Braun School of Public Health & Community Medicine
The Hebrew University of Jerusalem and Hadassah Medical Organisation, Israel

Thesis

Master's Degree in Public Health

An Economic Evaluation of Physical Activity and Implications for Its Promotion

30 December 2009

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Dedicated to my husband, David Sergio, without whom I would have completed this dissertation a year ago.

Acknowledgements

Thank you to Dr Matan Cohen for getting me started and for the use of his computer.

Special thanks to Yehudith Baruch, I greatly appreciate her kindness, efficiency, encouragement and cups of tea.

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1. Abstract

Physical activity (PA) is known to positively influence morbidity and mortality from many common chronic conditions. Despite this, it is evident that most people do not exercise as recommended. The reasons for this are complex. While the health benefits of physical activity are well documented the economic benefits are less clear.

Most studies on the subject either: investigate the direct costs of physical inactivity; analyse the cost-effectiveness of physical activity for a specific condition; or assess a particular intervention. Limited research published to date has compared the costs associated with promoting physical activity to those of the current minimal intervention in terms of the quality of life and life expectancy resulting from those conditions responsible for the majority of morbidity and mortality in the Western world today. The aim then, of this paper is to calculate the potential saving engendered when a sedentary person becomes active and, to extrapolate those findings to a population level by means of a comparison between the cost-effectiveness of enabling physical activity to a laissez-faire stance.

The study builds 2 decision-analysis models for a cohort of healthy 40yr olds using a decision tree: A cost minimisation (CMA) and a cost-utility analysis (CUA). Both include data collected from local and international literature on disease costs, utilities and lifetime risks coupled with the degree to which physical activity impacts on these factors. The CMA shows that one can expect a physically active adult to incur $117,000 less in disease-related costs compared to a sedentary individual. If all Israeli 40yr olds met recommended levels this would translate to a $9.5 billion saving over the lifetime of the cohort. If we assume that parameters are largely unchanged for a cohort aged 20-65 years we can multiply these figures by the over 3,2 million adults in Israel and see a potential annual saving of close to $10 billion. Even if only 1% becomes active one could invest $90 million a year and still realise a saving. The CUA then calculates at what levels of population adherence to PA recommendations and at what level of societal investment enabling PA would be cost-effective. Differences in benefits and cost-effectiveness ratios between the “Enabling” and “Laissez-faire” arms were highly significant with $p \approx 0$. In the base case, assuming a

$10,000 per person lifetime investment and a 25% increase in proportion of active individuals, the mean incremental cost-effectiveness ratio (ICER) of promoting PA is under $1000 per QALY gained. In univariate sensitivity analysis the most important variables are the effectiveness and cost of the intervention as well as the percentage of the population currently active. The model is less sensitive to the degree to which PA decreases disease risk and cost and increases utility. Enabling PA is cost-effective at costs up to $31,000 per person per lifetime, when increasing the active population by at least 22%, and when decreasing disease risk and cost by as little as 15% and 6% respectively.

The model is very robust and results are largely compatible with results from similar studies. It is hoped that the results of this study add to the growing literature giving weight to arguments that will convince policy-makers that investing in a national programme to promote physical activity is a worthwhile use of public funds.

2. תקציר

פעילות גופנית (פ"ג) ידועה ביכולה להשפיע על התחלואה והתמותה מרבים מהמצבים הכרוניים הנפוצים. למרות זאת, ברור כי רוב האנשים לא מתעמלים בהתאם להמלצות. הסיבות לכך הן מורכבות . למרות שהיתרונות הבריאותיים של פעילות גופנית מתועדים היטב, היתרונות הכלכליים ברורים פחות .

רוב המחקרים בנושא חוקרים את העלויות הישירות של פעילות גופנית,מנתחים את עלות / תועלת של פעילות גופנית בקשר למחלה ספציפית, או לחילופין מעריכים התערבות מסוימת . מעט מהמחקרים שפורסמו עד כה משווים את העלויות הכרוכות בקידום פעילות גופנית, לעומת אלה של התערבות המינימאלית, במונחים של איכות החיים ותוחלת החיים הנובעים מהמחלות הכרוניות, אשר אחראיות לרוב התחלואה והתמותה בעולם המערבי כיום . מטרת עבודה היא לחשב את החיסכון הפוטנציאלי כתוצאה מפ"ג ברמת היחיד, ולהגיע מתוך כך לממצאים ולמסקנות ברמת התערבות באוכלוסייה כולה.

המחקר בונה שני מודלים של ניתוח באמצעות עץ החלטות מבוסס על קוהורט מבוגרים בריאים בני 40 שנה: Cost-minimisation analysis (CMA) וגם Cost-utility analysis (CUA). המודלים מורכבים מנתונים אשר נאספו מן הספרות המקומית והבינלאומית על עלויות המחלה , התחלואה, איכות חיים והמידה שבה פעילות גופנית משפיעה על גורמים אלה. עולה כי ניתן להפחית כ117,000$ מההוצאות הרפואיות אצל אדם פעיל, לעומת אדם לא פעיל. אם כל הקוהורט בארץ היה מגיע לרמות המומלצות של פ"ג הרי יכולנו לצפות לחיסכון בסך 9.5 מיליארד דולר אמריקאי לאורך חייו של הקוהורט. . אם מניחים שפרמטרים אלה תקפים לקוהורט בני 20-65 ומכפילים את המספרים באוכלוסיית ישראל מגיעים לחיסכון שנתי של כ10$ מיליארד. זה אומר שאפילו אם רק 1% נהיים פעילים ניתן להשקיע כ90$ מיליון לשנה ולראות חיסכון. הCUA, מחשב מה רמות ההיענות של האוכלוסייה להמלצות ואיזו רמה של השקעה חברתית תאפשר כדאיות של הפעילות הגופנית. נמצא כי ההבדלים בתועלות וביחס עלות-תועלת בין מצב של השקעה חברתית לבין מצב של חוסר התערבות היו מאוד משמעותיים סטטיסטית ($p\approx 0$).
בהנחה של השקעת 10,000 $ לאדם וגידול של 25% באוכלוסיה הפעילה, היחס עלות-תועלת נוספת (Incremental Cost-Effectiveness Ratio – ICER) של איפשור פ"ג הוא פחות מ1000$ לQALY נוסף. בניתוח רגישות חד-משתני המשתנים החשובים ביותר הן יעילות ועלות של ההתערבות וכן אחוז האוכלוסייה הפעילה כעת . המודל הוא פחות רגיש למידה שבה העידוד מצמצם את הסיכון למחלות ומגביר את התועלת. איפשור פ"ג הוא cost-effective בעלות עד 31,000 $ לנפש לכל החיים, כאשר מגדילים את האוכלוסייה הפעילה ב 22% לפחות, וכאשר הפחתת הסיכון למחלות ועלות הם בסדרי גודל של 15% ו -6% בהתאמה.

המודל הוא מאוד חסון ותוצאותיו במידה רבה תואמות תוצאות מחקרים דומים. יש לקוות כי את תוצאות המחקר הזה יוסיפו לספרות ההולכת וגדלה שנותנת משקל לנימוקים שישכנעו את מעצבי המדיניות כי השקעה בתוכנית לאומית כדי לקדם פעילות גופנית הוא שימוש ראוי בכספי ציבור.

3. Literature review

3.1. Effectiveness of Physical Activity

In 1992 the American Heart Association declared that lack of regular physical activity is the most common of the four modifiable risk factors for many chronic conditions (Colman and Walker, 2004). This is borne out by Israeli figures whereby 27 - 30.1 % of the population smoke at least once a day, 11.2-20% are hypertensive, 6.1 - 16.5% report hypercholesterolaemia while a huge 72,3 – 78.8% are inadequately physically active (MABAT: First Israeli National Health and Nutrition Survey 1999-2001, Rennert and Peterburg, 2001, 2003-4 National Health Survey, 2006).

There is a growing body of evidence, including large cohort studies, demonstrating the role of physical activity in primary prevention of disease (Brukner and Brown, 2005). Beale et al (2007) assert that increasing activity levels will contribute to the prevention and management of over 20 conditions and diseases. They go on to state that people who are physically active reduce their risk of developing major chronic disease by up to 50% and the risk of premature death by about 20–30%.

The World Health Organization (World Health Report 2002) has reported that physical inactivity is one of the 10 leading causes of death in developed countries, producing 1.9 million deaths worldwide per year. A recent British study (Allender et al, 2007) attributes over 35000 annual deaths from ischaemic heart disease, cerebrovascular disease, breast cancer, colon/rectum cancer and diabetes mellitus to physical inactivity. This comprises 3.1% of mortality in the UK.

Epidemiological studies estimate that 36% of heart disease, 27% of osteoporosis, 20% of stroke, hypertension, Type II diabetes mellitus and colon cancer as well as 11% of breast cancer can be attributed to lack of physical activity. (Colman and Walker, 2004).

Regular physical activity has the added value of reducing tension and anxiety, increasing productivity, enhancing mental and sexual functioning, improving behavioural development in children and adolescents as well as maintaining function and preserving independence in older adults (Booth et al, 2002, Estabrooks et al 2003, Colman and Walker 2004) These health benefits hold for both women and men and even increase with advancing age (Stessman et al 2009).

According to studies, the health benefit exists already from a moderate intensity of physical activity – it is sufficient to burn just 150 calories a day, or 1000 calories a week - and the level of benefit is directly and positively correlated with the intensity, frequency and duration of physical activity.

Various evolutionary and physiological explanations have been posited for this. It is generally accepted that humans have inherited a genome within which important genes may only express themselves appropriately in an environment of regular physical activity. When activity levels fall below critical thresholds, there are changes in gene expression resulting in the manifestation of overt clinical disorders such as cardiovascular disease, metabolic disorders and some cancers. Until the modern era, energy expenditure has been inextricably linked to energy intake. With the industrial revolution and more recently the emergence of technological advances, a serious disparity has emerged between food availability and the energy required to access food – leading to new pandemic conditions of excess.

The United States Department of Health and Human Services conclude that regular physical activity and, possibly, caloric restriction, seem to be the only lifestyle factors which can favourably influence a wide range of physiological systems and chronic disease risk factors as well as mental health and social integration. Despite large genetic differences, it appears that physical activity may be the key that differentiates between those who do and do not experience successful aging.

In 1982 British epidemiologist Jeremy Morris defined physical activity as “today’s best buy of public health”. The aim of this thesis is to submit that claim to economic analysis.

3.2. Promoting physical activity

Few people, if any, today dispute the significant benefits of an active lifestyle, but human nature, societal changes and technological advances contrive to create disincentives to physical activity. According to Williams (2008) 41% percent of women and 35% of men engage in no leisure-time physical activity, while 73% of women and 66% of men are inadequately active. Thus the central question is how to promote the desired behaviour.

Most interventions to promote physical activity do show a significant increase (mean of 0.31 (95% CI 0.12 -0.50) for the duration of the intervention compared to the control group but very little long-term behavioural change (Hillsdon and Thorogood, 2005). In their analysis, Beale et al (2007) found a range of 7.5 – 41% (mean 22%) of sedentary people becoming active as a result of interventions, 2 of which were long-term - more than 5 years.

Many researchers have attempted to characterise the more successful interventions. For example, Van der Bij et al (2002) reviewed PA interventions specifically looking at participation rates and found higher rates for group-based interventions, for those aged over 60 years and for women. In their review of 17 randomised controlled trials, Hillsdon and Thorogood (2005) found that interventions with greater than 3 contacts between staff and participants had improved effect and that the effect is more consistent for self-directed physical activity with some professional guidance and on-going professional support. Perri et al (2002) in de Geus et al (2008) recommend prescribing a higher frequency (more sessions a week) rather than higher intensity as the former increases the accumulation of exercise without a decline in adherence, whereas the latter decreased adherence and results in the completion of less exercise.

Other important factors in the success of interventions are resources, well-trained staff and meticulous planning. Kahn et al (2002) highly recommend community-wide health education campaigns, and social support in community settings. They specifically suggest multi-site, multi-component interventions and note the roles that policy and environmental approaches combined with behavioural and social approaches can play in combating inactivity in our culture. Cobiac et al (2009) too recommend a mix of approaches to achieve a meaningful change in population physical activity levels.

Sallis et al (1998) make the following recommendations:

- Physical activity interventions should be conceptualized on a population basis; programmes based on individuals or small groups are unlikely to bring about population-wide change.
- Interventions are most effective when they target changes in the intrapersonal, social, environmental and policy domains. Ideally the intervention should use a combination of tactics, each targeting factors believed to mediate changes in physical activity.
- Interventions should be tailored to each setting. For example, installing a walking path may effectively promote activity at a suburban workplace, while in an urban workplace promoting stair climbing may be a better option. In some behaviour settings, the goal is to remove impediments to activity, such as poorly maintained sidewalks or the threat of street crime. In other settings the goal is to provide resources that facilitate activity such as showers at the workplace and providing sidewalks and bicycle trails in the community.
- Environmental interventions should be put in place before educational interventions are attempted. For examples, first policies should be adopted to reduce crime and provide opportunities for safe recreation and active living, and then educational programs are more likely to be effective.
- The combination of educational and environmental interventions depends on the behaviour setting. In settings in which physical activity is encouraged, such as schools, health clubs, parks, recreation centres, and some workplaces, educational and environmental interventions can be given equal emphasis. When interventions are conducted in behaviour settings in which people are not expected to be active (e.g., health care settings, movie theatres), then educational strategies should dominate. The usual goal of interventions then is to educate and motivate individuals or to encourage them to go to environments in which they could be active.

3.3. *Economic evaluations of physical activity*

Economics is the branch of social science that studies how societies allocate and manage their scarce resources. More than ever the public sector in general and the health sector in particular is confronted with dwindling resources and increasing costs whereby doing more of one thing requires doing less of another.
Economic evaluation is a widely accepted method for the appraisal of health care programmes and technologies. There are four methods of economic evaluation: cost minimisation; cost-benefit; cost-effectiveness (CEA) and cost-utility (CUA) analyses. Cost-minimisation analysis compares net costs and assumes that differences in health effects between alternatives are minimal or unimportant. Cost-benefit analysis usually considers just one intervention at a time. It adds up the costs of the intervention, puts monetary values on the benefits of the intervention and then assesses whether the value of the benefits is greater than the costs. Cost-effectiveness analysis, on the other hand, assumes that there is a certain desired outcome and that there are several methods by which this outcome may be achieved. It is a comparative approach. Outcomes of CEA are expressed in natural terms such as lives saved, cases averted or healthy days gained.

However, increased life expectancy is insufficient: Some interventions may extend life but the time remaining is full of pain and discomfort; while other interventions may not extend life expectancy by a great deal but are (relatively) inexpensive and considerably improve the patient's quality of life. An efficient allocation might shift resources from the first type of treatment to the second. Thus, a cost-utility analysis is a specific type of cost-effectiveness analysis (the terms are often used interchangeably) which takes into account the quality of the gain. The quality adjusted life year (QALY) combines quality and quantity of life, with one QALY being equivalent to one life year spent in full health. QALY's suffer from a number of limitations but they still currently provide the best methodology available for comparing outcomes from different health care interventions.
Outcomes of CUA are therefore expressed as quantity (duration) of health status multiplied by the quality of life (utility) of that health status.

An intervention is considered to cost-effective if it costs less and generates more

QALYs than the standard treatment. This is called dominance. It may also be judged to be cost-effective if the incremental cost-effectiveness ratio (ICER) falls below a certain threshold. The incremental cost-effectiveness ratio is calculated as the estimated difference in cost between the competing interventions/treatment divided by the difference in QALY's gained. A QALY of $50,000/QALY gained has historically been deemed an acceptable threshold but today there is evidence supporting thresholds of $100,000 - $300,00 per QALY gained (Ubel et al 2003, Braithwaite et al 2008). This is notwithstanding debate on the value of any threshold at all (Weinstein, 2008). In order to make the strongest case possible for the promotion of physical activity, this dissertation uses the conservative $50,000 threshold.

Many studies have examined the cost and health outcomes of physical activity compared to those of specific conditions and most found that physical activity is indeed cost-effective. For example, Hatziandreu et al’s (1988) analysis found that, compared to other preventive or therapeutic treatment modalities for Congestive Heart Disease (CHD), the $11,313 cost/QALY gained of regular PA is favourable for their total population. The incremental cost-effectiveness ratio for those ‘coerced’ to exercise was $48,775/QALY compared to the net cost savings yielded by investing in those who enjoy or are neutral towards PA (Hatziandreu et al, 1988). This was the only study found that takes into account the indirect costs of physical activity such as time and injuries sustained.

Other studies have attempted to calculate the overall costs of physical inactivity: Wang et al (2004) quote a 1987 study estimating the economic burden of physical inactivity in the US at $76.6 billion (in year 2000 dollars). More concretely, Pronk et al (1999) found health care charges are 4.7% lower per active day per week and Sari (2009) concludes that on average, an inactive person spends 38% more days in hospital, uses 5.5% more family physician visits, 13% more specialist services, and 12% more nurse visits than an active individual. Similarly, Hill et al (2009) assert that people who are physically inactive incur 1.4-fold higher total average annual costs than people with no risk factors. Overall Allender et al (2007) calculated that physical inactivity contributes more than £1 billion (2002 pounds) to the direct health cost burden of the UK National Health Service per year. Moreover, the authors mention that the Prime Minister’s Strategy Unit estimates the annual indirect cost of physical inactivity in England as £8.2 billion.

According to Colman and Walker (2004) a 10% decrease in physical inactivity could conceivably save the Canadian province of British Columbia C$36 million a year. The authors go on to assert that this is an absolute saving as regular exercisers have a lower overall lifetime morbidity, hence avoided medical costs are not just deferred to older ages.

There are contradicting opinions: Hellman (1997) argues that promoting wellness does not reduce healthcare costs but does defer and possibly increases them. A 1997 New York Times article agrees, but no further support for this view was found in a search of PubMed articles. Keuffel (2006, abstract only) contends that in the short-term (2-year follow-up), when adjustment is made for health state, income and other demographic characteristics the economic benefit from PA is modest, indeed persistent PA was found to significantly ($p<0.1$) increase the probability of having health care costs, albeit by 0.8-1.1%. However those who are physically active had 17% fewer days of work missed due to sickness. Keuffel's perspective for analysis is that of the employer and managed care organisation, hence the value of this article from a long-term, societal perspective is questionable.

Three studies were found that calculate the lifetime cost-effectiveness of physical activity compared to inactivity for several conditions:
The British National Institute of Clinical Excellence (NICE) commissioned a study in 2006 which assessed the cost-effectiveness of four physical activity interventions: brief interventions in primary care; pedometers; exercise referral and walking and cycling programmes in the community in an adult population. Diseases included in the model are: CHD, CVA, Type II Diabetes and colon cancer. Across all scenarios, in all four methods, the future discounted costs saved exceed intervention cost per participant. Benefits accrued range from 0.07 – 1.15 QALY's gained per person.

Annemans et al (2007) built a transition state model in which they investigated the impact of physical activity in a fitness centre environment on 3 different cohorts. Results of this Belgian study show clear advantages for physical activity versus inactivity study are with an ICER range of €2,000-15,000/QALY depending on the cohort risk profile.

Cobiac et al (2009) assessed the cost-effectiveness of 6 different interventions designed to promote PA in Australia and found that all, except general practitioner referral to an exercise physiologist, are cost-effective at the $50,000/DALY mark (Disability-Adjusted Life Years adjusts age-specific life expectancy by the loss of health and years of life due to disability from disease or injury as opposed to the QALY which adjusts by utility (http://www.who.int/healthinfo/global_burden_disease/metrics_daly/en/)). Programmes that encourage the use of pedometers and mass media-based community campaigns proved to be dominant (less expensive and greater benefit than laissez-faire) across all scenarios.

4. Thesis Goals and Objectives

Goal

To calculate medical cost reduction engendered by physical activity on an individual level and, based thereon, to infer threshold parameter values in terms of cost and efficiency whereby investing in interventions for the promotion of physical activity on a population level is cost-effective.

General Objective

Use a decision-tree analysis model to determine the absolute savings expected from a physically active compared to a sedentary individual and thereafter to establish the cost-effectiveness of investing in promoting physical activity versus a laissez-faire strategy for a cohort of healthy adults aged 40.

Specific Objectives

1. Identify the major chronic conditions preventable by physical activity, their incidence and prevalence in the Western world.
2. Determine the direct and indirect costs of these illnesses.
3. Determine the utility values of these conditions.
4. Determine the changes in life expectancy experienced as a result of these conditions and how they can be influenced by physical activity.
5. Examine the degree to which physical activity can decrease the incidence of these chronic conditions.
6. Build a decision tree using the TreeAge Pro 2009, Healthcare programme in order to assess potential savings from physical activity.
7. Build a second decision tree guide policy regarding population wide interventions.
8. Examine, based on the core economic evaluation, under which assumptions promoting PA would be appealing in comparison to not promoting PA.

5. Methods

5.1. Introduction

5.1.1. The Decision Tree

The analysis was performed using a decision tree model created in TreeAge Pro 2007 software (TreeAge Software Inc, Williamstown, Mass.). Modelling is becoming a crucial tool for economic evaluations, particularly when the question at hand is the allocation of resources. This is because of the difficulty of taking into consideration huge amounts of data regarding many conditions each with its own incidence and prevalence patterns, as well as differing costs and utilities.
All models are necessarily based on simplifications. If the relationships between factors involved in determining future outcomes were straightforward then a model would be unnecessary. Instead a model allows one to focus on those factors and relationships that are believed to have the greatest impact on outcomes. The model output then allows the user to make informed decisions based on the likely major outcomes of a scenario.
When building a model, the modeller must always decide what to include and what to exclude. There will always be elements that cannot be included within a model. The modeller also needs to make decisions as to what to represent in detail and what to approximate. These are very important decisions that can only be made in light of the intended use of the model and are, unfortunately, invariably influenced by the availability of data.
Despite these limitations, models are increasingly accepted as a good—and often the only—way to illustrate disease processes and their economic impact and to estimate the impact of changes in treatment strategies.

The analysis is taken from the perspective of society, specifically that of a public institution responsible for implementing health policy on a national level. It includes direct medical costs as well as productivity losses but excludes private expenditure and time loss as a result of physical activity.

5.1.2. Tree Parameters

Epidemiological data were used to determine those conditions most influenced by physical activity as well as the lifetime incidence thereof in a cohort of healthy adults aged 40, their effect on life expectancy and treatment costs. The measures of the effectiveness of physical activity are:

1. Reductions in disease incidence.
2. Gains in life expectancy.
3. Gains in quality of life.

These effectiveness measures serve as denominators for the cost-effectiveness ratio with the difference in the incurred costs of the two strategies (physical activity verses inactivity) serving as the numerators. The outcome measure for this study is thus cost per quality-adjusted life-year gained.

Table 1: Model steps

Process	Notes/Main assumptions
1. Select diseases for inclusion in the model.	• The model structure does not allow for all diseases prevented or ameliorated by physical activity to be included. • Inadequate data exists for some conditions.
2. Research the lifetime probability of developing the selected conditions.	• Assume that generated estimates apply to the sedentary population as probability risk calculations do not take into account activity levels. • Assume that the risks of experiencing the conditions are independent of one another. • Assume that probabilities generated in a specific population can be generalised to all Western populations.
3. Determine the degree to which physical activity reduces lifetime probability of disease.	• A range of probability reductions will be used for all diseases. • Assume reported effectiveness is independent of baseline activity level.
4. Determine average age of onset and life	• Assume that generated estimates apply to the sedentary population.

expectancy of each condition	• Assume that figures generated in specific populations can be generalised to all Western populations.
5. Research utility measures for each condition.	• Assume that generated estimates apply to the sedentary population. • Assume a baseline utility measure per disease despite variability in expression.
6. Determine the degree to which physical activity increases the utility of disease states.	• A range of utility increases will be used for all diseases. • Assume reported effectiveness is independent of baseline activity level.
7. Determine lifetime costs of each condition.	• Assume a baseline cost parameter despite variability in disease expression and treatment options.
8. Determine the degree to which physical activity decreases the cost of disease states.	• A range of cost decreases will be used for all diseases. • Assume reported effectiveness is independent of baseline activity level

5.1.3. Discounting

In cost-effectiveness analysis there is broad consensus that future costs and health consequences should be stated in terms of their present value. This is due to the prevalence of time preference for present over future outcomes (Gold et al, 1996). The accepted annual discount rate for costs ranges between 2.5 - 5% and in the publications reviewed, over half the cost studies used a 3% discount rate in their calculations, 10% did not discount, another 10% used a rate of 5% ,15% used rates varying from 3,5 - 8% and a further 15% did not state their discount policy at all. The discounting of QALY’s is more equivocal: there is empirical evidence from behavioural studies supporting inconsistent discounting effects at a different rate to that of costs and there are those who assert that, as real income increases over time, the value of a QALY increases too (hence debate over an appropriate threshold) therefore, health effects should not be discounted at all.. Weinstein (in Gold et al, 1996) asserts that QALY’s should be discounted at the same rate as costs as they are being valued relative to said costs. Furthermore if QALY’s are discounted at a lower rate it would result in the cost-effectiveness of an intervention increasing with delay – the Keeler-Cretin paradox (Gold et al 1996). In the current model QALY's were discounted at 3% as this was seen most compatible with prevailing norms. The model structure did not allow for sensitivity analysis on discount rate.

5.2. Tree input parameters

An initial English-language literature search was done in MEDLINE for reviews containing the MeSH term "exercise and "health" in order to get a cursory idea of the conditions affected by physical activity. Subsequent searches were performed using the terms "lifetime risk", "lifetime probability", "lifetime incidence", "life expectancy", "onset age", "lifetime cost" or "utility" combined with the condition name in order to ascertain input values for model parameters. The searches were then rerun adding the MeSH term "exercise" to the search strings. Additional publications were identified by reviewing the reference lists of the identified articles. Results were then analysed to determine the mean and standard deviation per parameter (see Appendices for details).
When multiple data sources were found, the averages and standard deviations were inputted into the model for the base case and sensitivity analyses.

5.2.1. Disease Selection

The basic tree structure requires that the probabilities of all options at a particular node sum to 1. Furthermore, for simplicity sake it was assumed that the risks of developing different disease states are independent of each other and that the disease states are mutually exclusive. These factors together constrain the number of disease states that can be used.

An example of this is the case of hypertension. If there is a 90% lifetime probability (Barlow et al 2006, Chobanian et al 2003, Goldstein et al 2006, Rosamond et al 2007 and Vasan et al 2002) of developing this condition then the model necessitates that the cumulative probability of developing any other condition can only be 10%. Reducing the risk of hypertension by half would still not allow for realistic probabilities of other conditions while concurrently diminishing the validity of the model. Additionally the cost of hypertension treatment is not significant compared to that of other conditions with annual costs ranging from £5-261 (Law et al, 2003) and 6-year drug costs in the ALLHAT trial being $1586-2792 (Heidenriech, 2008). Furthermore, while many studies were found that documented reductions in blood pressure, as measured in mm/Hg, due to physical activity only Whelton et al (2002) mention absolute reductions in lifetime risk. Therefore, despite the huge number of people being treated for this condition, hypertension was not included in the model.

Table 2: Level and strength of evidence for a relationship between physical activity and contemporary chronic conditions

(Adapted from Chief Medical Officer, British Department of Health, 2004, American College of Sports Medicine Position Stand, 2009 and Brukner and Brown 2005)

Condition	**Lifetime risk**	**Lifetime cost**	**Preventive effects**			**Therapeutic effects**	
			Level of evidence Volume and quality of data	**Strength of effect**	**Evidence of a dose-response relationship**	**Level of evidence** Volume and quality of data	**Strength of effect**
Cardiovascular disease							
Dyslipidaemia	50%	$450-2000	Medium	Moderate	Yes	High	Moderate
Hypertension	90%	No data	High	Strong	Yes	High	Weak
Coronary heart disease	M: 45% F: 30%	$500,000	High	Strong	Yes	Medium	Moderate
Stroke	15%	$60,000	High	Moderate	Yes	Low	Weak
Peripheral vascular disease	No data	No data	Medium Via treatment of risk factors related to exercise	Weak	-	Medium	Moderate
Cancer							
Overall	40%	No data	Medium	Moderate	Yes	No data/insufficient data However a low level of evidence indicates weak effects on physical function and fatigue during and following treatment	-
Colon	6%	$64,680	High	Strong	Yes		
Rectal	5%	$78,540	Medium	No effect	-		
Breast	12,5%	$250,000	High	Moderate	Yes		
Prostate	16%	$44,660	High	Equivocal	-		
Lung	7%	$50,820	Low	Moderate	-		
Endometrial	2%	No data	Low	Weak	Yes		

Condition	Lifetime risk	Lifetime cost	Preventive effects			Therapeutic effects	
			Level of evidence Volume and quality of data	Strength of effect	Evidence of a dose-response relationship	Level of evidence Volume and quality of data	Strength of effect
Musculoskeletal disorders							
Osteoporosis (defined in terms of bone mineral density)	No data	No data	High	Strong	-	Medium	Weak
Osteoarthritis	45% (knee)	$80,000	Possible Via prevention of obesity	Weak	-	Medium	Moderate
Low back pain	28%	No data	Medium	Weak	-	High	Moderate
Fractures and falls	M: 13% F: 40%	$91000 (hip)	Medium	Moderate	Weak	-	-
Reproduction							
Menopause	n/a	$14-22,000	-	-	Yes	High	Moderate
Infertility	17%	No data	Low	Equivocal	-	Low	Equivocal
Erectile dysfunction	No data	$4,000	Low	Moderate	Yes	Low	Moderate
Mental function							
Clinical depression	17%	No data	Low	Moderate	-	High	Moderate
Cognitive dysfunction	M: 14% F:25%	$215,000	Medium	High	-	Low	Weak
Insomnia	10% prevalence	$2000-5000 annual	Low	Weak	-	Medium	Moderate
Chronic fatigue syndrome	0.42% point prevalence	$20,000	No data/insufficient data	-	-	Low	Weak
Parkinson's Disease	6.70%	$100,000	Low	Equivocal	Yes	High	Moderate
GI Tract							
Gallbladder stones	M: 20% F: 35%	$9-24000 per event	High	Strong	-	-	-
Diverticulosis	No data	No data	Low	Moderate	Equivocal	Low	Moderate

Condition	Lifetime risk	Lifetime cost	Preventive effects			Therapeutic effects	
			Level of evidence Volume and quality of data	Strength of effect	Evidence of a dose-response relationship	Level of evidence Volume and quality of data	Strength of effect
Other							
Obesity and overweight	Overweight: 50% Obesity: 25%	£250,000.00	Medium	Moderate	Yes	High	Moderate
Type 2 diabetes	38%	$110,000	High	Strong	Yes	High	Strong
Asthma	34%	$30,000	No data/insufficient data	-	-	Medium	Weak
Fibromyalgia	No data	No data	No data/insufficient data	-	-	Medium	Moderate

5.2.1.1. Criteria for inclusion of diseases

- Availability of information on key model parameters: particularly lifetime incidence and cost.
- Diseases for which there is a high level of evidence regarding the efficacy of physical activity in prevention.

5.2.1.2. Other considerations:

- Musculoskeletal diseases and conditions of cognitive function were included despite not meeting the above criteria as it was felt to be important to include diseases affecting other body systems thereby making the model more comprehensive. These conditions were however grouped together in order to simplify the model and overcome the relative weakness and lack of data on individual diseases.
- Notwithstanding the will to include disease of the gastrointestinal tract the paucity of data on diverticulosis and the fact that gallstone disease is episodic rather than necessarily chronic, these were excluded. Similarly, limited data on conditions of

the reproductive system precluded their inclusion in the model.

