BMJ Open Diabetes Research & Care

Cost-effectiveness analysis of two interventions to promote physical activity in a multiethnic population at high risk of diabetes: an economic evaluation of the 48-month PROPELS randomized controlled trial

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To cite: Heathcote LE, Pollard DJ, Brennan A, *et al*. Cost-effectiveness analysis of two interventions to promote physical activity in a multiethnic population at high risk of diabetes: an economic evaluation of the 48-month PROPELS randomized controlled trial. *BMJ Open Diab Res Care* 2024;**12**:e003516. doi:10.1136/bmjdrc-2023-003516

► Additional supplemental material is published online only. To view, please visit the journal online (https://doi.org/10.1136/bmjdrc-2023-003516).

Received 9 May 2023
Accepted 25 January 2024

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ABSTRACT

Introduction Physical activity (PA) is protective against type 2 diabetes (T2D). However, data on pragmatic long-term interventions to reduce the risk of developing T2D via increased PA are lacking. This study investigated the cost-effectiveness of a pragmatic PA intervention in a multiethnic population at high risk of T2D.

Materials and methods We adapted the School for Public Health Research diabetes prevention model, using the PROPELS trial data and analyses of the NAVIGATOR trial. Lifetime costs, lifetime quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICERs) were calculated for each intervention (Walking Away (WA) and Walking Away Plus (WA+)) versus usual care and compared with National Institute for Health and Care Excellence's willingness-to-pay of £20 000–£30 000 per QALY gained. We conducted scenario analyses on the outcomes of the PROPELS trial data and a threshold analysis to determine the change in step count that would be needed for the interventions to be cost-effective.

Results Estimated lifetime costs for usual care, WA, and WA+ were £22 598, £23 018, and £22 945, respectively. Estimated QALYs were 9.323, 9.312, and 9.330, respectively. WA+ was estimated to be more effective and cheaper than WA. WA+ had an ICER of £49 273 per QALY gained versus usual care. In none of our scenario analyses did either WA or WA+ have an ICER below £20 000 per QALY gained. Our threshold analysis suggested that a PA intervention costing the same as WA+ would have an ICER below £20 000/QALY if it were to achieve an increase in step count of 500 steps per day which was 100% maintained at 4 years.

Conclusions We found that neither WA nor WA+ was cost-effective at a limit of £20 000 per QALY gained. Our threshold analysis showed that interventions to increase step count can be cost-effective at this limit if they achieve greater long-term maintenance of effect.

Trial Registration number ISRCTN registration: ISRCTN83465245: The PRomotion Of Physical activity through structuredEducation with differing Levels of ongoing Support for those with pre-diabetes (PROPELS)https://doi.org/10.1186/ISRCTN83465245.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Interventions that succeed in increasing physical activity in people at high risk of developing type 2 diabetes (T2D) may be an effective and cost-effective way to decrease the incidence of T2D and cardiovascular disease in this population.

WHAT THIS STUDY ADDS

⇒ We found that neither intervention tested in PROPELS was cost-effective using the usual threshold used by UK decision makers of £20 000 per quality-adjusted life year gained; an intervention that increased step count by 500 steps per day would be cost-effective if that increase were maintained longer-term.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE, OR POLICY

⇒ Researchers looking to develop similar interventions in similar populations should develop and test interventions with long-term support components if they are to be potentially cost-effective in England.

INTRODUCTION

It is estimated that diabetes affects just under half a billion people worldwide, of whom approximately 90% in high-income countries have type 2 diabetes (T2D).[1] People with T2D have an elevated risk of developing serious complications such as renal failure, blindness, amputation, cardiovascular disease (CVD), depression, and osteoarthritis. In the UK, treatment of diabetes and its complications costs approximately 10% of the total expenditure of

the National Health Service (NHS), and this is expected to rise further due to the increasing prevalence of T2D.[2 3] However, both development of T2D and progression to serious complications can be prevented or delayed by timely behavior change interventions targeting weight, diet, and physical activity (PA).[4]

PA, particularly walking-based behaviors, has been shown to improve glucose tolerance in intervention studies as well as being associated with a reduced risk of T2D and CVD in high-risk populations.[5–7]

Observational studies indicate that the incidence of T2D is lower in physically active individuals compared with inactive people.[8] The Nurses' Health Study found that 30-minute PA per day (analogous to the current UK guidelines) was associated with a 25% lower incidence of T2D over 8 years compared with no PA.[9] There is also evidence that increased PA in high-risk populations reduces the risk of developing T2D.[10] Observational studies also suggest that increased PA has a protective effect on development of CVD and CVD mortality in both the general population and people with T2D.[8] The National Health Interview Survey concluded that 2 hours of walking a week was associated with a 41% reduction in coronary heart disease compared with no walking.[11] However, a systematic review of experimental studies using increased PA as an intervention concluded that there was limited evidence that diabetes prevention studies have led to sustained increases in PA levels.[12]

