Date: 11th Jan 2019

Southampton and Bristol CTU efficient and innovative NIHR project final report

Gareth Griffiths, Amanda Blatch-Jones, Geoff Frampton, Jeremy Hinks, Athene Lane, Jacqui Nuttall, Karen Pickett, Jonathan Shepherd, Louise Worswick, Jeremy Wyatt.

(Section 1-6 word count: 2202)

1) Title of Project (20 words)

User-focused research to identify the benefits of innovative digital recruitment and retention tools for more efficient conduct of randomised trials.

2) Abstract (168 words)

Phase 1 included a scoping of literature and a survey of funder staff to determine what digital tools are currently available and success criteria. A total of 23 online tools/applications were identified with over 25 UK trials having used digital recruitment and retention tools. Phase 2 included a survey of CTUs and qualitative interviews with researchers, funders, hospital researchers, ethics committee members and trial participant representatives. For 24 CTUs database screening tools were the most widely used with saving GP time and reaching more patients reported as success criteria. Fewer retention tools were used, with SMS / email reminders most reported. 16 semi-structured qualitative interviews revealed there is a proliferation in use of digital tools without robust evidence with 5 main themes being security and transparency, inclusivity and engagement, human interaction, obstacles and risks and potential benefits. A definition of what constitutes a tool and two logic models have been developed. Phase 3 developed a systematic map describing the available evidence for each tool and the evidence gaps.

3) Introduction (370 words)

Background to project

Recruitment of participants to, and their retention in, RCTs is a key determinant of research efficiency, but is challenging (Treweek 2013). As a result, trialists and CTUs are increasingly exploring the use of digital tools to identify, recruit and retain participants. Examples of these tools include:

- Eligibility: searches and interactive record tools to support clinicians screening participants (e.g. Koepcke et al. 2013)
- Recruitment: trial websites, social media and email campaigns to engage with the public
- Retention: Emails, websites, text messages or apps to retain patients in trials and help them meet drug, behavioural adherence or outcome assessment criteria

These tools should benefit research by reducing costs, avoiding waste and speeding delivery of results, improve recruitment reach and reduce recruitment of ineligible patients (around 6% in Koepcke's study 2013).

However, selecting appropriate digital tools is challenging because few have been evaluated rigorously. Also, different success metrics are used: for example, reduced screening time, improved coverage of recruitment or percentage of patients recruited. We need to understand which metrics are most relevant to stakeholders, to ensure wider uptake of effective tools.

We identified only one systematic review in this area, on databases to improve trial recruitment [Koepcke 2014]. The methods used were not rigorous by current standards, and it located only 9 studies using reasonably robust methods. It concluded that databases could reduce the time taken to screen participants, improve participant coverage and actual recruitment rates by between 14% and 6 times, though 4 of 5 studies used an uncontrolled before-after design and the fifth was confounded.

Our view, is that the evidence base for these tools needs to be assembled, mapped and critically appraised before synthesis, where appropriate. Only then can we confidently advise on the wider use of such tools by trialists, or on further primary research.

Research questions

1. What digital tools are available that could help identify, recruit or retain people in trials, and what are the costs of these tools?

2. What performance characteristics do trialists and CTUs require of digital tools for them to be judged useful?

3. For the most promising digital tools, what is the evidence about their performance, and which important evidence gaps need to be filled with primary research?

4) Methods (597 words)

Light touch literature search to identify digital tools for trial recruitment and retention and survey of NETSCC trial Monitoring team

A light touch literature search was conducted to inform the research team of examples of digital tools used. In addition, a survey was sent to NIHR NETSCC trial monitoring staff to understand how many NIHR-funded trials used digital tools, and which tools these were.

CTU survey

A survey was sent to all UK Clinical Research Collaboration (UKCRC)-registered CTUs with a webinar to help increase completion. The survey asked CTUs to list up to five recruitment tools and five retention tools they have used and then to expand on up to two tools that have impressed them, within each category. Questions were about what digital tools are being used to identify, recruit and retain participant; their benefits; context (type of study and population); configuration requirements; characteristics of the digital tools for them to be judged useful; and estimated effectiveness.

Logic modelling

To help classify the digital tools into generic categories and identify potential outcome measures for studies, we developed draft logic models showing inputs, activities, outputs and outcomes [https://cyfar.org/what-logic-model] for both recruitment and retention which were iteratively refined after comments from team members then the Advisory Board and finally the CTU leads who responded to our survey. After 4 iterations, there were no further changes.

Qualitative research

Eligible participants for the stakeholder groups targeted in the qualitative research included medical research funding organisations; charities; individuals working on trials in all sectors (primary and secondary care); and research participant representatives.

Table 1: Stakeholders for qualitative interviews

Eligibility criteria	**Roles held by participant**	**Stakeholder groups**
Involvement in one of more of	***One or other of the following***	***(sample size**)***
Trial recruitment	Trialists and recruiters*	Trialists in Clinical Trials Units (secondary care) (n=3)
Management of trials		
Leading funding applications	Principal investigators	Research practitioners in Primary Care (n=3)
Making funding decisions	Funding committee members	Research funding bodies (n=3)
Making decisions on research ethics	Ethics committee members	Ethics committees and Health Research Authority (n=3)
As a trial patient	Patients/ participants	Research participant/patient representatives (n=4)

** e.g. researchers involved in setting up studies, CTU Head of trial management, Clinical Research Network contacts and research nurses. ** The sample of participants was purposive based on availability of resources, participant availability and number of participants required to reach data saturation.*

Participants participated in 45 minute, semi-structured telephone interviews. The interview framework was developed from findings of the CTU survey, and interviews undertaken May-June 2018. Data were captured on audio files, transcribed professionally and data stored securely on a University of Southampton server. **Appendix A** contains the theoretical framework for the interviews and schedules are in **Appendix B**. Ethics approval was granted by the Faculty of Medicine Ethics Committee, University of Southampton (Submission Number 32140).

The participant's identity remained anonymous in all reports and identifying data was password protected and only accessible by the qualitative research team. All participants were reassured that the research data obtained would be treated confidentially and adhere to principles outlined in the General Data Protection Regulation (GDPR) May 2018.

An inductive approach was used to establish clear links between the interview framework for data collection and the summary of findings from the raw data (e.g. the interviews). This

allowed the team to condense the raw material into a summarised format and show how the findings arose directly from analysis of the interview transcripts. The process was conducted manually and using Microsoft Excel.

A content analysis was conducted to provide a summary of the interview data and reveal which areas of the interview framework were discussed/not discussed. This was analysed using Microsoft Excel.

Systematic mapping

In accordance with the protocol, amended as agreed with the Project Board, the systematic map summarised comparative studies published 2008-present that used any digital approaches to recruit and/or retain participants in randomised controlled trials (RCTs).

From electronic literature database and internet searches, 353 publications passed the title + abstract screening step and were examined as full-text documents. Of these, we excluded 242 as not meeting all eligibility criteria, 3 remained unclear (no decision could be reached), and 8 full texts were unobtainable, so could not be assessed. The remaining 100 publications, reporting 101 studies met the systematic map eligibility criteria. These 101 studies were keyword coded by one reviewer; a 20%sample of studies was checked by a second reviewer for accuracy.

5) Results and Conclusions (983 words)

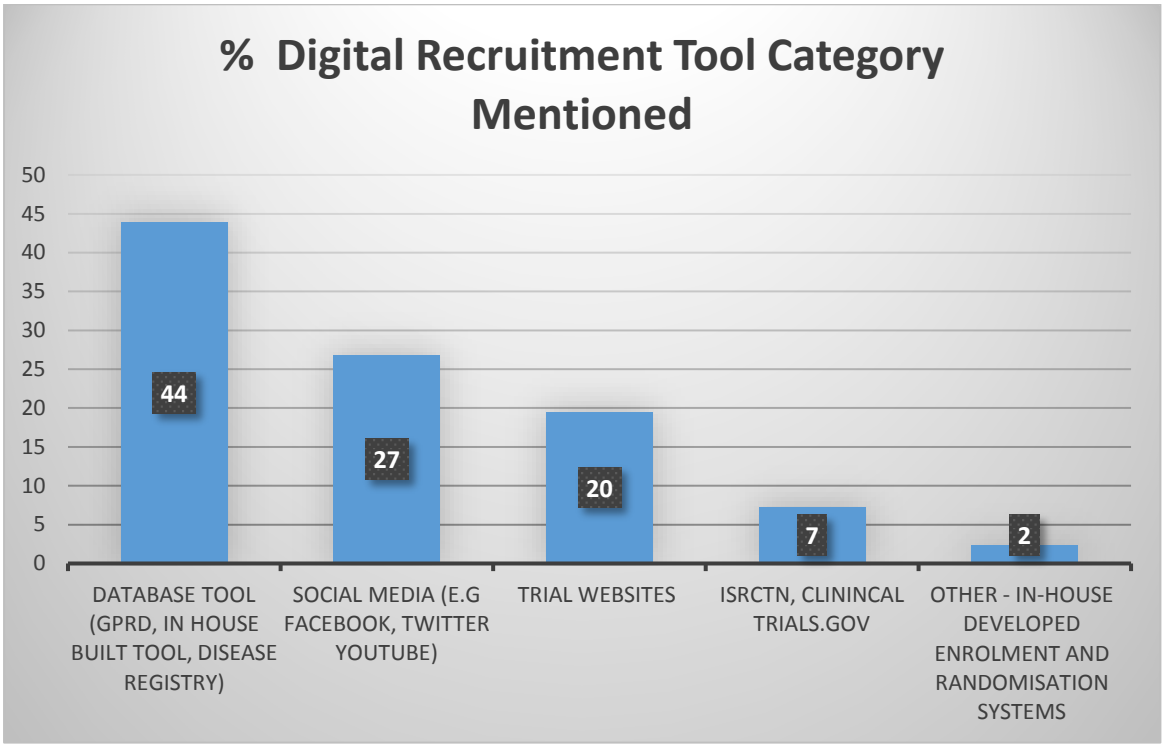
Light touch literature search and survey of NETSCC trial Monitoring team

The search revealed 23 online tools and applications, 16 clinical trial companies offering recruitment and retention services, and 7 online forums/companies facilitating patient involvement. 13 NETSCC staff completed the survey (46%) yielding 26 examples of NIHR trials using digital tools (either for recruitment or retention), but no evidence of (digital tool) efficacy was available. This information helped plan later phases of the work.

