

# Mobile-based technologies to support client to healthcare provider communication and management of care (Protocol)

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# TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
BACKGROUND	1
OBJECTIVES	2
METHODS	3
ACKNOWLEDGEMENTS	7
REFERENCES	7
APPENDICES	9
CONTRIBUTIONS OF AUTHORS	11
DECLARATIONS OF INTEREST	11
SOURCES OF SUPPORT	11
NOTES	12

[Intervention Protocol]

# Mobile-based technologies to support client to healthcare provider communication and management of care

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# ABSTRACT

This is a protocol for a Cochrane Review (Intervention). The objectives are as follows:

To assess the effectiveness of mobile-based technologies to support communication of healthcare information and management of care, on clients' health and well-being, as well as unintended consequences and resources use, compared to standard practice.

# BACKGROUND

The provision of healthcare at a distance, through telemedicine applications, can facilitate universal health coverage, decreasing health and social inequalities (Wootton 2008). The widespread use of information and communication technologies can potentially expand the use of telemedicine approaches to overcome health systems challenges associated with accessing care and coverage of services.

**Description of the condition** 

Access to healthcare is essential for the promotion of health and the management of diseases and chronic conditions. Extensive healthcare coverage traditionally leads to improved access to required healthcare and improved population health, especially for those from more deprived socio-economic backgrounds (Moreno-Serra 2012) and rural and remote areas (Jamison 2013). Mobile access to healthcare and health-related information becomes vital in contexts where access to healthcare is scarce, as those needing clinical information might be particularly vulnerable to ineffective treatment (Royston 2015).

## **Description of the intervention**

Telemedicine is defined as the use of information and communication technologies for medical diagnostic, monitoring, and therapeutic purposes, when participants are separated by distance, time, or both, with the ultimate goal of improving the health of indi-

viduals and communities (Hersh 2006). Although telemedicine and telehealth have been conceptualised separately, with the latter being a broader term that also encapsulates non-clinical activities such as professional education, they are often used synonymously (Hersh 2006; WHO 2016). Mobile health (mHealth) has been more recently defined and refers to the use of mobile telecommunication technologies for delivering healthcare (Steinhubi 2013). The exchange of information can occur synchronously (when interactions happen in real time) or asynchronously (when there is a lag between the clinical information being transmitted and the response) (WHO 2016), and through different channels, including videoconferencing, mobile applications, and secure messaging (Kruse 2017). The most common examples of telemedicine services are store and forward services, where medical data are transmitted to a healthcare provider for offline assessment; remote monitoring services, where a person is monitored at a distance by a healthcare provider through the use of technologies; and interactive services, where there is real-time interaction between a person and their healthcare provider (WHO 2012; WHO (in press)).

A global survey on eHealth was recently conducted by the World Health Organization (WHO) (WHO 2016), in which the terms telehealth and telemedicine were used interchangeably. Results showed that 57% of 122 surveyed countries had telehealth as part of the national eHealth policy or strategy (70 countries), and 22% (27 countries) had a dedicated national telehealth policy or strategy (WHO 2016). According to the surveyed countries, the most common areas where telehealth was used were teleradiology, telepathology, remote patient monitoring and teledermatology, all of which were in use in more than half of the surveyed countries (WHO 2016). Of those, teleradiology programmes were most established, whereas the other programme types were mainly informal or at the pilot stage.

In a bid to maximise the coverage of healthcare services, decrease the costs associated with providing healthcare, and optimise the shortage of healthcare professionals, governments and healthcare agencies all over the world have been funding telehealth programmes, in high-, middle- and low-income countries. Some examples include: the technology enabled care services programme in England (NHS Commissioning Assembly 2015); the Scottish Centre for Telehealth and Telecare (SCTT 2017); telehealth pilot programmes in Australia (Australian Government Department of Health 2017); telehealth services provided within the Medicare programme in the USA (MedPAC 2016); the Asia eHealth information network (AeHIN 20017); and the KwaZulu-Natal experience in South Africa (Mars 2012).

