Unsupervised remote spirometry vs supervised clinic spirometry: a protocol for a systematic review

Citation

Rohan Anand, Rebecca McLeese, Jonathan Stewart, John Busby, Mike Clarke, Judy Bradley. Unsupervised remote spirometry vs supervised clinic spirometry: a protocol for a systematic review. PROSPERO 2021 CRD42021272816 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42021272816

Review question

The primary objective of this methodology review is to determine if results from remote spirometry, completed unsupervised, are significantly different to those from clinic spirometry completed with the supervision of a clinician.

Secondary outcomes include: quality criteria, adherence, cost, participant satisfaction/acceptability and training standards.

Searches

Searches for relevant studies will be conducted from inception to present on the electronic databases MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), and a grey literature search will be done using Open Access Theses and Dissertations (OATD).

In addition, the websites of known manufacturers of spirometers will be searched, and the reference lists of eligible studies or related reviews will be checked for additional studies.

Forward citation screening of eligible studies will also be conducted.

The full search strategy including MeSH terms will be validated by a medical librarian.

Only publications in English will be included unless appropriate translation can be sourced.

Conference abstracts will be included.

Additional search strategy information can be found in the attached PDF document (link provided below).

Types of study to be included

This will be a methodology review assessing differences between methods used in trials and clinical practice rather than assessing the effects of the care itself (Clarke 2020). Studies will be included if they compare unsupervised spirometry performed by participants to spirometry performed by participants with clinician supervision. Eligible studies can be cross-sectional, longitudinal, randomised or non-randomised, or crossover studies as long as the participants receive both forms of spirometry. The methodology studies can be sub-studies embedded within another study, such as a clinical trial of medication. However, we will exclude studies in which there is no comparison group.

Condition or domain being studied

Measurements of lung function give an indication of the degree of airflow obstruction and disease severity in various respiratory conditions including chronic obstructive pulmonary disease (COPD), asthma and bronchiectasis (Halpin et al., 2021; Loponen et al., 2018; Pasteur et al., 2010). As per the definitions of the European Respiratory Society (ERS) and American Thoracic Society (ATS), spirometry is the term given to the series of lung function tests that measure the total air that is expired and inspired with maximal effort. Traditionally, patients perform spirometry in a clinic setting under the supervision of a trained clinician and using an acceptable technique according to standard criteria (Moore 2012; Graham et al., 2019). However, technological advances in spirometers have increased the opportunities for home monitoring and low-cost, self-calibrating, portable devices are now available for use by patients independently in clinical trials and in routine care (Carpenter et al., 2018). Remote lung function monitoring can allow for more pragmatic trial design and support the use of virtual visits and telemedicine. This has been accelerated by the COVID-19 pandemic where many trials and routine clinical services recommended the use of remote visits and

assessments where possible (Quer et al., 2021; Hartman et al., 2020).

Participants/population

Participants will be both adults and children of all ages. The eligible population will not be limited by any disease or clinical area and can include healthy individuals.

Intervention(s), exposure(s)

This will be the participants' use of unsupervised spirometry using a spirometer. 'Unsupervised' will be defined as the participants completing their lung function in the complete absence of a clinician or other professional support. This might be done outside of a hospital or healthcare clinic and be in an environment such as the participant's own home but could be done in a separate room in a health facility, away from the staff. A spirometer will be defined as any device or instrument that can measure common lung function parameters via the volume of air entering and leaving the lungs. The four commonly used measures that are derived from spirometry that are of particular interest in this review are the forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), forced expiratory flow (FEF25–75) and peak expiratory flow (PEF) (Moore 2012). Other related respiratory measurements such as the resting respiratory rate, respiratory sounds and oxygen levels will be excluded.

Comparator(s)/control

This will be the participants' use of supervised spirometry using a spirometer. This can be the same or be a different device to that in the intervention group but must fit the definition in the previous section. 'Supervised' will be defined as the presence of a clinician or other relevant professional along with the participant when they complete spirometry and can include virtual assistance via telephone or videolink. The supervision may include specific advice and encouragement to the participant. The location is likely to be, but is not limited to, a professional setting such as a hospital, healthcare clinic or GP surgery.

Main outcome(s)

There is no core outcome set available for assessing spirometry in the broad range of respiratory conditions to be covered by this methodology review.

The primary outcomes are:

• Measurements of lung function (supervised and unsupervised) including FEV1, FVC, FEF25–75, PEF, FEVx*, tidal volume (TV), forced inspiratory flow (FIF) and maximal voluntary ventilation (MVV). For each individual parameter, mean differences and 95% limits of agreement (LoA) with their 95% confidence intervals (CIs), will be primary outcome measures along with any correlations and the number of observations in the analysis.

**FEVx is Forced expiratory flow where x is any number representing time in seconds.*

Additional outcome(s)

Secondary outcomes include:

• Standards of quality criteria applied to the spirometers or analysis;

• Cost differences/cost analysis;

• Participant satisfaction/acceptability;

• Details of training protocols directed towards patient home spirometry;

• Technical issues/challenges.

Measures of effect

Measures of effect (secondary outcomes):

Secondary outcomes will be reported in tables and using simple summary statistics if appropriate.

In quantitative terms, ‘quality’ of FEV1 and FVC spirometry will be defined as 3 to 8 spirometry readings where the difference between the largest and the next largest value is ?0.150L and it meets various calibration criteria to ensure verification between flow or volume measured by sensors and the actual flow or volume (Graham et al., 2019). Three additional elements will be extracted: “accurate and precise instrumentation, a patient/subject capable of performing acceptable and repeatable measurements.” (Ruppel and Enright 2012).

