Self-management open online trials in health [SMOOTH] an analysis of existing online trials [Protocol]

BACKGROUND: The use of public engagement and self-management in online clinical trials is growing with benefits, boundaries and minimal methodological guidance. This analysis explores whether running self-recruited online trials can provide trustworthy and useful answers to research questions. **AIM:** To systematically explore existing self-recruited online randomized controlled trials of self-management interventions and analyze the trials to assess their strengths and weaknesses, the quality of trials reporting and to report how participants were involved in the research process. **METHODS**: The **O**nline **R**andomized **C**ontrolled Trials of **H**ealth **I**nformation **D**atabase (ORCHID) will be used as a sampling framework to identify a subset of self-management self-recruited interventions. The trials will be used to explore the qualities of self-recruited online randomized controlled trials and to evaluate how useful they are for obtaining trustworthy answers to questions about health self-management and citizen research involvement. This research employs participatory action research where researchers and participants work as collaborators. **SUMMARY**: This analysis can provide an overall view of effective methods for online trials and to provide insights into integration for online trials development as early as the protocol planning stage.

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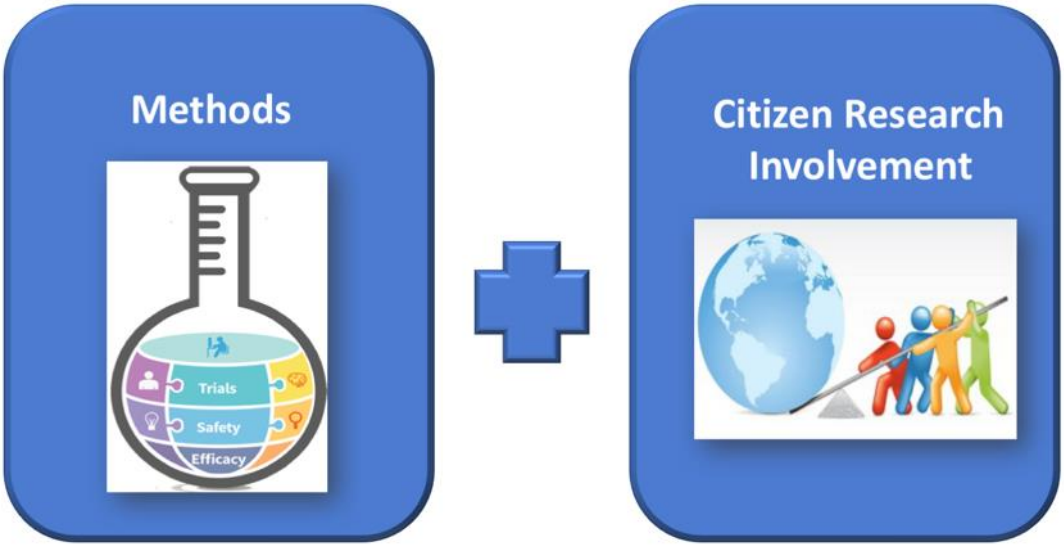
SMOOTH: Self-Management Open Online Trials in Health [Protocol]

An Analysis of Existing Online Trials



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Ethics Approval for interview and survey research: CUREC# MSD-IDREC-C1-2013-174 Research Organization: ThinkWell: Website address: http://ithinkwell.org Research Registry# 1986

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Self-Management Open Online Trials in Health (SMOOTH) What can we learn from existing trials?

BACKGROUND

The use of public engagement and self-management in online clinical trials is growing with benefits, boundaries and minimal methodological guidance. This analysis explores whether running self-recruited online trials can provide trustworthy and useful answers to research questions.

AIM

To systematically explore existing self-recruited online randomized controlled trials of self-management interventions and analyze the trials to assess their strengths and weaknesses, the quality of trials reporting and to report how participants were involved in the research process.

