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Telehealthcare for remote monitoring and consultations for people with chronic obstructive pulmonary disease (COPD) (Protocol)

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T A B L E   O F   C O N T E N T S

[Intervention Protocol]

Telehealthcare for remote monitoring and consultations for people with chronic obstructive pulmonary disease (COPD)

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A B S T R A C T

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

To assess the effectiveness of remote telehealthcare for monitoring and consultation with a healthcare professional for people with COPD.

B A C K G R O U N D

Description of the condition

Non-communicable or chronic diseases contribute to more than half of deaths globally (Benziger 2016). The World Health Organization has predicted that chronic obstructive pulmonary disease (COPD) will be among the top causes of death by 2030, and the Global Burden of Disease (GBD) study shows that it is the third leading cause of death claiming an estimated three million deaths from 2005 to 2015, with a prevalence of 251 million cases of COPD globally during this time period (GBD 2015; WHO 2018). Although most information about COPD deaths comes from high-income countries, it is known that 90% of COPD deaths occur in low-to-middle income countries (WHO 2018).

COPD represents 2.6% of the entire global burden of disease (GBD 2015), but it is still a growing global epidemic as people suffer as a result of under-recognition, underdiagnosis and under-treatment (Quaderi 2018).

While there is a significant burden of COPD on people in high-income countries, this is compounded in low- to middle-income countries by poverty and greater exposure to smoking and environmental factors including outside and household air pollution (Quaderi 2018). It is expected that continued exposure to risk factors, population growth and ageing will further increase the burden of this disease (Lopez-Campos 2016). Disease severity, symptoms (e.g. frequent exacerbations leading to hospitalisation) and other morbidities (e.g. cardiovascular disease) that commonly coexist (in approximately 30% to 57% of people with COPD), increase burden on people and their carers, as well as an economic burden on healthcare systems (Udsen 2017). Respiratory diseases

make up approximately 6% of the total healthcare budget in the EU, and more than half of this cost is attributed to COPD (ATS 2014). There is a direct correlation between severity of COPD, the number of coexisting conditions and increasing cost of care (GOLD 2018).

COPD is a chronic lung disease characterised by persistent respiratory symptoms and limited airflow due to airway or alveolar abnormalities (or both) resulting from significant exposure to noxious particles or gases (including tobacco smoking and environmental factors such as exposure to biomass fuel, and air pollution) (WHO 2018). Diagnosis of COPD is considered when an person has symptoms including dyspnoea, cough, sputum production, or a combination of these and demonstrated by spirometry (presence of postbronchodilator forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) of less than 70%) that confirms the presence of persistent airflow limitation (GOLD 2017). Exacerbations occur with increasing frequency as the disease progresses, leading to increased risk of hospitalisation or mortality (or both) (BLF 2018a; GOLD 2018). Despite optimisation of treatments, people with COPD experience debilitating symptoms (e.g. frequent exacerbations, lung infection, reduced self-care capability, limited physical function, anxiety, depression and cognitive deterioration) and that can have an impact on their functional status, access to health services and quality of life. There is also a burden on 'informal' carers as they are the main providers of care as they are often involved in long-term hands-on care, which can have a physical, emotional and financial impact on the career (Andrianopoulos 2017; Farquhar 2018).

Description of the intervention

Telehealthcare refers to the "use of information and communication technology to facilitate communication or transfer of information between patient and healthcare provider over a distance" (WHO 2010). Remote monitoring is a form of telehealthcare that can facilitate timely transfer of patient data, including physiological parameters (e.g. oxygen saturation, blood pressure) through digital devices (e.g. telephone line or web-based devices) to health professionals (Annandale 2011).

Remote monitoring has the potential to alert healthcare professionals to changes in a person's symptoms early in deterioration (McLean 2011), allowing the best opportunity for early intervention. Early intervention is known to decrease exacerbation severity, hospitalisation frequency and disease progression in COPD (GOLD 2018). Additionally, serial monitoring provides a more robust picture of a person's condition when compared with the single snapshot or retrospective symptoms recalled by the patient (or both), that clinicians commonly rely on in traditional face-to-face consultations (Breen 2015).

