National Institute for Health and Clinical Excellence
Public Health Intervention Guidance on Physical Activity
– Brief advice for adults in primary care:
Economic Analysis

Economic modelling of brief advice on physical activity for adults in primary care

Submitted to PHIAC 24th August 2012

(Commissioned by NICE Centre for Public Health Excellence to support update of PH2)

Anokye N, Lord J, Fox-Rushby J

Health Economics Research Group (HERG),
Brunel University
Uxbridge, Middlesex, UB8 3PH

Correspondence to: Julia Fox-Rushby PhD, Professor of Health Economics
Email:Julia.Fox-Rushby@brunel.ac.uk

Contribution of Authors

NA led the modeling with inputs from JL and JFR. JL reviewed the spreadsheet model. NA wrote the first draft and JFR edited drafts. JFR had overall responsibility for delivery to NICE.

Acknowledgements

This report was commissioned by the Centre for Public Health Excellence on behalf of the National Institute for Health and Clinical Excellence. The views expressed in the report are those of the authors and not necessarily those of the Centre for Public Health Excellence or the National Institute for Health and Clinical Excellence.

Declaration of interests

Authors declare *no co*nflicts of interest.

Executive Summary

Aim

To model the cost-effectiveness and present a consequences analysis of brief advice to promote physical activity and the local architecture that supports its provision in primary care settings.

Methods

A Markov decision model with annual cycles was used to compare the lifetime costs and outcomes of a cohort of 100,000 people exposed, at age 33 for one year, to brief advice with an unexposed population. By the end of the first year the cohort was either 'active' or 'inactive' (based on national definitions) and they could have one of 3 events (non-fatal CHD, non-fatal stroke, type 2 diabetes), remain event free (i.e. without CHD, stroke, or diabetes) or die either from CVD or non-CVD causes. Health outcomes were expressed in terms of Quality-Adjusted Life-Years (QALYs). Costs were assessed from a UK National Health Services perspective in £2010/11 prices.

Data to populate the model were primarily derived from the systematic literature reviews accompanying development of this public health guidance as well as literature searches of economic evaluations conducted for existing NICE guidelines. Deterministic and probability sensitivity analyses explore uncertainty in parameter estimates. The one-way deterministic sensitivity analyses, examines uncertainties in effectiveness, persistence of protective effect, discount rate and cost.

Main Results

Compared with usual care, brief advice is more expensive as it incurs additional costs of £806,809 but it is also more effective leading to 466 QALYs gained in the total cohort, which equates to a QALY gain of 0.0047 per person. The incremental cost per QALY of brief advice compared with usual care is £1,730 and thus can be considered cost-effective at the NICE threshold of £20,000.

Most changes in assumptions resulted in the ICER falling at or below £12,000/QALY gained. If recruitment to brief advice was changed from the opportunistic centres (base case) to disease register, the ICER increased from £1,730 to £12,010. However, when short term mental health gains associated with physical activity were excluded the ICER was

£27,000/QALY gained. The probabilistic sensitivity analysis showed that, at a threshold value of £20,000/QALY, there was a 99.9% chance that brief advice would be cost-effective.

The cost-consequences analysis showed that delivering brief advice to a cohort of 100,000 will cost the NHS £950,000 and result in an additional 6,994 people becoming physically active at year 1. In 10 years, brief advice would be expected to avert 2.4 events of CHD, 1.8 events of stroke, 3.1 events of diabetes and prevent 1 death, a 67-74% reduction in depressive symptoms, and impact positively on the prevention or/and management of health conditions including metabolic disease, cancer and muscoskeletal ailments. Potential non-health benefits comprise improvements in productivity via reduction in absenteeism at work. Whilst considered infrequent the potential adverse effects associated with brief advice include injuries and pain.

Further research is recommended to compare the cost effectiveness of brief advice with other interventions designed to increase physical activity interventions (e.g. exercise referral schemes, pedometer programmes) to ensure brief advice is not dominated (assuming the population accessing these interventions are similar). It is also important to observe the nature of mental health gains (size, duration) in terms of quality of life from physical activity participation with more precision and to establish good quality evidence on the impact of physical activity interventions beyond a year.

List of abbreviations

BA	Brief Advice
BMI	Body Mass Index
CCA	Cost Consequences Analysis
CEA	Cost Effectiveness Analysis
CHD	Coronary Heart Disease
CI	Confidence Interval
CPHE	Centre for Public Health Excellence
CUA	Cost Utility Analysis
CVD	Cardiovascular Disease
DH	Department of Health
EQ-5D	EuroQol 5 dimensional measure of health related quality of life
ERS	Exercise Referral Schemes
GP	General Practice/Practitioner
GPPAQ	General Practice Physical Activity Questionnaire
HERG	Health Economics Research Group
HRQL	Health Related Quality of Life
HSE	Health Survey for England
HTA	Health Technology Assessment
ICER	Incremental cost-Effectiveness Ratio
JFR	Julia Fox-Rushby
JL	Joanne Lord
NA	Nana Anokye
NCGC	National Clinical Guidelines Centre
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
OR	Odds Ratio
PH2	Public Health Guidance No 2
PHIAC	Public Health Interventions Advisory Committee
PSA	Probabilistic Sensitivity Analysis
QALY	Quality Adjusted Life Year
RCTs	Randomised Controlled Trials
RR	Relative Risk
ScHARR	School of Health and Health Related Research
SD	Standard Deviation

T2D	Type 2 Diabetes
UK	United Kingdom
USA	United States of America

Contents Page

Sections of report

List of tables

List of figures

1 Introduction

In 2006 NICE produced guidance with supporting documents on economic analysis (NICE 2006; MATRIX 2006a, and 2006b) on a small number of commonly used approaches to increasing physical activity; brief interventions in primary care, exercise referral schemes, pedometers and community-based exercise programmes for walking and cycling. Following a review in 2009, NICE decided to update the 'brief advice in primary care' recommendations with additional focus on mental wellbeing as an outcome of physical activity and the impact of infrastructure on efficiency of brief advice) as well as to consider mental wellbeing as an outcome (NICE 2011).

The updated guidance will supersede recommendations 1–4 from NICE public health guidance 2 on 'Four commonly used methods to increase physical activity' which covered recommendations to primary care practitioners to: identify inactive adults and advise 30 minutes of moderate activity 5 days a week; use of GPPAQ for monitoring; account for individual circumstances and agree individual-specific goals; monitor of strategies to promote physical activity locally; and cover the hard to reach and disadvantaged communities.

The updated guidance is due for publication in April 2013 and, in addition to aiming at guiding good practice among primary care practitioners and the general public, this guidance is expected to support at least six policy documents (NICE 2011) including; 'Healthy lives, healthy people: our strategy for public health in England' (DH 2010); Improving outcomes: a strategy for cancer' (DH 2011a); 'Let's get moving. Commissioning guidance: A new physical activity care pathway for the NHS' (DH 2009a); 'No health without mental health: a cross-government mental health outcomes strategy for people of all ages' (DH 2011); 'Start active, stay active: a report on physical activity from the four home countries' Chief Medical Officers' (Department of Health 2011b); and The 'public health responsibility deal' (Department of Health 2011c).

Assessing the cost-effectiveness of brief advice interventions will allow up to date knowledge on the efficiency of delivering brief advice. An accompanying systematic review of evidence on effectiveness of brief advice for physical activity shows brief advice results in improved physical activity participation compared with usual care (Campbell et al 2012). However, a

recent review of the cost-effectiveness of brief advice for physical activity (Anokye et al 2012) showed that little economic evidence exists to inform resource allocation; indeed only three economic evaluations were identified. The limited literature available suggests that brief advice, given by either GPs or other health workers and with or without written material is cost-effective. However, the paucity of evidence on effectiveness and concerns about its rigour (Campbell 2012) coupled with inadequate exploration of uncertainty point to the need for further evaluation.

The aim of this report is to present modelling of available evidence on the cost-effectiveness of brief advice to promote physical activity and the local architecture that supports its provision in primary care settings. The specific objectives were two-fold:

1. To use the literature reviews on effectiveness and cost-effectiveness to decide, with NICE, which intervention(s) or programme(s) (types of brief advice and types of local infrastructure/systems) are suitable for modelling expected cost utility and/or cost consequence, given the resources and deadlines.
2. To use, adapt or develop the best possible model(s), given resources, of the cost-utility/consequences of one or more interventions or programmes according to the deadlines set.

This report builds on a systematic review of effectiveness (Campbell et al 2012) and, as insufficient evidence of effectiveness was found on the local architecture that supports provision of brief advice for physical activity in primary care settings, this report on cost-effectiveness focuses on brief advice on physical activity.

Two economic analyses are presented in order: first the methods and results from modelling the cost utility of brief advice for physical activity in primary care and secondly, the methods and results from a cost consequence analysis summarises disaggregated costs and benefits. The results of these analyses are followed by a comparison and discussion.

2 Cost utility analysis

This analysis follows guidance set out by NICE for evaluating public health interventions (NICE, 2009). Any unexpected departures, for example through lack of data, were discussed and agreed with the CPHE team.

2.1 Methods

2.1.1 Conceptual framework

2.1.1.1 Overview and critique of existing model of brief advice for physical activity

The one model of the cost-effectiveness of brief advice in existence uses a decision tree approach (Matrix 2006). This study was commissioned by NICE for the development of PH2. It considers a cohort of individuals who enter the model in a sedentary state. Individuals are exposed to an intervention (brief advice) that affects their likelihood of becoming physically active. Physical activity is assumed to have a long-term effect on an individual's likelihood of developing a number of chronic conditions. Chronic conditions included in the model were selected given their view that there was evidence of a strong causal relationship between physical activity and the incidence coronary heart disease, stroke, type 2 diabetes mellitus and colon cancer. Estimates of the relative risk of developing each of these conditions, depending on physical activity status, were derived from published sources. The conditions were assumed to be independent of one another and individuals were only permitted to experience one condition within the model. Estimates of mortality rates and life years lost associated with each condition were derived from published sources and derived by assuming an average age of onset for each condition, dependent on the age of the population under consideration. Utilities and unit costs associated with each condition were also derived from multiple published sources.

This model is adaptable to a wide range of physical activity interventions including environmental interventions (Beale et al 2007) because the primary aim of the model was tied to the effects of physical activity per se rather than specific interventions. It formed the basis of a recent model developed (at Brunel), to evaluate the cost effectiveness of exercise referral schemes (ERS) in the UK (Anokye et al 2011). The ERS model considered the lifetime risk of developing a series of conditions known to be associated with being physically active and for which robust quantifiable evidence was available on the relationship between physical activity and incidence of disease; coronary heart disease, stroke and type II

diabetes. While physical activity has been associated with a wide range of conditions e.g. colon cancer, musculoskeletal or respiratory diseases, data limitations precluded their incorporation in the ERS model. The ERS model represents an improvement on the Matrix model in two ways; a short-term mental health benefit from exercise itself is included, and the effectiveness evidence is based on a meta-analysis rather than a single study (Pavey et al 2011).

A key consideration for future modelling is whether the simple decision analytic approach to modelling is warranted. Given that an individual's behaviour may change over time, an explicit recognition of time in modelling the cost effectiveness of brief advice may be useful, although once again this may be limited by available evidence.

2.1.1.2 Overview of conceptual model adopted

The modelling approach adopted in this report builds on the adapted model (ERS model) by developing a Markov model that considers a cohort of healthy individuals who present in a physically inactive state at the age of 33 years and follows them over their remaining life time (for a further 48 years). The age of the population was selected to reflect evidence on the effectiveness of brief advice (Campbell et al 2012).

Costs and outcomes of the cohort exposed (in the first one year cycle only) to brief advice are compared with the cohort not exposed to it (i.e. usual care). Those exposed to brief advice are assumed to have greater probabilities of becoming 'active' i.e. minimum of 150 minutes of at least moderate intensive physical activity/75 minutes of vigorous intensive physical activity was done per week or otherwise (inactive). The active state is defined in line with the literature on the effectiveness of brief advice and relative risks (RRs) for developing the disease conditions. It is recognised that this dichotomous specification of level of activity does not allow the impact of brief advice on people exercising below/above the threshold of active state to be explicitly modelled. Efforts were made to account for that through modelling a multinomial outcome i.e. inactive, active, and very active[1]. Eventually, in

[1] This process included: First, a thorough search for evidence on the impact of physical activity, where activity level is measured as varying degrees of activity comprising below/above the threshold, on health outcomes. Details of the search for data can be found in Appendix 1. Only 2 studies with relevant evidence were found. However, the specification of physical activity in those studies did not reflect the inactive, active, and very active categorisation discussed with NICE. Nevertheless, a model was developed that specified physical activity outcome as a multinomial variable and the details of this early model was discussed with NICE. The lack of a clear link to UK threshold values for physical

agreement with NICE, the binary outcome had to be used because of a lack of effectiveness data on people exercising below or above the threshold.

The 'active' state is associated with improved life expectancy and quality of life, as a result of a reduced risk of developing either coronary heart disease (CHD) (both non-fatal and fatal events), or stroke (both non-fatal and fatal events), or type 2 diabetes.
While the model does not explicitly include changes associated with activity levels over time, the impact of such changes is accounted through the use of the relative risk (RR) of developing CHD, stroke and type 2 diabetes as these are sourced from cohort studies that measured baseline physical activity (exposure) and related this to subsequent onset of CHD, stroke or diabetes (outcomes) over a defined follow-up period. By design, since these cohort studies (Hu et al 2003, 2005, 2007) followed up the same people (who were either active or inactive at baseline) for a number of years, during which some of the inactive people might have become active or vice versa, it means that irrespective of activity levels during the follow up years, once active (or inactive) at baseline, the relevant RR applies. The case-controls of these studies are only different in terms of baseline activity levels. Similarly, in the Markov model, as far as people are active or inactive at baseline i.e. Year 1 (through brief advice or usual care), the RR estimates are applicable regardless of activity levels in the subsequent years (equivalent to the follow-up years of the cohort studies). It is also important to note that the studies used as evidence further controlled for other potential confounders, including; BMI, other types of physical activity, smoking, and other morbidities. Given that such RR estimates already accounted for changes in physical activity that occurred during the cohort follow up periods, any further adjustment for changes in physical activity (e.g. decay rates) in the model would amount to double counting because any existing changes associated with physical activity during the follow-up is already incorporated in the RR estimate.