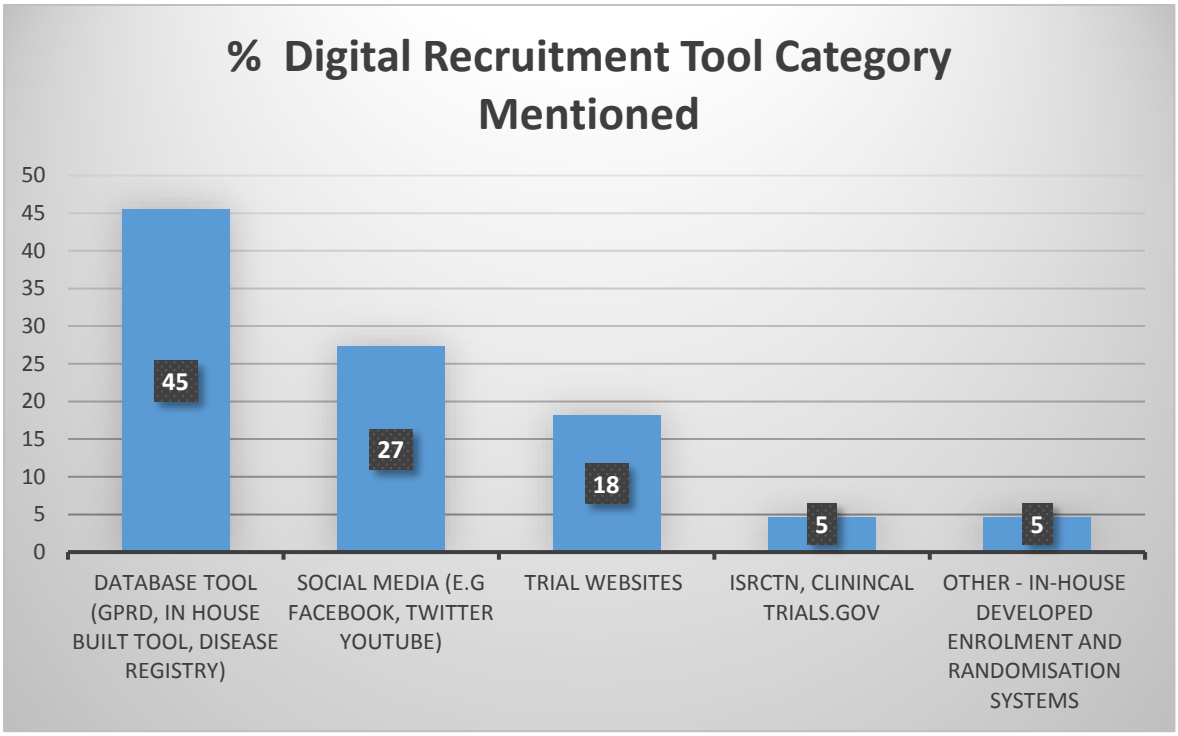
CTU survey results

Twenty four (46%) of 52 CTUs responded, 6 (25%) stating no prior tool use. Database screening tools (e.g. CPRD, EMIS) were the tools most widely mentioned (18/41, 44%) and chosen to expand upon (10/22, 45%) for recruitment and were considered very effective (7/10, 70%). The most mentioned success criteria were saving GP/clinician time and reaching more patients. Social media was second (27%), but estimated effectiveness varied considerably, with only 17% stating “very effective”. Fewer retention tools were used, with SMS / email reminders mentioned most (14/25, 56%) and expanded upon (10/15, 67%), but certainty about effectiveness varied. A detailed definition on what constitutes a digital tool with examples and logic models showing relationships between the resources, activities, outputs and outcomes for digital tools was developed (see **Graph 1-4**).

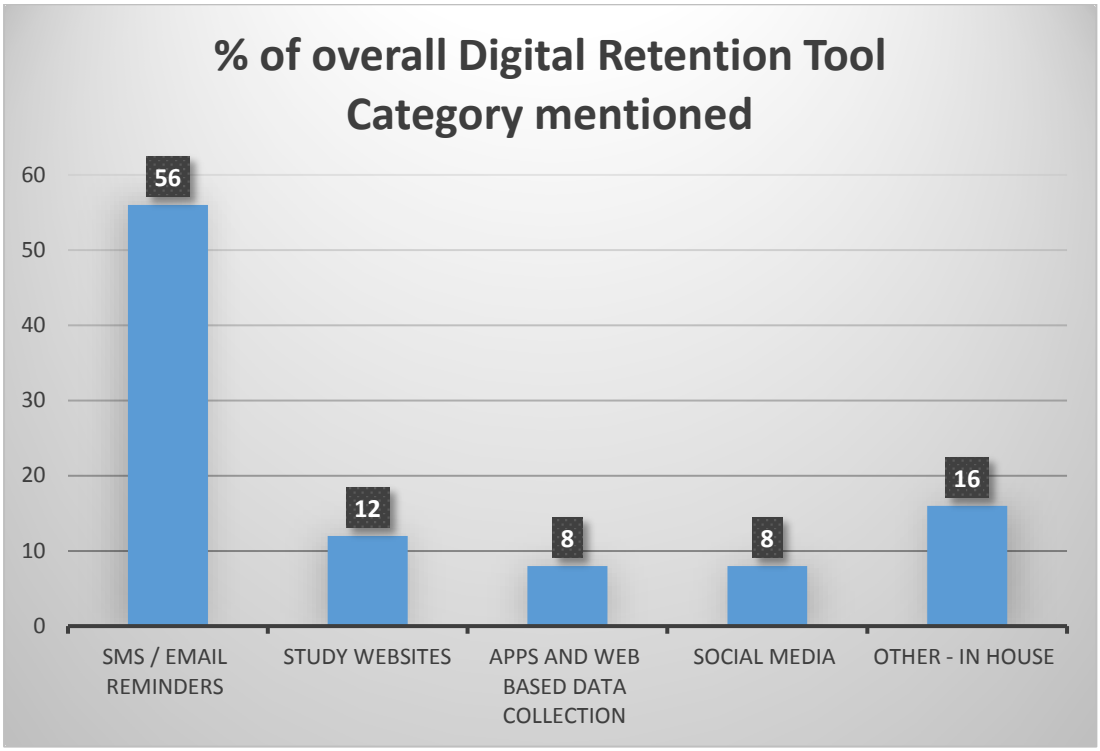
Graph 1: Percentage of Digital tools, by category, CTUs mentioned they have experience of in relation to recruitment (including identification)



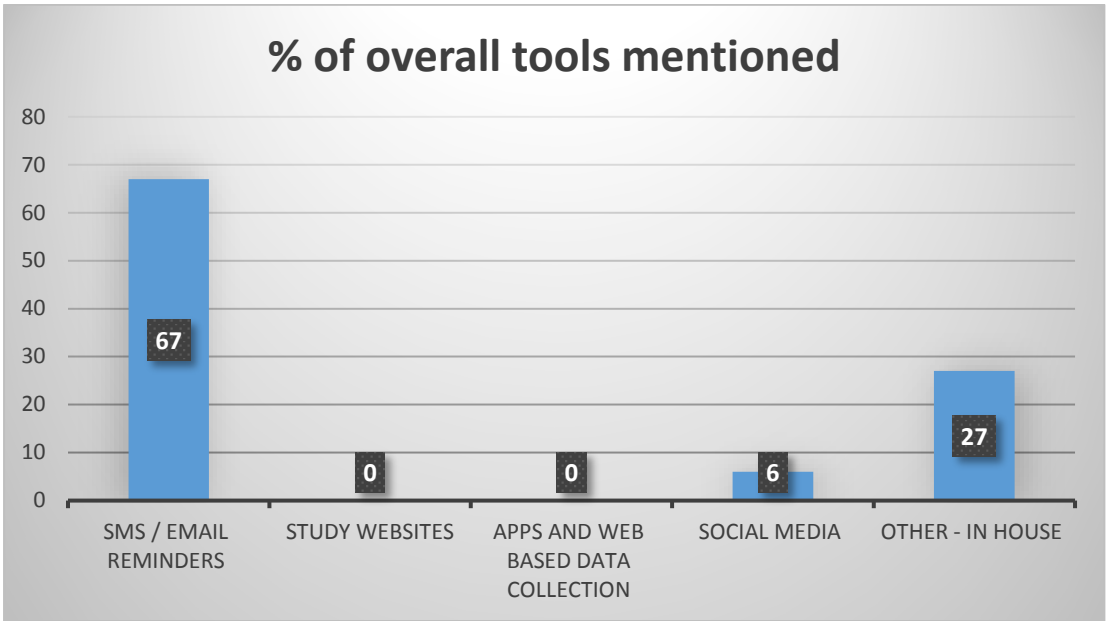
Graph 2: Percentage of digital recruitment tools CTUs mentioned that impressed them, by category.



Graph 3: Percentage of Digital tools, by category, CTUs mentioned they have experience of in relation to retention.



Graph 4: Percentage of digital retention tools that impressed CTUs, by category.



Logic modelling results

The final logic models for both recruitment and retention are show in **Appendix C**.

Qualitative work results

The content analysis provided an overview of the responses based on the interview framework topics. Table 2 provides a summary of results across stakeholder groups. There were some necessary differences in interview frameworks for professional and patient stakeholder groups.