Data extraction (selection and coding)

Selection of studies:

Searches will be completed by one review author. Search results will be imported into the systematic review manager software, Covidence. Any two review authors will independently screen titles and abstracts according to the eligibility criteria. Studies deemed potentially eligible will be retrieved for checking of their full text, which will also be done independently by any two reviewers and then passed to a third reviewer for confirmation. Any disagreements or uncertainties will be resolved through discussion with the other review authors.

Data extraction:

Data will be extracted independently for each included study by any two review authors using a customised data extraction form developed in Covidence. This will be adapted as necessary after piloting from an initial batch of studies. Information will be extracted on the type and setting of the study, eligibility criteria, recruitment information, participant characteristics (including sex, age and disease area), nature of the spirometers in each group (e.g. brand, lung function parameters measured, power analysis, limits of agreement, clinically important differences, quality criteria, training provided), nature of the supervision, setting and time-points of measurements, analysis conducted (e.g. Bland-Altman, type of correlation, regression analysis) and other outcomes as described above. For any Bland-Altman analysis, 13 key features as identified by Abu-Arafeh (2016) will be extracted. When LoA are not presented, data will be extracted from which the LoA could be derived (e.g., SD of the difference or root mean square error).

Any disagreements will be resolved through discussion between the two extractors and, if required, with consultation of the other review authors. If any of the required data are not available or insufficient from the included study publications, this will be requested from the corresponding author of the study.

Risk of bias (quality) assessment

Risk of bias of the included studies that are randomised trials will be assessed using the Cochrane Risk of Bias Tool Version 2 (RoB 2; Sterne et al., 2019). Version 2 of the tool replaces the first version, originally published in the 2008 Cochrane Handbook. As RoB 2 reflects current understanding of how the causes of bias can influence study results, it is most appropriate and validated way to assess this risk. There are three separate tools within RoB 2 that will be used accordingly for parallel, cluster and crossover trials. For non-randomised studies, the Risk Of Bias In Non-randomized Studies - of Interventions (ROBINS-I) tool will be used (Sterne et al., 2016).

If the included study is a substudy of a larger study or clinical trial then the risk of bias will be assessed towards the substudy as this review needs to focus the risk of bias in the design for the study comparing supervised versus unsupervised spirometry.

Two review authors will independently use these tools.

To minimise bias in the systematic review itself, it will be conducted using this protocol and any variations will be recorded with relevant reasons for these variations, in the final publication.

Strategy for data synthesis

Measures of effect (primary outcome):

As this is a methodology review with the primary outcome being the differences in measurements between two groups, we expect most eligible studies to have conducted a Bland-Altman analysis and/or correlation using continuous variables from common measurements of lung function such as FEV1 and FVC. For such spirometric parameters, we do not expect to find qualitative (nominal or ordinal) variables.

An average correlation coefficient will be presented for continuous data by calculating pooled correlation coefficients for each pair of comparisons/study. This will be done by transforming correlation coefficients (r values) to a Fishers *z* to determine 95% CI. This will be done using the Hedges-Olkin (1985) method under fixed effects, followed by the DerSimonian and Laird (1986) method, to pool the correlation coefficients under the random effects, all using Stata. Any correlation reported as Spearman's will be converted to Pearson's before meta-analysis.

Similarly, an average difference and limits of agreement from Bland-Altman analysis will be calculated based on the framework by Tipton and Shuster (2018). We will use a random effects approach for combining individual study estimates to obtain pooled estimates of mean difference (bias) and LoA, because of the expected variation in the patient populations and clinical settings, different spirometers, reference standards and quality criteria in the included studies.

All meta-analysis will be undertaken using Stata, with heterogeneity assessed using the I^2 statistic. Pooled analyses will be presented on forest plots and reported with 95% CI and associated p values, where the threshold for statistical significance will be set at 0.05.

Analysis of subgroups or subsets

Subgroup analyses:

If sufficient studies are available, we will undertake subgroup analyses for specific participant categories. This will include exploring benefits in participant with specific conditions and subgroups will be:

• Participant condition according to disease categories or healthy individuals;

• Age (children defined as <18 years old).

Sensitivity analysis:

If sufficient data are available, sensitivity analyses will be performed on the basis of the risk of bias of the included studies. This will include analysis of any change in the outcomes arising from inclusion of studies with higher risk of bias.

Contact details for further information

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Type and method of review
Diagnostic, Meta-analysis, Methodology, Systematic review

Anticipated or actual start date
15 July 2021

Anticipated completion date
30 September 2021

Funding sources/sponsors
Professor Judy Bradley, Queen's University Belfast

Conflicts of interest
RA, JB and MC are investigators in an NIHR HTA funded trial of mucoactives in bronchiectasis that is exploring unsupervised spirometry using PARI portable spirometers (Bradley et al., 2019).
Yes

Language
English

Country
Northern Ireland

Stage of review
Review Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
COVID-19; Delivery of Health Care; Forced Expiratory Volume; Humans; Reproducibility of Results; Respiratory Function Tests; Respiratory Tract Diseases; Self-Management; Self-Testing; Spirometry; Telemedicine

Date of registration in PROSPERO
10 August 2021

Date of first submission
10 August 2021

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.
The record owner confirms that they will update the status of the review when it is completed and will add

publication details in due course.

Versions

10 August 2021