Remote telehealthcare encompasses asynchronous and synchronous technologies. Asynchronous telehealthcare (e.g. store and forward technology) does not require live interaction with the person when data are collected. The data are collected in a file format that is then sent to the necessary healthcare professional via a secured encrypted internet connection, allowing healthcare professionals to receive and analyse these data as they would if the data were collected from the person in a usual clinic setting (McLean 2011). Synchronous telehealthcare refers to real-time technology that facilitates live streaming of medical images and video (AMD Global Telemedicine 2015; McLean 2011). Real-time remote consultations (i.e. interaction between the person and the healthcare professional via telephone or web-based applications (e.g. Skype or text messaging)) can be provided in addition to face-to-face home visits or clinic visits (Hernandez 2014).

How the intervention might work

Hospital admissions and readmissions pose significant burden on healthcare services, with respiratory disease contributing as the second most common cause of emergency-hospital admissions in the UK (BLF 2018b). As populations age, and as people live longer with chronic conditions, there is a need to explore more efficient approaches to healthcare delivery (McLean 2011) that are flexible and tailored, and emphasise people's participation to enable them to engage in management activities that affect their day-to-day activities (Luhr 2018). Remote monitoring and remote consultation (with a health professional), as forms of telehealthcare interventions in addition to usual care, provide closer and more timely monitoring of a person's condition in their own home, and early intervention for fluctuations and exacerbations of COPD. As there is a need for ongoing monitoring and management due to ongoing fluctuation in disease and symptoms, people with COPD often have difficulty accessing face-to-face services. Telehealthcare interventions may allow for serial collection of data over a longer period, a benefit over traditional face-to-face healthcare settings where the clinician often relies on a clinical snapshot provided by the patients at the time of the face-to-face consultation. Ultimately these types of interventions have the potential to optimise COPD management and consequently reduce hospitalisations and improve quality of life for people with COPD.

Why it is important to do this review

Although there is an argument for healthcare providers to promote telehealthcare interventions, it is not clear whether remote monitoring or consultations improve outcomes for people with COPD. Evidence from systematic reviews for effectiveness that have been published are mixed, as some report that there is a potential for telehealthcare interventions in improving health-related outcomes.

Two systematic reviews have been published on the topic (Lundell 2015; McLean 2011). Our current scoping searches suggest that

more than 50 new publications of potentially relevant studies may be available since the last Cochrane Review was published.

Similarly, evidence for cost-effectiveness of telehealthcare is limited and unclear, with one such trial showing that telehealthcare plus usual care had similar quality adjusted life years (QALY) to usual care alone and was not cost-effective in addition to standard support and treatment (Henderson 2013).

Therefore, it is essential to determine which remote telehealthcare interventions (i.e. remote telehealthcare for monitoring, or remote consultations with a health professional in addition to usual care) are clinically effective and safe for people with COPD, including those who may live a considerable distance from healthcare facilities.

OBJECTIVES

To assess the effectiveness of remote telehealthcare for monitoring and consultation with a healthcare professional for people with COPD.

METHODS

Criteria for considering studies for this review

Types of studies

We will include randomised controlled trials (RCTs) only. We will include cluster randomised trials, but will only meta-analyse data from such trials if they have been adjusted to account for clustering (or we can adjust them ourselves). We will include cross-over trials, but will only meta-analyse data from such trials if we can obtain outcome data pre-crossover, as we cannot exclude a carry-over effect. We will include studies reported in full text, those published as an abstract only and unpublished data. We will include studies from primary care and hospital settings.

Types of participants

We will include adults (aged 18 years and over) who have a diagnosis of COPD according to established criteria (e.g. Global Initiative for Chronic Obstructive Lung Disease (GOLD) staging, European Respiratory Society (ERS), or American Thoracic Society (ATS) criteria), and including adults with any comorbidities. We will exclude adults who are diagnosed with asthma, cystic fibrosis, bronchiectasis or other respiratory conditions.

