Long-term cost-effectiveness of Patient Empowerment Programme for Type 2 Diabetes Mellitus in primary care

Jinxiao Lian[1,2], Sarah M McGhee[3], Ching So[3], June Chau[3], Carlos KH Wong[1], William CW Wong[1], Cindy LK Lam[1]

[1] Department of Family Medicine and Primary Care, The University of Hong Kong, Hong Kong

[2] School of Optometry, The Hong Kong Polytechnic University, Hong Kong

[3] School of Public Health, The University of Hong Kong, Hong Kong

Running title: Long-term cost-effectiveness of PEP for T2DM

Corresponding author: William CM Wong

Address: Department of Family Medicine and Primary Care, The University of Hong Kong, 3/F, 161 Main Street, Ap Lei Chau Clinic, Ap Lei Chau, Hong Kong

Telephone number/fax number: 25185650/28147475

Email address: wongwcw@hku.hk

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1111/dom.13485

Abstract

Aims: To evaluate the long-term cost-effectiveness of a Patient Empowerment Programme (PEP) for Type 2 Diabetes Mellitus (DM) in primary care

Materials and methods: PEP participants were subjects with Type 2 DM who enrolled into PEP in addition to enrolment in the Risk Assessment and Management Programme for DM (RAMP-DM) at primary care level. The comparison group was subjects who only enrolled into RAMP-DM without participating in PEP (non-PEP). A cost-effectiveness analysis was conducted using a patient level simulation model (with fixed-time increments) from a societal perspective. We incorporated the empirical data from a matched cohort of PEP and non-PEP group to simulate lifetime costs and outcomes for subjects with DM with or without PEP. Incremental cost-effectiveness ratios (ICER) in terms of cost per quality adjusted life year (QALY) gained were calculated. Probabilistic sensitivity analysis was conducted with results presented as a cost-effectiveness acceptability curve.

Results: With an assumption that the PEP effect would last for 5 years as shown by the empirical data, the incremental cost per subject was US$197 and the incremental QALYs gained were 0.06 per subject, which resulted in an ICER of US$3,290 per QALY gained compared with no PEP across the life time. Probabilistic sensitivity analysis showed 66% likelihood that PEP is cost-effective compared with non-PEP when willingness-to-pay (WTP) for a QALY is US$46,153 or above (based on per capita GDP 2017).

Conclusions: Based on this carefully measured cost of PEP and its potentially large benefits, PEP could be highly cost-effective from a societal perspective as an adjunct intervention for patients with DM.

INTRODUCTION

Diabetes mellitus (DM) affects 422 million people in the world and is responsible for an increasing burden to healthcare spending.[1] In US and Europe, around 40 to 60% of the costs of DM management are attributable to inpatient care for complications.[2,3] The morbidity reflected by this economic burden is a strong motivation to develop effective interventions to prevent diabetic complications.

Apart from DM treatment, self-care and lifestyle changes are at the core of DM management.[4] A variety of self-management education programmes have been developed and shown to be effective.[5-8] The next question for decision makers is whether it is efficient to allocate resources to self-management programmes, given limited health care resources. Our recent systematic review identified 12 cost-effectiveness studies on self-management education programmes from 2003 to 2015.[9] Eight of the 12 studies had good quality estimations on both effectiveness and costs. Among these 8, four studies[10-13] found that the cost of an effective programme was modest at the 6- or 12-month follow up, three studies[14-16] found programmes likely to be cost-effective over the participants' life times and one study did not demonstrate cost-effectiveness at the 12-month follow up.[17] This review also showed that there were very few studies with good quality data and even then the clinical evidence for the simulation of cost-effectiveness over the lifetime was rarely sourced from patient-level population data. None of these studies were carried out on an Asian population so a population-based, cost-effectiveness study on an Asian population should be a useful addition to the literature.