## How the intervention might work

By enabling exchange of clinical information that otherwise might not be possible, telemedicine promotes access to healthcare services, overcoming barriers such as the existence of services and timeliness of access. The main benefits associated with telemedicine are improved access to healthcare, increased speed at which it can be accessed, and cost reduction (Wootton 2008). This is particularly relevant for settings with limited healthcare resources, for instance low- and middle-income countries and remote areas. By bringing together healthcare providers and clients who otherwise might not be able to exchange clinical information, telemedicine increases the uniformity of clinical practice, promotes universal health coverage, and decreases health and social inequalities. Techonological advances and better telecommunication systems enable broader and less expensive access to healthcare delivered remotely, making the intervention more accessible.

Notwithstanding the possibilities, telemedicine applications have been inconsistently implemented and with varying degrees of success, which can be explained by technological challenges, legal considerations, human and cultural factors, and uncertainty about its economic benefits and cost-effectiveness (WHO 2011). A global eHealth survey conducted recently reported that lack of funding, infrastructure, prioritisation, and legislation or regulations were the most commonly cited barriers to implementing telehealth programmes (WHO 2016). These barriers can only be overcome by the implementation of comprehensive regulatory guidelines, driven both by governmental and professional medical organisations; legislation on confidentiality, privacy and liability; and the involvement of all stakeholders in designing, implementing and evaluating telemedicine applications, focusing on the safety and the effectiveness of applications (Agboola 2016; WHO 2011).

# Why it is important to do this review

The rapid progress in information and communication technologies means that the field of telemedicine is also hastily evolving. Despite its potential and the exponential growth of telemedicine applications in recent decades, there are still unanswered questions about its effectiveness (Agboola 2016; WHO 2016). The rationale for conducting this review is to assess the effectiveness of mobilebased technologies to support communication of healthcare information. Although these technologies are now ubiquitous, their rapid expansion has not been accompanied by a close assessment of their impact, which led the WHO to commission guidelines that aim to inform investments of digital health applications for strengthening health systems. This is one of a suite of six Cochrane Reviews that will contribute to those guidelines. We aim to assess the effectiveness of telemedicine not only on relevant clinical outcomes, but also acceptability, satisfaction, resources use and unintended consequences. Research into unintended consequences has been particularly neglected, but can provide crucial information for the implementation of successful telemedicine programmes.

# OBJECTIVES

To assess the effectiveness of mobile-based technologies to support communication of healthcare information and management of care, on clients' health and well-being, as well as unintended consequences and resources use, compared to standard practice.

# METHODS

## Criteria for considering studies for this review

## **Types of studies**

We will include randomised trials and cluster randomised trials. We will include full-text studies, conference abstracts, and unpublished data. We will include studies irrespective of their publication status and language of publication.

## **Types of participants**

• Clients receiving healthcare accessible via mobile devices.

• All types of healthcare providers (i.e. professionals,

paraprofessionals and lay health workers), communicating and providing client care through mobile-based technologies.

We will include participants regardless of their location, setting, diagnoses, conditions or demographic factors such as age.

## **Types of interventions**

We will include trials comparing communication and management of care through a mobile device with standard practice. By mobile-based communication from client to healthcare provider, we mean the exchange of communication and provision of healthcare information and services at a distance (WHO 2012), in which communication is conducted between remote clients engaging with health services and healthcare providers. We will focus exclusively on the provision of healthcare information where the person's inquiry receives a response in real-time or response is as immediate as appropriate clinically. Standard practice is defined as the usual care provided in the setting where the study was conducted, which could include providing care or engaging with the client through face-to-face communication or other non-digital channels or referring the client to another provider.

We will focus exclusively on clinical information that can be exchanged over wireless and mobile technologies, as well as mobile phones of any kind (but not analogue landline telephones), laptops, tablets, personal digital assistants, and smartphones. Communication channels via mobile device can include text messaging, video messaging, social media, voice calls, voice over internet protocol (VoIP), and videoconferencing, through software such as Skype, WhatsApp, or Google Hangouts. We will include:

• studies in which the clients employ mobile-based technologies to engage with provider(s); this could also include partners, family members or other informal support providers engaging with providers on behalf of others;

 studies in which the provider(s) offering care is at a different location from the client;

• studies in which the client transmits clinical information via a mobile device; and

• studies in which the provider(s) offering guidance responds in real-time, defined as sufficiently immediate or as clinically appropriate.

