Trials

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Designing e-consent protocols for pragmatic clinical trials: case studies from a UKCRC clinical trials unit

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Abstract

Background Interest in and use of electronic consent (e-consent) in the conduct of academic clinical trials has increased since the COVID-19 pandemic. E-consent offers advantages including increased efficiency and accessibility, and reduced burden on site staff, which can be appealing to academic trialists anticipating challenges in recruitment to complex trial designs or with limited funding. However, there are many options to consider when using e-consent in a study protocol. This paper presents five case studies from Norwich Clinical Trials Unit, demonstrating how e-consent models can be effectively tailored to the needs of different trials. These examples illustrate the options around and benefits of e-consent, the acceptability of e-consent by participants, and the design considerations that were made during the development of the trial protocols.

Case studies Five randomised trials are presented, selected from a range of different trial designs, disease areas, interventions, and patient populations. E-consent was either offered as an alternative to paper consent, according to participant preference, or as the sole method of consent. E-consent was generally used to facilitate remote consent in decentralised trials but was also chosen to increase efficiency and reduce burden in an emergency department setting. The technical implementation of e-consent and detailed participant procedures were tailored to the needs of the trial settings and patient populations. For example, accompanying participant information sheets were provided in paper or electronic form, and electronic signatures could be typed or drawn. Administrative data on uptake of e-consent is presented where available.

Conclusion This paper demonstrates that the operational and technical aspects of implementing e-consent in clinical trials can be influenced by the trial design, the needs and characteristics of the trial population, financial/efficiency considerations, and level of risk. E-consent is not a one-size-fits-all tool for trials, and its use should be carefully considered during the development of the trial protocol, in conjunction with patient and public involvement contributors, site staff and other trial stakeholders.

Keywords Informed consent, E-consent, Decentralised clinical trials, Clinical trials

Background

In September 2018, the Health Research Authority (HRA) and Medicines and Healthcare products Regulatory Agency (MHRA) jointly published a statement outlining the legal and ethical requirements for seeking and documenting e-consent in research conducted within the UK [1]. This statement defined electronic

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consent (e-consent) as 'the use of any electronic media (such as text, graphics, audio, video, podcasts or websites) to convey information related to the study and to seek and/or document informed consent via an electronic device such as a smartphone, tablet or computer' [1].

The statement clarified that electronic methods can be used for seeking, confirming, and documenting informed consent in research studies; discussed appropriate use of the different types of electronic signatures (simple, advanced, and qualified); explored how e-consent can enhance participants' understanding of research by providing information through digital multimedia, improving recruitment processes, and reducing dropout rates; and put in place expectation regarding the use of e-consent in clinical trials [1].

E-consent is increasingly being adopted by academic clinical trials units (CTUs) in the conduct of randomised controlled trials. The move from traditional paper methods towards electronic methods of obtaining informed consent was accelerated during the COVID-19 pandemic, with the necessity for many trials to recruit remotely.

The benefits of e-consent were, however, evident prior to the pandemic. The use of e-consent can reduce burden on both participants and researchers, streamline remote recruitment, expand accessibility to research opportunities, and simplify centralised monitoring of consent procedures.

It is important to distinguish between e-consent and remote consent. Whilst e-consent involves the obtaining of consent via electronic methods, remote consent can be obtained electronically, on paper, or verbally, and is characterised by obtaining consent away from the research site, often in the participant's home. The ability to use electronic methods of consent has significantly enhanced the efficiency of remote consent processes.

Likewise it is important to delineate between methods that both deliver study information and seek consent electronically from participants and those that simply obtain consent using electronic methods. To maximise the benefits of e-consent, it is essential to recognise that a significant portion of its advantages lies in the effective dissemination of study information to potential participants electronically and that the e-consent process extends beyond merely documenting consent electronically.

Since the COVID-19 pandemic, there has been a growing awareness and adoption of remote or 'decentralised' clinical trial methods in the UK. This shift has been spearheaded by the commercial sector but is increasingly embraced by the non-commercial and academic sectors. The primary aim of these adaptations is to reduce burden on both patients and health and social care services.

