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Cost-Effectiveness and Value of Information Analysis of Brief Interventions to Promote Physical Activity in Primary Care

Vijay S. GC, MPH¹, Marc Suhrcke, PhD¹⁻³, Wendy Hardeman, PhD⁴, Stephen Sutton, PhD⁵, Edward C.F. Wilson, PhD^{1, 6, 7} on behalf of the VBI Programme Team

- ¹ Health Economics Group, Norwich Medical School, University of East Anglia, Norwich, UK;
- ² UKCRC Centre for Diet and Activity Research (CEDAR), University of Cambridge School of Clinical Medicine, Cambridge, UK;
- ³ Centre for Health Economics, University of York, York, UK;
- ⁴ School of Health Sciences, University of East Anglia, Norwich, UK;
- ⁵ Behavioural Science Group, Primary Care Unit, Institute of Public Health, University of Cambridge School of Clinical Medicine, Cambridge, UK;
- ⁶ Cambridge Centre for Health Services Research, Institute of Public Health, University of Cambridge School of Clinical Medicine, Cambridge, UK;
- ⁷ Cambridge Clinical Trials Unit, Cambridge University Hospitals NHS Foundation Trust, Hills Road, Cambridge, UK

Corresponding author: Vijay GC, Health Economics Group, Norwich Medical School, University of East Anglia, Norwich Research Park, Norwich NR4 7TJ, United Kingdom. Phone: +44 (0)1603 597164, email: vijay.gc@uea.ac.uk

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Running title: Cost-effectiveness of brief PA interventions

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Cost-Effectiveness and Value of Information Analysis of Brief Interventions to Promote Physical Activity in Primary Care

Abstract

Background: Brief interventions (BIs) delivered in primary care have shown potential to increase physical activity levels and may be cost-effective, at least in the short term, when compared with usual care.

However, there is limited evidence on their longer-term costs and health benefits.

Objectives: To estimate the cost-effectiveness of BIs to promote physical activity in primary care and to guide future research priorities using value of information analysis.

Methods: A decision model was used to compare the cost-effectiveness of three classes of BIs that have been used, or could be used, to promote physical activity in primary care: (1) pedometer interventions, (2) advice or counselling on physical activity and (3) action planning interventions. Published risk equations and data from the available literature or routine data sources were used to inform model parameters.

Uncertainty was investigated with probabilistic sensitivity analysis, and value of information analysis was conducted to estimate the value of undertaking further research.

Results: In the base-case, pedometer interventions yielded the highest expected net benefit at a willingness-to-pay of £20,000 per quality-adjusted life-year. However, there was a great deal of decision uncertainty: the expected value of perfect information surrounding the decision problem for the NHS Health Check population was estimated at £1.85billion.

Conclusion: Our analysis suggests that pedometer-based BIs are the most cost-effective strategy to promote physical activity in primary care, and that there is potential value in further research into the cost-effectiveness of brief (i.e. less than 30 minutes) and very brief (i.e. less than 5 minutes) pedometer-based interventions in this setting.

Introduction

Physical inactivity is a major public health problem associated with a significant burden of chronic disease, including type 2 diabetes, cardiovascular disease, some cancers and mental health problems [1-3]. Despite the well-documented health benefits of physical activity [4-7], in 2010, 33% of adults aged 18 years and over in high-income countries were insufficiently active: i.e. they did not meet the current World Health Organization (WHO) recommendations [8]. In England, using self-reported measures in 2012, 61% of adults aged 19 and over met the current UK guideline [9] for moderate/vigorous physical activity [10], a figure virtually unchanged since the 2008 Health Survey for England (HSE), reporting 59%. However, when physical activity was measured objectively using accelerometers, in 2008 only 6% of men and 4% of women aged 16 and over met the recommended physical activity level [11].

Physical inactivity is also associated with a considerable economic burden, accounting for 1.5% to 3% of total direct healthcare costs in high income countries [12]. The annual societal cost of physical inactivity in England (comprising the National Health Service (NHS) costs plus the value of morbidity/premature mortality-related lost productivity) is estimated at £8.2 billion per year, with an additional £2.5 billion for the contribution of physical inactivity to obesity-related costs [1].