The Hong Kong (HK) Hospital Authority (HA), which manages all publicly funded hospitals in HK, launched a Patient Empowerment Programme (PEP) in 2010 for subjects with Type 2

DM who attend public general outpatient clinics (GOPCs) for their diabetes care. A detailed description of the PEP has been published elsewhere.[18-24] Briefly, enrolled subjects attend generic education sessions that cover the importance of self-management and behaviour modification, diet, exercise, stress, coping skills and problem solving. They also attend disease-specific sessions covering knowledge of DM as well as DM management and self-care. Each PEP session is facilitated by an appropriately trained health care professional such as nurse or social worker but the non-government organizations (NGO) who run the sessions can choose their own level of staff and have some freedom in the style of their programme. Apart from the PEP, most of the subjects with Type 2 DM who attend public clinics have also been enrolled in a DM Risk Assessment and Management Programme (RAMP-DM) which provides regular check-ups and screening for complications and serves as their routine DM care.[25] We previously conducted a five-year cost-effectiveness analysis (CEA) based on empirical data which estimated that the cost to prevent one death from any cause for someone in the PEP programme was US$14,465 (HK$112,827) when compared with those enrolled only in RAMP-DM.[26] This cost to prevent one death is far below estimates of the statistical value of life in HK – at least HK$10 million[27] – which itself is a relatively low statistical value of life. However, this previous CEA did not evaluate the longer-term impact of PEP on healthcare costs over the lifetime (i.e. from subject's current age until death). In the current study we aimed to conduct a simulation study based on empirical data to estimate the long-term cost-effectiveness of PEP.

MATERIALS AND METHODS

We used empirical data on the programme cost, incidence of diabetic complications and mortality during the five-year PEP follow up, obtained other parameters from the RAMP-DM programme and incorporated these into a long-term model to simulate the lifetime impact of

PEP plus RAMP-DM on the health care costs and health related quality of life of participants versus those who participated in RAMP-DM only but not PEP. These empirical data were derived from a matched cohort of subjects with RAMP plus PEP and subjects with RAMP only, whose characteristics did not differ between the groups.[26] A societal perspective was taken in this CEA. All the costs are in US dollars (1 US$=7.8 HK$).

The long-term model structure

A patient level simulation model was used to simulate lifetime outcomes for subjects with DM with or without PEP. The model simulates the transitions between different disease states until estimated time of death, based on the average mortality rates of someone with the individual's profile and with a cycle length of one year. The main advantage of an individual-based model is that the transition probabilities can reflect disease history and so multiple complications can be included in the model. The United Kingdom Prospective Diabetes Study (UKPDS) outcome model was used as a reference to develop our model structure.[28] Each individual began in the no complication state, with age and sex randomly allocated from the distributions in the empirical data of a matched group of PEP and non-PEP subjects (Figure 1). Each yearly transition could include an initial occurrence of any of the six DM complications, i.e. acute myocardial infarction (AMI), other ischemic heart disease (IHD), heart failure, stroke, end-stage renal disease (ESRD) or sight-threatening diabetic retinopathy (STDR). In each year, an individual's probability of developing any of the complications or of dying were calculated based on the individual's profile. After developing any complication(s), the subject would have a higher risk of death in the event year, according to the risk associated with that complication, or they would survive the event year but enter the next cycle with the history of the complication for all subsequent years. Subjects with a history of a complication had a higher chance of death compared to those without. If a death

event occurred, the accumulated quality-adjusted life years (QALYs) and cost were calculated for that subject, while a subject who survived that cycle would carry on to the next with an updated age and complication history, if relevant. We simulated only the first development of any specific complication but a subject could have a first event of a different complication, even in the same year. All transition probabilities were estimated from the empirical data as described in more detail later.

Costs of healthcare utilisation and utility values were applied in each cycle (i.e. each year) according to the health states of individual subject (see later). When every individual in the model had died, total costs and QALYs gained were summed across the group. The simulation was repeated 10,000 times for both PEP and non-PEP groups. The model was developed in TreeAge Pro Suite 2013 (TreeAge Software, Inc, Williamstown, MA).

Estimation of transitional probabilities

Diabetic complications

The probabilities of developing the six DM complications were based on the incidence rates from matched PEP and non-PEP cohorts over a five-year follow up. The detailed subject selection and propensity score matching has been reported elsewhere.[26]

Sex-specific incidence rates of complications per person-year were calculated by dividing the five-year cumulative number of events by the total person-years at risk in the follow up period for each type of complication in the PEP and non-PEP groups (Table 1). The incidence rates were converted into an average annual transitional probability (P) for a subject aged 65 i.e. average age in the middle year of the follow-up period, by the equation (1):

$$P = 1 - \exp(-rt), \qquad (1)$$

where r is the average incidence rate over 5 years and t=1 for annual probability.[29]

Since age and sex were found to be associated with different risks of DM complications,[28,30-33] we investigated the association between age and the development of each complication by sex for the matched PEP and non-PEP groups using multivariable Cox proportional hazard regression models (Table 1). The hazard ratios for age were applied to the incidence rate (r) to estimate age-specific rates (r_{age}) using the equation (2):

$$r_{age} = r \times HR^{\wedge(age - 65)}, \qquad (2)$$

and, the transitional probability (P) for a specific age would be:

$$P_{age} = 1 - \exp(-r_{age}\, t), \qquad (3)$$

where t is the period of time, which t=1 for annual probability estimation.

