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Bristol Randomised Trials Collaboration

University of BRISTOL

Bristol Randomised Trials Collaboration (BRTC)

Travel to Work

Statistical and Health Economics Analysis Plan

Version 1.1 (21 April 2017)

The following people have reviewed the Statistical and Health Economic Analysis Plan and are in agreement with the contents			
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CONTENTS

Abbreviations/Glossary

AE	Adverse event
ASHE	Annual Survey of Hours and Earnings
BRTC	Bristol Randomised Trials Collaboration
CPM	Counts per minute
GPS	Global Positioning System
ICC	Intra-cluster correlation coefficients
ICECAP-A	ICEpop CAPability measure for Adults
ITT	Intention to treat
Modal Shift	Change in mode of transport e.g. from car to walking. To be measured by the number of journeys when walking was the major mode of transport to and from work
MVPA	Moderate to vigorous physical activity
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
NIHR-PHR	National Institute for Health Research – Public Health Research
PA	Physical activity
QoL	Quality of life
RCT	Randomised controlled trial
SAE	Serious adverse event
TSC	Trial Steering Committee
WHO	World Health Organisation

1. INTRODUCTION AND PURPOSE

This document details the rules proposed and the presentation that will be followed, as closely as possible, when analysing and reporting the main statistical results from the **Travel to Work** study.

The purpose of the plan is to:

1. Ensure that the analysis is appropriate for the aims of the trial, reflects good statistical practice, and that interpretation of a priori and post hoc analyses respectively is appropriate.
2. Explain in detail how the data will be handled and analysed to enable others to perform the actual analysis in the event of sickness or other absence.

Additional exploratory or auxiliary analyses of data not specified in the protocol are permitted but fall outside the scope of this analysis plan (although such analyses would be expected to follow good statistical practice).

The analysis strategy will be made available if required by journal editors or referees when the main papers are submitted for publication. Additional analyses suggested by reviewers or editors will, if considered appropriate, be performed in accordance with the analysis plan, but if reported the source of such a post-hoc analysis will be declared.

Amendments to the statistical analysis plan will be described and justified in the final report of the trial.

1.1 RATIONALE

Physical inactivity increases the risk of many chronic diseases including coronary heart disease, type 2 diabetes, obesity and some cancers[1]. Increasing physical activity levels, particularly among the most inactive, is an important aim of current public health policy in the UK[2]. There is also increasing interest in the relationship between time spent sedentary and poor health outcomes[3] and consequently UK health guidelines recommend that adults should minimise the amount of time spent sedentary (sitting) in addition to increasing physical activity.

In the UK, there are substantial opportunities to increase walking by replacing short journeys undertaken by car. For example, the 2011 National Travel Survey showed 22% of all car trips were shorter than two miles in length, while 18% of trips of less than one mile were made by car[4]. An opportunity for working adults to accumulate the recommended moderate activity levels is through the daily commute and, in addition, replacing the car for short journeys is likely to reduce sedentary time. Experts in many World Health Organisation (WHO) countries agree that significant public health benefits can be realised through greater use of active transport modes[5]. Furthermore, cost benefit analysis for the UK Department for Transport suggests the ratio of benefits to costs are high[6].

NICE public health guidance on workplace health promotion concluded that although schemes exist to encourage employees to walk or cycle to work, little is known about their impact[7]. Few studies used robust data collection methods to measure the impact of workplace interventions on employees' physical activity levels, with most using self-report. There was also a lack of information about how interventions are influenced by the size and type of workplace and the characteristics of employees.

In 2011, the National Institute for Health Research Public Health Research (NIHR-PHR) programme funded the Walk to Work feasibility study (Project 10/3001/04) which incorporated a Phase I development of a behavioural intervention followed by a Phase II exploratory trial in 17 workplaces in Bristol[8]. The intervention was tested in small, medium-sized and large workplaces, used objective measures of physical activity, and included process evaluation and an assessment of costs. Results from the feasibility study demonstrated that the intervention and its evaluation were feasible and funding was granted for a full-scale cluster randomised controlled trial (NIHR- PHR - 13/117/01)[9].

2. SYNOPSIS OF STUDY DESIGN AND PROCEDURES

This is a summary of the study design as described in the study protocol paper with the single purpose of ensuring an informed statistical analysis. For all other purposes reference MUST be made to the current version of the protocol.

The main aim of the Travel to Work trial is to examine the effectiveness, cost effectiveness and generalisability of a workplace-based 'Walk to Work' intervention.

2.1. TRIAL OBJECTIVES AND AIMS

2.1.1. PRIMARY OBJECTIVE

1. Does the intervention lead to an increase in daily minutes of moderate to vigorous physical activity (MVPA) after one year compared with the control group?

2.1.2. SECONDARY OBJECTIVES

1. Does the intervention lead to an increase in overall physical activity compared with the control group?
2. Does the intervention decrease the daily minutes of sedentary time, compared with the control group?
3. Does the intervention lead to an increased number of journeys where walking to work is the major mode of travel, compared with the control group?
4. Does the intervention increase the MVPA due to walking on the commute, compared with the control group?