- Obesity was excluded from the model due to the conflation of cause and effect when dealing with physical inactivity. There is much overlap between them and, in most cases, synergism of their effects on other conditions thereby complicating the model.

Conditions included in the decision tree are:

- Coronary Heart Disease
- Cerebrovascular Attacks
- Type 2 Diabetes Mellitus
- Colon Cancer
- Breast cancer (for women)
- Dementia
- Musculoskeletal disorders (arthritis and hip fracture)

5.2.2. Probability data

Probability and relative risk data were based on estimates from published studies and inputted separately for men and women. Where possible, lifetime incidence figures were preferred over annual and prevalence data. Appendix A details these papers. Disease risk figures were adjusted downwards such that their sum was less than 1.00. It was also decided to use a set, conservative relative risk reduction factor across all conditions in order to simplify the model. Both these factors would serve to underplay the impact of physical activity on health.

5.2.3. Disease Cost

Aggregating disease cost data proved to be the biggest challenge in the model: this is due firstly to the difficulty converting costs derived from disparate countries and time period to a common currency and time; secondly to the wide array of methodologies used and thirdly to the disparity in cost items included in the studies.

5.2.3.1. Converting disease cost data to a common currency and year

This was done in a 2-step process:

The first step entailed converting all disease cost estimates to US dollars. Because of market imperfections in health care, it is not recommended to use market exchange rates when comparing prices in health care but rather purchasing power parity ratios. PPPs are exchange rates that equalise the purchasing power of different currencies by eliminating the differences in price levels between countries thereby making possible more meaningful international comparisons. PPP's for the cost year used in each study were obtained from the Organisation for Economic Co-operation and Development (www.oecd.org/std/prices-ppp).

The second step entailed inflating figures to 2009 values using United States medical inflation data (http://www.bls.gov/data) and the following percentage change calculation:

(2009 1st Half Medical Inflation Index - index for publication cost year) ÷

Medical inflation index for publication cost year

5.2.3.2. Study methodologies

Study methodologies can be classified according to several criteria (Evers et al 2004):

1. *Perspective of Analysis*:
   The perspective of analysis indicates from which point of view the study is being considered and determines which costs will be examined. Ideally, the results of a cost-of-illness (COI) study are to be used for resource allocation on the societal level; therefore, it is preferable to perform these studies from the perspective of society thereby including both direct costs and productivity losses.

   As far as possible this analysis relies on studies performed from a societal perspective. In cases where only direct costs were available, indirect costs were estimated based on prevailing ratios between direct and indirect costs. For example, the indirect costs of breast cancer have been found to be 2-3 times greater than direct costs (Lidgren et al, 2007 and Radice and Redaelli, 2007). Only for conditions of cognitive dysfunction, where the average age of onset is about 65yrs, were productivity losses not included as patients are usually retired and life-expectancy is shortened.

2. *Prevalence- or Incidence-Based Study Design:*
   Prevalence is the fraction of the population that has the disease of interest during a certain period. Prevalence studies are thus based on the summation of costs associated with the disease during a particular period of time, usually 1 year. This approach usually results in an estimate of the annual cost of an illness to society or to a particular payer and, as such, provides useful data for health service planning
   Incidence is the fraction of a group initially free of the condition in which a disease develops over a given period of time. The incidence approach is based on the principle that the flow of costs associated with a disease should be assigned to the year in which that flow begins. The incidence approach is preferable when one is interested in the lifetime costs of new cases at an

individual level.

3. *Bottom-Up or Top-Down Estimation Procedure:*
   The top-down method calculates the national costs of a disease using data banks, such as the ones provided by the National Office of Statistics. In a bottom-up procedure, a group of patients with a certain disease is asked what the costs of their disease are. The results of this questionnaire are then extrapolated to a population level. The vast majority of studies used in the paper used the bottom-up procedure.

4. *Total or incremental costs:*
   Total disease costs provide estimates of the total health care expenditure of people diagnosed with the disease and hence include resource use related to co-morbidities the individual may have in addition to the condition being studied . Conversely, incremental cost studies estimate the increase in costs that is attributable solely to the presence of the disease. Akobundu et al (2006) identify two general methodological approaches for each category:

   1. *Sum_All Medical*: Identify all patients with a diagnosis and sum costs.
   2. *Sum_Diagnosis Specific*: Identify all patients with a primary diagnosis and sum costs for treatments for that diagnosis.
   3. *Matched Control*: Identify all patients with a diagnosis and sum costs. Subtract out the average cost of the sample to find incremental costs for treatment; alternatively, subtract out the average cost of a matched cohort instead
   4. *Regression*:
      a. Identify all patients with a diagnosis, complete a regression analysis and indicate the individual β for each diagnosis.
      b. Identify all patients with a diagnosis, find a matched cohort (similar to a clinical trial) and complete a regression analysis to quantify the individual β for each diagnosis – gold standard

50% of studies found used the Sum_Diagnosis Specific method, 34.5% used the Matched Control method. Only 5% made use of regression.

5.2.3.3. Standardising cost components

The difficulty in making cross-comparisons was compounded by the fact that the studies included different cost components within the basic cost categories: prescription medication, laboratory tests, paramedical costs such as dieticians, home nurses, and physiotherapists are examples of medical expenses not uniformly included.
To further complicate matters there did not seem to be a correlation between cost components included and overall disease cost. For example, Dewey et al (2003) included the most comprehensive costs (including productivity losses) for CVA but has the lowest cost of stroke at less than $45,000. Sandercock et al (2004) include only inpatient and rehabilitation costs but estimate the lifetime cost of stroke at $55,000.

Conversion to a common monetary unit and year cannot account for differences in healthcare systems, health service utilisation patterns, treatment paradigms and technologies nor costing structures. It also did not prove possible to redefine each study's cost components into a common set. Furthermore, while half the cost studies used a 3% discount rate in their calculations, 10% did not discount, another 10% used a rate of 5% ,15% used rates varying from 3,5 - 8% and a further 15% did not state their discount policy at all. Hence one is left with a general indication of the cost of each disease, relying on as many studies as possible in order to reduce bias.

A breakdown of all studies used to derive health costs can be seen in Appendix C.

5.2.4. Life expectancy data

Once again, this was based on data from published studies and inputted separately for males and females. Data was collected on average age at disease onset as well as average life expectancy from diagnosis. Where this was expressed as life years lost due to disease the number was subtracted from average life expectancy as published by the United States Social Security Administration. These details can be seen in Appendix E.

5.2.5. Utility data

In health economics the term “utility” refers to cardinal values that represent the strength of an individual’s preferences for specific outcomes under conditions of uncertainty. Health utilities specifically, are preferences for specific health states or treatment and they allow for the comprehensive measurement of health-related quality of life (Petrou 2003).

There are several methods for determining disease utilities/preference measures (Dennett et al 2008, Petrou 2003):

- Visual Analogue Scale: This involves asking an individual to indicate, on a visual aid ranging from 0 (death) to 1 (perfect health), where his or her preference for a particular health state lies.
- Time Trade-off: This method requires asking an individual to trade off length of life for gains in quality of life. Individuals are asked to assume they are living in a specific health state for the remainder of their lifetime. They are then asked to indicate how many years of life in their current health state they would be willing to give up to be returned to perfect health for their remaining years of life.
- Standard Gamble: This method is considered the gold standard for obtaining utilities and is based on paired comparisons from which an individual chooses one of two health states: a certain outcome or a gamble to achieve a better outcome while risking ending up with a worse outcome – usually death. The probability of experiencing either of these two choices is varied until the individual is indifferent between the lottery and the choice with the certain outcome. The utility value is the value of p at that point.
- Using multi-attribute utility scores: Because measuring utilities for health outcomes can be complex and time consuming, multi-attribute health status classification systems are frequently used. An individual completes a questionnaire about his or her health status, which is then scored using a multi-attribute scoring function derived from community preference measures for health states. Scores are presented on a scale from 0.0 (death) to 1.0 (full or perfect health).

Utility values obtained using the Standard Gamble method are typically greater than those obtained from using the Time Trade-Off method, which are greater than those using rating scales. This may be because the Standard Gamble procedure requires patients to rate health states relative to death. When death becomes a consideration, many individuals become risk averse, which leads to higher utilities. The majority of studies quoted in this paper used utility values converted from health status questionnaires, some were based on literature reviews and there are a few in which the method was not stipulated. Appendix D presents details of these papers.

Utility scores also differ based on who was asked. The advantage of asking patients to value their own health is that one does not need to describe the health state, thereby possibly ensuring a better understanding of the impact of the state on their lives (Brazier JE, et al., 2002). Some comparative studies have not found significant differences between the values assigned by those who have experienced the health state versus those who are asked to imagine the utility of the health state as described by the researcher, while other studies suggest that those experiencing the condition attach higher values to the resulting health states. This is important because if the latter is indeed the case then the choice of utility scores has an impact on the results of cost-utility evaluations. For example, in Patrick et al's (2001) study, aquatic classes for osteoarthritis were only cost-effective when using community-weighted measures but exceeded the $50000/QALY mark when using participant-weighted measures. Similarly Gabriel et al (1999) show that the CE of an intervention to prevent hip fracture cost $25,000/QALY using community-weighted measures compared to $94,000/QALY when using subjects' preferences. In general there is a tendency for those who have experienced a chronic condition to assign higher values to that health state than the general public. This is consistent with the widely held belief that people learn to cope with their conditions, change their reference point or even possibly lower expectations and that the general public has an exaggerated fear of disability and disease.

Except for Gabriel, Patrick and Brazier (incidentally all dealing with musculoskeletal conditions), all studies quoted in this paper used patient preferences.

Furthermore, there is wide variety in how people experience each health state. One can be comatose due to a stroke or one can suffer slight physical deficits, one's diabetes may be controlled by diet or it may complicate and result in blindness and amputation. For simplicity sake, the midpoint of each utility range was used in the base case.

5.3. Solution

The Monte Carlo method is a computerized mathematical technique used in widely divergent fields for analyzing uncertainty. The goal of the method is to determine how random variation, lack of knowledge, or error affects the conclusions of the scenarios being modelled. The technique was first used by scientists working on the Manhattan Project during World War II and it was named for the Monaco resort town renowned for its casinos.

The inputs into a Monte Carlo simulation are randomly generated from probability distributions (see below) to simulate the process of sampling from an actual population. These probability distributions are ranges of values for factors that are inherently uncertain.

By using probability distributions, variables can have different probabilities of different outcomes occurring.

Each set of samples is called an iteration, and the outcome from that sample is recorded. The system calculates results over and over, each time using a different set of random values from the full variable range. Monte Carlo simulation produces distributions of possible outcome values and how likely each outcome is. It shows the extreme possibilities along with all possible consequences for middle-of-the-road decisions.

TreeAge Pro 2009 offers three types of Monte Carlo simulations:

1. Micro-simulations: Used for first-order uncertainty i.e. variability among individuals, this consists of running a virtual cohort of subjects through the model. This process estimates expected values by averaging random, individual outcomes
2. Sampling: Also called probabilistic sensitivity; used for second-order uncertainty i.e. parameter uncertainty. Here, the analysis recalculates expected values for different sets of parameter samples.

3. Two-dimensional simulation: a combination of both trials and sampling

In this analysis there is both variability among individuals' experience of disease as well as parameter uncertainty, hence the latter simulation was used. 50,000 iterations were run in order to obtain the mean, median and the standard deviation for costs incurred and QALYs gained under each scenario.

5.3.1. Cost-minimisation analysis

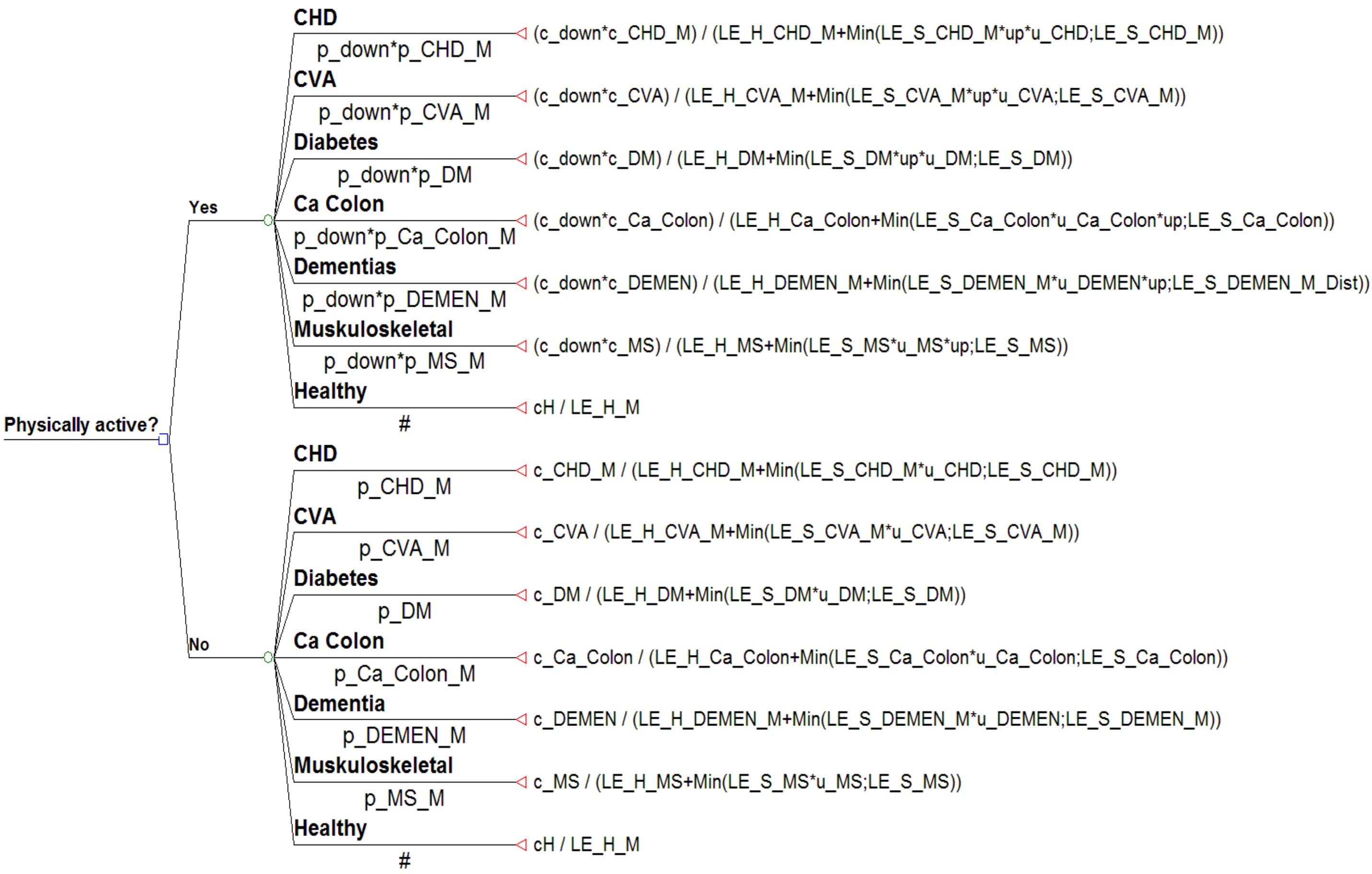

Figure 1: Tree model describing cost-minimisation analysis - males

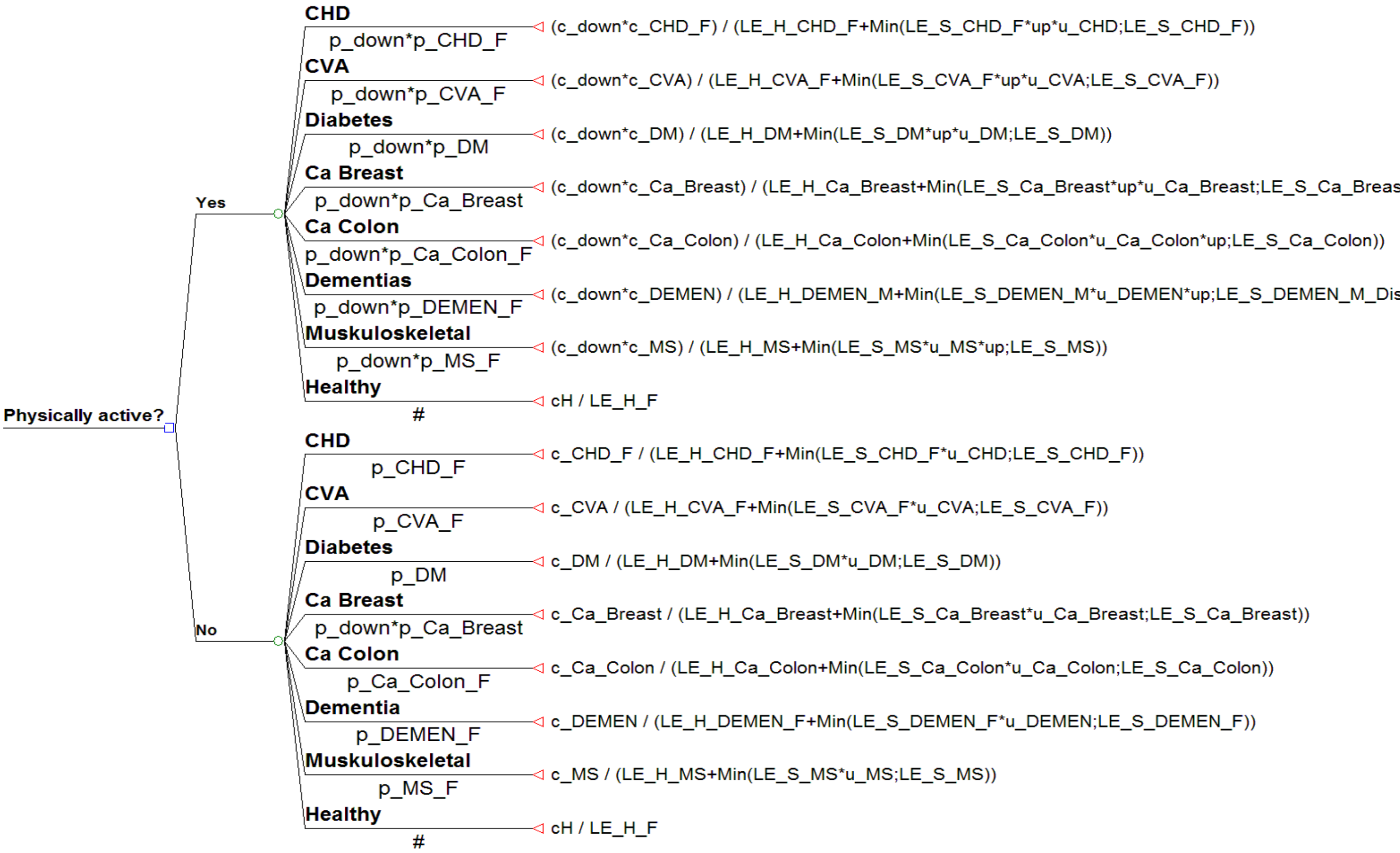

Figure 2: Tree model describing cost-minimisation analysis - females

In order to assess the range of possible cost savings from PA, the model was first run comparing a physically active to a sedentary individual. The assumptions of the basic tree are such that physical activity will be the dominant option in all scenarios, as costs and probabilities of illness always decrease. Neither costs nor detriments are assigned to PA.

People adhering to recommendations of at least 30 minutes of moderate exercise most days of the week are considered to be physically active. Sedentary is defined as less than 60 minutes a week of moderate physical activity.

The tree begins with a decision: to be physically active or to be sedentary. It then branches to “Yes” or “No” and then to male and female (not shown).
Each person then has the gender-linked probability of developing one chronic illness. As mentioned previously, model limitations dictate that:

- Conditions be mutually exclusive, such that once an individual develops one of the disorders the simulation ends.
- The sum of all probabilities equal to 1.0, resulting in lower probabilities than those quoted in the literature.

The hash mark (#) is the remainder symbol used in place of a probability expression in order for TreeAge Pro to automatically calculate the complement.

Active individuals have been shown to have a lower risk of contracting disease hence their probability is adjusted downward by the variable “p_down”.

For simplicity sake, it was decided to make this a uniform variable across conditions rather than varying it per disease. For this reason a conservative mean value (0.8) and standard deviation (0.1) were chosen despite evidence that physical activity can reduce lifetime disease incidence by up to 50%.

The tree concludes at the terminal node or “pay-off” which represents the net value of that particular scenario’s series of actions and events. In this case it is the cost divided by the effect.

As demonstrated by Andreyeva and Sturm (2006) as well as Lambert et al (2009), medical costs for active individuals tend to be lower thus are decreased by the factor “c_down”.

5.3.1.1. Variable distributions

By using probability distributions, variables can have different probabilities of different outcomes occurring. This analysis used Normal, Triangular and Beta distributions:

Normal distributions describe variables that cluster around a mean in a symmetrical manner that resembles a bell when drawn on a graph. In general it is assumed that the sum of a large number of random variables is approximately normally distributed. The cost of Enabling and all variables related to life expectancy and disease onset were defined as normal distributions.

Table 3: Parameters using normal distribution

Name	Description	Mean	Standard Deviation
LE_H_Ca_Breast_Dist	Healthy years before Breast cancer onset	10	5
LE_H_Ca_Colon_Dist	Healthy years before Colon Cancer onset	24	4
LE_H_CHD_F_Dist	Healthy years before CHD onset - women	25	5
LE_H_CHD_M_Dist	Healthy years before CHD onset - men	25	5
LE_H_CVA_F_Dist	Healthy years before CVA onset - women	28	5
LE_H_CVA_M_Dist	Healthy years before CVA onset - men	25	5
LE_H_DEMEN_F_Dist	Healthy years before dementia onset - women	37	5
LE_H_DEMEN_M_Dist	Healthy years before dementia onset - men	34	5
LE_H_DM_Dist	Healthy years before Diabetes Mellitus onset	10	2
LE_H_MS_Dist	Healthy years before Musculoeskeletal disorder onset	18	3
LE_S_Ca_Breast_Dist	Breast Cancer life expectancy	20	5
LE_S_Ca_Colon_Dist	Colon Cancer life expectancy	10.86	3
LE_S_CHD_F_Dist	CHD life expectancy - women	15	2
LE_S_CHD_M_Dist	CHD life expectancy - men	15	2
LE_S_CVA_F_Dist	CVA life expectancy - women	10	2
LE_S_CVA_M_Dist	CVA life expectancy -men	9	2
LE_S_DEMEN_F_Dist	Dementia life expectancy - women	5.5	1
LE_S_DEMEN_M_Dist	Dementia life expectancy - men	3	0.5
LE_S_DM_Dist	Diabetes Mellitus life expectancy	15	3
LE_S_MS_Dist	Muskuloskeletal life expectancy	20	2
c_E_Dist	Cost of Enabling	10,000.00	1,000.00

Triangular distributions are continuous distributions with a lower limit, mode and upper limit. Costs were defined as triangular distributions rather than normal distributions due to their large standard deviations which resulted in negative values. Similarly, the “up” variable required that a lower limit of 10 be set to avoid physical activity causing disutility.

Table 4: Parameters using triangular distribution

Name	Description	Minimum	Most Likely	Maximum
c_Ca_Breast_Dist	Indirect and direct costs of Breast Cancer	100.00	210,000.00	380,000.00
c_Ca_Colon_Dist	Indirect and direct costs of Colon Cancer	100.00	65,000.00	195,000.00
c_CHD_F_Dist	Indirect and direct costs of CHD - women	100.00	700,000.00	1,750,000.00
c_CHD_M_Dist	Indirect and direct costs of CHD - men	100.00	640,000.00	1,600,000.00
c_CVA_Dist	Indirect and direct costs of CVA	100.00	80,000.00	250,000.00
c_DEMEN_Dist	Direct costs of Dementia	100.00	295,000.00	465,000.00
c_DM_Dist	Cost of Diabetes Mellitus	100.00	220,000.00	630,000.00
c_MS_Dist	Indirect and direct costs of Musculoskeletal Disorders	100.00	195,000.00	370,000.00
up_Dist	QALY increase factor	1	1.1	2

A Beta distribution is a family of continuous probability distributions defined on the interval [0, 1] parameterized by two positive shape parameters, typically denoted by α and β. As utility and probability values are between 0 and 1, this is the most appropriate distribution to use. The parameters α and β were approximated in TreeAge Pro from the means and standard deviations found in the literature.

Table 5: Parameters using Beta distribution

Name	Description	α	β
c_down_Dist	Cost reduction factor	((0.8^2)*(1-0.8)/(0.1^2))	(0.8*(1-0.8)/(0.1^2))-((0.8^2)*(1-0.8)/(0.1^2))
p_Ca_Breast_Dist	Breast Cancer risk	((0.12^2)*(1-0.12)/(0.001^2))	(0.12*(1-0.12)/(0.001^2))-((0.12^2)*(1-0.12)/(0.001^2))
p_Ca_Colon_F_Dist	Colon Cancer risk - women	((0.05^2)*(1-0.05)/(0.001^2))	(0.05*(1-0.05)/(0.001^2))-((0.05^2)*(1-0.05)/(0.001^2))
p_Ca_Colon_M_Dist	Colon Cancer risk - men	((0.06^2)*(1-0.06)/(0.01^2))	(0.06*(1-0.06)/(0.01^2))-((0.06^2)*(1-0.06)/(0.01^2))

Name	Description	α	β
p_CHD_F_Dist	CHD risk - women	((0.2^2)*(1-0.2)/(0.001^2))	(0.2*(1-0.2)/(0.001^2))-((0.2^2)*(1-0.2)/(0.001^2))
p_CHD_M_Dist	CHD risk - men	((0.3^2)*(1-0.3)/(0.001^2))	(0.3*(1-0.3)/(0.001^2))-((0.3^2)*(1-0.3)/(0.001^2))
p_CVA_F_Dist	CVA risk - women	((0.15^2)*(1-0.15)/(0.001^2))	(0.15*(1-0.15)/(0.001^2))-((0.15^2)*(1-0.15)/(0.001^2))
p_CVA_M_Dist	CVA risk - men	((0.16^2)*(1-0.16)/(0.001^2))	(0.16*(1-0.16)/(0.001^2))-((0.16^2)*(1-0.16)/(0.001^2))
p_DEMEN_F_Dist	Dementia risk - women	((0.15^2)*(1-0.15)/(0.001^2))	(0.15*(1-0.15)/(0.001^2))-((0.15^2)*(1-0.15)/(0.001^2))
p_DEMEN_M_Dist	Dementia risk - men	((0.1^2)*(1-0.1)/(0.001^2))	(0.1*(1-0.1)/(0.001^2))-((0.1^2)*(1-0.1)/(0.001^2))
p_DM_Dist	Diabetes Mellitus risk	((0.2^2)*(1-0.2)/(0.001^2))	(0.2*(1-0.2)/(0.001^2))-((0.2^2)*(1-0.2)/(0.001^2))
p_down_Dist	Risk reduction factor	((0.8^2)*(1-0.8)/(0.1^2))	(0.8*(1-0.8)/(0.1^2))-((0.8^2)*(1-0.8)/(0.1^2))
p_LF_PA_Dist	Percentage physically active under Laissez-faire	((0.2^2)*(1-0.2)/(0.05^2))	(0.2*(1-0.2)/(0.05^2))-((0.2^2)*(1-0.2)/(0.05^2))
p_MS_F_Dist	Musculoskeletal disorder risk - women	((0.075^2)*(1-0.075)/(0.001^2))	(0.075*(1-0.075)/(0.001^2))-((0.075^2)*(1-0.075)/(0.001^2))
p_MS_M_Dist	Musculoskeletal disorder risk - men	((0.03^2)*(1-0.03)/(0.001^2))	(0.03*(1-0.03)/(0.001^2))-((0.03^2)*(1-0.03)/(0.001^2))
u_Ca_Breast_Dist	Utility of Breast Cancer	((0.6^2)*(1-0.6)/(0.1^2))	(0.6*(1-0.6)/(0.1^2))-((0.6^2)*(1-0.6)/(0.1^2))
u_Ca_Colon_Dist	Utility of Colon Cancer	((0.5^2)*(1-0.5)/(0.1^2))	(0.5*(1-0.5)/(0.1^2))-((0.5^2)*(1-0.5)/(0.1^2))
u_CHD_Dist	Utility of CHD	((0.683^2)*(1-0.683)/(0.15^2))	(0.683*(1-0.683)/(0.15^2))-((0.683^2)*(1-0.683)/(0.15^2))
u_CVA_Dist	Utility of CVA	((0.5^2)*(1-0.5)/(0.2^2))	(0.5*(1-0.5)/(0.2^2))-((0.5^2)*(1-0.5)/(0.2^2))
u_DEMEN_Dist	Utility of Dementia	((0.5^2)*(1-	(0.5*(1-0.5)/(0.2^2))-((0.5^2)*(1-

Name	Description	α	β
		0.5)/(0.2^2))	0.5)/(0.2^2))
u_DM_Dist	Utility of Diabetes Mellitus	((0.8^2)*(1-0.8)/(0.15^2))	(0.8*(1-0.8)/(0.15^2))-((0.8^2)*(1-0.8)/(0.15^2))
u_MS_Dist	Utility of Musculoskeletal disorders	((0.7^2)*(1-0.7)/(0.2^2))	(0.7*(1-0.7)/(0.2^2))-((0.7^2)*(1-0.7)/(0.2^2))

5.3.2. Cost-utility analysis

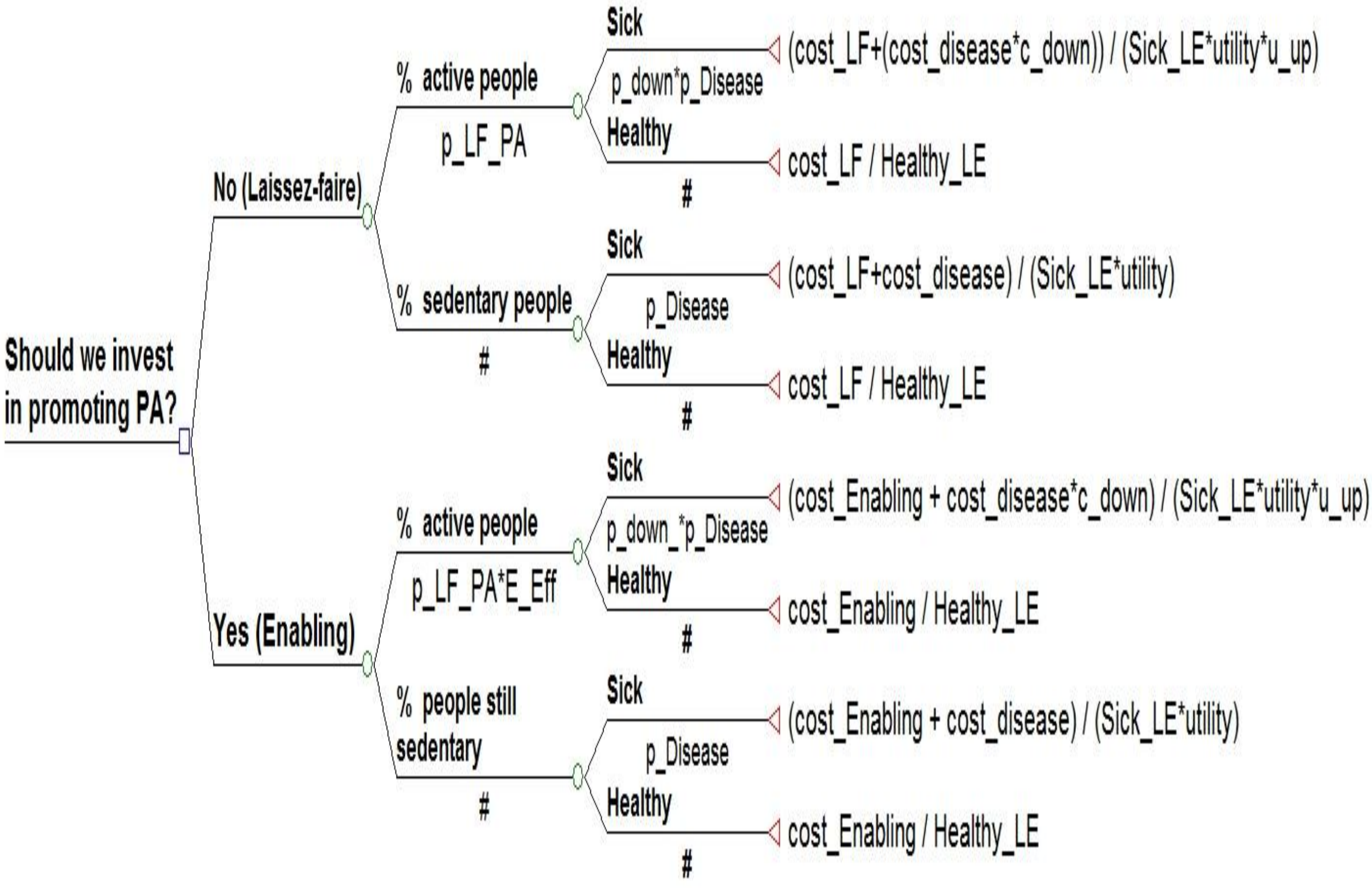

Figure 3: Schematic diagram of final model

The question of this dissertation is to determine whether promoting physical activity - the "Enabling" scenario – which involves investment of funds will bring benefit to society by increasing the number of active people as opposed to the current path of minimal involvement – the "Laissez Faire" scenario. Hence the cost-utility analysis moves the focus of the dilemma from an individual level to that of society in general and takes into account that physical activity does involve some cost.