The PRomotion Of Physical activity through structured Education with differing Levels of ongoing Support for those with prediabetes (PROPELS) trial was a large (n=1336) UK multicenter randomized control trial with 4-year follow-up which aimed to increase PA, assessed as accelerometer-measured daily step count, in a targeted population at high risk of developing T2D.[13 14] Two structured education and behavior change interventions were compared with a usual care arm: Walking Away (WA), which consisted of annual structured education sessions, and Walking Away Plus (WA+), which consisted of the same structured education sessions and additional follow-up support (tailored text messages and telephone calls).[15] Full details are reported in the trial protocol[13] and health technology assessment.[14] The PROPELS trial found a clinically and statistically significant increase in daily step count at 12 months in the WA+ arm versus usual care which was not maintained at 48 months; there was no significant change in step count in the WA arm.[14 16]

Although very little work has been done to establish the cost-effectiveness of PA interventions, exploratory modeling work has suggested they could be cost-effective.

Gillies *et al* estimated that a combined program of screening for those at risk of T2D and providing a combined lifestyle intervention (including dietetics and weekly group exercise classes) for high-risk individuals would have an incremental cost-effectiveness ratio (ICER) of £6242 per quality-adjusted life year (QALY) gained, which would be considered cost-effective at the usual National Institute for Health and Care Excellence (NICE) threshold ICER of £20 000–£30 000 per QALY gained.[17 18]

The objective of this analysis was to use data from the PROPELS trial to evaluate the cost-effectiveness of WA and WA+ compared with usual care, assessed against the NICE cost-effectiveness threshold of £20 000 per QALY gained.[18]

METHODS

This analysis was a lifetime horizon, model-based cost-utility analysis using the School for Public Health Research (SPHR) Diabetes Prevention Model v3.2 (hereafter referred to as "the model"),[19 20] as prespecified in the PROPELS health economics analysis plan. A model-based analysis was conducted for two reasons. First, the trial was not powered to detect differences in incidence of diabetes or its related health conditions, so a within-trial analysis would not capture differences in mean QALYs or costs associated with these potential benefits. Second, the trial was limited to a 4-year follow-up period, but the possible benefits could be accrued over a lifetime.

Perspective and discounting

In line with the NICE methods guide, the analyses took an NHS and personal social services perspective, and future costs and QALYs were discounted at 3.5% per annum.[18]

Model

The model was developed to estimate the lifetime effects of interventions targeting T2D prevention in England.[21] The model is an individual-level simulation model, with an annual time cycle. The key drivers of the model are changes in body mass index (BMI), systolic blood pressure, cholesterol, and blood glucose (eg, glycated hemoglobin (HbA1c)) which are updated annually using an analysis of the Whitehall cohort.[22] Each individual's level of these risk factors affects their probability of developing hypertension, CVD, T2D, retinopathy, neuropathy, nephropathy, heart failure, osteoarthritis, depression, dementia, and breast or colon cancer. Individuals can die in any time cycle and will experience an increased risk of death if they have or have a history of CVD, cancer, or T2D. Health-related quality of life (HRQoL) is estimated at the start of the model and declines with age. Each medical condition is associated with an HRQoL decrement and a cost based on published evidence; these are summarized in online supplemental appendix A. Our analysis was conducted using version 3.2 of the SPHR diabetes model in R V.3.5.3. Full details on the methods used in the model are presented elsewhere.[19 20]

Model population

A simulated population of individuals was generated based on trial data.[14] Individual characteristics were sampled from a multivariate normal distribution including steps per day, age, gender, ethnicity, smoking status, T2D status, index of multiple deprivation decile, height, BMI, waist measurement, cholesterol levels,

blood pressure, HbA1c, utility score at baseline, clinical event history, and treatment history. The trial collected EQ-5D-5L utility data; this was converted to EQ-5D-3L using the van Hout *et al* mapping algorithm in line with current NICE recommendations.[23–25]

As the PROPELS trial deliberately over-recruited South Asian participants compared with the general population (approximately 25% of trial participants vs approximately 5% in the UK overall), separate analyses were conducted in the South Asian and non-South Asian populations in the trial.[14 26] To obtain results relevant to the UK general population, the results of our South Asian and other ethnicity analysis were then combined by weighting the results according to the proportion of people in each ethnic subgroup in the UK general population.[26]

Modeling treatment effect

Three treatment effects from the PROPELS trial were included in the model: effect on HbA1c, T2D diagnoses, and CVD risk. HbA1c and T2D diagnoses were modeled directly using trial data; this replaced the Whitehall cohort analysis in the prior version of the model. The effect on CVD risk was modeled by assigning average daily step count to individuals in the model; this was estimated using trial data. This characteristic was then used to modify individuals' CVD risk using published data from the Nateglinide and Valsartan in Impaired Glucose Tolerance Outcomes Research (NAVIGATOR) study.[6]

HbA1c and diabetes diagnosis modeling

The HbA1c levels at 12 and 48 months were estimated using beta regressions applied to the PROPELS trial data (refer to online supplemental appendix B or Khunti *et al*[14] for more details).[27] Beta regression was chosen because it made it possible to generate variability in HbA1c values among individuals with identical baseline characteristics. In both regressions, ethnicity, gender, treatment arm, and site were controlled for. To predict HbA1c at 12 months, baseline HbA1c was also included as a control variable, and for HbA1c at 48 months, HbA1c at 12 months was controlled for. Since data for the 24- and 36-month time points were not available, a linear trajectory between 12 and 48 months was assumed for the HbA1c values.