However, academic trials often involve complex trial designs. These can include multi-stage consent processes, alternative randomisation models, dyad or triad recruitment, and the need to tailor consent procedures to specific patient groups or populations. This adds complexity and requires greater consideration when deciding whether to adopt e-consent and how.

A recent study undertaken by the UK e-consent collaborative group investigated the current practice, challenges, and evidence gaps related to the use of electronic consent (e-consent) in UK academic-led clinical trials. The study conducted a survey of UKCRC CTUs to gain insights into the implementation and perspectives on e-consent and explored the experiences of trial teams regarding the use of e-consent. Of the 34 CTUs responding to the survey, 21 CTUs (62%) had implemented e-consent in at least one of their trials including CTIMPs and non-CTIMPs demonstrating the increase in adoption of e-consent in academic UK CTUs. However, the paper concluded that there was insufficient guidance on the implementation of e-consent and its application across various study designs [2].

Published trial protocols often provide little insight into the details of trial-specific e-consent implementation due to word limits. The aim of this paper is to present useful examples, and results where known, to inform the development of future trial protocols, and to propose key aspects of e-consent requiring further methodological research.

The following case studies, summarised in Table 1, highlight examples of ongoing or recently completed trials utilising e-consent at Norwich Clinical Trials Unit (NCTU), a UKCRC-accredited unit based in the East of England with extensive experience in implementing e-consent [3]. These case studies were selected to demonstrate how different e-consent models can be employed effectively for diverse trial designs, bringing efficiencies, and enhancing the overall trial experience for both researchers and participants. All studies included below were funded by the National Institute for Health and Care Research (NIHR). The consent models utilised by each of the case studies were approved by NHS Ethics committees.

Case study 1: TIPAL—The effectiveness and risks of Treating people with Idiopathic Pulmonary fibrosis with the Addition of Lansoprazole: a randomised placebo-controlled multi-centre clinical trial

Recruitment period: 16/06/2021–ongoing.

Trial registration: ISRCTN13526307.

Ethical approval granted by East of England—Cambridgeshire and Hertfordshire Research Ethics

Table 1 Case studies

Acronym	Full title	Trial design	Type of e-consent	Intervention/control	Overview of main trial population	Published trial protocol
TIPAL	The effectiveness and risks of Treating people with Idiopathic Pulmonary fibrosis with the Addition of Lansoprazole	Placebo-controlled multicentre RCT; CTIMP	Remote e-consent with the option to use traditional paper methods at participants preference	Lansoprazole/placebo	People aged ≥ 40 years with a diagnosis of idiopathic pulmonary fibrosis (IPF)	In preparation
TYPPEX WP4	Addressing common mental disorder and psychotic experiences: a stepped wedge cluster randomised trial with nested economic and process evaluation of a training package for CBT therapists in Improving Access to Psychological Therapies (IAPT) services	Stepped wedge cluster RCT of a therapist training and supervision package, with nested economic and process evaluation	Remote e-consent or paper (postal) consent by participant preference	Enhanced training for cognitive behavioural therapists/usual care	Adults in England accepted onto IAPT (now NHS Talking Therapies) caseload for CBT therapy, with presence of psychotic symptoms (according to a Community Assessment of Psychic Experiences (CAPE-P15) questionnaire)	[4]
Quit Sense	Feasibility randomised controlled trial of a smoking cessation smartphone app that delivers 'context aware' behavioural support in real time	Two-arm feasibility randomised controlled trial delivered entirely online	Remote e-consent	Access to a smoking cessation app/usual care	People aged ≥ 16 years who are current smokers (at least 7 cigarettes per week); willing to make a quit attempt in the next 14 days; has primary use of an android smartphone; resident in England	[5]
COSTED	Cessation Of Smoking Trial in the Emergency Department	Two-arm randomised controlled trial of a brief smoking cessation intervention set in the emergency department	E-consent by participant at site with the option for paper consent if preferred	E-cigarettes/usual care	Adult daily tobacco smokers attending ED for medical treatment (or accompanying someone attending for medical treatment)	[6]
BabyBreathe	A randomised controlled trial of a complex intervention to prevent return to smoking postpartum	Two-arm randomised controlled trial with internal pilot including economic evaluation and process evaluation	Consent to contact followed by remote e-consent	E-cigarettes/usual care	Women who have stopped smoking in pregnancy	[7]

Committee on 29 April 2020 (REC reference 20/EE/0043).