Beyond a period equivalent to the follow-up period in the cohort studies, we assume a 100% decay rate of physical activity and hence the active people are given the same risk (as the inactive people) of developing the disease conditions. Therefore, after the run-in period of the intervention (Year 0), we do not assume that physical activity levels as result of brief

---

activity and therefore current policy guidance was the prime reason for not continuing the development of this model.

advice or usual care are sustainable. We recognise that this is a conservative approach and hence test its impact on the cost-effectiveness of brief advice in a sensitivity analysis.

2.1.2 Description of intervention and comparator

2.1.2.1 The intervention

In this guidance development, NICE defines brief advice to promote physical activity in adults as comprising: verbal advice, discussion, negotiation or encouragement, with or without written or other support or follow-up. It could be opportunistic and can typically take from less than a minute to up to 20 minutes. It can vary from basic advice to a more extended, individually-focused discussion. The advice might be delivered in a GP surgery, health centre or other primary care setting. It may also be delivered by primary care professionals in other settings (for example, a residential home).

2.1.2.2 Comparator

The comparator for the analysis is usual-care, which is specified as no active intervention, and is the common alternative in an inactive population (Campbell et al 2012). This acknowledges that some inactive individuals may choose to participate in physical activity without an intervention although the probability of doing so is assumed to increase as a result of exposure to an intervention.

2.1.3 Summary of effectiveness evidence

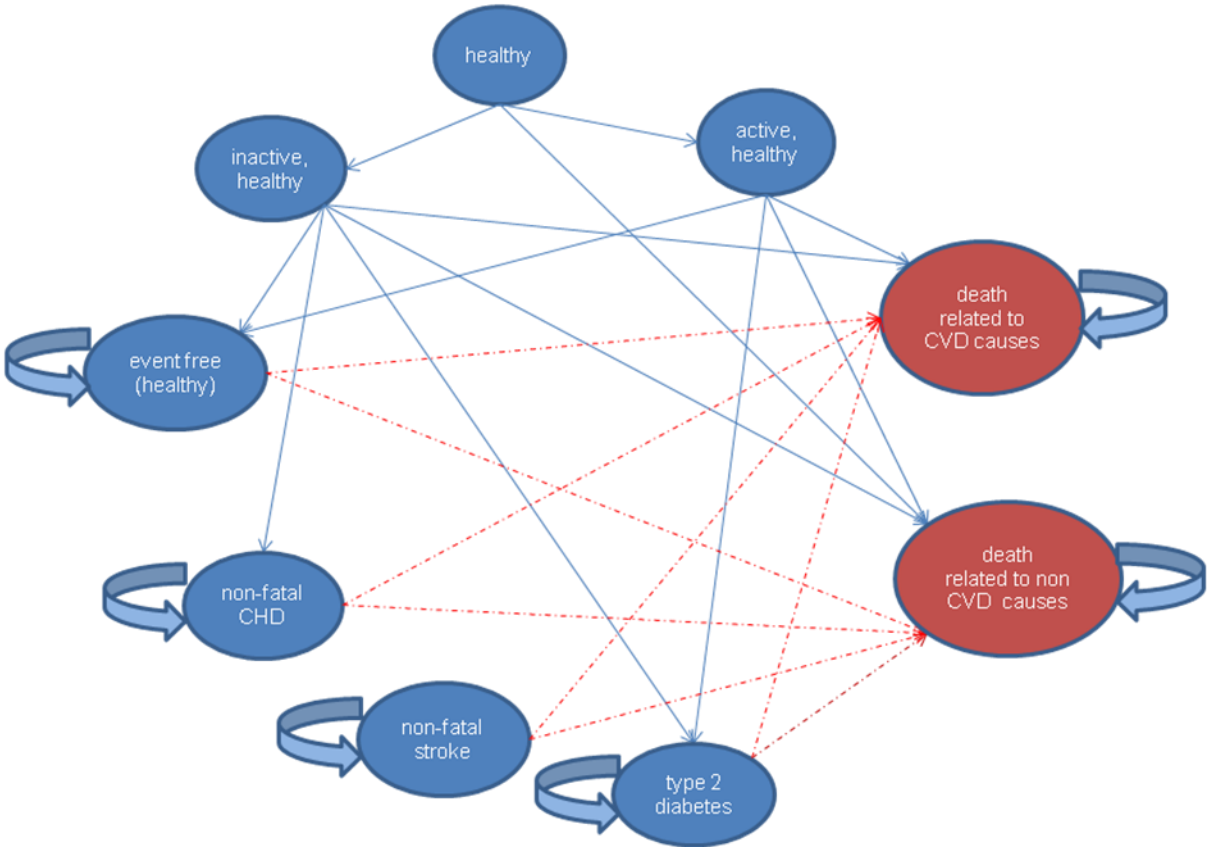
The systematic review of evidence on effectiveness of brief advice suggests that it leads to increased physical activity participation compared with usual care (Campbell et al 2012). This pattern was consistent for varied physical activity outcomes: continuous data (standard mean difference =0.20, 95%CI 0.09-0.31), dichotomous data (OR 1.89 95% CI= 1.23, 2.89). The addition of further interventions to support brief advice, however, yielded no clear benefit with no statistically significant difference found between physical activity levels of receiving a brief advice only intervention and those receiving brief advice, plus additional supportive elements (standardised mean difference. This finding was consistent across both continuous 0.10 (CI= -0.04 to 0.24)) and dichotomous physical activity measures (odds ratio 1.15 (CI= 0.71 to 1.88).

Notably, to match the physical activity outcomes used in the literature on the RR of developing the disease conditions used in the modelling and also allow of comparison of our results with the existing economic evidence on brief advice (i.e. NICE 2006), the modelling is based on the dichotomous data, which hereafter will be the focus.

2.1.4 Model structure

Figure 1 illustrates the path the cohort takes once it is exposed (or not) to brief advice. The intervention is delivered at the beginning of the first model cycle (Year 0). Then, over an initial 'run-in' period individuals settle into one of two states by the end of the first year: 'inactive, healthy' or 'active, healthy'. This allows transient effects of brief advice to have dissipated, so that we are left with more sustainable effects on activity, which may be expected to translate into health outcomes. We assume that one year is sufficient for people to reach a stable level of activity. The level of activity though changes overtime. During this run-in period, it is assumed that the cohort remains 'healthy' (i.e. they don't develop CHD, stroke, or diabetes), although they could die from non–CVD (defined as other conditions excluding CHD, stroke) related mortality, which are reflected at the beginning of year 1.

Figure 1: Diagrammatic presentation of model



At the beginning of year 1 (cycle 2), the cohort of people over this and subsequent cycles can transition into one of the following six health states (with probabilities of transition dependent on the activity states in the previous period):

- Event free (healthy) (i.e. don't have CHD, stroke, or diabetes)
- Non-fatal CHD
- Non-fatal stroke
- Type 2 diabetes (T2D)
- Death related to non–CVD (defined as other conditions excluding CHD, stroke) causes
- Death related to CVD (defined as CHD, stroke) causes

Annual costs of treatment for disease and utility values are attached to each of these health states. The average cost of brief advice is attached to each individual in the first year. At present there is no distinction between those who are contacted and those who access brief interventions, and making this distinction would not change the model results because this is a cohort rather than population model. In addition to costs, a utility gain for each year the active group is alive accounts for psychological benefits of physical activity.

From year 2 until the end of lifetime, the model comprises all the above health states plus death for people with a diagnosis of CHD, stroke or diabetes (non-fatal CHD event or stroke or onset of diabetes in a previous year). It is assumed that people with non-fatal CHD, non fatal stroke, and type 2 diabetes have a raised age specific all-cause mortality rate, compared with the 'healthy' population (those without CHD, stroke or diabetes).

Key assumptions of the model include: (a) Individuals are assumed to experience only one health state and therefore there is no transition to or from disease states once the first is experienced; (b) Physical activity is assumed to have health benefits via reduced risk for only CHD, stroke and diabetes.

2.1.5 Key features of analysis

The analysis adopts an NHS perspective; applies discounting to costs and health outcomes at the current NICE recommended rates (3.5%), and expresses outcomes as QALYs. The NHS perspective is adopted because the programmes under consideration are within the primary care setting (Drummond et al 2005) and because using a broader perspective

lacked data. Whilst it is acknowledged that physical activity may have important effects on non-healthcare costs and benefits, these are excluded from the cost utility analysis, although these broader considerations are addressed through the presentation of cost consequence analyses. A lifetime horizon is adopted to acknowledge the long-term benefits of physical activity.

Deterministic and probability sensitivity analyses explore uncertainty in parameter estimates. The one-way deterministic sensitivity analyses, examines uncertainties in effectiveness, persistence of protective effect, age of cohort, discount rate and cost. Table 1 sets out how these parameters are varied. The choice of effectiveness estimate and RR for developing disease conditions for the deterministic sensitivity is largely because of uncertainty and to test base-case assumptions around them. Changes in age of cohort are to provide an indication of the impact of targeting exposing to brief advice to older people. The choice of discount rate is a requirement stipulated in the methods manual (NICE 2009) whilst the variation in cost is to demonstrate how infrastructure or staff changes affect efficiency of brief advice given that per definition brief advice can be provided by various types of health professionals. In addition, infrastructure changes is reflected through differing recruitments to brief advice (i.e. opportunistic vs. disease register).

Table 1: Overview of deterministic sensitivity analysis

Purpose (Impact of.)	Parameter	Changes in parameter estimates
Changes in people who become physical active (at 1 year) after brief advice	Effectiveness estimate (via RR)	Percentage increases via the RR. If brief advice leads to a: 10% change=1.10 RR 25% change=1. 25 50% change=1.50 75% change=1.75 100% change=2.00
Changes in persistence of protective effects (adjusted for decay rates) of physical activity.	RR for developing disease conditions	Base case=protective effects persists up to 10 years Changes: 1.Protective effects persist over lifetime =applying the same RR used for the 10 years for the rest of the years 2. Protective effects persist just for a year = apply RR to first year(rather than 10 years) and the remaining years take RR =1

Changes in age of cohort (and impact on moving to dominant option)	Start-up age*	Change start-up age from 33 years to between 50 and 60 years
Changes in discount rate	Discount rate	Change discount rate for costs and QALYs from 3.5% to 1.5%
Changes in health professional delivering brief advice	Cost of intervention*	Base case-cost of intervention (that was delivered by GPs. Nurse and healthcare assistants) is changed to the a cost of brief advice intervention (delivered by healthcare assistants)
Changes in recruitment strategies for brief advice	Cost of intervention*	Base case-cost of intervention (recruitment via opportunistic) is changed to the a cost of brief advice intervention (recruitment via disease register)

**We recognise that a change in start-up age of cohort, infrastructure or person who delivers the brief advice potentially impacts on both effectiveness and cost of intervention. However, there was no effectiveness evidence to that effect and hence we focussed on costs in the case of the latter two. The former although had no adjustments for costs as well as effectiveness.

Uncertainties around all parameters in the model (except baseline mortality)[2] are addressed simultaneously using probabilistic sensitivity analyses (PSA). The choice of distributions and their respective alpha and beta calculations draws on Briggs et al (2006). In cases, where there are no data on standard errors, the standard approach of using 10% of mean estimates as standard error is followed (Pavey et al 2011). A total of 10,000 Monte Carlo simulations are generated from the PSA. The number of simulations required was assessed by plotting the net monetary benefit estimates (for brief advice vs. usual care) against number of iterations and identifies the point at which the distribution stabilises. The number of iterations corresponding to stability was considered the appropriate number of simulations to generate.

2.1.6 Model verification and validation

To ensure the credibility of the model, good practice guidance for verification and validation (Phillips et al 2004, Chilcott et al 2010) was followed. This comprised two main steps:

1. Verification of the computer model: ensuring that it behaves as expected according to the theoretical model. HERG has a checklist of methods to avoid and identify errors. This includes tips for model developers, for example on the use of sensitivity analysis

[2] Baseline mortality data was excluded in probabilistic sensitivity analysis because mortality data come from census data and national database that are less likely to have errors

to test the model is operating correctly, and re-programming complicated sections of code in another language. In addition, the model was reviewed and tested by experienced modellers both internal (both connected with and external to this project) and external to HERG.

2. Operational validity: comparing model results with real-world observations or the results of other models. For example, model predictions of the incidence of cardiovascular events were compared with observed event rates from clinical trials (not used in construction of the model).

