Health Economics Analysis Plan –SMART Work & Life intervention

ISRCTN11618007

Contents

1. Purpose

This health economics analysis plan (HEAP) outlines the intended analysis and reporting procedures for the economic analysis of the interventions evaluated in the SMART Work & Life trial. The HEAP is designed to ensure the rationale, objectives, methodologies and reporting of the economic analysis are prospective, explicit and consistent with the trial protocol and associated statistical analysis plan.

2. Overview

The SMART Work & Life trial is a three arm, clustered randomised controlled trial which seeks to evaluate the impact of a multicomponent intervention with and without a height-adjustable desk/platform on daily sitting time, physical activity, adiposity, mental health, health-related quality of life, and other work- and psychosocial-related variables. The SMART Work & Life intervention is grounded in several behaviour change theories and comprises organisational-level strategies (briefing events for managers, awareness training for staff), environmental-level strategies (modifications to office layout, motivational materials/signs, height adjustable desk), and individual/group strategies (educational sessions and materials, self-monitoring guidance and tailored goal-setting and progress reviews) in an effort to promote and maintain ≥60 minute per day reduction in overall daily sitting time compared to control (1). The economic analysis seeks to inform the cost-effectiveness of the SMART Work & Life Work intervention with or without a height-adjustable desk/platform compared to services as usual.

3. Trial background and design

Sedentary behaviour is associated with a variety of health issues, including increased risks of chronic disease and mortality (2–5), poor mental health (6,7), and a lower quality of life (8). In response, interventions which seek to reduce sitting time in the workplace have received significant attention. The SMART Work & Life randomised controlled trial is a three arm, clustered randomised controlled trial seeking to test the impact of a multi-component intervention with and without a height adjustable desk or desk platform on overall daily sitting time compared with control. Different office spaces (clusters) were randomised to receive one of the following:

Intervention 1): The multi-component SMART Work & Life intervention with a height-adjustable desk or desk platform

Intervention 2): The multi-component SMART Work & Life intervention without a height-adjustable desk or platform

Control 3): Usual practice (control condition)

The SMART Work & Life intervention was received throughout the trial (12 months) by those randomised to either intervention arm.

Participants for the trial were identified within local Councils in the Leicester, Greater Manchester and Liverpool areas. Staff ≥18 years of age were eligible if they were office based, spent ≥50% of their workday sitting (excluding mandatory breaks), worked at least 0.6 full time equivalent, willing and able to give informed consent, and were capable of walking without assistance.

The SMART Work & Life Work intervention is a multicomponent intervention designed to promote movement and reduce sedentary behaviour in office workers. The intervention was developed using input from a variety of relevant stakeholders (office workers, local council office workers, workplace champions, council stakeholders), experiences from other relevant programmes (9), and improvements that were noted following the evaluation of a previous version of the intervention - SMArT Work (10,11).

SMART Work & Life is grounded in several behaviour change theories and emphasises a 'whole-of-day' preventive approach in sedentary behaviour to overcome behaviour compensation (as observed in occupational-specific interventions). The intervention comprises organisational-, environmental- and individual/group-level strategies designed to promote positive changes in daily overall sitting and movement in office workers:

Organisational strategies: 1) briefing events to explain to managers the importance of reducing sitting time at work (e.g. benefits in performance and productivity); 2) a brief awareness session (online/video) for staff which reinforces the benefits of reducing sitting time in and outside of work, and encouraging staff to review current policies and to brainstorm new practices to promote movement of staff; 3) emphasised to managers the importance of their role in modelling positive behaviour.

Environmental strategies: 1) small-scale environmental restructuring in the office and at home; 2) motivational materials and reminder signs around the office space and at home; 3) the participant's choice of a height-adjustable desk/platform (within a set budget).