METHODS

The Online **R**andomized **C**ontrolled Trials of **H**ealth **I**nformation **D**atabase (ORCHID) will be used as a sampling framework to identify a subset of self-management self-recruited interventions. The trials will be used to explore the qualities of self-recruited online randomized controlled trials and to evaluate how useful they are for obtaining trustworthy answers to questions about health self-management and citizen research involvement. This research employs participatory action research where researchers and participants work as collaborators.

SUMMARY

This analysis can provide an overall view of effective methods for online trials and to provide insights into integration for online trials development as early as the protocol planning stage.

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FEEDBACK

We would appreciate, insights, practical ideas and suggestions to make this research better. Comments or email welcome. Amy Healingjia@msn.com and we will look for ways to integrate your feedback into our research plan.

Background

Why look at self-recruited online randomized controlled trials?

ThinkWell[1] is an organisation that was founded following a meeting in Birmingham of health researchers, health service users, and clinicians who thought that (a) there was a mismatch between the questions and outcomes of most importance to the public and those that were researched[2], (b) there was insufficient involvement of the public in health research[3] and (c) the internet and mobile communication were potentially useful and underused tools for re-dressing the balance. ThinkWell's stated mission was "to improve the health and wellbeing of citizens across the world by enabling them to make informed decisions about lifestyle, diet and health interventions through public-led health discussions, education and research, using the internet and the mass media as fundamental tools to reach the masses"[4]. In 2014 ThinkWell was converted into a charity.

Two key principles underlie ThinkWell's work – one is evidence-informed decision making and the other is public and patient involvement in all aspects of research process to promote, and generate the evidence required for, informed decisions (see Figure 1)

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Figure 1 Making informed decision

ThinkWell has identified several questions that are of high priority to the public about interventions people can do for themselves. ThinkWell has sought systematic reviews, or works towards undertaking new systematic reviews if no existing high quality up-to-date systematic reviews are available to establish which of these questions are true uncertainties. ThinkWell has worked with the public to collate potential self-management interventions whose effectiveness is uncertain that need testing in randomized controlled trials. Most of these do not require clinician involvement and have primary outcomes that are participant-reported measures. This makes it possible for the effectiveness of these interventions to be addressed in self-recruited online trials. ThinkWell has set up the Public Led Online Trials - Infrastructure and Tools Project, or PLOT-IT for short[5] to organize and run online trials addressing genuine uncertainties about health self-management identified as a priority for the public (Figure-2).

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SMOOTH: Self-Management Open Online Trials in Health
What can we learn from existing trials?

