati et al., 2021; Velligan et al., 2009) we observed that the severity of side effects and their impact on individual patients, rather than the mere presence of side effects, influenced treatment adherence. Understanding patients' experience of side effects and their impact on them will equip clinicians to provide better adherence support.

4.2. The role of knowledge and medicines information on adherence

Provision of knowledge is a frequently cited component of adherence interventions (Taibanguay et al., 2019). However, in our study, while knowing *how* medication works was not a significant barrier, a lack of knowledge about the consequences of stopping BD medication emerged as a key determinant. Given that excessive information can compromise recall (Kessels, 2003; Sarafis et al., 2013), prescribers should prioritise ensuring patients understand the harms associated with discontinuing treatment without medical advice.

Our findings also underscore the importance of timely access to medication information on an "as-needed" basis, reflecting patients' desire for greater involvement in decisions about their treatment. Current adherence interventions often focus on routine education (National Institute for Health and Care Excellence, 2009; Velligan et al., 2009), but there is a clear distinction between general education and the tailored advice patients seek. Universal provision of patient medication helplines, currently available in less than half of UK mental health trusts (Williams et al., 2018), could address this gap.

4.3. Forgetfulness as a barrier: Understanding its antecedents

Forgetfulness is a widely reported adherence barrier (Chauhan et al., 2021; Prajapati et al., 2021; Velligan et al., 2009), but our study reveals differences in its underlying causes. For some, forgetfulness stems from conflicting demands or cognitive impairments, while for others, it reflects a lack of prioritisation. These distinctions are critical for selecting appropriate BCTs. For instance, conscious decisions not to take medication, linked to motivational factors within the TDF domains of 'Beliefs about consequences' and 'Goals,' can be addressed by BCTs such as "Pros and Cons", "Action Planning". On the other hand, environmental barriers may be addressed by targeting the 'Environmental context and resources' domain, for example, recommending keeping medicine near bedside table. The conflicting evidence of effectiveness of reminders to improve adherence (Choudhry et al., 2017; Santo et al., 2019) may be explained by the failure to recognize these nuanced antecedents of forgetfulness in previous studies. The mainstay of current practice to support adherence, such as reminders and education (Care Quality Commission (CQC), 2018; National Institute for Health and Care Excellence, 2009), do not adequately target these diverse antecedents of forgetfulness.

4.4. Social and emotional influences on adherence

Despite global efforts to destigmatise mental illness (National Alliance on Mental Illness, 2024; World Health Organisation, 2024), stigma remains a barrier to adherence. Negative emotions such as anxiety about having a diagnosed physical health condition have been reported when taking antihypertensives (Easthall et al., 2019). In contrast, in the context of bipolar disorder, we have mapped this determinant to social influence, as it is primarily driven by the stigma of a BD diagnosis. To address this deeply ingrained stigma, healthcare professionals should support patients in reframing their perceptions of mental illness and medication using BCTs such as 'Framing/reframing', 'Social Comparison' and 'Comparative imagining of future outcomes' (The UCL Centre for Behaviour Change, 2024).

Fear is often portrayed in the literature as one of the barriers to adherence, such as fear of the negative effects of medication (García et al., 2016; MacDonald, 2017; Velligan et al., 2009). However, our study shows that fear had a dual effect, it could also act as a facilitator – such as when patient feared relapse or hospitalisation due to non-adherence. Reminders of past negative experiences using BCTs like 'Anticipated regret' or 'Imaginary Punishment' may improve adherence in these situations (The UCL Centre for Behaviour Change, 2024).

4.5. Patient-centred approaches to enhance adherence

Patients who believe that all chemicals are toxic or who do not want to take medication often show apathy toward their medications. These patients may benefit from BCTs such as 'Credible sources' or 'Social comparison' (The UCL Centre for Behaviour Change, 2024) and then negotiating a mutually agreeable and clinically appropriate action plan.

Shared decision making and treatment choices are known to affect adherence (Younas et al., 2016). However, since involvement in decision making and treatment options is a personal choice, healthcare professionals should tailor information to meet individual needs and preferences. Our study shows that patients should not feel medications are being imposed upon them, as this is a clear barrier to adherence.