We will include studies where mobile-based technologies were used for monitoring, consultation or delivering treatment, as long as there was clinical information exchanged between client and provider, and feedback given by the provider. We will include studies where the type of communication device that was used to transmit the clinical information is unknown, since the specificity of the type of communication device is not often reported.

We will include all health issues and will not restrict the content of clinical health information exchanged. We will include studies where the digital component of the intervention was delivered as part of a wider package if we have judged it to be the major component of the intervention.

We will exclude:

• Pilot and feasibility studies (pilot study defined as "a version of the main study that is run in miniature to test whether the components of the main study can all work together" (Arain 2010) and feasibility study defined as "pieces of research done before a main study" (Arain 2010)).

• Studies that compared different technical specifications of telecommunication technologies, e.g. different communication channels, software, etc.

• Studies in which the client used fully automated services to self-care or access clinical information without having any contact with a healthcare provider (e.g. webMD).

 Studies in which the use of telecommunications technology was not linked to direct client care.

• Studies in which the intervention consisted of client monitoring systems in which the client received only an automated voice response.

• Studies in which the intervention consisted of routine communication to the healthcare provider as part of usual follow-up care.

• Studies in which clients used an automated service to relay clinical information, without having any other interaction with the healthcare provider (e.g. client is fitted with a system that will send a message if glycated haemoglobin (HbA1c) drops below a certain range and there is no feedback from the healthcare provider), where the client has already had in-person contact with a healthcare provider.

• Studies in which there was no transfer/communication of

clinical information between client and provider. For example, a portable medical device is excluded if it does not transmit clinical information to a provider. The key functionality is that there is an exchange of clinical information between client and healthcare providers; the device/health equipment used for obtaining the clinical information to be exchanged is not as relevant.

• Studies in which providers engage with clients through predefined scheduled calls, where there is no mention of the client being able to contact the healthcare provider in between.

• Studies that explicitly used non-mobile devices to transfer clinical information, such as computers, videoconferencing, landlines, etc. We will not exclude studies based on the type of device or health equipment that was used to obtain the clinical information.

## Types of outcome measures

#### Main outcomes

1. Time between presentation and appropriate response (includes diagnosis, referral or treatment) by provider, including change in time for clients to receive/access health services and information.

2. Clients health status and well-being, using validated measures, such as the Notthingham Health Profile or the SF-36 (McDowell 2006).

## Other outcomes

1. Clients utilisation of healthcare services (e.g. reduced emergency room visits).

2. Clients acceptability of and satisfaction with the intervention; this will include both objective measures, such as the number of dropouts not explained by other reasons, and self-reported acceptability and satisfaction, measured with a validated scale, such as the Patient Satisfaction Scale (La Monica 1986).

3. Healthcare provider acceptability of and satisfaction with the intervention; this will include both objective measures, such as the number of dropouts not explained by other reasons, and self-reported acceptability and satisfaction, measured with a validated scale, such as the Physician Worklife Survey (Konrad 1999).

4. Resource use, including cost to the client and cost to the service (e.g. human resources/time, supplies and equipment). This measure will need to be pre-specified and available directly from the results section.

5. Unintended consequences. These could include: misreading or misinterpretation of data; transmission of inaccurate data; loss of verbal and non-verbal communication cues, including between provider and client; issues of privacy and disclosure; affecting interpersonal relationships; negative impacts on equity; failure or delay in the message delivery.