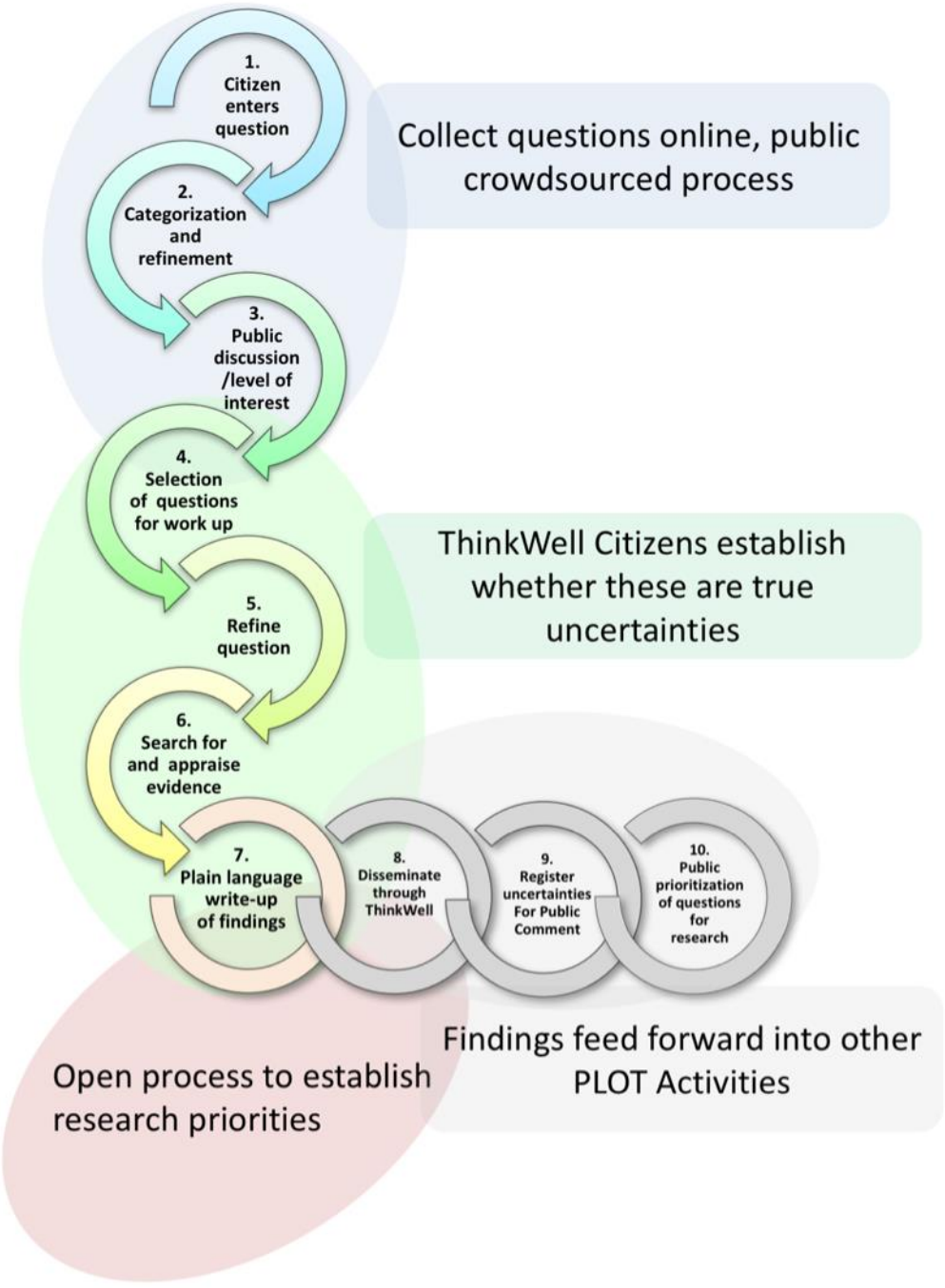

Figure 2 The ThinkWell research process adapted from Price and Burls[6]

ThinkWell commits to an evidence-based approach to investigate decisions that affect health and health care in all aspects of its work, such as, how to involve the public

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meaningfully in research and how to conduct research well. Before ThinkWell launches any online trial, we need to know about best practice for methods.

ThinkWell researchers looked for evidence about what constituted best practice in this area. Despite systematically searching for published methodological research in this area, little evidence was found.[7] This absence of methodological research has been confirmed by other researchers.[8] A high priority for ThinkWell therefore became to conduct its own research into online trials to help identify and develop best practice for conducting self-recruited online trials.

A starting point was to look at existing research that used online trials for health research to see if there were any lessons that could be drawn. A first step was to construct a database of the trials that had used the Internet in a significant way for health research. An **O**nline **R**andomized **C**ontrolled Trials of **H**ealth **I**nterventions **D**atabase (ORCHID) was primarily developed by Anne Brice and Amanda Burls with Amy Price contributing to development. data extraction, analysis, and adding of studies[9]. The aim was to identify as many relevant trials as possible to provide a comprehensive population of online trials that could be used as a substrate for research. Identifying relevant Internet health trials was a methodologically challenging project because of the lack of specific search terms that could be used; therefore, the construction of this database was underpinned by methodological research into search strategies to establish the optimal trade-off between exhaustiveness and efficiency. It is inevitable that some relevant studies will have been missed and, should any relevant studies come to light, these will be added to the database. Nonetheless the database contains 3636 relevant studies for screening Title and Abstract from the 26,000 studies that were searched[7]. Other researchers using data mining techniques have validated the database content and we believe that the database is sufficiently complete to permit meaningful and efficient methodological research[7]. A full description of methods used to develop the database is available in the paper by Brice, Burls, and Price 2015[7] and Appendix-1 contains the ORCHID search strategy and inclusion/exclusion criteria.