For modeling new cases of T2D at 12 and 48 months, a logistic regression model was used. This model incorporated coefficients for gender, site, treatment arm, and HbA1c at the respective time points. Moving beyond the 4-year trial period, the standard SPHR model methods (based on an analysis of the Whitehall dataset) were employed to model HbA1c trajectories. In subsequent health check-ups, individuals could be diagnosed with diabetes if their HbA1c exceeded 6.5% (48 mmol/mol).[20 22]

Step count modeling

Beta regressions were used to predict step count at 12 and 48 months. Ethnicity, gender, treatment arm, and site were controlled for at both time points. The 12-month regression also controlled for step count at baseline, and the 48-month regression controlled for step count at 12 months. Since data for the 24- and 36-month time points were not available, a linear trajectory between 12 and 48 months was assumed.

To model trends in step count after 48 months, an ordinary least squares regression was used to analyze the relationship between step count and age at baseline (adjusted for sex, ethnicity, trial site, and trial arm). This gave a coefficient equivalent to the annual change in step count in the absence of any ongoing intervention, which was a decrease in steps of 67.4 (SE=9.5) steps per day per year of age. This was applied equally to all individuals from the start of the trial to calculate their underlying trajectory for step count.

Therefore, for the first 4 years of the model, individuals were assigned two-step count trajectories: one representing the observed data in the trial (predicted using the beta regressions) and one representing the age-related change in step count (the underlying trajectory). If an individual's trial step count trajectory was converging with their underlying trajectory between 12 and 48 months, it was assumed to continue on the trial trajectory beyond 48 months until it converged with the underlying trajectory, at which point the individual continued on the underlying trajectory. On the other hand, if their trial trajectory was diverging from the underlying trajectory between 12 and 48 months, it was assumed that the trajectory beyond 48 months was parallel to the underlying trajectory, that is, that the change in step count (positive or negative) was maintained relative to the underlying trajectory.

Adapting the model to include the effect of step count on CVD risk

The model was extended to incorporate the effect of step count on CVD risk using a published cohort analysis of the NAVIGATOR study, which reported the relationship between PA and cardiovascular risk.[6] The fully adjusted model from this analysis was used, which gave an HR of CVD events of 0.90 (95% CI 0.84 to 0.96) for every 2000-step increment at baseline, and an HR of CVD events of 0.92 (95% CI 0.86 to 0.99) with a change from baseline of 2000 steps in 12 months. These HRs were used to modify the existing risk functions in the model. It was assumed that a person with the average baseline step count in the PROPELS data would have an HR of 1 (ie, their CVD risk would be unmodified).

Intervention costs

The cost of delivering WA and WA+ was microcosted using data collected by the trial administrators.[14] Two sets of cost were estimated: the first was based on how the interventions were delivered in the trial and the second set was based on advice from personnel involved in delivering WA in a real-world setting. The latter was used as our base case intervention costs for several reasons including the educators in the PROPELS trial were specifically recruited whereas if WA or WA+ were to be rolled out

NHS staff would be used; fewer staff would likely be used to train the educators; and, on average fewer courses would be delivered per educator as these staff would have other responsibilities in their role.

Health state cost and utility parameters

The methods and parameters for applying health state costs and calculating QALYs remained largely unchanged from version 3.1 of the model, which is detailed in Breeze *et al*.[20] In brief, costs were estimated additively, with a health state cost associated with each condition added when a patient had a history of an event. Furthermore, some events such as myocardial infarction are associated with a higher cost in the year of an event, and these additional costs were also applied additively. Lifetime costs were calculated by adding all costs accrued in all model years.

The baseline utility values for each patient were obtained from the PROPELS participants' baseline data. Furthermore, patients' utility declined by 0.004 per annum, based on data from Ward *et al*.[27] Once a patient experienced an event, we applied utility multipliers to each patient's baseline utility to account for their event history when calculating the patient's utility for that year.[28] As is standard in calculating QALYs, patients who died had a utility of 0. QALYs were calculated by summing the utility accrued by each patient in each year of the model. Full details of the utility parameters used are given in Breeze *et al*.[20]