Regardless of the policy decision there will be people who are physically active and those who are not, hence:

- p_LF_PA - the percentage of the population meeting recommended physical activity levels under the "Laissez-Faire" scenario
- p_LF_PA*(E_Eff + 1) – the percentage of the population meeting recommended physical activity levels under the "Enabling" scenario which is calculated by multiplying P_LF_PA by the percentage increase caused by the intervention (E_Eff – the effect of Enabling)

In the physical activity branch of the Enabling option, cost is represented as the sum of the cost of the intervention (c_E) and the cost of the disease, whereby disease cost is reduced by a set variable "c_down". For the sedentary branch cost is represented as the sum of the cost of the intervention and the cost of the disease. The variable cLF represents the cost of the Laissez-Faire option and was set to $0 in all iterations. This is based on the assumption that currently no money is being invested in facilitating physical activity on the national level but can theoretically be a range of values for policy makers considering increasing investment above a certain value.

Results of the CUA are expressed as an incremental cost-effectiveness ratio (ICER), that is, the ratio of change in costs to the change in effects. This represents the additional cost of one unit of outcome gained a healthcare intervention or strategy, when compared to its comparator. The formula is represented thus:

$$ICER = \frac{COST_{\text{new strategy}} - COST_{\text{current practice}}}{EFFECT_{\text{new strategy}} - EFFECT_{\text{current practice}}}$$

5.3.2.1. Additional variables used in CUA

Table 6: Additional variables used in CUA

Name	Description	Distribution Type	Minimum	Most Likely	Maximum
E_Eff_Dist	% change in PA due to Enabling	Triangular	0	0.25	1

Name	Description	Distribution Type	Mean	Standard Deviation
c_E_Dist	Cost of Enabling	Normal	10,000.00	1,000.00
Name	**Description**	**Distribution Type**	**α**	**β**
p_LF_PA_ Dist	Percentage physically active under Laissez-faire	Beta	((0.2^2)*(1-0.2)/(0.05^2))	(0.2*(1-0.2)/(0.05^2))-((0.2^2)*(1-0.2)/(0.05^2))

5.3.2.2. Calculating QALY's

Quality Adjusted Life Year's (QALY's) are calculated by multiplying years lived with a condition by the utility of that condition. For a cohort of healthy 40yr olds a combination of healthy life expectancy and life expectancy with disease is necessary. It was assumed that the utility of life before disease onset is 1.0 such that overall QALY's can be expressed as:

(Years between age 40 and disease onset * 1) + (Life expectancy at diagnosis * disease-specific utility)

Brønnum-Hansen et al (2007) estimate that physically active persons can expect to have 7 more QALY's than sedentary persons. Jonker et al (2006), Burnham and Wilcox (2002) and Franco et al (2005) also show increases in life expectancy and/or utility for active diabetic, cancer and CVD patients respectively compared to their sedentary counterparts. This was also demonstrated in a randomised control trial by Martin et al (2009) whereby post-menopausal women were assigned to groups in which they exercised at 0, 50, 100 and 150% of physical activity recommended levels. They report a significant, dose-dependent increase in 7 of 8 aspects of physical and mental quality of life. In this study the utility value for the physically active was multiplied by a set variable "up" in order to reflect this benefit.

Because utility and life expectancy for active individuals was further multiplied by the "up" variable it was necessary to ensure that the resulting figure did not exceed the total life expectancy at diagnosis.
For example: Life expectancy at diagnosis for Dementia is 6 years, utility ranges from 0.14 – 0.73 and "up" ranges from 1.0 – 2.0. If one was to take the upper ranges

the resultant life expectancy is 6 * 0.73 * 2 = 8.76 which is higher than life expectancy at diagnosis. The formula was therefore modified to take the lower of life expectancy at diagnosis and the utility adjusted life expectancy at diagnosis.

5.4. Sensitivity Analysis

An essential step in the modelling process is the sensitivity analyses. Given the uncertainty present in most economic evaluations, it is necessary to systematically vary the input parameters across their possible ranges and calculate the possible ratios based thereon thereby testing the assumptions used. If the conclusion remains unchanged the result can be said to be robust. If the results are not robust, the sensitivity analysis can point to areas where more information is needed, where uncertainty is most crucial and to variables that have greatest bearing on the conclusion (Shiell et al, 2002). Univariate sensitivity analyses plotted the results against key parameters within the full range of values used in the analysis.

5.5. Threshold Analysis

Threshold analysis seeks to identify the critical value of parameter that would need to be achieved in order for an intervention to be deemed cost-effective. Debate exists over the appropriate benchmark for societal willingness to pay per quality-adjusted life year (QALY) gained as well as the appropriateness of the measure itself. Most investigators subscribe to a $50,000/QALY cost-effectiveness threshold which corresponds to the CE of kidney dialysis when the end-stage renal dialysis programme was added as a new coverage under the U.S. Medicare system in 1972. However it is generally acknowledged that this is an arbitrary criterion, one that has not been revised to allow for inflation and national variation, and probably owes more to being a round number than to a well-formulated justification for a specific value.

6. Results

6.1. Cost-minimisation analysis

6.1.1. CMA Base case

Table 7: CMA Base case, Two-dimensional (Sampling and Trials) - 50,000 iterations

Statistic	C(PA)	C(no_PA)	Saving
Mean	$208,219	$325,260	-$117,041
Std Dev	$57,090	$68,286	
Minimum	$47,777	$104,130	-$56,353
2.50%	$109,045	$197,424	-$88,379
10%	$137,704	$237,945	-$100,241
Median	$204,006	$323,164	-$119,158
90%	$284,826	$415,623	-$130,797
97.50%	$331,020	$462,428	-$131,408
Maximum	$459,685	$606,695	-$147,010

The median life-time saving in health costs achieved by becoming physically active at age 40 is close to $120,000 with gain of 3.1 Quality adjusted life-years. Assuming a life expectancy of 40 years (39.39 based on United States 2004 Social Security Administration data and 39.81 based on Israeli 2000 Central Bureau of Statistics data) this equates to a saving of $3,000 per active vs. inactive person each year.

One can spend just $150 per person in the cohort, assuming that only 5% become physically active, multiplied by a population of 80,000 (Israeli Central Bureau of Statistics, 2008) this allows for an annual investment of $12 million per year to reap the benefits of physical activity and still have an overall zero cost to society.

6.1.2. CMA Sensitivity analyses

The key parameters varied in the sensitivity analyses are: p_down, c_down and up. Disease costs and life expectancies are the same in both arms of the tree and thus were not expected to make a difference to relative results.

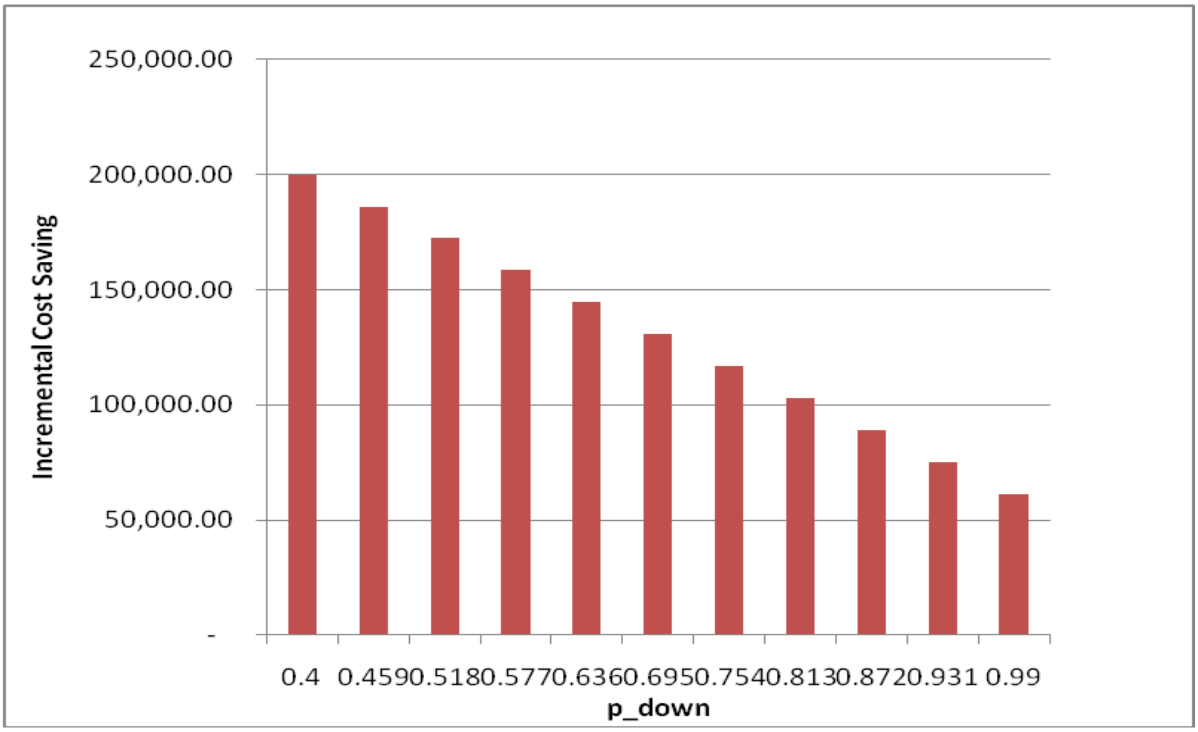

Figure 4: One-way sensitivity analysis on disease risk reduction and incremental cost savings

If disease risk is reduced by 60% a sedentary individual who becomes active can expect to incur $200,000 less in medical costs, Even a 1% decrease in lifetime risk will involve a substantial saving i.e. $60,000 over a lifetime.

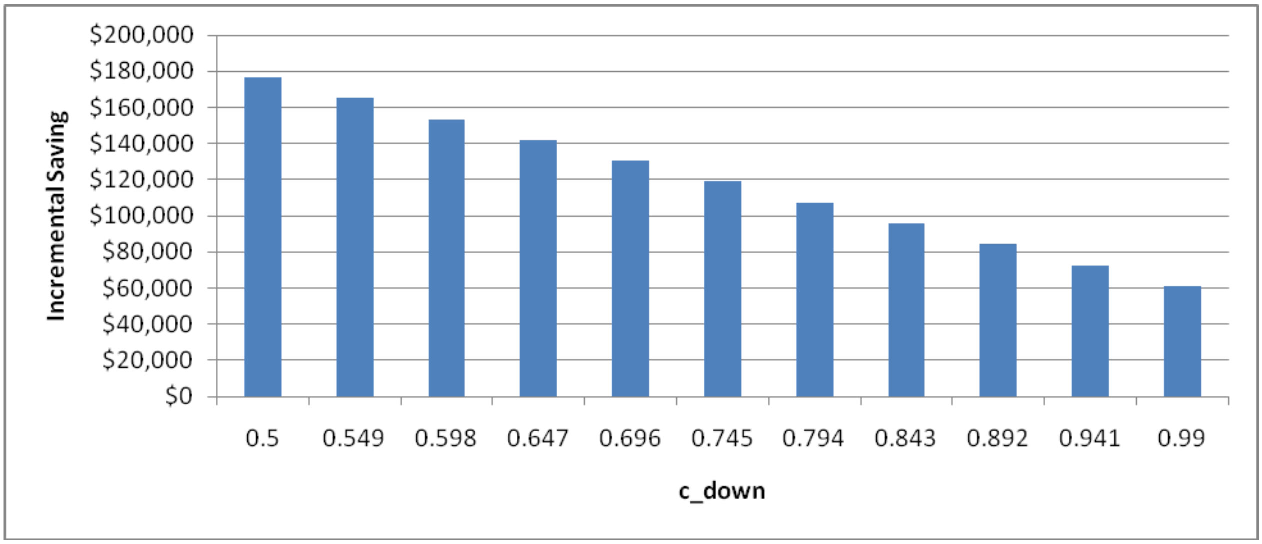

Figure 5: One-way sensitivity analysis disease cost reduction and incremental cost savings

Varying disease cost reduction from 1-50% for active people results in a lifetime saving of $61,000 – 175,000.

Since public health is concerned with the overall health of a community it is appropriate now to turn to the Cost-Utility Analysis which assesses the levels of population adherence to PA recommendations and the amount of financial investment required for Enabling to be cost-effective.

6.2. Cost-utility analysis

6.2.1. CUA Base case

Table 8: CUA Base case, Two-dimensional (Sampling and Trials) - 50,000 iterations

Statistic	**Cost(E)**	**QALY(E)**	**Cost(LF)**	**QALY(LF)**	***ICER***
Mean	$302,217	23.22	$302,017	22.87	$571.43
Std Dev	$62,974	1.52	$64,006	1.47	
Minimum	$86,484	16.84	$85,507	16.73	$8,881.82
2.50%	$184,170	20.24	$181,884	19.97	$8,466.67
10%	$221,686	21.28	$220,159	20.97	$4,925.81

Median	$300,671	23.21	$300,737	22.86	Dominant
90%	$385,125	25.16	$386,102	24.74	Dominant
97.50%	$428,742	26.21	$429,473	25.76	Dominant
Maximum	$570,102	30	$566,434	28.88	$3,275.00

As can be seen, in the base case scenario, Enabling physical activity has a median ICER of $571/QALY which is well below the most stringent of threshold values.

Differences between benefits and cost/benefit ratios in the Enabling and Laissez-faire arms were significant with $p \approx 0$. However differences in costs were not significant ($p = 0.64$). This is likely due to the baseline 20% reduction in disease cost being offset by the addition of the $10,000 per person per lifetime cost of enabling physical activity. The increased benefits from PA were not similarly offset by detrimental factors such as injuries.

6.2.2. CUA one-way sensitivity analyses

As in the cost-minimisation analysis, disease probabilities, costs and utilities were not significant deciding factors as identical parameters were used in all arms of the model. Important potential differences were assessed as:

- The cost of Enabling
- The proportion of people being physically active under each scenario
- The proportion of each sex out of the active population
- The degree to which physical activity increases life expectancy and quality
- The degree to which PA decreases probability of disease
- The degree to which PA decreases disease cost

Cost of Enabling

For lifetime costs of enabling ranging until approximately $5,000 per person the Enabling option is dominant. Up until $7,500 per person, per lifetime the Enabling option still remains below the $50,000/QALY mark, increasing to over $90,000/QALY at $50,000.

If in 2008 there were 82,000 Israelis aged 40 (Central Bureau of Statistics), over

US$400 million could be spent on promoting physical activity and still yield a net cost saving while improving the health status of this cohort. If one is prepared to spend $50,000 per QALY gained this would entail an investment of close to USD1 billion over the lifetime of this cohort or $25 million per year (undiscounted).

Proportion of physically active people (p_LF_PA)

The decision tree proved to be sensitive to the percentage of people who meet physical activity recommendations under the Laissez-faire scenario. Keeping in mind the base case value of E_Eff (a 25% increase in active people under the Enabling scenario), for values of p_LF_PA over 37% Enabling is the dominant option. If between 23% and 32% of the population is currently physically active (as reported in the Israeli Department of Health 2003-4 National Health survey, figures are for the population aged 21- 44 and 45-64 respectively) the ICER is approximately $19,200 - $68,600/QALY whereby the smaller the proportion exercising the higher the ICER.

Degree to which Enabling increases the active population (E_Eff)

Unsurprisingly, the greater the increase in the active population due to Enabling, the more cost-effective this option is. If the increase is less than 25% (under 30% in total being sufficiently active) the incremental cost per QALY of Enabling exceeds the $100,000/QALY mark. If it is greater than 31% (over 26% of the population meeting recommended physical activity levels) Enabling costs less than $50,000 per QALY gained. If there is no change Laissez-faire is obviously the dominant strategy. Should Enabling cause an increase of over 47,5% (30% of the population exercising at least 30 minutes on most days of the week) in the active population it becomes the dominant strategy.

Each percentage increase in the effectiveness of Enabling results in a cost reduction of about $211 per person per lifetime with the benefit of approximately 0.0022 QALY's. Assuming again a population of 82,000 this amounts to over $17million less in costs and a gain of 180 QALY's per percentage increase

The graph below shows the net health benefits (NHB) incurred (relative to a willingness-to-pay threshold of $50,000/QALY) with each percentage increase in the active population. NHB represents a new approach for the analysis of uncertainty in health economic evaluations. It is defined as the difference between the new interventions effects and its cost divided by the willingness-to-pay threshold. In order that the technology would be socially worthwhile, the NHB should be positive

If "Enabling" increases the active population by 20% the QALY's gained under the "Enabling" and "Laissez-faire" scenarios are equal at 26.74. Above this value "Enabling" (green line) represents an increasing QALY gain.

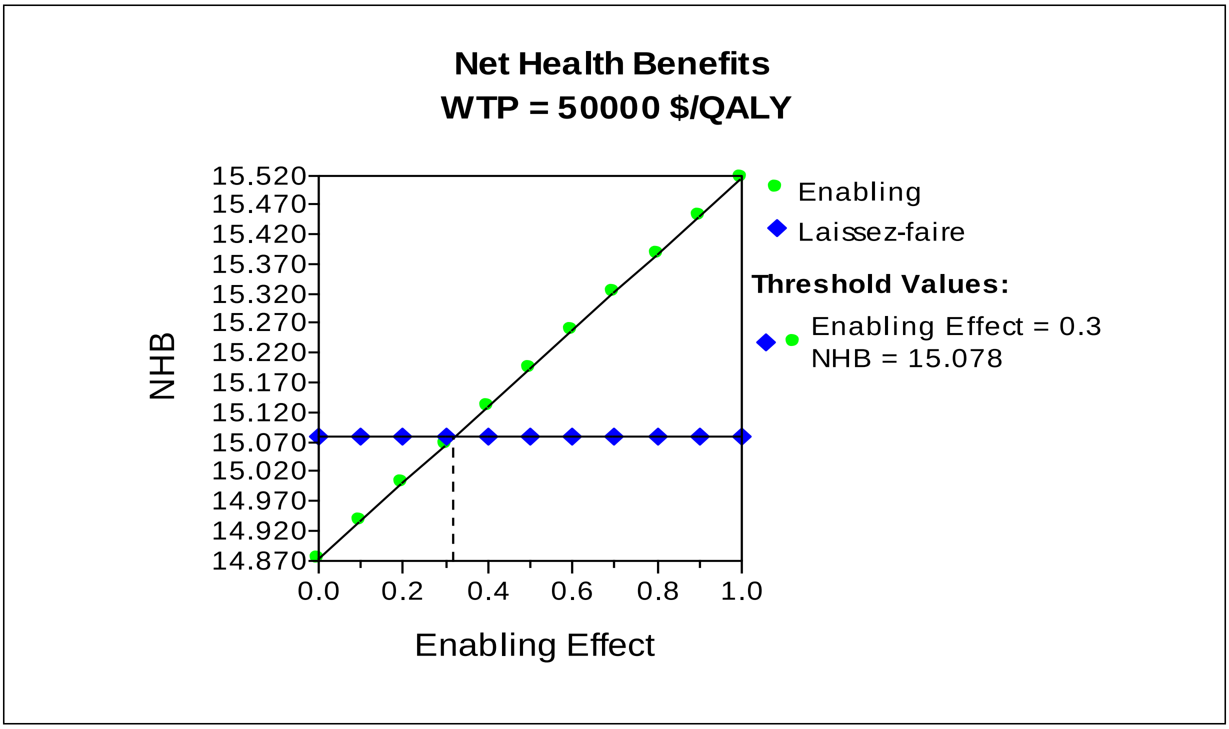

Figure 6: Net Health Benefits of increasing levels of Enabling's effectiveness

Proportion of females

The model assumes that males and females are distributed equally; this is despite studies that show that men tend to be more physically active than women. Hence a sensitivity analysis was run to determine if the proportion of men vs. women among the physically active has a bearing on results. The percentage of physically active women varied from 20-70% (by inference, the percentage of active men varied from 30-80%) and the ICER of Enabling was not significantly altered ranging from $99,700/QALY - $90,500/QALY with the lower ratio representing the higher percentage of active women (see Appendix F for data).

Reduction of disease probability

Model results proved sensitive to the degree to which physical activity decreases the risk of contracting one of the model ailments. For values of p_down until about 0.81, i.e. a 19% reduction in probability, Enabling remains cost effective at the $100,000/QALY mark. Enabling is below $50,000/QALY for values of p_down below 0.65.

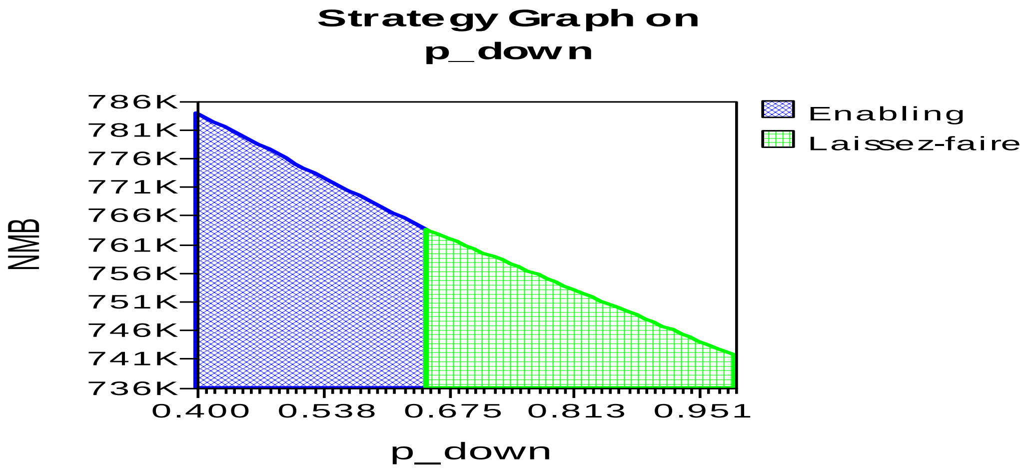

Figure 7: Sensitivity analysis on disease risk reduction and incremental cost/QALY

The lower the value of p_down the greater the decrease in disease risk and the lower the incremental cost paid per QALY gained.

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Decrease in disease cost

Similarly, enabling physical activity is cost-effective at the $50,000/QALY mark for values of c_down below 62% - hence disease costs would need to be at least 38% less for a physically active versus a sedentary person in order for Enabling to be cost-effective.

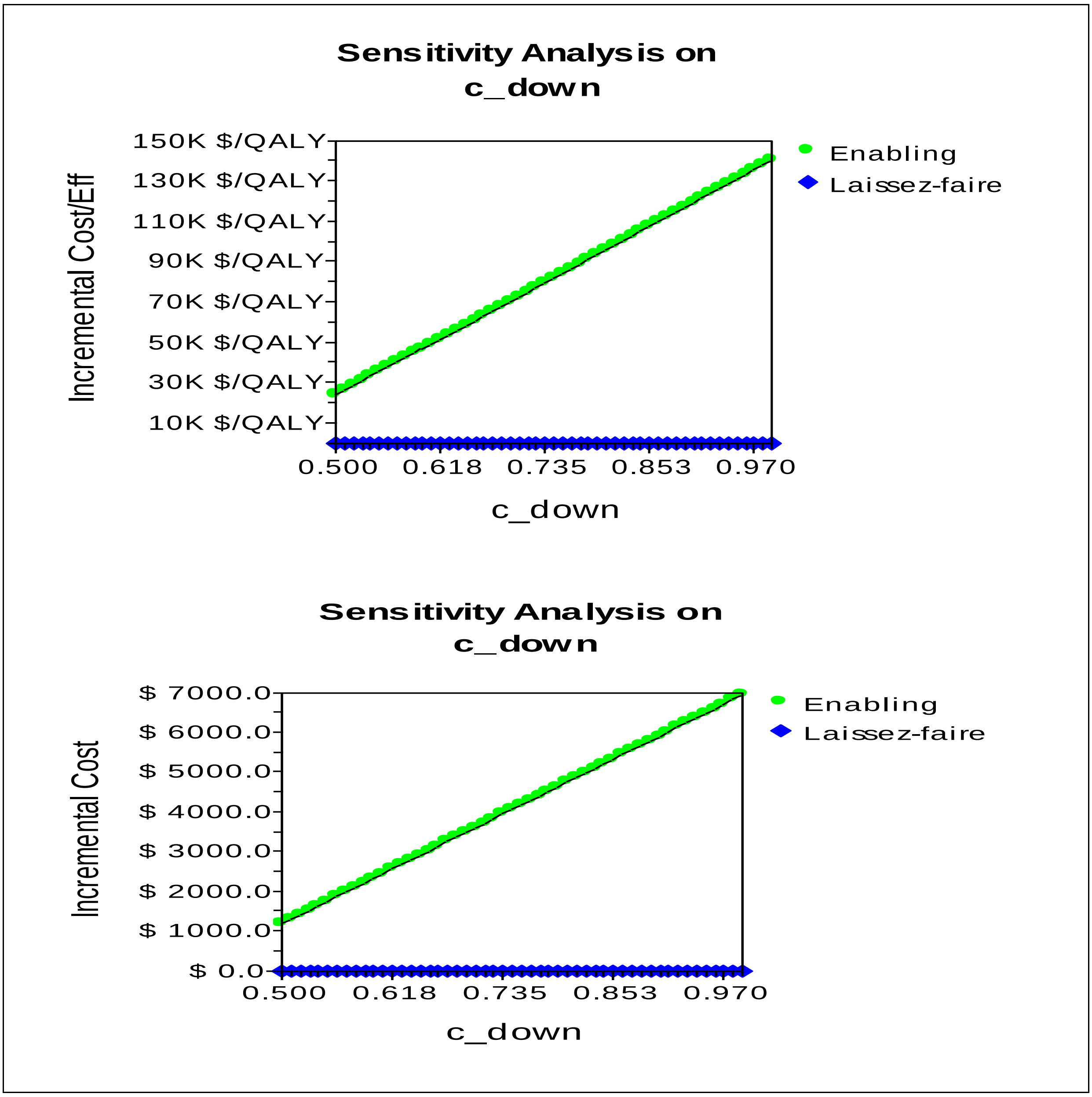

Figure 8: Sensitivity analysis on disease cost reduction and incremental cost

Increase in utility and life expectancy

The increase in “up” did not prove to be a significant factor in favour of Enabling with a best-case ICER of almost $52,000/QALY when PA doubles utility and life expectancy. For the more realistic value of 20% the ICER approaches $100,000/QALY.

Table 9: One-way sensitivity analysis threshold values

Variable	Dominant	<$50,000/QALY	<100,000/QALY	Dominated
Cost of Enabling	**$5,000**	**$7,700**	**$10,500**	**n/a**
Effectiveness of Enabling	**0.48**	**0.32**	**0.25**	**0.02**
Baseline active population	**0.38**	**0.25**	**0.20**	**n/a**
Females	**n/a**	**n/a**	**All values**	**n/a**
% increase in QALY	**n/a**	**n/a**	**1.2-2**	**n/a**
Disease risk reduction	**0.4**	**0.65**	**0.81**	**n/a**
Disease cost reduction	**n/a**	**0.61**	**0.82**	**n/a**

6.2.3. CUA Two-way sensitivity analyses and threshold analysis

The model was run several times in order to investigate the effect of varying 2 parameters at the same time.

6.2.3.1. Cost of Enabling and its effect

The most important combination was assessed as the interplay between the cost of Enabling (c_E) and its immediate results as measured as increase in percentage of people being physically active (E_Eff) where 1 represents a doubling of the active population (100% increase). At the $11,000 cost of Enabling per person-per lifetime one would require an increase of 32% in the active population for the ICER to be less than $50,000. If $100,000/QALY gained is the cut-off point one could spend closer to $13,000 per person with a 28% increase or perhaps $25,000 with a 56% increase and still remain within an acceptable range.