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Why engage the public in health research?

The public is the end recipient of healthcare interventions and it is important that research evidence guiding the use of healthcare interventions is relevant and useful to them[10,11]. The public can become participants in research trials without knowing whether a trial is well run, ethical or even if it will ever be published[12]. Patients can be confused, vulnerable and unsure of how to switch roles between patients and participants[13]. Few resources are available for patients themselves to distinguish between safe and ethical research. Through interactive collaboration the public can share real-life knowledge with practical life problem solving to increase adoption of best practice in research and health literacy. Mining the ORCHID database provides the opportunity to discover what works in terms of engagement and methodology in online trials. This will provide the foundation for building a network of participatory research in online trials where citizens can take part in every aspect of planning a trial and are not limited to being only participants within the trial.

What are the benefits of participatory research?

In other research, even novice human input can be more sophisticated than that of computer automated data mining to discriminate what is of value in research. [14]What has proved useful to bridge this gap in other sciences such as neuroscience and astronomy is to crowd source the public as citizen scientists[15]. They are given minimal training to classify scientific data and are able to volunteer and work online at their own pace and intensity[14]. This method may be useful for health research as information and demand are outstripping the ability of healthcare providers, academics and scientists to keep up with the present rate of health care research which doubles every 19 years. For example there are 75 new trials and 11 systematic reviews produced daily[16]. At the current rate health research outstrips medical school learning and becomes outdated during the lifetime of clinical practice [17]. This is where the public and patients can help, as they can become potential experts on their own conditions which is a narrow but important window where contributing to the chain to keep best research knowledge current is vital. This is a win/win scenario as the training and practice can enable the citizen scientists to become informed members of a health research team. Citizens can contribute to reducing the

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workload and become competent to engage in the complex informed shared decision making required for health science research particularly in the design and running of online clinical trials.

Why this Research is important

ThinkWell plans to train the public and motivated patients who can mentor others, influence existing patient advocacy groups and partner with ThinkWell and other researchers to develop research protocols[1]. This inspiration for an informed health public will spread across cultures and be an agent for change to facilitate communication between research, science and health care. The use of public engagement and self-management in online clinical trials is an emergent framework that will bring unique methodological challenges and benefits[3]. Working with a reliable established database for procuring primary studies can serve researchers and the public in terms of reducing start up research costs. This will be the first research of its kind using the ORCHID database and it is the only existing database that exclusively collates online trials.

This research is important to establish that running self-recruited online trials can be a trustworthy and useful methodology. This is relevant for both ethical and practical reasons, for example, to establish for funders that this is indeed a valid research approach. Currently online trials may not be perceived by funders to meet the threshold standards of validation or credibility[18]. This reduces their influence as a priority for funding bodies[19]. This project will employ participatory action research where researchers and participants will work as collaborators to answer the research questions[20]. This analysis can provide an overall view into what works for online trials and how methodology and public engagement might be best utilized and integrated into the development of online trials as early as the draft protocol stage.

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Research Question(s)

What can be learned about self-recruited online randomized controlled trials for self-management of health interventions from existing trials?

1. How useful were these trials for obtaining trustworthy answers to questions about health self-management?
2. To what extent did they engage the public in health research
3. What is the quality of these trials in their reporting?

Aim

To systematically explore existing self-recruited online randomized controlled trials of self-management interventions and analyze the trials to assess their strengths and weaknesses and to find whether, and if so how, participants were involved in the research process and the usefulness, if any, of public involvement.