Trial design

TIPAL is a phase III double blind, parallel group, 1:1 randomised, placebo controlled, multi-centre, clinical superiority trial of oral lansoprazole versus placebo in 298 participants with idiopathic pulmonary fibrosis in the UK. The primary outcome measure for the trial is the absolute change in percent predicted domiciliary forced vital capacity (FVC) measured between baseline and 12 months post-randomisation of lansoprazole versus placebo. FVC is measured on a weekly basis during the participants time on the trial by domiciliary spirometry.

E-consent procedure

At a pre-consent consultation (by phone, video, or face to face in clinic), the site staff discuss the trial with the patient. If the patient expresses an interest in participating, they can choose at this point whether to use e-consent or be provided with paper copies of the participant information sheet (PIS) and informed consent form (ICF).

If using e-consent, the participant is emailed a PIS and e-consent link and asked to attend a pre-arranged video call. During this call, which may occur at the participant's home, the trial is discussed with the participant, and they are able to consent through a link to the trial's REDCap database in the original email. Randomisation and data collection is performed by the same REDCap database.

Ongoing consent is established during each follow-up appointment. Any participant wishing to withdraw can record this via the database.

If a participant chooses at the pre-consent consultation to consent using the traditional paper method, a copy of the PIS and ICF are sent in the post or provided in clinic. Once completed, the paper ICF is returned to the site who then upload it on to the same REDCap database.

Design considerations

The trial protocol was developed prior to 2020, receiving all approvals during the first wave of COVID-19 in the UK. Whilst much of the trial was then extensively redesigned to facilitate decentralised elements, the intention to use e-consent pre-dated the pandemic.

Although the trial was largely designed as a decentralised clinical trial (DCT), the trial team permitted the use of paper ICFs if necessary, as an alternative to e-consent. This hybrid system was designed with the aim of having the most flexibility for participants and sites, and to address concerns with regard to digital exclusion. EMETIPAC, a precursor to the TIPAL study, which was undertaken in a similar population, reported a mean (SD) patient age of 71.3 (7.5) years. It was felt however that the preferred use of electronic methods for consent and follow-up in TIPAL would not necessarily be an issue in the trial population and previous studies examining the feasibility of using electronic consent for older populations have indicated that this is not necessarily a barrier [8].

Results

At the time of writing, 254 patients have consented to take part in the trial. Of these, 171 have been randomised. Of the 254 consented participants, 80 consenting electronically (31%) and 174 gave consent on paper (69%).

The participants to date have been recruited from 42 NHS sites. To date, only 11 of these sites (26%) have used a combination of both e-consent and paper consent when recruiting participants on to the trial with 31 sites (74%) solely using one of the two available methods.

In the 11 sites which have to date used a combination of both e-consent and paper consent to recruit, 50 participants consented electronically (39%) and 77 consented using paper methods (61%).

In the 31 sites that exclusively used one method of consent, the most common method was paper with 30 participants being consented electronically (23%), compared to 98 participants consenting on paper (77%).

The mean age at consent is currently 72 years, with no difference in mean age between the participants consenting electronically vs on paper. So far, the trial has demonstrated that e-consent can be effectively used alongside paper consent when recruiting participants in higher age brackets.

Case study 2: TYPPEX WP4—Addressing common mental disorder and psychotic experiences: a stepped wedge cluster randomised trial with nested economic and process evaluation of a training package for CBT therapists in Improving Access to Psychological Therapies (IAPT) services

Recruitment period: 11/3/2021–30/04/2024.

Trial registration: ISRCTN93895792.

Ethical approval granted by South Central—Berkshire Research Ethics Committee on 28 April 2020 (REC reference 20/SC/0135).