2.1.3. ECONOMIC OBJECTIVES

1. What are the intervention costs to participating employers and employees?
2. Does the intervention lead to increased or decreased costs in terms of healthcare use, commute costs and productivity losses?
3. Does the intervention lead to improved wellbeing as measured by the ICECAP-A questionnaire?

2.2. TRIAL DESIGN AND CONFIGURATION

The study is a multi-centre cluster randomised controlled trial, aiming to recruit 84 workplaces in south-west England and south Wales, and incorporates process and economic evaluations. The intervention will be implemented in 42 workplaces; and 42 workplaces will be randomised to the control arm.

2.3. ELIGIBILITY CRITERIA

2.3.1. INCLUSION CRITERIA (ALL CRITERIA MUST BE MET)

1. Employees in participating workplaces in urban and suburban areas of south-west England and south Wales will be eligible to take part.

2.3.2. EXCLUSION CRITERIA (IF ANY CRITERION MET)

1. Employees who already always walk/cycle to work
2. Employees who are due to retire before the one year follow-up data collection
3. Employees who are disabled in relation to walking
4. Employees for whom daily driving is a key part of their role (e.g. sales reps)
5. Workplaces with a large proportion of short-term/zero hour contracts as follow-up data may not be achievable
6. Workplaces with plans to significantly downsize/relocate during the study period

2.4. DESCRIPTION OF INTERVENTION

Workplace 'Walk-to-Work promoters' will be identified (volunteers, or nominated by participating employers) and trained by members of the research team about the benefits of walking during the daily commute and how to promote increased walking either by walking the entire route or mixing walking with other transport modes. Training will take place during the working day on site, or at a group external event, as appropriate to the needs of the workplace. The Walk-to-Work promoters will be given resource packs and trained to access relevant websites and toolkits. They will also be trained in the use of specific behaviour change techniques that form the basis of the intervention, including: providing information on the link between walking and health; prompting intention formation; identifying barriers to walking and ways to overcome them; prompting goal setting; prompting self-monitoring; identifying social support and encouragement; reviewing goals, and; relapse prevention. There is evidence that these techniques are effective in achieving behaviour change[10,11] and can be effectively delivered by non-specialists. There will be a maximum of 25 participants to each promoter. Additional booklets will be provided for employers/managers with information and ideas of how the workplace can support increased walking during the daily commute.

Participating employees will be contacted by the Walk-to-Work promoter and given a Walk-to-Work pack including an information booklet, travel diary and pedometer. Goals for incorporating walking into the journey to and from work will be set. Further encouragement will be provided through four contacts from the Walk-to-Work promoter over the following 10 weeks (face-to-face, email or telephone as appropriate to the workplace size, resources and work routines).

2.5. RANDOMISATION PROCEDURES

Randomisation will take place at the level of the workplace. Employers in workplaces expressing an interest will be asked to complete a short questionnaire. From the results of these questionnaires the randomisation will be carried out by creating pairs (or triples) of workplaces with similar characteristics such as the size of the company (micro, small, medium and large), location (Swansea (including Newport and Neath Port Talbot), Bath (including Swindon), Bristol (including South Gloucester) and type of business (using UK-SIC category). Assignment of workplaces will be carried out by the Bristol Randomised Trials Collaboration (BRTC) after pairing of workplaces with one workplace randomised to control and one (or two in a triple) to intervention using a concealed randomly computer generated allocation to minimise selection bias.

Given the nature of the intervention it is not possible to blind participants following randomisation.

2.6. SAMPLE SIZE AND JUSTIFICATION

Using the findings from the feasibility study, the sample size for the full scale trial was based on an average cluster size of 8, an ICC of 0.15 and participant attrition of 25%.

The calculation needed to allow equal numbers of workplaces between the intervention and control groups. We calculated that we needed 339 per study arm to detect a 15% difference in MVPA levels (equal to a difference of 0.36 standard deviations) with 80% power at the 5% significance level. Therefore 678 employees were required from 84 workplaces. The intervention would be implemented in 42 of the 84 workplaces; while the remaining 42 formed the control arm.

2.7. TRIAL COMMITTEES

The Travel to Work trial has a Trial Steering Committee, chaired by Dr David Ogilvie, Programme Leader, MRC Epidemiology Unit, University of Cambridge. Dr Obi Ukoumunne, Associate Professor in Medical Statistics, University of Exeter, is the independent statistician and Dr Emma Frew PhD, Dr Emma Frew, Reader in Health Economics, Institute of Applied Health Research, University of Birmingham, is the independent health economist for the Trial Steering Committee.

2.8. OUTCOME MEASURES

Raw accelerometer data will be downloaded using Actilife 6 software (ActiGraph LLC) and reintegrated to ten-second epochs for analysis and matching with GPS data. Reintegrated accelerometer data will be processed using Kinesoft (v3.3.75; KineSoft, Saskatchewan, Canada) data reduction software to generate outcome variables. Continuous periods of 60 minutes or more of zero values will be considered to be “non-wear” time and removed. The outcome variables of total physical activity volume (mean daily accelerometer counts per minute (cpm), time spent in moderate to vigorous physical activity (MVPA) and sedentary time, will be defined using validated thresholds (MVPA ≥ 1952 cpm; sedentary <100 cpm)[12].