Intensive face-to-face physical activity interventions delivered in primary care or community settings targeting sedentary adults can be effective at increasing activity levels [13]. They have been found to represent good 'value for money' as they can increase self-reported physical activity at reasonable cost [14, 15]. In recent years, there has been interest in brief interventions (BIs), defined as having a maximum duration of 30 minutes [16, 17], to promote physical activity in a primary care setting [18-20]. Systematic reviews and meta-analyses of randomised controlled trials (RCTs) showed that BIs, e.g. brief exercise advice/counselling delivered in primary care, increase physical activity [20, 21] and are cost-effective [15, 22] over the short-term (twelve months or less). However, the evidence on the longer-term costs and consequences of BIs has been sparse to date.

Findings from published RCTs of physical activity interventions are not sufficient on their own to inform decision makers about the cost-effectiveness of intervention strategies [23]. Evidence on the long term cost-effectiveness of health interventions is essential to inform resource allocation decisions aimed at

maximising health gains to the population from limited available resources [14]. Using a discrete event simulation model, we aim to evaluate the long-term cost-effectiveness of BIs to promote physical activity in adults eligible for an NHS Health Check in primary care.

If BIs are cost-effective, this raises the question of whether ‘very brief interventions’ (VBIs) could also be cost-effective. VBIs, defined as lasting no more than five minutes [18], are of interest as they can be delivered as part of a primary care consultation such as the NHS Health Check [24]. This is offered every five years to all adults in England aged 40-74 years without known pre-existing vascular disease and is intended to assess risk of certain conditions, including type 2 diabetes and heart disease, and provide preventative advice and interventions where indicated [25].

In this paper we present an economic evaluation of three classes of BIs (plus no intervention), reporting the incremental cost per quality-adjusted life-year (QALY) gained over 10 years. We also report a value of information analysis, a method to predict the return on investment in further research [26-28]. This information will inform the design of further research into the effectiveness and cost-effectiveness of VBIs delivered as part of the NHS Health Checks.

Methods

Study population

We used data from the 2011 HSE to generate a simulated cohort of 10,000 adults aged 40-74 years who do not have an existing diagnosis of diabetes, hypertension, cardiovascular or renal disease, representing the NHS Health Check population [25].

The PACE model

We developed a discrete event simulation model, the Physical Activity Cost Effectiveness (PACE) model in R [29] to estimate the cost-effectiveness of BIs. The model firstly generates a cohort of 10,000 representative individuals of the English population. It then follows each individual, predicting the incidence of chronic disease, mortality and associated costs and outcomes over ten years, specified with risk equations and data derived from the literature [30-38]. The model includes type 2 diabetes and

associated complications, heart disease, stroke and physical inactivity and obesity-related cancers (breast, colorectal, lung or kidney cancer). Increased physical activity is assumed to influence risk factors such as reduced blood pressure, cholesterol level and glycated haemoglobin (HbA1c). Modification of these risk factors leads to changes in the risk of chronic disease and comorbidities, such as reduced risk of cardiovascular disease. A decrease in chronic disease and comorbidities leads to a reduction in costs and to the prevention of a decrease in quality of life (Fig. 1). Effectiveness data for each comparator are entered in the model as an increase in metabolic equivalent (MET) hours per week compared with no intervention, which in turn influences risk of chronic disease. The random search method [39] was used to calibrate the model against seven calibration targets. Weighted mean deviation was used to assess the goodness-of-fit of calibration results [40]. Full details of the model and calibration are in Appendix 1 in Supplemental Materials.