Trial design

TYPPEX WP4 is a multisite, stepped-wedge cluster randomised controlled trial in NHS Talking Therapies (NHS TT) services in England [4]. The trial will evaluate the clinical and cost-effectiveness of an enhanced training for cognitive behavioural therapists that aims to address the unmet needs of patients experiencing distressing

psychotic experiences (PE) in addition to common mental disorder (CMD).

Participants are (1) 56–80 qualified cognitive behavioural therapists and (2) ~ 600 service users who are assessed as appropriate for cognitive behavioural therapy in an NHS TT service and have PEs according to the Community Assessment of Psychic Experiences—Positive 15-item Scale (CAPE-P15).

Pseudonymous clinical outcome data from NHS TT clinical records are collected for all eligible patients. A consented sub-group of patients are invited to complete health economic measures at baseline, 3-, 6-, 9-, and 12-month follow-up. The primary outcome is the proportion of patients with common mental disorder and psychotic experiences who have recovered by the end of treatment as measured by the standard NHS TT measure for recovery.

E-consent procedure

NHS TT patients with PE according to the CAPE-P15 screening questionnaire are asked by their therapist to provide consent to be contacted about participating in the health economic data collection. The online referral form creates a new record in the REDCap database, and its completion triggers an automatic email to the patient with a unique link to their participant information sheet and electronic consent form. If they submit a complete consent form, online baseline health economics questionnaires are presented on subsequent pages.

An automated reminder email is sent 3 days after the initial link is released. Following this, the research team may make up to three attempts to contact service users by telephone if they have not completed full consent after 1 week.

The 9-point consent form features yes/no buttons and automated scoring to validate complete consent. Participants sign the form by typing their full name. The date of consent was auto populated. Participants are automatically sent a pdf copy of their PIS and completed consent form by email.

Design considerations

The eligible patient population for this study has a broad adult age range with a median age of 35 (as of 04/10/2023). At the time of consent, patients are at the early stages of psychological therapy treatment for depression and/or anxiety in an NHS TT service and have reported psychotic experiences (of moderate to severe frequency or distress) which may include increased suspiciousness, unusual thought content, and visual or auditory hallucinations. It was anticipated that these symptoms could lead to recruitment challenges.

The use of remote e-consent administered by the central research team was chosen to increase trial efficiency and avoid the costs and time delays associated with paper consent. However, it was also part of a deliberate design choice to clearly delineate research and clinical treatment, allaying any patient concerns about the effect of disclosing research data on their access to treatment, and to preserve the therapeutic alliance.

The consent process is designed to be as flexible as possible and allow participants choice in how they interact with researchers. Remote e-consent allows patients to complete consent at home and in their own time, and they do not have to speak to a researcher if they prefer not to. Patients may also switch between email and postal contact at any time, and researchers are available for support by telephone or text message.

TYPPEX WP4 is a low-risk non-CTIMP study, and patients are referred by their treating therapist during a clinical contact, so separate verification of ID during consent is not required.

Results

In the period 11/3/2021–11/12/2023, 508 patients have agreed to be contacted by the research team, and 310 have consented. 87% of those agreeing to be contacted by the research team chose the email option (and therefore e-consent instead of paper), and 63% of those consented to take part in the study. By comparison, only 48% of patients who chose to be contacted by post went on to give full paper consent.

Case study 3: COSTED—Cessation of Smoking Trial in the Emergency Department

Recruitment period: 4th January 2022–7th August 2022.

Trial registration: NCT04854616.

The study was approved by the UK National Research Ethics Committee—Oxford B (reference 21/SC/0288).

Trial design

COSTED is a multi-centre, parallel-group, randomised controlled superiority trial in NHS Emergency Departments (EDs) in England and Scotland [6]. The trial evaluated the clinical and cost-effectiveness of an intervention which included brief advice on quitting smoking, e-cigarette starter kit, and referral to stop smoking services that aimed to support those attending the ED quit smoking.

Participants are 1010 smokers that attended the ED as a patient or someone accompanying a patient; smoking status was validated with a carbon monoxide breath test.

Participants were invited to complete health and economic outcome measures at baseline and 6-month follow-up, and were additionally asked about 7-day smoking

abstinence at 1, 3 and 12 months. The primary outcome is biochemically validated abstinence at 6 months.

