Full Study Title: Stand Out in Class: Restructuring the classroom environment to reduce sedentary behaviour – a pilot cluster randomised controlled trial (RCT)

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TABLE OF CONTENTS

1. AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made

2. SYNOPSIS

Study Title	Stand Out in Class: Restructuring the classroom environment to reduce sedentary behaviour – a pilot cluster randomised controlled trial (RCT)
Internal ref. no.	Loughborough University Ethical Advisory Committee reference: R16-P027
Trial Design	Pilot cluster RCT
Trial Participants	9-10 year old children
Planned Sample Size	8 schools (1 class in each school) with a minimum of 15 pupils in each
Follow-up duration	7 months
Planned Trial Period	7 months
Primary Objective	To undertake a pilot cluster RCT of the introduction of sit-stand desks in primary school classrooms to inform a future fully-powered definitive trial.
Secondary Objectives	1. Establish and refine a recruitment strategy for schools and pupils 2. Determine attrition in the trial (schools and children) 3. Determine completion rates for outcome measures (and whether these are sufficiently high to provide accurate data in a full trial) 4. Assess whether there are any differences in trial recruitment, retention and acceptability between ethnic groups 5. Assess the acceptability of randomisation to schools 6. Assess the acceptability of measurement instruments to teachers, children and parents, including the activPAL inclinometer as the tool for the measurement of the primary outcome 7. Assess the acceptability of the intervention to teachers, children and parents 8. Monitor any adverse effects, such as musculoskeletal discomfort and/or disruption to the classroom/learning to inform the design of a full trial and minimise or eliminate any such effects 9. Assess intervention fidelity over the intervention period 10. Derive preliminary estimates of the effect of the intervention on children's total daily sitting time, physical activity, indicators of health (markers of adiposity and blood pressure), cognitive function, and academic performance, engagement and behaviour; and to undertake preliminary analyses to examine whether any differences in the outcome measures over the intervention period occur between boys and girls and South Asian and White British children. 11. Estimate the standard deviation of the outcomes to inform a sample size calculation for a full RCT 12. Determine availability and completeness of economic data and conduct a preliminary assessment of potential cost-effectiveness
Primary Endpoint	End of overall study period at 20 months
Secondary Endpoints	

3. ABBREVIATIONS

AE	Adverse event
AR	Adverse reaction
CI	Chief Investigator
CRF	Case Report Form
CRO	Contract Research Organisation
EC	Ethics Committee (see REC)
GCP	Good Clinical Practice
ICF	Informed Consent Form
PI	Principal Investigator
PIL/S	Participant/ Patient Information Leaflet/Sheet
RCT	Randomised controlled trial
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAR	Serious Adverse Reaction
SOP	Standard Operating Procedure
SUSARs	Suspected Unexpected Serious Adverse Reactions
TMF	Trial Master File

4. BACKGROUND AND RATIONALE

Technological advances and changes to our environment and lifestyle have led to increased time in sedentary behaviours.[1] Sedentary behaviour (sitting and expending <1.5 METs) is ubiquitous in modern society, with individuals exposed to environments that promote prolonged periods of sitting. Whilst it is acknowledged that physical activity is beneficial to health, sedentary behaviour has been shown to adversely affect health. For example, high levels of sedentary behaviour have been associated with type 2 diabetes, cardiovascular disease, cancer and premature mortality in adults.[2,3] Sitting is the most prevalent behaviour exhibited during waking hours in UK children, accounting for >65% of wake time.[4] Data from our research group has shown that our target sample (9-10 year olds living in Bradford) spend >70% of their waking hours (~10 hours/day) sitting.[5] Adverse associations between sedentary behaviour and cardio-metabolic health risk markers (obesity, blood pressure, cholesterol, insulin) have been reported in children.[6,7] As sedentary behaviours track throughout childhood into adolescence and adulthood[8] the reduction of sedentary time in young people is pertinent for the primary and secondary prevention of chronic diseases that result from excessive sitting in adulthood.[2,3]

Children are exposed to environments and social norms that encourage prolonged sitting. To counter the detrimental effects of prolonged sitting on children's health,[6] strategies are needed to reverse the trend of increasing levels of sedentary behaviour. A meta-analysis of interventions targeting reductions in children's sedentary behaviour reported an overall decrease of 18 mins/day and a reduction in BMI of 0.25 kg/m².[9] Whilst most studies were school-based, sedentary behaviour was targeted via behaviour change strategies within non-school settings (i.e. screen time at home). No studies employed changes to the classroom environment. Classrooms are conducive to high volumes of sitting, children sit for longer during school hours than non-school hours.[10] Environmental change is an obvious means to target classroom sitting time, and may address health inequalities by being accessible to all children. Our feasibility study and others[5,11,12] have demonstrated the effectiveness of incorporating sit-stand desks in primary school classrooms over the short term (<12 weeks). We found sit-stand desks enabled pupils to alternate between sitting and standing, without disruption to teaching, learning or behaviour. In adults, regular breaks in prolonged sitting throughout the day are associated with metabolic health benefits and reductions in blood pressure.[13,14] International studies have shown sit-stand desks in school classrooms are effective in increasing energy expenditure[15,16] and standing and movement[17] during the school day. Further studies have shown sit-stand desks in classrooms lead to improvements in children's posture and musculoskeletal comfort[18,19] and levels of academic engagement[20] and achievement.[19] Two studies have assessed the impact on sitting directly, both showed reductions in children's daily sitting time of approximately one hour/day over 4 and 9 weeks follow-up.[12,21] The majority of studies conducted to date however have included relatively small samples and short intervention periods with no randomised controlled design. The present research will build on this earlier research by assessing the longer-term acceptability of this low burden environmental intervention, along with the acceptability of a range of health and education related outcome measures, informing a full RCT.

