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The impact of using spirometry on clinical decision making and quality of life in children: protocol for a single centre randomised controlled trial

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Abstract

Introduction: Spirometry as a tool for diagnosing and monitoring respiratory illnesses has been available for decades. However, it is underutilised in paediatric practice, other than in specialist clinics. This is unsurprising as there is limited evidence on the benefit of routine spirometry in improving clinical decision making and/or outcomes for children. We hypothesised that using spirometry for children being evaluated for respiratory diseases impacts on clinical decision making and/or improves patient-related outcome measures (PROMs) and/or quality of life (QoL), compared to not using spirometry.

Methods and analysis: We are undertaking a randomised controlled trial (commenced in March 2020) that will include 105 children (aged 4-18 years) recruited from respiratory clinics at Queensland Children's Hospital. Inclusion criteria are: able to perform reliable spirometry and a parent/guardian who can complete questionnaire(s). Children (1:1 allocation) are randomised to clinical medical review with spirometry (intervention group) or without spirometry (control group) within strata of consultation status (new or review), and cough condition (present or absent). The primary outcome is change in clinical decision making (diagnosis and management). The secondary outcomes are: change in PROM scores (State-Trait Anxiety Inventory and/or Parent-Proxy chronic cough QoL questionnaire). Additionally, we are quantifying the doctors' and participants' opinions regarding spirometry (10-point Likert scale).

Ethics and dissemination: The Human Research Ethics Committee (HREC) of the Queensland Children's Hospital approved the study. The trial results will be disseminated through conference presentations, teaching avenues and publications.

Trial registration: Australia and New Zealand Clinical Trials Register, ACTRN12619001686190

Key words: spirometry, child, lung, respiratory, randomised controlled trial

Article summary

Strengths and limitations

- This randomised controlled trial will provide important information on whether the routine use of spirometry in children being evaluated for respiratory problems impacts a doctor's clinical decision making (compared to clinical review alone) and will thus provide the first high-level evidence that may lead to a change in routine clinical practice.
- Patient-reported outcome measures (anxiety level, quality of life score and opinion towards spirometry) will be undertaken to determine the utility of routine spirometry.
- Although this study is randomised with a control group, the intervention could not be blinded to the doctors and participants. Therefore, the outcomes are subject to bias as perceptions may influence doctors' management and participants' scoring of the questionnaire(s).

Introduction

Of the many possible lung function tests used in clinical care, spirometry is the most widely available, established and used.[1] As such, many respiratory societies worldwide e.g. American Thoracic Society (ATS) and European Respiratory Society (ERS) support and/or provide training tools for spirometry testing. Undertaking spirometry is relatively simple as spirometers are portable and relatively inexpensive.

Data from spirometry provides invaluable contribution to the clinical assessment, including assisting in characterising respiratory pathophysiology, grading the severity of lung disorders and monitoring the course of lung disorders and therapeutic interventions.[2,3] Also, spirometry adds an objective element which is beneficial in both clinical practice and research. Hence, its use is recommended in many paediatric clinical guidelines including chronic cough, recurrent wheezing, cystic fibrosis and asthma.[4-7] Other conditions in which spirometry aids in management of children are transfusion-dependent disorders, oncology conditions, connective tissue disorders, neuromuscular weakness, chest wall deformities and scoliosis.[2,8]

Data obtained from spirometry differentiate normal lung function from abnormalities affecting airflow (forced expiratory volume in 1 sec, FEV_1) and lung size (forced vital capacity, FVC). It can also provide data on intra- and extra-thoracic obstruction when the inspiratory and expiratory loops are evaluated. Generally, spirometry can be reliably performed in most children aged >6 years. Improvements in equipment, technology, age-appropriate incentives in spirometer software and modified acceptability and reproducibility criteria for preschool children have meant even younger children (3 years and above) may be able to perform spirometry satisfactorily under the coaching of a well-trained technician.[1,9,10]

Intuitively, spirometry should assist clinicians in assessing and managing respiratory conditions and result in improved patient-related outcome measures (PROMs) e.g. quality of life (QoL) of the patients, however, there is limited published evidence. In the current era of evidence-based medicine, the effect of spirometry on clinical outcomes has rarely been studied with the few paediatric studies published looking only at its use in asthma management. Nair et al[11] found that spirometry changed management in 15% of children with asthma. When spirometry did change treatment decisions, they were more likely to increase (75%) than maintain (20%) or decrease (5%) therapy. Holt et al[12] found that 30% of paediatric asthma exacerbation treatment plans were changed after clinicians viewed spirometry, with an increased percentage of patients receiving steroid, bronchodilator or yellow zone treatment. Finally, Abramson et al[13] undertook a two clustered RCTs of spirometry integrated into regular general practice-based medical review for children with asthma over the duration of one year. They found that neither RCT demonstrated a significant improvement in health related QoL with the use of spirometry compared to not using (Odds Ratio (OR) -0.2 (95%CI -4.9, 4.6) for the first trial and OR 0.17 (95%CI -0.15, 0.5) for the other) nor a change in written asthma action plan (OR 1.11, 95%CI 0.43, 2.87).

While spirometry is widely advocated, it is currently under-utilised. Dombkoski et al[14] reported that only half of surveyed family physicians and general paediatricians use it in children and adults with asthma, and only 21% routinely use spirometry in asthma guideline-recommended situations i.e. establishing an asthma diagnosis, classifying asthma severity and classifying asthma control.[14] Another study by Blain et al[15] reported that only 10% of paediatricians used spirometry consistently on each asthma visit. Further, Bianchi et al[16] found that only a third of children with asthma were referred for spirometry and only one-half of hospitalised children with asthma underwent spirometry during 12-month follow-up. The

low utilisation of spirometry on a day-to-day basis outside of respiratory-focused practices is not surprising due to the limited published data supporting its benefits.

Given the paucity of relevant data, we are undertaking this RCT to compare clinical outcomes of out-patient consultation "with spirometry" versus "without spirometry" to assess the benefit of having spirometry data for both clinicians and patients.

Study objectives and hypotheses

Our primary question is: Does the routine use of spirometry improve the clinical decisions/management of children with suspected or known lung disease? We hypothesise that the routine use of spirometry in children managed by respiratory paediatricians in outpatient clinics alters clinical decision making in diagnosis and/or management.