2.1.7 Model inputs

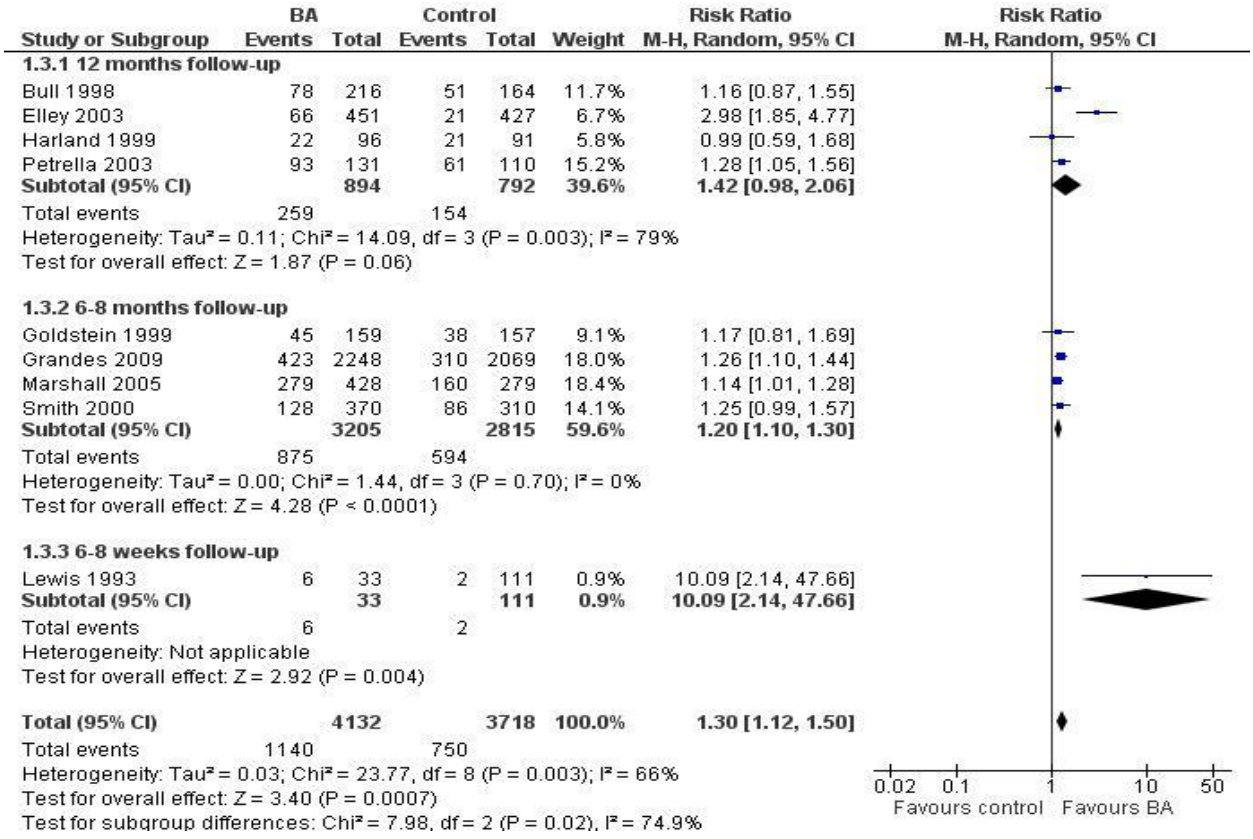
Data to populate the model were primarily derived from systematic literature reviews and literature searches of economic evaluations conducted for existing NICE guidelines. Further details are provided below.

2.1.7.1 Effectiveness of brief advice vs. usual care

Evidence of the effectiveness of brief advice vs. comparator are reflected as dichotomous outcome that was specified in terms of the probability of moving from an inactive state to an active state at one year after brief advice. This was obtained from a meta-analysis conducted as part of effectiveness review undertaken by Campbell et al (2012). The meta-analysis combined data from RCTs and non-randomised controlled studies with like populations, interventions and outcomes. The impact[3] of sources of heterogeneity on the meta-analysis was measured using the I^2 to quantify inconsistency across studies (Higgins 2008). Figure 2 give details of the meta-analysis conducted.

[3] A rough guide to interpretation of I^2 is suggested: 0% to 40% might not be important; 30% to 60% may represent moderate heterogeneity; 50% to 90% may represent substantial heterogeneity; 75% to 100% considerable heterogeneity.

Figure 2: Meta-analysis of the effectiveness of brief advice vs usual care (including studies measuring physical activity outcome as proportion of active people)



Source: Campbell et al (2012)

The estimate for 12 months follow-up from figure 1 (1.42 (95% CI:0.98, 2.06)) was used in the base case model because 12 months is considered relatively more capable of capturing sustainable effects on activity. This choice was discussed and agreed with the NICE team. Sensitivity analysis considered the other estimates[4] from Figure 1.

Table 2 shows that BA is associated with a higher probability of being active compared with usual care, although it is noted that the 95% CI falls just below 1. The active state is defined in line with the effectiveness literature. Thus, an inactive state corresponds not only to non-participation in physical activity but also participation below the requisite amount.

[4] The estimate at 6-8 weeks was however not considered given that the period was considered not sufficient enough and the potential implications on robustness given the relatively small number of studies.

Table 2: Proportion of people in activity states (after run-in period of BA)

	Usual care	Brief advice
Inactive	80.6%	73.6%
Active	19.4%	26.4%

Source: Figure 2

2.1.7.2 Risks of developing disease states associated with physical (in) activity

Evidence of the effect of physical activity on the development of the disease outcomes considered in the model (coronary heart disease, stroke and type II diabetes) is derived from a literature search of national and international guideline reports that set out the science-based guidance on physical activity, fitness, and health for UK, USA and Canada as well as NICE guideline documents. Our search for these sources involved inputs from the NICE team (details from Appendix 1).

Based on three indicators[5] (i.e. lengthy follow-up period; close match between physical activity indicator and meeting the recommended level; currency of evidence), data for RR estimate for developing CHD (non fatal and fatal), stroke (non fatal and fatal), and diabetes were selected from Hu et al (2007, 2005, 2003) respectively. The RR estimates were based on cohort follow up periods - 19 (CHD, stroke) and 12 years (diabetes) respectively. However, assuming that the RRs would be the same after the follow up periods might be unrealistic. We therefore assumed, conservatively, that these RR estimates hold for an initial 10 year period after which they change i.e. (a) the RR for developing CHD, stroke and T2D in the first 10 years of the model was based on Hu et al (2003, 2005, 2007) while; (b) the RR for developing CHD, stroke and T2D from the 11th year till death was assumed to equal to 1. Thus a 100% decay rate was assumed from the 11th year onwards (which represents 79% of the entire duration of the model). This assumption is tested through sensitivity analysis. The physical activity levels and study population used to measure the RR estimates were similar to those of the effectiveness estimate. (See Appendix 1 for details). The RR for developing

[5] These 3 indicators were chosen because (a) follow up: reflects how well decay rate had been accounted for in the analysis as a longer follow-up period allows adequate variations in activity levels to be adjusted for (b) currency of evidence: reflects up-to-date methods (c) meeting the recommended/being physically active is the thrust of physical activity guidelines in the UK including the guideline this study is meant to inform. Population setting was not a critical consideration here because the studies mainly found were from OECD countries.

CHD (non fatal and fatal), stroke (non fatal and fatal), and type 2 diabetes are provided in Table 3.

Table 3: RR estimates for developing the disease conditions

Disease conditions	RR(95% CI)	Source
CHD	0.9 (0.83,0.99)	Hu et al(2007)
Stroke	0.86 (0.79,0.93)	Hu et al (2005)
Diabetes	0.67 (0.53,0.84)	Hu et al (2003)

The baseline risks for developing CHD, and stroke were based on age-specific UK annual incidence rates used in an analysis of the cost effectiveness of statins developed for NICE/HTA technology appraisal (Ward et al 2005, 2007) and the model developed as part of the update of the NICE guideline on hypertension (NCGC 2011). In these models, data were obtained from the Bromley Coronary Heart Disease Register and the Oxfordshire Community Stroke project. The baseline risk for diabetes was taken from age-specific UK incidence rates for type 1 and type 2 diabetes from 1996 to 2005 estimated in Gonzalez et al (2009). Table 4 shows the baseline risks for the disease conditions in the general population.

Table 4: Baseline risks for CHD, stroke, diabetes

Age	CHD	Stroke	Diabetes*	Source(s)
33-34	0.000035	0.00008		Ward et al (2005, 2007); (NCGC 2011).
(33-39)			9E-05	Gonzalez et al (2009)
35-44	0.000465	0.00023		Ward et al (2005, 2007); (NCGC 2011).
(40-49)			0.00028	Gonzalez et al (2009)
45-54	0.002095	0.00057		Ward et al (2005, 2007); (NCGC 2011).
(50-59)			0.000632	Gonzalez et al (2009)
55-64	0.00631	0.00291		Ward et al (2005, 2007); (NCGC 2011).
(60-69)			0.001005	Gonzalez et al (2009)
65-74	0.0097	0.0069		Ward et al (2005, 2007); (NCGC 2011).
(70-79)			0.001116	Gonzalez et al (2009)
75-81	0.0097	0.01434		Ward et al (2005, 2007); (NCGC 2011).
(80-81)			0.001116	Gonzalez et al (2009)

*Converted into annual risks using Briggs et al (2006)

The derivation of the probabilities for developing CHD, stroke, and diabetes used in the model involved a number of steps. First, the probability of developing these conditions among inactive people was derived by adjusting the general population age-specific

incidence rates using the attributable risk fraction (Jamrosik 2005). To adjust these estimates appropriately, the second step estimated the probability of developing the health states among active individuals using the RR estimates identified from Hu et al (2003, 2005, 2007).

The probability that the primary stroke or CHD event is fatal is based on incidence data from the data from Bromley Coronary Heart Disease Register and the Oxfordshire Community Stroke project (Ward et al 2007). This is acknowledged as a simplification in the model, as in reality these probabilities might depend on level of physical activity. Lack of data, however, precluded accounting for such a possibility.

2.1.7.3 Mortality risks

The probability for CVD (CHD and stroke), and non–CVD related mortality for 'healthy people' were derived from age-specific UK interim life tables prepared Government Actuaries Department that were adjusted by age-specific UK annual incidence of mortality prepared by the Office of National Statistics (See Appendix 2). While it is recognised these estimates relate to the general population and hence include people with CHD, stroke and diabetes, the percentage of those disease groups are relatively small (<8%) and hence we assume these estimates are applicable to the 'healthy population'.

RR estimates for CVD (CHD and stroke), and non–CVD related mortality among people with CHD, stroke, and diabetes were used to adjust the probabilities for the 'healthy people' to derive probability of CVD (CHD and stroke), and non–CVD related mortality. The RR estimates for diabetic patients were based on a cohort of Framingham Heart Study (aged 45-74) that were followed for up to 25 years (Preis et al 2009) (see Table 5). For stroke patients, data was obtained from Bronum-Hansen et al (2001) that followed a Danish cohort of 25 + year olds after their first nonfatal stroke for 10 years (Table 5). As no equivalent data was found for CHD patients, we applied the same data for stroke patients.

Table 5: Relative risks for mortality after primary events

	After non-fatal CHD	After non-fatal stroke	After diabetes
Non-CVD mortality	1.71	1.71	1.49
CVD mortality	3.89	3.89	2.61

2.1.7.4 Primary Outcome Measure (QALY)

The NICE reference case (NICE 2009) requires that the primary outcome of the economic evaluation is expressed in terms of quality adjusted life years (QALYs) using estimates of survival and quality of life attributed to each health state.

Table 6 indicates the condition specific utility values used in the model. The health state utility values were taken from Ward et al (2005) (these were also used in NCGC (2011) who undertook a wide search[6] for available evidence on utility estimates associated with health states).

Table 6: Condition specific utility values (Ward et al 2005)

Conditions	Utility
Healthy	1
CHD 1st event	0.8
post CHD 1st event	0.92
Stroke 1st event	0.63
post stroke 1st event	0.65
Diabetes	0.9

Utility gains directly attributable to increased physical activity (Pavey et al 2011), so called process utility (0.072), and were also added to 'active' states to account for the psychological benefits of physical activity. Using a conservative approach, this utility gain was assumed to exist only at the 'run in' period (the first year) because that was the duration where we know that people had stayed active (Campbell et al 2012). Therefore, similar to the application RR estimates for developing disease conditions, we only assume the increased physical activity levels persist for one year. Sensitivity analysis considers the impact of changes in duration related the utility gain.

These quality of life gains were estimated using a sample of 5,537 adults (40–60 years) from the Health Survey for England (2008). The econometric estimation (a Tobit model) regressed EQ-5D mean scores on physical activity indicator assessed with an objective measure (accelerometer- actigraph model GT1M) controlling for confounders (Anokye et al 2012). Physical activity indicator was operationalised as a binary variable indicating being

[6] The literature search covered of electronic databases, hand searching, citation searching and reference list checking. Other sources examined were existing cost-effectiveness studies, the Cochrane Library and the Harvard catalogue of preference scores.

'active' or not (the definition in line with that of model). The regression model controlled for a set of socio-demographic, economic, health (including the disease conditions specified in the cost utility model) and other variables that were found in a separate literature review to be correlates of health related quality of life (HRQL). Models were subject to standard diagnostics and run separately including or excluding missing observations.

To account for the fact that health-related quality of life in the general population falls with age, the disease specific utilities were weighted using age specific utility scores for the general population. The age specific utility scores were estimated using data from the Health Survey for England (2008) (Table 7).

Table 7: Age-specific quality of life (HSE 2008)

Age	Mean	SD
33-44	0.90	0.184
45-54	0.86	0.229
55-64	0.82	0.264
65-74	0.78	0.266
75+	0.72	0.275

2.1.7.5 Intervention Costs

The cost of brief advice was derived from previously published research identified as part of the review of economic evaluations conducted as part of this study. Boehler et al (2011), presenting detailed patient level cost data was considered the best available evidence/estimate. The cost of brief advice was estimated using a time-driven variant of activity based cost analysis conducted from the health service perspective. Costs included salaries, practice overheads, capital costs, cost of support booklet for participants, cost of practitioner training, cost of contacting participants. Centre level resource use data was collected through a face to face survey of practice managers with telephone follow-up and contact with the Department of Health. All patient level resource use data was extracted using MIQUEST. Unit costs were based on national tariffs.