For the primary outcome analysis and the secondary outcome analyses of overall physical activity and sedentary time, participants are required to provide three days of valid accelerometer data of at least 600 minutes of accelerometer data. Participants are required to provide at least one valid day of accelerometer and GPS data to be included in the secondary outcome analyses of modal shift and daily MVPA of the commute.

Accelerometer and GPS data will be combined (accGPS) based upon the timestamp of the Actigraph data. For measurement of the journeys to and from work, the participant's workplace and home will be geocoded using the full postcode, and imported into a Geographical Information System (ArcMap v10.2.2). The merged accGPS files will then imported into ArcMap and journeys to and from work visually identified and segmented from other accGPS data using the "identify" tool. Journeys will be identified as a continuous (or near-continuous) sequence of GPS locations between the participant's home and workplace, and thus will include trips to other destinations (e.g. supermarkets) if taken as part of the journey to or from work. The data will also be visually analysed by the researcher to categorise participants' daily mode of travel to work over the measurement week using the variables: counts per 10 seconds, changes to sum of SNR, speed (km/hr) and GIS location. Where accelerometer and GPS data is not available, self-report data in the travel diaries will be used to define mode of transport on the commute.

Cycling journeys will be excluded from all analyses due to the inability of waist worn accelerometers to accurately record physical activity during cycling. For participants who used a mixed mode of travel (e.g. car and train) for a journey, the mode of transport of the greatest distance was considered to be their mode for that journey. If the modes were of equal distance, the data will be coded as the most active mode of travel. When an outward/return journey is missing, it will be assumed to be via the same mode of travel as the outward/return journey on the same day.

The economic evaluation will be presented as a cost-consequence analysis whereby costs and consequences are tabulated but no attempt will be made to combine results. A broad perspective will be taken to include employer, employee and health care costs and individual wellbeing over the one year follow-up period. Discounting will not be performed given the one year follow-up period.

Outcomes, data collection methods and timing

Outcome	Method	Timing
PRIMARY OUTCOME		
i) Daily minutes of MVPA	Accelerometers	Baseline data collection (DC1) and 1 year follow-up (DC3)
SECONDARY OUTCOMES		
ii) Overall level of physical activity (cpm)	Accelerometers	DC1, DC3
iii) Daily minutes of sedentary time	Accelerometers	DC1, DC3
iv) Daily minutes of moderate to vigorous activity during the commute (Mean MVPA over the number of valid working follow-up days completed)	Accelerometers and GPS Travel diaries	DC1, DC3
v) Modal shift (number of journeys, when walking was main mode of travel to/from work)	Accelerometers and GPS Travel diaries	DC1, DC3
ECONOMIC OUTCOMES		
vi) Commuting time and costs	Self-reported in the participant travel diaries	DC1, DC3 for a one week period
vii) Health care resource use	Self-reported in participant questionnaires	DC1 for the past 4 weeks, DC2 (post-intervention) & DC3 during the past 3 months
viii) Productivity and days off from work	Self-reported in participant questionnaires	DC1 for the past week, DC3 during the past 12 months
ix) ICECAP-A	Participant questionnaires	DC1, DC2, DC3
vi) Costs to employers of implementing the scheme	Employer questionnaires	DC2
xi) Overall workplace absentee rates	Pro forma sent to employers	Post DC3 for the 12 months between DC1 and DC3

2.8.1. PRIMARY OUTCOME

Primary outcome	**Type**	**Data Analysis**
i) Daily minutes of moderate to vigorous activity (Mean minutes of MVPA over the number of valid follow-up days completed, max. 7 days)	Continuous	Linear Regression (mixed-effects) *Covariates:-* - Treatment arm - Size of the company (categorical) - Location of the company (categorical) - Type of business (UK SIC category) - Baseline MVPA - Accelerometer wear-time (categorical) - Workplace as a random effect

2.8.2. SECONDARY OUTCOMES

Secondary Outcome	**Type**	**Data Analysis**
ii) Overall physical activity (mean counts per minute over the number of valid follow-up days completed, max. 7 days)	Continuous	Linear Regression (mixed-effects) *Covariates:-* - Treatment arm - Size of the company (categorical) - Location of the company (categorical) - Type of business (categorical) - Baseline overall physical activity - Workplace as a random effect
iii) Sedentary time (mean minutes per day over the number of valid follow-up days completed, max. 7 days)	Continuous	Linear Regression (mixed-effects) *Covariates:-* - Treatment arm - Size of the company (categorical) - Location of the company (categorical) - Type of business (categorical) - Baseline sedentary time - Accelerometer wear-time (categorical) - Workplace as a random effect
iv) Daily minutes of moderate to vigorous activity during the commute (mean MVPA over the number of valid working follow-up days completed, max. 7 days)	Continuous	Linear Regression (mixed-effects) *Covariates:-* - Treatment arm - Size of the company (categorical) - Location of the company (categorical) - Type of business (categorical) - Baseline daily minutes of moderate to vigorous activity during the commute - Workplace as a random effect
v) Number of journeys when	Categorical	Negative binomial regression (zero-inflated if appropriate) with an exposure variable of number of valid journeys,

walking was the major mode of travel to and from work (model shift, max. 14 journeys)		incorporating robust standard-errors to accommodate variation between workplaces *Covariates:-* - Treatment arm - Size of the company (categorical) - Location of the company (categorical) - Type of business (categorical) - Baseline number of journeys when walking was the major mode of travel to and from work