Outcome measures

The analyses produced discounted costs and discounted QALYs. ICERs were calculated and compared with a threshold of £20 000 per QALY gained in line with the lower limit of NICE's normal acceptable ICER.[29] Probabilistic sensitivity analysis (PSA) was used to explore uncertainty in the results. In a PSA, in each iteration every model parameter is sampled from its distribution and the model is run. This process is repeated multiple times and ICERs are calculated based on the mean costs and mean QALYs across all PSA iterations. One thousand iterations were run; results were assessed for stability using the method of Hatswell *et al*.[30]

In order to explore structural uncertainty in the model, three different scenario analyses were run: (1) the parameters for the predictive models for step count, HbA1c, and T2D diagnoses were replaced with values derived from statistical analyses conducted in the South Asian and non-South Asian subpopulations of PROPELS separately, as opposed to the base case where our statistical analyses were conducted in the whole population; (2) HbA1c and T2D diagnoses were predicted from the new regression equations, but the treatment arm effect was assumed to be zero (ie, the individual's value was predicted based solely on their demographic characteristics); and (3) the treatment effect for step count was applied, but the Whitehall equations were used to predict HbA1c trajectories (and associated T2D diagnoses) from baseline onwards.

A two-way threshold analysis was conducted using the deterministic base case version of the model whereby the increase in step count at 12 months and the proportion of that increase maintained at 48 months varied, in order to investigate the relationship between these two parameters and the cost-effectiveness of a hypothetical intervention that would improve objectively measured step count.

RESULTS

Simulated population

The simulated population showed close agreement with the characteristics of the PROPELS population at baseline, as shown in (table 1).[14]

Intervention costs

The real-world cost of providing the WA program was estimated to be £257 per person; the cost of providing WA+ was estimated to be £322 per person. A full breakdown of these costs is provided in online supplemental appendix C.

Changes in step count in the model

Figure 1A shows the average daily step count for individuals in all three arms of the PROPELS trial for the 4 years of the trial (A) and the first 30 years of the simulation (B). The model variated from the trial data only slightly: for instance, the actual baseline daily step count in each trial arm was slightly different (A), whereas in the model, all arms were assumed to have identical step counts at baseline. The model matched the trial data well in showing an initial increase in daily step count in both intervention arms, with a larger increase in the WA+ arm than WA. The model also accurately reflected an initial decrease in step count in the usual care arm, followed by a stabilization between years 1 and 4. The slight differences between the model averages and the trial data are well within the SD of the trial data.

In the model, individuals in both intervention arms converged with their underlying step count trajectory after 4 years and then continued to decline in daily step count. This is slightly below the rate of decline of 67 steps per day per year predicted by the ordinary least squares (OLS) regression model; individuals with lower step counts have a higher risk of experiencing CVD events and deaths over time compared with patients who have a higher step count. Therefore, over time individuals with higher step counts tend to be more likely to remain alive in the model at later time points.

Base case results

All model analyses used 20 000 simulated individuals through the model. Using the Hatswell *et al*[30] method, we found that 1000 PSA runs were sufficient to calculate robust ICERs. As shown in table 2, WA is dominated by usual care (ie, it is more expensive and less effective), and WA+ has an ICER exceeding £30 000 per QALY gained.

Table 1 A summary of the South Asian and non-South Asian population in the PROPELS data and in our simulated individual population for the economic model

		South Asian		Non-South Asian	
		Simulated	PROPELS	Simulated	PROPELS
Site	Leicester	97%	97%	58%	58%
	Cambridge	3%	3%	42%	42%
Arm	Usual care	35%	34%	34%	34%
	WA	32%	32%	32%	33%
	WA+	34%	34%	33%	33%
Sex	Male	58%	58%	49%	49%
	Female	42%	42%	51%	51%
Ethnicity	Indian	85%	86%	0%	0%
	Pakistani	5%	5%	0%	0%
	Bangladeshi	1%	1%	0%	0%
	Other South Asian (excluding Chinese)	9%	9%	0%	0%
	White British	0%	0%	88%	88%
	White Irish	0%	0%	1%	1%
	Other white	0%	0%	4%	4%
	White+back Caribbean	0%	0%	0%	0%
	White+black African	0%	0%	0%	0%
	White+South Asian	0%	0%	0%	0%
	Other mixed race	0%	0%	1%	1%
	Chinese	0%	0%	0%	0%
	Other	0%	0%	0%	0%
	Black Caribbean	0%	0%	2%	2%
	Black African	0%	0%	3%	3%
	Other black	0%	0%	0%	0%
Smoking	Never	74%	73%	47%	47%
	Ex-smoker	18%	18%	44%	43%
	Current smoker	8%	9%	10%	10%
Atrial fibrillation	No	100%	99%	94%	95%
	Yes	0%	1%	5%	4%
	Unknown	0%	0%	1%	1%
Statins	No	75%	75%	72%	71%
	Yes	24%	25%	28%	28%
	Unknown	0%	0%	0%	0%
Antihypertensives	No	69%	69%	59%	59%
	Yes	31%	31%	41%	40%
Diabetes	No	100%	100%	100%	100%
	Yes	0%	0%	0%	0%
Angina	No	99%	98%	93%	93%
	Yes	1%	2%	6%	6%
	Unknown	0%	0%	1%	1%
MI	No	99%	97%	97%	95%
	Yes	1%	3%	3%	5%
	Unknown	0%	0%	0%	0%