The intervention cost per patient varied depending on the recruitment strategy for brief advice intervention. The cost of brief advice, excluding training and set up costs[7], that recruited via disease register practices was estimated at £52 per patient and through opportunistic centres £8.60. The estimate used in this model was that of the opportunistic centre but sensitivity analysis considered the cost of recruitment via disease register. Costs were provided in 2007 prices and inflated to 2010/11 prices using the Personal Social Services Research Unit (2011) inflation indices.

Table 8: Intervention costs

	Cost per patient in 2007 prices (2010/11 prices)
Brief advice (recruitment via opportunistic centres)	£8.60[8] (£9.50)
Brief advice (recruitment via disease register practices)	£52 (£57.45)

2.1.7.6 Treatment costs associated with CHD, stroke and type II diabetes

Table 9 shows the annual costs per person attributed to health states provided in the model. These costs were taken from National Clinical Guidelines Centre (2011) that undertook an updated review of costs for various health states. Costs were inflated to 2010/11 prices using inflation indices from the Personal Social Services Research Unit (2011).

Table 9: Treatment costs related to conditions (Ward et al 2005)

Conditions	Annual cost per person (2010/11 prices)
Healthy	£0
CHD 1st event	£4,056
post CHD 1st event	£463

[7] Which, while we note a very significant proportion of the costs reported by Boehler et al (2011), were judged to constitute an additional intervention and hence excluded from costing in this analysis. Any training costs judged to be needed would need to be added, along with any potential changes to effectiveness.

[8] This is a population average cost, where non-completers are accounted for. The population average for consultation time per patient is 4 minutes. For completers only (16%), the mean cost is 53.22 with an average consultation time of 28 minutes.

Stroke 1st event	£10,471
post stroke 1st event	£2,300
Diabetes	£935

2.2 Results

2.2.1 Impact of brief advice on activity levels, and associated health states

Table 10 shows that considering a cohort of 100,000 brief advice compared with usual care, led to; 6,994 additional people becoming active (at the end of year one) at a total cost of £950,000, to the NHS (i.e.£136 per additionally active person). In addition, brief advice averted 2.4 CHD, 1.8 stroke, and 3.1 diabetes events, as well as 1 death in 10 years.

Table 10: Impact of brief advice vs. usual care

	Brief advice	Usual care	Difference
Cost* of intervention per person in cohort	£9.50	£0	£9.50
Number of 'active' people (at year 1)	26,438	19,444	6,994
Number of CHD events (in 10 years)	334.1.	336.5	-2.4
Number of stroke events (in 10 years)	178.8	180.6	-1.8
Number of diabetes events (in 10 years)	123.3	126.4	-3.1
Number of deaths (in 10 years)	987.7	988.4	-1

*In 2010/11 prices

2.2.2 Estimating the cost effectiveness of brief advice

Table 11 shows the estimated incremental cost effectiveness ratio (ICER) of the base-case analysis using a cohort of 100,000 individuals and a lifetime horizon. The incremental cost-effectiveness ratio was calculated with respect to the standard comparator 'usual care'. Compared with usual care, brief advice is more expensive as it incurs additional costs of £806,809 but it is also more effective leading to 466 QALYs gained in the total cohort, which equates to a QALY gain of 0.0047 per person. The incremental cost per QALY of brief advice compared with usual care is £1,730 and thus can be considered cost-effective at the NICE threshold of £20,000. Adopting this threshold results in brief advice generating a net benefit – that is the value of the health gains measured in monetary terms exceeds the cost of the intervention.

Table 11: Base-case incremental cost per QALY comparing brief advice with usual care (cohort of 100,000 individuals)

	Brief advice	Usual care	Difference	Incremental

				cost per QALY (ICER)
Lifetime total healthcare costs[a]	£155,004,599	£154,197,790	£806,809	£1,730
Total QALYs	1,827,971	1,827,505	466	

[a] In 2010/11 prices
*The numbers on this table have been rounded

2.2.3 Deterministic sensitivity analysis

Table 12 shows the impact of the varying parameter estimates in the one-way sensitivity analyses on the cost-effectiveness of brief advice. Assuming less effective or more effective brief advice resulted in an ICER below the threshold values for accepting cost-effectiveness. For example, when brief advice was assumed to be 32% (i.e. RR reduced from 1.42 to 1.10) less effective than the base case, the resultant ICER was still only around £8000.

Most changes in assumptions resulted in the ICER falling well below the £20,000 threshold value, indeed most fell at or below £12,000/QALY gained. If brief advice were delivered by healthcare assistants, or recruitment to brief advice undertaken via disease register, brief advice would still be cost-effective. Regardless of the health professional delivering brief advice, if the duration of brief advice was 5 minutes at minimum or 20 minutes at maximum, brief advice would still be cost-effective. In one case, assuming protective effects of physical activity (adjusted for potential decay rates) persist over lifetime, led to both lower costs and higher benefits and therefore brief advice dominating usual care. Similarly, using a start-up age of 54 years (and beyond) for the cohort resulted in brief advice dominating usual care.

The ICER was sensitive to the inclusion mental health gains associated with physical activity. The longer the length and the higher the value of gain, the lower the ICER is. However, moving from 0.072 to 0.01 still resulted in an ICER of less than £9,000/QALY. Excluding any short-term mental health gains from exercise itself led to an ICER of £27,000/QALY gained.

Table 12: Impact of changing assumptions (through one-way sensitivity analyses) on incremental cost effectiveness ratios of brief advice compared with usual care

Parameter	Incremental cost (£)	Incremental effect (QALY)	ICER (£)
Base case assumptions	£806,809	466	£1,730
Effectiveness estimate (Campbell et al 2012)[9]			
1.10	£914,869	115	£7,960
1.20	£880,294	227	£3,871
1.26	£859,905	294	£2,928
1.30	£846,458	337	£2,508
1.50	£780,942	551	£1,418
1.71	£715,133	765	£935
1.75	£702,933	804	£874
2.00	£629,029	1045	£602
2.2	£572,715	1228	£466
RR for developing disease conditions (Hu et al 2003, 2005, 2007)			
Protective effects persist over lifetime =applying the same RR used for the 10 years for the rest of the years	-£420,700	731	dominant
Protective effects persist just for a year = apply RR to first year(rather than 10 years) and the remaining years take RR =1	£942,129	439	£2147
Start-up age for the cohort			
50 years	£243,117	583	£417
53 years	£60,458	629	£96
54 years	-£2,153	644	dominant
60 years	-£257,983	681	dominant
Discount rate at 1.5% for both QALYs and costs (NICE 2009)	£747.345	491	£1,522
Cost of intervention (Boehler et al 2011)			
Recruitment to brief advice via disease register (i.e. cost of intervention increases from £9.50 to £57.45 per person)	£5,602,005	466	£12,010
Brief advice delivered by	£743,831	466	£1,595

[9] Percentage variations were suggested by NICE team

Parameter	Incremental cost (£)	Incremental effect (QALY)	ICER (£)
health care assistants (i.e. cost of intervention reduces from £9.50 to £8.03 per person)			
Brief advice lasting 5 mins and delivered by nurse (i.e. cost of intervention reduces from £9.50 to £3.58 per person)*	£214,609	466	£406
Brief advice lasting 20 mins and delivered by GP (i.e. cost of intervention increases from £9.50 to £51 per person)*	£4,956,609	466	£10,627
Mental health gain (Anokye et al 2012)			
If mental health gain was reduced from 0.072 to:			
0.06	£806,809	394	£2,050
0.04	£806,809	272	£2,966
0.02	£806,809	150	£5,363
0.01	£806,809	90	£8,997
0	£806,809	20	£27,913
If mental health gain persisted for:			
2 years (an additional year to base case)	£806,809	889	£908
5 years (4 additional years to base case)	£806,809	2,070	£390

*Data was based on Personal Social Services Research Unit (2011)

2.2.4 Probabilistic sensitivity analysis

Probabilistic sensitivity analysis, based on 10,000 simulations, was also conducted. A summary of the distributions adopted in the probabilistic analysis is presented in Appendix 3.

A scatter plot of the probabilistic findings, showing simulated estimates of cost difference against QALY difference between brief advice and usual care, is provided in Figure 3. The scatter plot shows that the majority of simulations generated improved effectiveness of brief advice but also at higher costs than usual care (i.e. points in the north-east quadrant of the cost effectiveness plane). In addition, a large proportion of the points lies below the £30,000 threshold (as indicated by the radiate).

The decision of whether these findings can be considered cost-effective depends on the maximum amount decision makers are willing to spend to obtain an additional unit of

effectiveness (in this case, a QALY). This can be presented in the form of a cost effectiveness acceptability curve, as shown in Figure 4. At a threshold of £2000 there is a 0.520 probability that brief advice is cost effective. This increases to 0.907 when a threshold of £5,000 is considered and the probability further rises to 0.9987 and 0.9997 when thresholds of £20,000 and £30,000 are considered respectively.

Figure 3: Cost-effectiveness plane showing the scatter plot of 10,000 Monte Carlo simulations for brief advice compared with usual care (expressed using a cohort of 100,000 individuals). Radiate represents a threshold of £30,000 per QALY

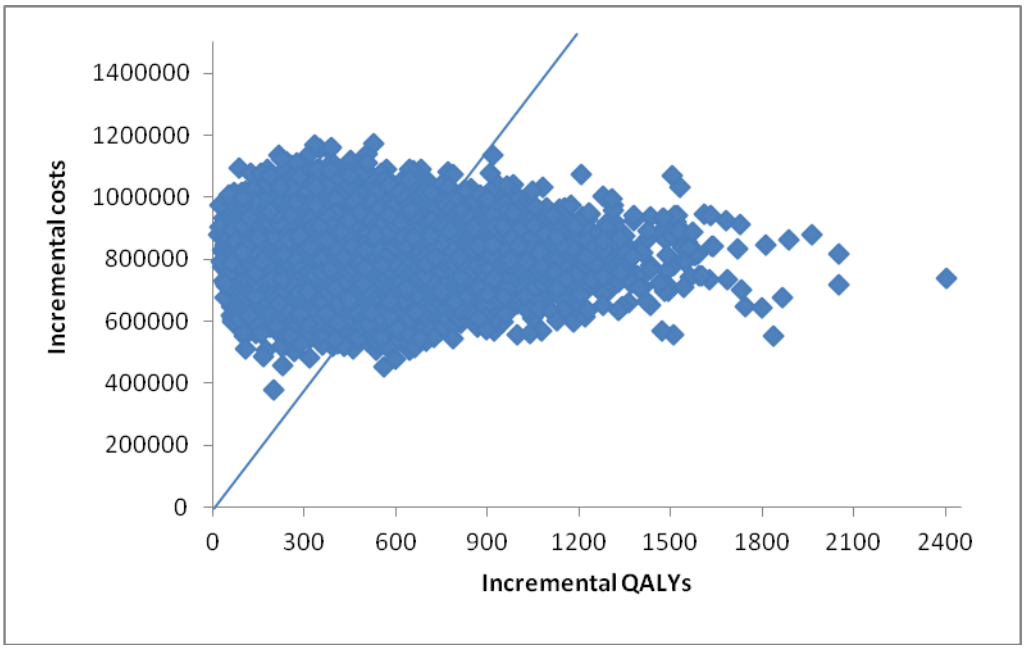
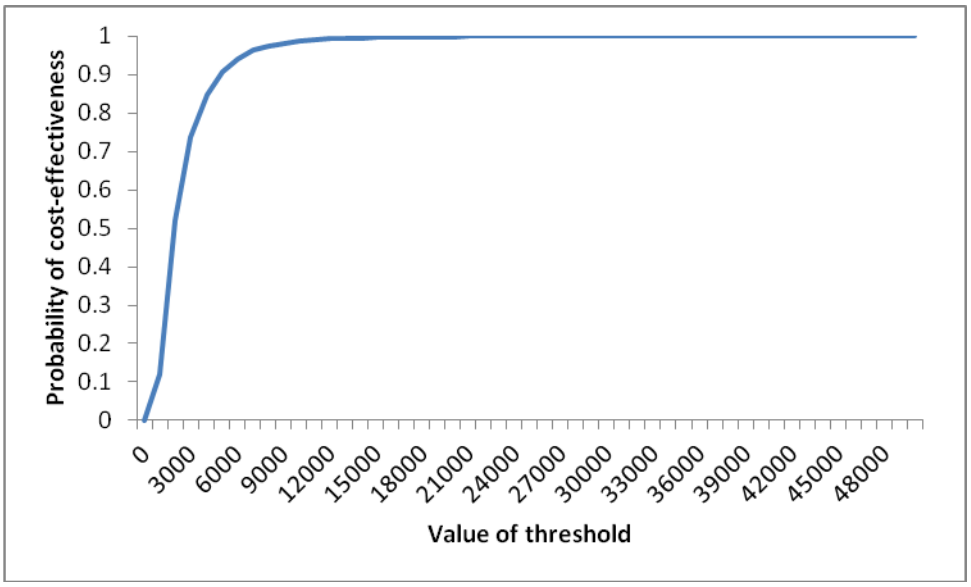


Figure 4: Cost-effectiveness acceptability curve showing the probability of cost-effectiveness for brief advice at varying levels of threshold



3 Cost consequence analysis

The cost consequence analysis (CCA) of brief advice was developed to acknowledge that the impacts of brief advice and physical activity might not be limited to the health states considered in the model. In addition, CCA tend to provide greater granularity than CUA in reporting the outcomes of public health interventions and can have greater resonance with commissioners (Trueman and Anokye 2012).