Table 2: Overview of responses from stakeholder professionals and patients

Stakeholder Group →	Trialist	Primary care	Ethics committee	Funding Committee	Patient/ participant	Totals
Interview framework topics ↓						
General	3	3	3	3	NA	**12**
Benefit	2	2	0	3	4	**11**
Intended outcomes of Digital Tools	1	0	0	1	NA	**2**
Acceptance	NA	NA	NA	NA	4	**4**
Challenges/barriers	2	3	3	3	4	**15**
Participant perspective	2	2	2	1	NA	**9**
Awareness of evidence	2	1	3	2	NA	**8**
Funding issues	2	1	0	2	1	**6**
Ethics	2	2	3	0	2	**9**
GDPR / Security	2	1	1	1	4	**9**
PPI	3	1	2	1	NA	**7**
Evidence	2	2	0	3	NA	**7**
Tools used	3	3	0	1	NA	**7**
Knowledge of Digital Tools	NA	NA	NA	NA	4	**4**

NA = not asked

During the analysis, specific themes were developed using an inductive approach. In order to help shape the analysis, we captured key headlines for each stakeholder group by the topic areas covered in the interviews to demonstrate the variability and/or similarities between stakeholders (See **Appendix D).**

A summary of the themes follows:

Box 1: Summary of themes identified

Theme 1: Security and transparency
- Security and legitimacy of information and data sharing
- Efficiency and transparency of information and data

Theme 2: Inclusivity and engagement
- Equity and inclusion of populations
- Recognition of the ability / inability to use digital tools

Theme 3: Human interaction
- Trading off between human face to face and digital tools
- Lose sight of human interface and the importance of face to face connection

Theme 4: Obstacles and risks
- Obstacles preventing the use of digital tools (e.g. evidence, barriers, solutions)
- Risk of technology overload

Theme 5: Potential benefits
- Unknown potential for the use of digital tools (e.g. evidence)
- Reducing the burden on participants (e.g. convenience, time)

(See **Appendix E** for further information)

Systematic mapping results

The 101 identified studies (further details in **Appendix F**) were conducted in a wide range of countries, with three-quarters (75%) in USA, and 13 (13%) in UK. Most (95, 94%) studies investigated digital approaches for recruitment (**see Table 3**). Seventeen (17%) investigated digital approaches for retention (**see Table 4**), of which eleven (11% overall) investigated both recruitment and retention. The most common aim of digital tools in recruitment (in 72% of recruitment studies) was to publicise or raise awareness of trials actively recruiting participants.

Table 3: Aims of digital tools for recruitment

Aim of the digital tool	**n (%)**
Raise awareness of an RCT/clinical trial	68 (72)
Search aid for people to identify specific health studies they may join	2 (2)
Enable study personnel/health professionals to identify eligible study participants	28 (29)
Provide and obtain participant informed consent	8 (8)
Other	3 (3)

Note. Percentages refer to the 95 studies that investigated digital tools for recruitment. Studies could focus on more than one recruitment aim, so the total number of studies and the percentages do not sum to N=95 and 100% respectively.

Table 4: Aims of digital tools for retention

Aim of digital tool	n (%)
Prompts/reminders to attend study appointments, to complete outcome assessments or to adhere to study intervention	13 (76)
Communication to maintain engagement with the study	2 (12)
Automation of data collection	1 (6)
Digital data capture	4 (24)
Other	3 (18)

Note: Studies could focus on more than one retention aim, so the total number of studies and the percentages do not sum to N=17 and 100% respectively

Twenty-nine percent of the recruitment studies aimed to assist trial personnel or health professionals to identify eligible participants. Whilst our intention was to map studies that investigated RCTs as their target study, the target trial design was not stated explicitly in 15 studies (15%); these were included in the map as the target study appeared to be an RCT (or at least a controlled clinical trial) in the review team's judgement. A wide range of health areas were addressed by the target RCTs, the most frequent being health promotion and public health (36 studies, 36%), cancers (17 studies, 17%), and circulatory system diseases (13 studies, 13%). The most frequent health promotion and public health topics were smoking cessation or tobacco control (10 studies) and sexual health promotion (7 studies); only 3 studies addressed alcohol misuse.

The map (**Appendix F**) contains primarily observational, including retrospective, studies (89%), with seven randomised experiments (7%) and five non-randomised experimental studies (5%) represented. Forty-three percent of studies investigated a single digital approach whilst the rest investigated digital approaches combined with non-digital approaches (52%), or multiple combined digital approaches (6%) (totals exceed 100% as one study included different approaches for recruitment and retention). The most frequently investigated digital recruitment approaches were social media (40 studies; 42% of the recruitment studies), internet sites (51 studies; 54%), television or radio (30 studies; 32%), and/or email (30 studies; 32%). Where the recruitment approach included both digital and non-digital components, the most frequent non-digital components were flyers (32 studies; 34% of the recruitment studies) or mail outs (27 studies; 28%). Among the 17 studies that investigated retention, the most frequently investigated digital retention approaches were email (10 of 17 retention studies; 59%) and/or instant messaging or text messaging (6 studies; 35%). The most frequently reported recruitment outcome was recruitment rate (79 of 95 recruitment studies; 83%), and 17 studies (18%) reported the quantitative accuracy of recruitment compared against a reference standard. The time to complete one or more parts of the recruitment process was reported in 17 (18%) of recruitment studies. The costs of the recruitment approaches were reported in 29 (29%) of studies but only 1 study mentioned any costs in relation to retention.

Conclusion

This study set out to answer the three research questions described previously. The four main activities described in this report contributed to answering these questions in the manner

captured in the mapping in **Table 5**. As well as providing direct contributions, each research activity provided critical information for the protocols for follow-on work, culminating in the systematic map.

Table 5: Mapping research outcomes to the research questions

	Direct contribution of research activity to developing understanding			
Research Questions	**CTU Survey**	**Logic Model**	**Qualitative research**	**Systematic Mapping**
1. What digital tools are available that could help identify, recruit or retain people in trials, and what are the associated costs of these tools?	✓	✓	✓	✓
2. What performance characteristics do trialists and CTUs require of these digital tools for them to be judged useful?	✓		✓	✓
3. For the most promising digital tools, what is the available evidence about their performance, and which important evidence gaps need to be filled with primary research?				✓

Our study demonstrates the variety of digital tools being used and of success criteria for these, as well as the empirical evidence that is currently available on each kind of tool to support this, which is of variable quality. Our detailed definition of what constitutes a digital tool, along with examples (see **Appendix G**), will inform the NIHR and wider research community about what is available and help them identify potential tools to help with recruitment to and retention within their studies. To help fill the gaps in the evidence base we have documented, we propose to carry out both specific, tool-focused systematic reviews and primary research to further develop this evidence base, including liaison with Trial Forge, so that assessment of promising digital tools can be evaluated within the NIHR Study within a Trial (SWAT) programme. Possible topics might include: (i) a randomised trial comparing email with social media for recruitment in different age groups and (ii) further Delphi research into appropriate tools for people with different disease types and prevention *vs* treatment.

6) Dissemination

Our plan for dissemination is as follows:

Activity	Detail		Where and when
Presentation of main results (oral/poster)	i)	A future UKCRC Clinical Trials Unit Directors meeting.	- London: Invited oral at future meeting in 2019.
	ii)	The Society of Clinical Trials (SCT), (abstract submitted).	- New Orleans, May 2019
	iii)	5th International Clinical Trials Methodology Conference, (we await abstract submission opening)	- Brighton, Oct 2019
Presentations of separate aspects of the research	i)	Health Technology Assessment International (HTAi), (abstracts for qualitative research and systematic mapping submitted).	- Cologne, June 2019
	ii)	NHS Research and Development Forum (qualitative research abstract submitted).	- Brighton, May 2019
	iii)	CRN Clinical Directors and Chief Op Officers executive meeting (TBC)	- London, Feb/April 2019
Publication of papers	i)	Development of Logic model informed by a survey of CTUs	- *Trials* in 2019
	ii)	Qualitative Research	- *Trials* in 2019
	iii)	Systematic mapping	- *Trials* in 2019
	iv)	Project editorial style Dissemination	- *BMJ Analysis* in 2019
Online access to results, guide dance materials	i)	Via Southampton Clinical Trials website	From Q2 2019
	ii)	Reference on Trial Forge website	
	iii)	Have registered a new website, www.digitaltools.org.uk , which we will use to upload this and future research.	

Other dissemination activities

We will also take the opportunity to disseminate results at national meetings, such as NIHR RDS Directors and CRUK/NCRI CTU Directors, undertake Southampton CTU seminar/webinars and circulate the open access publications across the groups involved (e.g. UKCRC CTUs, CRNs). Please see **Appendix H** for the pathways to impact related to the project dissemination plan.

7) Acknowledgements

To include a 'Contribution of authors' where the role of each author is recorded along with their job title and area of speciality.

Project Team

Amanda Blatch-Jones (Senior Research Fellow, NIHR Evaluations Trials and Studies Coordination Centre): was a member of the project team, led on phase 1, conducted analysis and write up of phase 2, and contributed to the early drafts of the report and reviewed a draft of the report.

Geoff Frampton (Senior Research Fellow, Southampton Health Technology Assessments Centre) was a member of the project team, contributed to phase 3 (design, data collection and analysis), contributed to early drafts of the report and reviewed a draft of the report.

Gareth Griffiths (Director of Southampton Clinical Trials Unit): was a co-lead of the project with Jeremy Wyatt and a member of the project team, overseeing all phases of the project and co-lead (with Jeremy Wyatt) in the writing of the report.

Jeremy Hinks (Director, Alpamayo Coaching Ltd) was contracted in as the project manager and served as a member of the project team.