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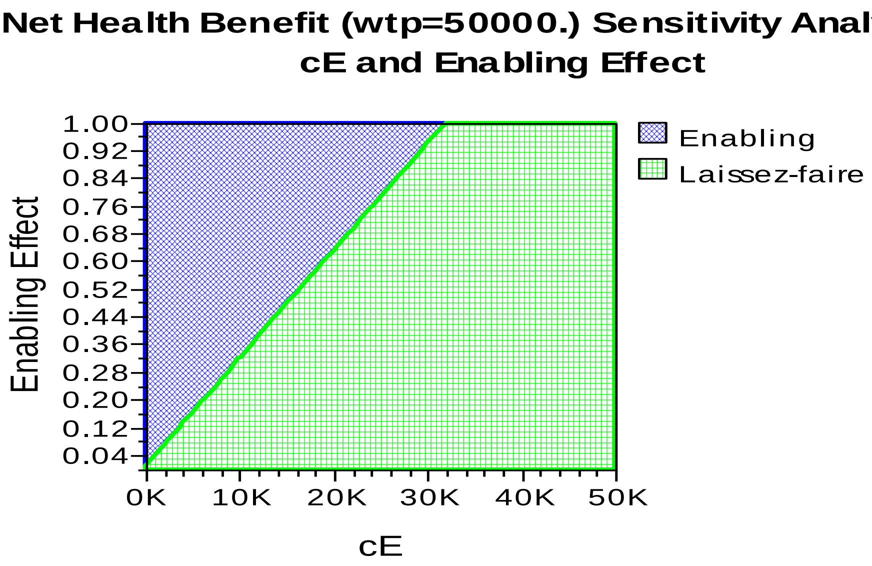


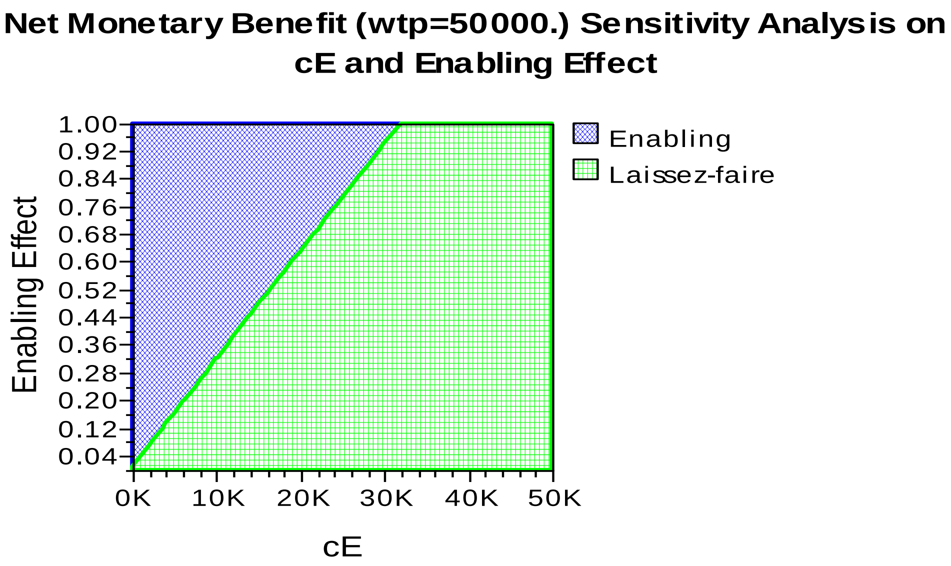


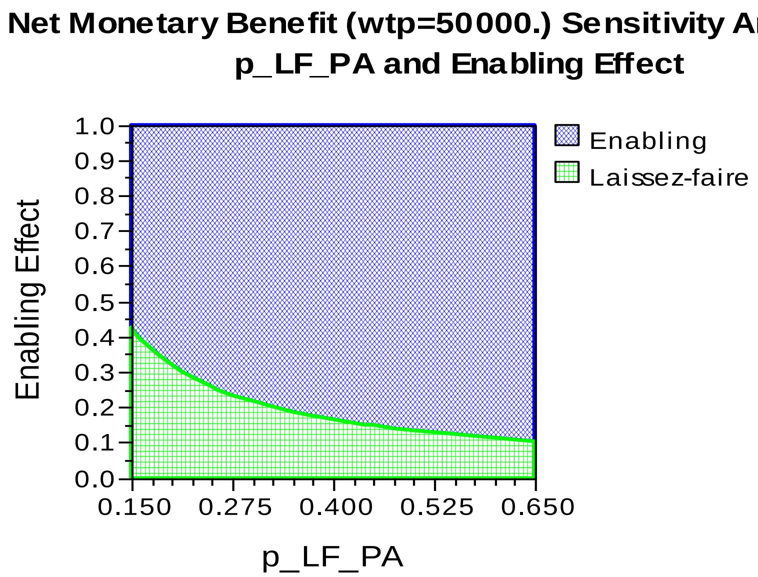
Figure 9: Sensitivity analyses on Cost and Effectiveness of Enabling

Net monetary benefits are defined as the effectiveness of the intervention multiplied by the willingness-to-pay threshold, less its cost.

6.2.3.2. Baseline active population and Enabling effect

The results show that the larger the active population at baseline, the greater the benefit from an increase. However if the increase is just 10% one would need a baseline of 52% of the population being active for the ICER to be below

$100,000/QALY gained. The 2003-4 Israeli Health Survey reported 32% of adults aged 45-64 being active at least 3 times a week in the month preceding the survey. While this includes some insufficiently active people, a 20% increase in this figure would be cost-effective at just under $50,000/QALY gained. Below these figures the ICER is not cost-effective.



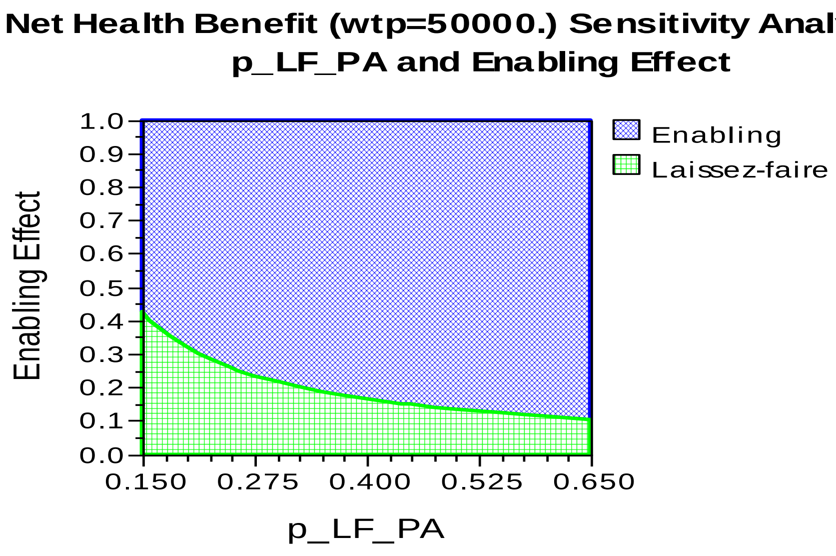


Figure 10: Sensitivity analyses on the percentage of the population meeting PA recommendations under the Laissez-faire scenario and Effectiveness of Enabling

Other combinations tested were:

1. Cost of enabling (cE) and

a. Degree of cost reduction (c_down)

- For all values of cE under $5,000 Enabling is dominant regardless of cost reduction.
- However, if c_down is greater than 70% (i.e. less than 30% reduction in disease costs due to physical activity), for values of cE greater than $15,000 the cost-utility of Enabling is greater than $100,000/QALY and potentially unaffordable.

b. Degree of disease risk reduction (p_down)

- For all values of cE under $5,000 Enabling is dominant regardless of risk reduction.

For values of cE greater than $15,700 and values of p_down greater than 87,2% (i.e. less than 13% reduction in disease risk) the cost-utility of Enabling is greater than $100,000/QALY. If PA reduces disease incidence by 40% (p_down = 0.6) Enabling is not dominant from $10,000 but cost/QALY remains below $100,000 even when Enabling itself costs $15,000 per person per lifetime.

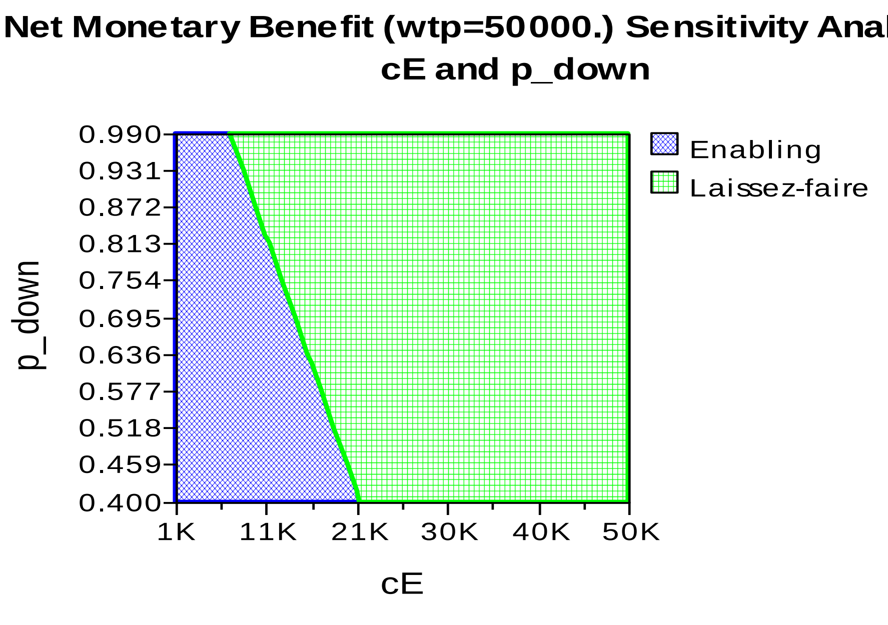


Figure 11: Sensitivity analysis on the cost of enabling and the degree of disease risk reduction

a. Degree of QALY increase (up)

- For all values of cE under $5,000 Enabling remained dominant.
- For values of cE greater than $10,000 and values of up below

1.1 (i.e. less than 10% increase in QALY) the cost-utility of Enabling is greater than $100,000/QALY.

1. Reduction in cost and risk (c_down and p_down)
   - For values of c_down and p_down below 0.9 and 0.84 respectively, the incremental cost-utility ratio of Enabling was less than $100,000/QALY. Hence, even if the probability of contracting a disease is reduced by just 13% and disease cost by 20%, Enabling PA remains close to the upper limit of acceptable values.

2. Reduction in cost and increased utility (c_down and up)
   - The maximum cost-utility ratio of Enabling for the ranges tested is $360,000/QALY
   - Enabling costs less than $50,000 per QALY gained in all cases where c_down is less than 0.75 (i.e greater than 25% reduction in cost) and where physical activity increases utility by more than 50%.

3. Reduction in risk and increased utility (p_down and up)
   - Only when physical activity decreases disease risk by less than 25% and increases utility by less than 50% do we obtain an ICER of greater than $50,000/QALY.
   - In all cases where p_down is less or equal to 0.75 the ICER of Enabling is less than $50,000/QALY.

6.2.4. CUA Three-way sensitivity analyses

Tree-Age also allows the user to simultaneously vary 3 parameters, creating an animated graph to illustrate the preferred option based on a predetermined willingness-to-pay threshold; in this case it was set at $50,000/QALY gained. One can see for example, the interplay between disease lifetime risk reduction (p_down) and disease cost reduction (c_down). Even when utility is unchanged (up) Enabling PA is still cost effective at most values.

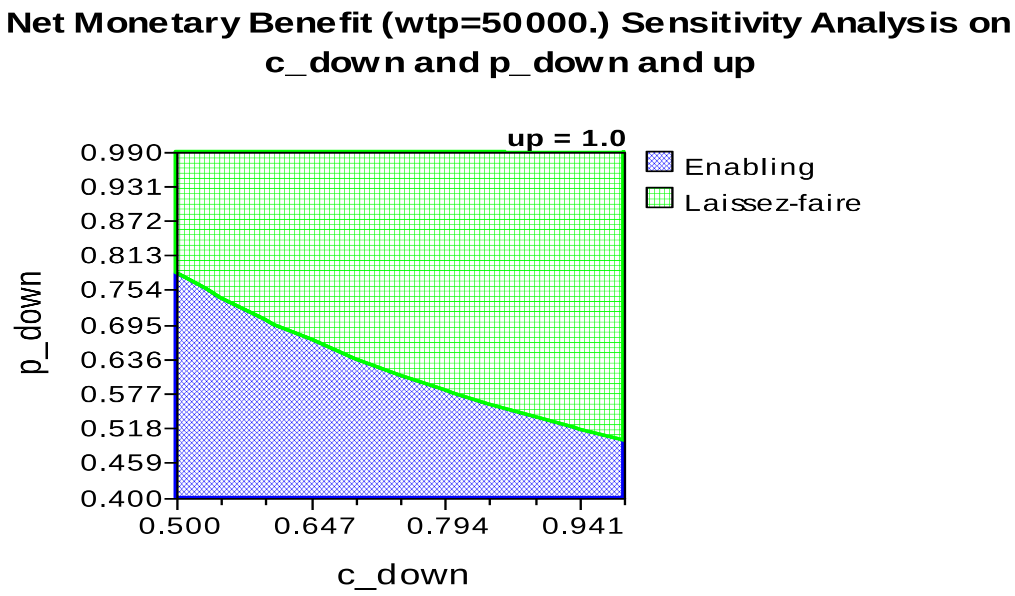


Figure 12: 3-way sensitivity analysis – degree of disease risk reduction, degree of disease cost reduction and up = 1

Just a 20% increase in utility gives even more favourable results:

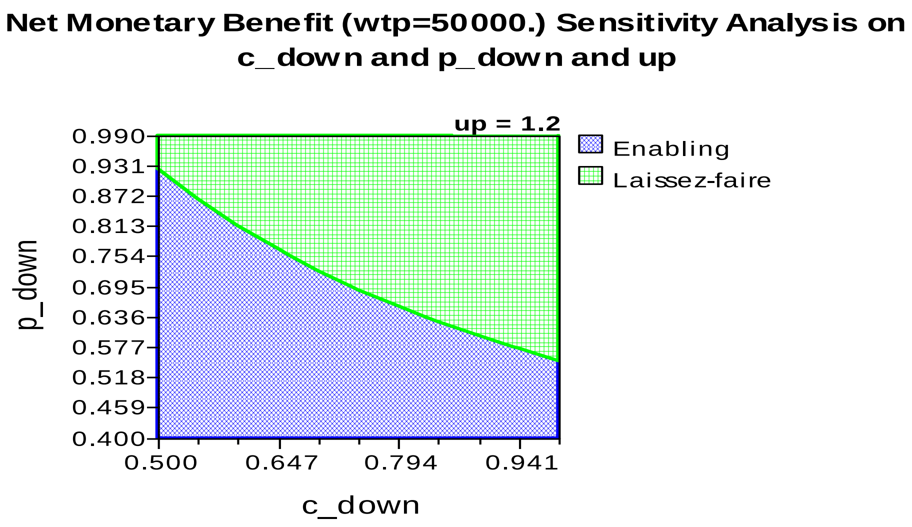


Figure 13: 3-way sensitivity analysis - degree of disease risk reduction, degree of disease cost reduction and up = 1.2

In the series below one can see the interaction between the cost of Enabling (cE), it's effectiveness (E_Eff) and reduction in disease risk (p_down). Here it is apparent that even at low levels of effectiveness promoting physical activity is cost-effective due its favourable impact on lifetime disease risk.

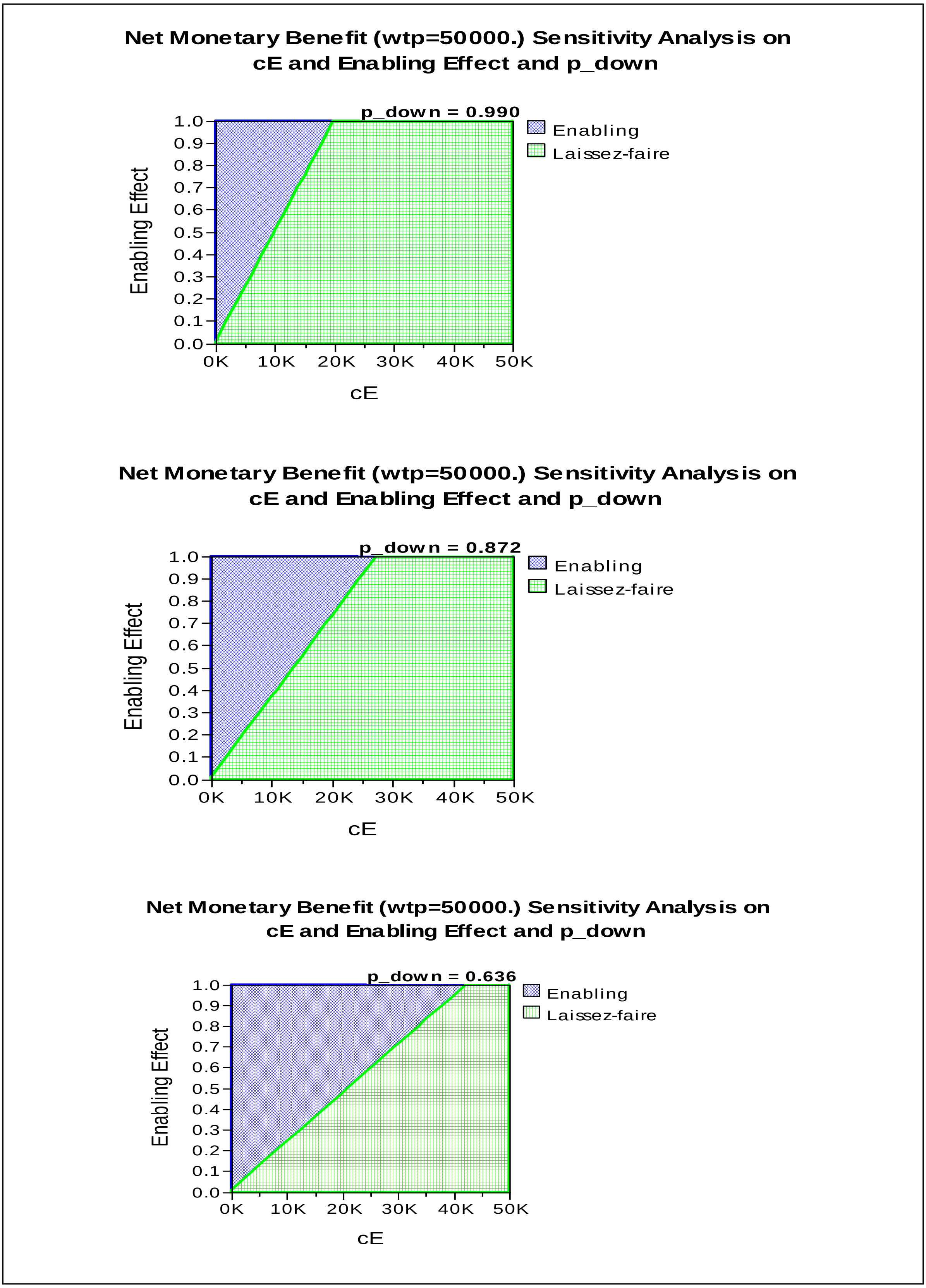


Figure 14: 3-way sensitivity analysis on the cost of Enabling, the effect of Enabling and the degree of disease risk reduction

7. Discussion

This paper reinforces current knowledge regarding the benefits of physical activity. A single person can save close to $120,000 in health costs over a lifetime or $3,000 a year, by initiating this lifestyle change. If we assume that parameters are largely unchanged for a cohort aged 20-65 years we can multiply these figures by the over 3.2 million adults in Israel and see a potential annual saving of close to $10 billion. Even if only 1% becomes active one could invest $90 million a year and still realise a saving. This is keeping in mind that savings are underestimated as many conditions are not included in the model and a person can suffer from more than one chronic disease. A “back-of-the envelope” calculation (see Appendix H) which ignores these constraints and shows a per-person saving of closer to $200,000 – albeit not an order of magnitude greater but still important, particularly since it still excludes conditions for which at least one parameter was missing and it does not take into consideration evidence that disease management is cheaper for physically active people.

As can be seen, the model makes a strong case for facilitating physical activity in a cohort of healthy 40yr olds. Differences in benefits and cost-benefit ratios between the “Enabling” and “Laissez-faire” arms were highly significant with $p \approx 0$.. In the base case, using mean parameter values, promoting physical activity costs less than $600 per QALY gained, 50% of all iterations resulted in Enabling being both less costly and more beneficial (dominant) compared to Laissez-faire. The incremental cost-effectiveness ratio is less than $10,000 making investing in PA far below even the most stringent willing-to-pay threshold in use today. The model does prove to be sensitive to variation in key model parameters such as cost of intervention, its effectiveness, baseline active population as well as degree of disease risk and cost reduction. Change in utility and proportion of females were not significant deciding factors.

Annemans and others have shown that the results would be even more dramatic for older populations and those already at risk of chronic disease (hyperlipidaemia, hypertension, metabolic syndrome) as well as showing benefit for younger, healthier cohorts as well.

These results are largely compatible with results from similar studies:
Annemans et al report a narrower but similar ICER's range of €2,000-15,000/QALY gained ($1500 - $11,000 based on mid-2007 exchange rate) for physical activity versus inactivity study. This difference can be attributed partly to a more limited condition set which would tend to reduce the uncertainty in the model and partly to use of a Markov model which allows for annual changes in risk as well as discounting.
The NICE cost-effectiveness analysis (2006) and Cobiac et al (2009), on the other hand, reported more favourable results. However, Cobiac et al assigned greater health benefits accruing from PA than those used in this model. Furthermore, intervention costs in the NICE study are low (maximum $544 per participant) and are accrued on an individual basis instead of a population-wide basis. The Cobiac study included both individual-based as well as population-based programmes which would also tend to decrease intervention costs. Lastly, both of these studies they measured effectiveness in terms of change in average community physical activity levels. This allows for the accumulation of benefits to sedentary people becoming inadequately active as well as inadequately active people becoming more active whereas this dissertation, like Annemans et al, calculates intervention effectiveness in terms of percentage of the sedentary population becoming adequately active.

It is hoped that the results of this study add to the growing literature giving weight to arguments that will convince policy-makers that investing in a national programme to promote physical activity is a worthwhile use of public funds as it has proved to be cost-effective in most scenarios and may even show to be cost-saving.

8. Model Limitations

Limited set of conditions

The main limitation of studies based on simulation modelling is that they are only as good as the data that are available to be incorporated into it. The desire to make the model as comprehensive as possible was hampered both by model structure and by the lack of appropriate data for some conditions. For instance, in the field of reproduction, while fertility is reported to be significantly improved by PA and while the cost of the medical therapy including in-vitro fertilisation is substantial, data on the lifetime cost of such treatment is unavailable and the volume of studies on physical activity and infertility is low. Similarly data has only recently begun to emerge on the beneficial effects of physical activity on kidney function (Robinson-Cohen et al, 2009) but to date there is not enough evidence to justify inclusion in the tree. This limitation would serve to underestimate the advantages of PA versus inactivity.

Measurement error

Physical activity consists of a complex set of behaviours including active commuting, occupational activities, recreational activities such as gardening, and more purposeful activities such as gym-based exercise and sport. This presents many measurement challenges, and no standardised instrument as yet exists that can effectively quantify the true level and pattern of an individual’s activity behaviour. Furthermore, physical activity cannot be easily dichotomised like smoking versus non-smoking, nor can it be placed on a simple continuum like cholesterol and blood pressure (Powell et al 1987). Hence the association between physical activity and disease is dependent on each study's definition of physical activity. However, Britain's Chief Medical Officer (2004) believes that measurement error is more likely to reduce rather than increase the strength of relationships between physical activity and health, thereby augmenting the argument in favour of investing in promoting physical activity.

Dichotomisation of Physical Activity

Despite the above, this model assumed that enabling physical activity will result in the benefits incurred from going from a state of inactivity to that of meeting recommended levels. However, enabling physical activity on a community-wide basis can also bring about the following changes in population physical activity levels:

1. Persuade the sedentary to become somewhat more active, albeit not meeting recommended levels of activity.
2. Encourage people who, at baseline, are somewhat active, to meet recommended levels.
3. Facilitate the already active population to exceed recommended activity levels.

By excluding these eventualities, the model underestimates the impact of physical activity on health. It is also assumed that levels of activity will be maintained throughout a person’s lifetime. This would tend to overestimate the impact of any intervention. However, since the baseline cost of the intervention is relatively high there is no reason to assume that it is a one-time investment rather than a steady budget allocated for this purpose. That said, there is a clear dose-response relationship between both duration and intensity of PA and morbidity and mortality hence any intervention that increases the dose will result in benefits to the individual and society.

Reconciliation of data sources

As discussed in-depth in the "Costs" section, considerable difficulty was encountered when attempting to reconcile data sources. Information was gathered from many studies, using diverse populations, different base assumptions, dissimilar treatment modalities and varying operational definitions of key concepts such as physical activity, costs, and disease states.

For example, definitions of physical activity in the literature range from relatively simple groupings based on self-report of time spent exercising and/or exercise intensity (defined either in terms of metabolic equivalents or as low, moderate, or high) to technical measurements of fitness using duration of a maximal graded treadmill exercise test or number of impacts within specified acceleration ranges. The most common definition of physical activity corresponds to the American Centers for Disease Control recommendation of at least 30 minutes of moderate activity on most days of the week.

It cannot be confidently asserted with any confidence the degree or direction of change this would imply. Some factors would serve to overestimate and others to underestimate the strength of effect between PA and outcomes. For example self-reported physical activity tends to overestimate time spent on sedentary activities and overestimate physical activity (Chinapaw et al 2009, Boon et al 2008). This would tend to strengthen the correlation between PA and health.

Excluded cost variables

Three cost factors were not taken into consideration in the model:

1. The monetary and time costs of physical activity:
   Time and money spent on physical activity are discretionary expenses which are dependent on individual preferences, needs and resources. Hatziandreu et al (1988) estimate that for 55% of people the opportunity cost is cancelled out by enjoyment, the 35% who are neutral would value their time at half their hourly pay rate whereas the 10% who dislike physical activity would value their time at their hourly pay rate.
   The monetary costs associated with physical activity are highly variable ranging from running shoes, which can be used for a few years, to fitness club membership with personal training and upwards. Most studies concur that the time and monetary costs of physical activity is most salient in studies of specific interventions.
2. The negative outcomes of physical activity:
   Risks of physical activity, for example injuries and exposure to environmental pollutants have not been quantified in terms of probability or cost.
   Researchers tend to agree that while these risks are often headline grabbing, for example sudden cardiac death, they are negligible.

3. Long term increased health costs occurring as result of increased life-expectancy:
   It is possible that any intervention that prevents/mitigates disease and consequently extends the life of a population will reduce health costs in the shorter term at the expense of increased health costs in the longer term: As human life expectancy increases, health-related costs are incurred for an extended period of time. A person whose colon cancer is averted due to a healthy lifestyle may go on to develop other, less preventable and possibly more expensive conditions. Also older patients tend to cost more to treat per episode of ill health and are at greater risk than younger people.
   This is a contentious issue; it is by no means obvious that the decline in mortality brings with it an increase in chronic illness and disability. There are many who posit that human life expectancy is approaching its biological limit such that postponement of disease onset leads to a "compression of morbidity" whereby incapacity is compressed into a shorter period of life. Regardless of this debate, preventing sickness has value in human terms that simple econometrics cannot capture.

These omissions are generally accepted in the literature and Beale et al (2007) believe that they are unlikely to significantly impact on QALY results.

Interactions and Co-morbidities

Physical inactivity is an independent risk factor for obesity, diabetes, cardiovascular disease, osteoporosis, and many other conditions. Furthermore, certain conditions are risk factors for others: obesity for diabetes for cardiovascular disease, for example. Similarly, an individual may have two or more unrelated conditions such as dementia and cancer. The multiple effects of increased activity across these many chronic conditions are rarely considered in study design as they would make the model unwieldy, so the true value of physical activity in terms of public health are likely under-estimated as while the beneficial effects seen within specific diseases are important in their own right, possibly the greatest public health contribution of physical activity is its strength of effect over such a wide range of common diseases.

9. Directions for further study

Barriers to Physical Activity

Barriers to physical activity are specific to gender, age and culture. For example, women tend to be less physically active, most often stating lack of time due to multiple competing commitments as a barrier to PA (Andajani-Sutjahjo et al, 2004). Older adults tend to attribute health problems to aging rather than illness (Sarkisian et al, 2005) hence they are not aware how physical activity can improve and preserve functioning. They also have a greater fear of falling and are more susceptible to injuries due to age-related physiological changes (Dergance et al, 2003). Despite these concerns Stessman et al found that, among the elderly, the frequency of falls, fractures, and chronic joint or musculoskeletal pain was consistently lower among the physically active population.

The interplay between factors is complex and has to do with personal factors such as self-efficacy, self-discipline, self-motivational characteristics, beliefs, expectations and knowledge regarding physical activity, previous experience in sports, family and peer support and degree of enjoyment.

Chinna et al (2006) stress the importance of categorising barriers as either internal or external, stating that external barriers, such as lack of transport are more amenable to change than internal barriers such as lack of motivation. Ideally one would want to quantify these barriers to enable a more accurate definition of the indirect costs of physical activities. This was outside the scope of this paper but can be a fruitful topic for further research.

Risks of physical activity

There are many potential hazards of physical activity resulting in acute or chronic, mechanical, metabolic, or psychological injury. However scant documentation of these detrimental effects exists. Powell and Paffenbarger (1985) report that even for the six most commonly reported aerobic activities among adults in the United States (walking, jogging, swimming, cycling, calisthenics, and racket sports) there is almost no information about injury incidence. A cursory search in PubMed shows this to be largely unchanged.

Other unquantified concerns are: increased exposure to air pollution and to sunburn, attacks from animals or humans, falls onto hard surfaces, injury from being struck by a bat or ball, colliding with other players, or being subjected to interpersonal violence. Unfavourable weather conditions coupled with severe or prolonged exertion can lead to dehydration, hyperthermia, heat stroke and, conversely, hypothermia with activities performed in cold conditions. The British Chief Medical Officer mentions that the risk of bacterial infection increases with activities such as swimming, and continued high volumes of exercise can increase the risk of infections due to immunosuppression. High levels of some activities (such as long-distance running) can also cause haematological disturbances such as haematuria.

Furthermore, it is also difficult to find information on the numbers of people who take part in different activities, and how frequently.

Studies that explore these fields would be of benefit to those wanting to quantify these risks in order to have a more realistic idea of all the costs of physical activity.