3.1 Methods

This analysis was conducted from an NHS provider and participants' perspective in 2010 prices for a cohort of 100,000 individuals. The intervention and its cost remained unchanged from the cost utility analysis. However, a broader range of benefits and disbenefits associated with brief advice and physical activity more generally were included.

Wherever possible, attempts were made to quantify the effects of brief advice for each outcome considered. Where quantification was possible, outcomes are expressed as the number of events per specified population. Nonetheless, in many cases it was only possible to indicate the direction rather than the magnitude of effect achieved through increased physical activity. Therefore disaggregated outcomes are presented.

The sources of data for the CCA were three-fold: (a) the disaggregated components of the cost utility model, (b) the additional outcomes reported in the papers selected for the meta-analysis by Campbell et al (2012) and used in the modelling, and (c) literature search conducted for a similar purpose undertaken as part of the economic evaluation of ERS (Pavey et al 2011).

Table 13 shows the inputs used for the cost consequence analysis and their sources of data.

Table 13: Inputs for cost consequence analysis

Measures in analysis	Data source	Methodology of study*
Costs		
Intervention cost to providers	Cost utility analysis	-
Benefits		
Physically active state	Cost utility analysis	-
Healthy state	Cost utility analysis	-
Deaths	Cost utility analysis	-
Mental health		
Anxiety	Conn (2010)	A meta-analysis that used data synthesized across 3,289 adult participants (mean age ranged from 21 to 71 years) from 15 studies based on interventions designed to increase physical activity delivered to healthy adults without anxiety disorders.
Depression	Craft and Pernia (2004)	A meta-analysis that converted the overall effect sizes of 3 meta-analyses (that included 37 studies investigating the effect of physical activity on depression) to a binomial effect size.
Metabolic		
Diabetes	Boule et al (2001); Cost utility analysis	A meta analysis of 14 controlled studies (11 RCT; findings did not differ according to study design) with synthesised data from 504 diabetes type II mellitus patients with mean age of 55.0 (7.2) years. 50% of participants were women. Studies, which examined the impact of physical activity on diabetes, covered different ethnicities (Northern Europeans, Southern Europeans, blacks, Asian, Middle-Easterners), age groups and medication status (no medication, oral hypoglycaemic agents, insulin therapy).
Cancer		
Colon Cancer	Lee (2003)	A narrative systematic review using data sourced from 50 published epidemiologic studies that had investigated the relationship between physical activity and the risk of developing cancer. Studies were conducted in North America, Europe,

Measures in analysis	Data source	Methodology of study*
		Asia, Australia, and New Zealand.
Breast cancer	Lee (2003)	See earlier
Lung cancer	Lee (2003)	See earlier
Cardiovascular		
Hypertension	Whelton et al (2002)	A meta-analysis of 54 RCTs (covering 2419 participants) that examined the impact of physical activity on hypertension. Studies were mainly Europe based. Sample covered both hypertensives and normatensives, diverse ethnic groups, and had mean age between 21 to 79 years
CHD	Taylor et al (2004); Cost utility analysis	A meta-analysis of 48 trials (covering 8940 participants who had CHD) that had observed the impact of physical activity on CHD. Mean age of participants were 48-71 years. Studies originated from Europe, North American, Asia/Australia.
Stroke	Cost utility analysis	-
Musculoskeletal		
Osteoporosis	Moayyeri (2008)	A meta-analysis of 13 prospective cohort studies showing association between physical activity and hip fracture is presented. The cohort was aged between 40 and 93 years
Osteoarthritis	Roddy et al (2005)	A systematic review of 13 RCTs showing the impact of physical activity on pain and disability among patients with knee osteoarthritis. Patients in the aerobic walking trials had mean age of 62 and 74 years.
Low back pain	Hayden et al (2005)	A meta-analysis of 61 randomized controlled trials (6390 participants) evaluating exercise therapy for adult nonspecific low back pain. Mean age of participants was 41 years.
Rheumatoid arthritis	Baillet et al (2010)	A meta analysis of 14 RCTs (including 1,040 patients). Patients were between 44-68 years. Age, disease duration, sex ratio, proportion of completers was same among the two groups. Studies originated from

Measures in analysis	Data source	Methodology of study*
		Europe, US, Canada.
Falls prevention	Chang et al (2004)	A meta analysis of 13 RCT's of participants who were 60 years and over.
Absenteeism at work	Conn et al(2009)	A meta analysis of worksite physical activity interventions with 38231 participants (138 reports).
Disbenefits		
Injury	Hootman et al (2001)	A study that investigated the relationship between physical activity and musculoskeletal injury using longitudinal data for 20 plus year olds.
Disability	Lamb et al (2000)	A cross sectional analysis of 769 older women (mean age 77.8, range 65–101) with physical disability, but no severe cognitive impairment.

Excluding the three health outcomes already considered in the cost utility analysis, our data sources identified evidence of an association between physical activity and improved outcomes in musculoskeletal disease, cancers and mental health. Non-health benefits and disbenefits were also identified. Relatively few disbenefits were, however, identified.

3.2 Results

The results are presented as incremental costs and outcomes attributable to brief advice/higher physical activity participation (compared with usual care/lower physical activity participation).

Delivering brief advice to a cohort of 100,000 will cost the NHS £950,000 (in 2010/11 prices). Compared with usual care, brief advice could result in an additional 6,994 people becoming physically active at year 1. In 10 years, brief advice could avert 2.4 events of CHD, 1.8 events of stroke, 3.1 events of diabetes and preventing 1 death. As a result there is a gain of 442 QALYs over 10 years. Of these QALY gains, 437 were attributable to mental health improvements. Other potential mental health gain as a result of improved physical activity is a 67-74% reduction in depressive symptoms (Table 14).

Table 14 shows that brief advice could also impact positively on the prevention or/and management of health conditions including metabolic disease, cancer and muscoskeletal ailments. Potential non-health benefits comprise improvements in productivity via reduction in absenteeism at work. Whilst considered infrequent the potential adverse effects associated with brief advice include injuries and pain which (Isaacs et al 2007; Munro et al 1997).

Table 14: Potential impacts of brief advice

Measures	Potential impact of brief advice on measures
Benefits	
Mental health	
Anxiety	Reduced anxiety in participants with the magnitude of the effect size being 0.219.
Depression	Increased the success rate to 67–74% reduction in depressive symptoms.
Metabolic	
Diabetes	• Led to small but significant reduction in glycoslated haemoglobin (0.7%). This amount is likely to reduce diabetes complications.
Cancer	
Colon Cancer	A 30–40% reduction in the risk of developing colon cancer.
Breast cancer	A 20–30% reduction in the risk of developing breast cancer.
Lung cancer	A 20% reduction in the risk of developing lung cancer.
Cardiovascular	
Hypertension	• Decreased systolic blood pressure by 3.8mm Hg and diastolic blood pressure by 2.6mm Hg in sample of both hypertensives and normatensives. • In hypertensives, systolic blood pressure was reduced by 4.94mm Hg and diastolic blood pressure by 3.73mm Hg. • In normatensives, systolic blood pressure was reduced by 4.04mm Hg and diastolic blood pressure by 2.33mm Hg.

CHD	• Reduced all-cause mortality (odds ratio [OR] 0.80; 95% confidence interval [CI]: 0.68 to 0.93) and cardiac mortality (OR 0.74; 95% CI: 0.61 to 0.96).
Musculoskeletal	
Osteoporosis	A hip fracture risk reduction of 45% (95% CI, 31-56%) and 38% (95% CI, 31-44%), respectively, among men and women.
Osteoarthritis	• Pooled effect sizes for pain were between 0.39 and 0.52. • For self reported disability, pooled effect sizes ranged from 0.32 and 0.46 •
Low back pain	Pooled mean improvement (measured on a scale of 100 points) was 7.3 points (95% CI, 3.7 to 10.9 points) for pain and 2.5 points (CI, 1.0 to 3.9 points) for function.
Rheumatoid arthritis	Improved function by 0.24 (measured via HAQ score) and pain by 0.31 (measured via HAQ score).
Falls prevention	Beneficial effect on the risk of falls (adjusted risk ratio 0.86, 0.75 to 0.99)
Absenteeism at work	Lower absenteeism at work (effect size=0.19)
Adverse effects	
Injury	Increased the risk of muscoskeletal injury by about 4 times
Disability	Walking (more than 3 city blocks) increased the risk of walking disability because of severe pain (OR=4.1 to 5.0)

4 Discussion

This study evaluates the cost-effectiveness of brief advice using cost utility and cost consequence analyses. The base case cost utility analysis resulted in a cost-effectiveness ratio of £1,730 per QALY gained from brief advice compared with usual care. This is significantly below the cost effectiveness threshold for England which ranges from £20,000 to £30,000 per QALY. The lifetime QALY gain per person as a result of brief advice is estimated at approximately 0.005. If each QALY gain is valued at £20,000 then brief advice could generate benefits that in monetary terms is about £93 pounds per person which exceeds the cost of the intervention (£9.50 per person).

The base case results were robust to both probabilistic and deterministic sensitivity analysis with the latter showing that at £20,000, there is a 99.9% chance that brief advice will be cost effective. The ICERs were, however, sensitive to the duration of protective effects of the reduced risks for developing disease as a result of being active. In addition, the cost-effectiveness of brief advice appears to improve when mental health gains from physical activity are increased and vice versa. In fact, when no mental health gains are added, brief advice is cost effective just below the £30,000 threshold, with an ICER equivalent to £27,913. Changes in infrastructure specifically around how patients are recruited to brief advice led to significant changes in the ICER. If recruitment to brief advice was changed from the opportunistic centres (base case) to disease register, the ICER increased from £1,730 to £12,010. Notably, given the lack of adequate effectiveness data around infrastructure, this analysis considered only cost of intervention and if the intervention were more effective at generating change then the ICER would be lower. Increases in start-up age of the cohort resulted in brief advice becoming more cost-effective. However, it must be acknowledged that lack of data precluded the adjustment of age-specific data for the cost and effectiveness of the intervention. Therefore this finding might be driven by base-case assumptions around the protective effects of physical activity, which mean that the older the age of the cohort the larger the proportion of years that the protective effects were spread over and hence the higher the benefits of physical activity.

The findings of the cost consequences analysis further confirm the potential cost-effectiveness of brief advice, showing that delivering brief advice to a cohort of 100,000 will cost the NHS £950,000 (in 2010/11 prices). The potential benefits of such an investment includes an additional 6,994 people becoming physically active at year 1; and averting 2.4 events of CHD, 1.8 events of stroke, 3.1 events of diabetes, as well as 1 death at 10 years.

The findings raise sets of issues about data and modelling, which are discussed in turn. The effectiveness estimate was derived from a meta-analysis that had substantial heterogeneity (Campbell et al 2012) and hence presents difficulties in drawing overall conclusions. However, the consequences of this heterogeneity might be reduced as the meta- analysis used a random effects model that allows study outcomes to vary (Higgins 2008).

It could be argued that the relative risk estimates for developing the disease conditions overestimate the benefits of physical activity, particularly for active individuals who were at the lower end of the threshold for being physical active. This is because 'active state' was defined as a minimum of 4 hours of moderate intensity activity per week (instead of the standard definition of 2.5 hours per week) in the epidemiology studies that produced those estimates. However, findings from HSE 2008 suggest that on the average, 'active individuals' (as per the standard definition) stated they undertake 6 hours (SD 4.9) of physical activity per week.

Given the sensitivity of the ICER to inclusion and size of mental health outcomes, it is important to consider the limitations of the supporting evidence (i.e. Anokye et al 2012). First, the analysis used cross-sectional data and though the findings point to a correlation between gain in health related quality of life and physical activity a causal relationship cannot be claimed. This is not to suggest that there is no mental health gain from physical activity as evidence, though scarce, exists (Conn 2010, Craft and Pernia 2004). The concern though is whether the utility gain from Anokye et al (2012) is attributable to mental health as physical activity is associated with both longer term effects via reduced risk for ill-health conditions, and shorter term mental health benefits (i.e. mental simulation during exercise, improved social interactions resulting from group participation, or improved self-esteem) (Penedo and Dahn 2005). However, as ill-health conditions associated with physical activity were adjusted for in the analysis[10], coupled with the cross-sectional nature of the data used, the utility gain might be said to more closely approximate mental health benefits (Anokye et al 2012). In addition, deterministic sensitivity analysis on the magnitude and duration of the mental health gains showed brief advice to be cost-effective given a threshold value of £30,000/QALY regardless of assumptions about short term mental health benefits.

[10] Self-reported data on having ill-health conditions including CHD, stoke and diabetes were included as control variables in the regression model.

The fatality cases associated with disease conditions were not allowed to differ among active and inactive people due to lack of data although such variation might exist. This potentially underestimates the cost effectiveness of brief advice.

The second set of issues around modelling includes assumptions made. First, the model examined only the long-term impact of physical activity on selected morbidities. It did not include other morbidities which may be affected by physical activity due to lack of robust evidence over the relationship between physical activity, incidence and quality adjusted life expectancy. This might underestimate the cost effectiveness of brief advice in ways indicated by the cost consequence analysis. Another reason for the ICERs to be underestimated are because secondary transitions between the disease conditions were not allowed and this may reduce the negative effects of physical inactivity.