Types of interventions

We will include studies that include the following intervention and comparator.

1. Remote monitoring (linked to a healthcare professional) plus usual care versus usual care alone (as reported by trialists).

2. Remote consultation (e.g. real-time contact with a health professional) plus usual care versus usual care alone (e.g. face-to-face visit for a check-up in a health service with a health professional, or as reported by trialists).

3. Remote monitoring or remote consultation versus usual care (e.g. where telehealthcare has replaced an element of usual face-to-face care).

We will analyse data from the above three groups separately.

We will include the following telehealthcare intervention categories.

1. Wired or wireless telehealthcare systems to monitor physiological parameters that are processed or authorised by a healthcare professional with feedback to the patient via telephone or video.

2. Store and forward telehealthcare systems to transfer data regarding the condition of the patient to healthcare professionals to assess offline.

3. Internet-based telecommunication such as video or telephone links with healthcare professionals (e.g. Skype, text messaging or email).

We will exclude interventions that deliver or monitor pulmonary rehabilitation remotely.

Types of outcome measures

Primary outcomes

1. Exacerbations (as defined by trialists, depending on the data available, we will extract either number of participants experiencing one or more exacerbation, or the exacerbation rate, or both).

2. Quality of life (validated scales, such as the St George's Respiratory Questionnaire (SGRQ)).

3. Hospitalisation utilisation (e.g. emergency department presentation, hospitalisation, readmission and length of stay. As defined by trialists, depending on the data available, we will extract number of participants who require hospitalisation, or the hospitalisation utilisation rate, or both).

4. Mortality (all-cause).

We will report outcomes using the following time points:

1. three months or greater to less than six months;

2. six months or greater to less than 12 months;

3. 12 months or greater.

Secondary outcomes

1. Adverse effects (i.e. the number of participants with adverse effects).
2. Anxiety and depression (validated scales, e.g. Hospital Anxiety and Depression Scale).
3. Self-efficacy (as defined by trialists, depending on the data available).
4. Participant satisfaction (as defined by trialists, depending on the data available).

Reporting one or more of the outcomes listed here in the study will not be an inclusion criterion for the review.

Search methods for identification of studies

Electronic searches

We will identify studies from the Cochrane Airways Trials Register, which is maintained by the Information Specialist for the Group. The Cochrane Airways Trials Register contains studies identified from several sources:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL), through the Cochrane Register of Studies Online (crso.cochrane.org);
2. weekly searches of MEDLINE OvidSP from 1946;
3. weekly searches of Embase OvidSP from 1974;
4. monthly searches of PsycINFO OvidSP from 1967;
5. monthly searches of CINAHL EBSCO (Cumulative Index to Nursing and Allied Health Literature) from 1937;
6. monthly searches of AMED EBSCO (Allied and Complementary Medicine);
7. handsearches of the proceedings of major respiratory conferences.

Studies contained in the Trials Register are identified through search strategies based on the scope of Cochrane Airways. Details of these strategies, as well as a list of handsearched conference proceedings are in Appendix 1. See Appendix 2 for the search terms we will use to identify studies for this review.

We will search the following additional sources with appropriately adapted search terms:

1. US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (www.clinicaltrials.gov);
2. World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch);
3. IEEE Xplore Digital Library.

We will search the Cochrane Airways Trials Register and additional sources from inception to present, with no restriction on language of publication.

Searching other resources

We will check the reference lists of all primary studies and review articles for additional references. We will search relevant manufacturers' websites for study information.

We will search for errata or retractions from included studies published in full text on PubMed and report the date this was done within the review.

Data collection and analysis

Selection of studies

Two review authors (SJ, CT) will screen titles and abstracts of the search results independently and code them as 'retrieve' (eligible or potentially eligible/unclear) or 'do not retrieve.' We will retrieve the full-text study reports of all potentially eligible studies and two review authors (SJ, CT) will independently screen them for inclusion, recording the reasons for exclusion of ineligible studies. We will resolve any disagreements through discussion or, if required, we will consult a third review author (RD). We will identify and exclude duplicates and 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 record the selection process in sufficient detail to complete a PRISMA flow diagram and 'Characteristics of excluded studies' table (Moher 2009).

