Full Study Title

A three arm cluster randomised controlled trial to test the effectiveness and cost-effectiveness of the SMART Work & Life intervention for reducing daily sitting time in office workers

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1. AMENDMENT HISTORY

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

2. SYNOPSIS

Study Title	A three arm cluster randomised controlled trial to test the effectiveness and cost-effectiveness of the SMART Work & Life intervention for reducing daily sitting time in office workers.
Internal ref. no.	0657
Trial Design	3 arm cluster randomised controlled trial
Trial Participants	Office workers within Councils
Planned Sample Size	660 (accounting for 30% dropout)
Follow-up duration	Follow up measures taken at 3, 12 and 24 months after baseline
Planned Trial Period	March 2018 – March 2021
Primary Objective	To investigate whether SMART Work & Life, delivered with and without a height adjustable desk, leads to reductions in objectively measured daily sitting time compared to usual practice at 24-month follow-up.
Secondary Objectives	To investigate whether SMART Work & Life, delivered with and without a height adjustable desk, leads to short (assessed at 3 months), medium (assessed at 12 months) and longer term (assessed at 24 months): • Reduction in daily sitting time (3 and 12 months) • Reductions in sitting time during work hours • Increases in time spent standing overall and inside/outside of work hours • Increases in light and moderate-to-vigorous physical activity overall and inside/outside of work hours • Increases in time spent stepping and number of steps overall and inside/outside of work hours • Reductions in adiposity (BMI, percent body fat, waist circumference) • Reductions in blood pressure • Improvements in blood markers (e.g. blood glucose, cholesterol, triglycerides) • Improvements in psychosocial variables (e.g. vitality, fatigue, stress, anxiety and depression, work engagement, job performance and satisfaction, presenteeism, sickness absence, and quality of life) • Improvements in sleep We will also conduct a full process evaluation and a full economic evaluation.

3. BACKGROUND AND RATIONALE

Sedentary behaviour levels and health

Technological innovations and economic advances have led to increases in physical inactivity and sedentary behaviour (Katzmarzyk & Mason, 2009). Evidence indicates that it is not only necessary to be physically active for at least 150 minutes a week, but also important to limit the number of waking hours spent being sedentary (i.e., sitting). A wealth of epidemiological evidence now exists that demonstrates that sedentary behaviour is associated with an increased risk of chronic disease (type 2 diabetes, cardiovascular disease, some cancers and mortality), often independently of BMI and physical activity (Wilmot et al 2012; Rezende et al 2014; Shen et al 2014; Biswas et al 2015). Office workers are one of the most sedentary populations, with data showing that they spend 70-85% of time at work sitting, with over a third of total sitting time being accumulated in bouts of prolonged sitting (greater than 30 minutes) (Healy et al 2013). Additionally, our research has shown that workers who spend large proportions of their time sitting at work also spend more time sitting during leisure time (Clemes et al 2014). Experimental evidence thus far demonstrates that avoiding long bouts of sitting by incorporating short but frequent bouts of more light intensity movement (standing and stepping) improves glucose, insulin and blood pressure levels (Henson et al 2016; Dunstan et al 2012; Thorp et al 2014; Larsen et al 2014). For example, breaking up sitting every 30 minutes for 5 minutes with standing (total sitting reduction of 60 minutes over the day) reduced glucose and insulin by 35% and 20% respectively in adults with raised glucose levels (Henson et al 2016). In overweight and obese adults, breaking up sitting every 20 minutes for 2 minutes (total sitting reduction of 28 minutes) with light walking over the course of 5 hours reduced glucose and insulin by 24% and 23% compared to uninterrupted sitting (Dunstan et al 2012). In office workers, Thorp and colleagues found an 11% reduction in glucose following a protocol of alternating sitting and standing postures to work (Thorp et al 2014a). Such sitting reduction strategies have also been shown to reduce musculoskeletal (e.g., low back) discomfort and fatigue in office workers (Thorp et al 2014b).

Recent evidence suggests that high levels of moderate-to-vigorous physical activity, for example, at least 60-120 minutes per day, may have a protective effect against the health consequences associated with high levels of sitting (Pulsford et al 2015; Ekelund et al 2016). However, the high levels of activity needed to be protective are unlikely to be achievable for the majority of the population. Therefore, evidence is emerging that a first “behavioural” step that might be more socially achievable than targeted exercise, could be to simply get people standing and moving more frequently as part of their day.

Existing literature

In 2016, a review was published summarising the effectiveness of workplace interventions for reducing sitting time at work (Shrestha et al 2015).The interventions included physical workplace changes such as providing height adjustable desks to enable sitting or standing at work, pedalling workstations and treadmill desks, policy changes, information provision and counselling and computer prompts. Providing height-adjustable workstations was the most frequently implemented intervention and was reported as the most promising for reducing sitting time at work (reductions ranged from 30 minutes – 2 hours/day). Whilst positive findings were observed, the review concluded that 'The quality of evidence was very low to low for most interventions' mainly because studies were very poorly designed, for example, there was a lack of non-biased cluster randomised controlled trials, and because they had very few participants (majority had 20-50 participants). They also concluded that 'sit-stand desks can reduce sitting at work in the short term but the evidence is very low quality' and 'there is a need for cluster-randomised trials with a sufficient sample size and long term follow-up'. A three-month follow up was typically the longest so knowledge on sustainability is currently lacking. To date only two studies currently address these limitations, both conducted by our research groups (O'Connell et al 2015; Dunstan et al 2013).

We have conducted two fully powered cluster RCTs (SMArT Work and Stand Up Victoria) with medium term follow up (12 months) (O'Connell et al 2015; Dunstan et al 2013). Both compared a multi-component intervention (i.e., group-based workshop, feedback on sitting behaviour, goal setting, and ongoing support e.g., emails or individual coaching sessions) with the provision of a height-adjustable workstation against control (see section 2.3 for more details on the SMArT Work intervention). Both studies successfully reduced workplace sitting time over the short and medium term (3, 6 and 12 months). For example, the Stand Up Victoria study, conducted by our collaborators, observed differences in sitting at work of 99 and 45 minutes/day at 3 and 12 months when comparing intervention and control groups (Healy et al 2016). In our SMArT Work intervention, we have shown (unpublished) differences in sitting in the workplace of 51, 64 and 83 minutes/day at 3, 6 and 12 months when comparing intervention and control groups. Although significant sitting reductions are observed at work we see some evidence of behaviour dilution outside of work i.e., when looking at the reduction in sitting across all waking hours, it is ~10-20 minutes less than that observed in the workplace indicating that participants sat for ~10-20minutes longer outside of work. We have also observed similar findings in another smaller workplace study. In a 3 month workplace

intervention involving height-adjustable desk attachments, sitting reductions at work of 19% were shown at 3 months but sitting outside of work increased by 8% at 3months (Mansoubi et al 2016). This evidence suggests that workplace interventions also need to target sitting time outside of working hours so that positive changes made at work are not 'cancelled out' during leisure time.