Our secondary aims are to: 1) determine whether the routine use of spirometry in children managed by respiratory paediatricians in outpatient clinics impacts on children or their parents PROMs and 2) quantify the benefits of routinely using spirometry in clinical practice assessed by a 10-point Likert scale.[17] Our secondary hypothesis is that the integration of spirometry into outpatient consultations with respiratory paediatricians improves PROM(s), specifically in emotional and social domains, evaluated by State-Trait Anxiety Inventory (STAI)[18,19] and/or Parent-Proxy QoL questionnaire for paediatric chronic cough (PC-QoL)[20,21] for those with chronic cough.

Methods and analysis

Study setting and design

We are conducting a single centre RCT with concealed allocation involving children seen at the Department of Respiratory and Sleep Medicine at the Queensland Children's Hospital, Brisbane, Australia. Our study design is summarised in Figure 1, and is in accordance with the recommendations of the Interventional Trial (SPIRIT) guidelines.[22] We recruited our first participant on 17th March 2020 and our study is ongoing with the study anticipated to be completed by early 2022.

Study population

Our inclusion criteria are: 1) children with parent/guardian in attendance and able to provide written consent, 2) children aged 4-18 years able to perform reliable spirometry, 3) parents/guardian able to complete the study questionnaire(s) and 4) children whose respiratory physician is willing to participate in the study.

Exclusion criteria are: 1) previously enrolled or 2) contraindication for spirometry including presence of acute dyspnoea, pneumothorax, haemoptysis, vital signs instability, lung cyst or bleb, and recent (<3 weeks) thoracic or ophthalmic surgery.

Recruitment

Parents/guardians with potentially eligible children are approached during a scheduled respiratory clinic appointment. A team member (WB) discusses the study using the parent/guardian information sheet. If the parent/guardian gives written informed consent and the child is able to perform acceptable spirometry then the child enters the study and is randomised.

All families approached are recorded in a screening log with details including name, date, whether informed consent was obtained or reason for refusal, whether the child was eligible and randomisation number if enrolled in the study.

Randomisation and allocation

A computer-generated permuted block (sizes of 2-6) randomisation sequence, generated by a statistician external to the study team, was prepared prior to commencement of the study. The randomisation is stratified by type of consultation (new patient or review), and presence of chronic cough condition (present or absent). On enrolment, the child is assigned to the next number on the stratified list that is opaque, i.e. the group allocation is concealed from investigators until the participant is recruited. Children are randomised to either routine use of spirometry (intervention) or delayed use of spirometry (controls) (Figure 1). Due to the obviously noticeable difference in intervention vs control groups, blinding is not possible.

Intervention groups

For both groups, the clinical management is at the discretion of the treating specialist. At baseline (T1), all participants undertake baseline PROM surveys (STAI[18,19] and if cough is present, the PC-QoL[20,21]) and are randomised to one of the two groups: intervention group where the doctor undertakes the consultation with the spirometry results being available, or controls where the doctor undertakes the initial consultation without the spirometry results.

After the consultation, the parents in both groups complete the questionnaire(s) for the second time (T2). At this same time point, the doctor is also asked to fill a data collection sheet

regarding the child's diagnosis and management. This completes the study for the intervention group.

In the control group, the doctor is then presented with the child's spirometry and completes the consultation. After completion of the consultation, the parents complete the same questionnaire(s) for a third time (T3) and the doctors complete a final data collection sheet with any change in diagnosis or management after spirometry results are known. Despite the delayed time point of presenting the spirometry to respiratory paediatricians, by the time the child leaves the clinic, all patients would have received the same standard of care. No restrictions on concomitant care were applicable in this study.

Data collection

An outline of study procedures (all occurring during a single outpatient visit) is summarised in Table 1. Data are collected from the interview of the parent/guardian and electronic medical records. On enrolment, demographic data, medical history, medications, tobacco smoke exposure and anthropometrics are recorded. Physical examination is performed and recorded by the treating doctor.

All children are tested using Vyntus Pneumo or Vyntus Spiro spirometers operated through SentrySuite Software (Carefusion Germany 234 GmbH, Hoechburg, Germany) undertaken by experienced paediatric respiratory scientists in accordance with standard guidelines (American Thoracic Society (ATS) and European Respiratory Society (ERS) criteria for lung function testing).[1,23] The measured values are compared with predicted reference values from the Global Lung Function Initiative (GLI)[24] based on the patient's height, age, race and sex.

As mentioned above, depending on study group, the parents complete the same questionnaire(s) two or three times. These time-points are prior to visiting the doctor (T1), after visiting the doctor (T2) and after second consultation with the doctor for controls only (T3). The questionnaires are: (i) STAI for all patients and (ii) PC-QoL for patients with cough. For both questionnaires, parents are given a hard copy of questionnaire(s) to complete on a self-report basis, with the investigator available if any clarification is needed.

The STAI is a long-standing psychological inventory frequently used to measure anxiety. It consists of two 20-item scales measuring 'state' or anxiety about an event, and 'trait' or anxiety proneness as a personality trait. In responding to the STAI, subjects rate their intensity of feeling for each item on a 4-point Likert scale. Based on its scoring key, the score of each of the two scales (state or trait) ranges from 20 to 80, where higher scores reflect higher levels of anxiety.[18,19] A license to reproduce/administer STAI was purchased from Mind Garden, Inc on 15th March 2020.

The PC-QoL is a validated parent-proxy quality of life measure specific for children with chronic cough.[20] The 27 item PC-QoL addresses parents' perception of three domains: the psychological (11 items), physical (11 items), and social (5 items) effect of their child's cough. Subjects are required to use a 7-point Likert-type scale to rate their perception (level of worry/ frequency of negative feelings); the highest intensity of perception gives a score of 1 and absence of perception gives a score of 7. Hence, higher scores reflect better QoL. For interpreting health-related QoL changes, the minimally important difference for the PC-QoL is 0.9.[25]

Prior to leaving the clinic at the completion of the consultation, the parents also score on a 10-point Likert scale "how much did the spirometry help with this clinic visit?", while the doctors are asked to score 3 aspects of its use; "how much did the spirometry (i) contribute to general management, (ii) increases confidence in clinical practice and (iii) aid education/counselling with each patient?" on a 10-point Likert scale. The unipolar scale of 1 to 10 is anchored by increasing degree of agreement, which one means "not at all", five means "somewhat" and ten means "very much so".