Data extraction and management

We will use a Microsoft Excel spreadsheet to collect data for study characteristics, interventions and outcomes, that has been piloted on at least one study in the review. One review author (SJ) will extract the following study characteristics from included studies.

1. Methods: study design, total duration of study, details of any 'run-in' period, number of study centres and location, study setting, withdrawals and date of study.
2. Participants: number, mean age, age range, gender, severity of condition, diagnostic criteria, baseline lung function, smoking history, inclusion criteria and exclusion criteria.
3. Interventions: intervention (including adherence), comparison.
4. Outcomes: primary and secondary outcomes specified and collected, and time points reported.
5. Notes: funding for studies and notable conflicts of interest of trial authors.

Two review authors (SJ, CT) will independently extract outcome data from included studies. We will note in the 'Characteristics of included studies' table if outcome data were not reported in a usable way. We will resolve disagreements by consensus or by involving a third review author (RD). One review author (SJ) will transfer data into Review Manager 5 (Review Manager 2014). We will double-check that data are entered correctly by comparing the data presented in the systematic review with the study reports. A

second review author (CT) will spot-check study characteristics for accuracy against the study report.

We will produce a table summarising the key characteristics of each study, including region, baseline characteristics of participants, size of study, interventions investigated and reported effect for each study.

Assessment of risk of bias in included studies

Two review authors (SJ, CT) will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). We will resolve any disagreements by discussion or by involving another review author (RD). 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. 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 judgement in the 'Risk of bias' table. We will summarise the risk of bias judgements 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 participant-reported pain scale). Due to the nature of the intervention, it is likely that it will not be possible to blind participants to the intervention. We will take this into account in the risk of bias and GRADE assessment and will consider the potential impact of lack of blinding on a case-by-case basis (e.g. subjective outcomes are likely to be more at risk than objective 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.

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

Assessment of bias in conducting the systematic review

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

Measures of treatment effect

We will analyse dichotomous data as odds ratios (OR) and continuous data as the mean difference (MD) if studies use the same scale or standardised mean difference (SMD) if studies use different scales. If data from rating scales are combined in a meta-analysis, we will ensure they are entered with a consistent direction of effect (e.g. lower scores always indicate improvement).

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.

We will present data as forest plots where it is possible to show size and direction of effect for treatments with 95% confidence intervals (CI) (certainty) using Review Manager 5 (Review Manager 2014).

We will describe skewed data narratively (e.g. medians and interquartile ranges for each group).

Where a single study reports multiple trial arms, we will include only the relevant arms. We will report details of the additional arms in the 'Characteristics of included studies' table, If two comparisons (e.g. intervention A versus usual care and intervention B versus usual care) are combined in the same meta-analysis, we will either combine the active arms or halve the control group to avoid double-counting.

If adjusted analyses are available (ANOVA or ANCOVA) we will use these as a preference in our meta-analyses. If both change from baseline and endpoint scores are available for continuous data, we will use change from baseline unless there is low correlation between measurements in participants. If a study reports outcomes at multiple time points, we will use the latest time point. If studies report post-treatment follow-up, we will extract this and report it narratively.

We will use intention-to-treat (ITT) or 'full analysis set' analyses where they are reported (i.e. those where data have been imputed for participants who were randomly assigned but did not complete the study) instead of completer or per protocol analyses.

Unit of analysis issues

For dichotomous outcomes, we will use participants, rather than events, as the unit of analysis (e.g. number of participants admitted to hospital, rather than number of admissions per participant). However, if a study reports rate ratios, we will analyse them on this basis. We will only meta-analyse data from cluster-RCTs if the available data are adjusted (or can be adjusted), to account for the clustering.

Dealing with missing data

We will contact investigators or study sponsors to verify key study characteristics and obtain missing numerical outcome data where possible (e.g. when a study is published as an abstract only). Where this is not possible, and the missing data are thought to introduce serious bias, we will take this into consideration in the GRADE rating for affected outcomes.