Athene Lane (co-Director, Bristol Randomised Trial Collaboration): was a member of the project team, co-led on CTU oversight of project and aspects including the phase 2 CTU survey, interpretation of analysis and write up, and contributed to the early drafts of the report and reviewed a draft of the report.

Jacqui Nuttall (Senior Trial Manager, Southampton Clinical Trials Unit): was a member of the project team, co-led on the phase 2 CTU survey and conducted analysis and write up, and contributed to the early drafts of the report and reviewed a draft of the report.

Karen Pickett (Research Fellow, Southampton Health Technology Assessments Centre) was a member of the project team, contributed to phase 3 (design, data collection and analysis), contributed to early drafts of the report and reviewed a draft of the report.

Jonathan Shepherd (Principal Research Fellow, Southampton Health Technology Assessments Centre) was a member of the project team, contributed to phase 3 (design, data collection and analysis), contributed to early drafts of the report and reviewed a draft of the report.

Louise Worswick (whilst on project - Research Fellow, NIHR Evaluations Trials and Studies Coordination Centre) was a member of the study team and lead researcher for phase 1 (qualitative study) from initiation to recruitment, data collection and commencement of data analysis (level one coding of the thematic analysis), and reviewed drafts of the final report.

Jeremy Wyatt (Director of the Wessex Institute): was a co-lead of the project with Gareth Griffiths and a member of the project team, overseeing all phases of the project and co-lead (with Gareth Griffiths) in the writing of the report.

Project Advisory Board

We would like to acknowledge the sustained and helpful support provided to this project by the Project Advisory board, whose members were:

Mark Mullee (NIHR RDS South Central), Robert Peveler (Chair, Wessex CRN),

Stephen Falk (Bristol and West CRN), Karen Underwood (UHS NHS foundation Trust),

Neil Tape UHS (NHS foundation Trust), Helen George (PPI),

Andrew Cook (NETSCC and Southampton CTU).

With Gareth Griffiths, Athene Lane, Jeremy Wyatt and Jeremy Hinks from the Project team.

8) References

Treweek S, Lockhart P, Pitkethly M, Cook JA, Kjeldstrøm M, Johansen M, Taskila TK, Sullivan FM, Wilson S, Jackson C, Jones R, Mitchell ED. Methods to improve recruitment to randomised controlled trials: Cochrane systematic review and meta-analysis. **BMJ Open**. 2013 Feb 7;3(2). pii: e002360. doi: 10.1136/bmjopen-2012-002360.

Koepcke F, Kraus S, Scholler A, Nau C, Schüttler J, Prokosch HU, Ganslandt T. Secondary use of routinely collected patient data in a clinical trial: an evaluation of the effects on patient recruitment and data acquisition. **Int J Med Inform**. 2013 Mar;82(3):185-92. doi: 10.1016/j.ijmedinf.2012.11.008.

Koepcke F, Prokosch HU. Employing computers for the recruitment into clinical trials: a comprehensive systematic review. **J Med Internet Res**. 2014 Jul 1; 16(7):e161.

9) Appendices

Appendix A - Using digital tools for recruitment and retention in trials - stakeholder perceptions from semi-structured interviews

Theoretical framework for data collection and analysis

Stakeholders	Concepts	Topics
Research funding bodies * Ethics Committees and Health Research Authority * Trialists in Clinical Trials Units (secondary care) * Research practitioners in primary care * Research participant/patient representative	Systems and processes - Seeking research funding - Appropriate ethical principles - Involvement of patients and the public - Privacy - Confidentiality - Data protection / GDPR About the digital tool - Evidence of effectiveness - Quality - what makes it good or bad - Type of digital tool Concerns about digital tools - Generic - Specific (to a patient or professional group) No concerns about digital tools - An integral part of our world - Any risks are no different from non-digital methods	Benefits To the study - Accuracy - Easy to use - Effective o Appropriate patients o Wider range of patients o More patients o Patients who stay in To the patient - No need to travel to hospital - Less time commitment - Easy to use Risk or harm To the study - More drop out - Privacy issues - Costs - False positives

Appendix B: Digital tools study - Preamble for all interviewees

Thank you for agreeing to participate in this research interview

Regarding the Participant Information Sheet we sent to you, did you have any questions about what we said about the study?

So just to clarify before we start:

Purpose of the study:
To explore the use of digital tools to support the recruitment and subsequent retention of patients in clinical trials.

Definition:
By 'digital tools' we mean things like searches and interactive medical record tools to support clinicians in screening participants for eligibility for studies or for recruitment of patients.
For eligibility, examples include trial websites, social media and email campaigns to engage with the broader public.
For retention of study participants examples include emails, interactive websites, text messages or apps.

Why are we doing this study?
A systematic review is needed but at the moment we don't really know what criteria stakeholders would use to judge the quality of digital tools, nor do we know how rigorous the studies of digital tools need to be to provide this evidence. So, we need to carry out this qualitative study first to provide information about the outcomes and methods that are relevant for the systematic review. The qualitative study includes interviews with stakeholders like yourself.

Who are the stakeholders we are interviewing?
Trialists, primary care researchers, research funders, ethics committee/HRA representatives and study participants (through focus groups).

Why you?
We are asking you in your capacity as [INSERT ROLE trialists, primary care researcher, research funders, ethics committee/HRA representatives] to give us your opinions about using digital tools.

Consent and confidentiality
Before we start the recording I will ask you to confirm that you agree with the following statements:

- Your participation is voluntary and you may withdraw at any time before the interview
- You give your consent to participate and for the audio-recording of the interview
- You have been offered the opportunity to ask any questions about the study

- Your role in this research will remain confidential. The audio file from the recording and the interview transcript will be stored securely in a password protected folder and accessed only by the researcher/s undertaking the interviews
- The final report and any subsequent publication will not contain any identifiable material
- You give your consent for anonymised quotes to be used in these reports.

Digital tools in trials recruitment and retention

Interview framework – version 3 1/6/18

Interview prompts for Research Funders

General

- Ethics
- Funding
- PPI
- Data protection, GDPR regulations
- Confidentiality
- Privacy

Interview prompts

What digital tools have you heard of?
What features would/do you look for?
What criteria would you use to decide whether it was a good tool or not?
What do board or panel members feel if they come across digital tools they've never heard of?
Do you think about what evidence is needed for digital tools?
What would put off the board about funding a proposal using digital tools?
Has the board funded or would it fund a Study within a Trial (SWAT) if it used digital tools? Which one? What would put the board off?
Would your view as a funder change if a proposal included the use of digital tools?

Digital tools in trials recruitment and retention

Interview framework – version 2 29/3/18

Interview prompts for Ethics committee / HRA

YOUR ROLE?

General

- Ethics
- Funding
- PPI
- Data protection. Did the new GDPR regulations have any influence?
- Did you have to think about any confidentiality issues?
- Privacy
- Will you use this for all your trials?

Interview prompts

Does the use of digital tools in research proposals pose any special issues for the committee?
Do you think about what evidence is needed for digital tools?
For example, is the use of digital tools seen to:

- put participants under stress?
- create privacy issues?

What digital tools have you heard of?
Are some types of digital tool better than others?
What features would/do you look for?
What criteria would you use to decide whether it was a good tool or not?
[Once we have an understanding of the criteria that are used by CTUs for determining the usefulness of a digital tools, we will ask an Ethics Committee representative their thoughts about these]

Digital tools in trials recruitment and retention

Interview framework – version 2 29/3/18

Interview prompts for trialists (e.g. Principal Investigators) and Research Nurses/Practitioners

YOUR ROLE?

General

- Ethics
- Funding
- PPI
- Data protection. Did the new GDPR regulations have any influence?
- Did you have to think about any confidentiality issues?
- Privacy
- Will you use this for all your trials?

Interview prompts

What do you think about using digital tools:
- When designing a study?
- When applying for funding?

What do you want to gain from using digital tools?
What digital tools do you use or have you heard of?
Are some types of digital tool better than others?
What features would/do you look for?
What criteria would you use to decide whether it was a good tool or not?
What outcomes are you looking for in using digital tools? Increase in number of enquiries?
What specific features are necessary for retention tools? Recruitment tools?
What evidence of success would you look for when deciding whether to use a particular tool?
What kind of evidence/level of evidence would convince you that the tool would work?
What tools have you tried using which didn't work? What was it that didn't work? What would have made it more effective for you? Why didn't you like it?
Do you know about any of the following for help with recruitment and retention in trials:
- Database tools off-line?
- Websites?
- Short message service (SMS or text)/email?
- Social media?
- Pop-up on the electronic patient record (EPR)?

Further prompts about specific tools from the list immediately above
- Have you ever used one of these tools?
- If you think this would be a useful tool what would be the useful features of this tool?
- What do you think would be the difficulties?
- What would need to happen to make this tool more useful for you?

Digital tools in trials recruitment and retention

Interview framework

Primary care staff

YOUR ROLE?

General

- Ethics
- Funding
- PPI
- Data protection. Did the new GDPR regulations have any influence?
- Did you have to think about any confidentiality issues?
- Privacy

Interview prompts

What do you think about using digital tools:
- When designing a study?
- When applying for funding?

What do you want to gain from using digital tools?
What digital tools do you use or have you heard of?
Are some types of digital tool better than others?
What features would/do you look for?
What criteria would you use to decide whether it was a good tool or not?
What outcomes are you looking for in using digital tools? Increase in number of enquiries?
What specific features are necessary for retention tools? Recruitment tools?
What evidence of success would you look for when deciding whether to use a particular tool?
What kind of evidence/level of evidence would convince you that the tool would work?
What tools have you tried using which didn't work? What was it that didn't work? What would have made it more effective for you? Why didn't you like it?
Do you know about any of the following for help with recruitment and retention in trials:
- Database tools off-line?
- Websites?
- Short message service (SMS or text)/email?
- Social media?
- Pop-up on the electronic patient record (EPR)?