Individual/group strategies: 1) an initial education session covering the health consequences of sitting and benefits of reducing sedentary behaviour, including a dedicated period for brainstorming barriers to reducing daily sedentary behaviour and strategies to overcome these. Individuals were encouraged to set a goal around sitting less and an action plan to achieve this; 2) self-monitoring of sitting behaviour to be encouraged with the use of free computer prompts, timers and mobile phone apps; 3) workplace champions trained to deliver

brief coaching/refresher sessions which review progress, goals, action plans, barriers and benefits with participants at 3, 6, and 12 months; 4) encouraging social support from colleagues and family members (e.g. through activity competitions inside and outside of work).

Participants randomised to intervention 1 received all the intervention components listed. Office workers in intervention 2 received all the intervention components listed minus the height-adjustable desk or desk platform. Participants in the control arm received usual practice for the 12 month study period (i.e. not given any lifestyle advice, guidance, or results from the activPAL device), but did receive the results of health measures (e.g. weight, blood pressure, etc.) taken at each time point.

The primary outcome from the trial was overall sitting time with the intervention goal being to maintain at least a 60 minute per day reduction in overall daily sitting time compared to control. Measurements were continuously taken by an activPAL micro accelerometer on the anterior aspect of the right thigh, for 24 hours/day over 7 days during each assessment period. Secondary outcome measurements included self-reported physical activity, musculoskeletal health, mood and affective states, work related measures, cognitive function, dietary behaviours, mental health, sickness absence, health-related quality of life and resources used (e.g. GP visits, outpatient attendances, accident and emergency visits). A series of self-reported questionnaires examined secondary outcomes. Mental health was assessed using the Hospital Anxiety and Depression Scale (HADS), a 14-item self-report screening scale developed to indicate the possible presence of anxiety and depressive states (12). Participants' emotion was evaluated using the Positive and Negative Affect Schedule (PANAS), a self-report questionnaire that consists of two 10-item scales to measure both positive and negative affect (13). The extent and severity of fatigue was assessed using the self-administered Chalder Fatigue Scale (14). Health-related quality of life was measured using the EQ5D-5L, a generic measure of health that incorporates five levels of severity across five health dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) (15). Primary and secondary outcomes were assessed at baseline and at 3 and 12 months.

Participant characteristics and factors including age, sex, ethnicity, smoking status, current job role, pay grade, working hours, body weight, body fat, height, waist circumference, medication and arterial blood pressure were collected at baseline. Follow-up questionnaires monitored changes in participant factors (e.g. location, smoking status, medication, etc.) at 3 and 12 months.

4. Economic analysis

4.1. Aims of economic evaluation

The economic evaluation seeks to address the question:

"*What is the cost-effectiveness of the SMART Work & Life intervention, with and without a standing desk/platform, compared with usual practice for office workers in the UK?*".

To address this question, the economic analysis of the SMART Work & Life trial will consist of:

i) a descriptive analysis of resource use, costs and outcomes;

ii) a cost-consequence analysis based on observed results within the trial period;

iii) a cost-effectiveness analysis with outcomes observed within the trial period and those extrapolated into the longer term;

iv) a series of sensitivity and scenario analyses considering alterative perspectives/assumptions

Outcomes will include quality-adjusted life-years (QALYs), in line with current UK guidance for economic evaluations (16), and other measures of health (e.g. mental health), well-being (fatigue and general mood) and productivity (e.g. sickness absence). The analysis will be performed initially from a public sector perspective, with financial impacts on individuals themselves incorporated using an alternative broader perspective (e.g. wage losses due to absence from work) subsequently considered. The base case cost-effectiveness analysis will extrapolate differences observed in the trial period into the longer-term. Results over the trial's time horizon (those within 12 months) will also be presented for comparison. Cost-effectiveness results will be expressed in terms of incremental cost-effectiveness ratios, showing the incremental cost per additional QALY compared to the other strategy, and incremental net health benefits to show the difference between the health generated with a strategy and the health which could be generated elsewhere in the health care system using the same resources at thresholds of £15,000, £20,000 and £30,000 per QALY (16,17).