Each participant completes the study on the day of enrolment when all study related forms have been completed and outcome data collected. All data are documented on paper-based case report forms (CRFs) using standardised data collection sheets.

Table 1: Timeline of study procedures during a single outpatient visit

	Before seeing doctor	After seeing doctor without spirometry (Only controls)	After seeing doctor with spirometry	Independent review
Written informed consent	√			
Randomised	√			
Medical history	√			
Medical Chart Review	√			
Spirometry with bronchodilator testing	√			√
Clinical assessment for diagnosis and treatment		√	√	√
PC-QoL assessment	√	√	√	
STAI QoL assessment	√	√	√	

Exit criteria during the study

Exit criteria are defined as occurrence within the visit of any of the following: (1) spirometry is unacceptable on independent review, (2) the doctor accidently viewed the spirometry at the start of consultation in the control group or (3) parents withdraw consent for participation, are unable to comply with study intervention or if spirometry related serious adverse event occurred.

Outcome measures

Our primary outcome is the proportion of change in clinical decision making (diagnosis and management) and difference of change scores between groups at T2 (Figure 1). This consists of an *a-priori* list that consists of (i) any change in diagnosis based on 2 categories (disease and severity) and (ii) management based on 4 categories (medication, investigation, follow-up schedule and education). Change in each category is dichotomised as 'yes' or 'no'. Each 'yes' scores one point, so the range in change score is 0 to a maximum of 6 (2 points from change in diagnosis and 4 points from change in management).

Our secondary outcomes are:

1) Difference in change of the questionnaire scores compared with baseline (T1) measured by STAI +/- PC-QoL (i) between two groups at T2 time point and (ii) between two time points, T2 and T3 of control group.
2) Opinions relating to the benefit of integrating spirometry into clinical practice are included as secondary outcomes. A 10-point Likert scale with a series of statements each designed to view a construct from a slightly different perspective is leveraged.

Sample size

The sample size is based on our primary outcome, the proportion of change in clinical decision making. We wish to detect a significant difference between the intervention and control groups. We assume the proportion change in the population is 30% (Ho: p = 0.30). To find a 45% proportion change (alternative p = 0.45) with 5% significance (alpha = 0.05, two-sided) and 90% power (power = 0.90), we require outcome data from 105 children. We did not account for any dropouts as this is a single visit study where a dropout rarely occurs. Participants who withdraw will be replaced to reach the total children of 105.

Data management and statistical analyses and reporting

CRFs are kept confidential and locked. Access to the data is available to research team, unless required by legislative or regulatory agencies and the Human Research Ethics Committee (HREC). No identifying information of the enrolled participants will be included in study reports in order to protect confidentiality.

Data coding and entry will be conducted in accordance with good clinical practice. Data is being entered directly into an SPSS database. Intention-to-treat analyses regardless of subsequent management will be used. We plan to develop a complete statistical analysis plan prior to data analyses, as done for our previous major RCTs.[26,27]

For our primary aim, the impact of utilising spirometry on change in diagnosis and management will be determined by the proportion of change and change scores at the T2 time point. Between the two groups, the proportion of change will be compared using Chi square test to determine the OR with 95% CIs. The difference of change scores will be examined by T-test or Mann-Whitney U test depending on normality of the data.

For secondary aims, the impact of spirometry will be determined by change in STAI and PC-QoL scores compared to baseline and quantified opinions by the 10-point Likert scale. Change in these scores is assessed at T2 for both groups and T3 for controls only. T-test or Mann-Whitney U test will be used to analyse the difference of change in these scores at T2 between the groups. For control group, paired T-test or Wilcoxon test will be used to analyse the difference of change in STAI and PC-QoL between T2 and T3. Other secondary outcomes, the quantified opinions, will be reported as mean with SD or median with range.

Patient and public involvement

Patients and public were not involved in the initial study design but were consulted subsequently.

Ethics, dissemination and safety monitoring

Ethical clearance was granted by the HREC of the Queensland Children's Hospital (HREC/19/QCHQ/58722; protocol version 1.3 dated 1st September 2020). We will publish the results in a major medical journal (using the International Committee of Medical Journal Editors [ICMJE] author guidelines) and share the outcomes with the academic and medical community, funding and relevant patient organisations. Professional writers will not be used.

During the study, participants may report any solicited and spontaneous adverse events at any time. All adverse events are being monitored and serious or unexpected adverse events will be reported to the HREC.

Discussion

We are currently undertaking a single centre open-label RCT to address the question of whether spirometry integrated into outpatient care, compared with not using spirometry, impacts the clinical decision making of specialist respiratory paediatricians and PROMs. The outcomes and time points were chosen carefully as described below.

Rationale for our chosen outcome measures and time frame

To measure the influence of using spirometry on clinical practice, choosing valid outcomes informed by consumers, i.e. the doctors and patients, are important. From the doctor's perspective, spirometry should contribute positively to clinical practice for it to be standard practice. Published observational studies also show that 15-30% of asthma management changed when spirometry was added to the practice.[11,12] Considering that spirometry plays a plausible role in decision-making to diagnose and/or treat patients with suspected or known respiratory conditions, these outcomes were chosen when developing our study design. Further, we clarified the outcomes as two categories of diagnosis: disease and severity, and four categories of management: medication, investigation, follow-up schedule and education. Therefore, the impact of spirometry can be clearly identified.

From the patient's viewpoint, we aim to determine the effect of our intervention (i.e. use of spirometry) on PROMs, especially in emotional and social domains, when patients attended the doctor consultation. PROMs are now considered essential for high quality clinical research in order to reliably measure and evaluate the efficacy of an intervention. As young children are unable to adequately communicate their opinion, the standard of PROMs assessment is to approach parents as proxy assessors. In addition, illness of the child usually puts a strain on the whole family, especially the parent or carer. The parent's own opinions

and QoL are undeniably relevant as an indirect measure of the child's QoL. Thus, PROMs used in paediatrics concern parents or carers themselves.