One active research trial in the US is evaluating the efficacy of sit-stand workstations on decreasing sitting time and increasing light-intensity physical activity in samples of office workers (Buman et al 2017).However, this randomised trial does not have a control group, it is comparing two interventions as follows: Intervention one: The *MOVE* + intervention is a multilevel individual, social, environmental, and organisational intervention targeting increases in light-intensity physical activity in the workplace. Intervention two: The *STAND* + intervention is the *MOVE* + intervention with the addition of the installation and use of sit-stand workstations. This trial will be the first trial with longer term follow up at 24 months.

This novel study will advance the current evidence by:

- Being fully powered to detect differences between groups in changes in sitting (address limitation identified in Cochrane review)
- Having a robust randomised controlled design (address limitation identified in Cochrane review)
- Emphasising a 'whole-of-day' preventive approach rather than just focusing on workplace sitting (to address behaviour compensation outside of work hours)
- Incorporating behaviour change maintenance strategies (to prevent the decline in positive behaviour change over the longer term)
- Including a long term (24 month) outcome assessment (to assess sustainability and address limitation identified in Cochrane review)
- Including a cost-effectiveness analysis
- Including two intervention arms to investigate how important providing a simple, but fairly expensive, environmental change (i.e., height-adjustable workstation) is for reductions in sitting.

4. AIM AND OBJECTIVES

4.1 Aim

The aim of this study is to determine the long term effectiveness and cost-effectiveness of the multi-component SMART Work & Life intervention (when provided with and without a height-adjustable desk) for reducing daily sitting time in office workers compared with no intervention. If both interventions are shown to be effective, a secondary aim will be to determine if one intervention is more effective than the other.

4.2 Primary Objective

To investigate whether SMART Work & Life, delivered with and without a height adjustable desk, leads to reductions in objectively measured daily sitting time compared to usual practice at 24-month follow-up.

4.3 Secondary Objectives

To investigate whether SMART Work & Life, delivered with and without a height adjustable desk, leads to short (assessed at 3 months), medium (assessed at 12 months) and longer term (assessed at 24 months);

- Reduction in daily sitting time (3 and 12 months)
- Reductions in sitting time during work hours
- Increases in time spent standing overall and inside/outside of work hours
- Increases in light and moderate-to-vigorous physical activity overall and inside/outside of work hours
- Increases in time spent stepping and number of steps overall and inside/outside of work hours
- Reductions in adiposity (BMI, percent body fat, waist circumference)
- Reductions in blood pressure
- Improvements in blood markers (e.g. blood glucose, cholesterol, triglycerides)
- Improvements in psychosocial variables (e.g. vitality, fatigue, stress, anxiety and depression, work engagement, job performance and satisfaction, presenteeism, sickness absence, and quality of life)
- Improvements in sleep

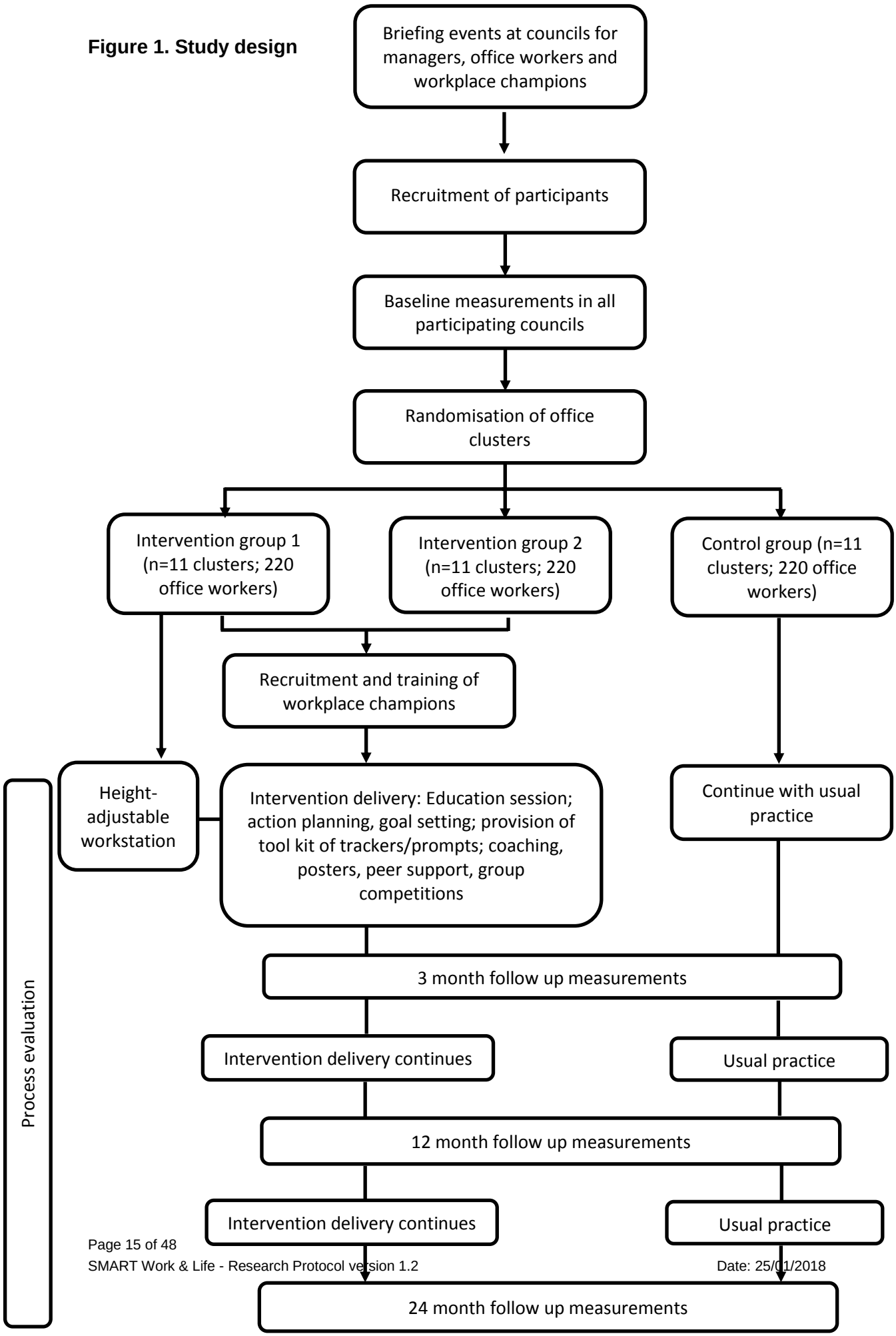
We will also conduct a full process evaluation and a full economic evaluation.