Continued

Table 1 Continued

		South Asian		Non-South Asian	
		Simulated	PROPELS	Simulated	PROPELS
Stroke	No	100%	99%	95%	97%
	Yes	0%	1%	3%	2%
	Unknown	0%	0%	1%	0%
IMD decile	1	9%	10%	10%	10%
	2	15%	15%	7%	7%
	3	13%	12%	7%	7%
	4	18%	18%	8%	8%
	5	14%	13%	10%	9%
	6	10%	10%	9%	9%
	7	10%	10%	12%	11%
	8	5%	5%	11%	11%
	9	5%	5%	14%	14%
	10	1%	2%	12%	12%
Height (m)		1.64 (0.001)	1.64 (0.005)	1.68 (0.001)	1.68 (0.003)
BMI (kg/m^2)		27.44 (0.034)	27.45 (0.263)	29.72 (0.038)	29.72 (0.178)
Total cholesterol		4.96 (0.007)	4.96 (0.058)	5.24 (0.008)	5.25 (0.034)
Systolic blood pressure		128.63 (0.113)	128.74 (0.974)	132.39 (0.127)	132.38 (0.550)
Waist (cm)		95.91 (0.082)	95.81 (0.649)	99.79 (0.099)	99.66 (0.446)
Drinks per occasion		1.61 (0.006)	1.60 (0.043)	2.07 (0.006)	2.07 (0.025)
Drinking occasions per week		2.07 (0.010)	2.06 (0.078)	3.08 (0.010)	3.08 (0.045)
Average steps per day at baseline		7042 (21.310)	7038 (168.9)	7164 (22.9)	7196 (99.7)
HDL		1.34 (0.002)	1.34 (0.020)	1.46 (0.003)	1.47 (0.013)
Age (years)		54.69 (0.072)	54.61 (0.580)	60.78 (0.057)	60.74 (0.254)
HbA1c at baseline (%)		5.81 (0.002)	5.81 (0.018)	5.86 (0.002)	5.85 (0.010)
GP visits in last year at baseline		4.05 (0.029)	5.12 (0.331)	3.20 (0.022)	4.20 (0.023)
EQ-5D utility score at baseline		0.787 (0.001)	0.778 (0.012)	0.799 (0.001)	0.797 (0.006)

Values are either percentages (for categorical or factor variables) or mean with SE in parentheses.
BMI, body mass index; GP, General practitioner; HbA1c, Glycated hemoglobin; HDL, high-density lipoprotein; IMD, Index of Multiple Deprivation; MI, myocardial infarction (history thereof); WA+, Walking Away Plus; WA, Walking Away.

Although both interventions achieved an increase in step count resulting in a reduction in modeled lifetime CVD events, WA was associated with a non-significant elevated lifetime risk of T2D in the PROPELS trial with an OR of 1.55 (97.5% CI 0.52 to 2.68) compared with usual care at 1 year postrecruitment and an OR of 1.58 (97.5% CI 0.74 to 3.39) 4 years post-recruitment. These increased risks account for much of the observed higher costs and lower QALYs in this arm than in the usual care arm.

As shown in the cost-effectiveness plane in figure 2A, there is substantial uncertainty around these results. Points to the right of the dashed line indicate an ICER that is cost-effective relative to £20 000/QALY, and points to the left indicate an ICER that is not. For both interventions, there are points on either side of the line. As shown in the cost-effectiveness acceptability curve in figure 2B, this equates to a probability of 0.53 that the most cost-effective option at £20 000/QALY is usual care, 0.38 that it is WA+, and 0.09 that it is WA. Figure 2C shows that none of the results of the scenario analyses were cost-effective at £20 000/QALY.

As shown in table 3, interventions designed to increase step count can be cost-effective at a threshold of £20 000 per QALY if they achieve a greater maintenance of effect at 48 months and/or a greater initial step count increase at 12 months than was observed in the PROPELS trial. In particular, the degree of increase in PA that is maintained at 48 months has a strong positive relationship with the cost-effectiveness of the intervention. Note that as these results are from a deterministic version of the model, they are not directly comparable with the PSA results for the PROPELS trial.