## Search methods for identification of studies

## **Electronic searches**

An information specialist developed the search strategies in consultation with the review authors and WHO content experts. We will use a cut-off search date of 2000, based on the increased availability and penetration of mobile devices used for telemedicine from that date (ITU 2017). Appendix 1 lists the search strategy for MEDLINE. We will search the following databases:

• Cochrane Central Register of Controlled Trials

(CENTRAL; latest issue), in the Cochrane Library;

- MEDLINE Ovid;
- Embase Ovid;
- POPLINE; and
- WHO Global Health Library.

## Searching other resources

## **Trial registries**

We will search clinicaltrials.gov (clinicaltrials.gov) and the World Health Organization International Clinical Trials Registry Platform (who.int/ictrp) trial registries.

## **Grey** literature

We will conduct a grey literature search to identify studies not indexed in the databases listed above. We will search for relevant systematic reviews and primary studies on similar topics using Epistemonikos (epistemonikos.org), which is a database of health evidence and a large source of health-related systematic reviews. We will search all the contributed content in mHealthEvidence ( mhealthevidence.org), a database of global literature on mHealth. We will contact authors of relevant studies and reviews to clarify reported published information and to seek unpublished results or data. We will contact researchers with expertise relevant to the review topic. Additionally, the WHO will issue a call for papers through popular digital health communities of practice such as the Global Digital Health Network and Implementing Best Practices, to identify additional primary studies as well as grey literature.

## Data collection and analysis

## Selection of studies

We will download all titles and abstracts retrieved by electronic searching to a reference management database and remove duplicates. For title and abstract screening, we will use a machine learning classifier that is able to assign a probability score that a given

record describes, or does not describe, a randomised trial (Wallace 2017). Titles and abstracts of studies with a 10% probability or greater of being a randomised trial will be screened by two review authors (of BB, NH, NM), and those with less than 10% probability of being a randomised trial will be screened by one review author. We will retrieve the full-text study reports/publications and two review authors (of BB, NH, NM) will independently screen the full-text and identify studies for inclusion and identify and record reasons for exclusion of the ineligible studies. We will resolve any disagreement through discussion or, if required, we will consult a third review author (DGB or SS).

We will list studies that initially appeared to meet the inclusion criteria but that we later excluded in the 'Characteristics of excluded studies' table. We will collate multiple reports of the same study so that each study rather than each report is the unit of interest in the review. We will also provide any information we can obtain about ongoing studies. We will record the selection process in sufficient detail to complete a PRISMA flow diagram (Liberati 2009).

## Data extraction and management

We will use the EPOC standard data collection form and adapt it for study characteristics and outcome data (EPOC 2017a); we will pilot the form on at least one study in the review. Two review authors (of BB, NH, NM) will independently extract the following study characteristics from the included studies.

1. Methods: study design, unit of allocation, location and study setting, withdrawals.

2. Participants: number, mean age, age range, gender,

inclusion criteria, exclusion criteria, other relevant characteristics. 3. Interventions: function of the intervention (monitoring, consultation, therapy), intervention components (including type of technology and mode of delivery, frequency of data transmission), comparison, fidelity assessment. For this review, we will define monitoring as to keep track or record the progress of symptoms or a condition over a period of time; consultation as an exchange between the healthcare provider and the client, where the latter's health status is discussed and guidance, support, or information are provided; and therapy as the ongoing management and care of a client, to counteract a disease or disorder.

4. Outcomes: main outcomes specified and collected, time points reported.

5. Notes: funding for trial, ethical approval.

Two review authors (of BB, NH, NM) will independently extract outcome data from included studies. We will contact authors of included studies to seek missing data. We will note in the 'Characteristics of included studies' table if outcome data were reported in an unusable way. We will resolve disagreements by consensus or by liaising with a third review author (DGB or SS). We will group the studies by health condition being targeted. We will create a miscellaneous category for studies focusing on rare conditions and single studies of a condition, for which we will extract basic study information and descriptive data, but not outcome data.

## Assessment of risk of bias in included studies

Two review authors (of BB, NH, NM) will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* Section (Higgins 2017), and guidance from the EPOC group (EPOC 2017b). Any disagreement will be resolved by discussion or by liaising with a third review author (DGB or SS). We will assess the risk of bias according to the following domains:

- 1. Random sequence generation.
- 2. Allocation concealment.
- 3. Blinding of participants and personnel.
- 4. Blinding of outcome assessment.
- 5. Incomplete outcome data.
- 6. Selective outcome reporting.
- 7. Baseline outcomes measurement.
- 8. Baseline characteristics.
- 9. Other bias.