2.8.3. ECONOMIC COSTS AND OUTCOMES

Economic/cost outcome	**Item**	**Valuation**	**Data Analysis**
Intervention cost	Trainer time	Unit cost estimated using basic salary, national insurance and superannuation, or using the trainer's day rate.	Intervention cost presented as a cost per workplace and a cost per participating employee. Costs will also be stratified by workplace size.
	Employer cost	Employee time: Unit cost estimated by dividing the upper quartile weekly earnings by the median number of hours worked per week from the ASHE[18].	
	Employee cost	Employee reported travel cost to promoter training.	
	Training materials	Printing costs of employee and promoter booklets. Pedometer cost.	
Health care use	Primary care	Resource use multiplied by unit costs from the Unit Costs of Health and Social Care[13].	Total health care cost estimated for the past 3 months at 1 year follow-up. Regression *Covariates:-* - Treatment arm - Size of the company (categorical) - Location of the company (categorical) - Type of business (categorical) - Baseline health care cost in the last 4 weeks - Workplace as a random effect
	Secondary care	Resource use multiplied by unit costs from the NHS reference costs[14].	
	Prescribed medications	Resource use multiplied by unit costs from the British National Formulary[15].	

Commute cost	Car travel	Time converted to mileage[16] and valued using AA Schedule of Motoring Costs[17] to estimate average daily cost.	Average daily commuting cost at 1 year follow-up. Regression *Covariates:-* - Treatment arm - Size of the company (categorical) - Location of the company (categorical) - Type of business (categorical) - Baseline average daily commute cost - Workplace as a random effect
	Permits and passes	Employee reported cost and duration of permits and passes used to estimate the average daily cost.	
	Employee daily expenses	Presented as the average daily cost.	
Productivity costs	Self-assessed productivity	Employee reported productivity based on the extent to which health problems affected productivity in the past 3 months measured on a 10-point scale. Converted to wages using median weekly earnings[18] assuming a 1-point decrement on the scale equates to a 10% loss in earnings.	Total productivity costs in the past 3 months at 1 year follow-up. Regression *Covariates:-* - Treatment arm - Size of the company (categorical) - Location of the company (categorical) - Type of business (categorical) - Baseline productivity costs over the past week - Workplace as a random effect
	Days of work missed	Employee self-reported number of days of work missed in the last 3 months. Converted to wages using median weekly earnings[18].	
Employee quality of life	Estimated using the ICECAP-A	ICECAP-A tariff scores estimated from questionnaire results and the ICECAP-A tariff[19]	ICECAP-A tariff score at 1 year follow-up. Regression *Covariates:-* - Treatment arm - Size of the company (categorical) - Location of the company (categorical) - Type of business (categorical) - Baseline ICECAP-A tariff score - Workplace as a random effect

2.9. INTERIM ANALYSIS

There are no pre-defined formal stopping rules. The trial may be prematurely discontinued by the Sponsor, Chief Investigator, Regulatory Authority or Funder on the basis of new safety information or for other reasons given by the Trial Steering Committee, regulatory authority or ethics committee concerned.

In the unlikely event that participants in the intervention arm experience a large number of adverse events, compared with the control arm, the trial may be stopped.

3. GENERAL ANALYSIS CONSIDERATIONS

3.1. STATISTICAL ANALYSIS

STATA will be used for all statistical analyses for this trial.

3.1.1 PRIMARY OUTCOME ANALYSIS

The primary analysis will be on an Intention to Treat (ITT) basis. The primary outcome measure of MVPA (mean minutes per day) at one year follow-up (measured on a continuous scale) will be compared between the intervention and control groups using multivariable linear regression, with covariates: treatment arm, baseline MVPA, accelerometer wear-time, size of the company, location, type of business and workplace as a random effect.

Assumptions:

#1 Continuous dependent variable (MVPA is numerical) ✓

#2 One or more independent variables, can be categorical or continuous (Group + Covariates) ✓

#3 Linear relationship between each independent variable vs. MVPA and collectively vs. MVPA [CHECK: Scatter plots and partial regression plots]

#4 Homoscedasticity [CHECK: Scatter plot of residuals]

#5 No outliers [CHECK: using plots in Stata]

#6 Normally distributed residuals [CHECK: Histogram and P-P, Q-Q plots]

3.1.2 SECONDARY OUTCOME ANALYSES

The secondary outcome analyses will be analysed on an ITT basis. The covariates are described in Section 2.8.2.

1) Overall physical activity (counts per minute) – multivariable linear regression [Assumptions above]
2) Sedentary time (minutes per day) – multivariable linear regression [Assumptions above]
3) Modal shift (number of journeys when walking was the major mode of travel to and from work) – negative binomial regression [Assumptions above]
4) MVPA due *only* to the commute (daily minutes of MVPA) – multivariable linear regression [Assumptions above]

3.2. ANALYSIS POPULATIONS

The primary analysis set is all randomised workplaces and employees within south-west England and south Wales that meet the inclusion criteria. Exclusion criteria can be found in Section 2.3.2.