Further prompts about specific tools from the list immediately above
- Have you ever used one of these tools?
- If you think this would be a useful tool what would be the useful features of this tool?
- What do you think would be the difficulties?
- What would need to happen to make this tool more useful for you?

Digital tools in trials recruitment and retention

Patient representative interview framework

Interview prompts

Do you have experience of being a study participant when digital tools were used for recruitment or retention of participants?

If you haven't had experience of using a digital tool as a trial participant we'd like you to try to imagine what it would be like to be a participant using digital tools which have been designed to help researchers with recruitment and retention of study participants.

What features of a digital tool would you want to have access to?

What criteria would make it a good tool or not from your perspective?

For recruitment and retention how would you feel about the use of:

- Text messaging
- Emails
- Interactive websites
- Social media
- Apps

How would these be helpful to you?

What would make them unsuitable for you to use?

What would make you want to use them?

What would put you off using them?

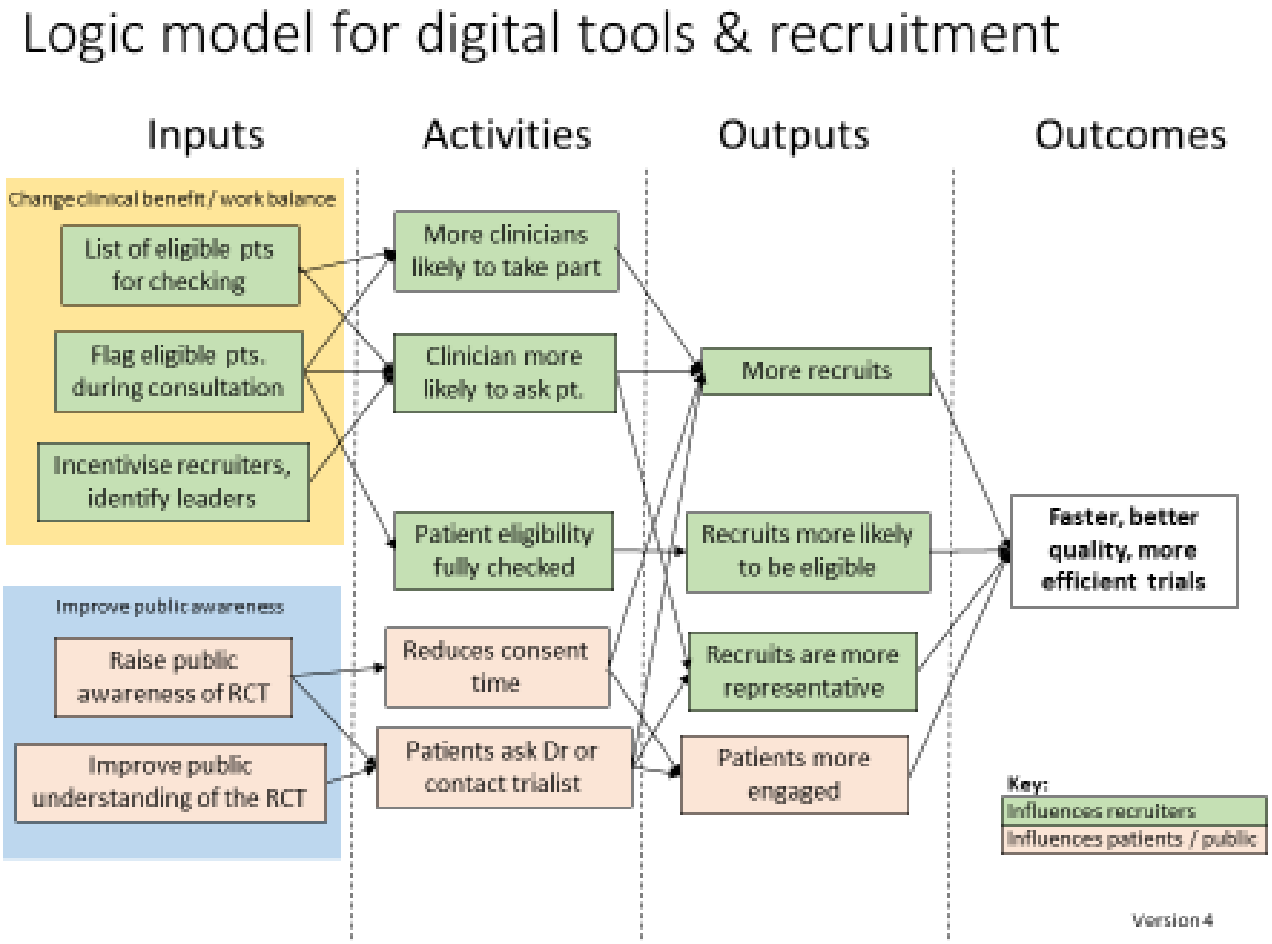
For those who have experience of using digital tools in trials

- What digital tools did you use?

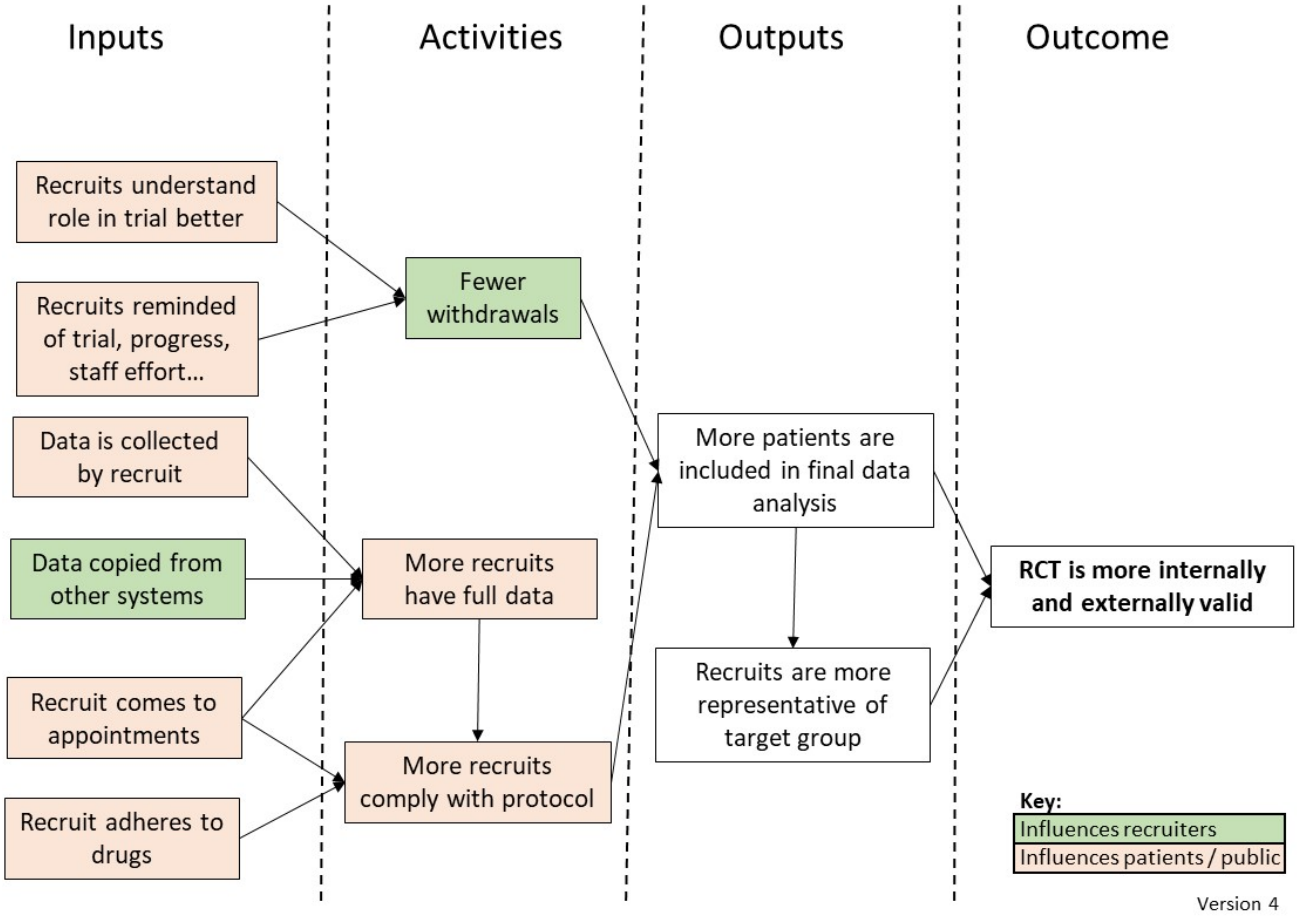
Do you know about any of the following for help with recruitment and retention in trials:

- Websites?
- Short message service (SMS or text)/email?
- Social media?
- Pop-up on your patient record in the GP practice (Pop-up on electronic patient record (EPR)?