We will judge each potential source of bias as high, low, or unclear and provide a quote from the study report together with a justification for our judgment in the 'Risk of bias' table. We will summarise the 'Risk of bias' judgments across different studies for each of the domains listed. We will consider blinding separately for different key outcomes where necessary (e.g. for unblinded outcome assessment, risk of bias for all-cause mortality may be very different than for a self-reported pain scale). We will assess incomplete outcome data separately for different outcomes. Where information on risk of bias relates to unpublished data or correspondence with a trialist, we will note this in the 'Risk of bias' table. We will not exclude studies on the grounds of their risk of bias, but will clearly report the risk of bias when presenting the results of the studies.

When considering treatment effects, we will take into account the risk of bias for the studies that contribute to that outcome.

We will conduct the review according to this published protocol and report any deviations form it in the 'Differences between protocol and review' section of the systematic review.

## Measures of treatment effect

We will estimate the effect of the intervention using risk ratio for dichotomous data, together with the appropriate associated 95% confidence interval and standardised mean difference for continuous data, together with the 95% appropriate associated confidence interval (Higgins 2011). We will ensure that an increase in scores for continuous outcomes can be interpreted in the same way for each outcome, explain the direction to the reader, and report where the directions were reversed if this was necessary.

## Unit of analysis issues

We will control for unit of analyses errors by re-analysing results while adjusting for clustering. If there is not enough information to re-analyse the results we will try to contact the study authors to obtain the necessary data. If we are not able to access all the data we will not report confidence intervals or P values (EPOC 2017c).

## Dealing with missing data

We will contact investigators to verify key study characteristics and obtain missing outcome data where possible (e.g. when a study is identified as abstract only). We will try to compute missing summary data from other reported statistics. Whenever it is not possible to obtain data, we will report the level of missingness and consider how that might impact the certainty of the evidence.

## Assessment of heterogeneity

If we find studies that are similar enough to combine, we will conduct a meta-analysis (Borenstein 2009). We will use the I<sup>2</sup> statistic to measure heterogeneity among the trials in each analysis. If we identify substantial heterogeneity we will explore it by prespecified subgroup analysis.

## Assessment of reporting biases

We will attempt to contact study authors, asking them to provide missing outcome data. Where this is not possible, and the missing data are thought to introduce serious bias, we will explore the impact of including such studies in the overall assessment of results. If we are able to pool more than 10 trials, we will create and examine a funnel plot to explore possible publication biases, interpreting the results with caution (Sterne 2011).

## Data synthesis

We will undertake meta-analyses only where this is meaningful, that is, if the treatments, participants, and the underlying clinical question are similar enough for pooling to make sense (Borenstein 2009). A common way that trialists indicate when they have skewed data is by reporting medians and interquartile ranges. When we encounter this we will note that the data were skewed and consider the implication of this. Where multiple trial arms are reported in a single trial, we will include only the relevant arms. If two comparisons (e.g. intervention A versus usual care and intervention B versus usual care) must be entered into the same meta-analysis, we will halve the control group to avoid double-counting.

## GRADE and 'Summary of findings' table

Two review authors will independently assess the certainty of the evidence (high, moderate, low, and very low) using the five GRADE considerations (risk of bias, consistency of effect, imprecision, indirectness, and publication bias) (Guyatt 2008). We will use methods and recommendations described in the *Cochrane Handbook for Systematic Reviews of interventions* (Schünemann 2017), and the EPOC worksheets (EPOC 2017d), and using GRADEpro software (GRADEpro GDT). We will resolve disagreements on certainty ratings by discussion and provide justification for decisions to down- or up-grade the ratings using footnotes in the table and make comments to aid readers' understanding of the review where necessary. We will use plain language statements to report these findings in the review (EPOC 2017e).