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11. Appendix A: Disease lifetime risk data

Author	**Disease**	**Risk**	**Women**	**Men**	**Type**	**Comment**
http://canques.seer.cancer.gov	Breast cancer		12.39%		lifetime risk	age 40-95+
Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, Thun MJ.	Breast cancer		12.50%		lifetime risk	
Merrill RM, Weed DL	Breast cancer		9.09%		lifetime risk	age 60
National Cancer Institute of Canada (NCIC)	Breast cancer		11.11%		lifetime risk	
Office for National Statistics, Health Statistics Quarterly Autumn 2000	Breast cancer		11.11%			
Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee.	Breast cancer		12.50%	0.10%	lifetime risk	age 40+
Singletary SE.	Breast cancer		11.11%		lifetime risk	
Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B,	Colon cancer		5.88%	6.25%	lifetime risk	from age 40

Author	Disease	Risk	Women	Men	Type	Comment
Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee.						
Office for National Statistics, Health Statistics Quarterly Autumn 2000	Colo-rectal cancer		4.90%	5.70%	lifetime risk	
http://canques.seer.cancer.gov	Colo-rectal cancer	5.56%	5.299	5.86%	lifetime risk	age 40-95+
Jemal A, Siegel R, Ward E, Hao Y, Xu J, Murray T, Thun MJ.	Colo-rectal cancer		5.26%	5.56%	lifetime risk	
Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, Thun MJ.	Colo-rectal cancer		5.56%	5.88%	lifetime risk	
National Cancer Institute of Canada (NCIC)	Colo-rectal cancer		6.25%	7.14%	lifetime risk	
Ness RM, Holmes AM, Klein R, Dittus R.	Colo-rectal cancer		5.50%	6%	lifetime risk	
Thomas GS.	CAD		49%	32%	incidence	age 40
Joyce GF, Keeler EB, Shang B, Goldman DP.	CHD	10,4%			lifetime prevalence	self-report
Joyce GF, Keeler EB, Shang B, Goldman DP.	CHD	10.90%			lifetime prevalence	age 65, self report

Author	Disease	Risk	Women	Men	Type	Comment
Liu JL, Maniadakis N, Gray A, Rayner M.	CHD		33%	50%	lifetime risk	age 40
Lloyd-Jones DM, Larson MG, Beiser A, Levy D.	CHD		31.70%	48.60%	lifetime risk	age 40
Oster G, Thompson D, Edelsberg J, Bird AP, Colditz GA.	CHD		28.75%	38.50%	lifetime risk	age 35-44
Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee.	CHD		49%	32%	lifetime risk	age 40+
Lloyd-Jones DM, Larson MG, Leip EP, Beiser A, D'Agostino RB, Kannel WB, Murabito JM, Vasan RS, Benjamin EJ, Levy D; Framingham Heart Study.	CHF		20.3% (95% CI 18.2% to 22.5%)	21.0% (95% CI 18.7% to 23.2%)	lifetime risk	age 40
Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong	Congestive Heart Disease	50%			lifetime risk	age 40+

Author	Disease	Risk	Women	Men	Type	Comment
Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee.						
Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee.	Congestive Heart Failure	20%			lifetime risk	age 40+
Fox CS, Pencina MJ, Wilson PW, Paynter NP, Vasan RS, D'Agostino RB Sr.	CVD		34.30%	49.2&	lifetime	age 50-89, non diabetic, normal weight
Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y; American Heart Association Statistics Committee	CVD		50.00%	66.67%	lifetime risk	age 40

Author	Disease	Risk	Women	Men	Type	Comment
and Stroke Statistics Subcommittee.						
Bushnell CD.	CVA	20%			lifetime risk	age 65
Joyce GF, Keeler EB, Shang B, Goldman DP.	CVA	7.50%			lifetime prevalence	sel-report
Lloyd-Jones DM, Leip EP, Larson MG, D'Agostino RB, Beiser A, Wilson PW, Wolf PA, Levy D.	CVA		39.2% (95% CI, 37.0 to 41.4)	51.7% (95% CI, 49.3 to 54.2)	lifetime risk	age 50
Oster G, Thompson D, Edelsberg J, Bird AP, Colditz GA.	CVA		16.60%	14.30%	lifetime risk	age 35-44
Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee.	CVA		20.00%	16.67%	lifetime risk	age 40+
Seshadri S, Beiser A, Kelly-Hayes M, Kase CS, Au R, Kannel WB, Wolf PA.	CVA		21.1% (19.4–22.7)	16.9% (15.3–18.6)	lifetime risk	age 65

Author	Disease	Risk	Women	Men	Type	Comment
Fox CS, Pencina MJ, Wilson PW, Paynter NP, Vasan RS, D'Agostino RB Sr.	Diabetes		38.50%	32.80%	lifetime risk	
Ackermann RT, Marrero DG, Hicks KA, Hoerger TJ, Sorensen S, Zhang P, Engelgau MM, Ratner RE, Herman WH.	Diabetes Mellitus	87%			lifetime risk	age 50
Joyce GF, Keeler EB, Shang B, Goldman DP.	Diabetes Mellitus	14.60%			lifetime prevalence	age 65, self report
Magliano DJ, Shaw JE, Shortreed SM, Nusselder WJ, Liew D, Barr EL, Zimmet PZ, Peeters A.	Diabetes Mellitus	38%			lifetime risk	age 25
Narayan KM, Boyle JP, Thompson TJ, Sorensen SW, Williamson DF.	Diabetes Mellitus		38.50%	32.80%	lifetime risk	born in US 20000
Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee.	Diabetes Mellitus	33.00%			lifetime risk	age 40
Gabriel SE, Michaud K.	OA	44.70%			lifetime risk	
Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK.	OA		14.7% (95% CI	10.5%	point	

Author	Disease	Risk	Women	Men	Type	Comment
			13.1-16.4)	(95% CI 9.0-12.1)	prevalence	
Urquhart DM, Soufan C, Teichtahl AJ, Wluka AE, Hanna F, Cicuttini FM.	OA	30%			prevalence age >60	
Dillon CF, Rasch EK, Gu Q, Hirsch R.	OA - knee		42.10%	31.20%	point prevalence	
Dennison E, Mohamed MA, Cooper C	Osteoporosis		40-50%	13- 22%	Lifetime risk	
Kanis JA, Stevenson M, McCloskey EV, Davis S, Lloyd-Jones M.	Osteoporosis		14%	4.80%		
Sasser AC, Rousculp MD, Birnbaum HG, Oster EF, Lufkin E, Mallet D	Osteoporosis	50%			lifetime risk	
World Health Organ	Osteoporotic fracture			40%	lifetime incidence	women age 50
Kvien TK	RA	0.5-1%			prevalence	
Wordsworth BP, Bell JI.	RA	1%			lifetime incidence	

12. Appendix B: Risk Reduction data

Author	Disease	Risk Reduction (95% CI)	Women	Men	Comment
Bernstein L, Patel AV, Ursin G, Sullivan-Halley J, Press MF, Deapen D, Berlin JA, Daling JR, McDonald JA, Norman SA, Malone KE, Strom BL, Liff J, Folger SG, Simon MS, Burkman RT, Marchbanks PA, Weiss LK, Spirtas R	Breast cancer		-20%		
Breslow RA, Ballard-Barbash R, Munoz K, Graubard BI.	Breast cancer		-67%		
Bucksch J, Schlicht W.	Breast cancer		0.82 (0.68–0.97)		
Chief Medical Officer, British Deparment of Health	Breast cancer		-30%		
Cobiac LJ, Vos T, Barendregt JJ.	Breast cancer		insufficient 0.84(0.78-0.91) sufficient 0.75		
Colditz GA, Feskanich D, Chen WY, Hunter DJ, Willett WC	Breast cancer		no significant association		
Friedenreich CM, Cust AE.	Breast cancer		-25-30%		
John EM, Horn-Ross PL, Koo J.	Breast cancer		premenopausal: = 0.74 (0.52-1.05) postmenopausal: 0.81, (0.64-1.02)		

Author	Disease	Risk Reduction (95% CI)	Women	Men	Comment
Katzmarzyk PT, Janssen I.	Breast cancer		-31% (95% CI 23-38%)		
Lee IM.	Breast cancer		-20-30%		
Margolis KL, Mucci L, Braaten T, Kumle M, Trolle Lagerros Y, Adami HO, Lund E, Weiderpass E.	Breast cancer		no difference		
Maruti SS, Willett WC, Feskanich D, Rosner B, Colditz GA	Breast cancer		-23%		
Matthews CE, Shu XO, Jin F, Dai Q, Hebert JR, Ruan ZX, Gao YT, Zheng W.	Breast cancer		(OR = 0.68 (0.53-0.88))		
Monninkhof EM, Elias SG, Vlems FA, van der Tweel I, Schuit AJ, Voskuil DW, van Leeuwen FE; TFPAC.	Breast cancer		-20- -80%		
Patel AV, Callel EE, Bernstein L, Wu AH, Thun MJ.	Breast cancer		-29%		
Peplonska B, Lissowska J, Hartman TJ, Szeszenia-Dabrowska N, Blair A, Zatonski W, Sherman ME, Garcia-Closas M, Brinton LA.	Breast cancer		-20%		highest vs lowest quartile
Renehan AG, Howell A.	Breast cancer		OR - 0.28		PA 3.4+hrs/week
Rockhill B, Willett WC, Hunter DJ, Manson JE, Hankinson SE, Colditz GA.	Breast cancer		-18%		
Willer A.	Breast cancer		-40-50%		
Calton BA, Lacey JV Jr, Schatzkin A, Schairer C, Colbert LH, Albanes D, Leitzmann MF	Colon cancer	no difference			

Author	Disease	Risk Reduction (95% CI)	Women	Men	Comment
Chief Medical Officer, British Deparment of Health	Colon cancer	-40-50%			
Cobiac LJ, Vos T, Barendregt JJ.	Colon cancer	insufficient 0.7 (0.625-0.70) sufficient0.59			
Katzmarzyk PT, Janssen I.	Colon cancer	-41% (95% CI 31-53%)			
Macfarlane GJ, Lowenfels AB.	Colon Cancer			-33%	
Mai PL, Sullivan-Halley J, Ursin G, Stram DO, Deapen D, Villaluna D, Horn-Ross PL, Clarke CA, Reynolds P, Ross RK, West DW, Anton-Culver H, Ziogas A, Bernstein L.	Colon Cancer	-75% 95%CI 0.43=1.0			
Martínez ME, Giovannucci E, Spiegelman D, Hunter DJ, Willett WC, Colditz GA.	Colon Cancer		0.54 (0.33-0.90)		> 21 MET-hours per week on leisure-time physical activity vs < 2 MET-hours per week
Miles, L	Colon cancer		0.86 (0.76 - 0.98)	0.80 (0.67 - 0.96)	
Peters HP, De Vries WR, Vanberge-Henegouwen GP, Akkermans LM.	Colon cancer	-50%			
Rissanen A, Fogelholm M.	Colon cancer	-50%			

Author	Disease	Risk Reduction (95% CI)	Women	Men	Comment
Slattery ML.	Colon Cancer	-12-14%			
Thune I, Lund E.	Colon Cancer	0.62, 95% CI 0.40-0.97)			
Willer A.	Colon Cancer	-40-50%			
Parkin DM, Olsen AH, Sasieni P.	Colo-rectal cancer	-30%			
Lee IM.	Cancer	-30-40%			
Thompson PD, Buchner D, Pina IL, Balady GJ, Williams MA, Marcus BH, Berra K, Blair SN, Costa F, Franklin B, Fletcher GF, Gordon NF, Pate RR, Rodriguez BL, Yancey AK, Wenger NK; American Heart Association Council on Clinical Cardiology Subcommittee on Exercise, Rehabilitation, and Prevention; American Heart Association Council on Nutrition, Physical Activity, and Metabolism Subcommittee on Physical Activity.	CAD	-50%			
Katzmarzyk PT, Janssen I.	CAD	-45% (95% CI 38-54%)			
Annemans L, Lamotte M, Clarys P, Van den Abeele E.	CHD	-40%			
Bucksch J, Schlicht W.	CHD	0.82; 95 % CI: 0.67–1.00)			

Author	Disease	Risk Reduction (95% CI)	Women	Men	Comment
Bucksch J, Schlicht W.	CHD			-14%	
Chief Medical Officer, British Deparment of Health	CHD	-50%	1.00, 0.73, 0.69, 0.68, and 0.47		Age-adjusted relative risks in increasing quintiles of activity
Haapanen N, Miilunpalo S, Vuori I, Oja P, Pasanen M.	CHD		Moderate -42% High -20%	Moderate: -33% High -50%	
Haapanen N, Miilunpalo S, Vuori I, Oja P, Pasanen M.	CHD		-12%	-30%	
Hu G, Jousilahti P, Borodulin K, Barengo NC, Lakka TA, Nissinen A, Tuomilehto J.	CHD		Moderate: 0.85 High: -0.77	Moderate: -0.95 High: 0.84	
Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE.	CHD	Moderate: 0.55 Most active: 0.75			
Lee IM, Sesso HD, Oguma Y, Paffenbarger RS Jr.	CHD	-31-24%			
Munro J, Brazier J, Davey R, Nicholl J.	CHD	-35%			
Munro J, Brazier J, Davey R, Nicholl J.	CHD	-40%			
Powell KE, Thompson PD, Caspersen CJ, Kendrick JS.	CHD	-52% range: -41% - -66%			
Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy	CHD	0.41- 0.625			

Author	**Disease**	**Risk Reduction (95% CI)**	**Women**	**Men**	**Comment**
C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y; American Heart Association Statistics Committee and Stroke Statistics Subcommittee.					
Snell PG, Mitchell, JH	CHD	-50%			
Sofi F, Capalbo A, Cesari F, Abbate R, Gensini GF.	CHD	-7 - -35%			
Stampfer MJ, Hu FB, Manson JE, Rimm EB, Willett WC.	CHD	<1h/w 1.41 (1.15–1.75) 1.0–2.2h/w1.23 (0.99–1.53) 2.3–3.5h/w1.18 (0.94–1.47) 3.6–5.5h/w1.05 (0.82–1.34) >5.5h/w 1.0 (reference)			
Tanasescu M, Leitzmann MF, Rimm EB, Willett WC, Stampfer MJ, Hu FB.	CHD	-18% for walking			higher for running, rowing, weights
Annemans L, Lamotte M, Clarys P, Van den Abeele E.	CVA	-27%			
Chief Medical Officer, British Deparment of Health	CVA	-27%			

<u>**Author**</u>	<u>**Disease**</u>	<u>**Risk Reduction (95% CI)**</u>	<u>**Women**</u>	<u>**Men**</u>	<u>**Comment**</u>
Chiuve SE, Rexrode KM, Spiegelman D, Logroscino G, Manson JE, Rimm EB.	CVA	-18-39%			
Goldstein LB, Adams R, Alberts MJ, Appel LJ, Brass LM, Bushnell CD, Culebras A, Degraba TJ, Gorelick PB, Guyton JR, Hart RG, Howard G, Kelly-Hayes M, Nixon JV, Sacco RL; American Heart Association/American Stroke Association Stroke Council; Atherosclerotic Peripheral Vascular Disease Interdisciplinary Working Group; Cardiovascular Nursing Council; Clinical Cardiology Council; Nutrition, Physical Activity, and Metabolism Council; Quality of Care and Outcomes Research Interdisciplinary Working Group; American Academy of Neurology.	CVA	0.6296			
Hu G, Sarti C, Jousilahti P, Silventoinen K, Barengo NC, Tuomilehto J.	CVA	moderate 0.86 high 0.74			Hazard ratio
Katzmarzyk PT, Janssen I.	CVA	-60% (42-80%)			
Lee IM, Paffenbarger RS Jr.	CVA	-46%			
Shinton R, Sagar G	CVA	0,33 (0-2 - 0.6).			history of vigorous exercise during the ages 15-25

Author	Disease	Risk Reduction (95% CI)	Women	Men	Comment
Wannamethee G, Shaper AG	CVA	Moderate 0.8 Vigorous 0.3			
Wendel-Vos GC, Schuit AJ, Feskens EJ, Boshuizen HC, Verschuren WM, Saris WH, Kromhout D.	CVA	Moderate: occupational 0.64, (0.48-0.87) Moderate leisure time 0.85(: 0.78-0.93). High level: leisure RR = 0.78 (0.71-0.85)			
Scottish Intercollegiate Guidelines Network	CVD	-50%			
Ackermann RT, Marrero DG, Hicks KA, Hoerger TJ, Sorensen S, Zhang P, Engelgau MM, Ratner RE, Herman WH.	Diabetes Mellitus	-58%			High risk patients
Annemans L, Lamotte M, Clarys P, Van den Abeele E.	Diabetes Mellitus	-29%			
Chief Medical Officer, British Deparment of Health	Diabetes Mellitus	-35-50%			
Haapanen N, Miilunpalo S, Vuori I, Oja P, Pasanen M.	Diabetes Mellitus		mod -66% high -62%	mod: -22% high -35%	energy expenditure
Haapanen N, Miilunpalo S, Vuori I, Oja P, Pasanen M.	Diabetes		-55%	-29%	exercise intensity

Author	Disease	Risk Reduction (95% CI)	Women	Men	Comment
	Mellitus				
Jonker JT, De Laet C, Franco OH, Peeters A, Mackenbach J, Nusselder WJ.	Diabetes Mellitus	0.63 (0.48–0.82)			
Mozaffarian D, Kamineni A, Carnethon M, Djoussé L, Mukamal KJ, Siscovick D.	Diabetes Mellitus	-26%			
Munro J, Brazier J, Davey R, Nicholl J.	Diabetes Mellitus	-29%			
Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C.	Diabetes Mellitus	-58%			includes diet changes
Spelsberg A, Manson JE.	Diabetes Mellitus	-30-50%			
Waugh N, Scotland G, McNamee P, Gillett M, Brennan A, Goyder E, Williams R, John A	Diabetes Mellitus		-30%	-40%	
Williams PT, Franklin B.	Diabetes Mellitus		-65%	-58%	most vs least fit runners
Williams PT.	Diabetes Mellitus		Fittest quintile: -86% Greatest distance: -70%	Fittest quintile: -50% Greatest distance: -70%	
Williams PT.	Diabetes Mellitus		-68%	-59%	walking speed <1.2m/1 vs >2,1m/s

Author	Disease	Risk Reduction (95% CI)	Women	Men	Comment
Cobiac LJ, Vos T, Barendregt JJ.	DM Type II	Insufficient 0.85 (0.76-0.96) Sufficient 0.69			age 15-69
Henriksson F, Agardh CD, Berne C, Bolinder J, Lonnqvist F, Stenstrom P, Ostenson CG, Jonsson B	DM Type II				direct
Katzmarzyk PT, Janssen I.	DM Type II	-50% (37-63%)			
Krause MP, Hallage T, Gama MP, Goss FL, Robertson R, da Silva SG.	DM Type II	-30%			
Lindström J, Tuomilehto J.	DM Type II	-24%			>= 4hrs PA/week
Cobiac LJ, Vos T, Barendregt JJ.	Ischemic CVA	Insuffucient 0.719 Sufficient 0.654			
Cobiac LJ, Vos T, Barendregt JJ.	Ischemic heart disease	Insufficient : 0.842 (0.749-0.947) Sufficient: 0.585			age 15-69
Hardoon SL, Whincup PH, Lennon LT, Wannamethee SG, Capewell S, Morris RW.	MI	-5% (0-11%)			
Lakka TA, Venäläinen JM, Rauramaa R, Salonen R, Tuomilehto J, Salonen JT.	MI	0.34 (0.12 to 0.94)			highest vs lowst 3rd
Shaper AG, Wannamethee G, Walker M.	MI			-50%	
Spencer CA, Jamrozik K, Lambert L.	MI	-29.70%			population attributable

Author	Disease	Risk Reduction (95% CI)	Women	Men	Comment
					fraction
Yusuf S, Hawken S, Ounpuu S, Dans T, Avezum A, Lanas F, McQueen M, Budaj A, Pais P, Varigos J, Lisheng L; INTERHEART Study Investigators.	MI	0.86 (CI 99% 0·76–0·97),	F(99% CI) OR 0·48 (0·39–0·59)	(99% CI) OR 0·77 (0·69–0·85)	
Felson DT, Niu J, Clancy M, Sack B, Aliabadi P, Zhang Y.	Osteoarthritis	No difference			
Lane NE, Hochberg MC, Pressman A, Scott JC, Nevitt MC.	Osteoarthritis	+60%			
Mehrotra C, Naimi TS, MD, Serdula M, Bolen J, Pearson K	Osteoarthritis	-20% prevalence			prevalence
Rogers LQ, Macera CA, Hootman JM, Ainsworth BE, Blairi SN.	Osteoarthritis		moderate/high joint stress: 0.24 (0.11–0.52), low stress: 0.58 (0.34–0.99)	0.62 (0.43–0.89)	
Spector TD, Harris PA, Hart DJ, Cicuttini FM, Nandra D, Etherington J, Wolman RL, Doyle DV.	Osteoarthritis	OR: +1.6-3.57			
Sutton AJ, Muir KR, Mockett S, Fentem P.	Osteoarthritis	No significant relation			
White JA, Wright V, Hudson AM.	Osteoarthritis	Protective			
Zeller L, Sukenik S.	Osteoarthritis	No impact			
Szoeke C, Dennerstein L, Guthrie J, Clark M, Cicuttini F	Osteoarthritis	Higher prevalence for			

Author	**Disease**	**Risk Reduction (95% CI)**	**Women**	**Men**	**Comment**
	knee	certain manifestations of OA			
Szoeke CE, Cicuttini FM, Guthrie JR, Clark MS, Dennerstein L.	Osteoarthritis knee	Increasing level of PA at ages 20-29 associated with increased risk			
Devine A, Dhaliwal SS, Dick IM, Bollerslev J, Prince RL	Osteoporosis		-17%		with high calcium intake
Katzmarzyk PT, Janssen I.	Osteoporosis	-59% (95% CI 40-80%)			
Seavey WG, Kurata JH, Cohen RD.	Rheumatoid Arthritis and Osteoarthritis	OR 0.69, 95% CI 0.51–0.95			

13. Appendix C: Disease cost data

13.1. Breast Cancer

	Max W, Sung HY, Stark B.	Riley GF, Potosky AL, Lubitz JD, Kessler LG.	Taplin SH, Barlow W, Urban N, Mandelson MT, Timlin DJ, Ichikawa L, Nefcy P.	Will BP, Berthelot JM, Le Petit C, Tomiak EM, Verma S, Evans WK	Fireman BH, Quesenberry CP, Somkin CP, Jacobson AS, Baer D, West D, Potosky AL, Brown ML.
Country	USA	USA	USA	Canada	USA
Basis of analysis	Database	Database	Database	POHEM: Microsimulation model	Database
Study design	Prevalence	Prevalence	Prevalance	Prevalance	Prevalence
Methodological approach	IH: Sum_Diagnosis Specific OH: Sum_All_Medical Indirect: Sum_All_Medical	Sum_Diagnosis Specific	Matched control	Sum_Diagnosis Specific	Matched control
Data sources	Hospital Discharge Data released by the California Office of Statewide Health Planning and Development- OSHPD, Medical Expenditure Panel Survey (MEPS) medical event files, National Nursing Home Survey, 2001 California Mortality File, California Department of Health Services	Medicare claims and National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program.	Group Health Cooperative (GHC) of Puget Sound (Washington State), the Surveillance, Epidemiology, and End Results (SEER) Program' of the National Cancer Institute (NCI) registry	Canadian Cancer Registry, Statistics Canada's national person-oriented data-base of hospital discharges and national surveys of medical, surgical and radiation oncologists. Provincial cancer registry data, provincial fee schedules and special costing studies and chart reviews	HMO
Population n	12934	59,822	incident: 645 prevalent :2299	17700	8152
age	all	65+	35+	all	all
Perspective	3rd party payer	3rd party payer	3rd party payer	not stated	3rd party payer
Time horizon	lifetime	lifetime	lifetime	lifetime	15yr
Year of costs	2008	1990	1992	1995	1992

	Max W, Sung HY, Stark B.	Riley GF, Potosky AL, Lubitz JD, Kessler LG.	Taplin SH, Barlow W, Urban N, Mandelson MT, Timlin DJ, Ichikawa L, Nefcy P.	Will BP, Berthelot JM, Le Petit C, Tomiak EM, Verma S, Evans WK	Fireman BH, Quesenberry CP, Somkin CP, Jacobson AS, Baer D, West D, Potosky AL, Brown ML.
Discount rate	2001 Costs were adjusted to 2008 dollars using the appropriate component of the Consumer Price Index (CPI) for medical care components. Future costs: 3%	not stated	average change in the Consumer Price Index for medical care from mid-1990 through 1991 (8.7%) and mid-1991 through 1992 (7.2%)	0%	3%
COI Estimation Procedure	Bottom-up	Bottom-up	Bottom-up	Bottom-up	Bottom-up
Cost component	charges converted to costs	Medicare payments	HMO costs incl admin overhead	Fees	
In-patient care	✓	✓	✓	✓	✓
Out-patient care	✓	✓	✓	✓	✓
Prescription Drugs	✓	some	✓	×	✓
Skilled nursing facility	✓	✓	✓		✓
Home nursing	✓	✓	✓	×	
Doctors' visits	✓		✓	✓	
Therapists' vists		some			
Emergency Room	✓				✓
Nursing home		×	×		×
Aid tools			✓		✓
Lost productivity	✓	×	×	×	
Co-morbidities			✓		
Hospice		✓	✓		✓
Radiology			✓	✓	✓
Laboratory			✓	✓	✓
Other			admin overhead	diagnostic costs, facility overhead costs	admin overhead
excludes			long-term nursing care		
Per person cost	303,735	50448	30507.8	25660	35000
Currency	USD	USD	USD	Ca$	USD

	Max W, Sung HY, Stark B.	Riley GF, Potosky AL, Lubitz JD, Kessler LG.	Taplin SH, Barlow W, Urban N, Mandelson MT, Timlin DJ, Ichikawa L, Nefcy P.	Will BP, Berthelot JM, Le Petit C, Tomiak EM, Verma S, Evans WK	Fireman BH, Quesenberry CP, Somkin CP, Jacobson AS, Baer D, West D, Potosky AL, Brown ML.
Conversion to US$	1	1	1	1.214607	1
Value	303735	50448	30507.8	31166.8177	35000
CPI for 1H2009	394.9	394.9	394.9	394.9	394.9
CPI for article period	384.943	162.7	190.5	224.2	190.5
current-previous	9.957	232.2	204.4	170.7	204.4
%change	1.025866167	2.42716656	2.072965879	1.76137377	2.07296588
Inflated total	$311,591.46	$122,445.70	$63,241.63	$54,896.42	$72,553.81
total with 19% herceptin*		*$145,710.38*	$75,257.54	$65,326.73	$86,339.03
with 100% indirect costs		*$291,420.76*	$150,515.08	$130,653.47	$172,678.06

*Drukner et al

Mean	211,371.77
Median	172,678.06
Standard Deviation	83,916.64
Minimum	130,653.47
Maximum	311,591.46

13.2. Colon Cancer

	Etzioni R, Ramsey SD, Berry K, Brown M	**Maroun J, Ng E, Berthelot JM, Le Petit C, Dahrouge S, Flanagan WM, Walker H, Evans WK**	**Riley GF, Potosky AL, Lubitz JD, Kessler LG.**	**Brown ML, Riley GF, Potosky AL, Etzioni RD.**	**Taplin SH, Barlow W, Urban N, Mandelson MT, Timlin DJ, Ichikawa L, Nefcy P.**	**Ramsey SD, Berry K, Etzioni R.**	**Fireman BH, Quesenberry CP, Somkin CP, Jacobson AS, Baer D, West D, Potosky AL, Brown ML.**
Disease subtype	per stage	per stage	per stage	per stage	per stage	>5yr survival	per stage
Country	USA	Canada	USA	USA	USA	USA	USA
Basis of analysis	Database	Microsimulation	Database	Database	Database	Database	Database
Study design	Prevalance	Incidence	Prevalence	Prevalance	Prevalence	Prevalance	Prevalence
Methodological approach	Matched Control	Sum_Diagnosis Specific	Sum_Diagnosis Specific	Matched control	Matched control	Matched control	Matched control
Data sources	Surveillance, Epidemiology and End Results (SEER)–Medicare database, US life tables	Canada-wide survey of oncologists 1998, Canadian Cancer Registry (CCR) 195 Statistics Canada, 1995 population estimates Ottawa Chart Review - 1991-92, Manitoba Medical Services Foundation and Manitoba Cancer Treatment and Research Foundation (MCTRF) - 1990, National Person-oriented Database of Hospital Discharges - 1998, Study by Earle and Grunfeldb, Ontario Health Insurance Plan (OHIP) - 1998, Study by Earle et al., 1997, Chemotherapy costs study, National Surgical Adjuvant Breast and Bowel	SEER- Medicare linked database	SEER- Medicare linked database	Group Health Cooperative (GHC) of Puget Sound (Washington State), the Surveillance, Epidemiology, and End Results (SEER) Program' of the National Cancer Institute (NCI) registry	SEER database	HMO

		Etzioni R, Ramsey SD, Berry K, Brown M		Maroun J, Ng E, Berthelot JM, Le Petit C, Dahrouge S, Flanagan WM, Walker H, Evans WK	Riley GF, Potosky AL, Lubitz JD, Kessler LG.	Brown ML, Riley GF, Potosky AL, Etzioni RD.	Taplin SH, Barlow W, Urban N, Mandelson MT, Timlin DJ, Ichikawa L, Nefcy P.	Ramsey SD, Berry K, Etzioni R.		Fireman BH, Quesenberry CP, Somkin CP, Jacobson AS, Baer D, West D, Potosky AL, Brown ML.
				Project (NSABP), The Resource Intensity Weights study - 1996, Ontario Case Cost Project - 1998						
Population	**Sex**	M	F	both	both	both	both	M	F	both
	n	583	829	11,430	76,723	40094+	incident: 290 prevalent: 1046	2493	2138	3321
	age	65+	65+	all	65+	65+	35+	65-69	65-69	not stated
Perspective		3rd party payer		3rd party payer	3rd party payer	3rd party payer	3rd party payer	3rd party payer		3rd party payer
Time horizon		25yr		lifetime	lifetime	25yr	lifetime	lifetime		15yr
Year of costs		1994		1998	1990	1994	1992	2000		1992
Discount rate		3%		0%	not stated	3%	average change in the Consumer Price Index for medical care from mid-1990 through 1991 (8.7%) and mid-1991 through 1992 (7.2%)	3%		3%
COI Estimation Procedure		Bottom-up		Bottom-up	Bottom-up	Bottom-up	Bottom-up	Bottom-up		Bottom-up
Cost component		Medicare payments		Medicare payments	Medicare payments	Medicare payments	HMO costs incl admin overhead	Medicare payments		Medicare payments
In-patient care		✓		✓	✓		✓	✓		✓
Out-patient care		✓		✓	✓	not stated	✓	✓		✓
Presciption Drugs		×			×		✓	×		✓
Home nursing		✓		×	✓		✓	✓		✓

	Etzioni R, Ramsey SD, Berry K, Brown M	Maroun J, Ng E, Berthelot JM, Le Petit C, Dahrouge S, Flanagan WM, Walker H, Evans WK	Riley GF, Potosky AL, Lubitz JD, Kessler LG.	Brown ML, Riley GF, Potosky AL, Etzioni RD.	Taplin SH, Barlow W, Urban N, Mandelson MT, Timlin DJ, Ichikawa L, Nefcy P.	Ramsey SD, Berry K, Etzioni R.	Fireman BH, Quesenberry CP, Somkin CP, Jacobson AS, Baer D, West D, Potosky AL, Brown ML.
Doctors' visits	✓	✓	✓		✓	✓	
Therapists' vists					✓		
Emergency Room							
Skilled nursing facility	✓		✓			✓	✓
Nursing home			×		×	×	×
Aid tools		×			✓		✓
Lost productivity		×			×		
Co-morbidities		×			✓		
Hospice	✓		✓		✓	✓	✓
Radiology and lab tests	✓	✓			✓	✓	✓
Laboratory		✓			✓	✓	✓
Other		Diagnostic work-up	non cancer-related care	deductibles and coinsurance	Admin overhead		admin overhead
excludes		travel and accommodation, costs of caregivers in the home	deductibles, coinsurance, charges in excess of Medicare allowed charges, and costs of non- covered services				
Per person cost	20544 19188	29,110	51865	31300	28119.2	8573 4511	42000
Currency	USD	Ca$	USD	USD	USD	USD	USD
Conversion rate to US$	1	1.187293	1	1	1	1	1
Value	20544 19188	34562.094	51865	31300	28119.2	8573 4511	42000
CPI 1H 2009	394.9	394.9	394.9	394.9	394.9	394.9	394.9
CPI for article	213.4	246.8	162.7	213.4	190.5	266	190.5

	Etzioni R, Ramsey SD, Berry K, Brown M		Maroun J, Ng E, Berthelot JM, Le Petit C, Dahrouge S, Flanagan WM, Walker H, Evans WK	Riley GF, Potosky AL, Lubitz JD, Kessler LG.	Brown ML, Riley GF, Potosky AL, Etzioni RD.	Taplin SH, Barlow W, Urban N, Mandelson MT, Timlin DJ, Ichikawa L, Nefcy P.	Ramsey SD, Berry K, Etzioni R.		Fireman BH, Quesenberry CP, Somkin CP, Jacobson AS, Baer D, West D, Potosky AL, Brown ML.
period current-previous	181.5		148.1	232.2	181.5	204.4	128.9		204.4
%change	1.85		1.6	2.43	1.86	2.07	1.48		2.07
Inflated total	*$38,016.99*	*$35,507.69*	*$55,302.15*	*$125,884.99*	*$57,921.13*	*$58,290.14*	*$12,727.36*	*$6,696.97*	*$87,064.57*
total with 21% avastin*	$45,240.22	$42,254.15	$66,915.60	$149,803.14	$68,926.15	$69,365.27	$15,145.56	$7,969.39	$103,606.83

*Drukner et al

Mean	63247.36902
Median	66915.60357
Standard Deviation	43786.88878
Minimum	7969.393763
Maximum	149803.1427