3.3. DERIVED VARIABLES

See Section 10 and *Protocol: Coding commute to work and assessment of mode of commute to work.*

3.4. PROCEDURES FOR MISSING DATA

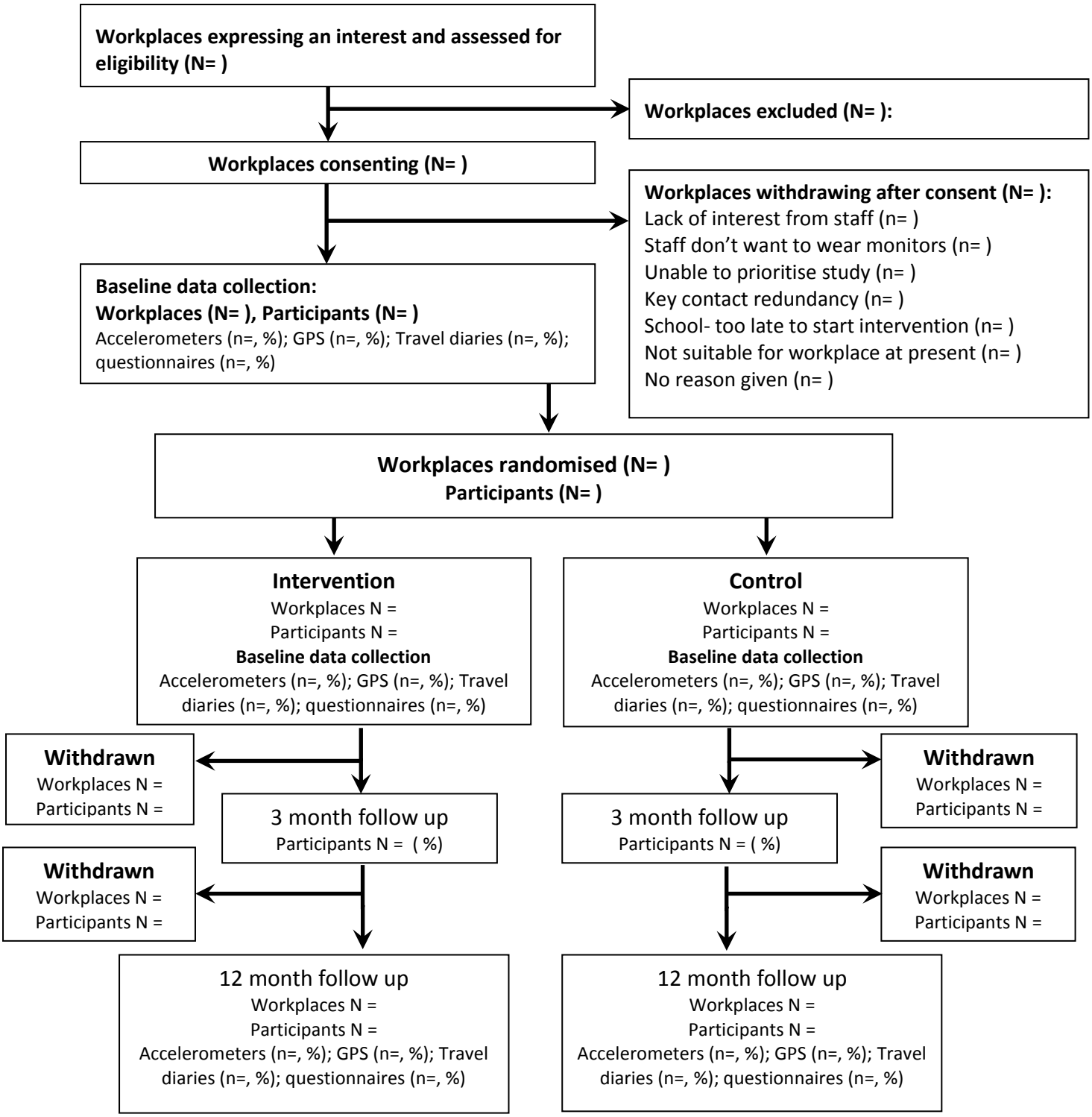
A sensitivity analysis will be conducted for the impact of missing data on the primary analysis (if required), using the most appropriate imputation technique. We will conduct this analysis if around 20% of the data needed is missing for the primary analysis.

In order to more appropriately classify the missingness mechanism of the data the distribution of baseline data will be compared for those missing either the primary outcome, or covariates needed for the primary analysis model, and those that are not missing the data. If we are able to assume that the data is "Missing at Random (MAR)", multiple imputation will be used. Packages, such as REALCOM Impute, that incorporate methods for clustered data and multi-level analyses will be used.

4. RECRUITMENT AND RETENTION

4.1. DISPOSITION

A flow of workplaces, and participants, through the trial will be summarised in a CONSORT diagram.



4.2. BASELINE CHARACTERISTICS

The study cohort will be described by the baseline characteristics in Table 1 (Section 8). These will be compared between the two arms by reporting relevant summary statistics in order to determine whether any potentially influential imbalance occurred, by chance, between the two arms.