5. STUDY DESIGN

5.1 Summary of Trial Design

This is a three arm cluster randomised controlled trial (RCT) involving 660 office workers (220 per arm). Clusters (different office spaces) will be randomised to receive one of the following conditions: 1) The multi-component SMART Work & Life intervention with a height-adjustable desk or desk platform (intervention 1), or 2) The multi-component SMART Work & Life intervention without a height-adjustable desk or platform (intervention 2) or 3) usual practice (control condition). Baseline measurements will precede randomisation. Measurements will be repeated, using identical standardised procedures, at 3 months to assess any short term changes and 12 months and 24-months to assess any longer term changes. Observations, questionnaires and focus groups with office workers and workplace champions will be conducted throughout the intervention period as part of our full process evaluation. Figure 1 shows the overall study design.

Figure 1. Study design



5.2 Primary and Secondary Endpoints/Outcome Measures

Primary outcome

The primary outcome will be daily sitting time, objectively measured using the activPAL device (worn 24hrs/day for 7 days by waterproofing)**.**

Secondary outcomes

The secondary outcomes in this study are:

- Other activity outputs from the activPAL
- Moderate-to-vigorous physical activity (MVPA):
- Measures of adiposity
- Blood pressure
- Blood markers
- Dietary intake
- Work-related psychosocial variables and mental health
- Process evaluation (qualitative and quantitative data collection)

6.0 TRIAL PARTICIPANTS

6.1 Overall Description of Trial Participants

Office-based employees aged ≥18 years of age within local Councils in the Leicester and Manchester areas.

6.2 Recruitment strategy

The study may be advertised in several ways (these have been informed by Councils themselves):

- Using the council's weekly newsletter (Interface)
- Using the council's newpod
- Through more targeted strategies directly to appropriate office-based departments via departmental emails/posters/office walk arounds

Employees who want to hear more about the study will be invited to a short briefing event at the Council where the study will be presented and explained to managers and employees. At the end of the briefing event participant information sheets will be given out to employees who are interested in taking part. The study team's contact details will also be given on emails and posters so that interested employees can request a participant information sheet.

6.3 Inclusion Criteria

- Office-based employees ≥ 18 years of age within the Councils
- Spend the majority of their day sitting. This will be used as screening criteria prior to the consent and baseline measurement visit and will subsequently be confirmed using the objective data collected via the activPAL device.
- They must also work for the council at least 3 days/week.
- Participant is willing and able to give informed consent to take part in the study.
- Able to walk without the use of an assistive device or requiring assistance form another person.

6.4 Exclusion Criteria

The participant may not enter the study if ANY of the following apply:

- They are currently pregnant

- Currently using a height-adjustable workstation at their primary work location.
- Unable to communicate in English.
- Unable to provide written informed consent.

7 STUDY PROCEDURES

7.1 Informed Consent

Before any study related procedure can take place, the participant must sign and date the latest approved version of the informed consent form. Participant information with full details of procedures, expectations, potential risks and withdrawal rights will be sent to the participants prior to their baseline visit to give them time to read through it. It will then be presented both in writing and verbally on arrival at their first study visit prior to consent being taken. It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to future care, and with no obligation to give the reason for withdrawal. If a participant wishes to withdraw from the study intervention, we will encourage them to continue participating in the data collection visits. It will be made clear on the participant information sheet (PIS) and consent form that their anonymised data will be used for analysis even if they withdraw from the study.

The consent form will be signed and dated based upon an informed decision from this information. Consent will be taken by someone who has received generic consent training and has been authorised by the Principal investigator to do so. The original signed form will be retained at the study site within the Trial Master File (TMF) and a copy will be given to the participant.

7.2 Eligibility Assessment

Prior to commencing the study, participants will complete a reply form with some basic information about themselves (e.g., work site, work hours etc) and their contact details. This information will be used to assess eligibility for the study. Once this has been completed and the participant has decided to take part, informed consent will be sought. Baseline measurements will then be taken. Please note that no baseline measurements other than those used to check eligibility will be taken until the participant has given their informed consent and been confirmed as eligible.

7.3 Baseline and Follow Up Assessments

Once eligibility has been confirmed, baseline measurements will be taken. These are described here.

Demographic

During their baseline visit, participants will be asked their age and date of birth, ethnicity, education level, current job role and grade, working site, working hours, length of time in post, and postcode. At each follow up visit, participants will be asked if there has been any change in these aspects.

Medical history and medication

Details of any history of disease or injuries that may indicate an inability to participate in the study will be measured. If needed, results will be reviewed to define eligibility. Medication will also be recorded.

Anthropometrics and blood pressure measurements

Height will be measured in centimetres (cm), to 1 decimal place, using a Leicester portable height measure. Waist circumference (WC) will be measured using a standard anthropometric tape measure, with the tape measure being placed around the abdomen midway between the uppermost border of the iliac crest and the lower edge of the chest (thorax) formed by the bottom edge of the rib cage. A reading in cm, to 1 decimal point, will be taken when the tape is snug, but not compressing the skin. Weight, in kilograms (kg), and body composition are measured using a Body Composition Analyser. Participant's height, age, gender and a clothing allowance of 1.5 kg will be entered into the scales. Participants will remove shoes, socks and heavy outerwear clothing and to ensure their pockets were empty before stepping on to the scales. Body mass index (BMI) is calculated by the scales as kg/m^2. Blood pressure (BP) will be assessed using an Omron automated blood pressure monitor (Omron Healthcare Europe). Participants will be asked to sit quietly and relax prior to having their BP measurements taken and three readings will be taken, with the average of the last 2 readings being used.