13.3. CHD

	Oster G, Epstein AM.	**Shaw LJ, Merz CN, Pepine CJ, Reis SE, Bittner V, Kip KE, Kelsey SF, Olson M, Johnson BD, Mankad S, Sharaf BL, Rogers WJ, Pohost GM, Sopko G; Women's Ischemia Syndrome Evaluation (WISE) Investigators**	**Joyce GF, Keeler EB, Shang B, Goldman DP.**	**Beale S, Bending M, Trueman P**	**Hay JW, Sterling KL.**	**Birnbaum H, Leong S, Kabra A.**	**Eisenstein EL, Shaw LK, Anstrom KJ, Nelson CL, Hakim Z, Hasselblad V, Mark DB.**	**Hlatky MA, Boothroyd DB, Melsop KA, Brooks MM, Mark DB, Pitt B, Reeder GS, Rogers WJ, Ryan TJ, Whitlow PL, Wiens RD.**
Disease	CHD	CHD	CHD	CHD	CAD	CHD	CAD	CAD
Disease subtype	Sudden Death, Nonsudden Death, MI, Coronary Insufficency, Angina Pectoris	non-obstructive, 1- and 3-vessel CAD			Acute MI, angina pectoris, unstable AP, sudden death, nonsudden death		Unstable AP, Acute MI	Multi-vessel coronary disease
Country	USA	USA	USA	*United Kingdom*	USA	USA	USA	USA
Basis of analysis	Microsimulation	Microsimulation	Microsimulation	?	Microsimulation	Database	Database	RTC
Study design	Incidence	Incidence	Incidence	?	Incidence	Prevalence	Incidence	Incidence
Methodological approach	Sum_Diagnosis Specific	Sum_Diagnosis Specific	Regression	?	Sum_Diagnosis Specific	Matched control	Sum_Diagnosis Specific	Sum_Diagnosis Specific
Data sources	informal survey of	WISE cost methods, published reports, 2003 Red Book, National Vital Statistics	Future Elderly Project (FEP):	NHS	Wittels et al: cardiologists,	Claims data, US government stats,	Global Use of Strategies to Open Occluded Coronary	Hospital bills, Red Book

		Oster G, Epstein AM.	Shaw LJ, Merz CN, Pepine CJ, Reis SE, Bittner V, Kip KE, Kelsey SF, Olson M, Johnson BD, Mankad S, Sharaf BL, Rogers WJ, Pohost GM, Sopko G; Women's Ischemia Syndrome Evaluation (WISE) Investigators	Joyce GF, Keeler EB, Shang B, Goldman DP.	Beale S, Bending M, Trueman P	Hay JW, Sterling KL.	Birnbaum H, Leong S, Kabra A.	Eisenstein EL, Shaw LK, Anstrom KJ, Nelson CL, Hakim Z, Hasselblad V, Mark DB.	Hlatky MA, Boothroyd DB, Melsop KA, Brooks MM, Mark DB, Pitt B, Reeder GS, Rogers WJ, Ryan TJ, Whitlow PL, Wiens RD.
		doctors, Framingham	Report	link extendedMedicare claims (1991–1999) to the Medicare Current Beneficiary Survey (MCBS)		Framingham, Health Care Financing Administration (HCFA), IMS America, Houston area surveys	Health Care Financing Administration	Arteries (GUSTO IIb) Economics and Quality of Life (EQOL) Substudies, Red Book	
Population	**Sex**	M	F	both	both	both	F	both	both
	n		883	not specifically stated for CHD	not stated for this age group		9528	9876	934
	age	45	all	65+	40-44	45-74	all	52-71	not stated
	other		after angiography			low levels of HDL-cholesterol and no prior history of CHD		after cardiac catheterisation	randomised to CABG or PTCA
Perspective		society	society	3rd party payer	3rd party payer	3rd party payer	3rd party payer	3rd party payer	3rd party payer
Time horizon		lifetime	lifetime	lifetime	lifetime	lifetime	lifetime	10yr	10yr
Year of costs		1980	2006	1999	2007	2004	2002	1997	2002
Discount rate		3%	5% annual rate, corrected for inflation by the US medical service sector estimate (city average) of the consumer price index (for	3%	not stated	3%	inflated using the inflation rate of the medical care	3%	3%

	Oster G, Epstein AM.	Shaw LJ, Merz CN, Pepine CJ, Reis SE, Bittner V, Kip KE, Kelsey SF, Olson M, Johnson BD, Mankad S, Sharaf BL, Rogers WJ, Pohost GM, Sopko G; Women's Ischemia Syndrome Evaluation (WISE) Investigators	Joyce GF, Keeler EB, Shang B, Goldman DP.	Beale S, Bending M, Trueman P	Hay JW, Sterling KL.	Birnbaum H, Leong S, Kabra A.	Eisenstein EL, Shaw LK, Anstrom KJ, Nelson CL, Hakim Z, Hasselblad V, Mark DB.	Hlatky MA, Boothroyd DB, Melsop KA, Brooks MM, Mark DB, Pitt B, Reeder GS, Rogers WJ, Ryan TJ, Whitlow PL, Wiens RD.
		urban wage earners and clerical workers)				component of the consumer price index, which averaged 3.8% per year. No discounting		
COI Estimation Procedure	Bottom-Up	Bottom-Up	Bottom-Up	Top-down	Bottom-up	Bottom-up	Bottom-up	Bottom-up
Cost component				NHS costs	Prices Based on Wittels et al 1990	Employer medical payments	Charges converted to costs	Charges converted to costs
In-patient care	✓	✓	✓		✓	✓	✓	✓
Out-patient care	✓	✓	✓		✓	✓	✓	✓
Presciption Drugs	✓	✓	✓		✓	✓	✓	✓
Skilled nursing facility			✓					✓
Home nursing			✓					
Doctors' visits	✓	✓	✓		✓	✓	✓	✓

	Oster G, Epstein AM.	Shaw LJ, Merz CN, Pepine CJ, Reis SE, Bittner V, Kip KE, Kelsey SF, Olson M, Johnson BD, Mankad S, Sharaf BL, Rogers WJ, Pohost GM, Sopko G; Women's Ischemia Syndrome Evaluation (WISE) Investigators	Joyce GF, Keeler EB, Shang B, Goldman DP.	Beale S, Bending M, Trueman P	Hay JW, Sterling KL.	Birnbaum H, Leong S, Kabra A.	Eisenstein EL, Shaw LK, Anstrom KJ, Nelson CL, Hakim Z, Hasselblad V, Mark DB.	Hlatky MA, Boothroyd DB, Melsop KA, Brooks MM, Mark DB, Pitt B, Reeder GS, Rogers WJ, Ryan TJ, Whitlow PL, Wiens RD.
Therapists' vists		✓						
Emergency Room visits	✓				✓		✓	
Nursing home			✓					
Aid tools			✓					
Lost productivity	✓	✓				×		×
Co-morbidities						✓		
Radiology	✓				✓			✓
Laboratory	✓				✓			✓
Other	ambulance, coroner	travel, out-of-pocket			ambulance			
Per person cost	114040	881,093.59	11691	36675.90028	32505	423,000.00	45253	121875
Currency	USD	USD	USD	GBP	USD	USD	USD	USD
Conversion rate to US$	1	1	1	0.6462187	1	1	1	1
Value	114040	881093.59	11691	23700.65194	32505	423000	45253	121875
CPI for	394.9	394.9	394.9	394.9	394.9	394.9	394.9	394.9

	Oster G, Epstein AM.	Shaw LJ, Merz CN, Pepine CJ, Reis SE, Bittner V, Kip KE, Kelsey SF, Olson M, Johnson BD, Mankad S, Sharaf BL, Rogers WJ, Pohost GM, Sopko G; Women's Ischemia Syndrome Evaluation (WISE) Investigators	Joyce GF, Keeler EB, Shang B, Goldman DP.	Beale S, Bending M, Trueman P	Hay JW, Sterling KL.	Birnbaum H, Leong S, Kabra A.	Eisenstein EL, Shaw LK, Anstrom KJ, Nelson CL, Hakim Z, Hasselblad V, Mark DB.	Hlatky MA, Boothroyd DB, Melsop KA, Brooks MM, Mark DB, Pitt B, Reeder GS, Rogers WJ, Ryan TJ, Whitlow PL, Wiens RD.
1H2009 CPI for article period	74.8	350.6	255.1	369.302	321.3	292.9	239.1	292.9
current-previous	320.1	44.3	139.8	25.598	73.6	102	155.8	102
%change	5.27	1.12	1.54	1.06	1.22	1.35	1.65	1.35
Inflated total	602,064.12	992,424.01	18,097.91	25,343.45	39,950.90	570,306.25	74,740.32	164,316.96
with 1000% indirect costs	-	-	180,979.06	253,434.52	399,509.01		747,403.17	1,643,169.60

	M	F
Mean	637,759.91	702,819.89
Median	500,786.56	573,456.089
Standard Deviation	536,146.01	554,324.51
Minimum	180,979.06	180,979.06
Maximum	1,643,169.60	1,643,169.60

13.4. CVA

	Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, Donnan GA.	**Kolominsky-Rabas PL, Heuschmann PU, Marschall D, Emmert M, Baltzer N, Neundorfer B, Schooffski O, Krobot KJ**	**Taylor TN, Davis PH, Torner JC, Holmes J, Meyer JW, Jacobson MF.**	**Chung CW, Wang JD, Yu CF, Yang MC.**	**Joyce GF, Keeler EB, Shang B, Goldman DP.**	**Beale S, Bending M, Trueman P**	**Bergman L, van der Meulen JH, Limburg M, Habbema JD.**	**Sandercock P, Berge E, Dennis M, Forbes J, Hand P, Kwan J, Lewis S, Lindley R, Neilson A, Wardlaw J.**	**Lightowlers S, McGuire A.**
Sub-type	cerebral infarction, intracerebral hemorrhage, unclassified stroke	Ischemic stroke	subarachnoid hemorrhage (SAH), intracerebral hemorrhage (ICH), and ischemic stroke (ISC).				cerebral infarction (CI) , primary intracerebral hemorrhage (PICH)	Ischemic stroke	Ischemic stroke
Country	Australia	Germany	USA	Taiwan	USA	*United Kingdom*	Netherlands	*United Kingdom*	United Kingdom
Basis of analysis	Database	Database	Microsimulation	Database	Microsimulation	?	Database	Microsimulation	Microsimulation
Study design	incidence	incidence	incidence	prevalence	Incidence	?	Incidence	Incidence	Incidence
Methodological approach	Sum_Diagnosis Specific	Sum_Diagnosis_Specific	Sum_Diagnosis_Specific	?Sum_All Medical	Regression	?	Sum_Diagnosis_Specific	Sum_Diagnosis_Specific	Sum_Diagnosis_Specific
Data sources	North East Melbourne Stroke Incidence Study (NEMESIS), Oxfordshire Community Stroke Project, Australian Bureau of Statistics ,hospital medical records, hospital	Elangen Stroke Project	Medicare claims data, the 1987 National Medical Expenditure Survey (NMES), and insurance claims data representing a group of large, self-insured employers,	National Death Registry and National Health Insurance databases, patients at the National Taiwan University Hospital (NTUH).	Future Elderly Project (FEP): link extendedMedicare claims (1991–1999) to the Medicare Current Beneficiary Survey (MCBS)	NHS	Literature review	Lothian Stroke Register, literature review, expert panel	BAATAF, Oxfordshire Community Stroke Project, South of England Study, Royal College of Physicians report

		Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, Donnan GA.	Kolominsky-Rabas PL, Heuschmann PU, Marschall D, Emmert M, Baltzer N, Neundorfer B, Schooffski O, Krobot KJ	Taylor TN, Davis PH, Torner JC, Holmes J, Meyer JW, Jacobson MF.	Chung CW, Wang JD, Yu CF, Yang MC.		Joyce GF, Keeler EB, Shang B, Goldman DP.	Beale S, Bending M, Trueman P	Bergman L, van der Meulen JH, Limburg M, Habbema JD.	Sandercock P, Berge E, Dennis M, Forbes J, Hand P, Kwan J, Lewis S, Lindley R, Neilson A, Wardlaw J.	Lightowlers S, McGuire A.
		financial costing system, nursing home and hostel case notes.		US Bureau of Economic Analysis, literature review							
Population	Sex	both	both	both	M	F	both	both	both	both	both
	n	275	2458	n/a	3758	2630			24001	n/a	n/a
	age	all	all	all	>=35		65+	40-44	all	all	all
Perspective		societal	3rd party payer	societal			3rd party payer	3rd party payer	3rd party payer	3rd party payer	3rd party payer
Time horizon		lifetime	lifetime	lifetime	lifetime		lifetime	lifetime	15yr	lifetime	10yr
Year of costs		1997	2004	1990	?2001		1999	2007	1991	1999-2000	1997
Discount rate		5%	3%	5%	3%		3%	not stated	none	6%	6%
COI Estimation Procedure		Bottom-up	Bottom-up	Bottom-up	Top-down		Bottom-up	Top-down	Bottom-up	Bottom-up	Bottom-up
Cost component				Cost-to-charge ratios	NHI costs			NHS costs			
In-patient care		✓	✓	✓	✓		✓		✓	✓	✓
Out-patient care		✓	✓	✓	✓		✓				✓
Presciption Drugs		✓	✓	✓			✓				✓
Skilled nursing facility		✓	✓	✓			✓		✓		
Home nursing		✓	✓	✓			✓		✓		
Doctors' visits		✓	✓				✓				✓
Therapists' vists		✓	✓						✓		

	Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, Donnan GA.	Kolominsky-Rabas PL, Heuschmann PU, Marschall D, Emmert M, Baltzer N, Neundorfer B, Schooffski O, Krobot KJ	Taylor TN, Davis PH, Torner JC, Holmes J, Meyer JW, Jacobson MF.	Chung CW, Wang JD, Yu CF, Yang MC.	Joyce GF, Keeler EB, Shang B, Goldman DP.	Beale S, Bending M, Trueman P	Bergman L, van der Meulen JH, Limburg M, Habbema JD.	Sandercock P, Berge E, Dennis M, Forbes J, Hand P, Kwan J, Lewis S, Lindley R, Neilson A, Wardlaw J.	Lightowlers S, McGuire A.
Emergency Room visits	✓								
Nursing home	✓	✓	✓		✓				
Rehabiliation	✓	✓	✓				✓	✓	
Aid tools	✓				✓		✓		
Lost productivity	✓		✓	×		×		×	
Co-morbidities							✓		
Radiology	✓								✓
Laboratory	✓								✓
Other	OTC, Home modifications, Ambulance transfers, Day hospitals (community rehabilitation centers) and day centers, Provision of community services, Aged care and psychogeriatric assessment teams, Paid domestic assistance, Respite care, Informal care provided by family and friends		Hospice	"all other claims data"					blood transfusions
Per person cost	33,658.00	43,129.00	103,576.00	8,641.00 7,535.00	3,807.00	50,028.74	78,000.00	26,208.62	17,819.58
Currency	USD	Euro	USD	USD	USD	GBP	Dfl	GBP	GBP

	Dewey HM, Thrift AG, Mihalopoulos C, Carter R, Macdonell RA, McNeil JJ, Donnan GA.	Kolominsky-Rabas PL, Heuschmann PU, Marschall D, Emmert M, Baltzer N, Neundorfer B, Schooffski O, Krobot KJ	Taylor TN, Davis PH, Torner JC, Holmes J, Meyer JW, Jacobson MF.	Chung CW, Wang JD, Yu CF, Yang MC.	Joyce GF, Keeler EB, Shang B, Goldman DP.	Beale S, Bending M, Trueman P	Bergman L, van der Meulen JH, Limburg M, Habbema JD.	Sandercock P, Berge E, Dennis M, Forbes J, Hand P, Kwan J, Lewis S, Lindley R, Neilson A, Wardlaw J.	Lightowlers S, McGuire A.
Conversion rate to US$	1	0.895912701	1	1	1	0.6462187	0.53	0.636819185	0.6344894
Value	33658	38639.81888	103576	8641 7535	3807	32329.5036	41340	16690.15203	11306.33452
CPI for 1H2009	394.9	394.9	394.9	394.9	394.9	394.9	394.9	394.9	394.9
CPI for article period	239.1	321.3	162.7	278.8	255.1	369.302	177.1	266	239.1
current-previous	155.8	73.6	232.2	116.1	139.8	25.598	217.8	128.9	155.8
%change	1.651610205	1.229069406	2.427166564	1.41642755	1.54802	1.069314545	2.229813665	1.484586466	1.6516102
Inflated total	55,589.90	47,491.02	251,396.20	12,239.35 10672.78	5,893.31	34,570.41	92,180.50	24,777.97	18,673.66
with 100% indirect costs		94,982.04		24,478.70 21345.56	11,786.63	69,140.82	184,360.99	49,555.95	37,347.31

Mean	79998.41
Median	52572.92
Standard Deviation	78264.67
Minimum	11786.63
Maximum	251396.2

13.5. Dementia/Cognitive Dysfunction

		McDonnell J, Redekop WK, van der Roer N, Goes E, Ruitenberg A, Busschbach JJ, Breteler MM, Rutten FF.	Ernst RL, Hay JW.
Disease subtype		Alzheimers	Alzheimers
Country		Netherlands	USA
Basis of analysis		Microsimulation	Microsimulation
Study design		Incidence	Incidence
Methodological approach		Sum_Diagnosis Specific	Sum_Diagnosis Specific
Data sources		Dutch healthcare system data,The Rotterdam Study, Dutch Central Bureau for Statistics, Ministry of National Health, Welfare and Sport and published yearbooks containing data on costs of homecare, care in a home for the elderly and nursing home care.	Literature review
Population	Sex	both	both
	n	306 prevalent, 95 incident	n/a
	age	55+	65+
	other		
Perspective		3rd party payer	Societal
Time horizon		10yr	Lifetime
Year of costs		1996	1991
Discount rate		-	4%
COI Estimation Procedure		Bottom up	Bottom up
Cost component			
In-patient hospital care			✓
Out-patient hospital care			
Long-term mental hospital		✓	✓
Presciption Drugs			×
Skilled nursing facility		✓	
Home nursing		✓	✓
Doctors' visits		✓	✓
Therapists' vists			×

	McDonnell J, Redekop WK, van der Roer N, Goes E, Ruitenberg A, Busschbach JJ, Breteler MM, Rutten FF.	Ernst RL, Hay JW.
Emergency Room visits		
Nursing home	✓	✓
Aid tools		
Lost productivity		✓
Co-morbidities		
Radiology		
Laboratory		
Other		Caregiver costs, unpaid home care, diagnostic costs
excludes	Caregiver costs	transportation
Per person cost	100000	173932
Currency	Euro	USD
Conversion rate to US$	1.17	1
Value	117000	173932
CPI for H12009	394.9	394.9
CPI for article period	232.4	177.1
current-previous	162.5	217.8
%change	1.69922547	2.22981366
Inflated total	198,809.38	387,835.95

Mean	293,322.67
Median	293322.665
Standard Deviation	133,661.97
Minimum	198809.38
Maximum	387835.95

13.6. Diabetes Mellitus

	Ackermann RT, Marrero DG, Hicks KA, Hoerger TJ, Sorensen S, Zhang P, Engelgau MM, Ratner RE, Herman WH.	**Birnbaum H, Leong S, Kabra A.**	**Joyce GF, Keeler EB, Shang B, Goldman DP.**	**Beale S, Bending M, Trueman P**
Disease subtype	Type 2	Type 1 and Type 2		
Country	USA	USA	USA	*United Kingdom*
Basis of analysis	Microsimulation	Database	Microsimulation	Microsimulation
Study design	Incidence	Prevalence	Incidence	?
Methodological approach	Sum_Diagnosis Specific	Matched control	Regression	?
Data sources	UK Prospective Diabetes Study, Herman et al 2003, Center for Medicare and Medicaid Services (CMS) reimbursement rates	Claims data, US government stats, Health Care Financing Administration	Future Elderly Project (FEP): link extended Medicare claims (1991–1999) to the Medicare Current Beneficiary Survey (MCBS)	?
Popul ation **Sex**	both	F	both	both
n	3234	3759	not specifically stated for DM	not stated for this age group
age	25+	all	65+	40-44
Perspective	3rd party payer	3rd party payer	3rd party payer	3rd party payer
Time horizon	lifetime	lifetime	lifetime	lifetime
Year of costs	2000	2002	1999	2007
Discount rate	3%	inflated using the inflation rate of the medical care component of the consumer price index, which averaged 3.8% per year. No discounting	3%	not stated
COI Estimation Procedure	Bottom-up	Bottom-up	Bottom-up	Top-down
Cost component		Employer medical payments		NHS costs
In-patient care	✓	✓	✓	
Out-patient care	✓	✓	✓	
Presciption Drugs	✓	✓	✓	

	Ackermann RT, Marrero DG, Hicks KA, Hoerger TJ, Sorensen S, Zhang P, Engelgau MM, Ratner RE, Herman WH.	Birnbaum H, Leong S, Kabra A.	Joyce GF, Keeler EB, Shang B, Goldman DP.	Beale S, Bending M, Trueman P
Skilled nursing facility			✓	
Home nursing			✓	
Doctors' visits		✓	✓	
Therapists' vists				
Emergency Room visits	✓			
Nursing home			✓	
Aid tools				
Lost productivity	✓	×	✓	
Co-morbidities		✓		×
Radiology				
Laboratory	✓			
Other	value of the time that spent traveling to and attending appointments, exercising, shopping, and cooking; the costs of exercise classes, exercise equipment, special foods, and food preparation items; and the costs of transportation to and from appointments, monitoring and treating side effects			
Per person cost	45,362.00	233000	13,032.00	53,621.75
Currency	USD	USD	USD	GBP
Conversion rate to US$	1	1	1	0.646218682
Value	45,362.00	233,000.00	13,032.00	34,651.37
CPI for 1H2009	394.9	394.9	394.9	394.9
CPI for article period	266	292.9	255.1	369.302
current-previous	128.9	102	139.8	25.598
%change	1.484586466	1.348241721	1.548020384	1.069314545
Inflated total	67,343.81	314,140.32	20,173.80	37,053.22

	Ackermann RT, Marrero DG, Hicks KA, Hoerger TJ, Sorensen S, Zhang P, Engelgau MM, Ratner RE, Herman WH.	Birnbaum H, Leong S, Kabra A.	Joyce GF, Keeler EB, Shang B, Goldman DP.	Beale S, Bending M, Trueman P
with 100% indirect costs	134687.6226	628280.6419	40347.60329	74106.43619

Mean	219355.576
Median	104397.0294
Standard Deviation	275396.4044
Minimum	40347.60329
Maximum	628280.6419

13.7. Musculoskeletal disorders

		Kobelt G, Jönsson L, Lindgren P, Young A, Eberhardt K.		Wong JB, Ramey DR, Singh G	Wong JB, Ramey DR, Singh G	Patrick DL, Ramsey SD, Spencer AC, Kinne S, Belza B, Topolski TD.	Braithwaite RS, Col NF, Wong JB.	Gabriel SE, Crowson CS, Luthra HS, Wagner JL, O'Fallon WM
Disease		Arthritis		Arthritis	Arthritis	Arthritis	Hip fracture	Arthritis
Disease subtype		RA		RA	RA	OA		RA
Country		United Kingdom	Sweden	USA	USA	USA	USA	USA
Basis of analysis		Microsimulation		Microsimulation	Microsimulation	RTC	Microsimulation	Microsimulation
Study design		Incidence		Incidence	Incidence	Prevalence	Incidence	Prevalence
Methodological approach		Sum_Diagnosis Specific		Sum_Diagnosis Specific	Sum_Diagnosis Specific	Sum_Diagnosis Specific	Sum_Diagnosis Specific	Matched control
Data sources		Cohort studies, price lists		Arthritis, Rheumatism, and Aging Medical Information System (ARAMIS) Post-Marketing Surveillance Program cohort	Arthritis, Rheumatism, and Aging Medical Information System (ARAMIS) Post-Marketing Surveillance Program cohort	RTC	Literature review: Longitudinal Study of Aging and the Established Populations for Epidemiologic Studies of the Elderly, 1997 National Hospital Discharge Survey	Study
Population	**Sex**	both		both	both	both	80% female	74% F
	n	183	916	4258	4258	249	n/a	193
	age	18+		45	45	55-75	80+	36-93 mean: 65.2
	other			healthy cohort	healthy cohort	OA		RA
Perspective		society		society	society	societal	societal	societal
Time horizon		10yr		lifetime	lifetime	lifetime	lifetime	lifetime
Year of costs		2001		1998	1998	1997	2001	1995
Discount rate		3%		3%	3%	3%	3%	3%
COI Estimation		Bottom-up		Bottom-up	Bottom-up	Bottom-up	Bottom-up	Bottom-up

	Kobelt G, Jönsson L, Lindgren P, Young A, Eberhardt K.	Wong JB, Ramey DR, Singh G	Wong JB, Ramey DR, Singh G	Patrick DL, Ramsey SD, Spencer AC, Kinne S, Belza B, Topolski TD.	Braithwaite RS, Col NF, Wong JB.	Gabriel SE, Crowson CS, Luthra HS, Wagner JL, O'Fallon WM
Procedure						
Cost component		Medicare reimbursement rates	Medicare reimbursement rates	Medicare reimbursement rates	Medicare reimbursement rates	Charges
In-patient hospital care	✓	✓	✓		✓	✓
Out-patient hospital care	✓	✓	✓		✓	✓
Presciption Drugs	✓	✓	✓	✓	×	✓
Skilled nursing facility					✓	
Home nursing		✓	✓	✓	✓	
Doctors' visits	✓	✓	✓	✓	×	
Therapists' vists	✓	✓	✓	✓		
Emergency Room visits		✓	✓			
Nursing home		✓	✓		✓	
Aid tools				✓		
Lost productivity	✓	✓	✓		×	✓
Co-morbidities						
Radiology		✓	✓			
Laboratory		✓	✓			
Rehabilitation		✓	✓		✓	
Other		Non-traditional treatment	Non-traditional treatment	Non-traditional treatment, chore help		transportation, child care, chore help
excludes	nonmedical direct costs, costs of informal care				transport	
Per person cost	38331 78911	130680	141686	59689	75500	122,000
Currency	USD	USD	USD	USD	USD	USD
Conversion rate to US$	1	1	1	1	1	1
Value	38331 78911	130680	141686	59689	75500	122000
CPI for 1H2009	394.9	394.9	394.9	394.9	394.9	394.9
CPI for article period	278.8	246.8	246.8	239.1	278.8	190.5

	Kobelt G, Jönsson L, Lindgren P, Young A, Eberhardt K.	Wong JB, Ramey DR, Singh G	Wong JB, Ramey DR, Singh G	Patrick DL, Ramsey SD, Spencer AC, Kinne S, Belza B, Topolski TD.	Braithwaite RS, Col NF, Wong JB.	Gabriel SE, Crowson CS, Luthra HS, Wagner JL, O'Fallon WM
current-previous	116.1	148.1	148.1	155.8	116.1	204.4
%change	1.42	1.6	1.6	1.65	1.42	2.07
Inflated total	54,293.084 111,771.7	209,098.6	226,709.082	98,582.9615	106,940.3	0
with 200% indirect costs				295,748.885	320,820.8	

Mean	192596.699
Median	211993.095
Standard Deviation	94056.3958
Range	266527.755
Minimum	54293.0843
Maximum	320820.839

14. Appendix D: Disease utility data

Author	Disease	Utility	Preference	Method
Kobelt G, Eberhardt K, Jönsson L, Jönsson B.	RA	0.2245 - 0.7154	Patient	VAS/QOL questionnaire
Kobelt G, Jönsson L, Lindgren P, Young A, Eberhardt K.	RA	0.2245 - 0.7459	Patient	QOL questionnaire
Patrick DL, Ramsey SD, Spencer AC, Kinne S, Belza B, Topolski TD.	OA	0.599	Community and Patient	QOL questionnaire
van den Hout WB, de Jong Z, Munneke M, Hazes JM, Breedveld FC, Vliet Vlieland TP.	RA	0.659 - 0.796	Patient	VAS/QOL questionnaire
Neumann PJ, Kuntz KM, Leon J, Araki SS, Hermann RC, Hsu MA, Weinstein MC	Alzheimer's	0.14 - 0.73	Patient Caregiver	QOL questionnaire
Earle CC, Chapman RH, Baker CS, Bell CM, Stone PW, Sandberg EA, Neumann PJ	Breast cancer	0.16-1.0	Clinicians 18 Author 11 Patients 10 Community 8	SG 4 10.0 TTO 7 17.5 RS 23 57.5 Estimates 6
Ko CY, Maggard M, Livingston EH	Breast cancer	0.62	Patient	QOL questionnaire
Millar JA, Millward MJ	Breast cancer	0.41 - 0.98	From Earle et al	From Earle et al
Salpeter SR, Buckley NS, Liu H, Salpeter EE.	Breast cancer	0.65	Lit review (incl Ko	Lit review (incl Ko etal)

Author	Disease	Utility	Preference	Method
			etal)	
Ward S, Simpson E, Davis S, Hind D, Rees A, Wilkinson A.	Breast cancer	0.5 - 0.94	Patients and Clinicians	TTO, VAS
Earle CC, Chapman RH, Baker CS, Bell CM, Stone PW, Sandberg EA, Neumann PJ	Colon cancer	0.75-0.96	Clinicians 18 Author 11 Patients 10 Community 8	SG 4 10.0 TTO 7 17.5 RS 23 57.5 Estimates 6
Ko CY, Maggard M, Livingston EH	Colon cancer	0.67 - 0.71	Patient	QOL questionnaire
Ness RM, Holmes AM, Klein R, Dittus R.	Colo-rectal cancer	0.25 - 0.74	Patient	SG
Salpeter SR, Buckley NS, Liu H, Salpeter EE.	Colon cancer	0.7 (0.55 - 0.85)	from Ko et al	from Ko et al
Sandercock P, Berge E, Dennis M, Forbes J, Hand P, Kwan J, Lewis S, Lindley R, Neilson A, Wardlaw J.	CVA	0.29 - 0.79	Patient	QOL questionnaire
Ward S, Lloyd Jones M, Pandor A, Holmes M, Ara R, Ryan A, Yeo W, Payne N.	CVA	0.52 – 0.87	Not stated	review of 53 measures
Salpeter SR, Buckley NS, Liu H, Salpeter EE.	CVD event	0.75 (0.6 - 0.85)	Not stated	Lit review
Ward S, Lloyd Jones M, Pandor A, Holmes M, Ara R, Ryan A, Yeo W, Payne N.	Unstable angina	0.77	Patient	QOL questionnaire
Ward S, Lloyd Jones M, Pandor A, Holmes M, Ara R, Ryan A, Yeo W, Payne N.	Stable angina	0.808	Patient	TTO, QOL questionnaire

Author	Disease	Utility	Preference	Method
Ackermann RT, Marrero DG, Hicks KA, Hoerger TJ, Sorensen S, Zhang P, Engelgau MM, Ratner RE, Herman WH.	Diabetes	0.69	Patient	QOL questionnaire
Adler AI.	Diabetes	0.78	Patient	QOL questionnaire
Annemans L, Lamotte M, Clarys P, Van den Abeele E.	Diabetes	0.689	From Coffey	
Clarke PM, Gray AM, Briggs A, Farmer AJ, Fenn P, Stevens RJ, Matthews DR, Stratton IM, Holman RR; UK Prospective Diabetes Study (UKDPS) Group	DM Type II - uncomplicated	0.78	Patient	QOL questionnaire
Coffey JT, Brandle M, Zhou H, Marriott D, Burke R, Tabaei BP, Engelgau MM, Kaplan RM, Herman WH.	Diabetes	0.36 - 0.69	Patient	QOL questionnaire
Herman WH, Hoerger TJ, Brandle M, Hicks K, Sorensen S, Zhang P, Hamman RF, Ackermann RT, Engelgau MM, Ratner RE; Diabetes Prevention Program Research Group.	DM Type II	0.54 – 0.69	Patient	QOL questionnaire
Manuel DG, Schultz SE, Kopec JA	Diabetes	F: 0.92 M: 0.929	Patient	QOL questionnaire
Manuel DG, Schultz SE.	Diabetes	0.872	Patient	QOL questionnaire