Assessment of heterogeneity

We will use the I² statistic to measure heterogeneity among the studies in each analysis. If we identify substantial heterogeneity (I² of 40% or more), we will report it and explore the possible causes by prespecified subgroup analysis.

Assessment of reporting biases

If we are able to pool more than 10 studies, we will create and examine a funnel plot to explore possible small-study and publication biases.

Data synthesis

We will use a random-effects model, with the assumption that the included studies may have heterogeneous, but related, intervention effect estimates (due to the clinical nature of the intervention). We will perform a sensitivity analysis with a fixed-effect model.

'Summary of findings' table

We will create a 'Summary of findings' table using the following outcomes: exacerbations, quality of life, hospitalisation utilisation, mortality and adverse effects. We will present effect size with 95% CIs for each outcome as well as absolute effects (generated by GRADEpro GDT software). We will use the five GRADE considerations (risk of bias, consistency of effect, imprecision, indirectness and publication bias) to assess the overall certainty of a body of evidence (low, moderate or high certainty) as it relates to the studies that contribute data for the prespecified outcomes. We will use the methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), using GRADEpro software (GRADEpro GDT). We will justify all decisions to downgrade the quality of studies using footnotes and we will make comments to aid the reader's understanding of the review where necessary.

We will apply clinical importance of results using published minimal important difference (MID) if available (e.g. SGRQ has well established MIDs in the literature).

Subgroup analysis and investigation of heterogeneity

We plan to carry out the following subgroup analyses.
1. Recent hospitalisations (within six months versus no hospitalisations).
2. Cognitive function (presence or absence, e.g. Mini-Mental State Examination score less than 26).
3. Mean number of comorbidities (one or fewer versus more than one; e.g. Charleson index).
We will use the following outcomes in subgroup analyses.
1. Exacerbations.
2. Quality of life.
3. Hospitalisation utilisation.
4. Mortality.
We will use the formal test for subgroup interactions in Review Manager 5 (Review Manager 2014).

Sensitivity analysis

We plan to carry out the following sensitivity analyses, removing the following from the primary outcome analyses.
1. Studies with high risk of bias in one or more domains.
We will compare the results from a fixed-effect model using the random-effects model.

ACKNOWLEDGEMENTS

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* Indicates the major publication for the study

APPENDICES

Appendix 1. Sources and search methods for the Cochrane Airways Trials Register

Electronic searches: core databases

Database	Frequency of search
CENTRAL (the Cochrane Library)	Monthly
MEDLINE (Ovid)	Weekly
Embase (Ovid)	Weekly
PsycINFO (Ovid)	Monthly
CINAHL (EBSCO)	Monthly
AMED (EBSCO)	Monthly

Handsearches: core respiratory conference abstracts

Conference	Years searched
American Academy of Allergy, Asthma and Immunology (AAAAI)	2001 onwards
American Thoracic Society (ATS)	2001 onwards
Asia Pacific Society of Respirology (APSR)	2004 onwards

British Thoracic Society Winter Meeting (BTS)	2000 onwards
Chest Meeting	2003 onwards
European Respiratory Society (ERS)	1992, 1994, 2000 onwards
International Primary Care Respiratory Group Congress (IPCRG)	2002 onwards
Thoracic Society of Australia and New Zealand (TSANZ)	1999 onwards

MEDLINE search strategy used to identify studies for the Cochrane Airways Trials Register