Data inputs and sources

Model inputs

Data on demographic characteristics of individual participants (age, gender, ethnicity) were derived from the UK Office for National Statistics [41, 42]. The risk factor profile (systolic blood pressure, total cholesterol, high density lipoprotein cholesterol, body mass index, smoking status and HbA1c) and prevalence of type 2 diabetes and cardiovascular events (ischaemic heart disease, myocardial infarction (MI), stroke and heart failure) for individual participants in the cohort was generated using data from the 2011 HSE [43]. The severity of breast cancer was classified according to Nottingham Prognostic Index (NPI) prognostic groups – ductal carcinoma in situ (DCIS), excellent, good, moderate and poor [44] – and age-specific prevalence data for breast cancer was taken from the estimates for 2008 in the UK [45]. The baseline parameter values for colorectal cancer were derived from Frazier et al [35] and applied to the baseline population to generate prevalence data for colorectal cancer. The baseline prevalence data of lung and kidney cancers were based on estimates from Cancer Research UK [37, 46].

Interventions

We selected three classes of BIs: pedometer interventions, advice/counselling in primary care, and action planning interventions. Evidence of effectiveness was extracted from published meta-analyses of RCTs

[47-49]. The three classes are somewhat heterogeneous, therefore descriptions of the classes (and associated costings) below reflect the scope of interventions included in the respective meta-analyses. This selection of BIs was based on the strength of evidence of effectiveness and their relevance in a primary care setting. Full details are provided in Appendix 2 in Supplemental Materials. We also included current practice where no physical activity intervention is delivered.

Pedometer-based interventions: Participants were given a pedometer to wear and encouraged to view and record their daily step counts. They were also asked to set a physical activity goal such as to walk 20 minutes on all or most days of the week, or walk 10,000 steps on five days per week. In some interventions, participants received individualised exercise feedback or additional 'behavioural counselling' from a nurse or physiotherapist.

Advice or counselling in primary care: Typically, participants received written materials with exercise advice or an exercise prescription; and two or more sessions of advice or counselling on physical activity. Advice or counselling was mostly delivered face-to-face, in some cases by phone (or both). In most cases, the interventions were delivered by primary care doctors or nurses.

Action planning interventions: These BIs employed 'implementation intentions', a commonly used form of action planning. Participants were asked to formulate an action plan for physical activity in the format of what, when and where, and to record their action plan in a logbook or calendar. In most interventions, participants were encouraged to write down an action plan assisted by a trained interviewer.

Current practice: Participants received no intervention.

Short-term effectiveness of interventions

The intervention effects of the BIs were converted to MET-hours by estimating the time spent in activities with higher MET intensities as a result of the intervention [50]. We extracted physical activity outcomes from individual studies included in the three meta-analyses which were translated into MET-hours by selecting the estimates from the compendium of physical activity [51]. Finally, we updated the meta-analysis using translated values (MET-hours). However, it was not possible to translate intervention effects into MET-hours for five of the nineteen RCTs included in the meta-analysis of action planning

interventions [47] as either these studies did not provide details on changes in intensity, duration and/or frequency of activity required for MET-hours translation, or the outcome was expressed in composite units (e.g. a sum of scores where responses were rated on a scale). Thus, we excluded those five studies.

Intervention costs

We first extracted resource use data based on the intervention description provided for individual studies in the meta-analyses. We then costed each intervention based on the quantities of resources used multiplied by the unit cost of each resource component. The cost per participant was then evaluated as weighted average of intervention costs from each RCT in the meta-analysis (Table 1). Full details on translating the intervention effects into MET-hours and costing of each intervention are provided in Appendix 2 in Supplemental Materials.

Disease costs and health outcomes

The price year and currency of the study was 2011 UK pounds sterling (£). The annual costs associated with each health state were derived from previous studies [33, 36, 52-63]. The health outcomes were evaluated in QALYs. Utilities for health states included in the model were obtained from published sources [64-69]. Details on costs and utilities related to comorbid disease conditions in the model are available in Appendix 1 in Supplemental Materials. We performed the analysis from the English NHS perspective to estimate the costs and benefits of BIs over a ten-year time horizon. All health outcomes and costs were discounted at 3.5% per annum [70].