In this study, both the STAI and PC-QoL are employed for assessing PROMs to maximise relevant data without overburdening parents/guardians. First and foremost, we select the STAI and PC-QoL because both have demonstrated reliability and repeatability.[18,21,28] The STAI clearly differentiates between a temporary condition and general long-standing quality of anxiety. It could help distinguish feelings of anxiety at a particular time from anxious personality, so we can precisely compare the outcome between timepoints that the parents meet the doctor with or without spirometry. The PC-QoL is utilised given that cough is very common symptom of children with respiratory illness and cough-specific QoL inventories for adults have been shown better specificity and sensitivity over generic QoL inventories.[29,30] The domains of psychological, social and physical concerns in the PC-QoL could provide insight into impacts of the intervention across aspects of life. Finally, both the questionnaires are scale-based inventories. The inventory simplicity also makes it ideal for all individuals regardless of educational backgrounds.

Another secondary outcome is doctors' and patients' opinions towards spirometry via three questions for the doctor and one question for the patient. A unipolar 10-point Likert scale model is utilized to measure these opinions. The scale is feasible for collecting the additional outcome since it is easy to employ and communicate. A Likert scale survey can achieve valuable data which gives insight into the complex views of participants on a single subject matter.[17] Because perception of an opinion generally ranges along a continuum of positive to negative, a more refined scale with more points presumably permit individuals to express their opinions precisely and comfortably. Consequently, distortion in data decreases as the

number of scale points increases, although the improvement is relatively modest beyond 5 to 7 points,[31] hence the 10 point scale is utilized.

We chose to evaluate the outcomes at a single visit because spirometry information is a measure used for a single point in time for clinical decisions. However, this timeframe limits us from assessing other health related outcomes that require long-term observation such as improvement of symptoms, limitation of activities and unscheduled visits.

In summary, this RCT addresses a current gap in evidence to assess the benefit of spirometry in routine clinical practice. If this study shows that spirometry has a positive impact on clinical decision making and/or PROMs, this evidence will promote the use of spirometry as an important clinical assessment tool in multi-level care settings.

Author contributions

AC originally conceived and designed the study. IM, WB, JM and MM co-designed the study. All authors were involved in protocol preparation. WB obtained ethics and governance, prepared study materials, recruited participants, collected data and developed database. AC and SY supervised in statistical analyses and reporting. The first draft of manuscript was written by WB. All authors read and approved the final manuscript.

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Conflicts of interest/Competing interests

There are no financial conflicts of interest/competing interests to be declared.

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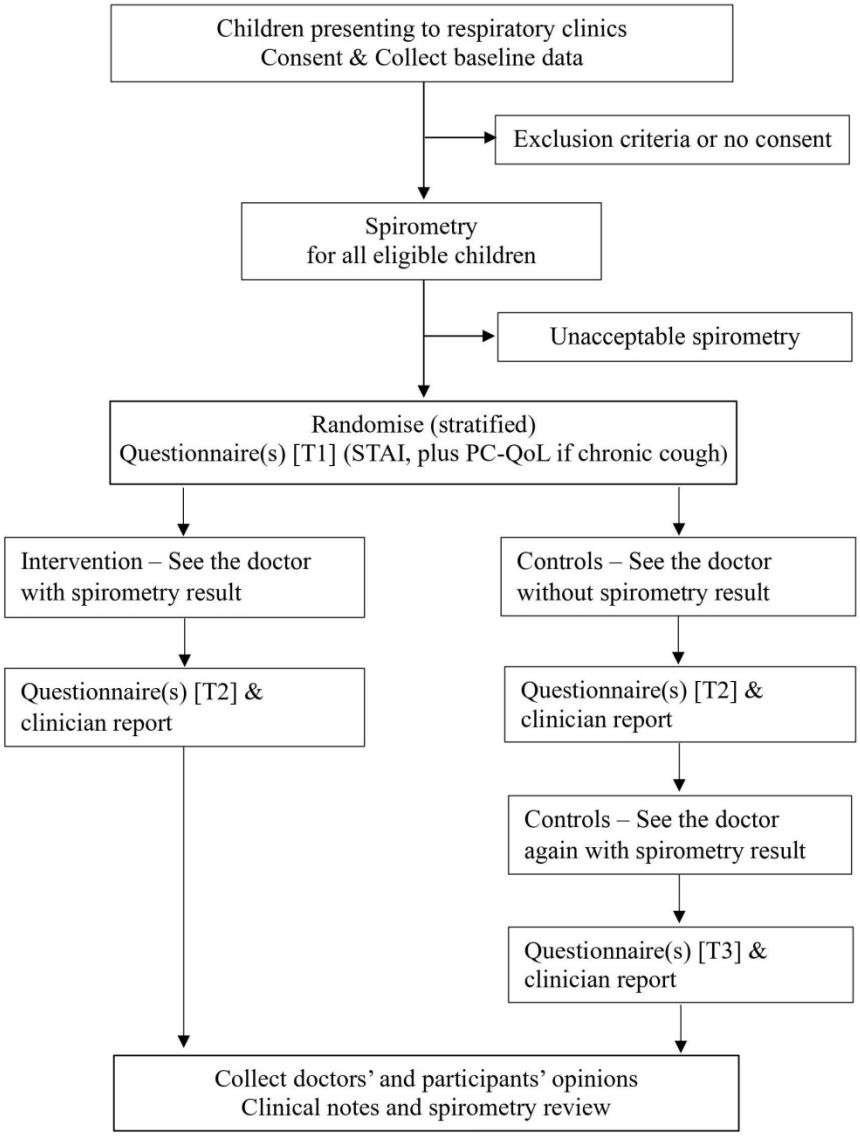

Figure 1: Schematic study design

490x632mm (96 x 96 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

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In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	#3	Date and version identifier	14
Funding	#4	Sources and types of financial, material, and other support	18
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	17

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	n/a
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	n/a
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	6
Objectives	#7	Specific objectives or hypotheses	6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	7
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will	7

		perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	n/a
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	n/a
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	11
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	13
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8

Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	n/a
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	13
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	n/a

Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	n/a
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	n/a
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	14
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	14
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	n/a
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	13

Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	18
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	13
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	14
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	14
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	n/a
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a

BMJ Open

The impact of using spirometry on clinical decision making and quality of life in children: protocol for a single centre randomised controlled trial

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The impact of using spirometry on clinical decision making and quality of life in children: protocol for a single centre randomised controlled trial

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Abstract

Introduction: Although spirometry has been available for decades, it is underutilised in paediatric practice, other than in specialist clinics. This is unsurprising as there is limited evidence on the benefit of routine spirometry in improving clinical decision making and/or outcomes for children. We hypothesised that using spirometry for children being evaluated for respiratory diseases impacts on clinical decision making and/or improves patient-related outcome measures (PROMs) and/or quality of life (QoL), compared to not using spirometry.