Characteristics will be reported as means (SD), medians (IQR) or number (%) depending of the nature of the data and its respective distribution. For those that follow a symmetrical distribution, the mean and standard deviation will be calculated for each group. For those following a skewed distribution, the medians (IQR) will be presented for each group. Categorical data will be summarised in terms of frequency counts and percentages.

P-values will not be reported for differences between the two groups at baseline since randomisation will have accounted for this. If the baseline characteristics of the intervention and control groups differ then the effect of this variable on the outcome will be investigated in a sensitivity analysis.

5. ASSESSMENT OF STUDY QUALITY

5.1. STUDY COMPLETION

The final follow up, for both arms of the study, is one year after baseline data collection.

5.2. COMPLIANCE

The CONSORT diagram (Section 4.1) will give an overview of how many patients left the study. Compliance for the primary outcome only is defined as 3 days of valid accelerometer data received by each employee.

6. ANALYSIS OF EFFECTIVENESS

6.1 SUMMARY OF THE PRIMARY OUTCOME

Baseline and one year follow-up MVPA will be collected for both groups. Both group's MVPA (after one year follow up) will be compared using multivariable linear regression with 95% confidence intervals, adjusting for baseline MVPA, accelerometer wear-time, randomisation variables (size, location and type of workplace) and workplace as a random effect.

6.2. PRIMARY OUTCOME ANALYSIS

The null hypothesis for the primary analysis is "no difference in the MVPA" between employees in the intervention and control groups at one year's follow up. Both group's MVPA levels will be compared using multivariable linear regression with 95% confidence intervals.

$$y_{ij} = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4 + \beta_5 x_5 + \gamma_j + e_{ij}$$

for i =1,…,n employees within j =1,…,J workplaces, where $e_{ij} \sim N(0, {\sigma_a}^2)$ and $\gamma_j \sim N(0, {\sigma_b}^2)$

Where y is MVPA, β_1 is the parameter regression coefficient for treatment group and x_1 is the variable for treatment group (1= intervention, 0=control). The following variables (x_2, x_3, x_4 and x_5) are the potential confounding variables that are being adjusted for. They include baseline MVPA, accelerometer wear-time and the size, location and type of workplace. γ_j and e_{ij} will adjust for the between workplace and within workplace variation, by inclusion of the workplace as a random effect.

The estimated treatment effect will be presented as the adjusted difference in means between the intervention and control groups with a 95% confidence interval and p-value. The results of this analysis will be recorded in Table 2 (Section 8.3).

6.3. SECONDARY OUTCOME ANALYSES

The analysis in Section 6.2 will be adapted to the analysis of other physical activity measures, apart from modal shift which will be analysed using a Poisson (or negative binomial, if data is over-dispersed) regression model.

- Null hypothesis: "No difference in overall physical activity (counts per minute) between groups"

- Null hypothesis: "No difference in sedentary time (minutes per day) between groups"

- Null hypothesis: "No difference in the number of journeys where walking is the main mode of travel to/from work between groups"

- Null hypothesis: "No difference in MVPA due *only* to the daily commute between groups"

The results of these analyses will be recorded in Tables 2 and 3 (Section 8.3).

6.4. SUBGROUP ANALYSIS

Subgroup analysis of the primary outcome will explore differences in the effect of intervention according to baseline participant age (below or above the median), gender, baseline socioeconomic status defined using self-reported household income (below or above £30,000) and distance to work (2km or less, more than 2km). These subgroup analyses are exploratory and will be conducted by adding interaction terms to the regression models used for the primary analysis. We recognise there will be low power for these subgroup analyses and therefore only cautious conclusions will be drawn from them.

The results of these analyses will be recorded in Table 7 (Section 8.5).

6.5. SENSITIVITY ANALYSIS OF PRIMARY OUTCOME

- The sensitivity of the results to assumptions about the missing data will be assessed using the most appropriate imputation technique for missing primary outcome data (if required).

- Where there are imbalances in baseline characteristics (Table 1) a sensitivity analysis will be carried out for the primary outcome, adjusting for the identified variable.

- If there is concern that the MVPA distribution is non-normally distributed and therefore the multivariable linear regression model is unsuitable, a sensitivity analysis will be investigated using a log-transformation of the MVPA outcome.

- For the primary outcome only (MVPA); different quality assurance thresholds for accelerometer data will be investigated (see Section 10) and the primary analysis will be repeated using data from working and non-working days independently.

The results of these analyses will be recorded in Tables 4 and 5 (Section 8.4).

6.6. ANALYSIS OF COSTS AND CONSEQUENCES

All analyses will be conducted on an intention-to-treat basis comparing the intervention and control groups as randomised. The cost-consequence analysis will include the cost of the intervention, health care costs, commuting costs, productivity costs and the ICECAP-A. Information needed for costing the intervention will be collected by the study team.

Table 7 outlines the cost-consequence table where the final results will be presented. The cost of the intervention will be estimated by employee and employer. For the remaining costs and outcomes the results will be presented by arm along with the adjusted difference in means between the intervention and control groups with a 95% confidence interval and p-value

Missing economic data will be explored and if required a sensitivity analysis will be conducted using the most appropriate imputation technique (see Section 3.4 for more details).