Some impacts identified in the cost consequence analysis were negative (e.g. injuries) and their exclusion from the CUA implies estimates could be overestimated.
Whilst risk of injury may affect delivery of brief advice or take-up of physical activity, particularly in the elderly, the evidence on injuries suggests that they are rare (Munro et al. 2004) and not expected to significantly affect results when considered at a population level. Nonetheless, observing few injuries does not necessarily mean that differences are rare as studies may not have been sufficient powered to detect these differences.

Finally, this model only presents evidence on the cost-effectiveness of brief advice compared with usual care. It excludes all other interventions designed to increase physical activity interventions. Other interventions may even dominate brief advice and, if the population profiles accessing brief advice and these other interventions were identical, it would suggest the information here is not sufficient for making decisions around resource allocation. This possibility was suggested in the last report providing inputs to public health guidance in this area (Matrix, 2006) as it found that although brief advice (compared with usual care) was cost-effective, it was dominated by exercise prescription intervention. However, no evidence was provided on the populations accessing the different types of intervention.

Comparison of our findings with previous research

The existing limited literature on the cost effectiveness of brief advice suggests that it is cost effective at £20,000/QALY. Although Pringle (2011) did not report an ICER for brief advice per se, results of a similar intervention (motivational interviews) shows that the cost per

completer improving moderate physical activity is between £2,659 and £2,789 and the cost per QALY was £47 to £229 with NHS cost savings per completer between £3,036 to £3,286. In Boëhler et al (2011), an incremental cost of £886.50 to increase self reported physical activity levels to 150 minutes of moderate intensity activity per week (3 months post intervention) was observed when disease register screening was compared with opportunistic patient recruitment. Matrix (2006) found that brief advice compared with usual care leads to a cost per QALY of £159 for stage based advice by a GP during consultation; and £425 for stage based advice plus a booklet (mailed 2 weeks after). The differences between outcomes used in Pringle et al (2011) & Boëhler et al (2011) and ours makes, combined with the paucity of information on the effectiveness of moving from opportunistic to disease register screening, make it difficult to compare the two sets of results with the findings in this report. Therefore the remainder of this section focuses on Matrix (2006) which used cost per QALY and was the basis for the first set of NICE guidance in this area.

Although this study and the analysis undertaken by Matrix (2006) both suggest brief advice is highly cost effective, Matrix (2006) estimated a much lower cost per QALY. The difference in results might be explained by a number of reasons. First, the approach to accounting for changes in physical activity was more conservative in our model; Matrix (2006) assumed that once people become active, the active state 'is maintained long enough to obtain the health benefits of that physical activity level' but allows for a one-off '50% drop off' in the number of people who enter the active state *only* at the beginning. Our analysis, however, not only accounted for changes in physical activity levels (potentially decay rates) throughout the lifetime of people but also had a relatively more conservative assumption around decay rates (i.e. 100%) for majority of the lifetime of active individuals. After having accounted for potential changes in physical activity levels at year 1 (via effectiveness estimate that followed people for 12 months), we also reflected subsequent changes in physical activity at the initial 10 years of the model (via RR estimates for developing disease conditions that are adjusted for variations in physical activity). In addition, from year 11 for the remaining life years, 79% of their lifetime, active individuals at year 1 were assumed to be inactive. To test the 'validity' of this argument, we replicated the broad findings of the Matrix model by abandoning the assumption of 100% decay rate although still adjusting for changes in physical activity through use of the adjusted RR estimates.

Secondly, Matrix(2006) included different disease states; a) they included colon cancer as an additional disease condition in addition to CHD, stroke and diabetes and hence their

analysis were likely to reflect more benefits of brief advice through impacts on disease conditions; b) we included short term mental health gains, which was not included by in their analysis. We were able to test the exclusion of mental health gain in our model and produced relatively consistent findings with Matrix (2006) in that brief advice was cost-effective than usual care. However, even with mental health benefits included, their analysis potentially had wider coverage of health benefits because mental health gain is captured in our model as a one-off benefit whereas Matrix (2006) captured lifetime benefits of reducing colon cancer. Nevertheless, one caveat to this last argument is that the impact of physical activity on both conditions is not significantly different.

We have based our approach to modelling the cost effectiveness on an adapted version of Matrix (2006) model. However, this model offers a number of improvements including; (a) time-based modelling (b) more extensive exploration of uncertainty around the ICERs, (c) more conservative assumptions around changes in physical activity overtime, and (d) use of meta-analysed effectiveness data. Nevertheless, the limitations of this analysis point to the need both for new data and for more accurate evidence on factors contributing to the cost effectiveness of brief advice to increase physical activity.

Recommendations for further research

1. Compare the cost effectiveness of brief advice with other interventions designed to increase physical activity interventions (e.g. exercise referral schemes, pedometer programmes)
2. Explore the nature of mental health gains (size and duration) from physical activity participation, and when and how they can be measured. Their relationship to quality of life gains for inclusion in economic evaluation is important to account for in this research.
3. Good quality evidence on the impact of physical activity interventions over time.
4. Greater quantity of better quality evidence on effectiveness of physical activity interventions, ideally with a broader range of head to head comparisons.
5. Development of a population model that accounts for a range of patient (and potential provider) characteristics and is able to consider, more directly, information from infrastructure based interventions that influence access to services.

References

Anokye N, Jones T, Fox-Rushby J. *National Institute for Health and Clinical Excellence Public Health Intervention Guidance physical activity: brief advice for adults in primary care: component 2 economic analysis. Review of economic evidence*. 2012. London: NICE

Anokye NK, Trueman P, Green C, Pavey TG, Taylor RS. Physical activity and health related quality of life. *BMC Public Health.* 2012 Aug 7;12(1):624. [Epub ahead of print]

Anokye, NK., Trueman, P., Green, C., Pavey, TG., Hillsdon, M. and Taylor, RS., The cost-effectiveness of exercise referral schemes, *BMC Public He*alth 2011 **11**:954 doi:10.1186/1471-2458-11-954

Baillet A, Zeboulon N, Gossec L, Combescure C, Bodin LA, Juvin R, et al. Efficacy of cardiorespiratory aerobic exercise in rheumatoid arthritis: meta-analysis of randomized controlled trials. *Arthritis Care.Res.(Hoboken*) 2010 Jul;62(7):984-992.

Beale S, Bending M, Trueman P. *An economic analysis of environmental interventions that promote physical activity.* York: University of York, York Health Economics Consortium, 2007.

Boehler CEH, Milton KE, Bull FC, Fox-Rushby J. The cost of changing physical activity behaviour: evidence from a "physical activity pathway" in the primary care setting. *BMC Public Health* 2011, 11:370. doi:10.1186/1471-2458-11-370

Boule NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. *JAMA* 2001 Sep 12;286(10):1218-1227.

Briggs A, Sculpher M, Claxton K: *Decision Modelling for Health Economic Evaluation*. New York: Oxford University Press Inc.; 2006.

Brønnum-Hansen H, Davidsen M, Thorvaldsen P. Long-Term survival and causes of death after stroke. *Stroke.* 2001**;** 32: 2131-2136 doi: 10.1161/hs0901.094253

Campbell F, Blank L, Messina J et al. *National Institute for Health and Clinical Excellence Public Health Intervention Guidance physical activity: brief advice for adults in primary care*. *Review of effectiveness evidence*. 2012. London: NICE

Chang JT, Morton SC, Rubenstein LZ, Mojica WA, Maglione M, Suttorp MJ, et al. Interventions for the prevention of falls in older adults: systematic review and meta-analysis of randomised clinical trials. *BMJ 2004* Mar 20;328(7441):680

Chilcott J, Tappenden P, Rawdin A, Johnson M, Kaltenthaler E, Papaioannou D, Shippam A. Avoiding and identifying errors in health technology assessment models: qualitative study and methodological review. *Health Technology Assessment* 2010., 14(25)**:**1-107

Conn VS. Anxiety outcomes after physical activity interventions: meta-analysis findings. *Nurs.Res*. 2010 May-Jun;59(3):224-231.

Conn VS, Hafdahl AR, Cooper PS, Brown LM, Lusk SL. Meta-analysis of workplace physical activity interventions. *Am.J.Prev.Med*. 2009 Oct;37(4):330-339.

Craft LL, Perna FM. The benefits of exercise for the clinically depressed. prim.care.companion *J.Clin.Psychiatry*. 2004;6(3):104-111.

Department of Health. *Let's Get Moving: Commissioning guidance*. *A new physical activity care pathway for the NHS*. London: Department of Health physical activity care pathway" by Paul Stonebrook, 2009a.

Department of Health. *Healthy lives, healthy people: our strategy for public health in England*. London: Department of Health, 2010.

Department of Health. *Improving outcomes: a strategy for cancer*. London: Department of Health, 2011a.

Department of Health *Start active, stay active: a report on physical activity from the four home counties*' Chief Medical Officers [online], 2011b. Available from www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh128210.pdf

Department of Health. *The public health responsibility deal* [online]. 2011c. Available from www.dh.gov.uk/en/Publichealth/Publichealthresponsibilitydeal/index.htm

Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL: *Methods for the Economic Evaluation of Health Care Programmes*. 3rd edition. Oxford: Oxford University Press; 2005.

Gonzalez ELM, Johansson S, Wallander MA, Rodriguez LAG. Trends in the prevalence and incidence of diabetes in the UK: 1996–2005. *J Epidemiol Community Health* 2009;63:332–336. doi:10.1136/jech.2008.080382

Higgins JPT. Commentary: Heterogeneity in meta-analysis should be expected and appropriately quantified. *Int. J. Epidemiol.* 2008; 37 (5): 1158-1160. doi: 10.1093/ije/dyn204

Hu G, Qiao Q, Silventoinen K, Eriksson JG, Jousilahti P, Lindstrom J et al,

Occupational, commuting, and leisure-time physical activity in relation to risk for Type 2 diabetes in middle-aged Finnish men and women *Diabetologia* 2003; 46:322–329

Hu G, Sarti C, Jousilahti P, Silventoinen K, Barengo NC, Jaakko Tuomilehto Leisure Time, Occupational, and Commuting Physical Activity and the Risk of Stroke*. Stroke.* 2005; 36:1994-1999.

Hu G, Jousilahti P, Borodulin K, Barengo NC, Lakka TA, Nissinen A et al.

Occupational, commuting and leisure-time physical activity in relation to coronary heart disease among middle-aged Finnish men and women. *Atherosclerosis* 2007; 194: 490–497

Isaacs AJ, Critchley JA, Tai SS et al. Exercise Evaluation Randomised Trial (EXERT): a randomised trial comparing GP referral for leisure centre-based exercise, community-based walking and advice only. *Health Technol Assess* 2007;11(10):1–184.

Jamrozik K. Estimate of deaths attributable to passive smoking among UK adults: database analysis. *BMJ*. 2005 Apr 9;330(7495):812.

Joint Health Surveys Unit of Social and Community Planning Research and University College London. *Health Survey for England* 2008; SN: 5809.

Lamb SE, Guralnik JM, Buchner DM, Ferrucci LM, Hochberg MC, Simonsick EM, et al. Factors that modify the association between knee pain and mobility limitation in older women: the Women's Health and Aging Study. *Ann.Rheum.Dis.* 2000 May;59(5):331-337.

Lee IM. Physical activity and cancer prevention--data from epidemiologic studies. *Med.Sci.Sports Exerc*. 2003 Nov;35(11):1823-1827.

Matrix. *Rapid review of the economic evidence of physical activity interventions*. 2006b . Available at http://www.matrixknowledge.com/wpcontent/uploads/physical_activity_economic_review_april20061.pdf

Matrix . *Modelling the cost-effectiveness of physical activity interventions*. 2006b Available at http://www.matrixknowledge.com/wpcontent/uploads/physical_activity_economic_modelling_report_april20061.pdf

Moayyeri A. The association between physical activity and osteoporotic fractures: a review of the evidence and implications for future research. *Ann.Epidemiol*. 2008 Nov;18(11):827-835.

Munro J, Brazier J, Davey R et al. Physical activity for the over-65s: could it be a cost-effective exercise for the NHS? *J Public Health Med* 1997;19(4):397–402.

National Clinical Guideline Centre. *Hypertension: the clinical management of primary hypertension in adults. Clinical guideline: methods, evidence and recommendations*. Commissioned by National Institute for Health and Clinical Excellence. 2011

NICE. *Four commonly used methods to increase physical activity: brief interventions in primary care, exercise referral schemes, pedometers and community-based walking and cycling Public Health Guidance No 2*: 2006. Available at http://www.nice.org.uk/nicemedia/pdf/PH002_physical_activity.pdf

NICE. *Public Health Guidance Draft Scope 1: Physical activity: brief advice for adults in primary care.* 2011. Available at http://www.nice.org.uk/nicemedia/live/13443/56937/56937.pdf

NICE. *Methods for the development of NICE public health guidance (second edition).* 2009. Available at http://www.nice.org.uk/media/2FB/53/PHMethodsManual110509.pdf

Pavey T, Anokye N, Taylor A et al. The effectiveness and cost effectiveness of exercise referral schemes: a systematic review and economic evaluation. *Health Technol Assess* 2011;15(44):1–254.

Penedo FJ, Dahn JR: Exercise and well-being: a review of mental and physical health benefits associated with physical activity. *Curr Opin Psychiatry* 2005, 18(2):189–193.

Personal Social Services Research. *Unit costs of health & social care*. Kent: University of Kent. 2011

Philips Z, Ginnely L, Sculpher M, Claxton K, Golder S, Riemsa R, et al (2004). Review of guidelines for good practice in decision-analytic modelling in health technology assessment. *Health Technology Assessment* 8:36:1-172

Preis SR, Hwang SJ, Coady S, Pencina MJ, D'Agostino RB Sr, Savage PJ et al. Trends in all-cause and cardiovascular disease mortality among women and men with and without diabetes mellitus in the Framingham Heart Study, 1950 to 2005. *Circulation*. 2009 Apr 7;119(13):1728-35.