5. OBJECTIVES

5.1 Primary aim

The primary objective of this research is to undertake a pilot cluster RCT of the introduction of sit-stand desks in primary school classrooms to inform a future fully-powered definitive trial.

If successful, we will seek funding to undertake a cluster RCT comparing the effects of the introduction of sit-stand desks over 1 school year on daily sitting time, health and education related outcomes, with sub-group analyses for ethnicity. Before the full trial can be delivered, key information needs to be established around recruitment, acceptability, attrition and data collection. We therefore propose to undertake a pilot trial in the classrooms of 4 intervention and 4 control schools over a 7-month period.

5.2 Pilot trial study objectives:

1. Establish and refine a recruitment strategy for schools and pupils
2. Determine attrition in the trial (schools and children)
3. Determine completion rates for outcome measures (and whether these are sufficiently high to provide accurate data in a full trial)
4. Assess whether there are any differences in trial recruitment, retention and acceptability between ethnic groups
5. Assess the acceptability of randomisation to schools
6. Assess the acceptability of measurement instruments to teachers, children and parents, including the activPAL inclinometer as the tool for the measurement of the primary outcome
7. Assess the acceptability of the intervention to teachers, children and parents
8. Monitor any adverse effects, such as musculoskeletal discomfort and/or disruption to the classroom/learning to inform the design of a full trial and minimise or eliminate any such effects
9. Assess intervention fidelity over the intervention period
10. Derive preliminary estimates of the effect of the intervention on children's total daily sitting time, physical activity, indicators of health (markers of adiposity and blood pressure), cognitive function, and academic performance, engagement and behaviour; and to undertake preliminary analyses to examine whether any differences in the outcome measures over the intervention period occur between boys and girls and South Asian and White British children.
11. Estimate the standard deviation of the primary outcome to inform a sample size calculation for a full RCT
12. Determine availability and completeness of economic data and conduct a preliminary assessment of potential cost-effectiveness

6. STUDY DESIGN

6.1 Summary of Trial Design

This is a school-based, pilot two-armed cluster RCT with economic and process evaluations. Individuals (children) will be the unit of analysis and schools (clusters) randomly assigned to one of two conditions: 1) manually adjustable sit-stand desks incorporated into the classroom environment (intervention condition), or 2) current practice (control condition).

Baseline measurements will precede randomisation and be completed when the participants are near the beginning of year 5 (November/December 2016) (see Appendix 1 for an overview of the trial design). The demand on participant's time will be minimal. All participants taking part in the evaluation of the intervention will be required to have a series of health and learning related measurements taken at 2 time points throughout the study (baseline and follow-up, follow-up measurements will be conducted in June/July 2017). The health and learning related measurements will take place during school hours and will take approximately 15 minutes per child. In addition to these measurements, participants will be issued with an accelerometer and inclinometer to wear continuously whilst they continue with their normal daily routine for 7 days at each measurement time point. This will have minimal impact on the participant as they will be requested to wear the devices for 24 hours/day, only removing the accelerometer for water-based activities.

To assess the acceptability of the intervention, interviews will take place with teachers from the intervention classrooms and a sub-sample of children from the intervention schools will be invited to participate in two focus groups undertaken throughout the study. These focus groups will likely last for no more than 30 minutes and will be conducted either during school time, or immediately after school.

6.2 Primary and Secondary Outcome Measures

In this pilot study, the primary outcome will be the feasibility of the long-term use of sit-stand desks and outcome measures proposed for inclusion in a full RCT (objectively measured total daily sitting time, physical activity during and outside school hours, adiposity, blood pressure, cognitive function, academic progress, engagement and behaviour). Acceptability of the trial will be assessed by monitoring recruitment uptake, compliance and attrition rates. We will conduct a full process evaluation and an exploratory economic evaluation to further inform a full trial. Full details of all outcome measures are described in section 8.3.

7. TRIAL PARTICIPANTS

7.1 Overall Description of Trial Participants

Study participants will be Year 5 children (aged 9 – 10 years) from participating Bradford primary schools.

Eight primary schools (1 class in each school, selected by the Head Teacher if there is more than 1 year 5 class per school), with at least 15 participants (approximately 50% of a typical class), will be recruited giving a minimum total sample of 120. A minimum of 15 pupils per class volunteering to participate in the study will be required.

Schools will be recruited following ethical approval. The study will initially be publicised to Bradford primary schools through email/telephone contact and visits to schools using existing contacts within the Bradford Institute for Health Research. To assess the acceptability of the intervention and proposed outcome measures for use in a full trial across an ethnically diverse sample, recruited schools will be stratified based on the ethnic composition of their pupils. We will aim to recruit four schools with predominantly South Asian pupils (>50%) and four schools with predominantly White British pupils (>50%). Interested schools and year 5 teachers will receive a detailed information sheet explaining the study. Consent will be sought from School Management (head teacher, senior teachers, governors) and Year 5 teachers to participate in the study. During recruitment, schools will be told they have a 50% chance of being randomised to a current practice control condition where they will maintain their usual classroom practice.