7. ANALYSIS OF SAFETY

7.1. ADVERSE EVENTS

This is a low risk intervention and there were no reported adverse events during the feasibility study. However, we will be mindful of the potential for harm in terms of road traffic injuries and collisions, personal safety of walkers, difficulties experienced by Walk-to-Work promoters (including disrupting usual working relationships and employers attitudes towards time taken out of usual work activities) and costs to employers (including disruption to work routines due to permitting the intervention during working hours).

Participating workplaces and Walk-to-Work promoters will have the contact details of the Principal Investigator (PI) and will be encouraged to report adverse and serious adverse events which will be recorded and reported to the ethics committee.

If adverse events are attributable to the intervention, relevant participants will be informed immediately e.g. other employees taking a similar route. It is also possible that people with low activity and no history of walking will suffer initial muscle stiffness. In most cases this would be mild and is a normal consequence of increased physical activity. However, participants will be given information about symptoms which may require medical attention and temporary or permanent cessation of walking to work: for example, where underlying joint weakness is exposed. Such incidents will be recorded and monitored throughout the trial.

8. FINAL REPORT TABLES AND FIGURES

8.1. SUBJECT CHARACTERISTICS AND BACKGROUND SUMMARIES

Table 1. Baseline characteristics of participants and workplaces

		Control		Intervention
	N*	**Mean (SD), median (IQR) or n (%)**	**N***	**Mean (SD), median (IQR) or n (%)**
Participant Demographics				
Total number of participants				
Gender: Male				
Age (years)				
BMI:				
Underweight				
Normal				
Overweight				
Obese				
Household income:				
Up to £10,000				
£10,001 - £20,000				
£20,001 - £30,000				
£30,001 - £40,000				
£40,001 - £50,000				
More than £50,000				
Don't know				
Ethnicity:				
White British				
White other				
Mixed ethnic group				
Asian or British Asian				
Black or Black British				
Chinese				
Other				
Education:				
Higher degree, degree or equivalent				
A levels or equivalent				
GCSEs or equivalent				
No formal qualifications				
Other				
Current method of travel to work				
Car				
Train/Bus				
Walk				
Cycle				

Distance between workplace and home (km):				
2km or less				
Over 2km				
Current occupation				
Sedentary				
Standing				
Manual				
Heavy manual work				
Primary outcome				
Daily minutes of MVPA				
Secondary outcomes				
Overall physical activity (counts per minute)				
Sedentary time (minutes per day)				
Daily minutes of moderate to vigorous activity (MVPA) during the commute				
Number of journeys when walking was the major mode of travel to and from work				
0 journeys				
1 journey				
2 journeys				
3 journeys				
4 journeys				
5 journeys				
6 journeys				
7 journeys				
8 journeys				
9 journeys				
10 journeys				
11 journeys				
12 journeys				
13 journeys				
14 journeys				
Number of valid journeys				
Sensitivity outcomes: Daily minutes of MVPA				
Adjusted quality assurance thresholds				
a) at least 2 weekdays and 1 weekend day				
b) at least 1 day				
Data from working days only				
Data from non-working days only				
Accelerometer wear-time				
Number of valid days				
Workplace demographics				
Total number of employees				
Location				
Swansea (including Newport and Neath Port Talbot)				

Bath (including Swindon)				
Bristol (including South Gloucestershire)				
Size of business				
Micro				
Small				
Medium				
Large				
Most often used method of travel to work by employees				
Car or motorised transport				
Public transport				
Walk or cycle				
Unknown				
Proportion of employees that walk or cycle all the way to work				
None or hardly any				
Less than half				
Most				
All				
Unknown				
UK SIC Categories 2007				
A: Agriculture, forestry and Fishing				
B: Mining and quarrying				
C: Manufacturing				
D: Electricity, gas, steam and air conditioning supply				
E: Water supply; sewerage, waste management and remediation activities				
F: Construction				
G: Wholesale and retail trade; repair of motor vehicles and motor cycles				
H: Transport and storage				
I: Accommodation and food service activities				
J: Information and Communication				
K: Financial and insurance Activities				
L: Real estate activities				
M: Professional, scientific and technical activities				
N: Administrative and support service activities				
O: Public administration and defence; compulsory				

social security				
P: Education				
Q: Human health and social work activities				
R: Arts, entertainment and Recreation				
S: Other service activities				
T: Activities of households as employers; undifferentiated goods and services-producing activities of households for own use				
U: Activities of extraterritorial organisations and bodies				

*Total number of employees or employers (as appropriate) that responded to this question (those with missing values excluded)

8.2. STUDY QUALITY SUMMARIES

Summarised in the CONSORT chart (see Section 4.1)

8.3. OUTCOME SUMMARIES

Table 2. Continuous outcome analyses

Outcome	Control mean (SD)	Intervention mean (SD)	Adjusted difference in means* (95% CI)	Additionally adjusted difference in means**(95% CI)	P-value
Primary					
i) Daily minutes of MVPA					
Secondary					
ii) Overall physical activity (counts per minute)					
iii) Sedentary time (minutes per day)					
iv) Daily minutes of moderate to vigorous activity (MVPA) during the commute					
*Adjusted for baseline outcome **Adjusted for size, location and type of business, baseline outcome, accelerometer wear-time (for outcomes i and iii) and workplace as a random effect.					