Author	Disease	Utility	Preference	Method
Manuel DG, Schultz SE.	Diabetes	0.799	Physician	QOL questionnaire
Salpeter SR, Buckley NS, Liu H, Salpeter EE.	Fracture	0.85 (0.65-0.9)	Not stated	Review
Earnshaw SR, Graham CN, Ettinger B, Amonkar MM, Lynch NO, Middelhoven H.	Hip Fracture	1st year: 0.598 (+/- 20%) subsequent years: 0.857	Not stated	Review
Kanis JA, Stevenson M, McCloskey EV, Davis S, Lloyd-Jones M.	Fracture	1st year: 0.792 2nd year:0.813	Community	QOL questionnaire
Gabriel SE, Kneeland TS, Melton LJ 3rd, Moncur MM, Ettinger B, Tosteson AN.	Fracture	0.28 (SD: 0.37)	Non-Fracture Subjects	Time trade off
Gabriel SE, Kneeland TS, Melton LJ 3rd, Moncur MM, Ettinger B, Tosteson AN.	Fracture	0.65 (SD: 0.45)	Fracture Subjects	Time trade off
Gabriel SE, Kneeland TS, Melton LJ 3rd, Moncur MM, Ettinger B, Tosteson AN.	Fracture	0.72 (SD: 0.16)	Fracture Subjects	Directly measured: vertical rating scale
Gabriel SE, Kneeland TS, Melton LJ 3rd, Moncur MM, Ettinger B, Tosteson AN.	Fracture	0.70 (SD: 0.41)	Fracture Subjects	Directly measured:TTO
Gabriel SE, Kneeland TS, Melton LJ 3rd, Moncur MM, Ettinger B, Tosteson AN.	Fracture	0.68 (SD: 0.18)	Fracture Subjects	Derived using population-based values: Health utility index
Gabriel SE, Kneeland TS, Melton LJ 3rd, Moncur MM, Ettinger B, Tosteson AN.	Fracture	0.61 (SD: 0.08)	Fracture Subjects	Derived using population-based

Author	**Disease**	**Utility**	**Preference**	**Method**
				values: Quality of well-being
Davies A, Hutton J, O'Donnell J, Kingslake S	MI	1st year: 0.718, post MI 0.74	Review	?QOL questionnaire
Ward S, Lloyd Jones M, Pandor A, Holmes M, Ara R, Ryan A, Yeo W, Payne N.	MI	0.683-0.78	Not stated	Review
Goodacre S, Nicholl J, Dixon S, Cross E, Angelini K, Arnold J, Revill S, Locker T, Capewell SJ, Quinney D, Campbell S, Morris F.	MI	0.76	Patient	QOL questionnaire
Lacey EA, Walters SJ.	MI (6 weeks) MI (1yr)	68.3 (SD:23.3) 71.8 (SD: 24.3)	Patient	QOL questionnaire
Brazier JE, Green C, Kanis JA; Committee Of Scientific Advisors International Osteoporosis Foundation.	Hip fracture Vertebral fracture Wrist fracture in first year Proximal humerus	0.797 (0.651-1.012) 0.909 (0.84-0.97) 0.981 (0.978-0.986) 0.981 (0.978-0.986)	Community	TTO
Gabriel SE, Kneeland TS, Melton LJ 3rd, Moncur MM, Ettinger B, Tosteson AN.	Osteoporosis	0.43 (SD: 0.4)	Non-Fracture Subjects	Time trade off
Gabriel SE, Kneeland TS, Melton LJ 3rd, Moncur MM, Ettinger B, Tosteson AN.	Osteoporosis	0.84 (SD: 0.29)	Fracture Subjects	Time trade off

15. Appendix E: Disease-onset and life expectancy data

Author	Disease	Onset	Onset: F	Onset: M	LE	LE: F	LE: M	Comment
Ernst RL, Hay JW.	Alzheimer's					4.3	3.3	
Ganguli M, Dodge HH, Shen C, Pandav RS, DeKosky ST.	Alzheimer's	80.2 ± 6	80.3 ± 5.8	80.1 ± 6.3	5.9 ± 3.7			
Jost BC, Grossberg GT.	Alzheimer's	74.7	75.4	72.8		6.083333	5	
Larson EB, Shadlen MF, Wang L, McCormick WC, Bowen JD, Teri L, Kukull WA.	Alzheimer's					5.7	4.2	
Loveman E, Green C, Kirby J, Takeda A, Picot J, Payne E, CleggA	Alzheimer's	75.2			5.25			
Loveman E, Green C, Kirby J, Takeda A, Picot J, Payne E, CleggA	Alzheimer's							
McDonnell J, Redekop WK, van der Roer N, Goes E, Ruitenberg A, Busschbach JJ, Breteler MM, Rutten FF.	Alzheimer's	84.3			4.5			
Chu PC, Wang JD, Hwang JS, Chang YY.	Ca breast	50.5			20.01			
Chu PC, Wang JD, Hwang JS, Chang YY.	Ca colon	63.8			10.86			
Maroun J, Ng E, Berthelot JM, Le Petit C, Dahrouge S, Flanagan WM, Walker H, Evans WK	Ca colon				7.6			
Eisenstein EL, Shaw LK, Anstrom KJ, Nelson CL, Hakim Z, Hasselblad V, Mark DB	CHD				16.2			
Chung CW, Wang JD, Yu CF, Yang MC.	CVA		67.7	65.1		10.1	9.1	
Kolominsky-Rabas PL, Heuschmann PU, Marschall D, Emmert M, Baltzer N, Neundorfer B, Schooffski O, Krobot KJ	CVA		76.3	70.6	7.3	6.3	8.6	
Hill GB, Forbes WF, Lindsay J.	Dementia					19.98	15.8	

Author	Disease	Onset	Onset: F	Onset: M	LE	LE: F	LE: M	Comment
Meerman L, van de Lisdonk EH, Koopmans RT, Zielhuis GA, Olde Rikkert MG.	Dementia	81.7 ± 7.1			2.3			
Wolstenholme J, Fenn P, Gray A, Keene J, Jacoby R, Hope T.	Dementia	73 ± 7.5						
Koopman RJ, Mainous AG 3rd, Diaz VA, Geesey ME.	Diabetes	46						
Manuel DG, Schultz SE.	Diabetes					24.7	18.7	LE age 50
Clarke PM, Gray AM, Briggs A, Farmer AJ, Fenn P, Stevens RJ, Matthews DR, Stratton IM, Holman RR; UK Prospective Diabetes Study (UKDPS) Group	DM Type II	52.59				26.8	25.54	LE age 45-49
Gilmer TP, Roze S, Valentine WJ, Emy-Albrecht K, Ray JA, Cobden D, Nicklasson L, Philis-Tsimikas A, Palmer AJ.	Diabetes	44.7			17.3			
Jonker JT, De Laet C, Franco OH, Peeters A, Mackenbach J, Nusselder WJ.	Diabetes					24.3	23.8	
Valentine WJ, Palmer AJ, Nicklasson L, Cobden D, Roze S.	Diabetes	47			25			
Braithwaite RS, Col NF, Wong JB.	Hip fracture				5.4			
Chung CW, Wang JD, Yu CF, Yang MC.	MI		68.6	61.3		11.4	13.6	
Gabriel SE, Crowson CS, O'Fallon, WM	Rheumatoid Arthritis	66.5			30			LE age 50
Gonzalez A, Icen M, Kremrees HM, Crowson CS, David JM, Therneau TM, Roger VL, Gabriel SE	Rheumatoid Arthritis	58			17			
Wong JB, Ramey DR, Singh G	Rheumatoid Arthritis				28.5			LE age 45
Ramos-Remus C, Sierra-Jimenez G, Skeith K, Aceves-Avila FJ, Russell AS, Offer R, Olguin-Redes JE, Homik J, Sanchez L, Sanchez-Ortiz A, Navarro-Cano G.	Rheumatoid Arthritis	48						Canada

Author	Disease	Onset	Onset: F	Onset: M	LE	LE: F	LE: M	Comment
Ramos-Remus C, Sierra-Jimenez G, Skeith K, Aceves-Avila FJ, Russell AS, Offer R, Olguin-Redes JE, Homik J, Sanchez L, Sanchez-Ortiz A, Navarro-Cano G.	Rheumatoid Arthritis	36						Mexico

16. Appendix F: Detailed results

16.1. CUA Base case

Probabilistic sensitivity analysis - 1,000,000 iterations

Statistic	C(Enabling)	E(Enabling)	C/E(Enabling)	C(Laissez-faire)	E(Laissez-faire)	C/E(Laissez-faire)	ICER
Mean	$302,352	32.33 QALY	9378 $/QALY	$302,107	32.07 QALY	9445 $/QALY	942 $/QALY
Std Dev	$63,022	1.58 QALY	2028 $/QALY	$64,051	1.58 QALY	2066 $/QALY	n/a
Minimum	$74,975	25.08 QALY	2315 $/QALY	$70,606	24.95 QALY	2209 $/QALY	33,608 $/QALY
2.50%	$185,135	29.2 QALY	5665 $/QALY	$182,311	28.96 QALY	5637 $/QALY	11,767 $/QALY
10%	$221,984	30.3 QALY	6814 $/QALY	$220,211	30.05 QALY	6826 $/QALY	7092 $/QALY
Median	$300,514	32.34 QALY	9296 $/QALY	$300,485	32.08 QALY	9369 $/QALY	112 $/QALY
90%	$385,377	34.35 QALY	12051 $/QALY	$386,403	34.09 QALY	12163 $/QALY	Dominant
97.50%	$429,727	35.4 QALY	13555 $/QALY	$430,985	35.14 QALY	13676 $/QALY	Dominant
Maximum	$574,094	39.78 QALY	19578 $/QALY	$571,607	39.47 QALY	19436 $/QALY	8023 $/QALY

Two-dimensional (Sampling and Trials) - 50,000 iterations

Statistic	C(Enabling)	E(Enabling)	C/E(Enabling)	C(Laissez-faire)	E(Laissez-faire)	C/E(Laissez-faire)	ICER
Mean	$302,442	32.33 QALY	9,382 $/QALY	$302,254	32.07 QALY	9,451 $/QALY	723 $/QALY
Std Dev	$63,061	1.58 QALY	2,030 $/QALY	$64,146	1.58 QALY	2,070 $/QALY	n/a
Minimum	$97,473	26.10 QALY	2,911 $/QALY	$92,043	25.81 QALY	2,763 $/QALY	18,724 $/QALY
2.50%	$184,887	29.19 QALY	5,658 $/QALY	$181,599	28.95 QALY	5,620 $/QALY	13,700 $/QALY
10%	$222,302	30.29 QALY	6,816 $/QALY	$220,359	30.04 QALY	6,828 $/QALY	7,772 $/QALY
Median	$300,376	32.34 QALY	9,303 $/QALY	$300,469	32.07 QALY	9,382 $/QALY	Dominant
90%	$385,487	34.35 QALY	12,054 $/QALY	$386,832	34.09 QALY	12,180 $/QALY	Dominant
97.50%	$431,066	35.38 QALY	13,577 $/QALY	$432,961	35.12 QALY	13,707 $/QALY	Dominant
Maximum	$556,608	38.66 QALY	18,913 $/QALY	$555,362	38.52 QALY	18,857 $/QALY	8,900 $/QALY

t-Test: Two-Sample Assuming Equal Variances

	C(Enabling)	C(Laissez-faire)
Mean	302441.8	302254.4971
Variance	3976776815	4114765774
P(T<=t) one-tail	0.320742	
P(T<=t) two-tail	0.641483	
	E(Enabling)	***E(Laissez-faire)***
Mean	32.32848	32.06610988
Variance	2.493096	2.48386777
P(T<=t) one-tail	$3.4 * 10^{-152}$	
P(T<=t) two-tail	$6.8 * 10^{-152}$	
	C/E(Enabling)	***C/E(Laissez-faire)***
Mean	9381.567	9450.669352
Variance	4121997	4286633.899
P(T<=t) one-tail	$4.96 * 10^{-8}$	
P(T<=t) two-tail	$9.91921 * 10^{-8}$	

t-Test: Two-Sample Assuming Unequal Variances

	C(Enabling)	C(Laissez-faire)
Mean	302441.8	302254.4971
Variance	3976776814.84364	4114765774
P(T<=t) one-tail	0.320742	
P(T<=t) two-tail	0.641483	
	E(Enabling)	***E(Laissez-faire)***
Mean	32.32848	32.06610988
Variance	2.493096	2.48386777
P(T<=t) one-tail	$3.4 * 10^{-152}$	
P(T<=t) two-tail	$6.8 * 10^{-152}$	
	C/E(Enabling)	***C/E(Laissez-faire)***
Mean	9381.567	9450.669352
Variance	4121997	4286633.899
P(T<=t) one-tail	$4.96 * 10^{-8}$	
P(T<=t) two-tail	$9.92 * 10^{-8}$	

16.2. One-way sensitivity analyses

16.2.1. Percentage of women among the physically active

F	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.2	Enabling	$274,609		32.17 QALY		8537 $/QALY	
	Laissez-faire	$279,283	$4,674	32.29 QALY	0.12 QALY	8650 $/QALY	38530 $/QALY
0.25	Enabling	$274,454		32.17 QALY		8531 $/QALY	
	Laissez-faire	$279,131	$4,677	32.29 QALY	0.12 QALY	8644 $/QALY	38509 $/QALY
0.3	Enabling	$274,299		32.17 QALY		8526 $/QALY	
	Laissez-faire	$278,979	$4,680	32.30 QALY	0.12 QALY	8638 $/QALY	38487 $/QALY
0.35	Enabling	$274,145		32.18 QALY		8520 $/QALY	
	Laissez-faire	$278,827	$4,683	32.30 QALY	0.12 QALY	8633 $/QALY	38466 $/QALY
0.4	Enabling	$273,990		32.18 QALY		8514 $/QALY	
	Laissez-faire	$278,675	$4,686	32.30 QALY	0.12 QALY	8627 $/QALY	38445 $/QALY
0.45	Enabling	$273,835		32.18 QALY		8509 $/QALY	

F	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
	Laissez-faire	$278,523	$4,689	32.30 QALY	0.12 QALY	8622 $/QALY	38424 $/QALY
0.5	Enabling	$273,680		32.19 QALY		8503 $/QALY	
	Laissez-faire	$278,372	$4,692	32.31 QALY	0.12 QALY	8616 $/QALY	38402 $/QALY
0.55	Enabling	$273,525		32.19 QALY		8497 $/QALY	
	Laissez-faire	$278,220	$4,695	32.31 QALY	0.12 QALY	8611 $/QALY	38381 $/QALY
0.6	Enabling	$273,370		32.19 QALY		8492 $/QALY	
	Laissez-faire	$278,068	$4,698	32.31 QALY	0.12 QALY	8605 $/QALY	38360 $/QALY
0.65	Enabling	$273,215		32.20 QALY		8486 $/QALY	
	Laissez-faire	$277,916	$4,701	32.32 QALY	0.12 QALY	8599 $/QALY	38339 $/QALY
0.7	Enabling	$273,061		32.20 QALY		8480 $/QALY	
	Laissez-faire	$277,764	$4,704	32.32 QALY	0.12 QALY	8594 $/QALY	38318 $/QALY

16.2.2. Increase in percentage of physically active people under Enabling

E_Eff	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$283,061		32.19 QALY	-0.009	8793 $/QALY	(Dominated)
0.025	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$282,531	$9,470	32.203 QALY	0.0044 QALY	8773 $/QALY	2167462 $/QALY
0.05	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$282,001	$8,941	32.216 QALY	0.0175 QALY	8753 $/QALY	510237 $/QALY
0.075	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$281,472	$8,411	32.229 QALY	0.0307 QALY	8733 $/QALY	274191 $/QALY
0.1	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$280,942	$7,881	32.243 QALY	0.0438 QALY	8713 $/QALY	179821 $/QALY
0.125	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$280,412	$7,352	32.256 QALY	0.0570 QALY	8693 $/QALY	129018 $/QALY

E_Eff	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.15	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$279,883	$6,822	32.269 QALY	0.0701 QALY	8673 $/QALY	97270 $/QALY
0.175	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$279,353	$6,292	32.282 QALY	0.0833 QALY	8654 $/QALY	75550 $/QALY
0.2	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$278,823	$5,763	32.295 QALY	0.0964 QALY	8634 $/QALY	59754 $/QALY
0.225	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$278,294	$5,233	32.308 QALY	0.1096 QALY	8614 $/QALY	47750 $/QALY
0.25	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$277,764	$4,704	32.321 QALY	0.1227 QALY	8594 $/QALY	38318 $/QALY
0.275	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$277,234	$4,174	32.335 QALY	0.1359 QALY	8574 $/QALY	30713 $/QALY
0.3	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	

E_Eff	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
	Enabling	$276,705	$3,644	32.348 QALY	0.1491 QALY	8554 $/QALY	24449 $/QALY
0.325	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$276,175	$3,115	32.361 QALY	0.1622 QALY	8534 $/QALY	19201 $/QALY
0.35	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$275,646	$2,585	32.374 QALY	0.1754 QALY	8514 $/QALY	14741 $/QALY
0.375	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$275,116	$2,055	32.387 QALY	0.1885 QALY	8495 $/QALY	10903 $/QALY
0.4	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$274,586	$1,526	32.4 QALY	0.2017 QALY	8475 $/QALY	7565 $/QALY
0.425	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$274,057	$996	32.414 QALY	0.2148 QALY	8455 $/QALY	4637 $/QALY
0.45	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	
	Enabling	$273,527	$466	32.427 QALY	0.2280 QALY	8435 $/QALY	2046 $/QALY

E_Eff	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.475	Enabling	$272,997		32.44 QALY		8416 $/QALY	
	Laissez-faire	$273,061		32.199 QALY	0.2411	8480 $/QALY	(Dominated)
0.5	Enabling	$272,468		32.453 QALY		8396 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.525	Enabling	$271,938		32.466 QALY		8376 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.55	Enabling	$271,408		32.479 QALY		8356 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.575	Enabling	$270,879		32.492 QALY		8337 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.6	Enabling	$270,349		32.506 QALY		8317 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.625	Enabling	$269,819		32.519 QALY		8297 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)

E_Eff	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.65	Enabling	$269,290		32.532 QALY		8278 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.675	Enabling	$268,760		32.545 QALY		8258 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.7	Enabling	$268,231		32.558 QALY		8238 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.725	Enabling	$267,701		32.571 QALY		8219 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.75	Enabling	$267,171		32.585 QALY		8199 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.775	Enabling	$266,642		32.598 QALY		8180 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.8	Enabling	$266,112		32.611 QALY		8160 $/QALY	

E_Eff	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.825	Enabling	$265,582		32.624 QALY		8141 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.85	Enabling	$265,053		32.637 QALY		8121 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.875	Enabling	$264,523		32.65 QALY		8102 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.9	Enabling	$263,993		32.663 QALY		8082 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.925	Enabling	$263,464		32.677 QALY		8063 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
0.95	Enabling	$262,934		32.69 QALY		8043 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)

E_Eff	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.975	Enabling	$262,404		32.703 QALY		8024 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)
1	Enabling	$261,875		32.716 QALY		8004 $/QALY	
	Laissez-faire	$273,061		32.199 QALY		8480 $/QALY	(Dominated)

16.2.3. Percentage of physically active people under Laissez-faire

p_LF_PA	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.1	Laissez-faire	$283,653		31.9312 QALY		8883 $/QALY	
	Enabling	$291,005	$7,352	31.9926 QALY	0.0614 QALY	9096 $/QALY	119785 $/QALY
0.1275	Laissez-faire	$280,740		32.0048 QALY		8772 $/QALY	
	Enabling	$287,364	$6,624	32.0830 QALY	0.0783 QALY	8957 $/QALY	84643 $/QALY
0.155	Laissez-faire	$277,827		32.0783 QALY		8661 $/QALY	
	Enabling	$283,723	$5,895	32.1734 QALY	0.0951 QALY	8819 $/QALY	61970 $/QALY
0.1825	Laissez-faire	$274,914		32.1519 QALY		8550 $/QALY	
	Enabling	$280,081	$5,167	32.2639 QALY	0.1120 QALY	8681 $/QALY	46130 $/QALY

p_LF_PA	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.21	Laissez-faire	$272,001		32.2254 QALY		8441 $/QALY	
	Enabling	$276,440	$4,439	32.3543 QALY	0.1289 QALY	8544 $/QALY	34439 $/QALY
0.2375	Laissez-faire	$269,088		32.2990 QALY		8331 $/QALY	
	Enabling	$272,799	$3,710	32.4447 QALY	0.1458 QALY	8408 $/QALY	25455 $/QALY
0.265	Laissez-faire	$266,175		32.3725 QALY		8222 $/QALY	
	Enabling	$269,157	$2,982	32.5352 QALY	0.1626 QALY	8273 $/QALY	18336 $/QALY
0.2925	Laissez-faire	$263,262		32.4461 QALY		8114 $/QALY	
	Enabling	$265,516	$2,254	32.6256 QALY	0.1795 QALY	8138 $/QALY	12555 $/QALY
0.32	Laissez-faire	$260,349		32.5196 QALY		8006 $/QALY	
	Enabling	$261,875	$1,526	32.7160 QALY	0.1964 QALY	8004 $/QALY	7768 $/QALY
0.3475	Laissez-faire	$257,436		32.5932 QALY		7898 $/QALY	
	Enabling	$258,233	$797	32.8064 QALY	0.2133 QALY	7871 $/QALY	3739 $/QALY
0.375	Laissez-faire	$254,523		32.6667 QALY		7792 $/QALY	

p_LF_PA	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
	Enabling	$254,592	$69	32.8969 QALY	0.2302 QALY	7739 $/QALY	301 $/QALY
0.4025	Enabling	$250,951		32.9873 QALY		7607 $/QALY	
	Laissez-faire	$251,610		32.7403 QALY		7685 $/QALY	(Dominated)
0.43	Enabling	$247,310		33.0777 QALY		7477 $/QALY	
	Laissez-faire	$248,697		32.8138 QALY		7579 $/QALY	(Dominated)
0.4575	Enabling	$243,668		33.1682 QALY		7346 $/QALY	
	Laissez-faire	$245,784		32.8874 QALY		7474 $/QALY	(Dominated)
0.485	Enabling	$240,027		33.2586 QALY		7217 $/QALY	
	Laissez-faire	$242,871		32.9609 QALY		7368 $/QALY	(Dominated)
0.5125	Enabling	$236,386		33.3490 QALY		7088 $/QALY	
	Laissez-faire	$239,958		33.0345 QALY		7264 $/QALY	(Dominated)
0.54	Enabling	$232,744		33.4394 QALY		6960 $/QALY	
	Laissez-faire	$237,045		33.1080 QALY		7160 $/QALY	(Dominated)

p_LF_PA	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.5675	Enabling	$229,103		33.5299 QALY		6833 $/QALY	
	Laissez-faire	$234,132		33.1816 QALY		7056 $/QALY	(Dominated)
0.595	Enabling	$225,462		33.6203 QALY		6706 $/QALY	
	Laissez-faire	$231,219		33.2551 QALY		6953 $/QALY	(Dominated)
0.6225	Enabling	$221,821		33.7107 QALY		6580 $/QALY	
	Laissez-faire	$228,306		33.3287 QALY		6850 $/QALY	(Dominated)
0.65	Enabling	$218,179		33.8012 QALY		6455 $/QALY	
	Laissez-faire	$225,393		33.4022 QALY		6748 $/QALY	(Dominated)

16.2.4. Risk reduction

p_down	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.4	Enabling	$254,224		32.8746 QALY		7733 $/QALY	
	Laissez-faire	$254,229		32.6548 QALY		7785 $/QALY	(Dominated)
0.459	Laissez-faire	$257,006		32.5875 QALY		7887 $/QALY	
	Enabling	$257,696	$690	32.7930 QALY	0.2055 QALY	7858 $/QALY	3358 $/QALY
0.518	Laissez-faire	$259,784		32.5203 QALY		7988 $/QALY	
	Enabling	$261,169	$1,384	32.7114 QALY	0.1912 QALY	7984 $/QALY	7243 $/QALY
0.577	Laissez-faire	$262,562		32.4530 QALY		8091 $/QALY	
	Enabling	$264,641	$2,079	32.6298 QALY	0.1768 QALY	8110 $/QALY	11755 $/QALY
0.636	Laissez-faire	$265,339		32.3857 QALY		8193 $/QALY	
	Enabling	$268,113	$2,773	32.5482 QALY	0.1625 QALY	8237 $/QALY	17063 $/QALY
0.695	Laissez-faire	$268,117		32.3184 QALY		8296 $/QALY	
	Enabling	$271,585	$3,468	32.4666 QALY	0.1482 QALY	8365 $/QALY	23396 $/QALY

p_down	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.754	Laissez-faire	$270,895		32.2511 QALY		8400 $/QALY	
	Enabling	$275,057	$4,162	32.3850 QALY	0.1339 QALY	8493 $/QALY	31082 $/QALY
0.813	Laissez-faire	$273,673		32.1838 QALY		8503 $/QALY	
	Enabling	$278,529	$4,857	32.3034 QALY	0.1196 QALY	8622 $/QALY	40608 $/QALY
0.872	Laissez-faire	$276,450		32.1166 QALY		8608 $/QALY	
	Enabling	$282,001	$5,551	32.2218 QALY	0.1053 QALY	8752 $/QALY	52724 $/QALY
0.931	Laissez-faire	$279,228		32.0493 QALY		8712 $/QALY	
	Enabling	$285,473	$6,245	32.1402 QALY	0.0910 QALY	8882 $/QALY	68653 $/QALY
0.99	Laissez-faire	$282,006		31.9820 QALY		8818 $/QALY	
	Enabling	$288,945	$6,940	32.0586 QALY	0.0767 QALY	9013 $/QALY	90528 $/QALY

16.2.5. Cost reduction

c_down	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.5	Laissez-faire	$258,937		32.1987 QALY		8042 $/QALY	
	Enabling	$260,109	1173	32.3214 QALY	0.1227 QALY	8048 $/QALY	9553 $/QALY
0.549	Laissez-faire	$261,244		32.1987 QALY		8113 $/QALY	
	Enabling	$262,993	1749	32.3214 QALY	0.1227 QALY	8137 $/QALY	14251 $/QALY
0.598	Laissez-faire	$263,550		32.1987 QALY		8185 $/QALY	
	Enabling	$265,877	2326	32.3214 QALY	0.1227 QALY	8226 $/QALY	18950 $/QALY
0.647	Laissez-faire	$265,857		32.1987 QALY		8257 $/QALY	
	Enabling	$268,760	2903	32.3214 QALY	0.1227 QALY	8315 $/QALY	23648 $/QALY
0.696	Laissez-faire	$268,164		32.1987 QALY		8328 $/QALY	
	Enabling	$271,644	3480	32.3214 QALY	0.1227 QALY	8404 $/QALY	28346 $/QALY
0.745	Laissez-faire	$270,471		32.1987 QALY		8400 $/QALY	
	Enabling	$274,527	4056	32.3214 QALY	0.1227 QALY	8494 $/QALY	33045 $/QALY

c_down	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
0.794	Laissez-faire	$272,778		32.1987 QALY		8472 $/QALY	
	Enabling	$277,411	4633	32.3214 QALY	0.1227 QALY	8583 $/QALY	37743 $/QALY
0.843	Laissez-faire	$275,085		32.1987 QALY		8543 $/QALY	
	Enabling	$280,295	5210	32.3214 QALY	0.1227 QALY	8672 $/QALY	42442 $/QALY
0.892	Laissez-faire	$277,392		32.1987 QALY		8615 $/QALY	
	Enabling	$283,178	5786	32.3214 QALY	0.1227 QALY	8761 $/QALY	47140 $/QALY
0.941	Laissez-faire	$279,699		32.1987 QALY		8687 $/QALY	
	Enabling	$286,062	$6,363	32.3214 QALY	0.1227 QALY	8851 $/QALY	51838 $/QALY
0.99	Laissez-faire	$282,006		32.1987 QALY		8758 $/QALY	
	Enabling	$288,945	$6,940	32.3214 QALY	0.1227 QALY	8940 $/QALY	56537 $/QALY

16.2.6. Increase in utility and life expectancy

up	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
1	Laissez-faire	$273,061		31.9532 QALY		8546 $/QALY	
	Enabling	$277,764	4704	32.0146 QALY	0.0614 QALY	8676 $/QALY	76627 $/QALY
1.1	Laissez-faire	$273,061		32.0759 QALY		8513 $/QALY	
	Enabling	$277,764	4704	32.1680 QALY	0.0921 QALY	8635 $/QALY	51089 $/QALY
1.2	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$277,764	4704	32.3214 QALY	0.1227 QALY	8594 $/QALY	38318 $/QALY
1.3	Laissez-faire	$273,061		32.3022 QALY		8453 $/QALY	
	Enabling	$277,764	4704	32.4508 QALY	0.1486 QALY	8560 $/QALY	31646 $/QALY
1.4	Laissez-faire	$273,061		32.3865 QALY		8431 $/QALY	
	Enabling	$277,764	4704	32.5563 QALY	0.1697 QALY	8532 $/QALY	27714 $/QALY
1.5	Laissez-faire	$273,061		32.4478 QALY		8415 $/QALY	
	Enabling	$277,764	4704	32.6329 QALY	0.1850 QALY	8512 $/QALY	25419 $/QALY

up	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
1.6	Laissez-faire	$273,061		32.4791 QALY		8407 $/QALY	
	Enabling	$277,764	4704	32.6720 QALY	0.1929 QALY	8502 $/QALY	24388 $/QALY
1.7	Laissez-faire	$273,061		32.5069 QALY		8400 $/QALY	
	Enabling	$277,764	4704	32.7068 QALY	0.1998 QALY	8493 $/QALY	23539 $/QALY
1.8	Laissez-faire	$273,061		32.5278 QALY		8395 $/QALY	
	Enabling	$277,764	4704	32.7329 QALY	0.2050 QALY	8486 $/QALY	22939 $/QALY
1.9	Laissez-faire	$273,061		32.5488 QALY		8389 $/QALY	
	Enabling	$277,764	4704	32.7590 QALY	0.2103 QALY	8479 $/QALY	22369 $/QALY
2	Laissez-faire	$273,061		32.5697 QALY		8384 $/QALY	
	Enabling	$277,764	4704	32.7852 QALY	0.2155 QALY	8472 $/QALY	21826 $/QALY