7.2 Inclusion Criteria

All children within the Year 5 class of participating schools will be invited to participate in the intervention evaluation. In cases when there is more than one Year 5 class in the school, the head teacher will select the class to participate.

7.3 Exclusion Criteria

Children without parental consent for their participation in the evaluation, or those who do not give their assent to participate in the evaluation will be excluded. For those children whose parents refuse consent, they will still be exposed to the sit-stand desks in their classroom (if they are in the intervention schools) but no evaluation data will be collected from them and no assessments undertaken. Children in the intervention schools with known contraindications that would preclude periods of standing will be encouraged to use the sit-stand desk in a seated posture for inclusivity. These individuals will be excluded from the analyses. Children with any disabilities or injuries/illnesses that prevent them from going about their usual routine will be excluded from the evaluation component of the study.

8. STUDY PROCEDURES

8.1 Informed Consent

All year 5 children from participating classes in schools will be invited to take part in the intervention evaluation. Recruitment of schools will take place in September/October 2016, while recruitment of children and baseline measurements will take place when the children are early in year 5, November/December 2016. Parents will be sent a detailed information sheet about the study via the schools so that they can make an informed decision about their child's participation. They will also be invited to a school meeting where the researchers will conduct a presentation outlining the study and hold a question and answer session. Researchers will also be present in school playgrounds at the beginning and end of the school day to talk to parents about the study.

The parent/guardian must personally sign and date the latest approved version of the informed consent form before any study specific procedures are performed. Written and verbal versions of the Participant Information sheet and Informed Consent form will be presented to parent/guardians during the school presentation events. It will be clearly stated that the parent/guardian can withdraw their child from the study, or the child can withdraw from the study, at any time for any reason without prejudice, and with no obligation to give the reason for withdrawal.

Parents/guardians will be allowed at least 48 hours to consider the information, and the opportunity to question the Investigator or other independent parties to decide whether they wish their child to participate. Written Informed Consent will then be obtained by means of a parent/guardian dated signature and dated signature of the person who obtained the informed consent. The person who obtained the consent must be suitably qualified and experienced, and have been authorised to do so by the Principal Investigators. The original signed form will be retained at the study site within the Investigator Site File (ISF). A copy of the signed Informed Consent will be given to parents/guardians and a copy retained in the participant's notes.

8.2 Screening and Eligibility Assessment

All children within the participating year 5 classes of recruited schools will be eligible to participate in the intervention evaluation.

8.3 Primary Feasibility Outcomes

To inform the feasibility outcomes of the study, we will monitor study uptake by recording the number of schools and pupils approached, and the number agreeing to participate. Withdrawal rates of schools and children and completion rates for outcome measures (described below) will be summarised as a whole group and by ethnic groups.

All measurements described below will be undertaken at the schools, by trained research staff. The measurements will be taken at baseline (November/December 2016) and at follow-up (June/July 2017).

8.3.1 Primary outcomes (pilot tested in the present study for use in a full trial):

- School hours sitting/standing time, and breaks in sitting – measured using the activPAL3 inclinometer (PAL Technologies Ltd).

The activPAL3 will be waterproofed and worn continuously on the anterior aspect of the right thigh for 24 hours/day for seven consecutive days during each measurement period.

8.3.2 Secondary physiological outcomes:

- Total and non-school hours sitting, standing and stepping time - measured using the activPAL3.
- Physical activity - measured using the ActiGraph GT3X+ accelerometer, worn on the hip for 24 hours/day over seven consecutive days.
- Time in bed – measured using a self-report diary for seven days whilst participants wear the activPAL3 and ActiGraph GT3X+.
- Blood pressure - measured using a portable blood pressure digital monitor with a paediatric cuff after a period (5 minutes) of quiet sitting.
- Height - measured without shoes using a portable stadiometer.
- Body weight - measured without shoes using electronic weighing scales.
- Body mass index - calculated from the child's height and weight.
- Body fat percentage - estimated using Tanita DC-360S body composition scales.

All of these measurements will be conducted in a private setting within the school by trained researchers; at least two researchers will be present during all measurements.

8.3.3 Secondary cognitive, behaviour, comfort and self-report outcomes:

- Cognitive function (visuo-spatial working memory, executive function, vigilance and sustained attention) - administered via a validated software package. The software will be loaded onto school computers enabling a group of students (those with parental consent to participate in the intervention evaluation) to undertake these assessments at the same time, under the supervision of research staff.
- Pupil behaviour - assessed using the Strengths and Difficulties Questionnaire, completed by teachers.
- Engagement Vs Disaffection With Learning - self-report questionnaire, completed by children.
- Academic achievement – routine data collected by schools at half-termly intervals.
- Postural comfort - assessed using a self-assessment survey, completed by children.
- Attitudes to sit-stand desk use – self-report questionnaire, completed by children.

8.3.4 Economic outcomes

- Paediatric Quality of Life inventory (PEDS-QL) – completed by children.
- EQ-5D Youth – completed by children.
- Sit-stand desk costs – obtained from manufacturers.
- Health and education resource use – questionnaires completed by parents and teachers.