Probabilistic sensitivity analysis

We performed a Monte-Carlo simulation (n=10,000 iterations) to simultaneously account for uncertainty in all input parameters (Appendix 1 in Supplemental Materials). The net monetary benefit (NB; UK 2011 £), that is, the health effect (QALYs) multiplied by a societal willingness-to-pay (WTP) per QALY gained minus the cost was calculated for each BI [71]. At any given WTP threshold, the cost-effective intervention was identified as the one with the highest expected NB, which is mathematically identical to sequentially identifying the most cost-effective intervention with an incremental cost-effectiveness ratio (ICER) below the threshold compared with the next best non-dominated alternative. We constructed cost-

effectiveness acceptability curves (CEACs) to illustrate the decision uncertainty surrounding the adoption of BIs, conditional on the WTP per QALY [72]. The NBs were estimated at a WTP of £20,000 per QALY.

Scenario analyses

The sustainability of intervention effects over time plays an important role in the cost-effectiveness analysis. There is considerable uncertainty about the maintenance of any effects of BIs as very few studies have follow-up measurement beyond one year. We performed sensitivity analysis with decay rates for the intervention effect ranging between 0% (lifelong behaviour change) and 100% (behaviour change reversed to baseline after the first year post-intervention). In the base case, we assumed that the intervention effects were sustained for the first year, but decayed at a rate of 55% per annum thereafter. We also evaluated the cost-effectiveness of BIs if they were repeated once every two, five and ten years, and finally explored the direct impact of a short-term quality of life boost from increased physical activity. Only a few studies have measured these short-term improvements in the general population [73, 74], as most studies focus on older adults and people with chronic conditions [75]. A pragmatic RCT evaluating the national exercise referral scheme in Wales estimated a utility boost of 0.03 +/- 0.023 [76]. We added this in the first year of intervention to reflect the short-term benefits of physical activity.

Value of information analysis

We had originally intended to conduct a value of information analysis on the entire decision problem. However, due to computational difficulties for such a complex model, we limited this to a comparison between the pedometer BIs and current practice. This was chosen as we selected a pedometer-based intervention as the most promising VBI for trial evaluation in our wider research programme [77]. Thus the analysis established whether or not there was an economic case for a trial of a pedometer-based BI.

We estimated the expected value of perfect information (EVPI) as the difference between the expected value of decision (i.e. the maximum expected NB) with perfect information and that with current information [78]. As the value for additional information is related to the size of the eligible population, the EVPI was multiplied with the estimated Health Check population to estimate the population EVPI. Given that approximately 30% of the population are on a primary care disease register [79], the eligible Health

Check population (i.e. adults aged 40-74) over 10-years equates to approximately 19.1 million. The population EVPI provides the upper bound on the value of future research. To identify a parameter or group of parameters that contribute to most of the overall decision uncertainty and for which future research is the most promising, we estimated the expected value of partial perfect information (EVPPI) [78, 80, 81]. For this, we grouped model parameters into the following six sub-groups: research on 1) intervention effects, 2) health state utilities, 3) costs, 4) risk of MI, 5) risk of stroke, and 6) parameters used in systolic blood pressure equation. The EVPPI was calculated using a two-level Monte-Carlo sampling loop, in which the parameter(s) of interest were sampled 500 times in the outer loop, and for every iteration the remaining parameters were sampled 1,000 times in the inner loop [82, 83]. Multiplying the EVPPI values per patient with the eligible Health Check population resulted in the population EVPPI.

Results

Cost-effectiveness analysis

In the base-case, the point estimates for per person costs and QALYs for all interventions were similar (Table 2). Pedometer BIs dominated both advice/counselling and action planning BIs, i.e. pedometer BIs were both less expensive and more effective. When compared with current practice, all three BIs were both more effective and more costly.

Analysis of Uncertainty

The scatterplot of incremental costs versus incremental QALYs (comparing each BI with current practice) for the 10,000 iterations showed points scattered across all four quadrants of the cost-effectiveness plane, with the majority of the points overlapping with each other (Fig. 2A). The CEAC (Fig. 2B) showed that pedometer BIs were the optimal option in 56% of the 10,000 model simulations at a WTP of £20,000 per QALY. Advice/counselling intervention was optimal in 22% of the iterations at a WTP of £20,000 per QALY. Current practice and action planning interventions had similar CEACs showing less than 13% probability of being the most cost-effective.