E-consent procedure

Smokers were recruited by the research team in the ED waiting room and were provided with a paper PIS. On reading the PIS, if the patient and/or the person accompanying them were interested in taking part, the research team member accessed the trial's REDCap database using a tablet device, created a new record, and completed an eligibility assessment. If eligible, the patient and/or accompanying person provided e-consent using the tablet, or via a link sent to their phone. In Scotland, a tablet was not accessible in the ED and so a computer was used.

The 11-point electronic consent form featured yes/no buttons and automated rules to ensure consent was complete prior to questionnaire completion and randomisation. Participants signed the form using their finger on the tablet to generate their signature after completing their full name. The date of consent was auto populated. Participants were automatically sent a pdf copy of their completed consent form by email or post.

Design considerations

The eligible patient population for this study were those attending the ED, where there is little space for researchers to screen and consent potential participants. This can cause recruitment challenges in research and so the trial team purposefully designed this study to use e-consent where possible, and provided sites with tablets set up specifically to only be accessed to use the COSTED REDCap database and the camera (to upload paper copies if required).

The use of e-consent administered by the research team where possible was chosen to increase trial efficiency and avoid the costs, time delays, and inconvenience associated with paper consent forms. It was specifically chosen to allow easy consent in a busy ED. The option to provide consent on paper ICF was available upon request, if preferred by the participant.

COSTED is a low-risk non-CTIMP study, and as participants were screened and recruited face-to-face in the ED (and treated at the same visit), verification of ID during consent or future visits was not required.

Results

Between January and August 2022, the COSTED trial assessed 1443 participants for eligibility in six EDs. Of these, 975 patients were subsequently consented and randomised plus 35 accompanying people. The population for this trial had a mean age of 40 years and mean deprivation decile of approximately 4 (1 = most deprived, 10 = least deprived) indicating that participants were from slightly more deprived neighbourhoods than average.

Prior to consent, during screening, researchers asked participants whether they would prefer to consent on paper or via e-consent. In total, 954 (98%) opted for e-consent and just 21 (2%) paper consent.

This study shows that e-consent was acceptable and accessible as a method for written informed consent in busy EDs if an electronic device is available for use. It helped that in this trial participants could be supported by the research team as e-consent was face to face and not undertaken remotely as in other trials.

Case study 4: Quit sense—Feasibility randomised controlled trial of a smoking cessation smartphone app that delivers 'context aware' behavioural support in real time

Recruitment period: 27/11/2020–18/01/2021.

Trial registration: ISRCTN12326962.

Ethical approval granted by HRA Wales REC 7 committee on 11th December 2019 (REC reference 19/WA/0361).

Trial design

Quit Sense is a feasibility randomised controlled trial among online smokers of a smoking cessation smartphone app that delivers 'context aware' behavioural support in real time [5, 9]. Quit Sense recruited 209 smokers to a two-arm feasibility RCT between 27/11/2020 and 18/01/2021. Participants self-referred by responding to adverts via a Google search and/or Facebook, with recruitment, e-consent, randomisation, and data entry completed entirely online.

E-consent procedure

Participants clicking on trial adverts (limited to England-based IP addresses) were directed to the trial specific website. If the participant confirmed they were a current smoker aged over 16 years, they could view online or download a participant information sheet. Once they confirmed they had read this, met some further eligibility criteria, and were willing to give consent, they were directed to give e-consent in the trial specific REDCap database. Consenting participants were emailed a copy of the PIS together with their signed consent form.

Design considerations

As this was a low-risk intervention with self-assessment of eligibility, a simple E-signature was used, and the form was not countersigned by the research team. The participant completed online baseline questionnaires before being randomised, receiving either the intervention (Quit Sense app and standard care) or standard care (link to

the NHS smokefree website) and thereafter receiving automated links to complete follow-up questionnaires online at 6 weeks and 6 months. The primary outcome was smoking cessation at 6 months, but being a feasibility trial all aspects of the trial process were reviewed including ease of recruitment and the enrolment process.