16.2.7. Cost of Enabling

cE	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
1000	Enabling	$268,764		32.3214 QALY		8315 $/QALY	

cE	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	(Dominated)
3450	Enabling	$271,214		32.3214 QALY		8391 $/QALY	
	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	(Dominated)
5900	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$273,664	604	32.3214 QALY	0.1227 QALY	8467 $/QALY	4,917 $/QALY
8350	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$276,114	3054	32.3214 QALY	0.1227 QALY	8543 $/QALY	24,876 $/QALY
10800	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$278,564	5504	32.3214 QALY	0.1227 QALY	8619 $/QALY	44,836 $/QALY
13250	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$281,014	7954	32.3214 QALY	0.1227 QALY	8694 $/QALY	64,795 $/QALY
15700	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$283,464	$10,404	32.3214 QALY	0.1227 QALY	8770 $/QALY	84,755 $/QALY

cE	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
18150	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$285,914	$12,854	32.3214 QALY	0.1227 QALY	8846 $/QALY	104,714 $/QALY
20600	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$288,364	$15,304	32.3214 QALY	0.1227 QALY	8922 $/QALY	124,673 $/QALY
23050	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$290,814	$17,754	32.3214 QALY	0.1227 QALY	8998 $/QALY	144,633 $/QALY
25500	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$293,264	$20,204	32.3214 QALY	0.1227 QALY	9073 $/QALY	164,592 $/QALY
27950	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$295,714	$22,654	32.3214 QALY	0.1227 QALY	9149 $/QALY	184,552 $/QALY
30400	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$298,164	$25,104	32.3214 QALY	0.1227 QALY	9225 $/QALY	204,511 $/QALY
32850	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$300,614	$27,554	32.3214 QALY	0.1227 QALY	9301 $/QALY	224,470 $/QALY

cE	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
35300	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$303,064	$30,004	32.3214 QALY	0.1227 QALY	9377 $/QALY	244,430 $/QALY
37750	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$305,514	$32,454	32.3214 QALY	0.1227 QALY	9452 $/QALY	264,389 $/QALY
40200	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$307,964	$34,904	32.3214 QALY	0.1227 QALY	9528 $/QALY	284,348 $/QALY
42650	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$310,414	$37,354	32.3214 QALY	0.1227 QALY	9604 $/QALY	304,308 $/QALY
45100	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$312,864	$39,804	32.3214 QALY	0.1227 QALY	9680 $/QALY	324,267 $/QALY
47550	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	
	Enabling	$315,314	$42,254	32.3214 QALY	0.1227 QALY	9756 $/QALY	344,227 $/QALY
50000	Laissez-faire	$273,061		32.1987 QALY		8480 $/QALY	

cE	Strategy	Cost	Incr Cost	Eff	Incr Eff	C/E	Incr C/E (ICER)
	Enabling	$317,764	$44,704	32.3214 QALY	0.1227 QALY	9831 $/QALY	364,186 $/QALY

16.3. Two-way sensitivity analyses

16.3.1. Cost of enabling and increase in people who are physically active under enabling

cE =>	**1.0K**	**5.9K**	**10.8K**	**15.7K**	**20.6K**	**25.5K**	**30.4K**	**35.3K**	**40.2K**	**45.1K**	**50.0K**
Enabling Effect											
1											
Inc. cost	- 20,186	- 15,286	- 10,386	- 5,486	- 586	4,314	9,214	14,114	19,014	23,914	28,814
Inc. QALY	0.52	0.52	0.52	0.52	0.52	0.52	0.52	0.52	0.52	0.52	0.52
ICER	**Dominant**	**Dominant**	**Dominant**	**Dominant**	**Dominant**	8,339	17,811	27,282	36,753	46,225	55,696
0.9											
Inc. cost	- 18,067	- 13,167	- 8,267	- 3,367	1,533	6,433	11,333	16,233	21,133	26,033	30,933
Inc. QALY	0.46	0.46	0.46	0.46	0.46	0.46	0.46	0.46	0.46	0.46	0.46
ICER	**Dominant**	**Dominant**	**Dominant**	**Dominant**	3,298	13,842	24,386	34,929	45,473	56,016	66,560
0.8											
Inc. cost	- 15,949	- 11,049	- 6,149	- 1,249	3,651	8,551	13,451	18,351	23,251	28,151	33,051
Inc. QALY	0.41	0.41	0.41	0.41	0.41	0.41	0.41	0.41	0.41	0.41	0.41
ICER	**Dominant**	**Dominant**	**Dominant**	**Dominant**	8,860	20,750	32,639	44,529	56,419	68,308	80,198
0.7											

cE =>	1.0K	5.9K	10.8K	15.7K	20.6K	25.5K	30.4K	35.3K	40.2K	45.1K	50.0K
Enabling Effect											
Inc. cost	- 13,830	- 8,930	- 4,030	870	5,770	10,670	15,570	20,470	25,370	30,270	35,170
Inc. QALY	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36	0.36
ICER	**Dominant**	**Dominant**	**Dominant**	2,420	16,050	29,679	43,309	56,939	70,568	84,198	97,828
0.6											
Inc. cost	- 11,711	- 6,811	- 1,911	2,989	7,889	12,789	17,689	22,589	27,489	32,389	37,289
Inc. QALY	0.31	0.31	0.31	0.31	0.31	0.31	0.31	0.31	0.31	0.31	0.31
ICER	**Dominant**	**Dominant**	**Dominant**	9,738	25,704	41,671	57,637	73,603	89,570	105,536	121,502
0.5											
Inc. cost	- 9,593	- 4,693	207	5,107	10,007	14,907	19,807	24,707	29,607	34,507	39,407
Inc. QALY	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25	0.25
ICER	**Dominant**	**Dominant**	815	20,084	39,354	58,624	77,894	97,164	116,434	135,704	154,974
0.4											
Inc. cost	- 7,474	- 2,574	2,326	7,226	12,126	17,026	21,926	26,826	31,726	36,626	41,526
Inc. QALY	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20
ICER	**Dominant**	**Dominant**	11,532	35,830	60,127	84,424	108,721	133,019	157,316	181,613	205,910
0.3											
Inc. cost	- 5,356	- 456	4,444	9,344	14,244	19,144	24,044	28,944	33,844	38,744	43,644
Inc. QALY	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
ICER	**Dominant**	**Dominant**	29,816	62,690	95,563	128,437	161,310	194,184	227,057	259,931	292,805
0.2											

cE =>	1.0K	5.9K	10.8K	15.7K	20.6K	25.5K	30.4K	35.3K	40.2K	45.1K	50.0K
Enabling Effect											
Inc. cost	- 3,237	1,663	6,563	11,463	16,363	21,263	26,163	31,063	35,963	40,863	45,763
Inc. QALY	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
ICER	**Dominant**	17,242	68,049	118,856	169,663	220,471	271,278	322,085	372,892	423,700	474,507
0.1											
Inc. cost	- 1,119	3,781	8,681	13,581	18,481	23,381	28,281	33,181	38,081	42,981	47,881
Inc. QALY	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04	0.04
ICER	**Dominant**	86,275	198,070	309,866	421,662	533,457	645,253	757,048	868,844	980,639	1,092,435
0											
Inc. cost	1,000	5,900	10,800	15,700	20,600	25,500	30,400	35,300	40,200	45,100	50,000
Inc. QALY	- 0.01	- 0.01	0.01	- 0.01	0.01	- 0.01	0.01	- 0.01	0.01	- 0.01	0.01
ICER	**Dominated**	**Dominated**	**Dominated**	**Dominated**	**Dominated**	**Dominated**	**Dominated**	**Dominated**	**Dominated**	**Dominated**	**Dominated**

16.3.2. Cost of Enabling and degree of disease cost reduction

cE =>	1000	5900	10800	15700	20600	25500	30400	35300	40200	45100	50000
c_down											
0.99											
Inc. cost	- 2,060.16	2,839.84	7,739.84	12,639.84	17,539.84	22,439.84	27,339.84	32,239.84	37,139.84	42,039.84	46,939.84
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12

cE =>	1000	5900	10800	15700	20600	25500	30400	35300	40200	45100	50000
c_down											
ICER	**Dominant**	23,135.33	63,054.19	102,973.05	142,891.91	182,810.77	222,729.63	262,648.49	302,567.34	342,486.20	382,405.06
0.941											
Inc. cost	- 2,636.88	2,263.12	7,163.12	12,063.12	16,963.12	21,863.12	26,763.12	31,663.12	36,563.12	41,463.12	46,363.12
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	18,436.94	58,355.80	98,274.66	138,193.52	178,112.38	218,031.24	257,950.10	297,868.95	337,787.81	377,706.67
0.892											
Inc. cost	- 3,213.61	1,686.39	6,586.39	11,486.39	16,386.39	21,286.39	26,186.39	31,086.39	35,986.39	40,886.39	45,786.39
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	13,738.55	53,657.41	93,576.27	133,495.13	173,413.99	213,332.85	253,251.71	293,170.57	333,089.42	373,008.28
0.843											
Inc. cost	- 3,790.33	1,109.67	6,009.67	10,909.67	15,809.67	20,709.67	25,609.67	30,509.67	35,409.67	40,309.67	45,209.67
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	9,040.16	48,959.02	88,877.88	128,796.74	168,715.60	208,634.46	248,553.32	288,472.18	328,391.03	368,309.89

cE =>	1000	5900	10800	15700	20600	25500	30400	35300	40200	45100	50000
c_down											
0.794											
Inc. cost	- 4,367.05	532.95	5,432.95	10,332.95	15,232.95	20,132.95	25,032.95	29,932.95	34,832.95	39,732.95	44,632.95
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	4,341.77	44,260.63	84,179.49	124,098.35	164,017.21	203,936.07	243,854.93	283,773.79	323,692.64	363,611.50
0.745											
Inc. cost	- 4,943.77	- 43.77	4,856.23	9,756.23	14,656.23	19,556.23	24,456.23	29,356.23	34,256.23	39,156.23	44,056.23
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	**Dominant**	39,562.24	79,481.10	119,399.96	159,318.82	199,237.68	239,156.54	279,075.40	318,994.25	358,913.11
0.696											
Inc. cost	- 5,520.50	- 620.50	4,279.50	9,179.50	14,079.50	18,979.50	23,879.50	28,779.50	33,679.50	38,579.50	43,479.50
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	**Dominant**	34,863.85	74,782.71	114,701.57	154,620.43	194,539.29	234,458.15	274,377.01	314,295.86	354,214.72
0.647											
Inc.	-	-	3,702.78	8,602.78	13,502.78	18,402.78	23,302.78	28,202.78	33,102.78	38,002.78	42,902.78

cE =>	1000	5900	10800	15700	20600	25500	30400	35300	40200	45100	50000
c_down											
cost	6,097.22	1,197.22									
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	**Dominant**	30,165.46	70,084.32	110,003.18	149,922.04	189,840.90	229,759.76	269,678.62	309,597.47	349,516.33
0.598											
Inc. cost	- 6,673.94	- 1,773.94	3,126.06	8,026.06	12,926.06	17,826.06	22,726.06	27,626.06	32,526.06	37,426.06	42,326.06
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	**Dominant**	25,467.07	65,385.93	105,304.79	145,223.65	185,142.51	225,061.37	264,980.23	304,899.09	344,817.94
0.549											
Inc. cost	- 7,250.66	- 2,350.66	2,549.34	7,449.34	12,349.34	17,249.34	22,149.34	27,049.34	31,949.34	36,849.34	41,749.34
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	**Dominant**	20,768.68	60,687.54	100,606.40	140,525.26	180,444.12	220,362.98	260,281.84	300,200.70	340,119.55
0.5											
Inc. cost	- 7,827.39	- 2,927.39	1,972.61	6,872.61	11,772.61	16,672.61	21,572.61	26,472.61	31,372.61	36,272.61	41,172.61
Inc.	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12

cE =>	1000	5900	10800	15700	20600	25500	30400	35300	40200	45100	50000
c_down											
QALY											
ICER	**Dominant**	**Dominant**	16,070.29	55,989.15	95,908.01	135,826.87	175,745.73	215,664.59	255,583.45	295,502.31	335,421.16

16.3.3. Cost of Enabling and degree of disease risk reduction

cE =>	1.0000K	5.9000K	10.8000K	15.7000K	20.6000K	25.5000K	30.4000K	35.3000K	40.2000K	45.1000K	50.0000K
p_down											
0.990											
Inc. cost	- 2,060	2,840	7,740	12,640	17,540	22,440	27,340	32,240	37,140	**42,040**	46,940
Inc. QALY	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	0.08	**0.08**	0.08
ICER	**Dominant**	37,045	100,965	164,884	228,803	292,723	356,642	420,562	484,481	**548,401**	612,320
0.931											
Inc. cost	- 2,755	2,145	7,045	11,945	16,845	21,745	26,645	31,545	36,445	**41,345**	46,245
Inc. QALY	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09
ICER	**Dominant**	23,584	77,447	131,310	185,173	239,037	292,900	346,763	400,627	**454,490**	508,353
0.872											
Inc. cost	- 3,449	1,451	6,351	11,251	16,151	21,051	25,951	30,851	35,751	**40,651**	45,551

cE =>	1.0000K	5.9000K	10.8000K	15.7000K	20.6000K	25.5000K	30.4000K	35.3000K	40.2000K	45.1000K	50.0000K
p_down											
Inc. QALY	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11	0.11
ICER	**Dominant**	13,782	60,323	106,863	153,404	199,945	246,486	293,026	339,567	**386,108**	432,649
0.813											
Inc. cost	- 4,143	757	5,657	10,557	15,457	20,357	25,257	30,157	35,057	**39,957**	44,857
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	6,326	47,297	88,269	129,240	170,211	211,182	252,154	293,125	**334,096**	375,068
0.754											
Inc. cost	- 4,838	62	4,962	9,862	14,762	19,662	24,562	29,462	34,362	**39,262**	44,162
Inc. QALY	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13	0.13
ICER	**Dominant**	464	37,056	73,649	110,241	146,833	183,426	220,018	256,610	**293,202**	329,795
0.695											
Inc. cost	- 5,532	- 632	4,268	9,168	14,068	18,968	23,868	28,768	33,668	**38,568**	43,468
Inc. QALY	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
ICER	**Dominant**	**Dominant**	28,793	61,852	94,911	127,970	161,029	194,088	227,147	**260,206**	293,265
0.636											

cE =>	1.0000K	5.9000K	10.8000K	15.7000K	20.6000K	25.5000K	30.4000K	35.3000K	40.2000K	45.1000K	50.0000K
p_down											
Inc. cost	- 6,227	- 1,327	3,573	8,473	13,373	18,273	23,173	28,073	32,973	**37,873**	42,773
Inc. QALY	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16
ICER	**Dominant**	**Dominant**	21,985	52,133	82,281	112,428	142,576	172,724	202,871	**233,019**	263,167
0.577											
Inc. cost	- 6,921	- 2,021	2,879	7,779	12,679	17,579	22,479	27,379	32,279	**37,179**	42,079
Inc. QALY	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18	0.18
ICER	**Dominant**	**Dominant**	16,279	43,987	71,695	99,403	127,111	154,819	182,527	**210,236**	237,944
0.518											
Inc. cost	- 7,616	- 2,716	2,184	7,084	11,984	16,884	21,784	26,684	31,584	**36,484**	41,384
Inc. QALY	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19
ICER	**Dominant**	**Dominant**	11,428	37,061	62,695	88,328	113,962	139,595	165,229	**190,862**	216,496
0.459											
Inc. cost	- 8,310	- 3,410	1,490	6,390	11,290	16,190	21,090	25,990	30,890	**35,790**	40,690
Inc. QALY	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21
ICER	**Dominant**	**Dominant**	7,252	31,100	54,948	78,796	102,643	126,491	150,339	**174,187**	198,035

cE =>	1.0000K	5.9000K	10.8000K	15.7000K	20.6000K	25.5000K	30.4000K	35.3000K	40.2000K	45.1000K	50.0000K
p_down											
0.400											
Inc. cost	- 9,004	- 4,104	796	5,696	10,596	15,496	20,396	25,296	30,196	**35,096**	39,996
Inc. QALY	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22
ICER	**Dominant**	**Dominant**	3,620	25,915	48,210	70,505	92,800	115,095	137,390	**159,685**	181,979

16.3.4. Cost of Enabling and degree of increase in quality of life and life expectancy

cE =>	2000	6800	11600	16400	21200	26000	30800	35600	40400	45200	50000
up											
2											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22
ICER	**Dominant**	2,800.80	25,538.83	48,276.86	71,014.89	93,752.92	116,490.95	139,228.98	161,967.01	184,705.04	207,443.07
1.9											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21
ICER	**Dominant**	2,870.43	26,173.69	49,476.95	72,780.21	96,083.47	119,386.73	142,689.99	165,993.25	189,296.51	212,599.78

cE =>	2000	6800	11600	16400	21200	26000	30800	35600	40400	45200	50000
up											
1.8											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21
ICER	**Dominant**	2,943.60	26,840.91	50,738.22	74,635.53	98,532.84	122,430.15	146,327.46	170,224.77	194,122.08	218,019.39
1.7											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20
ICER	**Dominant**	3,020.62	27,543.18	52,065.74	76,588.30	101,110.86	125,633.42	150,155.98	174,678.54	199,201.10	223,723.66
1.6											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19
ICER	**Dominant**	3,129.55	28,536.45	53,943.35	79,350.24	104,757.14	130,164.04	155,570.94	180,977.84	206,384.74	231,791.64
1.5											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19
ICER	**Dominant**	3,261.80	29,742.42	56,223.04	82,703.66	109,184.28	135,664.89	162,145.51	188,626.13	215,106.75	241,587.36

cE =>	2000	6800	11600	16400	21200	26000	30800	35600	40400	45200	50000
up											
1.4											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17
ICER	**Dominant**	3,556.32	32,427.91	61,299.50	90,171.09	119,042.69	147,914.28	176,785.87	205,657.46	234,529.05	263,400.65
1.3											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
ICER	**Dominant**	4,060.79	37,027.90	69,995.00	102,962.11	135,929.22	168,896.33	201,863.43	234,830.54	267,797.65	300,764.75
1.2											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	**Dominant**	4,917.09	44,835.95	84,754.80	124,673.66	164,592.52	204,511.38	244,430.24	284,349.10	324,267.96	364,186.82
1.1											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09

cE =>	2000	6800	11600	16400	21200	26000	30800	35600	40400	45200	50000
up											
ICER	Dominant	6,555.81	59,778.50	113,001.19	166,223.88	219,446.57	272,669.25	325,891.94	379,114.63	432,337.32	485,560.01
1											
Inc. cost	- 4,296.43	603.57	5,503.57	10,403.57	15,303.57	20,203.57	25,103.57	30,003.57	34,903.57	39,803.57	44,703.57
Inc. QALY	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06
ICER	Dominant	9,832.81	89,659.47	169,486.14	249,312.80	329,139.46	408,966.12	488,792.78	568,619.45	648,446.11	728,272.77

16.3.5. Reduction in cost and risk

p_down =>	0.40	0.46	0.52	0.58	0.64	0.70	0.75	0.81	0.87	0.93	0.99
c_down											
0.99											
Inc. cost	1,113.76	1,973.11	2,832.46	3,691.80	4,551.15	5,410.49	6,269.84	7,129.19	7,988.53	8,847.88	9,707.22
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	5,067.60	9,602.95	14,817.51	20,876.04	28,001.38	36,503.13	46,822.00	59,610.58	75,876.04	97,260.43	126,628.64
0.94											
Inc. cost	825.40	1,642.21	2,459.03	3,275.84	4,092.65	4,909.47	5,726.28	6,543.09	7,359.90	8,176.72	8,993.53
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	3,755.57	7,992.52	12,863.98	18,523.90	25,180.45	33,122.83	42,762.79	54,709.96	69,905.26	89,882.69	117,318.65
0.89											
Inc. cost	537.04	1,311.32	2,085.60	2,859.88	3,634.16	4,408.44	5,182.72	5,957.00	6,731.28	7,505.56	8,279.84
Inc.	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08

p_down =>	**0.40**	**0.46**	**0.52**	**0.58**	**0.64**	**0.70**	**0.75**	**0.81**	**0.87**	**0.93**	**0.99**
c_down											
QALY											
ICER	2,443.53	6,382.08	10,910.46	16,171.76	22,359.51	29,742.53	38,703.57	49,809.34	63,934.47	82,504.94	108,008.67
0.84											
Inc. cost	248.68	980.43	1,712.17	2,443.92	3,175.66	3,907.41	4,639.16	5,370.90	6,102.65	6,834.40	7,566.14
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	1,131.49	4,771.65	8,956.93	13,819.63	19,538.58	26,362.24	34,644.36	44,908.72	57,963.69	75,127.19	98,698.68
0.79											
Inc. cost	- 39.68	649.53	1,338.74	2,027.96	2,717.17	3,406.38	4,095.60	4,784.81	5,474.02	6,163.23	6,852.45
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	**Dominant**	3,161.21	7,003.41	11,467.49	16,717.65	22,981.94	30,585.15	40,008.10	51,992.91	67,749.45	89,388.69
0.75											
Inc. cost	- 328.04	318.64	965.32	1,612.00	2,258.68	2,905.36	3,552.03	4,198.71	4,845.39	5,492.07	6,138.75
Inc.	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08

p_down =>	0.40	0.46	0.52	0.58	0.64	0.70	0.75	0.81	0.87	0.93	0.99
c_down											
QALY											
ICER	**Dominant**	1,550.78	5,049.89	9,115.35	13,896.72	19,601.64	26,525.93	35,107.48	46,022.13	60,371.70	80,078.71
0.70											
Inc. cost	- 616.40	- 12.26	591.89	1,196.03	1,800.18	2,404.33	3,008.47	3,612.62	4,216.77	4,820.91	5,425.06
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	**Dominant**	**Dominant**	3,096.36	6,763.22	11,075.79	16,221.34	22,466.72	30,206.86	40,051.35	52,993.95	70,768.72
0.65											
Inc. cost	- 904.77	- 343.15	218.46	780.07	1,341.69	1,903.30	2,464.91	3,026.53	3,588.14	4,149.75	4,711.37
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	**Dominant**	**Dominant**	1,142.84	4,411.08	8,254.86	12,841.04	18,407.51	25,306.25	34,080.57	45,616.21	61,458.73
0.60											
Inc. cost	-1,193.13	- 674.05	- 154.97	364.11	883.19	1,402.27	1,921.35	2,440.43	2,959.51	3,478.59	3,997.67

p_down =>	0.40	0.46	0.52	0.58	0.64	0.70	0.75	0.81	0.87	0.93	0.99
c_down											
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	**Dominant**	**Dominant**	**Dominant**	2,058.95	5,433.92	9,460.75	14,348.30	20,405.63	28,109.79	38,238.46	52,148.75
0.55											
Inc. cost	-1,481.49	-1,004.94	- 528.40	- 51.85	424.70	901.24	1,377.79	1,854.34	2,330.88	2,807.43	3,283.98
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	**Dominant**	**Dominant**	**Dominant**	**Dominant**	2,612.99	6,080.45	10,289.08	15,505.01	22,139.01	30,860.71	42,838.76
0.50											
Inc. cost	-1,769.85	-1,335.84	- 901.82	- 467.81	- 33.80	400.22	834.23	1,268.24	1,702.26	2,136.27	2,570.28
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	**Dominant**	**Dominant**	**Dominant**	**Dominant**	**Dominant**	2,700.15	6,229.87	10,604.39	16,168.23	23,482.97	33,528.77

16.3.6. Reduction in cost and increased quality of life and life expectancy

c_down =>	0.50	0.55	0.60	0.65	0.70	0.75	0.79	0.84	0.89	0.94	0.99
up											
2.00											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22	0.22
ICER	5,441.41	8,117.64	10,793.87	13,470.10	16,146.34	18,822.57	21,498.80	24,175.03	26,851.26	29,527.50	32,203.73
1.90											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21
ICER	5,576.67	8,319.43	11,062.19	13,804.95	16,547.71	19,290.47	22,033.23	24,775.98	27,518.74	30,261.50	33,004.26
1.80											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21	0.21
ICER	5,718.83	8,531.51	11,344.19	14,156.87	16,969.54	19,782.22	22,594.90	25,407.58	28,220.25	31,032.93	33,845.61
1.70											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20	0.20
ICER	5,868.46	8,754.73	11,641.00	14,527.27	17,413.54	20,299.80	23,186.07	26,072.34	28,958.61	31,844.88	34,731.15

c_down => up	0.50	0.55	0.60	0.65	0.70	0.75	0.79	0.84	0.89	0.94	0.99
1.60											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19
ICER	6,080.09	9,070.45	12,060.80	15,051.15	18,041.51	21,031.86	24,022.21	27,012.57	30,002.92	32,993.28	35,983.63
1.50											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19	0.19
ICER	6,337.04	9,453.77	12,570.50	15,687.23	18,803.96	21,920.69	25,037.42	28,154.14	31,270.87	34,387.60	37,504.33
1.40											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17	0.17
ICER	6,909.22	10,307.37	13,705.51	17,103.65	20,501.79	23,899.94	27,298.08	30,696.22	34,094.37	37,492.51	40,890.65
1.30											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15	0.15
ICER	7,889.31	11,769.49	15,649.67	19,529.85	23,410.03	27,290.21	31,170.39	35,050.57	38,930.75	42,810.93	46,691.10
1.20											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84

c_down =>	0.50	0.55	0.60	0.65	0.70	0.75	0.79	0.84	0.89	0.94	0.99
up											
Inc. QALY	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.12
ICER	9,552.93	14,251.32	18,949.71	23,648.10	28,346.49	33,044.88	37,743.27	42,441.66	47,140.05	51,838.44	56,536.83
1.10											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09	0.09
ICER	12,736.65	19,000.88	25,265.11	31,529.34	37,793.57	44,057.80	50,322.03	56,586.26	62,850.50	69,114.73	75,378.96
1.00											
Inc. cost	1,172.61	1,749.34	2,326.06	2,902.78	3,479.50	4,056.23	4,632.95	5,209.67	5,786.39	6,363.12	6,939.84
Inc. QALY	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06	0.06
ICER	19,103.21	28,498.69	37,894.17	47,289.65	56,685.13	66,080.60	75,476.08	84,871.56	94,267.04	103,662.52	113,058.00

16.3.7. Reduction in risk and increased quality of life and life expectancy

p_down =>	0.40	0.46	0.52	0.58	0.64	0.70	0.75	0.81	0.87	0.93	0.99
up											
2.00											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.27	0.26	0.25	0.24	0.24	0.23	0.22	0.21	0.21	0.20	0.19
ICER	Dominant	2,667.54	5,511.16	8,529.13	11,737.99	15,156.44	18,805.71	22,709.98	26,896.97	31,398.37	36,251.48

p_down =>	0.40	0.46	0.52	0.58	0.64	0.70	0.75	0.81	0.87	0.93	0.99
up											
1.90											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.26	0.26	0.25	0.24	0.23	0.22	0.22	0.21	0.20	0.19	0.18
ICER	**Dominant**	2,698.82	5,586.44	8,663.13	11,948.16	15,463.42	19,233.88	23,288.57	27,660.66	32,389.05	37,519.34
1.80											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.26	0.25	0.24	0.24	0.23	0.22	0.21	0.20	0.19	0.19	0.18
ICER	**Dominant**	2,730.87	5,663.77	8,801.44	12,166.00	15,783.01	19,681.92	23,897.29	28,468.99	33,444.10	38,878.87
1.70											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.26	0.25	0.24	0.23	0.22	0.22	0.21	0.20	0.19	0.18	0.17
ICER	**Dominant**	2,763.67	5,743.31	8,944.20	12,391.92	16,116.17	20,151.52	24,538.69	29,325.98	34,570.39	40,340.86
1.60											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.25	0.25	0.24	0.23	0.22	0.21	0.20	0.19	0.18	0.17	0.16

p_down =>	0.40	0.46	0.52	0.58	0.64	0.70	0.75	0.81	0.87	0.93	0.99
up											
ICER	**Dominant**	2,808.56	5,852.68	9,141.52	12,705.82	16,581.71	20,812.12	25,447.62	30,549.50	36,191.89	42,465.76
1.50											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.25	0.24	0.23	0.22	0.21	0.20	0.19	0.18	0.17	0.16	0.15
ICER	**Dominant**	2,860.80	5,980.69	9,374.00	13,078.33	17,138.49	21,608.34	26,553.32	32,052.97	38,206.92	45,138.63
1.40											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.24	0.23	0.22	0.21	0.20	0.19	0.18	0.17	0.16	0.15	0.13
ICER	**Dominant**	2,969.02	6,248.54	9,865.70	13,875.51	18,345.66	23,360.05	29,024.63	35,474.61	42,885.81	51,489.74
1.30											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.23	0.22	0.21	0.20	0.18	0.17	0.16	0.15	0.13	0.12	0.11
ICER	**Dominant**	3,132.03	6,658.79	10,633.06	15,145.69	20,314.07	26,292.33	33,287.02	41,581.75	51,575.38	63,849.84
1.20											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84

p_down =>	0.40	0.46	0.52	0.58	0.64	0.70	0.75	0.81	0.87	0.93	0.99
up											
Inc. QALY	0.22	0.21	0.19	0.18	0.16	0.15	0.13	0.12	0.11	0.09	0.08
ICER	**Dominant**	3,358.41	7,242.62	11,755.51	17,063.07	23,395.85	31,082.19	40,608.18	52,724.03	68,652.84	90,528.69
1.10											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.20	0.19	0.17	0.15	0.14	0.12	0.10	0.09	0.07	0.06	0.04
ICER	**Dominant**	3,673.13	8,082.65	13,436.99	20,076.24	28,525.99	39,643.72	54,929.94	77,271.04	113,010.60	179,374.99
1.00											
Inc. cost	- 4.37	690.05	1,384.47	2,078.89	2,773.31	3,467.73	4,162.15	4,856.58	5,551.00	6,245.42	6,939.84
Inc. QALY	0.19	0.17	0.15	0.13	0.11	0.09	0.08	0.06	0.04	0.02	0.00
ICER	**Dominant**	4,052.91	9,143.18	15,679.92	24,381.62	36,537.84	54,714.79	84,857.69	144,579.80	319,360.70	9,678,994.42

17. Appendix G: Back-of-the-envelope calculation of absolute savings as a result of PA

		Males	LE age 40:	37.28		
Disease	**Risk**	**Cost**	**p-down**	**risk * cost**	**risk * cost * risk reduction**	**difference**
Ca_Colon	0.05	$65,000	0.6	$3,250	$1,950	$1,300
CHD	0.4	$700,000	0.5	$280,000	$140,000	$140,000
CVA	0.15	$275,000	0.65	$41,250	$26,813	$14,438
DEMEN	0.15	$295,000	0.7	$44,250	$30,975	$13,275
DM	0.38	$110,000	0.3	$41,800	$12,540	$29,260
HTN	0.9	$10,000	0.7	$9,000	$6,300	$2,700
Dyslipidaemia	0.5	$2,000	0.97	$1,000	$970	$30
Rectal	0.058	$78,540	0.68	$4,555	$3,098	$1,458
Prostate	0.16	$44,660	0.9	$7,146	$6,431	$715
Lung	0.07	$50,820	0.75	$3,557	$2,668	$889
Fractures and falls	0.13	$91,000	0.75	$11,830	$8,873	$2,958
Parkinson's Disease	0.067	$100,000	0.8	$6,700	$5,360	$1,340
Total	**3.015**			**$454,338**	**$245,977**	**$208,362**
saving per year						**$5,589**

		Females	**LE age 40:**	**42.46**		
Disease	**Risk**	**Cost**	**p-down**	**risk * cost**	**risk * cost * risk reduction**	**difference**
Ca_Breast	0.125	$210,000	0.8	$26,250	$21,000	$5,250
Ca_Colon	0.05	$65,000	0.6	$3,250	$1,950	$1,300
CHD	0.4	$700,000	0.5	$280,000	$140,000	$140,000
CVA	0.15	$275,000	0.65	$41,250	$26,813	$14,438
DEMEN	0.25	$295,000	0.7	$73,750	$51,625	$22,125
DM	0.38	$110,000	0.3	$41,800	$12,540	$29,260
HTN	0.9	$10,000	0.75	$9,000	$6,750	$2,250
Dyslipidaemia	0.5	$2,000	0.98	$1,000	$980	$20
Rectal	0.052	$78,540	0.81	$4,084	$3,308	$776
Lung	0.07	$50,820	0.62	$3,557	$2,206	$1,352
Fractures and falls	0.4	$91,000	0.75	$36,400	$27,300	$9,100
Parkinson's Disease	0.067	$100,000	0.8	$6,700	$5,360	$1,340
Total				**$527,041**	**$299,831**	**$227,210**
saving per year						**$5,351**