Scenario analyses

As the intervention decay rate increases, BIs become less cost-effective (Fig. 2C). At higher intervention decay rates, the expected NBs of all interventions were quite similar, ultimately dropping below that of current practice. This is to be expected as the treatment effect declines to that of current practice. For the scenario analysis with the interventions being repeated once every two, five and ten years (Fig. 2D) respectively, pedometer BIs were found to be the optimal option for all three repeat year scenarios. The expected NB for pedometer interventions was highest when the intervention was repeated once every two years.

The inclusion of short-term health gains (utility boost) from increased physical activity (Appendix Table 4.1 in Supplemental Materials) had similar results as the base-case analysis, with pedometer BIs as the most cost-effective intervention. However, there was a parallel shift upwards for the three BIs. The probabilities of pedometer and advice/counselling BIs being cost-effective at a WTP of £20,000 per QALY increased to 61% and 24%, respectively, up from 56% and 21% in the base-case scenario.

Value of information analysis

At a WTP of £20,000 per QALY, the base-case per person EVPI associated with a decision between pedometer BIs and current practice was £97, or £1.85bn to the NHS Health Check population (Fig. 3A). This means that, at a WTP of £20,000 per QALY, the upper limit for research into which intervention is most cost-effective is £1.85 bn. Among the groups of different parameters, intervention effects had the highest population EVPPPI of £708 million followed by costs (£690) and risk of stroke (£684 million) parameters at a WTP of £20,000 per QALY (Fig. 3B).

Discussion

What this study shows

In this study we estimated the expected long-term costs and health outcomes of BIs that could potentially be used to increase physical activity among apparently healthy adults who are eligible for NHS Health

Checks in primary care in England. The health benefits of increasing physical activity levels were simulated using effects of BIs reported in the meta-analyses of RCTs, and synthesised in a decision analytic cost-effectiveness model. In the base-case analysis, we found that pedometer BIs were dominant, i.e. they were less costly and had better outcomes (QALY gains) than other BIs. The value of information analysis for pedometer BIs versus current practice showed that the expected value of conducting further research to eliminate decision uncertainty was £1.85 billion, assuming a time horizon of ten years, and that further research that would eliminate uncertainty in intervention effects for the NHS Health Check population would be worth £708 million (Fig. 3B). We explored the impact of repeating the BI, and repetition every two years seems to be the most efficient interval.

Care must be taken in interpreting the value of information statistics. A new study will not eliminate uncertainty, but is expected to reduce it. Therefore, the expected value of sample information (EVSI) of such a study will be less than the EVPI. We attempted to calculate the EVSI and the expected net gain of sampling (ENGs, defined as the EVSI less the total cost of a proposed study) but due to computational demands we were unable to generate meaningful and stable results. Nevertheless, given the size of the EVPI, it may be reasonable to suggest that there is scope for further research to be efficient. Whilst all parameter groups had a similar EVPI, the highest was in intervention effectiveness.

Implications for policy

Our results show that pedometer BIs appear to be a cost-effective way of promoting physical activity when compared with other BIs such as advice or counselling in primary care. Delivering the pedometer BI once every two years appears to be the most efficient repeat interval. However, this is contingent on the assumed 'decay rate' of the intervention effect, and the ability of repeat contacts to maintain physical activity.

The value of information analysis suggests that there may be value in further exploring the effectiveness of a general class of pedometer-based brief interventions: the population EVPI of £1.85bn is certainly very much above the cost of any plausible design of a RCT, suggesting that further research could be efficient. However, a definitive answer requires calculation of the expected net gain of sampling for a particular trial. Given that this analysis is part of a research programme on VBIs, the logical next question

is whether it is worth investigating whether a shortened VBI pedometer intervention, incorporated as part of the NHS Health Check, would be of value. Given that (1) it is highly likely that future research into pedometer-based BIs is efficient, and (2) less is known about the effectiveness and cost-effectiveness of VBIs, it is reasonable to suggest that exploration of the effectiveness and cost-effectiveness of a pedometer-based VBI is efficient.