Biochemical assessments

The 'A1c Now' point-of-care analyser to measure glycated haemoglobin which is a marker of long-term glucose regulation used in clinical care. Additionally, we will use the Cardiocheck point-of-care analyser to measure circulating cholesterol (total, HDL, LDL) and triglycerides. Both of these systems are manufactured by PTS Diagnostics and possess analyte validation certificates from the International Federation of Clinical Chemistry and Laboratory Medicine. Capillary blood samples will be taken from each participant using the finger prick method (we will not be taking blood from a vein via a needle). The CardioChek® system, which is a portable hand-held device that requires between 15-40 µL (millions per microliter) of blood taken using a finger-stick, will be used for these measurements. No blood will be stored and all blood contaminated testing sticks will be deposed of appropriately. All participants will

receive a results report with their blood test results clearly documented, they can share these with their GP if they have any concerns.

Objectively measured sitting and physical activity

The activPAL device will be worn on the thigh 24hrs/day for up to 7 days at each measurement time point. It will be made waterproof using a nitrile sleeves and waterproof medical dressing. This device will assess a variety of aspects of behaviour including sitting, standing and stepping time, prolonged sitting and standing, number of steps and number of transitions from sitting to an upright posture and vice versa. These variables can be calculated daily (i.e., across all waking hours) and during work hours only. We will ensure good compliance with this device by checking each device on return and requesting a re-wear if the participant does not provide enough valid days (e.g., at least four). The importance of this measure and the re-wear will be emphasised in the briefing events before the participants sign up to the study and in the participant information sheets. The participants will be offered a £10 gift voucher on the provision of valid activPAL data at each measurement time point. A wrist-worn accelerometer will also be worn on the non-dominant wrist 24hrs/day for up to 7 days at each measurement time point. Time spent in different intensities of physical activity as well as sleep duration and other sleep variables such as efficiency will be calculated. Participants will be asked to complete a short log each day to note the time they went to bed, went to sleep, woke up and got out of bed each day, work times, as well as recording any periods throughout the day if they removed the devices.

Self-reported sitting, standing, walking and breaks in sitting and time at desk and in office

Participants will be asked to complete an adapted version of the Occupational Sitting and Physical Activity Questionnaire (Chau et al 2012) as well as estimated the hours they spend sitting and breaking up sitting as part of their job (Clarke et al 2011). Participants will be asked to estimate the percentage of their working day that they spend at their desk space and their office space.

Dietary behaviours, smoking and alcohol

Dietary behaviours and alcohol intake will be assessed using questions from the Whitehall II study (http://www.ucl.ac.uk/whitehallII). Information on smoking status will also be gathered by self-report.

Self-reported sleep

Self-report sleep duration and quality will be assessed using the Pittsburgh Sleep Quality Index (PSQI).

Physical and mental fatigue

We will use the Fatigue Scale (Chalder, 1993) to measure fatigue severity. The Fatigue Scale is one of the most widely used measures assessing fatigue and includes 11 items, seven assessing physical fatigue and four assessing mental fatigue. Responses to items are measured using a 4-point Likert-style.

Work-related health

Job performance (Bond et al 2001) and job satisfaction (Nagy, 2002) will be measured using single-item 7-point likert scales, while participants will also be asked to indicate the extent to which they intentionally changed their work priorities and objectives to accommodate the change in sitting behaviour (6-point fully anchored scale). Work engagement (characterized by vigour, dedication, and absorption) will be measured using the Utretcht Work Engagement Scale (UWES) (Schaufeli et al, 2002); a multi-item 7-point likert scale. The Need for Recovery (NFR) Scale (van Veldhoven et al, 2003) will be used to measure occupational fatigue, while The Standardised Nordic Questionnaire (SNQ) for the analysis of musculoskeletal symptoms will be used to assess self-reported ratings of symptoms most often encountered in an occupational setting (Kuorinka et al,1987). Presenteeism will also be assessed both by using the validated 8-item Work Limitations Questionnaire (Lerner et al, 2001) that asks participants to rate on a six-point Likert scale how their health has affected aspects of their work in the past two weeks. Data on sickness absence will be collected using both self-report and from employer records and include frequency and duration of self-certified and certified sickness. Reasons for sickness absence will also be recorded. Data on sickness absence will be collected for 12 months prior to the intervention and for the 24 months of the intervention period.

Mental health, well-being and quality of life

Health-related quality of life will be assessed using the EQ5D-5L (Herdman et al 2011). Anxiety and depression will be measured using the Hospital Anxiety and Depression Scale (HADS) (Zigmond et al, 1983). Stress will be measured using the Perceived Stress Scale (Cohen et al, 1983).Emotion will be assed using the Positive and Negative Affect Schedule (PANAS) which comprises of two mood scales (positive and negative) (Watson et al, 1988). Wellbeing will be measured using the WHO-5 scale (Bech 1998).

Health-related resource use

The health related resource use will be based on a variant of the Client Service Receipt Inventory (Chisholm et al, 2000) and will include services that this population are likely to utilise such as GPs and Practise nurse appointments, occupational health visitors and other professionals that are deemed appropriate.

Table 1. Measurement schedule of the above outcomes and when they will be taken.

Measure	Baseline	3 months +/- 15 days	12 months +/- 15 days	24 months +/- 15 days
Objective sitting and physical activity	✔	✔	✔	✔
Self-report sitting and breaks	✔	✔	✔	✔
Office/desk dwell time	✔	✔	✔	✔
Job performance	✔	✔	✔	✔
Job satisfaction	✔	✔	✔	✔
Work engagement (UWES)	✔	✔	✔	✔
Occupational fatigue (NFR)	✔	✔	✔	✔
Fatigue (physical and mental)	✔	✔	✔	✔
Musculoskeletal symptoms (SNQ)	✔	✔	✔	✔
Presenteeism (WLQ)	✔	✔	✔	✔
Quality of Life	✔	✔	✔	✔
Sleep duration and quality (PSQI)	✔	✔	✔	✔
Self-reported sickness absence	✔		✔	✔

Sickness absence via employee records	✔		✔	✔
Anthropometric and blood pressure	✔	✔	✔	✔
Biochemical	✔	✔	✔	✔
Diet, smoking and alcohol	✔	✔	✔	✔
Mental health	✔	✔	✔	✔
Medical history and medication	✔	✔	✔	✔
Demographics	✔			
Job descriptives	✔	✔	✔	✔
Client Service Receipt Inventory	✔	✔	✔	✔

Process evaluation

The process evaluation methods will be a mix of questionnaires, interviews, focus groups and direct observation. The process evaluation will be used to understand the participants' experiences of the intervention and it's different components, help explain any discrepancies between expected and observed outcomes, understand the influence of intervention components and context on the observed outcomes, understand sustainability, extent of any contamination between intervention and control, any unexpected events arising from participation, and to provide insight for any further intervention development and implementation. For example, workplace champions from each site will report on a regular basis if there were any organisational changes (e.g. job changes) or events that may affect participation. They will also record attendance for sessions. Self-report questionnaires provided to study participants will evaluate their opinions of the various intervention components (e.g. education, coaching, self-monitoring). Interviews and focus groups with study participants (sub-sample) will further examine engagement in the various components of the intervention, along with any barriers or facilitators to participating in the various components. Focus groups with workplace champions will further examine the intervention implementation and the champions' experiences of delivery. All interviews and focus groups will be audio-recorded.