Appendix C: **Logic models for recruitment and retention**



Draft logic model for digital tools & **retention**



Appendix D: Matrix describing the key headlines for each stakeholder group (Qualitative analysis)

Transcript summaries	Trialist	Primary Care	Ethics	Funder	Participant representatives
Benefits	- Facilitates outcomes of data / reduces the issue regarding its loss. - Benefits studies recruiting hard to reach groups. - Easier to identify suitable patients for trials.	- Enables new opportunities, such as the increase of data collection/ reduction of paper trails. - Easier to identify suitable patients for trials.	- Recruits the correct trial participants at a faster rate.	- Easier to identify suitable patients for trials. - A wider reach and coverage of the general population. - The value, purpose and scope of DTs is vast. (when used in the correct way)	- Convenient (travel/ parking.) - Relieves pressure felt by participants. - Important to share data with others who will benefit rather than being overly cautious about data protection.
Intended outcomes of DTs	- More convenient means of collecting outcome data/ increasing output of data. - Studies at a lower risk of bias.			- Funders engage in trialling innovative DTs to aid recruitment	
Challenges / barriers	- Requires expertise of technical staff not always available (high staff turnover/ staff retention issues). - Lack of face-to-face contact. - Larger risk of data breach.	- Cost and time of DTs needs to be considered and compatibility with other platforms. - DTs pose security issues, e.g. with text messaging. - Potential to exclude populations on age, accessibility/ usability of device	- Fear/ reluctance regarding innovation/ security of data collected. - Exclusion of populations. - not one size fits all and sometimes only suitable to specific disease areas. - Loss of human interaction.	- Not one size fits all – only suitable to specific disease areas. - DTs at risk of being obsolete with rapid movement of technology. - Privacy/ confidentiality considerations instead of cultural/ behavioural barriers.	- Participants need to be pre-warned by a source they trust regarding the invitation to participate. - Exclusion - relates to age and preferences to use more traditional means of communication (face-to-face/ pen and paper). - A trade-off between the use of DTs and human interaction.
Participant perspective	- Trial recruitment information to be transparent and clear. - Remote recruitment to trials provides impression that potential patients are being cold called.	- Patients feel more included on a personal level – have more autonomy and control. - Diversity across clinical practice, some patients can use DTs and others would find it challenging.	- Learning a new piece of technology inhibits involvement and fear of the new - Different populations are embracing the 'cyber divide'. - Inclusion of hard to reach participants/ groups.	- Quicker and easier for participants.	- Legitimacy of source increases likelihood of participant responding. - Convenience Vs security - Level of acceptance associated with DTs.

Transcript summaries	**Trialist**	**Primary Care**	**Ethics**	**Funder**	**Participant representatives**
		- Flexibility is key.			
Awareness of evidence	- Limited evidence exists. - Awareness generated from personal experience of their use.	- Lack of awareness/ expertise in DT regulations. - Development of digital tools not attractive to commercial companies due to regulations.	- Trial recruitment information to be transparent and clear (for PPI as well) -Limited evidence on use of DTs. -Pilot evidence of DTs is invaluable.	- Evidence challenging to obtain. - Evidence is anecdotal and not formally reported. - Alternative non-digital methods to be available.	
Funding issues	- Challenges experienced with funders understanding and appreciating the value of DTs for recruitment and retention purposes (e.g. IT investment). -Reluctance to cost for appropriate staffing and skills to develop DTs	- Cost of technology: development costs and tools expensive. - Costs cause evident gaps in market for higher-level DT platforms.		- Evidence needed to support use of DTs at funding stage. - Time limitations/ neglect to mention use of DTs prevent detailed review at funding stage. - DTs to help or hinder recruitment?	- DTs to be piloted before patients start using them.
Ethics	- Lack of understanding of technological advances/ security measures by Ethics Committee. - Ensure that data security and data protection standards are upheld. - Wary of use of apps due to security measures.	- Ensure equity across the board but raising awareness of alternative approaches.	- Concerns around confidentiality/ security of data / verification of identify / storage of data/ information. - Alternative methods to be made available. - Lose sight of the importance of human interaction.		- Essential in ensuring inclusivity/ security measures for participants.
GDPR / security	- GDPR is timely and will help to resolve issues around confidentiality/ security.	- Concerns surrounding third party involvement/ confidentiality.	- GDPR has not changed over time.	- Concerns around confidentiality/ security of data. - Pilot data and evidence required.	- The perceived perception of the participant is not as others might expect. - Data/ information shared openly and transparently in relation to supporting others/ advancing research. - Important to know that the invitation (to participate) has originated from a legitimate source.

Transcript summaries	**Trialist**	**Primary Care**	**Ethics**	**Funder**	**Participant representatives**
PPI	- PPI members need to be consulted and reassured regarding what is and isn't acceptable when using DTs.	- PPI is important - Challenges to be overcome if DTs need development prior to funding approval.	- PPI is critical to the development/ appropriateness/ acceptability of DTs. - Inclusion of PPI is key.	- PPI is critical to the development of DTs at the funding stage.	
Evidence	- Evidence is 'previous experience of using a similar tool' and not written evidence.	- More evidence required. - Some have not considered evidence around DTs. - Evidence based on one's own evaluation.		- Scepticism around the re-use of DTs in different clinical settings. - Consideration of heterogeneity -Some funders identify consumer behaviour (not research evidence) to engage participants.	
Tools used	- NW e-health system – Farsite - CPRD GP data - SAIL databank in Wales - Social media (e.g. Twitter) - Online data collection forms (follow up recruitment and delivery of intervention) - Bespoke systems - Telephone triage - Tablet software tools - Power tools app (took too long to set up) - Personalised and diagnostic apps - SMS - Patient electronic records - Somerset Cancer Database	- Bespoke systems - Tablet software tools - Personalised and diagnostic apps - Virtual techniques (e.g. collecting blood pressure results) - Videos using Tablet - ePRO for sending questionnaires - Self management techniques e.g. Google - DotMail		Social media (e.g. Facebook)	- Emails - Self management techniques e.g. Google - Websites

Appendix E: Qualitative study thematic analysis

Theme one: Security and transparency.

There was unified acceptance of the use of digital tools for recruiting and retaining participants, however issues around security, legitimacy and transparency of data were significant barriers and/or concerns to stakeholders to some varying degree.

- "…you just have to make sure that everything is held securely and that that information is conveyed. In terms of recruitment, I think one of the issues is recruiting people remotely could potentially be seen as a kind of cold calling type of exercise." (ID1)
- "…it's a case of making sure that all those controls are in place, isn't it? To make sure that the data doesn't get into the wrong hands." (IDPR04)
- "We clearly need to make sure that we've got the cyber security and everything in place and consent sorted out." (ID12)

Theme two: Inclusivity and engagement

Embracing the use of digital tools across different types of population groups was considered essential for participants to feel inclusive. This not only focused on the perspective of the individual but also the availability and acceptance of using a digital device as well as applications or tools using a digital interface. Consideration of the user interface is required before deciding whether digital tools are the appropriate method for recruitment.

- "Approaching people by a different route is potentially a way of providing information to people that they wouldn't otherwise be given through the typical kind of health professionals route. It opens up an avenue for actually getting greater dissemination about research opportunities." (ID1)
- "Some patients, they're quite happy having everything emailed, others want telephone calls…its different for everyone so I think you just have to be flexible." (ID10)

[flexibility, diversity and 'not one size fits all' were key considerations]

Theme three: Human interaction

Trade-off between the use of digital tools and having human interface. This was seen as an important consequence for the use of digital tools. However, it was felt by most that as long as the ethical and legal frameworks are in place along with reassurances then there is less risk involved. A difference between recruitment and retention was noted under this theme.

- "that digital recruitment can kind of be seen as a somewhat arm's length approach, as opposed to a face-to-face discussion. And I'm not saying that you have one

without the other, but I have seen some research that suggests people recruited digitally if you like, whilst the recruitment was better the retention was poorer than recruitment via a face-to-face meeting." (ID1)

- "I suppose the potential participants might be a bit frightened of the new…once you stop to think about it, they don't worry, but I think the initial thing is…this bit of a fear of the new…the cyber divide is breaking down and even older people will be able to embrace it." (ID4)

Theme four: Obstacles and risks

Three noticeable obstacles were around

i. staffing and the lack of technical experience

ii. expense and time associated with digital tools

iii. level of acceptance from funders/ethics

- "…the rapidity with which things become obsolete, in terms of digital platforms, is frighteningly rapid. I think that does complicate this space; it makes it more difficult to identify what's best practice and then replicate it at an industrial scale." (ID11)
- "You have to fight hard to explain clearly why you need that much money. It's easier to justify costs in CTIMPS because of MHRA regulation." (ID2)
- "…the evidence for using for example text messages for reminding I think is compelling...I think that's where maybe the funders need to be more proactive and say 'well this is, as far as we're concerned, this is best practice and we'll expect to see it' and actually help people achieve that best practice." (ID11)

Theme five: Potential benefits

There was a strong sense of the potential benefits associated to the use of digital tools in terms of their value, purpose and scope. There was an appreciation that 'not one size fits all' and how the perceived benefits are 'just not realised yet'.

- "I can't see any reason why you wouldn't want to store the data digitally. The data is going to end up in an electronic format anyway." (IDPR03)
- "…my own anecdotal evidence is that, having used it in studies, it's been so much easier to manage recruitment. Not only could you recruit better, but you could also manage the people who are actually doing the recruiting." (ID2)
- "You've got to demonstrate that you've got the expertise to handle the electronic aspect of your research...and have people been offered a choice…the principles of fair consent are the same whether its electronic or face-to-face…the principles of

good research are still the same whether you're doing it electronically or by traditional methods." (ID4)

Appendix F: Systematic Map

This appendix contains:

- A flowchart showing the flow of publications during the map screening process.
- Tables and a figure showing selected results from the map.