Comparison with other studies

Our cost-effectiveness results were mostly more favourable than the Over et al [84] and Gulliford et al [85] studies of pedometer and brief exercise advice/counselling interventions, respectively, but were not as favourable as reported by Cobiac et al [86] for pedometer interventions. This could be because intervention costs in our study were lower than in Over et al [84] and Gulliford et al [85]. However, Cobiac et al [86] used much lower intervention costs per person than our model. In addition, differences in the target population, modelling methods, inclusion of diseases/co-morbidities and short-term health gains, and assumptions on intervention decay could explain the observed differences in the cost-effectiveness results. Two modelling studies [85, 86] were driven by a disease burden modelling strategy and Anokye and colleagues [87] included short-term mental health gains in their cost-effectiveness analysis. However, in their analyses [85, 87] they did not take into account any decay in the intervention effects over time.

Strengths and limitations

Our model is comprehensive and complex in terms of the inclusion of physical activity dose-response relationship and comorbidities related to physical inactivity and obesity. Our analysis was based on meta-analyses of RCTs evaluating the effect of BIs on physical activity levels, incorporated into a comprehensive decision model to project costs and outcomes associated with each intervention (plus current practice) over the long term. We included interventions that are low cost and relevant to a primary care setting.

However, there are limitations to our approach, including the structure of the model and data inputs. Not all the data sources, e.g. transition probabilities and health state utilities were available for the NHS Health Check population. We only included disease conditions related to physical inactivity and obesity

for which dose-response evidence was available. Only one of the meta-analyses [49] focused on interventions delivered in primary care, and all three meta-analyses included several studies in which participants had a chronic condition. However, based on the intervention descriptions (Appendix 2 in Supplemental Materials), many of them are arguably amenable to delivery in a primary care setting and suitable for apparently healthy populations. Translating a wide range of physical activity measures used in the primary studies into a common metric (here: MET hours) entails potential for error. It was not always possible to translate intervention effects directly into MET-hours. Although we excluded five of the nineteen studies included in the meta-analysis of action planning interventions [47], the intervention effect size after excluding those five studies did not change.

The true rate of decline in intervention effects and how it differs across interventions over time is unknown, as much of the evidence is based on studies with short (i.e. 12 months or less) follow-up [88, 89]. Moreover, the 'active ingredients' differ across interventions as well as the extent to which interventions are able to prompt enactment of behaviour change techniques in daily life (e.g. goal setting, action planning) and only the meta-analysis of advice/counselling interventions [49] included studies with 12 months or longer of follow-up.

In the base-case analysis, we assumed that the intervention effects are sustained for the first year and decay at a rate of 55% per annum thereafter, irrespective of intervention duration and length of follow-up. This assumption may have overestimated the intervention effects of pedometers and action planning interventions, leading to an underestimation of the ICER. In addition, our assumptions on sustained effects of intervention beyond one year is arbitrary and may be a strong assumption. However, previously reported modelling studies [84, 86, 90] assumed similar base-case decay rates, varying between 50% and 55%.

The effect of pedometers BI was based on a meta-analysis that included only 277 participants in total. In addition, the pooled intervention effects of BIs included in this analysis are based on a broad range of similar interventions and not all the included interventions are sufficiently brief to be used in primary care. Hence this category represents a broad class of interventions. Although "no intervention" was the typical

comparator in the studies included in the three meta-analyses, some of the studies evaluated the intervention against a comparator intervention only (Appendix 2 in Supplemental Materials).

Conclusion

In conclusion, based on currently available data, pedometer-based BIs appear the most cost-effective strategy to increase physical activity in primary care. However, there is substantial uncertainty, and BIs yielded only relatively small health benefits. The sensitivity analysis suggests that repeating BIs once every two years could be the most efficient repeat interval. If further research were to be conducted, research on the effectiveness of brief and very brief pedometer BIs in primary care would be a worthwhile investment.