Throughout the intervention we will monitor the fidelity of the intervention implementation using the Normalisation Process Theory framework (NPT) (May et al 2015) in line with guidance from the National Institutes of Health Behaviour Change Consortium and the DESMOND collaborative. Observations of sessions (e.g., coaching) will take in both intervention arms to assess whether the content was delivered as expected and receipt by attendees.. Observations will be undertaken by a trained observer who is assessed as reliable in the use of the structured observation tool that will be completed during the observations. During the observations a case report form will also be completed. The case report form will combine an 'adherence measure' to capture delivery (mode of delivery (dose)/duration/content) and use of resources (materials/activities). The structured observation tool will assess facilitator delivery of prescribed behaviours and behaviour change techniques. The case report form will also contain specific objective 'receipt' measures and will likely include examples related to how well the participants understand the content and engage in the session.

Observations in the office clusters will also take place in a random sample of offices in both intervention arms at several time points during the intervention period. Each observation will be done over one whole working day. This observation work will be guided by the four domains of the NPT and an observation guide will highlight the types of behaviours of focus, such as: use of height adjustable desks, sitting and standing time, engagement with colleagues, walking/standing meetings as well as office structure, posters displayed. Practically, the observation work will include keeping structured field notes and collating relevant documentation for further context and insight, and may include informal discussions with office workers and workplace champions. A random sample of control offices will also be observed to judge contamination and other practices that may impact on our behaviours of interest.

7.4 Randomisation

A participant unique identifier number will be assigned as each participant is consented into the study. Once all participants in a particular office cluster have been measured, the office cluster will be assigned to an arm by a CTU statistician using a pre-generated list.

7.5 Definition of End of Trial

The end of trial is the date the last participant completes their final study visit.

7.6 Discontinuation/Withdrawal of Participants from Study Treatment

Each participant has the right to withdraw from the study at any time. The reason for withdrawal will be recorded in the CRF. However, participants will not need to provide a reason for their

withdrawal if they do not wish not to do so. Any data collected up to the point of consent withdrawal will be included in the analysis.

7.7 Source Data

Source data is the first place a value or measurement is recorded. These include case report forms, lab reports, participant diaries and questionnaires. All documents will be stored safely under confidential and secure conditions.

8 TREATMENT OF TRIAL PARTICIPANTS

8.1 Intervention background

The proposed SMART Work & Life intervention is a multicomponent intervention promoting positive changes in daily overall sitting and movement in office workers. SMART Work & Life, has been developed with input from office workers, local council office workers, workplace champions, council stakeholders, recently published research, experiences in Australia (the Stand Up Australia programme of research e.g., Stand Up Comcare and Stand Up Victoria) (http://www.iea.cc/congress/2015/1904.pdf), and a 12-month RCT of a previous version of the intervention - SMArT Work (O'Connell et al, 2015). As a result SMArT Work has been refined and extended to become SMART Work & Life. SMART Work & Life incorporates improvements that were noted following the SMART Work RCT and addresses the gaps in existing interventions by going beyond sitting in the workplace to also focus on behaviour change outside of work, emphasising a novel 'whole-of-day' preventive approach to overcome the behaviour compensation that is observed.

SMART Work & Life is grounded in several behaviour change theories (Social Cognitive Theory (Bandura, 1986), Organisational Development Theory (Steckler et al 2002), Habit Theory (Verplanken et al 1999), Self-Regulation Theory (Baumeister et al 2004) and Relapse prevention Theory (Marlatt et al 1984)) and implemented through the Behaviour Change Wheel (BCW) and the associated COM-B approach (Michie et al, 2011).The latter has 'capability', 'opportunity', and 'motivation' as central components in guiding 'behaviour' SMART Work & Life emphasises not just behaviour change per se, but the under-developed area of behavioural maintenance (Kwasnicka et al, 2016). While behaviour change has been achieved through sedentary behaviour as well as physical activity interventions, it is recognised that changing some behaviours can be a challenge. Moreover, few studies are willing or able to tackle the greater challenge of behavioural maintenance. It was over 30 years ago when it was stated that health reasons may help people engage in behaviour change (e.g. physical activity) but feelings of enjoyment are likely to be more powerful for the maintenance of such behaviour (Dishman et al, 1985). Yet studies often fail to emphasise behavioural maintenance or are not long enough to test for such effects. Moreover, strategies aimed at enjoyment ('positive affect') are not always included.

A recent review of health behaviour maintenance stated that people would be more likely to maintain changes in behaviour if they enjoyed engaging in the behaviour and were satisfied with the outcomes, could successfully monitor their behaviour, have effective strategies to overcome barriers, have psychological and physical resources, have their behaviour

supported by more 'automatic' cues in the social and physical environment, and have a generally supportive environment (Kwasnicka et al, 2016). Our own review has shown that successful behaviour change techniques might involve education, environmental restructuring, persuasion, and training as they showed potential for engineering reduction in sedentary behaviour. (Gardner et al, 2016).

8.2 Intervention goal

The aim of the intervention will be to promote and maintain at least a 60 minute per day reduction in overall daily sitting time compared to control. Recent experimental evidence has demonstrated a reduction in glucose, insulin and blood pressure following regular standing and walking breaks (Henson et al 2016; Dunstan et al 2012; Larsen et al 2014). Furthermore, using statistical modelling we have observed that interchanging 30 mins/day of sitting (measured with the activPAL) with standing and stepping is associated with favourable differences in insulin sensitivity (Edwardson et al, 2017). In a similar analysis, our collaborators in Australia (GH,DD) have observed that interchanging 2 hour of sitting/day with standing or stepping is associated with favourable differences in glucose, triglycerides, cholesterol and waist circumference (Healy et al, 2015). Others have also shown that each additional hour/day of sitting past 7 hours is associated with a 5% higher risk of mortality in the general population (Chau et al, 2013).Thus based on the available evidence, a reduction in sitting time of 60 minutes is likely to represent a clinically meaningful difference in behaviour.