Condition search

1. exp Asthma/
2. asthma$.mp.
3. (antiasthma$ or anti-asthma$).mp.
4. Respiratory Sounds/
5. wheez$.mp.
6. Bronchial Spasm/
7. bronchospas$.mp.
8. (bronch$ adj3 spasm$).mp.
9. bronchoconstrict$.mp.
10. exp Bronchoconstriction/
11. (bronch$ adj3 constrict$).mp.
12. Bronchial Hyperreactivity/
13. Respiratory Hypersensitivity/
14. ((bronchial$ or respiratory or airway$ or lung$) adj3 (hypersensitiv$ or hyperreactiv$ or allerg$ or insufficiency)).mp.
15. ((dust or mite$) adj3 (allerg$ or hypersensitiv$)).mp.
16. or/1-15
17. exp Aspergillosis, Allergic Bronchopulmonary/
18. lung diseases, fungal/
19. aspergillosis/
20. 18 and 19
21. (bronchopulmonar$ adj3 aspergillosis).mp.
22. 17 or 20 or 21
23. 16 or 22
24. Lung Diseases, Obstructive/
25. exp Pulmonary Disease, Chronic Obstructive/
26. emphysema$.mp.
27. (chronic$ adj3 bronchiti$).mp.
28. (obstruct$ adj3 (pulmonary or lung$ or airway$ or airflow$ or bronch$ or respirat$)).mp.
29. COPD.mp.
30. COAD.mp.
31. COBD.mp.
32. AECB.mp.
33. or/24-32

34. exp Bronchiectasis/
35. bronchiect$.mp.
36. bronchoect$.mp.
37. kartagener$.mp.
38. (ciliary adj3 dyskinesia).mp.
39. (bronchial$ adj3 dilat$).mp.
40. or/34-39
41. exp Sleep Apnea Syndromes/
42. (sleep$ adj3 (apnoea$ or apnoea$)).mp.
43. (hypopnoea$ or hypopnoea$).mp.
44. OSA.mp.
45. SHS.mp.
46. OSAHS.mp.
47. or/41-46
48. Lung Diseases, Interstitial/
49. Pulmonary Fibrosis/
50. Sarcoidosis, Pulmonary/
51. (interstitial$ adj3 (lung$ or disease$ or pneumon$)).mp.
52. ((pulmonary$ or lung$ or alveoli$) adj3 (fibros$ or fibrot$)).mp.
53. ((pulmonary$ or lung$) adj3 (sarcoid$ or granulom$)).mp.
54. or/48-53
55. 23 or 33 or 40 or 47 or 54

Filter to identify randomised controlled trials

1. exp "clinical trial [publication type]"/
2. (randomised or randomised).ab,ti.
3. placebo.ab,ti.
4. dt.fs.
5. randomly.ab,ti.
6. trial.ab,ti.
7. groups.ab,ti.
8. or/1-7
9. Animals/
10. Humans/
11. 9 not (9 and 10)
12. 8 not 11

The MEDLINE strategy and RCT filter are adapted to identify studies in other electronic databases.

Appendix 2. Search strategy to identify relevant studies from the Cochrane Airways Trials Register

Search line	Search term	Comments
#1	MESH DESCRIPTOR Pulmonary Disease, Chronic Obstructive EXPLODE ALL AND INSEGMENT	
#2	MeSH DESCRIPTOR Bronchitis, Chronic AND IN-SEGMENT	

#3	(obstruct*) near3 (pulmonary or lung* or airway* or air-flow* or bronch* or respirat*) AND INSEGMENT	
#4	COPD:MISC1 AND INSEGMENT	MISC1=field in record where reference has been coded for condition i.e. COPD
#5	(COPD OR COAD OR COBD OR AECOPD):TI,AB, KW AND INSEGMENT	
#6	#1 OR #2 OR #3 OR #4 OR #5	Combines all population (COPD) terms
#7	MESH DESCRIPTOR Telemedicine EXPLODE ALL AND INSEGMENT	Index term includes remote consultation
#8	telehealth* or tele-health* AND INSEGMENT	
#9	telemedicine* or tele-medicine* AND INSEGMENT	
#10	telemanagement or tele-management AND INSEGMENT	
#11	telecare* or tele-care* AND INSEGMENT	
#12	telematic* AND INSEGMENT	
#13	telepharmacy or tele-pharmacy AND INSEGMENT	
#14	telenurs* or tele-nurs* AND INSEGMENT	
#15	tele-homecare or telehomecare AND INSEGMENT	
#16	teleconsultation or tele-consultation AND INSEGMENT	
#17	(remote* or distant or distance) NEAR (consult* or monitor* or care or treat* or therap*) AND INSEGMENT	
#18	(mobile* or digital*) NEXT health* AND INSEGMENT	
#19	ehealth or e-health AND INSEGMENT	
#20	mhealth or m-health AND INSEGMENT	
#21	MESH DESCRIPTOR Technology EXPLODE ALL AND INSEGMENT	
#22	MESH DESCRIPTOR Telephone EXPLODE ALL AND INSEGMENT	Includes cell phones & answering services
#23	MESH DESCRIPTOR Videoconferencing EXPLODE ALL AND INSEGMENT	Includes web casts/podcasts