The trial was funded by the NIHR PHR (17/92/31) and received NHS Research Ethics Committee approval (19/WA/0361) but did not use NHS sites.

Results

A total of 1275 people landed on the webpage after clicking a link in the adverts. Of these, 323 undertook eligibility self-assessment and 267 provided informed consent ($n=26$ did not meet detailed eligibility criteria and $n=30$ declined to give consent).

210 participants were randomised ($n=57$ did not proceed after consent, $n=1$ withdrawn from trial outcomes due to their partner signing them up without their knowledge) and 160 participants completed follow-up at 6 months (76%).

The population for this trial had a mean age of 40 years (upper age of 61 years), 57% female, 91% described their ethnicity as white, and based on answers given to employment status, occupation type, and highest educational qualification, 71% were described as 'high socioeconomic status (SES)'. These characteristics may reflect the way participants were recruited and their access to technology, though the trial did actively seek to recruit a broad range of individuals and SES through targeted advertising. As no other consent options were offered, this may lead to some bias in who was recruited. The use of e-consent in this trial saved considerable resource and allowed recruitment to be completed quickly.

Case study 5: BabyBreathe trial—A randomised controlled trial of a complex intervention to prevent return to smoking postpartum

Recruitment period: 28/07/2021–01/09/2023.

Trial registration: ISRCTN70307341.

Ethical approval granted by North West—Preston Research Ethics Committee on 12 March 2021 (REC reference 21/NW/0017).

Trial design

BabyBreathe is a two-arm randomised controlled trial with internal pilot to compare the BabyBreathe™ intervention with usual care, to assess long-term smoking abstinence for those who have recently given birth and have stopped smoking during pregnancy or during the 12 months prior to pregnancy [7]. The primary effectiveness outcome is self-reported continuous postpartum smoking abstinence, biochemically validated by carbon monoxide (CO) monitors at 12 months postpartum. The CO cut-off is less that 8 ppm for those who are not pregnant or less than 4 ppm if they are pregnant at this timepoint. A target of 880 participants are randomised (1:1) to either the BabyBreathe intervention arm or standard care arm by the trial's REDCap database. The database captures initial 'consent to contact', full e-consent, baseline and follow-up measures.

E-consent procedure

Participants are identified via two main routes.

The first route, used since the start of the trial, is screening through NHS trusts taking part in the trial. NHS staff used clinics and patient records to create a list of potentially eligible participants to contact. They then introduced the trial over the phone, text, email, or face to face to gain consent to pass on their contact details (phone number and email) to the research team. The contact details were then entered onto the REDCap database.

The second route was added midway through the trial due to under-recruitment. This involved targeted online advertising where participants from across the UK were shown an advert for the trial and if interested could follow a link to confirm they meet the eligibility criteria and provide their contact details to the research team. A member of the BabyBreathe research team then entered their contact details onto the database.

Once a potential participant's contact details are entered into the database, a link was sent automatically (by email or text depending on stated preference) to the online PIS, e-consent form, and final eligibility questionnaire. Once full informed consent is provided, copies of the PIS and consent form were emailed to the participant. Each participant that self-reported as eligible was sent an individual use CO monitor to complete the final step of the eligibility check by providing a CO reading of below 4 ppm.

Design considerations

When designing the initial trial, a decentralised model of remote recruitment, intervention delivery, and follow-up was not considered, but the pandemic required the trial to adapt as services in the NHS changed. The team developed remote methods of gaining consent to contact and full consent, using posted individual use CO monitors to confirm eligibility and primary outcome data as well as delivering the intervention within health visiting services and across the wider population using digital elements and telehealth. This approach allowed the trial to begin recruitment with COVID-19 restrictions still in place.

Results

Twelve NHS trusts manually screened for potentially eligible patients across England (London, Norfolk, and the North East) and Scotland (Lothian). A total of 1953 patients consented to be contacted by the research team, of which 927 provided full informed electronic consent and 685 went on to be randomised.