8.3 Intervention Group 1

Organisational strategies grounded in Social Cognitive Theory and Organisational Development Theory (targeting 'opportunity' & 'motivation' through BCW intervention functions: enablement, persuasion, environmental restructuring, modelling, positive emotion): 1) we will seek buy-in from the management through the briefing events by explaining the importance of reducing and breaking up sitting at work and how this may lead to workplace benefits without negatively affecting performance and productivity; 2) a brief awareness session (online/video) which will reinforce the benefits for the workforce and employers of reducing sitting time in and outside of work, and encourage them to brainstorm organisational strategies that could take place, review any current policies around being active at work and as well creating new policies around topics such as standing and walking meetings, provision for lunch time walking, internal competitions and displaying signs around the workplace. We will also encourage managers to review the layout of their office space to promote increased movement of staff e.g., location of printers, waste bins, water coolers; 3) Modelling of the positive behaviour from managers will also be emphasised.

Environmental strategies grounded in Social Cognitive Theory, Organisational Development Theory and Habit Theory (targeting 'capability', 'motivation' & 'opportunity' through BCW intervention functions: environmental restructuring, enablement as well as 'automatic' forms of motivation, including emotion): 1) Small-scale environmental restructuring in the office and at home (e.g., relocation of printers and waste bins), 2) Motivational and reminder signs around the office space and at home to sit less and move more, 3) A height-adjustable desk or desk platform to allow the individual to sit or stand to work. The individual will get a choice of desk/desk platform within a set budget. This allows flexibility for office set up, participant preference and avoids testing the effectiveness of a specific type of desk rather than the concept.

Individual and group strategies grounded in Social Cognitive Theory, Self-Regulation Theory and Relapse Prevention Theory (targeting 'capability, 'motivation' & 'opportunity' through BCW intervention functions: enablement, persuasion, education and training): 1) An initial education session which covers health consequences of sitting and benefits of reducing and regularly breaking up sitting. During the session they will brainstorm strategies to reduce sitting at work and outside of work, think about barriers to reducing and breaking up sitting and ways to overcome these. At the end of the session individuals will be encouraged to set a goal around sitting less and an action plan to achieve this. The focus on overall daily sitting will be emphasised rather than just workplace sitting; 2) Self-monitoring of sitting behaviour across the whole waking day will be encouraged through the use of free computer prompts, timers and mobile phone apps. An app named Rise & Recharge has shown promise in participant acceptability and short term effectiveness for reducing and breaking up sitting (Dunstan et al 2016).The Rise & Recharge app specifically targets prolonged sitting by encouraging breaks every 30 minutes (http://www.riserecharge.com/). The app is available on both Apple and Android phones making it accessible to most individuals. The importance of self-monitoring and the apps will be introduced during the education session and individuals will be encouraged to download the app during the session 3) Workplace champions will receive training to deliver brief coaching/refresher sessions. These sessions will be used to review key messages, discuss progress, review goals and action plans, discuss barriers and any benefits experienced. These coaching /refresher sessions will likely take place at 3, 6, 12 and 18 months5) Social support, from colleagues and family members, will be encouraged through regular activity competitions inside and outside of work.

8.4 Intervention Group 2

This group will receive all of the intervention components listed in the previous sections above minus the height-adjustable desk allowing us to investigate how important providing a simple, but fairly expensive, environmental change is for significant reductions in sitting.

8.5 Control Group

Office clusters assigned to the usual practice control arm will be asked to continue with their usual occupational health promotion conditions. Participants in the control arm will be asked to complete the same study measurements as those in the intervention arms, at the same time points.

8.6 Storage of Study Equipment or Related apparatus

Study equipment will be stored at the Leicester Diabetes Centre, Leicester General Hospital/ University of Leicester or at the University of Salford.

9 SAFETY REPORTING

9.1 Definitions

9.1.1 Adverse Event (AE)

An AE or adverse experience is:

Any untoward medical occurrence in a participant or clinical investigation participants, which does not necessarily have to have a causal relationship with this 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.

9.1.2 Severe Adverse Events

This study is a non-invasive lifestyle modification study, therefore no SAEs are expected.

9.1.3 Expected Serious Adverse Events/Reactions

This study is a non-invasive lifestyle modification study, therefore no SAE/Rs are expected.

9.1.4 Suspected Unexpected Serious Adverse Reactions

This study is a non-invasive lifestyle modification study, therefore no SUSARs are expected.

9.2 Reporting Procedures for Adverse Events

All AEs occurring during the study observed by the trial team or reported by the participant, whether or not attributed to study, will be recorded on the CRF. The following information will be recorded: description, date of onset and end date, severity, assessment of relatedness to study, other suspect device and action taken. Follow-up information should be provided as necessary.

AEs considered related to the study as judged by the Chief Investigator will be followed until resolution or the event is considered stable. All related AEs that result in a participant's withdrawal from the study or are present at the end of the study, should be followed up until a satisfactory resolution occurs.

10 STATISTICS

10.1 Description of Statistical Methods

Primary and secondary outcomes

This study will be analysed and reported according to the CONSORT statement for cluster RCTs. A statistical analysis plan will be written prior to database lock for the cluster RCT.

The aim of the primary analysis is to investigate whether the multi-component intervention, with and without a height-adjustable desk, leads to reductions in objectively measured overall sitting time compared to usual practice at 24-month follow-up. The primary outcome analysis was powered to detect a clinically significant difference in sitting time of 60 minutes at 24 months. However, discontinuation of the study due to futility will be considered in a formal interim analysis at 12 months. An Independent Data Monitoring and Ethics Committee (DMEC) will be convened to review the primary outcome at 12 months. The conditional probability of the final study results being statistically significant given the data observed at 12 months will be calculated and the DMEC will make a recommendation based on this and other important factors (i.e. trial conduct, data quality, participant retention) of whether or not to continue follow-up until 24 months. If the DMEC decide the data from the interim analysis at 12 months provides satisfactory evidence to continue, the trial will continue to follow-up participants to 24 months as there is evidence that this magnitude of difference at 24 months improves long-term health. Furthermore, only if both arms are determined to be futile at the interim analysis stage will the trial be stopped early.