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TABLES

Table 1 – Intervention effects and costs associated with implementing BIs promoting physical activity

Brief interventions	No. of studies	Total no of participants	Median (range) duration of follow-up	Unit of measurement; (95% CI)	Effect (in MET- hours per day)	Intervention costs*	Source
Advice/counselling in primary care	9 RCTs	3,445	12 months	Standardised mean difference; 0.25 (0.11 – 0.38)	0.33 (0.16 – 0.49)	£71.26	[49]
Action planning interventions	14 RCTs	1,864	10 (2–52) weeks	Standardised mean difference; 0.23 (0.10 – 0.35)	0.05 (0.02 – 0.08)	£33.21	[47]
Pedometer interventions	8 RCTs	277	11 (4–24) weeks	Increase in steps per day; 2,491 (1,098 – 3,885)	1.06 (0.47 – 1.65)	£54.33	[48]
Current practice ('doing nothing')			-	-	-	-	

*All costs are inflated to 2011 UK £ sterling using the Hospital and Community Health Services (HCHS) index [53]

Table 2 – Cost-effectiveness of brief interventions over 10 years (base-case costs, QALYs and NBs)

Brief intervention	Mean cost (SE)		Mean QALY (SE)		Mean NB* (SE)		ICER
Current practice	£1,712	(583)	7.848	(0.228)	£ 155,254	(5,072)	-
Action planning	£1,738	(583)	7.851	(0.228)	£ 155,291	(5,079)	Extendedly dominated
Advice/counselling in primary care	£1,758	(580)	7.857	(0.229)	£ 155,378	(5,084)	Dominated by pedometers
Pedometer interventions	£1,723	(579)	7.864	(0.229)	£ 155,549	(5,097)	£ 687.50

*NB calculated at a WTP of £20,000 per QALY, ICER: incremental cost-effectiveness ratio