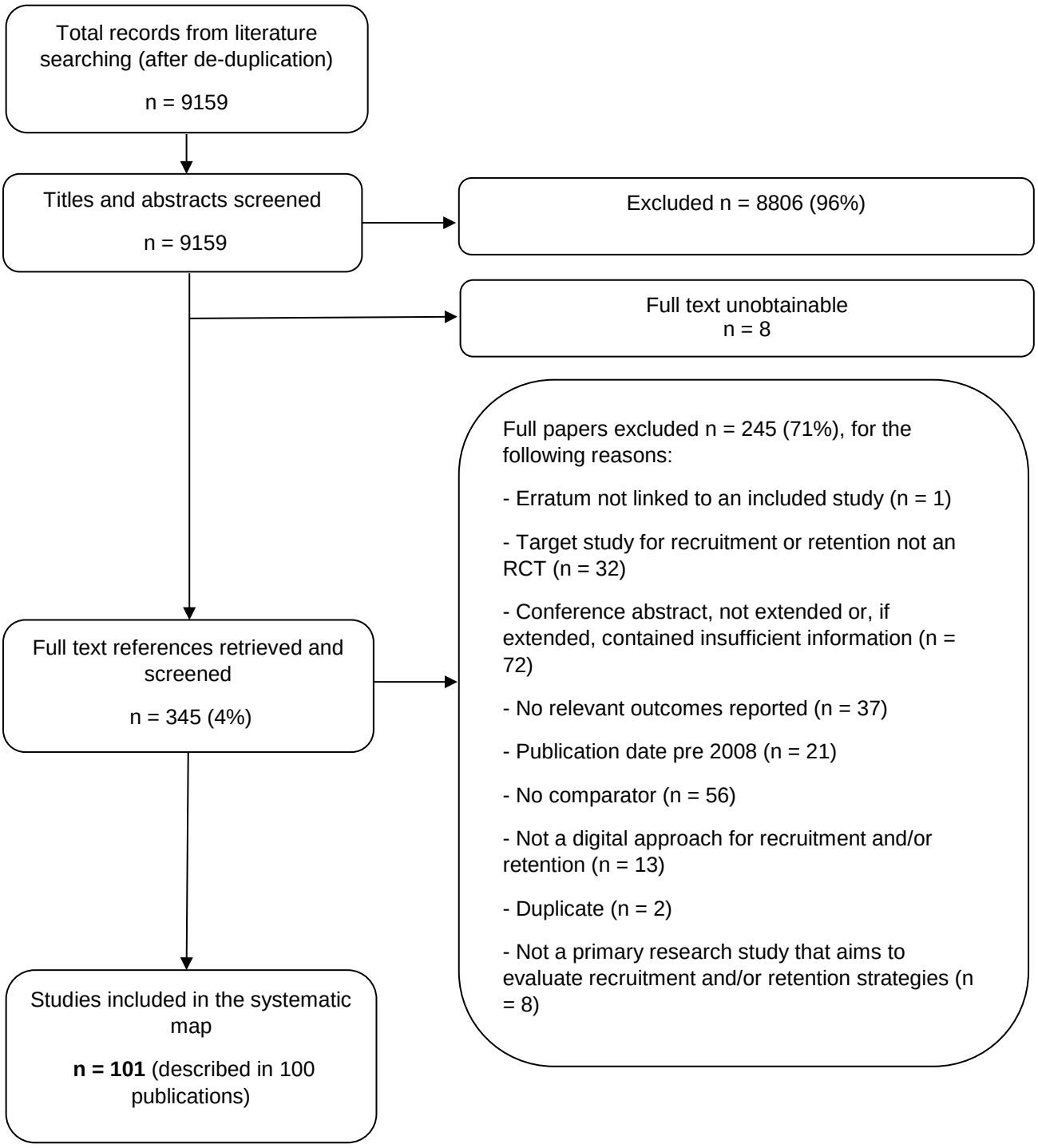


Figure F1 Flowchart showing the number of publications and studies identified, excluded and included at each stage of the screening process for the systematic map

Selected map results

Selected results from the map are presented below. The tables present basic frequencies, showing the number and proportion of the studies included in the map (N = 101) that were recorded against each code. All numbers and percentages refer to the 101 included studies, unless otherwise stated.

Table F1 Study location

Country	n (%)
USA	63 (62)
UK	13 (13)
Australia	10 (10)
Canada	5 (5)
Germany	4 (4)
Netherlands	2 (2)
New Zealand	2 (2)
Republic of Korea	1 (1)
France	1 (1)
Norway	1 (1)
Multinational (conducted in more than 3 countries)	2 (2)

Note. Three studies were conducted in two of the listed countries so the total number of studies and the percentages do not sum to N=101 and 100% respectively.

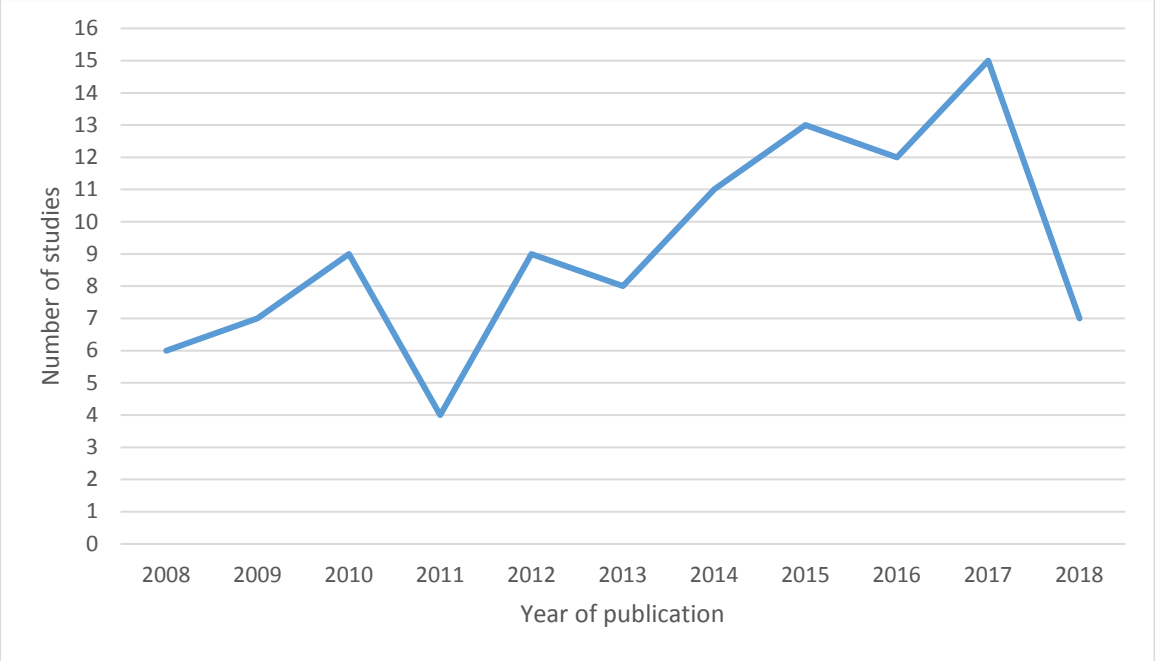


Figure F2 Number of studies by year of publication (N=101)

Table F2 Study design

Design	n (%)
Experimental - randomised	7 (7)
Experimental - non-randomised	5 (5)
Observational study or retrospective analysis	90 (89)
Simulation study	0 (0)
Other	0 (0)

Note. One study incorporated two different designs so the total number of studies and the percentages do not sum to N=101 and 100% respectively.

Table F3 Purpose of digital approach(es) investigated

Purpose	n (%)
Recruitment	95 (94)
Retention	17 (17)
Both recruitment and retention	11 (11)

Table F4 Aims of digital tools for recruitment

Types of approach	n (%)
Raise awareness of an RCT/clinical trial	68 (72)
Search aid for people to identify specific health studies they may join	2 (2)
Enable study personnel/health professionals to identify eligible study participants	28 (29)
Provide and obtain participant informed consent	8 (8)
Other	3 (3)

Note. Percentages refer to the 95 studies that investigated digital tools for recruitment. Studies could focus on more than one recruitment approach type, so the total number of studies and the percentages do not sum to N=95 and 100% respectively.

Table F5 Aims of digital tools for retention

Types of approach	n (%)
Prompts/reminders to attend study appointments, to complete outcome assessments or to adhere to study intervention	13 (76)
Communication to maintain engagement with the study	2 (12)
Automation of data collection	1 (6)
Digital data capture	4 (24)
Other	3 (18)

Note. Percentages refer to the 17 studies that investigated digital tools for retention. Studies could focus on more than one retention approach type, so the total number of studies and the percentages do not sum to N=17 and 100% respectively.

Table F6 Types of digital tools used in the studies

Digital tools	**n (%)**
Internet site for recruitment	51 (50)
Internet site for retention	2 (2)
Internet forum for recruitment	5 (5)
Internet forum for retention	0 (0)
Internet pop-up adverts for recruitment	0 (0)
e-mail for recruitment	30 (30)
e-mail for retention	10 (10)
Automated identification of trials for which people are potentially eligible, for recruitment	4 (4)
Automated screening method used to identify potential participants, for recruitment	22 (22)
Digital lecture/presentation (e.g. Powerpoint) for recruitment	0 (0)
Digital lecture/presentation (e.g. Powerpoint) for retention	0 (0)
Other computer programme software for recruitment	2 (2)
Other computer programme software for retention	3 (3)
Social media for recruitment	40 (40)
Social media for retention	2 (2)
Crowdsourcing platform for recruitment	1 (1)
Digital (i.e. automated) phone calls for recruitment	2 (2)
Digital (i.e. automated) phone calls for retention	0 (0)
Virtual assistant/gadget for retention	0 (0)
Chatbot for recruitment	1 (1)
Chatbot for retention	0 (0)
"Virtual snowballing" for recruitment	1 (1)
Instant messaging / text messaging for recruitment	4 (4)
Instant messaging / text messaging for retention	6 (6)
Smartphone/tablet App for recruitment	5 (5)
Smartphone/tablet App for retention	2 (2)
Smartphone/tablet other use for recruitment (specify in comment)	1 (1)
Smartphone/tablet other use for retention (specify in comment)	1 (1)
Videos for recruitment	5 (5)
Videos for retention	0 (0)
Television or radio for recruitment	30 (30)
Other	17 (17)

Note. Studies could use more than one tool type, so the total number of studies and the percentages do not sum to N=101 and 100% respectively.

Table F7 Type of recruitment and/or retention intervention investigated (study intervention group)

Intervention	n (%)
Single digital approach	43 (43)
Multiple combined digital approaches	6 (6)
Combined digital & non-digital approaches	53 (52)

Note. One of the 101 studies investigated two approaches so the total number of studies and the percentages do not sum to N=101 and 100% respectively.