The primary analysis will be performed using a linear multilevel model with sitting time as the outcome variable, levels to indicate the clustering of workers within office sites, a categorical variable for randomisation group as the explanatory variable, and terms for the stratification factors (area and cluster size) and baseline values as confounders. In these linear multilevel models, office clusters will be incorporated as a random effect to model worker heterogeneity within office sites. The structure of the variance-covariance matrix for the random effect will be assumed to be unstructured and the models will be estimated using restricted maximum likelihood. For the primary analysis, missing data will not be replaced (complete case analysis) and participants will be included in the intervention group in which their clusters were randomised irrespective of the intervention that was actually received. The number of clusters per arm was inflated to allow for multiple comparisons against the control group and to allow for whole cluster drop out. The sample size was also inflated by 30% to account for potential loss to follow-up and non-compliance with the primary outcome measure. The baseline characteristics of those who have complete primary outcome data will be compared with those who dropped out from the study in order to investigate differences between them.

A sensitivity analysis using multiple imputation will be performed to evaluate the impact of missing outcome data on the results obtained and to account for uncertainty associated with imputing data (full intention-to-treat analysis). Missing data will be replaced using multiple imputation methods in Stata using the MI command. With the MI command, missing data is replaced with multiple sets of simulated values in order to complete the data, standard analysis on each completed dataset is performed, and the obtained parameter estimates are adjusted for missing-data uncertainty using Rubin's rules to combine estimates. The effect size will also be estimated using a per-protocol analysis, which will only include those who were compliant with the protocol and follow-up visits. Secondary outcomes, including those measured at other time-points, will be analysed using similar methodology. We will additionally assess data from all time points for the primary outcome in a single analysis using repeated measured. We will also conduct a subgroup analysis which compares the treatment effect in those clusters in which other work place health initiatives were taking place at the same time as the study compared to those where there were no such initiatives.

All tests and reported p-values will be two-sided. Estimates will be presented with 95% confidence intervals.

Process evaluation

Audio-recordings of interviews and focus groups with office workers and workplace champions will be transcribed verbatim and analysed using framework analysis using the Normalisation Process Theory as the overarching framework.

Cost-effectiveness

The economic evaluation will consist of two analyses. i) a cost-consequence analysis based on the observed results within the trial period. ii) a cost-effectiveness analysis where differences between groups in the trial will be extrapolated to the longer term where appropriate.

For both analyses, costs in both arms will be estimated from a NHS and Personal Social Services (PSS) perspective (consistent with that used by NICE) as well as a wider public sector perspective. In each analysis, the cost of the SMART Work & Life groups will include an estimate of the cost of the intervention, with and without the height adjustable desk. The cost of the intervention consists of the cost of equipment (such as desks) and the cost of training and delivery of intervention, including the time of those attending educational sessions. We will estimate the cost of the equipment from manufacturers estimates of costs. Estimates of the

cost of training for participating individuals will be generated through a staff questionnaire completed at the end of each education session; we will also include the cost of training and delivery of intervention by the workplace champions.

Within-trial analysis: Within the period of the trial, we will collect resource use estimates from participant questionnaires. These questionnaires will record health related resource use as well as absence from employment. The health related resource use will be based on a variant of the Client Service Receipt Inventory and will include services that this population are likely to utilise such as GPs and Practise nurse appointments, occupational health visitors and other professionals that are deemed appropriate. Costs of resources will be calculated by applying published national unit cost estimates (e.g. NHS reference costs or PSSRU Unit costs of health and social care), where available, to estimates of relevant resource use.

A range of outcomes will be assessed in the trial including health related quality of life, measured using the EQ5D-5L The within trial analysis will present incremental results for the primary and secondary outcomes (including EQ5D) in both intervention and control arms and will be compared with the incremental costs measured above. We will also present the results in terms of the differences between the groups in time absent from work. As there is some controversy over inclusion of productivity losses in the assessment of cost-effectiveness, the within trial analysis will be presented both with and without estimates of the cost of absenteeism. This will allow decision makers to assess the importance of inclusion of absenteeism costs when deciding whether to implement the intervention.

Longer term analysis: While there may be short term health benefits from reducing levels of sitting time, the longer term effects on mortality on office workers is likely to be more important. We will therefore use existing evidence that links short-term trial endpoints and longer term outcomes. While some existing evidence used covariates to adjust for confounding factors, it is not possible to assess unmeasured confounders. Therefore, we will use existing evidence to extrapolate costs and effects to a more appropriate time horizon; however, as recommended by Taylor and Elston (Taylor & Elston, 2008) we will explain how the surrogate-final outcomes relationship is quantified and explore the uncertainty around the use of the surrogate outcome (in this case sitting time) through sensitivity analysis.

If appropriate an Incremental Cost-effectiveness Ratio for the extrapolated period will be reported using the Quality Adjusted Life Year (QALY). As with the within-trial analysis, we will conduct analyses where productivity losses are included/excluded to assess the impact on decision making. Costs and effects will be discounted at the prevailing recommended rate (currently 1.5% per annum on both costs and effects), but will be the subject of sensitivity analysis to reflect the ongoing uncertainty around appropriate discount rates for public health

interventions. We will conduct probabilistic sensitivity analyses to allow a characterisation of the uncertainty around the adoption decision which we will depict using cost-effectiveness acceptability curves. Sensitivity analyses will be performed to determine the robustness of the results to altering certain assumptions such as the discount rate, inclusion/exclusion of productivity losses and the robustness of the relationship between sitting time and mortality.

10.2 The Number of Participants

In this study, the primary outcome measure used for the sample size calculation is the change in objectively measured overall daily sitting time, measured by activPAL, after 24 months. The study has been powered to detect a difference of 60 minutes between both intervention arms and the control arm which reflects the goal of the intervention.

The primary analysis will be performed using linear multilevel models, which require a minimum of 10 clusters per arm in order to robustly estimate random effects.[65] Power calculations indicated that with a sample size of 420 participants and 10 clusters per arm, this study would have over 90% power to detect a 60 minute reduction in overall sitting time using multilevel models with a two-tailed significance level of 5%. The calculations assumed an SD of 90 minutes (informed by SMArT Work), a conservative ICC of 0.05 (informed by Stand Up Victoria (Healy et al, 2016)), a coefficient of variation to allow for variation in cluster size of 0.54 (cluster range 15-45), and an average cluster size of 20. These calculations allowed for multiple comparisons against the control group, and then the number of clusters per arm was inflated by 1 to allow for whole cluster drop out and the sample size was also inflated by 30% to allow for potential individual loss to follow-up and non-compliance with the primary outcome, giving a total sample size of 660 to be recruited, with 11 clusters per arm. Finally, the sensitivity of power was assessed against alternative ICC values of 0.021 and 0.10 (Healy et al, 2016). Adequate power for RCTs is widely accepted as 80%, and with these ICC values the power was above the required level at 98% and 81%, respectively. Furthermore, the study we have referenced (Healy et al, 2016) employed an ICC=0.021 for overall sitting, while we have chosen a more conservative value, ICC=0.05.