Methods and analysis: We are undertaking a randomised controlled trial (commenced in March 2020) that will include 106 children (aged 4-18 years) recruited from respiratory clinics at Queensland Children's Hospital, Australia. Inclusion criteria are able to perform reliable spirometry and a parent/guardian who can complete questionnaire(s). Children (1:1 allocation) are randomised to clinical medical review with spirometry (intervention group) or without spirometry (control group) within strata of consultation status (new/review), and cough condition (present/absent). The primary outcome is change in clinical decision making. The secondary outcomes are change in PROM scores, opinions regarding spirometry and degree of diagnosis certainty. Inter-group differences of these outcomes will be determined by Chi-square test or unpaired T-test (or Mann-Whitney if not normally distributed). Change in outcomes within the control group after review of spirometry will also be assessed by McNemar test or paired T-test/Wilcoxon Signed Rank test.

Ethics and dissemination: The Human Research Ethics Committee (HREC) of the Queensland Children's Hospital approved the study. The trial results will be disseminated through conference presentations, teaching avenues and publications.

Trial registration: Australia and New Zealand Clinical Trials Register, ACTRN12619001686190

Key words: spirometry, child, lung, respiratory, randomised controlled trial

Article summary

Strengths and limitations

- This randomised controlled trial will provide important information on whether the routine use of spirometry in children being evaluated for respiratory problems impacts a doctor's clinical decision making (compared to clinical review alone) and will thus provide the first high-level evidence that may lead to a change in routine clinical practice.
- Patient-reported outcome measures (anxiety level, quality of life score and opinion towards spirometry) will be undertaken to determine the utility of routine spirometry.
- Although this study is randomised with a control group and concealed allocation, the intervention could not be blinded to the doctors and participants. Therefore, the outcomes are subject to bias as perceptions may influence doctors' management and participants' scoring of the questionnaire(s).

Introduction

Of the many possible lung function tests used in clinical care, spirometry is the most widely available, established and used.[1] As such, many respiratory societies worldwide e.g. American Thoracic Society (ATS) and European Respiratory Society (ERS) support and/or provide training tools for spirometry testing. Undertaking spirometry is relatively simple as spirometers are portable and relatively inexpensive.

Data from spirometry provides invaluable contribution to the clinical assessment, including assisting in characterising respiratory pathophysiology, grading the severity of lung disorders and monitoring the course of lung disorders and therapeutic interventions.[2,3] Also, spirometry adds an objective element which is beneficial in both clinical practice and research. Hence, its use is recommended in many paediatric clinical guidelines including chronic cough, recurrent wheezing, cystic fibrosis and asthma.[4-7] Other conditions in which spirometry aids in management of children are transfusion-dependent disorders, oncology conditions, connective tissue disorders, neuromuscular weakness, chest wall deformities and scoliosis.[2,8]

Data obtained from spirometry differentiate normal lung function from abnormalities affecting airflow (forced expiratory volume in 1 sec, FEV_1) and lung size (forced vital capacity, FVC). It can also provide data on intra- and extra-thoracic obstruction when the inspiratory and expiratory loops are evaluated. Generally, spirometry can be reliably performed in most children aged >6 years. Improvements in equipment, technology, age-appropriate incentives in spirometer software and modified acceptability and reproducibility criteria for preschool children have meant even younger children (3 years and above) may be able to perform spirometry satisfactorily under the coaching of a well-trained technician.[1,9,10]

Intuitively, spirometry should assist clinicians in assessing and managing respiratory conditions and result in improved patient-related outcome measures (PROMs) e.g. quality of life (QoL) of the patients, however, there is limited published evidence. In the current era of evidence-based medicine, the effect of spirometry on clinical outcomes has rarely been studied with the few paediatric studies published looking only at its use in asthma management. Nair et al[11] found that spirometry changed management in 15% of children with asthma. When spirometry did change treatment decisions, they were more likely to increase (75%) than maintain (20%) or decrease (5%) therapy. Holt et al[12] found that 30% of paediatric asthma exacerbation treatment plans were changed after clinicians viewed spirometry, with an increased percentage of patients receiving steroid, bronchodilator or yellow zone treatment. Finally, Abramson et al[13] undertook a two clustered RCTs of spirometry integrated into regular general practice-based medical review for children with asthma over the duration of one year. They found that neither RCT demonstrated a significant improvement in health related QoL with the use of spirometry compared to not using (adjusted difference of Pediatric Asthma Impact Scale -0.2 (95%CI -4.9, 4.6) for the first trial and of Pediatric Asthma Quality of Life Questionnaire 0.17 (95%CI -0.15, 0.5) for the second) nor a change in written asthma action plan (Odds Ratio 1.11, 95%CI 0.43, 2.87).

While spirometry is widely advocated, it is currently under-utilised. Dombkoski et al[14] reported that only half of surveyed family physicians and general paediatricians use it in children and adults with asthma, and only 21% routinely use spirometry in asthma guideline-recommended situations i.e. establishing an asthma diagnosis, classifying asthma severity and classifying asthma control.[14] Another study by Blain et al[15] reported that only 10% of paediatricians used spirometry consistently on each asthma visit. Further, Bianchi et al[16] found that only a third of children with asthma were referred for spirometry and only one-half

of hospitalised children with asthma underwent spirometry during 12-month follow-up. The low utilisation of spirometry on a day-to-day basis outside of respiratory-focused practices is not surprising due to the limited published data supporting its benefits.

Given the paucity of relevant data, we are undertaking this RCT to compare clinical outcomes of out-patient consultation "with spirometry" versus "without spirometry" to assess the benefit of having spirometry data for both clinicians and patients.

Study objectives and hypotheses

Our primary question is: Does the routine use of spirometry improve the clinical decisions/management of children with suspected or known lung disease? We hypothesise that the routine use of spirometry in children managed by respiratory paediatricians in outpatient clinics alters clinical decision making in diagnosis and/or management.

Our secondary aims are to: 1) determine whether the routine use of spirometry in children impacts on diagnostic certainty and PROMs and 2) quantify the benefits of routinely using spirometry in clinical practice assessed by a 10-point Likert scale.[17] Our secondary hypothesis is that the integration of spirometry into outpatient consultations with respiratory paediatricians improves diagnosis certainty, PROM(s), specifically in emotional and social domains, evaluated by State-Trait Anxiety Inventory (STAI)[18,19] and/or Parent-Proxy QoL questionnaire for paediatric chronic cough (PC-QoL)[20,21] for those with chronic cough.