8.3.5 Demographic information (provided from school records)

- Date of birth.
- Ethnicity.
- Postcode (to determine IMD as an indicator of socio-economic status).
- Sex.

8.3.6 Process Evaluation:

Appendix 2 outlines our detailed process evaluation plan. We will monitor the fidelity of the intervention implementation in line with guidance from the NIH Behaviour Change Consortium; for example at the end of each day teachers in the intervention classes will record the number of

children exposed to the sit-stand desks, number of children present and engagement of the children. Additionally, observations of the intervention will be carried out by trained research staff and a standardised form completed. Observations will take place at a frequency of one per term in the intervention schools. Participant, teacher and parental perceptions and experiences of the intervention and outcome measures (including any negative effects such as discomfort from the monitoring equipment or class disruption) will be obtained during the intervention through interviews (with intervention teachers, 4 teachers in total) and focus groups (with children and parents). Interviews with the intervention teachers will take place during the beginning and end of the intervention period. The focus groups with children and parents will be conducted using participants (and their parents) from the intervention classrooms. These focus groups will be conducted at the beginning and end of the intervention. We will aim to run at least 4 focus groups with children and 4 focus groups with parents at each time point. Our target sample within each focus group will be 4 to 6 participants (32-48 participants in total). Parents will be asked to complete an informed consent form for their participation in the focus groups, all participants will be informed that their comments made during the focus groups will remain confidential.

8.4 Randomisation and Codebreaking (if applicable)

We will aim to recruit four schools with predominantly South Asian pupils (>50%) and four schools with predominantly White British pupils (>50%). Schools within each stratum will be randomised into the two study arms by the Leicester CTU following the completion of baseline measurements. Two schools with predominantly South Asian pupils and two schools with predominantly White British pupils will be randomised into the intervention and control arms (4 schools in each arm).

8.5 Subsequent Assessments

The outcome measurements collected at baseline (November/December 2016) will be repeated at the end of the intervention period, in June/July 2017.

8.6 Definition of End of Trial

The end of trial is the date of the last follow up assessment of the last participant.

8.7 Discontinuation/Withdrawal of Participants from Study Treatment

Each participant and/or parent/guardian has the right to withdraw their child from the study at any time. In addition, the investigator may discontinue a participant from the study at any time if the investigator considers it necessary for any reason including:

- Significant protocol deviation
- Significant non-compliance with the outcome measurements
- An adverse event which requires discontinuation of the study or results in inability to continue to comply with study procedures
- Consent withdrawn
- Lost to follow up

Withdrawal from the study will result in exclusion of the data for that participant from analysis.

The reason for withdrawal will be recorded in the CRF.

If the participant is withdrawn due to an adverse event, the investigator will arrange for follow-up visits or telephone calls until the adverse event has resolved.

8.8 Source Data

Source documents are original documents, data, and records from which participants' CRF data are obtained. These include, but are not limited to, demographic information, anthropometric measurements (height, weight, BMI, % body fat), ratings of perceived comfort, and teacher and child reported behaviour. CRF entries will be considered source data if the CRF is the site of the original recording (e.g., there is no other written or electronic record of data). All documents will be stored safely in confidential conditions. On all study-specific documents, other than the signed consent, the participant will be referred to by the study participant number/code, not by name.

9. TREATMENT OF TRIAL PARTICIPANTS

9.1 Description of Study Treatment

Six sit-stand desks (plus 1 for the teacher) will be placed in one Year 5 classroom in each intervention school for the majority of the academic year (February/March 2017 – July 2017). These desks have been used successfully over the short term (9 weeks) and have led to reductions in sitting time and increases in movement on school days.[5] In consultation with teachers, the study should ensure that all pupils are exposed to the sit-stand desks for at least one hour/day. The research team will support teachers with the development of a rotation plan for desk use and will recommend the use of naturally occurring breaks during class time (e.g. when moving from one subject or task to another) and the school day (morning break and lunch time) as a time for desk rotation. Stools or chairs will remain and children will be free to choose whether they sit or stand.

Teachers and children in the intervention classrooms will receive training on sit-stand desk use by the research team. Teachers will receive a Professional Development Manual containing information on the health benefits of reducing prolonged sitting and information on correct posture when standing at the desks. The manual and training will be based on the Theoretical Domains Framework[22] and use standardised behaviour change techniques (e.g. goal setting) to address any perceived barriers and facilitators, with the aim to increase self-efficacy and motivation for sit-stand desk use.[23]

Once the desks have been installed, the demands and disruption placed on the teacher and the school are minimal. Teachers in the intervention classrooms will need to be familiar with the functionality of the sit-stand desks and the health benefits of reducing periods of prolonged sitting, which will be provided via training by the research team prior to implementation. During the intervention, the teacher will be asked to emphasize to pupils that they have the option to stand or sit and to change between the two as they wish.

9.2 Control Condition

Schools assigned to the usual practice control arm will be asked to continue with their usual lesson delivery, no environmental changes will be made to their classrooms. Participants in the control schools (year 5 children) will be asked to complete the same study measurements as those in the intervention schools, at the same time points. Upon completion of the study, control schools will receive a report summarising their pupils' sitting and physical activity data. They will also receive adapted materials (i.e., the Professional Development Manual provided to teachers in the intervention schools, which excludes references to sit-stand desks) upon completion of all follow-up evaluation measures.