The primary objective of the economic analysis is to evaluate the cost-effectiveness of the SMART Work & Life intervention with and without a standing desk or platform to assess the value for money that they may offer the NHS and personal social services (PSS). Secondary objectives of the analysis include calculating the cost-effectiveness of the SMART Work & Life intervention with and without a standing desk or platform using a within-trial economic evaluation (12-month time horizon), and the cost-effectiveness when accounting for financial

impacts outside of public services, and an exploration into key model and structural uncertainties (e.g. treatment effects, service delivery, etc.).

4.2. Resource use

Data on health-related resource use by participants was collected at baseline and at each trial follow-up time point (3 and 12 months) through a questionnaire with participants (18). The following resource use items were measured: primary health service resource use (e.g. GP and practice nurse appointments), occupational health visitors and counsellors, mental health services and secondary care (e.g. hospital appointments and accident and emergency). Resource use data collection in each period was conducted retrospectively, with participants asked to record their resource utilisation since the previous study visit. Resource use will be presented for each resource item within and across follow-up periods by trial arm. All intervention-related resource use will be retrieved from trial procurement documentation and descriptively summarised.

4.3. Costs

Costs will be estimated based on applying appropriate unit costs to estimates of resource use. An individual-level costing framework will be employed such that each participant in the trial has a cost based on their reported resource use and their associated relevant unit costs. Costs in both trial arms will be estimated initially from a public sector perspective, and subsequently from a broader perspective encompassing the financial impacts the SMART Work & Life interventions have on individuals and companies. Total costs will be estimated by summating estimated costs across resource categories. All resource use will be valued in monetary terms (UK pound sterling) at the time of the analysis (2019-2020). Within-trial average participant costs will be summarised and presented both by item (including delivering the intervention) and by aggregated total cost.

4.3.1. Intervention costs

A micro costing framework will be used to estimate the cost of delivering both versions of the SMART Work & Life intervention to office workers. Intervention costs will include all relevant set-up and training of practitioners, costs associated with the procurement of intervention equipment (desk, materials, etc.) and the delivery of the interventions themselves (administrative time, transportation costs, etc.). This information will be retrieved from the trial manager/project documentation. Alternative assumptions will be explored about the cost of each SMART Work & Life intervention per office worker where uncertainties remain about how the intervention may be delivered in the event of a large-scale roll-out (e.g. potential cost-sharing arrangements for enrolments in institutions outside of public health, number of individuals a practitioner can assist, etc.).

4.3.2. Unit costs

Unit costs for all relevant resource use will be sourced from published sources. Resources related to the health and social care sector will be costed using published national sources, including NHS reference costs (19) and the Personal Social Services Research Unit (PSSRU) Unit Costs of Health and Social Care (20). Productivity losses due to sickness absence from work will be calculated using the human capital approach where caregivers time off work is multiplied by their salary (21). Where up to date cost estimates are not available, earlier cost estimates will be inflated using the hospital and community services pay and prices index (HCHS) reported in the latest available PSSRU report (20).

4.4. Outcomes

Outcomes relevant to the economic evaluation of the two versions of the SMART Work & Life intervention include health-related quality of life scores (HRQoL) (EQ5D-5L), mental health status (HADS), and measures of fatigue (CFS), mood (PANAS) and productivity (e.g. sickness absence). In line with current UK guidance for economic evaluations (16), the primary outcome of the cost-effectiveness analysis will use quality-adjusted life-years (QALYs), a composite measure of health encompassing both morbidity and mortality (with one QALY equalling a year in perfect health).

4.5. Methods for analysis

The economic analysis will be conducted on an intention to treat (ITT) basis and encompass cost-effectiveness analyses using costs and QALYs estimated from the trial data. A secondary analysis will include a descriptive analysis presenting within-trial costs and secondary outcomes in a disaggregated format (e.g. HADS scores).

4.5.1. Statistical software

Stata version 15.1 or higher will be used for all statistical analyses, including imputing data, descriptive statistics, calculating costs, HRQoL scores and QALYs, and all regression analyses. Any existing models used for extrapolation will be conducted in the model's chosen statistical software.