Methods and analysis

Study setting and design

We are conducting a single centre RCT with concealed allocation involving children seen at the Department of Respiratory and Sleep Medicine at the Queensland Children's Hospital, Brisbane, Australia. Our study design is summarised in Figure 1, and is in accordance with the recommendations of the Interventional Trial (SPIRIT) guidelines.[22] We recruited our first participant on 17th March 2020 and our study is ongoing with the study anticipated to be completed by early 2022.

Study population

Our inclusion criteria are: 1) children with parent/guardian in attendance and able to provide written consent, 2) children aged 4-18 years able to perform reliable spirometry, 3) parents/guardian able to complete the study questionnaire(s) and 4) children whose respiratory physician is willing to participate in the study.

Exclusion criteria are: 1) previously enrolled or 2) contraindication for spirometry including presence of acute dyspnoea, pneumothorax, haemoptysis, vital signs instability, lung cyst or bleb, and recent (<3 weeks) thoracic or ophthalmic surgery.

Recruitment

Parents/guardians with potentially eligible children are approached during a scheduled respiratory clinic appointment. A team member (WB) discusses the study using the parent/guardian information sheet. If the parent/guardian gives written informed consent and the child is able to perform acceptable spirometry then the child enters the study and is randomised.

All families approached are recorded in a screening log with details including name, date, whether informed consent was obtained or reason for refusal, whether the child was eligible and randomisation number if enrolled in the study.

Randomisation and allocation

A computer-generated permuted block (sizes of 2-6) randomisation sequence, generated by a statistician external to the study team, was prepared prior to commencement of the study. The randomisation is stratified by type of consultation (new patient or review), and presence of chronic cough condition (present or absent). On enrolment, the child is assigned to the next number on the stratified list that is opaque, i.e. the group allocation is concealed from investigators until the participant is recruited. Children are randomised to either routine use of spirometry (intervention) or delayed use of spirometry (controls) (Figure 1). Due to the obviously noticeable difference in intervention vs control groups, blinding is not possible.

Intervention groups

For both groups, the clinical management is at the discretion of the treating specialist. At baseline (T1), all participants undertake baseline PROM surveys (STAI[18,19] and if cough is present, the PC-QoL[20,21]) and are randomised to one of the two groups: intervention group where the doctor undertakes the consultation with the spirometry results being available, or controls where the doctor undertakes the initial consultation without the spirometry results.

After the consultation, the parents in both groups complete the questionnaire(s) for the second time (T2). At this same time point, the doctor is also asked to fill a data collection sheet regarding the child's diagnosis and management. This completes the study for the intervention group.

In the control group, the doctor is then presented with the child's spirometry and completes the consultation. After completion of the consultation, the parents complete the same questionnaire(s) for a third time (T3) and the doctors complete a final data collection sheet with any change in diagnosis or management after spirometry results are known. Despite the delayed time point of presenting the spirometry to respiratory paediatricians, by the time the child leaves the clinic, all patients would have received the same standard of care. No restrictions on concomitant care were applicable in this study.

Data collection

An outline of study procedures (all occurring during a single outpatient visit) is summarised in Table 1. Data are collected from the interview of the parent/guardian and electronic medical records. On enrolment, demographic data, medical history, medications, tobacco smoke exposure and anthropometrics are recorded. Physical examination is performed and recorded by the treating doctor.

All children are tested using Vyntus Pneumo or Vyntus Spiro spirometers operated through SentrySuite Software (Carefusion Germany 234 GmbH, Hoechburg, Germany) undertaken by experienced paediatric respiratory scientists in accordance with standard guidelines (American Thoracic Society (ATS) and European Respiratory Society (ERS) criteria for lung function testing).[1,23] The measured values are compared with predicted reference values from the Global Lung Function Initiative (GLI)[24] based on the patient's height, age, race and sex.

As mentioned above, depending on study group, the parents complete the same questionnaire(s) two or three times. These time-points are prior to visiting the doctor (T1),

after visiting the doctor (T2) and after second consultation with the doctor for controls only (T3). The questionnaires are: (i) STAI for all patients and (ii) PC-QoL for patients with cough. For both questionnaires, parents are given a hard copy of questionnaire(s) to complete on a self-report basis, with the investigator available if any clarification is needed.

The STAI is a long-standing psychological inventory frequently used to measure anxiety. It consists of two 20-item scales measuring 'state' or anxiety about an event, and 'trait' or anxiety proneness as a personality trait. In responding to the STAI, subjects rate their intensity of feeling for each item on a 4-point Likert scale. Based on its scoring key, the score of each of the two scales (state or trait) ranges from 20 to 80, where higher scores reflect higher levels of anxiety.[18,19] A license to reproduce/administer STAI was purchased from Mind Garden, Inc on 15th March 2020.

The PC-QoL is a validated parent-proxy quality of life measure specific for children with chronic cough.[20] The 27 item PC-QoL addresses parents' perception of three domains: the psychological (11 items), physical (11 items), and social (5 items) effect of their child's cough. Subjects are required to use a 7-point Likert-type scale to rate their perception (level of worry/ frequency of negative feelings); the highest intensity of perception gives a score of 1 and absence of perception gives a score of 7. Hence, higher scores reflect better QoL. For interpreting health-related QoL changes, the minimally important difference for the PC-QoL is 0.9.[25]

Prior to leaving the clinic at the completion of the consultation, the parents also score on a 10-point Likert scale "how much did the spirometry help with this clinic visit?", while the doctors are asked to score 3 aspects of its use; "how much did the spirometry (i) contribute to

general management, (ii) increases confidence in clinical practice and (iii) aid education/counselling with each patient?" on a 10-point Likert scale. The unipolar scale of 1 to 10 is anchored by increasing degree of agreement, which one means "not at all", five means "somewhat" and ten means "very much so".

Each participant completes the study on the day of enrolment when all study related forms have been completed and outcome data collected. All data are documented on paper-based case report forms (CRFs) using standardised data collection sheets.