9.3 Compliance with Study Treatment and Assessment Methods

As part of a process evaluation, interviews and focus groups with teachers, children and parents will be conducted to explore the acceptability of trial procedures and the intervention. Participant, teacher and parental perceptions and experiences of the intervention and outcome measures

(including any negative effects such as discomfort from the monitoring equipment or class disruption) will be obtained during the intervention through interviews (with teachers) and focus groups (with children and parents). As part of the assessment of intervention fidelity some lessons in intervention classrooms will be observed once per school term to enable the examination of compliance to the intervention (i.e. the number of children choosing to stand when using the sit-stand desks) and participant's posture during sit-stand desk use.

10. SAFETY REPORTING

10.1 Definitions

10.1.1 Adverse Event (AE)

Any untoward medical occurrence in a patient or clinical investigation participant, which does not necessarily have to have a causal relationship with the treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the study, whether or not considered related to the study.

10.1.2 Adverse Reaction (AR)

All untoward and unintended responses related to the study.
All cases judged by either the reporting medically qualified professional or the sponsor as having a reasonable suspected causal relationship to the study qualify as adverse reactions.

10.1.3 Severe Adverse Events

To ensure no confusion or misunderstanding of the difference between the terms "serious" and "severe", which are not synonymous, the following note of clarification is provided:
The term "severe" is often used to describe the intensity (severity) of a specific event (as in mild, moderate, or severe myocardial infarction); the event itself, however, may be of relatively minor medical significance (such as severe headache). This is not the same as "serious," which is based on patient/event outcome or action criteria usually associated with events that pose a threat to a participant's life or functioning. Seriousness (not severity) serves as a guide for defining regulatory reporting obligations.

10.1.4 Serious Adverse Event or Serious Adverse Reaction

A serious adverse event or reaction is any untoward medical occurrence that at any dose:

- Results in death,
- Is life-threatening,

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

- Requires inpatient hospitalisation or prolongation of existing hospitalisation,
- Results in persistent or significant disability/incapacity, or
- Is a congenital anomaly/birth defect.
- Other important medical events*

*Other events that may not result in death, are not life threatening, or do not require hospitalisation, may be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the patient and may require medical or surgical intervention to prevent one of the outcomes listed above.

10.1.5 Expected Serious Adverse Events/Reactions

No serious Adverse Events/Reactions are expected to occur within the present study.

10.1.6 Suspected Unexpected Serious Adverse Reactions

A serious adverse reaction, the nature or severity of which is not consistent with the applicable product information

10.2 Reporting Procedures for All Adverse Events

Due to the nature of this study we do not anticipate any adverse events to occur; however should any arise, we will follow Loughborough University guidelines for managing and reporting adverse events, serious adverse events and suspected, unexpected serious adverse reactions which follow those outlined in good clinical practice guidance. If an adult or child has an adverse event relating either to the study measurements or the intervention the researcher or teacher will record this on a report form. Report forms relating to the intervention will be collected at the end of the intervention, unless the adverse event requires further NHS treatment. In this case, the teacher will be asked to contact the local study coordinator immediately and fax/email the completed report form to the coordinator immediately.

10.3 Reporting Procedures for Serious Adverse Events

All SAEs must be reported to the Sponsor within one working day of discovery or notification of the event. The Sponsor will perform an initial check of the information and ensure that it is reviewed at the next R&D Management meeting. All SAE information must be recorded on an SAE form and sent to the Sponsor using the appropriate reporting form and the contact details on there. Additional information received for a case (follow-up or corrections to the original case) needs to be detailed on a new SAE form which must be sent to the Sponsor using the appropriate reporting form and the contact details on there.

The Sponsor will report all SUSARs to the Research Ethics Committee concerned. Fatal or life-threatening SUSARs must be reported within 7 days and all other SUSARs within 15 days. The CI will inform all investigators concerned of relevant information about SUSARs that could adversely affect the safety of participants.

In addition to the expedited reporting above, the CI shall submit once a year throughout the study or on request an Annual Report to the Ethics Committee which lists all SAEs / SUSARs that have occurred during the preceding 12 months.

11. STATISTICS

A statistical analysis plan will be written and approved before database lock.

Analysis will mainly utilise descriptive statistics. We will summarise the number of schools approached, the number agreeing to participate, the proportion of children within each school with parental consent to participate in the study evaluation, the number of children completing the study protocol, retention rates, and the number providing valid outcome measurement data at baseline and follow-up. Reasons for non-compliance to the outcome measurements and reasons for withdrawal from the study evaluation derived from the process evaluation (interviews and focus groups) will be reported. The study acceptability data (described above) will be presented for the sample as a whole, and stratified according to study arm (intervention and control) and ethnicity (South Asian and White British).

While the main aim of this study is to establish acceptability, feasibility, recruitment rates and sample size in order to inform a full trial, and although effectiveness will unlikely be established with the small sample size, we will examine the primary and secondary outcomes to mimic practice

for a full trial. Results from this analysis will be treated as preliminary and interpreted with caution.[24,25] As the number of clusters is low, cluster summary statistics will be used rather than multi-level modelling.[26,27] The analysis will be carried out using children as the unit of analysis with change in total daily sitting time as the primary outcome. A weighted linear regression model will be used to compare the intervention arms weighted by the number of participants followed up in each cluster and adjusted for baseline total daily sitting time on school days for each cluster. To examine preliminary effects of the intervention on the secondary outcomes, the same analytical approach will be adopted as for the primary outcome. Due to the exploratory nature of the trial, all results will be presented as confidence intervals. No p-values will be calculated.