Mortality

The mortality rates used in the model were based on the subject's age, sex, and presence of complications and the coefficients for the association with mortality were from the RAMP-DM data using four statistical models to estimate mortality rates: 1) rate of death in each year for subjects who have not yet developed any of the six complications; 2) rate of death in an event year for subjects without history of complications; 3) rate of death in an event year for those who have other pre-existing complications; and, 4) rate of death in a non-event year for subjects who have developed complications previously (Supplemental Table S1).[34] Probability of death occurring in non-event years (models 1 and 4) was estimated using Gompertz models. The probability of death at age (t) for a subject was estimated by equation (4):

$$1 - \exp\left[\left(H(t \mid x_j) - H(t+1 \mid x_j)\right)\right], \qquad (4)$$

where the $H(t \mid x_j) = h_0(t) \exp(\beta_i x_i)$, with baseline hazard $h_0(t) = \exp(\gamma t) \exp(\beta_0)$ and the parameters γ, β_0, and β_i were the coefficients for each factor as shown in Supplemental Table S1.

For probability of death in event years (models 2 and 3), logistic models were used. The probability of death was estimated by the equation (5):

$$P = 1 - (\exp(-z))/(1+\exp(-z)), \quad (5)$$

where $z = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_n x_n$ and β was the coefficient for each factor.

Estimation of health utility scores

QALYs were used as the long term outcome in the CEA model. The disease-related health state utility values were taken from RAMP-DM data and the same cross sectional sample as used for the private medical costs (see later).[35] The health-related quality of life (HRQOL) data were collected using the SF-12v2 health survey and were transformed into SF-6D health utility scores using a local algorithm.[36,37] Ordinary least squares (OLS) regression was used to estimate the association between each type of DM complication and SF-6D health utility scores, adjusted for socio-demographic factors and clinical parameters (Table 1). We applied the utility value of DM without complications and utility decrements according to individual health status. The loss in utility due to multiple complications was assumed to be additive. No age-related health utility values were applied. The QALYs were calculated by multiplying the utility values with the time spent in that health state. Details of utility decrements associated with DM complications were obtained from published literature.[38]

Estimation of costs

Programme cost

An in-depth costing of the PEP was conducted from a societal perspective and is described elsewhere.[26] The costs included the operation costs of the NGOs providing service, the administrative cost of HA head office and cluster office, subjects' and accompanying persons' travel and time cost for attending the PEP sessions and community resources needed to run the programme which covers the value of volunteer workers' time and of 'free' venues

for holding sessions. The average of the annualized costs during the study period was converted to the year 2017 cost using the Consumer Price Index (CPI) rate[39] and was US$276 per subject. It was assumed to be a one-off cost and was applied to each PEP subject at the initial stage of the model.

Cost of health service utilization

The cost of public health service utilization included the costs of hospitalization, GOPC visits, specialist outpatient clinic (SOPC) visits, allied health clinic visits, and accident and emergency department visits. Data from the RAMP-DM cohort of 128,309 subjects over five years were used to estimate the incremental cost due to DM complications in the event and subsequent years and corresponding cost multipliers (Table 2).[35] The cost multipliers were applied to the baseline cost to calculate the extra cost due to increases in age as well as sex grouping and presence of complications. For example, the annual utilization cost for a 65-year old female with a new MI and history of heart failure was calculated as: US$1,650 × $1.02^{(65-63)}$ × 1.01 × 4.50 × 2.10 = US$16,385. It was assumed that the age and sex-related utilization cost was the same for PEP and non-PEP subjects.

The cost of private medical care included out-patient clinics, inpatient stays and self-financed drugs and was estimated from a cross-sectional survey of 1,275 RAMP-DM subjects.[35] Cost multipliers for age, sex and DM complications were generated using the same methods as described for the public health care costs and the values are shown in Table 2. The cost multipliers were derived from the empirical data from people who may or may not have used private care so it reflects the frequency of use and the costs of each episode and was applied to every individual in the model.