4.5.2. *Costs*

Unadjusted costs for each trial participant for the first 12-months will be estimated as the product of recorded resource use and corresponding relevant unit costs. Regression methods will be used to produce adjusted estimates of costs (see section 4.5.4). The long-term health effects of increased physical activity and/or reduced sedentary behaviour and corresponding changes to health costs over an expanded time horizon will be calculated through extrapolation (see section 4.5.6).

4.5.3. *Outcomes*

HRQoL weights and survival data will be combined to estimate QALYs over the trial period (12 month) (22). An area under the curve approach using linear interpolation between time points will be used to estimate QALYs. Each EQ5D-5L defined health state will be transformed into a HRQoL score by using UK social tariffs obtained from a sample of the general population which assigns values to each health state described by the EQ5D-5L (23). In line with guidance from the National Institute for Health and Care Excellence (NICE) (16), the base case analysis will map EQ5D-5L scores to HRQoL values based on a population survey using the EQ-5D-3L instrument and estimate QALYs using these values (24). As a scenario analysis we will directly use EQ5D-5L scores to estimate QALYs. The remaining secondary outcomes will be presented descriptively and can be used to inform cost-consequence analyses where applicable. Extrapolation will be used to project the long-term QALY impacts of increased physical activity and/or reduced sedentary behaviour over an extended time horizon (see section 4.5.6).

4.5.4. Regression methods

Average sitting time for each trial arm will be estimated from an analysis using a linear multilevel model that adjusts for area-level clustering effects, baseline values, and activPAL waking wear time across baseline and 12-month follow-up (further details see statistical analysis plan). In order to account for site-level clustering effects and skewed and non-negative distributions in costs, multilevel generalised linear models (MGLM) will be used to analyse costs while controlling for baseline covariates. The MGLM random effects approach will specify two levels (participants nested within sites) and consider a number of distributions (i.e. normal, gamma, Poisson, inverse gaussian) and functional forms (i.e. identity, log-transformed). QALYs will also be analysed using MGLMs. Baseline covariates will include age, gender, ethnicity (White vs. Other), BMI, site area (Leicester; Salford; Liverpool), and cluster size (Small <10; Large ≥10). QALY regressions will also control for baseline EQ-5D.

4.5.5. Missing data

To account for the hierarchical nature of the data (I.e. participants within site areas), missing cost and outcome variables will be imputed using a multilevel multiple imputation (MI) approach. Predictive mean matching will be used to ensure imputed values are in the appropriate range (e.g. no negative costs) with MI by chained equations (MICE) (26) and Rubin's rules applied for the subsequent analysis of multiple data sets (27).The multi-level design will allow clusters to be incorporated as a random effect as to account for heterogeneity between sites. The imputation model will include: average daily sitting time at baseline, average daily sitting time at 3 months, age, gender, ethnicity (White vs. Other),

BMI at baseline, BMI at 3 months, site area (Leicester; Salford; Liverpool), cluster size (Small <10; Large ≥10), and costs and QALYs. A scenario analysis only using participants with complete data will be conducted for comparison (i.e. a complete case analysis).

4.5.6. Extrapolation

A pragmatic search of the literature will be conducted to identify and review existing cost-effectiveness models in sedentary behaviour that link short-term end points measured in the trial (e.g. sitting time) and long-term survival and quality of life. Medline and Embase databases will be searched using a systematic search strategy based on the terms "sedentary behaviour", "sitting", and those aligned with the nomenclature in cost-effectiveness analysis in health technology assessment (e.g. cost, QALY, economic model, HRQoL, etc.). Decision analytic models identified from the search will be assessed for applicability, adapted where necessary and used to project the long-term QALY and cost impacts of increased physical activity and/or reduced sedentary behaviour.