An intention to treat population will be used for the analysis, with pupils and schools assigned to the group they were randomised to. Missing data will not be imputed.

Audio-recordings of interviews and focus groups with teachers, parents and children will be transcribed verbatim and analysed using framework analysis,[28,29] using the Normalisation Process Theory[30] as the overarching framework, along with field notes from observation sessions.

Availability and completeness of economic data and preliminary assessment of potential cost-effectiveness will be established. We will assess the likely cost-effectiveness of the intervention in two analyses. Firstly, a “within trial” approach will be used to assess whether the intervention is likely to provide value for money based on the time horizon of the trial (half a school year). It is acknowledged that the outcomes measured in the trial period may not capture all of the costs and benefits associated with the intervention. Therefore, a further analysis will be conducted to explore likely costs and effects of the intervention over a more appropriate time horizon (e.g. the lifetime of the individual).

12. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

Direct access will be granted to authorised representatives from the sponsor, host institution and the regulatory authorities to permit trial-related monitoring, audits and inspections.

13. QUALITY CONTROL AND QUALITY ASSURANCE PROCEDURES

The study will be conducted in accordance with the current approved protocol, ICH GCP, relevant regulations and standard operating procedures.

Regular monitoring will be performed according to ICH GCP. Data will be evaluated for compliance with the protocol and accuracy in relation to source documents. The standard operating procedures will be followed for all assessments and documented and reported in compliance with the protocol, GCP and the applicable regulatory requirements.

14. CODES OF PRACTICE AND REGULATIONS

14.1 Ethics

Ethical consideration has been given to the study design in relation to participant exposure and participant burden as well as to the collection of meaningful data.

14.2 Sponsor Standard Operating Procedures

All relevant Sponsor SOPs will be followed to ensure that this study complies with all relevant legislation and guidelines

14.3 Declaration of Helsinki

The Investigator will ensure that this study is conducted in full conformity with the current revision of the Declaration of Helsinki (last amended October 2000, with additional footnotes added 2002 and 2004).

14.4 ICH Guidelines for Good Clinical Practice

The Investigators will ensure that this study is conducted in full conformity with relevant regulations and with the ICH Guidelines for Good Clinical Practice (CPMP/ICH/135/95) July 1996.

14.5 Approvals

Once Sponsor authorisation has been confirmed, the protocol, informed consent form, participant/parent/teacher/school information sheets and any proposed advertising material will be submitted to an appropriate Research Ethics Committee (REC), regulatory authorities and host institution(s) for written approval.

Once Sponsor authorisation has been confirmed, the Investigator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

14.6 Participant Confidentiality

The trial staff will ensure that the participants' anonymity is maintained. The participants will be identified only by initials and a participants ID number on the CRF and any electronic database. All documents will be stored securely and only accessible by trial staff and authorised personnel. The study will comply with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so.

14.7 Other Ethical Considerations

The 'Stand Out in Class' intervention is low risk and we have received ethical approval for previous work of this nature so we do not anticipate ethical concerns. However, there are a number of specific ethical issues that may be considered "more than minimal risk", as per ESRC Research Ethics Framework (paragraph 1.2.2). These include:

- *Research with children (considered a vulnerable population)*: All researchers will have an Enhanced Disclosure and Barring Service check and at least two trained researchers will be present during the anthropometric measurements.
- *Gatekeepers*: To gain access to children in the schools we will go through the relevant gatekeepers (i.e. the head teacher, the teacher, the school board, board of governors). We will provide information for the school governor boards (or similar) in advance, and will attend the school in person to give information or presentations to the relevant gatekeepers.

Teacher consent and parental/guardian consent (through an opt-in form for their child to participate in the intervention evaluation, see Section 8.1) will be obtained to ensure that they fully understand what the intervention evaluation involves. Parents will be sent a detailed information sheet about the evaluation so that they can make an informed decision about their child's participation. Children will be asked to provide written assent at each data collection time point for the evaluation measures.

We will also ask parents to provide informed consent for long-term follow-up of their children. Future funding will be sought to make use of the routine data collected as part of the National Child Measurement Programme which participants will undertake in Year 6. Data collected in the proposed study from children with parental consent for long-term follow-up will be linked to the National Child Measurement Programme data, enabling us to make preliminary assessments of

longer term effects of the intervention on body composition.

15. DATA HANDLING AND RECORD KEEPING

The Leicester CTU use an 'off the shelf' commercial Clinical Data Management System (CDMS) called InferMed MACRO v4 (Macro) to implement compliant database solutions. Macro is an integrated electronic data collection system developed for running multi-centre clinical research studies and trials. It is intuitive to use, has interactive tools for study definition, and supports on-line data entry and remote study monitoring.

All study data will be entered into the database and checked visually and verbally at entry. The participants will be identified by a study specific number and/or code in the database. The name and any other identifying detail will NOT be included in the study data electronic file. A separate secure database will be used to record participant information and contact details, in addition to their follow up dates.