(Continued)

#24	MESH DESCRIPTOR Electronic Mail EXPLODE ALL AND INSEGMENT	
#25	MESH DESCRIPTOR Text Messaging EXPLODE ALL AND INSEGMENT	
#26	MESH DESCRIPTOR Software EXPLODE ALL AND INSEGMENT	Includes web browsers, video games & mobile applications
#27	MESH DESCRIPTOR Software EXPLODE ALL AND INSEGMENT	Includes smartphones
#28	MESH DESCRIPTOR Computers, Handheld EXPLODE ALL AND INSEGMENT	
#29	MESH DESCRIPTOR Computer-Assisted Instruction AND INSEGMENT	
#30	MESH DESCRIPTOR Decision Making, Computer-Assisted EXPLODE ALL AND INSEGMENT	
#31	MESH DESCRIPTOR Wireless Technology AND INSEGMENT	
#32	MESH DESCRIPTOR Internet EXPLODE ALL AND INSEGMENT	
#33	(internet* or computer* or web* or online*):ti,ab,kw AND INSEGMENT	
#34	(telephone or phone*):ti,ab,kw AND INSEGMENT	
#35	(sms or mms or texting or text messag*):ti,ab,kw AND INSEGMENT	
#36	(video* or skype*):ti,ab,kw AND INSEGMENT	
#37	(email or e-mail or electronic mail):ti,ab,kw AND INSEGMENT	
#38	interactive* or telecommunication* AND INSEGMENT	
#39	wireless* or bluetooth* AND INSEGMENT	
#40	smartphone* or cellphone* AND INSEGMENT	
#41	(iphone* or ipod* or podcast* or ipad* or android* or blackberr* or palm pilot*):ti,ab,kw AND INSEGMENT	

(Continued)

#42	(pda* or personal digital assistant*):ti,ab,kw AND INSEGMENT	
#43	(tablet* or hand-held*) near3 (device or computer) AND INSEGMENT	
#44	social* near3 (media* or network*) AND INSEGMENT	
#45	smart watch or smartwatch AND INSEGMENT	
#46	wearable*:ti,ab,kw AND INSEGMENT	
#47	#7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46	Combines all m-health and technology intervention terms
#48	#47 AND #6	Combine population and intervention terms

CONTRIBUTIONS OF AUTHORS

SJ: drafting of background and methods of protocol. Sifting, data extraction, risk of bias assessment and write-up of full review.

CT: drafting of background and methods of protocol. Sifting, data extraction, risk of bias assessment and write-up of full review.

SP: critical review of protocol, analysis and interpretation, approval of final draft of full review.

RD: conceptual and clinical advice, drafting of background and methods of protocol. Arbitrating conflicts, analysis and interpretation, approval of final draft of full review.

DECLARATIONS OF INTEREST

SJ: is employed full-time as a systematic reviewer by a National Institute for Health Research (NIHR) Programme Grant to complete work on this review.

CT: is employed part-time by an NIHR Programme Grant to complete work on this review and is an academic clinical fellow in pharmacology.

SP: has received payment for lectures including speaking services from Boehringer Ingelheim, NAPP, Novartis, Pfizer, Nutricia, Astra Zeneca and TEVA, and travel expenses from Nutricia, Astra Zeneca and TEVA. SP has no conflicts of interests related to the review.

RD: has no conflict of interest and is employed full time as a Senior Research Fellow within an academic unit.

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