Objectives

1. To critically appraise and extract a subset of self-recruited online trials of self-management interventions to:
   - Identify their strengths and weaknesses
   - Assess the quality of their reporting
2. Identify how public or patients were involved in the research process
3. To use information obtained during the critical appraisal to see to what extent these factors influence the success or failure of trials.
4. To inform the development of guidance for the design, conduct and reporting of online RCTs of self-management interventions

Methods

1. The ThinkWell **O**nline **R**andomized **C**ontrolled Trials of **H**ealth **I**nformation **D**atabase (ORCHID) will be used as a sampling framework to identify a subset of self-management self-recruited interventions. The trials will be used to explore the qualities of self-recruited online randomized controlled trials and to evaluate how useful they are for obtaining trustworthy answers to questions about health self-management and public engagement/involvement in research. Usefulness will be identified as ways the trial can contribute to evidence based practice and

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clinical application. Evaluation will be conducted through systematic review of a subset of the qualifying trials, critical appraisal, surveys and interviews.

Identification of Trials

The ORCHID database represents the most comprehensive collation of online health trials available and was last updated July 2016. It will be used to identify the sub-set of trials that were self-recruited and investigated interventions involving the self-management of health. If relevant online trials are identified that were published before this publication cut-off date, they will be added to ORCHID and included in this study.

Inclusion and Exclusion Criteria

Inclusions

- Randomized controlled trial
- Self-enrolled online
- Use of internet-based technologies, computer, tablet, smartphone, in the trial process
- Interventions of health and well-being including educational or behavioral components
- Outcomes recorded or reported by the participants themselves

Exclusions

- Studies investigating interventions in social care or educational settings, where the outcome of investigation is not health related.
- Data not collected online or by mobile technology
- Studies where the population was exclusively health professionals, educators, or students for training and not a specific health intervention

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- Studies where the population are enrolled as patients for trial purposes and require physician intervention for reporting outcomes
- Studies that are not randomized controlled trials or are secondary analysis, cost effectiveness research
- No abstract available
- Conference presentation or poster only
- Aborted/Withdrawn Trials

Definitions of Self-management and Enrolment

Self-management

For the purposes of this research, self-management or self-monitoring of health is defined as use of a medical device, intervention or process that, while it may be recommended by a physician or other clinician, can be used or undertaken by the participant without assistance of a health care professional. For example, self-help, wellness, diet, activity, therapy online or anti coagulation medication that is monitored and titrated by the patient could be included, likewise asthma medications with peak flow measurement recorded by the patients are included, however interventions that are fully physician dependent for interpretation such as radiological films or lab work would not.

Self-Enrolment

Self-enrolment (self-recruitment) online is defined as when participants themselves sign up to, or enroll in, a trial online, via smart phone, tablet or computer.

Screening Title and Abstracts

Two researchers will screen the title and abstract of all citations in ORCHID that match health, self-management, self-help, intervention, self-recruit, self-enroll, and community for citations that match inclusion/exclusion criteria. The citations will be categorized as include, unsure (references to be checked), exclude. Full papers will be retrieved for

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categories; include and unsure based on screening of the title and abstract. Exclusions will not be documented at this stage.

Full Paper Retrieval

Two researchers will screen the retrieved full papers to match them against the inclusion and exclusion criteria and categorize them as include, exclude or unsure. There will be discussion between the two researchers to resolve the status of an unsure paper to reach consensus on exclusion or inclusion. A third researcher will be consulted if there is still uncertainty. The rationale for exclusions will be documented in text and with a PRISMA[21] diagram outlining the fate of full papers. The degree of agreement and reasons for discrepancies will be reported in the results.

Obtaining a Representative Sample

The study will use a proportionate stratified sampling technique to include a percentage of subgroups from eligible citations. This allows representation of the online trials population avoiding artificially constraining the size to accommodate resource costs. This method makes it possible to include all subgroups or strata equally and allows for the observation of existing relationships between subgroups. The random selection of all the trials was not used as it could result in groups not having equal representation. We will group the studies into the following strata or sub groups:

- Feasibility or Pilot studies
- Full trials

We will randomly select 50% percent of the studies from each stratum.