The database management system which stores the databases underlying the MACRO application is Microsoft SQL Server. SQL Server and its supporting hardware infrastructure is provided by the University of Leicester's IT Services (ITS).

The database solutions implemented by the CTU using MACRO are validated.

The CTU has procedures in place to manage the Study Definition Life Cycle, covering the Design, Build, Verification, Routine Use, Maintenance (including change management) and Archiving of trial databases.

16. STUDY GOVERNANCE

Two groups will be created to oversee the study; a TSC and a Project Committee. As the study is regarded as low risk, we request not to have a separate Data Monitoring Committee, rather the TSC will take on the role of a Data Monitoring Committee and review any serious adverse events which are thought to be intervention related and monitor progress with data collection. The TSC will meet every 6 months and include the principle investigators (Drs Clemes and Barber), an independent chair, two independent external members, two school representatives and a statistician. The TSC will act as an independent strategic oversight body to ensure transparency and that relevant milestones are being met and will report back to the NIHR PHR Programme. The TSC will provide advice and updates to the Project Committee which will comprise the PI's, all co-investigators, a financial representative and those concerned with the day to day running of the study (research associates, administrator, etc.). The Project Committee will meet monthly and provide an update report for the TSC. The TSC and the study investigators will be responsible for the strategic direction and performance monitoring of the research including study delivery, risk management, public and stakeholder engagement, dissemination of results, communications, and strategic planning. The study will comply with 'The Medicines for Human Use (Clinical Trials) Regulations 2004' and all study documentation and data will be retained for the set number of years specified by the study sponsor.

17. FINANCING AND INSURANCE

As a thank you for participating in the pilot trial, all schools will receive a donation of £200 which will be given at the end of the trial.

All children will also receive £10 in vouchers as a thank you for taking part at baseline and at follow-up (£5 at each time point). Due to using the inclinometers and accelerometers for 7 days, we feel that it is appropriate to give children a voucher as a thank you for committing to the measurements in the study.

The Study will be covered by the Sponsor's Insurance.

18. PUBLICATION POLICY

Publications from this study will be co-authored and internally reviewed by Dr Stacy Clemes, Dr Sally Barber, Dr Natalie Pearson, Dr Daniel Bingham, Dr Yu-Ling Chen, Dr Rosie McEachan, Dr Keith Tolfrey, Dr Charlotte Edwardson, Dr Lorraine Cale, Dr Stephan Bandelow, Dr Gerry Richardson, and Dr Mike Fray. All study publications will acknowledge the funder (the NIHR PHR stream).

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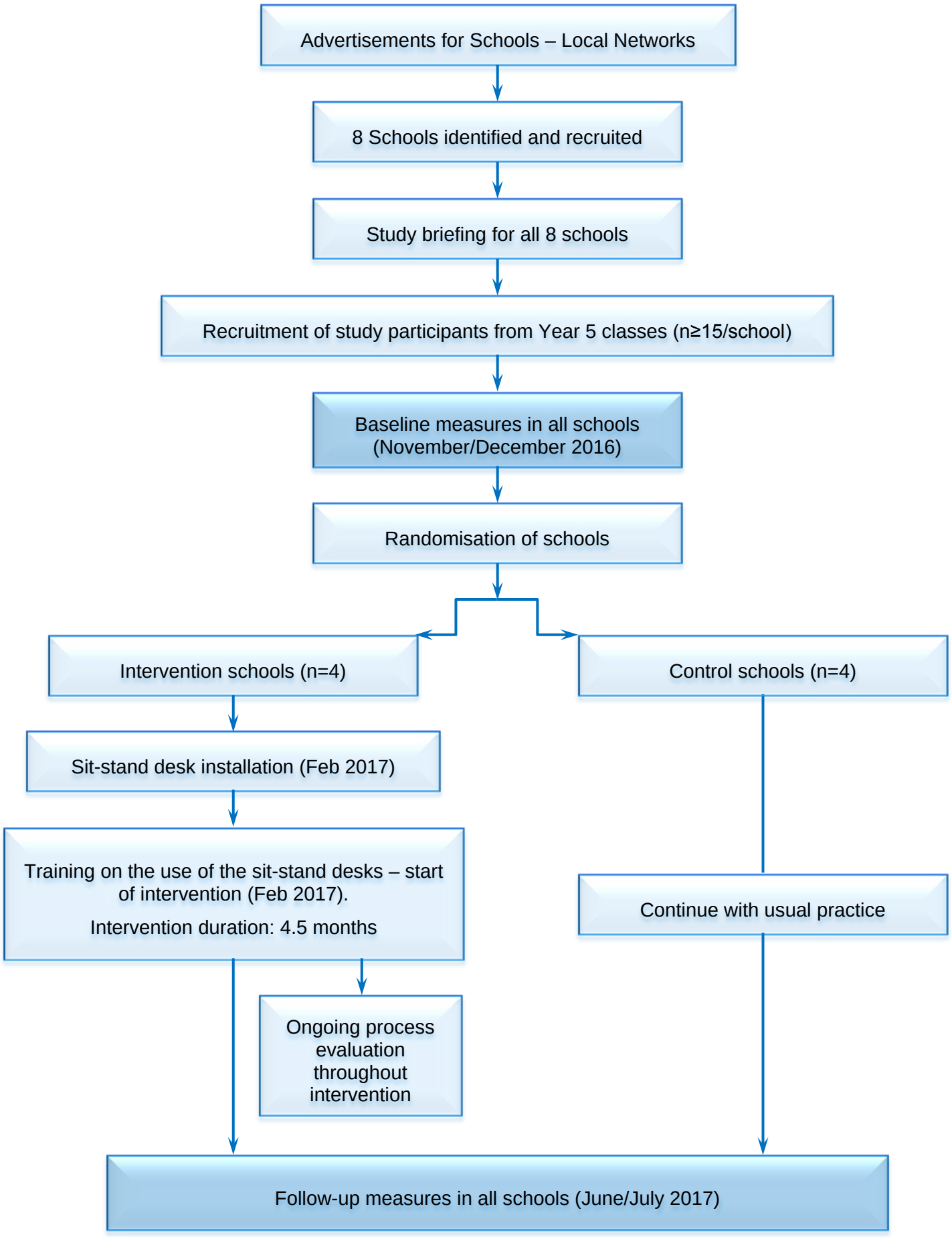
20. APPENDIX 1: STUDY FLOWCHART