Table 3. Categorical outcome analyses

Outcome	Control participants N (%)	Intervention participants N (%)	Adjusted incidence rate ratios* (95% CI)	Additionally adjusted incidence rate ratios** (95% CI)	P-value
Secondary					
v) Number of journeys when walking was the major mode of travel to and from work					
0 journeys					
1 journey					
2 journeys					
3 journeys					
4 journeys					
5 journeys					
6 journeys					
7 journeys					
8 journeys					
9 journeys					
10 journeys					
11 journeys					
12 journeys					
13 journeys					
14 journeys					
*Adjusted for baseline outcome **Adjusted for size, location and type of business, baseline outcome and workplace as a random effect.					

8.4. SENSITIVITY ANALYSES

Table 4. Sensitivity analyses of primary outcome

Outcome	Control mean (SD)	Intervention mean (SD)	Adjusted difference in means* (95% CI)	Additionally adjusted difference in means* (95% CI)	P-value
Daily minutes of MVPA					
Additionally adjusted for imbalances in baseline characteristics					
Imputation of missing data (if appropriate)					
Adjusted quality assurance thresholds					
a) at least 2 weekdays and 1 weekend day					

b) at least 1 day					
Data from working days only					
Data from non-working days only					
*Adjusted for baseline daily minutes of MVPA **Adjusted for size, location and type of business, baseline daily minutes of MVPA, accelerometer wear-time and workplace as a random effect.					

Table 5. Sensitivity analysis of primary outcome (if non-normally distributed)

Outcome	Control log-mean (SD)	Intervention log-mean (SD)	Adjusted ratio of geometric means* (95% CI	Additionally adjusted ratio of geometric means** (95% CI)	P-value
Daily minutes of MVPA					
Linear regression of log-transformed outcome					
*Adjusted for baseline daily minutes of MVPA *Adjusted for size, location and type of business, baseline daily minutes of MVPA, accelerometer wear-time and workplace as a random effect.					

8.5. SUBGROUP ANALYSIS

Table 6. Subgroup analysis of primary outcome

Outcome	Control mean (SD)	Intervention mean (SD)	Adjusted difference in means* (95% CI)	Additionally adjusted difference in means** (95% CI)	Interaction P-value
Daily minutes of MVPA in each subgroup					
Age (<median)					
Age (≥median)					
Sex (Male)					
Sex (Female)					
Household income (below £30,000)					
Household income (above £30,000)					
Distance from work (2km or less)					
Distance from work (more than 2km)					
*Adjusted for baseline daily minutes of MVPA *Adjusted for size, location and type of business, baseline daily minutes of MVPA, accelerometer wear-time and workplace as a random effect.					

8.6. ECONOMIC RESULTS

Table 7. Cost-consequence analysis

	Intervention	Control	Adjusted incremental difference
Intervention costs:			
Average intervention cost per participating employee			
Average intervention cost per workplace			
Health care cost			
Commute cost			
Productivity cost			
ICECAP-A			

8.7. SAFETY RESULTS

Table 8. Adverse events

	Control N (%)	Intervention N (%)
Severity:		
Not Serious		
Serious unexpected		
Serious expected		

10. ACCELEROMETRY AND GPS; DECISIONS AND OUTCOMES

Accelerometry: decisions and outcomes	
Initialising	Accelerometers initialised to start recording on day after distribution and to store data for 7 days including a weekend.
Data collection points	Baseline (DC1), one year follow-up (DC3)
Protocol	Single Actigraph GT1M monitor, worn around the waist over the same hip during waking hours (except when swimming/bathing/showering).
Wear time	Waking hours
Valid length of day	≥10 hours (600 minutes) for primary analysis
Days required	Primary analysis: Any 3 days (for outcomes i, ii and iii), 1 day (outcome iv and v) Sensitivity analysis (outcome i only): a) at least 2 weekdays and 1 weekend day, b) at least 1 day
Epoch length	10 seconds
Zero counts	Bouts of 60 minutes of continuous/consecutive zero counts excluded
Spurious data	≥ 20,000 cpm
Activity cut-points	Sedentary <100 cpm ; MVPA ≥ 1952 cpm[40]
Outcomes	i) Moderate to vigorous physical activity (MVPA) ii) Sedentary time iii) Overall physical activity, mean counts per minutes (cpm) iv) Modal shift (number of journeys when walking was main mode of travel to/from work) v) Moderate to vigorous physical activity (MVPA) during the commute

GPS: decisions and outcomes	
Initialising	GPS records when switched on
Data collection points	Baseline (DC1), one year follow-up (DC3)
Protocol	Switch on to 'log' before leaving for work. Switch to 'off' when finishing the commute.
Wear time	Commute and working hours
Valid data	One journey on given day required
Days required	1 valid working day
Spurious data	Aberrant speed: all GPS points recorded as travelling at more than 100 kph Outliers for each participant: removal of GPS points that are further than 500 metres from any other GPS points
Missing data	Use mode of travel from self-reported travel diary
Outcomes	iv) Modal shift (number of journeys when walking was main mode of travel to/from work) v) Moderate to vigorous physical activity (MVPA) during the commute

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