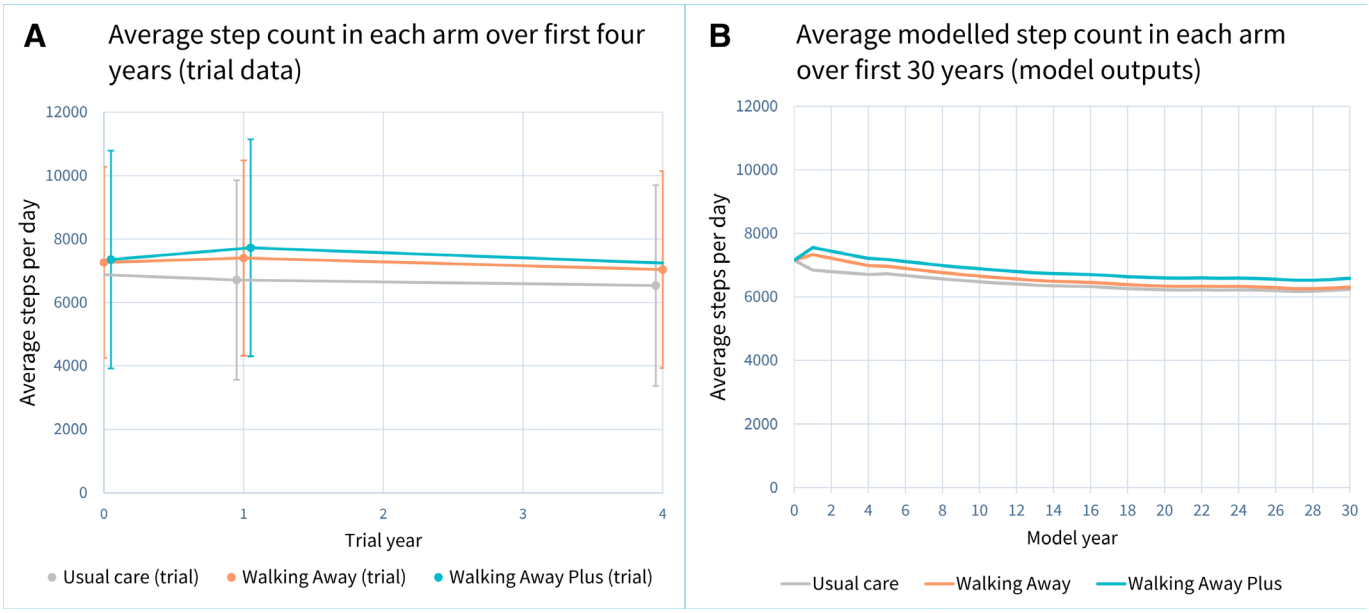

Figure 1 (A) Average step count in each arm over the first 4 years (trial data). Error bars denote 1 SD. Note that points are shown spaced around the year marks to allow vertical error bars to be visible. (b) Average step count in each arm over the first 30 years (model outputs).

DISCUSSION

Neither WA nor WA+ was cost-effective at a threshold of £20 000 per QALY gained. Despite having a positive impact on lifetime CVD risk, neither intervention achieved enough reduction in the risk of T2D and/or CVD to give substantial lifetime QALY gains and reductions in lifetime costs. However, the results of the threshold analysis showed that interventions targeting step count have the potential to be cost-effective at this threshold. Interventions to increase step count should aim to maintain the increase long-term (in this case, at 48 months). Even a modest increase in step count at 12 months (such as 500 steps per day, as achieved by the WA+ arm of the PROPELS trial) can give cost-effective results at £20 000/QALY if this is fully maintained at 48 months. Five hundred steps/day is equivalent to just 5 min of brisk walking per day and the minimum clinically important difference in overall activity levels.[31]

The findings that WA and WA+ are not cost-effective are contrary to previous modeling work supporting the cost-effectiveness of behavior change interventions.[17] There are several possible reasons for this difference. First, Gillies *et al* modeled a reduction in T2D diagnoses because of lifestyle interventions, a reduction in T2D diagnoses was not observed in the PROPELS trial. Moreover, because there was no treatment effect on HbA1c in the PROPELS trial, there was no reason to extrapolate differences in rates of diagnosis beyond the trial period. Therefore, the only clinical effect included in the model was the protective effect on CVD risk of increasing step count. These differences may also be because the intervention in Gillies *et al* was a more intensive intervention than those modeled here; it was also a combined diet and exercise program, rather than a primary focus on PA as was the case in the PROPELS interventions. The Gillies *et al* study was also conducted in a slightly different population: it was defined based on impaired glucose tolerance

Table 2 The results of the base case probabilistic analysis

	Weighted population		
	Usual care	WA	WA+
Clinical outcomes (lifetime probability of events per person)			
T2D	0.464	0.474	0.464
CVD events	0.411	0.409	0.407
T2D complications	0.213	0.215	0.213
Cost-effectiveness			
Costs			
T2D	£1549	£1628	£1576
CVD events	£8440	£8436	£8410
T2D complications	£1328	£1382	£1339
Other clinical events	£11 284	£11 318	£11 301
Intervention	£0	£257	£322
Total	£22 598	£23 018	£22 945
QALYs	9.323	9.312	9.33
Incremental costs	–	£421	£347
Incremental QALYs	–	−0.01029	0.00705
ICER (95% CI)	–	Dominated by usual care	£49 273 (£30 011–£82 987)

CVD, cardiovascular disease; ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years; T2D, type 2 diabetes; WA, Walking Away; WA+, Walking Away Plus.