21. APPENDIX 2: PROCESS EVALUATION PLAN

A thorough process evaluation will be key to understanding the i) implementation ii) receipt and iii) setting of the intervention and help in the interpretation of results (Oakely et al, 2006). Based on the conceptual frameworks of Hasson et al (2010) and Carroll et al (2007) our process evaluation will include a range of qualitative methods (including semi-structured interviews, focus groups and observations). We will explore factors related to adherence (content, delivery, uptake of intervention) at both school and individual levels. We will also explore key moderating factors such as responsiveness (how satisfied schools/ individuals are), strategies to facilitate implementation, quality of delivery, and context. We will use Normalisation Process Theory (May and Finch, 2009) as a lens through which we structure our analysis

Key elements of process evaluation: Based on Hasson et al (2010)

Areas to measure	**General process questions**	**Data source and data collection method**	**Total numbers and sampling strategy**
Acceptability of randomisation and measurement tools (objectives 5 and 6)	How did schools feel about being randomised to intervention / control arms? How did schools / children / parents experience recruitment, and outcome assessments? Did schools / children / parents find outcome assessments acceptable? What were the reasons for not participating in the trial, and/or not complying to the outcome measures?	Interviews with teachers In-class focus groups with children Focus groups with parents Recruitment data (numbers consenting), and missing data from outcome assessments 1-to-1 interviews with parents and children not participating and/or not complying	8 teachers from participating schools (end of summer term, July 2017) 8 focus groups with children (1 per school), Autumn term after baseline assessments (Dec 2016) 8 focus groups with parents (1 per school), Autumn term after baseline assessments (Dec 2016) Data collected at baseline and follow-up Interviews conducted after baseline assessments (Dec 2016)
Intervention acceptability and fidelity (objectives 7 and 9)	Was the intervention implemented as planned?	Interviews with intervention teachers Observations of lessons	4 intervention teachers Time-points: T1: Autumn term (Dec 2016) T2: End of summer term (July 2017) 4 intervention schools, observed once per term (12 observations)

Areas to measure	General process questions	Data source and data collection method	Total numbers and sampling strategy
Intervention acceptability and fidelity (objectives 7 and 9)	What proportion of the target group participated in the intervention?	Teachers logs and telephone interviews with intervention teachers	4 intervention teachers recording use of desks in log book and brief telephone contact every two weeks
Intervention acceptability and fidelity - potential moderating factors (objectives 7 and 9)	How were children engaged with sit-stand desks? How satisfied were schools / children / parents with sit-stand desks? How did schools / children / parents perceive the outcomes and usefulness of sit-stand desks	Focus groups with children (in class) Interviews with teachers Focus groups with parents	4 in class focus groups with children from intervention schools: T1: Autumn term (Dec 2016) T2: Beginning of summer term (May 2016) 4 intervention teachers Time-points: T1: Autumn term (Dec 2016) T2: End of summer term (July 2017) 4 parent focus groups from intervention schools (Dec 2016)
Intervention acceptability and fidelity - strategies to facilitate implementation (objective 7 and 9)	What strategies were used to support introduction of standing desks? How were these strategies perceived by staff involved within project?	Interviews with teachers	4 intervention teachers Time-points: T1: Autumn term (Dec 2016) T2: End of summer term (July 2017)
Intervention acceptability and fidelity - Quality of delivery (objectives 7 and 9)	How well were sit-stand desks introduced? What is the quality of the sit-stand desks and professional manual?	Interviews with teachers Focus groups with children (in class)	4 intervention teachers Time-points: T1: Autumn term (Dec 2016) T2: End of summer term (July 2017) 4 in class focus groups with children from intervention schools: T1: Autumn term (Dec 2016) T2: Beginning of summer term (May 2017)

Areas to measure	General process questions	Data source and data collection method	Total numbers and sampling strategy
Intervention fidelity – Context (objective 9)	What factors at political, economical, organisational and work group levels affected the implementation?	Interviews with teachers and headteachers	4 intervention teachers (end of Summer term, July 2017) 4 interviews with head teachers from intervention schools (end of summer term, July 2017)

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