Online advertising across Google, Facebook, and Twitter ran for 57 weeks covering England, Scotland, Wales, and Northern Ireland. The BabyBreathe advert was displayed 1,909,877 times converting to 31,917 'clicks' and 3471 form starts. A total of 2138 people completed the self-report eligibility check of which 1132 were eligible. 820 of these potential participants provided their contact details and were added to the REDCap consent to contact page so they could receive the link to the PIS and provide full consent. 333 remotely recruited participants provided full informed electronic consent and 202 went on to be randomised. By implementing online advertising and electronic consent for both contact and trial participation, the study observed a clear increase in recruitment rate. The modifications proved decisive in achieving the recruitment target within the timelines, a goal that would have been otherwise very challenging.

Overall, 2773 individuals provided their contact details, of which 1263 provided full informed electronic consent. The mean age of participants providing consent was 29 with a range of 16–47. Of those providing full consent, 911 provided a confirmatory CO reading and 887 were randomised.

Conclusion

This paper aims to provide practical examples of e-consent in studies conducted by a UKCRC CTU. Whilst we have included five trials, a limitation is the diversity of intervention type included. Three of the trials included as case studies (60%) are relatively low-risk smoking cessation trials. Only one of the examples (TIPAL) relates to a CTIMP. This said, the examples provided are still able to provide a range of methods and design considerations that will be of interest to adoptees of e-consent.

Unfortunately, no studies were available to include in this paper which require the consent of dyads (for example patient and caregiver). This is a common requirement in social care research and requires additional design considerations. Likewise, consent of participants with impaired capacity or consent/assent in studies involving children and young people requires additional considerations to ensure that the method employed is appropriate.

E-consent offers promising efficiency and accessibility benefits for pragmatic trials and is becoming an increasingly popular approach to obtaining informed consent. Offering e-consent only, with no paper option, risks disproportionately excluding those with limited digital literacy, access, or resources, leading to potential bias in the trial sample. When designing and implementing e-consent in a study, a consideration of population and setting and whether to include alternative methods for consent should be undertaken.

E-consent, when used remotely, can introduce issues around verification of patient identity and even cast doubt on the validity of informed consent. Therefore, a risk-based approach is crucial. Thoroughly assessing the target population, research setting, and intervention risk should inform the type of consent used and the level of burden placed on participants. This may involve offering hybrid paper-electronic options, deploying trained research assistants for in-person support, or tailoring e-consent platforms to accommodate varying levels of digital fluency.

Proper e-consent implementation further necessitates robust site training. Researchers must be equipped to navigate the nuances of electronic platforms, address digital literacy concerns, and ensure informed and autonomous decision-making for all participants. Ongoing monitoring and feedback loops remain essential to identify and address any emerging vulnerabilities or accessibility issues.

Looking ahead, research is crucial to establish the optimal e-consent models for diverse settings and populations. Future studies should investigate whether different e-consent formats impact on participant comprehension, understanding, and satisfaction.

It is unclear whether online engagement and consent in studies such as Quit Sense helped or perhaps was detrimental to follow-up rates. Further work is required to understand whether there is a relationship between the type of consent and attrition/withdrawal in studies.

A critical area of inquiry lies in assessing potential health and research inequalities associated with e-consent. Studies should explore if e-consent disproportionately excludes or disadvantages participants from lower socioeconomic backgrounds or minority groups who may lack reliable internet access or digital literacy skills, or conversely, improves engagement by allowing digital tools such as automated translation software. By addressing these complexities and refining e-consent practices, we can ensure that pragmatic trials leverage technological advancements without compromising ethical foundations or exacerbating existing health inequities.

Embracing e-consent for pragmatic trials holds promise, but only if paired with careful consideration of potential exclusion risks and a commitment to inclusive design, responsible implementation, and ongoing assessment of its impact on participant autonomy, understanding, and overall well-being. It is therefore essential that trialists

continue to share experience and learning regarding the implementation of e-consent within clinical trials to facilitate greater understanding. This could be supported by workshops and webinars, through dissemination of case studies and best practice at conferences (such the MRC-NIHR Trials Methodology Research Partnership supported International Clinical Trials Methodology conference) and through existing clinical trials communities and professional networks such as the UKCRC CTU Network.

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