Pringle A, Marsh K, Gilson N, McKenna J, Cooke C Cost-effectiveness of interventions to improve moderate physical activity: A study in nine UK sites. *Health Education Journal* 2010; 69 (2) 211–224

Hayden JA, van Tulder MW, Malmivaara AV, Koes BW. Meta-analysis: exercise therapy for nonspecific low back pain. *Ann.Intern.Med*. 2005 May 3;142(9):765-775.

Hootman JM, Macera CA, Ainsworth BE, Martin M, Addy CL, Blair SN. Association among physical activity level, cardiorespiratory fitness, and risk of musculoskeletal injury. *Am.J.Epidemiol*. 2001 Aug 1;154(3):251-258.

Roddy E, Zhang W, Doherty M. Aerobic walking or strengthening exercise for osteoarthritis of the knee? A systematic review. *Ann.Rheum.Dis*. 2005 Apr;64(4):544-548.

Taylor RS, Brown A, Ebrahim S, Jolliffe J, Noorani H, Rees K, et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized controlled trials. *Am.J.Med*. 2004 May 15;116(10):682-692.

Ward S, Jones ML, Pandor A, Holmes M, Ara R, Ryan A et al**.** A systematic review and economic evaluation of statins for the prevention of coronary events. *Health Technology Assessment* 2007; Vol. 11: No. 14; 1-160

Ward S, Jones ML, Pandor A, Holmes M, Ara R, Ryan A et al. *Statins for the prevention of coronary events*. Technology assessment report commissioned by the HTA Programme on behalf of The National Institute for Clinical Excellence. 2005

Whelton SP, Chin A, Xin X, He J. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. *Ann.Intern.Med*. 2002 Apr 2;136(7):493-503.

Appendix 1: Overview of search for RR estimates

The documents presented in the Table 15 shows the guideline documents that were searched for relevant literature on epidemiological data on the disease conditions used in the model. The search for these documents, which was discussed and agreed with the NICE team, mainly covered reports suggested by the NICE team and our contact persons involved in physical activity policy development. To identify the relevant epidemiological literature, the evidence base informing the impact of physical activity spelt in these guideline documents was searched. The reference list of these guideline documents were screened for relevant literature. In addition, the references of the relevant primary studies were further screened.

Table 15: Guideline documents

Document	Which country's guideline is this relevant to?	Source
U.S. Department of Health and Human Services: Physical Activity Guidelines Advisory Committee Report. Washington, DC: U.S. Department of Health and Human Services 2008	US	NICE team
Department of Health: Start Active, Stay Active A report on physical activity for health from the four home countries' Chief Medical Officers. 2011: London: DH	UK	Sports England (contact person)
Warburton DE, Charlesworth S, Ivey A et al (2010) A systematic review of the evidence for Canada's Physical Activity Guidelines for Adults. International Journal of Behavioral Nutrition and Physical Activity 7: 39.	Canada	snowballing (via Stay active document)
O'Donovan G, Blazevich AJ, Boreham C et al (2010) The ABC of physical activity for health: a consensus statement from the British Association of Sport and Exercise Sciences. Journal of Sports Sciences 28(6): 573–591.	UK	snowballing (via Stay active document)
Department of Health: At least five a week: Evidence on the impact of physical activity and its relationship to health 2004: London: DH (this is superseded by second document on the list)	UK	NICE team

Table 16, Table 17 and Table 18 below describes the relevant literature reviewed. The review focussed on: (a) prospective cohort studies as they are likely to have accounted for the changes in physical activity given the longitudinal nature of their data (b) studies that used both female and male sample as the relative risk estimates for disease conditions tend to differ by gender.

CHD: 5 papers were identified. The sample used by the studies was aged 35 to 74 years. The follow up periods for data collection/analysis ranged from 5 to 16 years with most studies (n=4) considering >10 years. Based on 3 indicators (i.e. lengthy follow-up period; close match between physical activity indicator and meeting the recommended level; currency of evidence), two studies (Sattelmaeir et al 2011, Hu et al 2007) described below appear to be potential data source for the model. Hu et al (2007) was selected to ensure coherency in the model, as it has similar methods to the other potential sources for stroke and diabetes (forthcoming).

Stroke: 7 papers were identified. The sample used by the studies was aged 20 to 101 years. The follow up periods for data collection/analysis ranged from 5 to 40 years with most studies (n=5) considering >10 years. Using the same 3 indicators, Hu et al (2005) was selected as data source for the model.

Diabetes: 4 papers were identified. The sample used by the studies was mainly aged 35 to 65 plus years. The follow up periods for data collection/analysis ranged from 6 to 12 years with most studies (n=3) considering >10 years. Using the same indicators as previous, Hu et al (2003) was selected as data source for the model.

Table 16: Evidence on data for CHD

Author	Sample	Study type	Specification of PA (collected at baseline)	Specification of outcome	Control variables	Remarks
Sundquist et al (2005)	A national, Swedish, random sample of 2,551 women and 2,645 men, aged 35–74, was interviewed in 1988 and 1989 and followed until December 31, 2000.	11–12-year follow-up study. A Cox regression model was used to estimate the hazard ratio (HR) of CHD	Leisure-time physical activity was categorized into four groups, based on the response alternatives in the survey: (1) I get practically no exercise at all; (2) I exercise occasionally (e.g., 1-h walks, skiing a couple of times every year, swimming, picking mushrooms); (3) I exercise about once to twice a week (e.g., fast walks, skiing, swimming, jogging, cycling); (4) I exercise vigorously at least twice a week (e.g., skiing, swimming, running,	*CHD*: It was specified as CHD events-these were identified using a unique personal identification number to link the participants to the Swedish National Hospital Discharge Register and the Cause-of-Death Register. Participants were followed from date of interview to first hospitalization due to CHD, death from all causes, emigration, or end of study on December 31, 2000 (mean follow-up time of 11.7 years). Coronary heart disease (CHD): first hospitalization for nonfatal or fatal CHD event according to the International Classification of Diseases, ICD 9 (410–	gender, smoking, income, BMI	Follow-up period was 11-12 years and might not be long enough to constitute long -term It is not clear if the amount of exercise matches the meeting recommended level because duration was not provided

Author	Sample	Study type	Specification of PA (collected at baseline)	Specification of outcome	Control variables	Remarks
			cycling for quite a while, ball games).	414) and ICD 10 (I20–I25). Data were obtained from the Swedish National Hospital Discharge Register and the Cause-of-Death Register. Out-of-hospital deaths due to CHD were included in the analysis. Participants hospitalized for a CHD event during the interview year or 2 years preceding the interview year were excluded. We did not exclude participants with a CHD event earlier than 1986 because the In-Care Register only records complete information from 1986 onwards.		
Satellmaier et al 2011	9 studies that had quantitative estimates were included in the dose-response	This was an aggregate data meta-analysis of epidemiological studies investigating physical	150 min/wk of moderate-intensity leisure-time physical activity; 300 min/wk of moderate-intensity leisure-time physical activity; no	CHD: mortality, incidence,	The following factors were adjusted for the individual studies: Age, employment, marital status, perceived	n/a

Author	Sample	Study type	Specification of PA (collected at baseline)	Specification of outcome	Control variables	Remarks
	analysis. The average age range for the studies was 43 to 67 years.	activity and primary prevention of CHD. It included prospective cohort studies published in English since 1995. 33 studies were included 13 years follow –up (average across of 9 studies)	leisure-time physical activity;		health status, smoking, alcohol, saturated fats, diet and lifestyle factors, MI history, SBP, diabetes, cholesterol, disease at study entry, history of MI, history of CHD, income, job physical activity, sex. The meta-analysis adjusted for geography, CHD outcome (nonfatal, fatal, and combined)	
Schnoor et al 2006	2136 men and 2758 women aged 20–79 years at the first examination	5 year follow up	Physical activity was operationalised as: 1 was considered low physical activity, 2 was	CHD& Stroke: mortality Sourced from National Central Person Register and The Register of Causes of Death	smoking, total cholesterol, HDL-cholesterol, systolic blood pressure,	Adjustment of decay rate not relatively strong (in our context) considering the relatively short follow-up period, and the restriction of analysis with those whose

Author	Sample	Study type	Specification of PA (collected at baseline)	Specification of outcome	Control variables	Remarks
	, who attended both examinations, and did not change leisure-time physical activity level from the first to the second examination.		considered moderate physical activity and categories 3 and 4 were combined and considered as high physical activity in leisure time. We assumed that low, moderate, and high physical activity corresponded to <4, 4–6 and >6 metabolic equivalents, respectively.[11]		diabetes mellitus, alcohol consumption, body mass index, education, income and FEV1% predicted	exercise levels did not change during the course of the study. The effect of physical activity was not significant for stroke but for CHD RR are estimated for mortality and not morbidity
Wisloff et al 2006	>=20 years (mean age at entry was 47 years-men; 48 years women)	16 year follow up	Physical activity was operationalised as: (a)no activity (<1 per week) (b)1 per week =< 30 mins at low	Ischemic Heart Disease: mortality National Cause of Death Registry in Norway	Age, body mass index, marital status, education, alcohol consumption, smoking	RR are estimated for mortality and not morbidity

[11] Physical activity were defined as follows: (1) almost entirely sedentary (e.g. reading, watching television or movies, engaging in light physical activity such as walking or biking for less than 2 h per week); (2) light physical activity for 2–4 h per week; (3) light physical activity for more than 4 h per week or more vigorous activity for 2–4 h per week (e.g. brisk walking, fast biking, heavy gardening, sports that cause perspiration or exhaustion); and (4) highly vigorous physical activity for more than 4 h per week or regular heavy exercise or competitive sports several times per week.

Author	Sample	Study type	Specification of PA (collected at baseline)	Specification of outcome	Control variables	Remarks
	n=27143(men) n=28929(women)		intensity (c)1 per week >30 mins at high intensity (d)2-3 per week =< 30 mins at low intensity (e) 2-3 per week >30 mins at high intensity (f) >= 4 per week =< 30 mins at low intensity (e) >= 4 per week c>30 mins at high intensity		status, systolic blood pressure, diastolic blood pressure. n/B: estimates were presentation separately for men and women	
Haapanen et al 1997	35-63 year olds N=1340 men, n=1500 women	10 year follow up	An index representing weekly net energy expenditure from physical activity. This was operationalised as: <u>men</u> 0-1100 kcal /week 1101-1900 kcal/week >1900 kcal/week <u>Women</u>	Diabetes: incidence rates of non-fatal CHD obtained from self-administered questionnaire	Age, BMI, smoking, diabetes, hypertension	The PA specification can be converted (with adjustments) to the meeting recommended level via British Association of Sports Sciences consensus statement (O'Donovan et al 2010) that indicates that the recommended level is equivalent to 800-1200 kcal

Author	Sample	Study type	Specification of PA (collected at baseline)	Specification of outcome	Control variables	Remarks
			0-900 kcal/week 901-1500 kcal/week >1500 kcal/week			
Hu et al 2007	22,877 men and 24,963 women(25 to 64 years of age)	18.9 year follow up	Self-reported leisure-time physical activity was classified into three categories: (i) 'low' was defined as almost completely inactive, such as reading, watching TV, or doing some minor physical activity but not of moderate or high level; (ii) 'moderate' was doing some physical activity more than 4 h a week, such as walking, cycling, or light gardening, excluding travel to work; (iii) 'high' was performing vigorous physical activity more than 3 h a week, such	CHD: Combined non-fatal (myocardial infarction) and fatal (deaths due to CHD) cases were defined as CHD incidence in the analysis Sourced from Finnish Hospital Discharge Register for non-fatal outcomes (hospitalized myocardial infarctions) and the Finnish Causes of Death Register for fatal outcomes	age, sex, area, study year, body mass index, systolic blood pressure, cholesterol, education, smoking, alcohol consumption, diabetes, and other 2 types of physical activity	A mix of mortality and morbidity stroke events Considerable high follow-up years

Author	Sample	Study type	Specification of PA (collected at baseline)	Specification of outcome	Control variables	Remarks
			as running, jogging, swimming, or heavy gardening, or competitive sports several times a week. The subjects reported their occupational physical activity according to the following three categories: (i) 'low' was physically very easy, sitting office work, e.g. secretary; (ii) 'moderate' was work including standing and walking, e.g. store assistant, light industrial worker; (iii) 'high' was work including walking and lifting, or heavy manual labor, e.g. industrial or farm work.			

Author	Sample	Study type	Specification of PA (collected at baseline)	Specification of outcome	Control variables	Remarks
			Daily commuting return journey was categorized into three categories: (i) motorized transportation or no work (no walking or cycling); (ii) walking or bicycling 1–29 min/day; (iii) walking or bicycling more than 30 min/day.			