4.6. Cost-consequence (within-trial analysis)

A cost-consequence analysis framework is helpful to inform decision-makers where alternative outcomes may be of be interest, and where costs and outcomes fall on different domains. The within-trial analysis will present average and incremental results for the costs and the primary and secondary outcomes in and between the intervention with and without a standing desk or platform and the control arm.

4.7. Cost-effectiveness analysis

The cost-effectiveness of the SMART Work & Life interventions will be investigated based on the differences in QALYs gained and costs over the trial time horizon and over the longer term. Estimated costs and QALYs from the trial will inform cost-effectiveness results in the first year; extrapolation will be used to estimate results thereafter. Differences in QALYs will be compared with differences in costs measured from the public sector perspective and presented as both incremental cost-effectiveness ratios (ICERs) and incremental net health benefits (NHBs). Net health benefit will be presented at three measures of health opportunity cost: £15,000 per QALY, based on an approximation of recent empirical estimates and the department for health's chosen threshold (17,28), alongside £20,000 and £30,000 per QALY, the range used by NICE (16). An annual discount rate of 1.5% will be applied to both costs and outcomes as per the NICE public health economics base-case guidance (29).

To reflect the levels of uncertainty in parameter inputs a probabilistic sensitivity analyses will be conducted. The probability of each intervention being cost-effective (i.e. having the highest positive net health benefit) at each cost-effectiveness threshold will be calculated using Monte Carlo simulation. The uncertainty surrounding the adoption decision will also be

depicted using cost-effectiveness acceptability curves (30). Uncertainty around the incremental cost and outcome estimates will be represented on cost-effectiveness planes. Given that not all financial impacts of the SMART Work & Life intervention fall on the public sector budget we will conduct analyses where productivity losses are included/excluded to assess the impact on decision-making (31).

4.8. Subgroup analysis

The cost-effectiveness of interventions will be considered for the following subgroups:

- Site (Leicester vs. Liverpool vs. Manchester)
- Small vs large clusters (Small <10; Large ≥10)
- Sex (male, female)
- Age (< median, ≥ median)
- BMI (normal, overweight/obese (≥ 25 kg/m2)

Subgroup analyses will be conducted using sitting times, costs, immediate and extrapolated outcomes estimated specifically from those patients pertaining to a given sub-group.

4.9. Sensitivity analysis

In both the cost-consequence analysis and cost-effectiveness analysis, sensitivity analyses will be performed to determine the robustness of the results to altering underlying assumptions and inputs for each analysis. We will consider the following scenarios, among others:

- Alternative intervention costs
  - those possible with cost sharing arrangements (e.g. public-funded subsidies for the use by private enterprises)
  - those likely borne in the event of a wider roll-out (i.e. fixed costs spread over a larger cohort).
- EQ5D-5L preference-based HRQoL scores used to estimate QALYs
- Alternative discount rates
  - 0 to 5% cost and QALY discount rates (16)
- Alternative treatment effects from the SMART Work & Life interventions
  - Changes in efficacy
  - Changes in persistence of treatment effects beyond the trial period
- A broader costing perspective
  - including impacts from changes to productivity

Additional analyses will consider productivity impacts more broadly, considering both the effects on absenteeism and exploring whether it is possible to capture effects on

presenteeism. Moreover, given the potential for each version of the SMART Work & Life intervention to be implemented outside of the public sector, additional analyses will also explore alternative cost-sharing arrangements and their impacts on alternative stakeholders (32). Threshold analyses will be conducted to show the interventions cost and/or the expected duration of benefit required for the interventions to be deemed cost-effective at the chosen threshold values of £15,000, £20,000 and £30,000 per QALY.

Funding

This project is funded by the NIHR Public Health Research (project No PR-R5-0213-25004).

Roles and Responsibilities

This HEAP was prepared by Edward Cox (Research Fellow) and approved by Simon Walker (Senior Research Fellow) and Professor Gerry Richardson. The trial health economist(s) [Edward Cox, Simon Walker, Gerry Richardson] are responsible for conducting and reporting the economic evaluation in accordance with the HEAP.

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