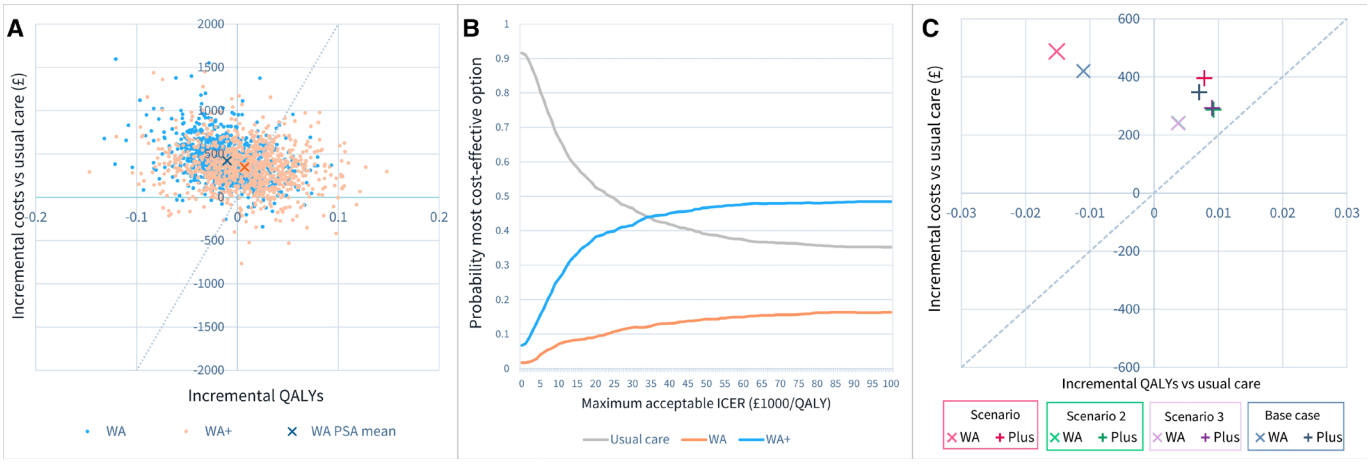

Figure 2 The results of the economic analyses: (A) the cost-effectiveness plan in the whole population with the interventions compared with usual care; (B) the cost-effectiveness acceptability curve in the whole population; and (C) the results of the scenario analyses on a cost-effectiveness plane with the interventions compared with usual care (scenario 1: regressions were based on each ethnic subgroup separately; scenario 2: statistically non-significant treatment effects were removed; scenario 3: Whitehall risk equations used in all model years). ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; WA, Walking Away; WA+, Walking Away Plus.

rather than HbA1c as in PROPELS. The threshold analysis suggests that maintaining the intervention effect of over 500 step/day observed after 12 months in WA+ to 48 months would give an ICER of £15 986/QALY, (ie, it would be cost-effective at a threshold of £20 00/QALY).

Both WA and WA+ were estimated to be substantially more expensive than other structured education programs for people with T2D (eg, the Diabetes Education and Self-Management for Ongoing and Newly Diagnosed (DESMOND) program for T2D self-management); if they were as inexpensive as DESMOND, WA+ would be cost-effective.[32] As well as the costs of providing an education course, WA+ incurs additional costs related to delivering follow-up support. It is worth noting that while the in-trial costs for delivering DESMOND were £203 per person (roughly equivalent to WA), the "real-world" estimate was just £76 per person. It is likely that the assumptions underlying the estimation of real-world costs are a key driver of the discrepancies in cost-effectiveness estimates.

The key strengths of this study are that it is based on a clinical trial which is to our knowledge unique in two important ways: first, it uses accelerometer-measured PA as a primary outcome, and thus allows inferences to be made about the relationship between PA, health outcomes (including diabetes diagnosis), and quality of life. Second, it collected follow-up data for 4 years, which is an unusually long follow-up period for a clinical trial of this nature. Finally, the model used is a well-validated model that has been used in many previous evaluations, some of which were conducted for UK decision makers.[20 21 33 34] However, there are several limitations that may have affected the strength of the conclusions. First, data on the date of diabetes diagnosis were not collected in the PROPELS trial for all participants, so diagnoses were based on logistic regression models, rather than time-to-event analysis. It was necessary to make the simplifying assumption that diagnosis was made at either 12 or 48 months (ie, at a PROPELS clinic visit). This is not representative of the real world, where some

Table 3 Results of the threshold analyses on the ICER for the change in step count at 12 months postintervention and the percentage of the step count that is maintained at 48 months postintervention

		Percentage of step count change at 12 months maintained at 48 months					
		0%	20%	40%	60%	80%	100%
Absolute average daily step count increase at 12 months	500	£42 344	£31 837	£27 936	£24 623	£20 574	£15 986
	600	£42 583	£32 157	£26 838	£23 039	£17 150	£13 959
	700	£46 089	£33 551	£25 064	£20 055	£15 916	£12 362
	800	£41 314	£29 209	£23 103	£16 868	£13 707	£10 776
	900	£44 137	£29 954	£20 668	£15 725	£12 253	£9772
	1000	£45 233	£29 604	£19 589	£14 515	£10 552	£8396