Table F8 Type of recruitment and/or retention comparator investigated (study comparator group)

Comparator	n (%)
Single digital approach	8 (8)
Multiple combined digital approaches	1 (1)
Single non-digital approach	27 (27)
Multiple combined non-digital approaches	10 (10)
Combined digital & non-digital approaches	10 (10)
Other comparison type (specify in comment)	4 (4)
No formally-defined comparator - but a multi-component approach with results separable for the components	46 (46)

Note. Studies could include more than one comparator, so the total number of studies and the percentages do not sum to N=101 and 100% respectively.

Table F9 Effectiveness outcomes assessed

Outcome	n (%)
Recruitment rate	79 (78)
Recruitment accuracy - quantitative	17 (17)
Recruitment accuracy - qualitative	1 (1)
Time to complete recruitment (for part or all of the process)	17 (17)
Recruitment reach	19 (19)
Retention rate	22 (22)
Retention accuracy	1 (1)
Other	4 (4)

Note. Studies could assess more than one outcome, so the total number of studies and the percentages do not sum to N=101 and 100% respectively.

Table F10 Other outcomes assessed

Outcome	n (%)
Attitudes towards use of the tool	2 (2)
Study participant satisfaction	2 (2)
Study personnel satisfaction	5 (5)
Cost of recruitment/retention	29 (29)
Efficiency of tool	27 (27)
Other (specify in comment)	14 (14)

Note. Studies could assess more than one outcome, so the total number of studies and the percentages do not sum to N=101 and 100% respectively. Of the 29 studies reporting costs, all reported costs of recruitment; only one also reported overall costs per retained patient.

Table F11 Type of health study for recruitment and retention

Outcome	n (%)
RCT	87 (86)
Clinical trial (not explicitly stated as an RCT)	15 (15)

Note. One of the 101 studies included several target trials, some of which were clearly labelled RCTs, while others were not.

Table F12 Health topics under study

Digital tools	n (%)
Bone and joint diseases	1 (1)
Brain and nervous system diseases	4 (4)
Cancers	17 (17)
Ear diseases	0 (0)
Endocrine, nutritional and metabolic conditions	7 (7)
Eye diseases	0 (0)
Genito-urinary system diseases	1 (1)
Health promotion and public health (specific topic investigated is shown in italics)	36 (36)
Smoking cessation or tobacco control	*10 (10)*
Sexual health promotion	*7 (7)*
Physical activity promotion	*6 (6)*
Healthy eating	*1 (1)*
Alcohol misuse	*3 (3)*
Cardiovascular health promotion	*1 (1)*
Lifestyle interventions for diabetes prevention	*2 (2)*
Lifestyle interventions for weight gain or obesity prevention	*4 (4)*
Health checks or screening	*1 (1)*
Falls and fracture prevention in older adults	*1 (1)*
Cancer chemoprevention	*1 (1)*

Infectious diseases	3 (3)
Mental health	10 (10)
Respiratory diseases	1 (1)
Skin diseases	1 (1)
Digestive system diseases	2 (2)
Circulatory system diseases	13 (13)
Maternal health and pregnancy	4 (4)
Other	8 (8)

Note. Studies could focus on more than one health topic, so the total number of studies and the percentages do not sum to N=101 and 100% respectively.

Table F13 Number and proportion of studies focusing on minority or under-served populations

Minority or under-served population	**n (%)**
Yes	16 (16)
No	85 (84)

Appendix G: Tables of potential digital tools to support recruitment and retention tasks

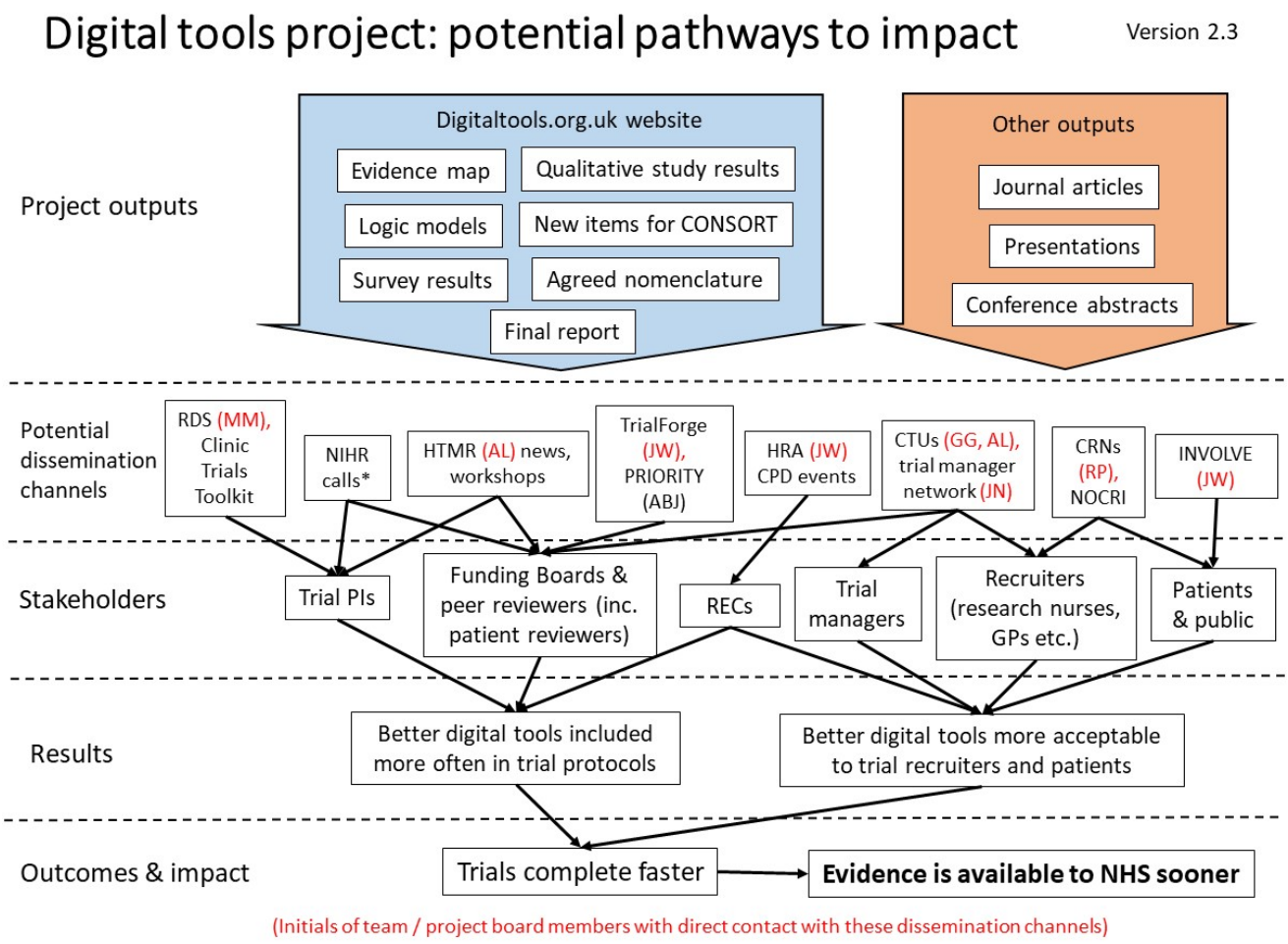
Possible tools to support recruitment tasks

Task	Target	Possible tools
Publicise a trial	Recruiters	Social media, email campaign
Identify possible patients for a trial offline	Recruiters	Database screening (eg. CPRD) Trial eligibility checklist on trial website
Identify pts for trial during consultation	Recruiters	Automated flag based on EPR
Ensure pt really was eligible for trial when recruited	Recruiter	EPR database check on entry
Incentivise recruiters	Recruiters	Automated league table, lottery for recruiters Simplified trial recruitment workflow Online pt. info / video etc.
Raise public awareness about trials in general	Public / patients	Social media, email campaigns
Help pts. find a specific trial	Public / patients	clinicaltrials.gov, trial website; Google ads or pop up on disease website
Improve public understanding of a specific trial	Patients	Trial website eConsent video, animated patient information leaflet Web chat with trial nurse App providing tailored info for patient

Possible tools to support retention tasks

Task	Target	Possible tools
Ensure recruits & trial staff fully understand the trial	Recruits & trial staff	eConsent video, better pt. info leaflets checked by automated tool; online protocol documents
Remind pts about visits	Recruits	Email, app, SMS reminders
Remind pts about data capture	Recruits	Smartphone app, freetext SMS
Remind pts about drug adherence	Recruits	Email, app, SMS reminders Smart pill box with reminders
Minimise human data entry	Recruits and trial staff	Copy data from lab, EPR etc. systems
Motivate people about the trial & adherence to protocol	Recruits and trial staff	Social media, league table, trial newsletter / blog

Appendix H: Pathways to impact related to the project dissemination plan



10) Conflict of interest declaration

Amanda Blatch-Jones: is employed by the University of Southampton to work for NETSCC. ABJ is employed as the Senior Research Fellow for the Research on Research programme and has worked for NETSCC (and its predecessor organisation) in various roles since 2008.

Geoff Frampton is employed by the University of Southampton to work for Southampton Health Technology Assessments Centre (SHTAC).

Jonathan Shepherd is employed by the University of Southampton to work for Southampton Health Technology Assessments Centre (SHTAC).

Karen Pickett is employed by the University of Southampton to work for Southampton Health Technology Assessments Centre (SHTAC).

Louise Worswick: is currently employed by the UK National Health Service in a management role. Previously she was employed by the University of Southampton working for NETSCC in a research role and has held research and management roles in NHS and academic institutions for over 30 years.

Gareth Griffiths, Athene Lane, Jacqui Nuttall and Jeremy Hinks have no conflicts of interest.