Sampling Rationale

There may be fewer feasibility and pilot trials than full trials or other groups however a scoping of the literature and consultation with content experts of trials methodology informed us that important choices about methodology and engagement may be detailed in the feasibility or pilot trial but not included in the final trials report. Sampling increases possibilities for representative inclusion.

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Missing Information

Investigators and authors will be contacted for missing information in instances where this information would contribute meaningfully to fulfilling the objectives of the study. This could be by questionnaire with room for free text, by structured interviews or email. A record of the communication will be reported indicating if study authors could be contacted, response rates after three attempts and percentage of information answered or if they made themselves available for contact some other way.

Methods for Data Extraction and Synthesis

Data extraction will be constructed by AP after reading a sub sample of 10 studies to inductively develop a draft data extraction form. AP and LV will independently code 4 studies and adapt the form for best use of resources and information quality. They will then extract the balance of the studies. Results will be presented in graphical or tabular form using descriptive statistics and some of the data extracted will be used in the narrative summary for each included study. A characteristic of studies table is shown in Table-1.

Characteristics of included studies Table-1

These will be collected using the EPPI Reviewer code set.

Characteristics of Included Studies

Citation	Authors, title, year, journal
Research Question	Research question, Aims, Objectives
Methods	Trial design
Participants	Study setting, health status of participants, age, sex, country,
Enrolment	sample size calculated and reached? time to recruitment
Intervention	active condition, controls, intervention details, duration
Outcomes	Outcome measures, time–points and follow-up

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Quality Assessment and Reporting

The included trials will be quality assessed for methodology strengths and weaknesses by two review authors. Discrepancies will be discussed and resolved by consensus, or by consultation with a third review author.

Reporting Tools

Critical Appraisal Skills Programme, (CASP) 11 questions to help you make sense of a trial[22] will be used and scored as unacceptable 0-2, Low 3-4, Medium 5-7 Medium High 8-9, High 10-11. The CASP and may be supplemented by Equator[23] guidelines as they pertain to qualities commonly used in reporting randomized controlled online trials for example: Items may be used from CHERRIES[24] for online surveys, CONSORT[25], CONSORT PRO[26] for reporting patient reported outcomes. The quality tools will be piloted and adapted for best use of time and resources to capture the methodology. Skip technology (branching) will be used to make the critical appraisal process more efficient so that only questions that are relevant to the paper are evaluated and every piece of evidence needs to be handled only once per reviewer.

Cochrane Risk of Bias assessment

The risk of bias will be assessed using the Cochrane 'Risk of Bias' tool categorizing the risks as 'low', 'high', or 'unclear' risk. Individual bias items will be evaluated as described in the Cochrane Handbook for Systematic Reviews of Interventions[27]where any of the specified criteria for a judgment on 'low', unclear' or 'high' risk of bias justifies the associated categorization.

Public and Patient Involvement

There will be a narrative summary of how, when and at what stage(s) public and patient involvement occurred in each included study and whether the impact or value of the public involvement within the study was recorded.

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Public and Patient Collaboration

Citizens are invited to comment on this protocol which will be registered and available on a publicly available repository, and shared via social media. There may be important outcomes that citizens can suggest to make online trials useful, engaging or a safer vehicle of research. We will ask how could quality and participation better be improved for online trials. In a recent review citizen input was credited with contributing to clinical safety standards[28]. Citizens will be invited to review, add to, clarity check and prioritize our list of quality assessment criteria and they may be included in the formation of a panel for a future Delphi concerning what to include for a protocol in an online trial.

SMOOTH Survey

Useful details about public and participant involvement in online trials might not be reported in the research publication. Further questions about the use of PPI in the trials will be investigated by inviting trial investigators or corresponding authors of the full sample of included studies to participate in a survey (protocol in appendix-2). The survey will be conducted using a validated survey program and will use guidelines available from Equator "Improving the Quality of Web Surveys: The Checklist for Reporting Results of Internet E-Surveys (CHERRIES) [24]".