Cells in red are not cost-effective at £30 000/QALY; cells in yellow are cost-effective at £30 000/QALY but not at £20 000/QALY; cells in green are cost-effective at £20 000/QALY.
ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year.

people will have been diagnosed between the 1- and 4-year follow-ups. Furthermore, the trial would need to be much larger to be powered to detect differences in diabetes diagnoses between the arms. Moreover, it was only possible to model the independent effect of PA on one group of health outcomes: CVD events; effects of PA on other health outcomes (eg, cancer[35] and depression[36]) are not captured here. However, as the evidence linking objectively measured step count to these outcomes is currently poor, these effects cannot be included in the model. Key areas of research that would improve decision making in PA in people at high risk of developing T2D include research into PA interventions that can maintain small (but clinically meaningful) changes to PA over the longer-term, and research linking accelerometer-measured PA to outcomes other than CVD.

In conclusion, neither WA nor WA+ has an ICER below English decision makers' cost-effectiveness threshold. However, for PA interventions to be cost-effective in a population at high risk of developing T2D, only relatively small changes to behavior need to be maintained over the longer term.

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Acknowledgements We acknowledge the support and contribution of the study management team who worked tirelessly for the successful completion of this program of research. We thank Bernie Stribling (Southwark Council) for her advice and input into the real-world costs of delivering the Walking Away program. We acknowledge and thank the independent trial steering committee which was responsible for the overall management and oversight of the trial. The TSC was made up of: Chair: Simon Heller, Professor of Clinical Diabetes, University of Sheffield; Richard Morris, Professor in Medical Statistics, University of Bristol; Des Johnston, Professor of Clinical Endocrinology, Imperial College London. We acknowledge and thank the Data Monitoring and Ethics Committee (DMEC) which held responsibility for the interests of participant safety and data integrity and reviewed all reported adverse events. They also reviewed and agreed the statistical analysis plan. The DMEC comprised: Chair: Graham Hitman, Professor of Molecular Medicine and Diabetes, Queen Mary, University of London. Naveed Sattar, Professor of Cardiovascular and Medical Sciences, University of Glasgow. Michael Campbell, Emeritus Professor of Medical Statistics, University of Sheffield. KK, LJG, and HE are supported by the National Institute for Health Research (NIHR) Applied Research Collaboration East Midlands (ARC EM). KK, MJD, and TY are supported by the NIHR Leicester Biomedical Research Centre (BRC). Finally, we would like to acknowledge and thank the research participants, without whom the research could not have taken place.

Contributors Conceived the work: MG, KK, TY, SJG, WH, HE, StephenSu, MJD, and LJG. Designed the work: MG, DJP, AB, LEH, TY, SJG, and KK. Acquisition of data: HE and CLE. Accelerometer data processing: CLE. Data analysis: LEH, TY, DJP, AB, and StephenSh were involved in the analysis of data. Interpretation of data: LEH, TY, KK, SJG, DJP, and AB were involved in the interpretation of data. LEH acted as the lead author and acts as the guarantor for this work. All authors were involved in the final approval of the version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions relating to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding This study/project is funded by the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) Programme (grant number 09/162/02). The NIHR had no control over the conduct of the study. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care. Accelerometer processing and analysis were supported by the NIHR Leicester Biomedical Research Centre. The costs of the intervention were supported by the NHS Leicester City Clinical Commissioning Group, NHS West Leicestershire Clinical Commissioning Group, NHS East Leicestershire and Rutland Clinical Commissioning Group, and NHS England. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR, or the Department of Health.The publication costs of this article were funded by the University of Sheffield Institutional Open Access Fund.

Competing interests KK reports that he acted as an advisor to NICE Guidance. SJG reports grants from NIHR HTA, during the conduct of the study. DJP reports non-financial support from Novo Nordisk, non-financial support from Eli Lilly and Company Limited, non-financial support from Abbott, Diabetes Care, non-financial support from Sanofi-Aventis, and non-financial support from Medtronic, outside the submitted work. TY reports grants from NIHR Leicester Biomedical Research Unit, during the conduct of the study and was involved in contributing to an adapted version of the Walking Away intervention that is part of the framework for the National Health Service Diabetes Prevention Programme, led by Ingeus (main contractor) and the Leicester Diabetes Centre, University Hospitals of Leicester (subcontractor).

Patient consent for publication Not applicable.

Ethics approval Ethical approval was granted by the NHS National Research Ethics Service, East-Midlands Leicester Committee (Ethics number: 12/EM/0151). Participant recruitment commenced in December 2013 and was completed in February 2015, with follow-up data collection completed in July 2019. This is a health economics study. Patients consented to participation in the PROPELS RCT on which this analysis is based.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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