10.3 The Level of Statistical Significance

Statistical analyses tests will be two-sided with a 5% significance level.

10.4 Criteria for the Termination of the Trial.

There is no official criteria for trial termination. The trial will be conducted in accordance to the sponsors SOPs and in accordance to the HRA.

10.5 Procedure for Accounting for Missing, Unused, and Spurious Data.

Assessment of the primary outcome and secondary outcomes will follow an intention to treat and per-protocol analysis, with missing data being replaced using multiple imputation or another appropriate method.

10.6 Procedures for Reporting any Deviation(s) from the Original Statistical Plan

Any deviation(s) from the original statistical plan will be described and justified in protocol and/or in the final report, as appropriate.

10.7 Inclusion in Analysis

All analysis will be conducted via intention to treat and per-protocol.

11 DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

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

12 QUALITY CONTROL AND QUALITY ASSURANCE PROCEDURES

University of Leicester as sponsor operate a risk based audit programme to which this study will be subject. The study team and the Leicester Clinical Trials Unit (LCTU) will be responsible for elements of study management as defined in the Service Level Agreement on an on-going basis. A documented monitoring log and audit trail will be maintained throughout the lifetime of the study. The Principal Investigator, Leicester CTU and study co-ordinator will oversee the set-up of and conduct of study procedures at each site. All source data, study documents will be made available for Sponsor monitoring, and any external audits and inspections as appropriate.

13 CODES OF PRACTICE AND REGULATIONS

13.1 Ethics

Approval from Sponsor (University of Leicester) and ethics representatives at both the University of Leicester and University of Salford will be sought prior to the commencement of the research. This will ensure that all ethical and indemnity issues are dealt with. The Study Co-ordinator will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents. The Chief Investigator will ensure that this study is conducted in full conformity with relevant regulations and with the International Conference on Harmonisation Guidelines for Good Clinical Practice.

Participants will be free to withdraw at any time from the study without giving a reason and without their legal rights being affected. We do not anticipate any harm, discomfort or risk to any participant enrolled in this study. The overall care and comfort of the participant will be considered paramount at all times during the study.

13.2 Sponsor Standard Operating Procedures

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

13.3 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).

13.4 ICH Guidelines for Good Clinical Practice

The Investigator will ensure that this study is conducted in full conformity with relevant regulations and with the latest version of ICH Guidelines for Good Clinical Practice

13.5 Approvals

The protocol, informed consent form, participant information sheet and any proposed advertising material will be submitted to appropriate University of Leicester and University of Salford ethics representatives and the Sponsor for written approval. Once Sponsor authorisation has been confirmed, the Investigator will submit and, where necessary, obtain approval from the above parties for amendments to the original approved documents.

13.6 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. Direct access to all documents will be granted where appropriate to authorised representatives from the sponsor, and LCTU, for monitoring, audits and inspections. The study will comply with the Data Protection Act which requires data to be anonymised as soon as it is practical to do so.

13.7 Other Ethical Considerations

N/A

14 DATA HANDLING AND RECORD KEEPING

All data collected will be kept strictly confidential and in accordance with all relevant legislation. The research staff will ensure that the participants' anonymity is maintained. On all study-specific documents, other than the signed consent form enrolment log and blood test results card, the participant will be identified by initials and/or a participant ID number, not by name.

All research data will be kept in a secure location within University of Leicester, University of Salford or the University Hospitals of Leicester, accessible only by named members of the research team during the active phase of the study and until the data have been analysed. It will then be archived in line with University of Leicester policy.

Direct access to information gathered in this study will only be available to individuals who have been granted access. The sponsor and host institution can permit trial related monitoring, audits and inspections. Information will only be obtained from the participant if necessary for the study.

All electronic data will be stored on secure university or hospital systems , to which only the relevant study staff have access, which is granted by the research team. All study documents and data will be kept for 5 years or the minimum determined by the funder, whichever is longer. The study file will be archived in line with the Sponsor/LCTU SOPs.

LCTU has a well-established IT infrastructure and will be providing a GCP-compliant database solution using a Clinical Data Management System (CDMS) called InferMed Macro. This is a secure and validated database solution with quality control mechanisms to ensure that the data collected are complete and accurate. The CTU works within a Quality Management System framework and will ensure that the relevant staff utilising CTU services are adequately trained and supported.

Neither hard copies nor electronic files containing personal information will be removed from the research office or stored in a non-secure manner electronically. The study research team will comply with the Data Protection Policy of Councils, and Universities and Sponsor/LCTU SOP.

15. STUDY GOVERNANCE

15.1 Committees/Meetings

The study will be sponsored by the University of Leicester. Five groups will be created to oversee the study; a Data Monitoring and Ethics Committee (DMEC), a Trial Steering Committee (TSC), an Employer Advisory Group (EAG), an Investigator Committee (IC) and a Project Co-ordination Committee. We will appoint a fully independent DMEC comprising of at least three members, including an independent chair and a statistician which will make recommendations to the TSC. They will meet every 6 months 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 Chief Investigator (Dr Edwardson), an independent chair, two independent external members, two council 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 EAG will consist of senior managers from the local Councils and they will meet at least once per year over the three year project to advise on recruitment, delivery, dissemination and translation.

The Investigator Committee will meet every 3 months and comprise of all Investigators listed on the application as well as the International Collaborators in Australia (Profs Biddle and Dunstan and Dr Healy). 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 Project Co-ordination Committee will meet fortnightly to discuss the day-to-day running of the project and they will provide an update report for the TSC and IC. This committee will comprise of the PI, CTU Study Manager, the Research Assistants and Administrators at both sites (Leicester and Salford).

16 FINANCING AND INSURANCE

Funder: This research will be funded by a research grant awarded by the NIHR Public Healh Research funding stream (80% - £905,133)

Sponsorship and indemnity for the study will be provided by the University of Leicester.

17 PUBLICATION POLICY

It is envisaged that the results of the study will be published in relevant medical or behavioural journals, used for educational purposes and presented at academic conferences. Acknowledgement of any supporting organisations will be included.

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