Table 17: Evidence on Stroke

Author	Sample	Study type	Specification of physical activity (at baseline)	Specification of outcome	Control variables	Remarks
Gillium et al 1996	25-74 years of age	11.6 year follow up	"Do you get much exercise in things you do for recreation (sports, or hiking, or anything like that), or hardly any exercise, or in between?" "hi your usual day, aside from recreation, are you physically very active, moderately active, or quite inactive?" This were operationalised into high, moderate, or low activity	**Stroke**: Incident stroke cases met at least one of the following criteria : 1) a death certificate with the underlying or nonunderlying cause of death coded 431-434.9, 436, or 437.0-437.1 using the *International Classification of Diseases,* Ninth Revision (ICD-9); or 2) one or more hospital and/or nursing home stays during the follow-up period with any discharge diagnosis with these codes using the Clinical Modification of ICD-9.	age, smoking, history of diabetes, history of heart disease, education, systolic blood pressure, serum total cholesterol, body mass Index, and hemoglobin	Challenge is how to translate the categories of PA into meeting recommended level Analysis were run separately for different gender and ethnicity Although only baseline PA was collected, the decay rate is likely to be picked up over time given the random sample used
Schnohr et	2136 men and	5 year	Physical activity was	CHD&	smoking, total	Adjustment of decay rate

al 2006	2758 women aged 20–79 years at the first examination, who attended both examinations, and did not change leisure-time physical activity level from the first to the second examination.	follow up	operationalised as: 1 was considered low physical activity, 2 was considered moderate physical activity and categories 3 and 4 were combined and considered as high physical activity in leisure time. We assumed that low, moderate, and high physical activity corresponded to <4, 4–6 and >6 metabolic equivalents, respectively.[12]	Stroke: mortality Sourced from National Central Person Register and The Register of Causes of Death	cholesterol, HDL-cholesterol, systolic blood pressure, diabetes mellitus, alcohol consumption, body mass index, education, income and FEV1% predicted	not relatively strong (in our context) considering the relatively short follow-up period, and the restriction of analysis with those whose exercise levels did not change during the course of the study. The effect of physical activity was not significant for stroke (although the RR was below 1 for higher levels of physical activity) but for CHD RR are estimated for mortality and not morbidity
Wisloff et al 2006	>=20 years (mean age at entry was 47 years-men; 48 years women) n=27143(men)	16 year follow up	Physical activity was operationalised as: (a)no activity (<1 per week) (b)1 per week =< 30 mins at low intensity	Stroke: mortality National Cause of Death Registry in Norway	Age, body mass index, marital status, education, alcohol consumption,	RR are estimated for mortality and not morbidity

[12] Physical activity were defined as follows: (1) almost entirely sedentary (e.g. reading, watching television or movies, engaging in light physical activity such as walking or biking for less than 2 h per week); (2) light physical activity for 2–4 h per week; (3) light physical activity for more than 4 h per week or more vigorous activity for 2–4 h per week (e.g. brisk walking, fast biking, heavy gardening, sports that cause perspiration or exhaustion); and (4) highly vigorous physical activity for more than 4 h per week or regular heavy exercise or competitive sports several times per week.

	n=28929(women)		(c)1 per week >30 mins at high intensity (d)2-3 per week =< 30 mins at low intensity (e) 2-3 per week >30 mins at high intensity (f) >= 4 per week =< 30 mins at low intensity (e) >= 4 per week c>30 mins at high intensity		smoking status, systolic blood pressure, diastolic blood pressure. n/B: estimates were presentation separately for men and women	
Evenson et al 1999	45 to 64 years (N=14 575;both gender)	7.2 year follow up	Baecke score was calculated for sport, leisure physical activity, and work related physical activity based on their frequency, intensity, and duration. Each physical activity was therefore operationalised as a continuous variable, unit increase in physical activity	Ischemic stroke: stroke events (hospitalizations) Sourced from self-reports, community-wide hospital surveillance, complete medical records.	age, sex, race-center, education, smoking, hypertension, diabetes, fibrinogen, and BMI	Operationalisation of physical activity does not match the categorical specification of physical activity in the model
Hu et al 2005	47 721 men and women (25 to 64 years of age)	19 year follow up Between 1972 and 1997, every	Self-reported leisure time physical activity was classified into 3 categories: (1) low (almost completely inactive or doing some minor physical activity	Stroke: events, defined as either the first nonfatal stroke event or stroke death without a preceding nonfatal event.	age, sex, area, study year, body mass index, systolic blood pressure,	A mix of mortality and morbidity stroke events

	5 years, 6 independent population surveys were performed in 5 geographic areas of Finland among the population. The study cohorts were followed until the end of 2003 through computerized register linkage by identification numbers	that was not of a moderate or high level), (2) moderate (some physical activity for >4 hours per week), and (3) high (vigorous physical activity for >3 hours per week). Occupational physical activity was classified as: (1) light (physically very easy, sitting office work, eg, secretary), (2) moderate (standing and walking, eg, store assistant, light industrial worker), and (3) active (walking and lifting, or heavy manual labor, eg, industrial or farm work). The daily commuting return journey was categorized into 3 categories: (1) using motorized transportation or no work (0 minutes of walking or cycling), (2) walking or bicycling 1 to 29 minutes, and (3) walking or bicycling for	Sourced from Statistics Finland and data on nonfatal events from the National Hospital Discharge Register; as well as death register.	cholesterol, education, smoking, alcohol consumption, diabetes, and other 2 types of physical activity

			≥30 minutes.			
Kiely et al 1994	n=1897 men, n=2299 women 28-62 years	32 years follow up	This was specified as composite score, the physical activity index, calculated by summing the products of the hours spent at each level of activity and a weighting factor based on the oxygen consumption required for that activity. The index was subsequently converted into tertiles for analysis	Stroke was defined as the first occurrence of atherothrombotic brain infarction, cerebral embolism, or other type of stroke.	age, systolic blood pressure, serum cholesterol (, number of cigarettes smoked per day, glucose intolerance , total vital capacity, BMI, left ventricular hypertrophy by electrocardiogram, atrial fibrillation, valvular disease ,history of congestive heart failure, history of ischemic heart disease, and occupation.	Challenge is how to translate the physical activity index scores to match a known indicator eg meeting recommended level

Table 18: Evidence on type 2 Diabetes

Author	Sample	Study type	Specification of PA	Specification of outcome	Control variables	Remarks
Haapanen et al 1997	35-63 year olds N=1340 men, n=1500 women	10 year follow up	An index representing weekly net energy expenditure from physical activity. This was operationalised as: Men 0-1100 kcal /week 1101-1900 kcal/week >1900 kcal/week Women 0-900 kcal/week 901-1500 kcal/week >1500 kcal/week	Diabetes: incidence rates obtained from self-administered questionnaire	Age, BMI, hypertension, alcohol consumption	The PA specification can be converted (with adjustments) to the meeting recommended level via British Association of Sports Sciences consensus statement (O'Donovan et al 2010) that indicates that the recommended level is equivalent to 800-1200 kcal
Hu et al 2003	35-64 year olds N=14290 men&women	12 year follow up	Self-reported leisure-time PA[13] was classified into: (i) 'low' was defined as almost completely inactive, e.g. reading, watching TV, or doing some minor PA but not of moderate or high level; (ii) 'moderate' was doing some	Type 2 diabetes: incident cases of type 2 diabetes from the National Hospital Discharge Register and the National Social Insurance Institution's Register.	age, study year, education, systolic blood pressure, smoking, the other two types of physical activity (i.e. occupational,	Moderate and high categories can be classified as meeting the recommended level although it must be recognised that the cut-offs here exceed the recommended level

[13] Analyses were also ran separately for other types of physical activity i.e. occupational and active travel

Author	Sample	Study type	Specification of PA	Specification of outcome	Control variables	Remarks
			physical activity more than 4 h a week, e.g. walking, cycling, light gardening, fishing, hunting, but excluding travel to work; (iii) 'high' was performing vigorous physical activity more than 3 h a week, e.g. running, jogging, skiing, swimming, ball games, heavy gardening, or regular exercise or competitive sports several times a week.		active travel)BMI, and for sex	
Katzmarzyk et al 2007	N=1543 (men & women) Mean age: 36.8 – 37.5 years	6 years	Physical activity was measured as a continuous variable indicating energy expenditure,	Type 2 diabetes: incident cases of type 2 diabetes sourced from questionnaire	Age, sex, smoking status, alcohol consumption and parental history of diabetes	Difficult to match PA specification with meeting recommended level
Dziura et al 2004	N=2135 (men & women) Age:>= 65 years	12 years	Total physical activity operationalised as: *never* (coded as 0), *sometimes* (coded as 1), or *often* (coded as 2).	Type 2 diabetes: incident cases of type 2 diabetes sourced from questionnaire	age, sex, race, education, body mass index (BMI), smoking, chronic	Difficult to match PA specification with meeting recommended level. The study explicitly

Author	Sample	Study type	Specification of PA	Specification of outcome	Control variables	Remarks
					conditions, physical function, and alcohol intake	adjusted for a 3 year change in physical activity (ostensibly to account for decay rate)

Appendix 2: Mortality data

Age	All cause mortality	CVD cause mortality	Non -CVD cause mortality
33	0.00074	0.00006	0.00068
34	0.000826	0.00007	0.00076
35	0.000893	0.00007	0.00082
36	0.000889	0.00007	0.00082
37	0.000994	0.00008	0.00091
38	0.001119	0.00009	0.00103
39	0.001136	0.00009	0.00104
40	0.001282	0.00010	0.00118
41	0.001369	0.00011	0.00126
42	0.001411	0.00012	0.00130
43	0.001551	0.00013	0.00142
44	0.001718	0.00014	0.00158
45	0.00187	0.00036	0.00151
46	0.001992	0.00038	0.00161
47	0.002128	0.00040	0.00172
48	0.00232	0.00044	0.00188
49	0.002548	0.00048	0.00206
50	0.002854	0.00054	0.00231
51	0.003087	0.00059	0.00250
52	0.003413	0.00065	0.00276
53	0.003693	0.00070	0.00299
54	0.004115	0.00078	0.00333
55	0.004513	0.00086	0.00366
56	0.004949	0.00094	0.00401
57	0.005334	0.00101	0.00432
58	0.005799	0.00110	0.00470
59	0.006403	0.00122	0.00519
60	0.006948	0.00132	0.00563
61	0.007478	0.00142	0.00606
62	0.008051	0.00153	0.00652
63	0.009034	0.00172	0.00732
64	0.010004	0.00190	0.00810
65	0.010801	0.00240	0.00840
66	0.011984	0.00266	0.00932
67	0.013043	0.00290	0.01015
68	0.014685	0.00326	0.01142
69	0.016104	0.00358	0.01253
70	0.017616	0.00391	0.01370
71	0.01932	0.00429	0.01503
72	0.021385	0.00475	0.01663
73	0.023881	0.00531	0.01858

Age	All cause mortality	CVD cause mortality	Non -CVD cause mortality
74	0.02628	0.00584	0.02044
75	0.029173	0.00776	0.02141
76	0.032836	0.00874	0.02410
77	0.036376	0.00968	0.02670
78	0.040763	0.01085	0.02992
79	0.045782	0.01218	0.03360
80	0.051718	0.01376	0.03796
81	0.057861	0.01540	0.04246

Sources: ONS, GAD

Appendix 3: Inputs for probabilistic sensitivity analysis

Parameter	mean	standard error	distribution
Incidence rates for:			
CHD (available by age groups)			
33-34	0.000035	1.0881E-05	beta
35-44	0.000465	3.9654E-05	
45-54	0.002095	8.41E-05	
55-64	0.00631	0.00014565	
65-74	0.0097	0.00018027	
75-81	0.0097	0.00018027	
Stroke (available by age groups)			
33-34	0.00008	2.7602E-05	beta
35-44	0.00023	4.6797E-05	
45-54	0.00057	7.3658E-05	
55-64	0.00291	0.00016623	
65-74	0.0069	0.00025546	
75-81	0.01434	0.0003669	
Diabetes (available by age groups)			
33-39	9.00365E-05	6.9895E-06	beta
40-49	0.000280353	1.2332E-05	
50-59	0.000631793	1.851E-05	
60-69	0.001004529	2.3336E-05	
70-79	0.001115584	2.459E-05	
80-81	0.001115584	2.459E-05	
Probability:			
Fatality cases for CHD			
33-34	0.08773	0.008773	beta
35-44	0.08773	0.008773	
45-54	0.08773	0.008773	
55-64	0.11553	0.011553	
65-74	0.21065	0.021065	
75-81	0.14763	0.014763	
Fatality cases for stroke			
33-34	0.234636872	0.02346369	beta
35-44	0.234636872	0.02346369	
45-54	0.234636872	0.02346369	

Parameter	mean	standard error	distribution
55-64	0.23279352	0.02327935	
65-74	0.23466258	0.02346626	
75-81	0.23420074	0.02342007	
Relative risks for: To be active (at year 1) as a result of brief advice	1.42	0.19	lognormal
Developing disease conditions for active people:			
CHD	0.90	0.04	
Stroke	0.86	0.04	
T2 Diabetes	0.67	0.12	
Non-CVD mortality after:			
non-fatal CHD	1.71	0.14	
non-fatal Stroke	1.71	0.14	
diabetes	1.49	0.13	
CVD mortality after:			
non-fatal CHD	3.89	0.04	
non-fatal Stroke	3.89	0.04	
diabetes	2.61	0.14	
Utility			
Age specific quality of life			
33-44	0.90	0.01	beta
45-54	0.86	0.01	
55-64	0.82	0.01	
65-74	0.78	0.01	
75+	0.72	0.01	
Health state utility weight			
Healthy	1.00	0.10	gamma
CHD 1st event	0.80	0.08	
Post CHD 1st event	0.92	0.09	
Stroke 1st event	0.63	0.06	
Post stroke 1st event	0.65	0.07	
Diabetes	0.90	0.09	
Mental health gain	0.07	0.04	beta
Cost			
Brief advice	£9	£1	normal
CHD 1st event	£3,947	£395	

Parameter	mean	standard error	distribution
Post CHD 1st event	£451	£45	
Stroke 1st event	£10,190	£1,019	
Post stroke 1st event	£2,238	£224	
Diabetes	£910	£91	

Appendix 4: Plots of net monetary benefit (cumulative) against number of iterations for probabilistic sensitivity analysis