We will create 'Summary of findings' tables for the main intervention comparison(s) and include the following outcomes to draw conclusions about the certainty of the evidence within the text of the review: time between presentation and appropriate response by provider; mortality and health-related quality of life; clients acceptability of and satisfaction with the intervention; resource use; and unintended consequences. If we find enough studies, we will create one summary of findings table each for more common health conditions (e.g., heart failure, diabetes, mental health, asthma). If we find enough studies, we will separate studies according to their main function (monitoring, consulting, and delivering treatment).

We will consider whether there is any additional outcome information that was not able to be incorporated into meta-analyses and note this in the comments and state if it supports or contradicts the information from the meta-analyses. If it is not possible to meta-analyse the data we will summarise the results in the text.

## Subgroup analysis and investigation of heterogeneity

We plan to carry out the following subgroup analyses.

1. Healthcare provider type (e.g. lay versus professional healthcare provider). Lay health workers often provide healthcare in settings where healthcare resources are scarcer, for example targeting epidemics in low- and middle-income countries and the specific health needs of minority communities in high-income countries (Lewin 2010). Because lay health workers have no formal professional tertiary education, their knowledge and beliefs might moderate the effects of the intervention (Akinlua 2016).

2. Type of communication channel (e.g. voice, SMS, interactive voice response, image exchange). Different communication channels might be used differently and serve distinct purposes (Ventola 2014), as well as providing a more comprehensive and realistic opportunity for communication.

3. Setting/income level (e.g. low-income versus high-income settings). Traditionally, the quality of healthcare is lower in lowand middle-income countries (Mills 2014), which might

increase heterogeneity and pre-empt the pooled analysis of studies conducted in different settings.

We will use the following outcomes in subgroup analysis.

1. Time between presentation and appropriate management by provider, including change in time for clients to receive/access health services and information;

- 2. clients' health status and well-being; and
- 3. clients' utilisation of healthcare services.

We will use the formal statistical techniques of Mantel-Haenszel and regression to test for subgroup interactions (Mantel 1959).

## Sensitivity analysis

We will perform sensitivity analyses defined a priori to assess the robustness of our conclusions and explore its impact on effect sizes. This will involve restricting the analysis to published studies and restricting the analysis to studies with a low risk of bias.

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\* Indicates the major publication for the study

# APPENDICES

## Appendix 1. MEDLINE search strategy

Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) 1 exp Health Personnel/

2 (((health or medical or healthcare) adj (personnel or worker\* or auxiliar\* or staff or professional\*)) or doctor\* or physician\* or GP or general practitioner? or family doctor or nurse\* or midwi\* or clinical officer\* or pharmacist\* or dentist\* or ((birth or childbirth or labor or labour) adj (attendant? or assistant?))).ti,ab,kw.

3 ((lay or voluntary or volunteer? or untrained or unlicensed or nonprofessional? or non professional?) adj5 (worker? or visitor? or attendant? or aide or aides or support\$ or person\$ or helper? or care? or caregiver? or care giver? or consultant? or assistant? or staff)).ti,ab,kw.

4 (paraprofessional? or paramedic or paramedics or paramedical worker? or paramedical personnel or allied health personnel or allied health worker? or support worker? or home health aide?).ti,ab,kw.

5 ((community or village? or lay) adj3 (health worker? or health care worker?) .ti,ab,kw.

6 (doula? or douladural? or barefoot doctor?).ti,ab,kw.

7 1 or 2 or 3 or 4 or 5 or 6

8 Cell Phones/

9 Smartphone/

10 MP3-Player/

11 Computers, Handheld/

12 ((cell\* or mobile\*) adj1 (phone\* or telephone\* or technolog\* or device\*)).ti,ab,kw.

13 (handheld or hand-held).ti,ab,kw.

14 (smartphone\* or smart-phone\* or cellphone\* or mobiles).ti,ab,kw.

15 ((personal adj1 digital) or (PDA adj3 (device\* or assistant\*)) or MP3 player\* or MP4 player\*).ti,ab,kw.