4.6. The underrated role of family and friends

While the impact of effective collaboration between healthcare professionals and patients on medication adherence is well-documented (García et al., 2016; MacDonald, 2017; Velligan et al., 2009; Younas et al., 2016); the role of family and friends is underappreciated in the literature. Our findings highlight the significant influence of patients' family and friends in managing medication adherence in mental health patients. Thus, clinicians should systematically explore and utilize this influence to enhance adherence.

4.7. Reflexivity

Acknowledging researcher's influence in qualitative research, facilitators (AP, SS, and DB) were mindful of their impact on participant responses during focus groups and interviews, striving to create an open and non-judgmental environment and regularly debriefed to address any biases or preconceptions. Additionally, during data analysis, multiple reviewers (AP, AD, DB, and SS) independently mapped adherence determinants to TDF domains and resolved discrepancies through discussion. This reflexive approach enhanced the reliability and validity of findings.

4.8. Strengths and limitations

One of the key strengths of this study is the use of a framework of behaviour change, the TDF, to explore not only barriers but also facilitators of adherence. This enabled the identification of previously unreported modifiable adherence determinants. Secondly, the focus on modifiable determinants provides patients and healthcare professionals with determinants to consider when working together to improve adherence. Thirdly, the refinement and prioritisation of the modifiable determinants provided a better understanding of those determinants and those needing more attention. Finally, this study addresses a significant gap in the literature by incorporating patients' family and friends' views on medication adherence determinants.

COVID-19 restrictions may have excluded individuals without access to or comfort with online platforms for focus groups. However, offering optional one-on-one phone interviews likely mitigated this risk.

Participants, mainly white British or European women, do not fully represent the broader UK bipolar patient (Smith et al., 2013). The lack of ethnic diversity and relatively small number of male participants are limitations in this study. Nonetheless, we believe that the findings remain transferable due to the relevance of core themes, alignment with existing literature but with additional insights and new determinants, and the structured application of the TDF. For instance, while stigma, denial of illness and medication may be more prominent in ethnic minority groups (Bansal et al., 2022; Eylem et al., 2020), these determinants were still identified in this study too. Similarly, although the limited number of male participants may underrepresent their perspectives, the determinants themselves did not differ substantively, only in the magnitude.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jad.2025.04.149.

CRediT authorship contribution statement

Asta Ratna Prajapati: Writing – review & editing, Writing – original draft, Visualization, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Sion Scott:** Writing – review & editing, Validation, Investigation, Formal analysis, Data curation. **Alexandra L. Dima:** Writing – review & editing, Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization. **Allan Clark:** Writing – review & editing, Supervision. **Jo Taylor:** Writing – review & editing, Validation, Supervision, Methodology, Formal analysis, Data curation. **Jonathan Wilson:** Writing – review & editing, Supervision. **Debi Bhattacharya:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Formal analysis, Data curation, Conceptualization.

Consent for publication

All authors have reviewed and consented for publication.

Funding and disclaimer

Asta Ratna Prajapati is funded by Health Education England (HEE)/National Institute for Health Research (NIHR) (Clinical Doctoral Research Fellowship) (NIHR reference number: ICA-CDRF-2017-03-054) for this research project. This paper presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author(s) and not necessarily those of the NHS, the HEE/NIHR, or the Department of Health and Social Care.

AD has been funded by the Agence Nationale de la Recherche, Grant/Award Number: ANR-16-IDEX-0005 and Instituto de Salud Carlos III, Grant/Award Number: CP21/00062 unrelated to this research.

Declaration of competing interest

No other conflicts of interest related to this study have been declared by the authors.

Acknowledgements

We would like to thank members of the Collaborative Medication Adherence in Bipolar disorder (C-MAB) Research Advisory Board members for their support. We are also grateful to colleagues from NSFT and UEA libraries for help with the literature search and sourcing articles.

Data availability

Most data and materials are provided as supplementary file.

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