Table 1: Timeline of study procedures during a single outpatient visit

	Before seeing doctor	After seeing doctor without spirometry (Only controls)	After seeing doctor with spirometry	Independent review
Written informed consent	√			
Randomisation	√			
Medical history interview and chart review	√			
Spirometry with bronchodilator testing	√			√
Clinical assessment for diagnosis and management		√	√	√
STAI ± PC-QoL assessment	√	√	√	
Opinion survey			√	

Exit criteria during the study

Exit criteria are defined as occurrence within the visit of any of the following: (1) spirometry is unacceptable on independent review, (2) the doctor accidently viewed the spirometry at the start of consultation in the control group or (3) parents withdraw consent for participation, are unable to comply with study intervention or if spirometry related serious adverse event occurred.

Outcome measures

Our primary outcome is the proportion of children with any change in clinical decision making (diagnosis and management) and change scores between groups at T2 (Figure 1). This consists of an *a-priori* list that consists of (i) any change in diagnosis based on 2 categories (disease and severity) and (ii) management based on 4 categories (medication, investigation, follow-up schedule and education). Change in each category is dichotomised as 'yes' or 'no'. Each 'yes' scores one point, so the range in change score is 0 to a maximum of 6 (2 points from change in diagnosis and 4 points from change in management).

Our secondary outcomes are:

1) Change of the PROM scores (STAI ± PC-QoL) assessed at T2 compared with T1 between two groups.
2) Opinions relating to the benefit of integrating spirometry into clinical practice are included as secondary outcomes. A 10-point Likert scale with a series of statements each designed to view a construct from a slightly different perspective is leveraged.
3) Degree of diagnosis certainty (definite, probable or doubtful) assessed at T2, between both groups
4) In the control group only, changes in the primary outcome and secondary outcomes 1 and 3, (T3 versus T2)

Sample size

The sample size is based on our primary outcome, the proportion of children with any change in clinical decision making. We wish to detect a significant difference between the intervention and control groups. We assume the proportion in the population is 30% (Ho: p = 0.30). To find 45% proportion of children with any change (alternative p = 0.45) with 5% significance (alpha = 0.05, two-sided) and 90% power (power = 0.90), we require outcome data from 105 children (rounded up to 106 children). We did not account for any dropouts as this is a single visit study where a dropout rarely occurs. Participants who withdraw will be replaced to reach the total children of 106.

Data management and statistical analyses and reporting

CRFs are kept confidential and locked. Access to the data is available to research team, unless required by legislative or regulatory agencies and the Human Research Ethics Committee (HREC). No identifying information of the enrolled participants will be included in study reports in order to protect confidentiality.

Data coding and entry will be conducted in accordance with good clinical practice. Data is being entered directly into an SPSS database. Intention-to-treat analyses regardless of subsequent management will be used. We plan to develop a complete statistical analysis plan prior to data analyses, as done for our previous major RCTs.[26,27]

For our primary aim, the impact of utilising spirometry on change in diagnosis and management will be determined by the proportion of children with any change and change scores at the T2 time point. Between the two groups, the proportion will be compared using

Chi-Square test to determine the OR with 95% CIs. The difference of change scores will be examined by T-test or Mann-Whitney U test depending on normality of the data.

For secondary aims:

1) Change in PROM (STAI ± PC-QoL) score from T1: The difference of the change between groups assessed at T2 will be compared using t-test or Mann-Whitney test.
2) Opinions towards spirometry quantified by 10-point Likert scales: The result will be reported as mean with standard deviation or median with 25^{th}-75^{th} percentile.
3) Degree of diagnosis certainty as definite, probable and doubtful for both groups assessed at T2 will be reported as frequency.
4) For controls only, outcomes at T2 and T3 will be compared. These outcomes include change in diagnosis and management, change scores of clinical decisions, change of PROMs and degree of diagnosis certainty. Difference of the outcomes between T2 and T3 will be analysed using McNemar test, paired t-test/Wilcoxon Signed Rank regarding data characteristics.

Patient and public involvement

Patients and public were not involved in the initial study design but were consulted subsequently.

Ethics, dissemination and safety monitoring

Ethical clearance was granted by the HREC of the Queensland Children's Hospital (HREC/19/QCHQ/58722; protocol version 1.3 dated 1st September 2020). We will publish the results in a major medical journal (using the International Committee of Medical Journal

Editors [ICMJE] author guidelines) and share the outcomes with the academic and medical community, funding and relevant patient organisations. Professional writers will not be used.

During the study, participants may report any solicited and spontaneous adverse events at any time. All adverse events are being monitored and serious or unexpected adverse events will be reported to the HREC.

Discussion

We are currently undertaking a single centre open-label RCT to address the question of whether spirometry integrated into outpatient care, compared with not using spirometry, impacts the clinical decision making of specialist respiratory paediatricians and PROMs. The outcomes and time points were chosen carefully as described below.

Rationale for our chosen outcome measures and time frame

To measure the influence of using spirometry on clinical practice, choosing valid outcomes informed by consumers. From the doctor's perspective, spirometry should contribute positively to clinical practice for it to be standard practice. Published observational studies also show that 15-30% of asthma management changed when spirometry was added to the practice.[11,12] Considering that spirometry plays a plausible role in decision-making to diagnose and/or treat patients with suspected or known respiratory conditions, these outcomes were chosen when developing our study design. Further, we clarified the outcomes as two categories of diagnosis: disease and severity, and four categories of management: medication, investigation, follow-up schedule and education. Therefore, the impact of spirometry can be clearly identified.

From the patient's viewpoint, we aim to determine the effect of our intervention (i.e. use of spirometry) on PROMs, especially in emotional and social domains, when patients attended the doctor consultation. PROMs are now considered essential for high quality clinical research in order to reliably measure and evaluate the efficacy of an intervention. As young children are unable to adequately communicate their opinion, the standard of PROMs assessment is to approach parents as proxy assessors. In addition, illness of the child usually puts a strain on the whole family, especially the parent or carer. The parent's own opinions and QoL are undeniably relevant as an indirect measure of the child's QoL. Thus, PROMs used in paediatrics concern parents or carers themselves.