16 (samsung or nokia).ti,ab,kw.

17 (windows adj3 (mobile\* or phone\*)).ti,ab,kw.

18 android.ti,ab,kw.

19 (ipad\* or i-pad\* or ipod\* or i-pod\* or iphone\* or i-phone\*).ti,ab,kw.

20 (tablet\* adj3 (device\* or computer\*)).ti,ab,kw.

21 Telemedicine/

22 Videoconferencing/ or Webcasts as topic/

23 Text Messaging/

24 Telenursing/

25 (mhealth or m-health or "mobile health" or ehealth or e-health or "electronic health").ti,ab,kw.

26 (telemedicine or tele-medicine or telehealth or tele-health or telecare or tele-care or telenursing or tele-nursing or telepsychiatry or tele-psychiatry or teleconsult\* or

27 (videoconferenc\* or video-conferenc\* or webcast\* or web-cast\*).ti,ab,kw.

28 (((text\* or short or voice or multimedia or multi-media or electronic or instant) adj1 messag\*) or instant messenger).ti,ab,kw.

29 (texting or texted or texter\* or ((sms or mms) adj (service\* or messag\*)) or interactive voice response\* or IVR or voice call\* or callback\* or voice over internet or VOIP).ti,ab,kw.

30 (Facebook or Twitter or Whatsapp\* or Skyp\* or YouTube or "You Tube" or Google Hangout\*).ti,ab,kw.

31 Mobile Applications/

32 "mobile app\*".ti,ab,kw.

33 Social Media/

34 (social adj (media or network\*)).ti,ab,kw.

35 Reminder Systems/

36 (remind\* adj3 (text\* or system\* or messag\*)).ti,ab,kw.

37 Electronic Mail/

38 (electronic mail\* or email\* or e-mail or webmail).ti,ab,kw.

39 Medical informatics/ or Medical informatics applications/

40 Nursing informatics/ or Public health informatics/

41 ((medical or clinical or health or healthcare or nurs\*) adj3 informatics).ti,ab,kw.

42 Multimedia/

43 Hypermedia/

44 Blogging/

45 (multimedia or multi-media or hypermedia or hyper-media or blog\* or vlog\* or web-log\*).ti,ab,kw.

46 Interactive Tutorial/

47 Computer-Assisted Instruction/

48 ((interactive or computer-assisted) adj1 (tutor\* or technolog\* or learn\* or instruct\* or software or communication)).ti,ab,kw.

49 or/8-48

50 randomized controlled trial.pt.

51 controlled clinical trial.pt.

52 randomized.ab.

53 placebo.ab.

54 drug therapy.fs.

55 randomly.ab.

56 trial.ab.

57 groups.ab.

58 or/50-57

59 exp animals/ not humans.sh.

60 58 not 59

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10

61 7 and 49 and 60 62 limit 61 to yr="2000 -Current"

# CONTRIBUTIONS OF AUTHORS

Conceiving and designing the protocol: MF, DGB, CG, SL, GM, SS, TT Co-ordinating the protocol: DGB, SS Writing the protocol: DGB, SS Providing general advice on the protocol: BB, MF, CG, SL, NH, GM, NM, TT Securing funding for the protocol: GM, TT

# DECLARATIONS OF INTEREST

DGB: I was commissioned by the WHO to conduct this review.

BB: none known.

MF: none known.

CG: none known.

NH: Since June 2016 I have been employed by Cochrane Response, an evidence services unit operated by the Cochrane Collaboration. Cochrane Response was contracted by the WHO to produce this review.

SL: I am the Joint Co-ordinating Editor for the Cochrane Effective Practice and Organisation of Care Review Group.

NM: I previously worked for Enhanced Reviews Ltd, a company that conducts systematic reviews mostly for the public sector. Since June 2016 I have be employed by Cochrane Response, an evidence services unit operated by the Cochrane Collaboration. Cochrane Response was contracted by the WHO to produce this review.

GM: owns stock in Apple Computer.

TT: none known.

SS: none known.

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