Analysis

The analysis will explore interactions and correlates for areas of interest across or within the studies. It is not known at the protocol stage the exact areas that contain sufficient data to make this exploration feasible. For example, one question might be "*How does participant resource cost throughout the trial and length of the trial influence the compliance, completion rates and effect size of the trial?*" is one question that could be asked of the data. It is not known whether there will be sufficient data or homogeneity to perform meta-analysis. If regression modeling is indicated statistical software will be used. The numerical analysis will be supported using graphs and tables for ease of understanding and visual comparisons.

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Results

The study will report on the methodological quality, mechanical operation and bias potential in existing online trials and how these may influence outcomes of PPI for online trials. Some of the outcomes of PPI the study shall consider should the data allow will include usefulness of question prioritization, agenda setting, ethical decisions, methodology, data collection, implementation of results, PPI with multi-stages of research such as a community or participatory action group, and the usefulness in very large research studies.

Descriptions of Information Presentation Forms

There will be summary description of each study. A summary table for included studies will be provided in table format. The table will consist of citations, type of review, population, research question, aims, number of studies and participants in each review, outcome measures, findings and comments. The excluded studies summary will consist of the citation and reason for exclusion. A narrative description for each included study will be available. The narrative discussion will focus on items specific to the research objectives and questions.

Discussion Points

A short summary of the main finding will be included here along with the overall completeness and applicability of the evidence that is found and its external validity. In addition to discussion of the results the discussion will be expanded to include whether different methodological approaches and areas of involvement used to engage the public and patients in trials could have a measurable positive or negative effect on the research results, conduct of the trial and outcomes, and the patients or public.

Quality of the Evidence

Were the relevant studies identified and could methodology for search, study selection, data collection or analysis be strengthened. Was the quality of evidence stronger for some outcomes of key interest than others?

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Bias Potential Within the Review

What were the strengths and limitations of the study about reducing bias and were these aspects within the control of the review authors? If the answer is affirmative, we will discuss how this might be resolved in future studies.

Agreements and disagreements with other reviews

Here authors will look at how the included reviews fit into the context of other evidence and whether that evidence was systematically reviewed. This information will be collected through our overview of Participant involvement in trials design.

Conclusion

Implications for Research

Implications for best practice and areas in need of further review will be suggested. Discussion of potential areas of public and patient involvement in trials that have not yet been systematically reviewed and ripe areas for future research will be included. The findings will be reported in peer-reviewed journals where others involved or wanting to learn about online trials can learn from what was found and improve on it to build a stronger foundation for online clinical trials health science research. This project will enable the ThinkWell team and other researchers to build methodologically viable, PPI enabled and user-friendly protocols for interventional online trials

Implications for Practice

Gaps and key issues that remain unresolved after a review of the evidence will be clearly noted. What can we learn from existing trials? The findings will be used to develop a working protocol for online trials that will include effective ways to incorporate PPI in the trials design.

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Contributions of authors

All authors will fulfil the ICJME requirements for authorship

Declarations of interest

No authors have any conflict or interests to declare

Differences between protocol and review

The preliminary protocol may be amended following public feedback so the input can be incorporated into the data extraction.

Ethics Approval for interview and survey research: CUREC# MSD-IDREC-C1-2013-174 Research Organization: ThinkWell: Website address: http://ithinkwell.org

Research Registry# 1986 http://www.researchregistry.com/browse-the-registry.html#home/registrationdetails/5856b9bd759db5ec4609d880/

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Appendix-1 ORCHID search strategy and inclusion/exclusion criteria

The inclusion and Exclusion criteria plus the literature strategy is included below.:

Inclusion criteria
All studies that meet the following criteria were included:

- randomised controlled trials using internet-based technologies in the trial process
- studies using mobile technologies where there is also internet-based activity
- studies investigating health research, public health research topics and settings.
- Studies that include educational or behavioral interventions of health and well being topics
- Studies involving patients or members of the public

Exclusion criteria:
The following studies were excluded:

- Studies using mobile telecommunications technologies exclusively, with no internet-based content
- Studies investigating interventions in social care or educational settings, where the main topic of investigation is not health related, or where clinical interventions are not included in ICD10.
- Studies where participants were health professionals or students

The ORCHID Search Rationale

A comprehensive literature search was completed to retrieve and import relevant studies into a bibliographic software package where they were screened against inclusion and exclusion criteria.

- Included studies were indexed and coded for the core stages of the research process, topic of study, interventions used, and location of the trial setting. The results were then included in the database to create a known set of internet-based randomised clinical trials in health and well-being
- The studies were identified with a broad and comprehensive search strategy to accommodate the wide variations in terminology, definitions and applications of internet-based technologies within the research environment and limited indexing.
- Terms were mined from the search sources below, along with exploring core articles identified from scoping searches; and by experts in the field. A process of text word analysis was undertaken, and the identified relevant thesaurus and free-text terms, and combinations of terms, tested where possible.

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Medline – Ovid Medline 1948 – July 2016

Search sources

The following sources were searched:

• Medline

• Embase

• CINAHL

• PsycInfo

• The Cochrane Controlled Trials Register (CCTR)

• Physiotherapy Evidence Database

• OT Seeker

• ERIC

• LILACS

Searches using Internet search engines were not used, due to the lack of specificity possible when searching for terms such as "internet" in this context. The ORCHID search was conducted without limits due to the uncertainty about how and when Internet trials originated.

1. exp Computer Communication Networks/
2. (internet$ or web$ or online or on-line).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
3. 1 or 2
4. randomized controlled trial.pt.
5. controlled clinical trial.pt.
6. randomized.ab.
7. placebo.ab.
8. clinical trials as topic.sh.
9. randomly.ab.
10. trial.ti.
11. 4 or 5 or 6 or 7 or 8 or 9 or 10
12. exp animals/ not humans.sh.
13. 11 not 12
14. 3 and 13

Embase : Ovid Embase 1980 – 2015 Week 02: 18/1/16
Update from 13/01/13

1. (internet$ or online or on-line).mp. [mp=title, abstract, subject headings, heading word,

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drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
2. random$.tw. or placebo$.mp. or double-blind$.tw.
3. 1 and 2

PyscINFO: 1987 to July 2016

1. (internet$ or web$ or online or on-line).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]
2. (random$ adj assigned).tw.
3. double-blind.tw.
4. control.tw.
5. 2 or 3 or 4
6. 1 and 5

Cinahl: EBSCO 01 July 2016

1. (MH "Internet+")
2. web* OR internet* OR online
3. s1 OR s2
4. PT clinical trial
5. MH "Treatment Outcomes+"
6. TX randomized
7. s4 OR s5 OR s6
8. s3 AND s7

ERIC: ProQuest 03 July 2016

tbc

Pedro

1. Internet OR web OR online in Abstract or Title AND Method: clinical trial

OT Seeker

1. internet OR web OR online AND Method: Randomised Controlled Trial

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Supplementary

Appendix-2 CUREC Questionnaire Protocol (see in supplementary file)
Appendix -3 Sample Interview Protocol (see in supplementary file**)**

For more information contact Corresponding author by leaving a comment**.**

The ThinkWell Online Randomized Controlled Trials of Health Information Database (ORCHID) will be used as a sampling framework to identify a subset of self-management self-recruited interventions. The trials will be used to explore the qualities of self-recruited online randomized controlled trials and to evaluate how useful they are for obtaining trustworthy answers to questions about health self-management and public engagement in research. Usefulness will be identified as ways the trial can contribute to evidence based practice and clinical application. Evaluation will be conducted through systematic review of a subset of the qualifying trials, critical appraisal, surveys and interviews.

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