In this study, both the STAI and PC-QoL are employed for assessing PROMs to maximise relevant data without overburdening parents/guardians. First and foremost, we select the STAI and PC-QoL because both have demonstrated reliability and repeatability and been validated.[18,21,28] The STAI clearly differentiates between a temporary condition and general long-standing quality of anxiety. It could help distinguish feelings of anxiety at a particular time from anxious personality, so we can precisely compare the outcome between timepoints that the parents meet the doctor with or without spirometry. The PC-QoL is utilised given that cough is very common symptom of children with respiratory illness and cough-specific QoL inventories for adults have been shown better specificity and sensitivity over generic QoL inventories.[29,30] The domains of psychological, social and physical concerns in the PC-QoL could provide insight into impacts of the intervention across aspects of life. Finally, both the questionnaires are scale-based inventories. The inventory simplicity also makes it ideal for all individuals regardless of educational backgrounds.

Another secondary outcome is doctors' and patients' opinions towards spirometry via three questions for the doctor and one question for the patient. A unipolar 10-point Likert scale model is utilized to measure these opinions. The scale is feasible for collecting the additional outcome since it is easy to employ and communicate. A Likert scale survey can achieve valuable data which gives insight into the complex views of participants on a single subject matter.[17] Because perception of an opinion generally ranges along a continuum of positive to negative, a more refined scale with more points presumably permit individuals to express their opinions precisely and comfortably. Consequently, distortion in data decreases as the number of scale points increases, although the improvement is relatively modest beyond 5 to 7 points,[31] hence the 10 point scale is utilized.

We chose to evaluate the outcomes at a single visit because spirometry information is a measure used for a single point in time for clinical decisions. However, this timeframe limits us from assessing other health related outcomes that require long-term observation such as improvement of symptoms, limitation of activities and unscheduled visits.

In summary, this RCT addresses a current gap in evidence to assess the benefit of spirometry in routine clinical practice. If this study shows that spirometry has a positive impact on clinical decision making and/or PROMs, this evidence will promote the use of spirometry as an important clinical assessment tool in multi-level care settings, especially in primary care and outreach settings where respiratory specialists are limited. Thus, respiratory healthcare for children could be optimised to maximal benefit.

Author contributions

AC originally conceived and designed the study. IM, WB, JM and MM co-designed the study. All authors were involved in protocol preparation. WB obtained ethics and governance, prepared study materials, recruited participants, collected data and developed database. AC and SY supervised the plan for statistical analyses and reporting. The first draft of manuscript was written by WB. All authors read and approved the final manuscript.

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Conflicts of interest/Competing interests

There are no financial conflicts of interest/competing interests to be declared.

Word count

3,594 words

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Figure 1: Schematic study design

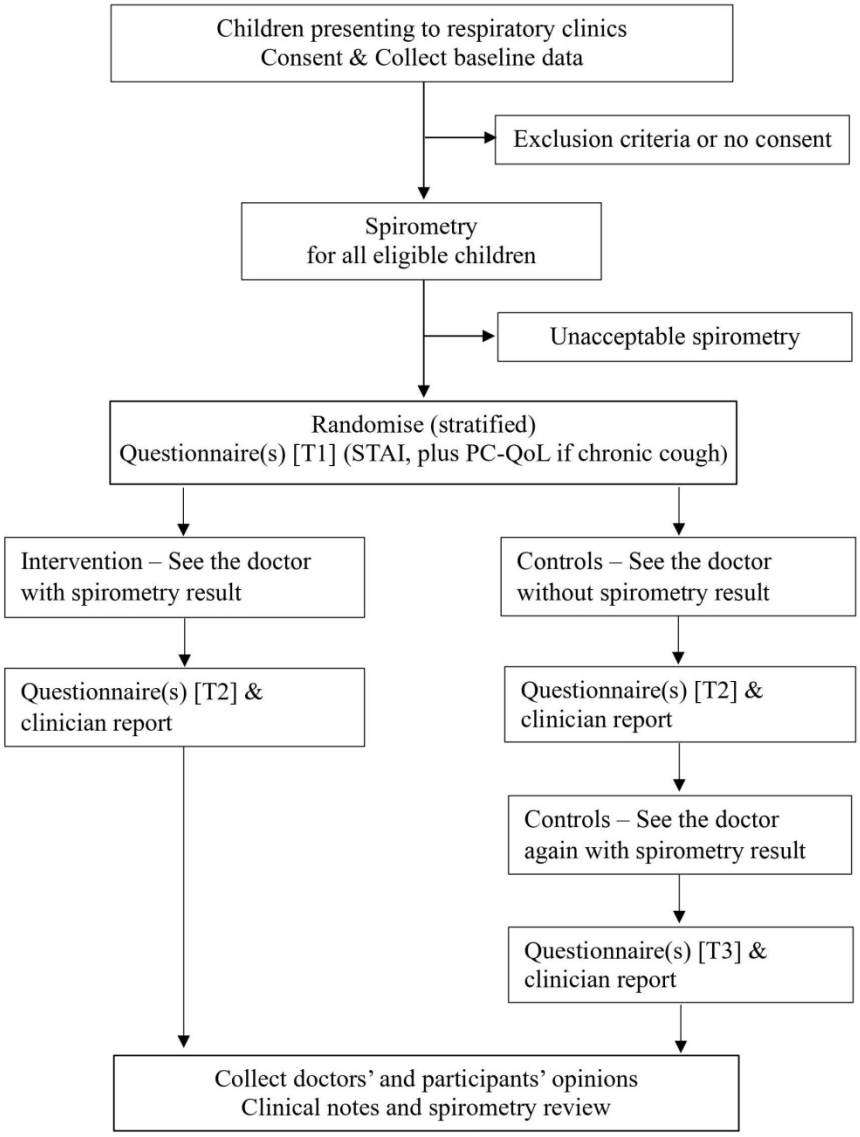

Figure 1: Schematic study design

490x632mm (96 x 96 DPI)

Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	n/a
Protocol version	#3	Date and version identifier	14
Funding	#4	Sources and types of financial, material, and other support	18
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	17

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	n/a
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	n/a
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	n/a
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	6
Objectives	#7	Specific objectives or hypotheses	6
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	7
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	7
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will	7

		perform the interventions (eg, surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	8
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	n/a
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	n/a
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	9
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	12
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	11
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	13
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	7
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	8

Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	8
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	8
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	n/a
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	9
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	n/a
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	13
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	13
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	n/a

Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	n/a
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	n/a
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	n/a
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	14
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	n/a
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	14
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	n/a
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	7
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	n/a
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	13

Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	18
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	13
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	n/a
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	14
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	14
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	n/a
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	n/a
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	n/a