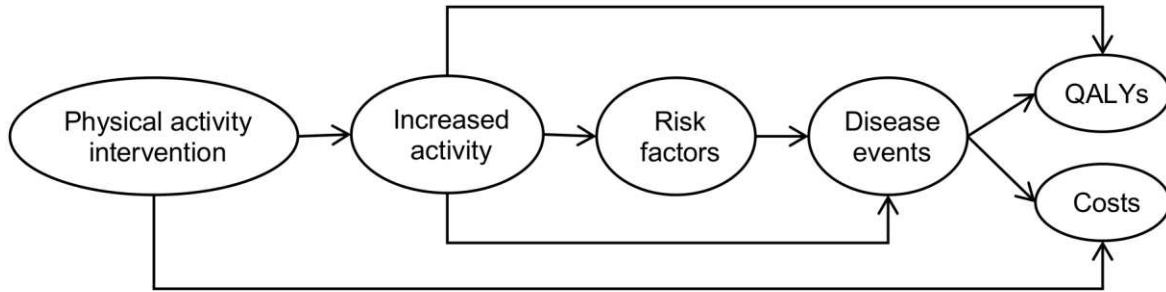


Fig. 1 – A schematic of the PACE model

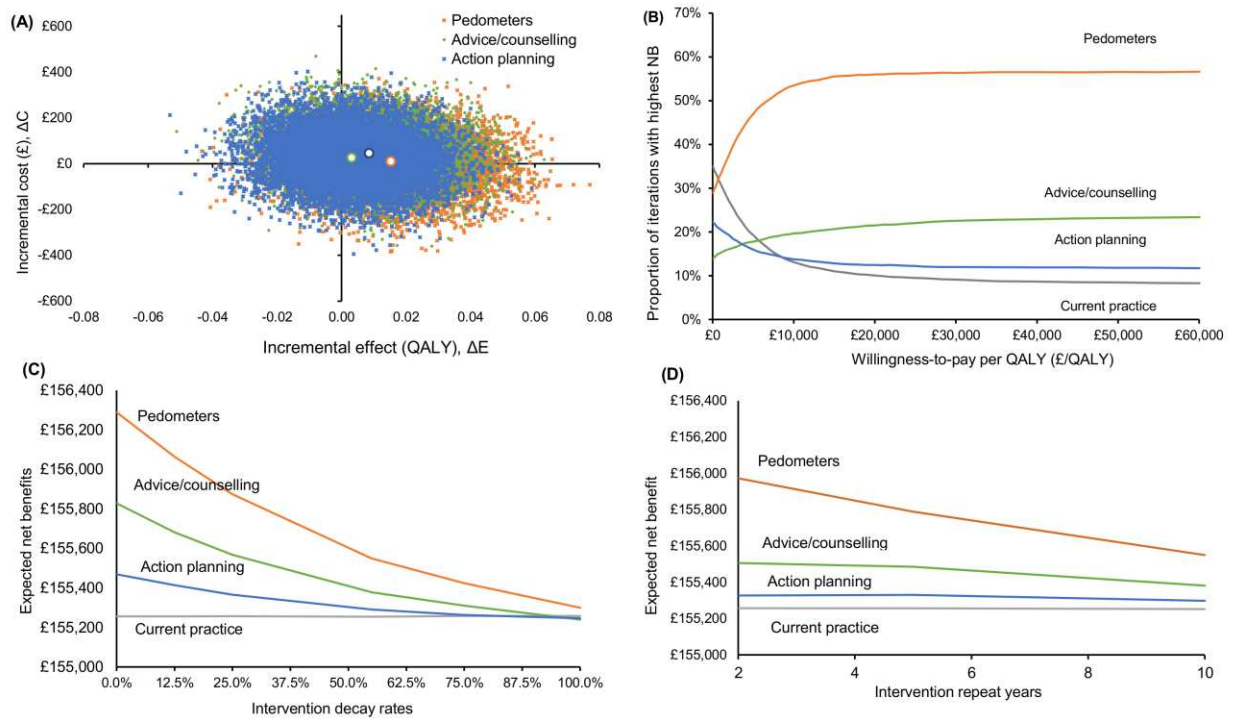


Fig. 2 – (A) Cost-effectiveness plane showing incremental costs and effects of BIs as compared with current practice (10,000 simulation), circles represent mean point estimates and **(B)** CEACs showing probability of interventions being optimal by threshold value **(C)** Sensitivity analysis of intervention cost-effectiveness to decay in intervention effects at a WTP of £20,000/QALY and **(D)** sensitivity analysis of intervention cost-effectiveness to the intervention repeat year at a WTP of £20,000/QALY. WTP, willingness-to-pay.

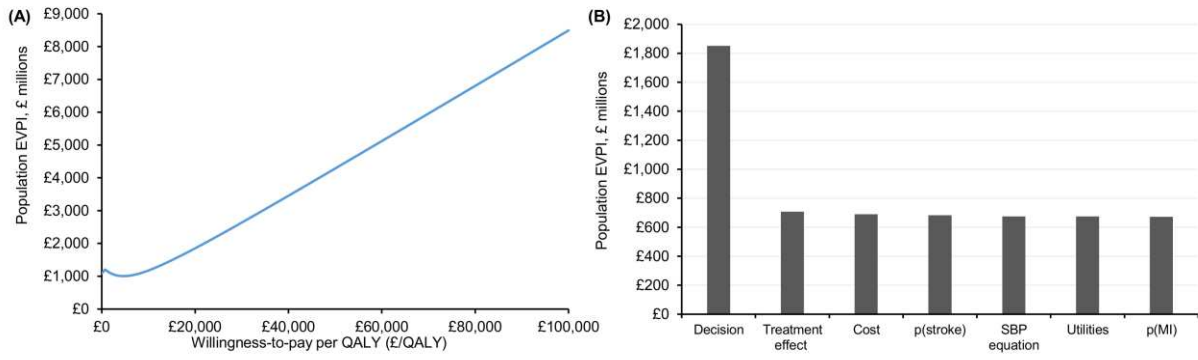


Fig. 3 – (A) Expected value of perfect information (EVPI) against varying WTP values for cost-effectiveness and (B) Partial EVPI results for the base-case at a WTP of £20,000 per QALY.