Cost-effectiveness analysis

All future costs and QALYs were discounted at 3.5% per year. In the base case model. The effect of PEP was assumed to last for 5 years after the baseline as observed from the empirical data and assumed to have no further effect after 5 years i.e. have the same transition probabilities of complications as the non-PEP group. Although the effectiveness of PEP last for 5-year, the impact on the health care cost could be long-term across people's life time as a results from the prevented or postponed complication and death. For example, overall there would be fewer subjects with complications developed during their lifetime in the PEP group, which would result in reduced risk of mortality which is associated with the history of complication(s) compared with subjects in the non-PEP group. This is a conservative approach. Incremental cost-effectiveness ratios (ICER) between the PEP and non-PEP groups were calculated by dividing the difference in cost by the difference in QALYs. The ICERs were compared with the willingness to pay (WTP) threshold for a QALY according to the WHO guideline that interventions with a cost per QALY gained of less than 1 × GDP per capita (HK$359,996 in year 2017; at US$1=HK$7.8 = US$46,153) would be considered highly cost-effective.[40-43]

Sensitivity analyses

Sensitivity analyses were conducted to test assumptions on the duration of PEP effect and uncertainties around the parameters. Two alternative assumptions about duration of effect were: 1) a 3-year effect and 2) a lifelong effect. One-way sensitivity analyses were used to identify which parameters had the largest effects on cost-effectiveness. One model parameter was varied at a time while the others remained unchanged. The variables tested included discount rates, programme cost, cost multipliers for public and private health service use, effectiveness of PEP versus non-PEP for each complication, and utility values (Table 1 and 2). The results are displayed as Tornado Charts. Probabilistic sensitivity analysis was

conducted to capture the uncertainties around some of the parameters using the same variables and ranges as in the one-way sensitivity analyses (Table 1 and 2). Random values from the distribution of the selected parameters were used in each iteration of the model. The model was repeated 1,000 times for 1,000 individuals simulated in the model, selecting random values for each parameter each time. The results were plotted on a cost-effectiveness plane and are displayed with cost-effectiveness acceptability curves. All the above sensitivity analyses were based on the CEA model from a societal perspective.

RESULTS

Base case results

The lifetime cost, from a societal perspective and assuming a 5-year intervention effect, for the PEP group was US$30,621 with nearly 90% of the cost derived from public health service use. For the non-PEP group, the lifetime cost was US$30,423 (Table 3). The incremental cost and QALYs gained for the PEP versus non-PEP group were US$197 and 0.06 QALYs respectively per subject. This gives an ICER of US$3,290 per QALY gained for PEP.

Sensitivity analysis

The scenario analysis showed that PEP remained consistently cost-effective when a shorter (3-year) duration of effect was assumed. The ICER for the 3-year effect model slightly increased to US$6,675 per QALY gained from the base case scenario of a 5-year effect while that for the lifelong effect model reduced to US$478 per QALY gained (Table 3).

The results of other one-way sensitivity analyses showed that the ICER varied from US$478 to US$7,897 (Figure 2). Varying staff cost had the greatest impact on the ICER among those cost parameters tested and the assumed duration of the PEP effect had the biggest impact

among the effectiveness parameters tested. However, none of the above analyses would change the conclusion that PEP was cost-effective at the stated threshold value of US$46,153 per QALY.

The results of the probabilistic sensitivity analysis are shown a cost-effectiveness plane (Supplemental Figure S1). More than half of the estimated ICERs fall below the WTP threshold of US$46,153 (dotted line) but 15.6% of the simulations are located in the south east quadrant, indicating that PEP is cost saving with QALYs gained compared with no PEP. The cost effectiveness acceptability curve (Figure 3) shows that the PEP intervention had a 37% probability of being cost-effective even under the assumption of zero willingness to pay (US$0) for a QALY gained, increasing to 66% probability of being cost-effective at the WTP threshold of US$46,153 for a QALY. The likelihood of PEP being cost-effective remains even when the value of a QALY is lowered to US$40,000 or raised to US$80,000.

DISCUSSION

In this lifetime model, we found that, if the PEP effect lasted for five years, PEP was highly cost-effective from a societal perspective with an ICER of US$3,290 per QALY gained compared with no PEP. This value is far below the WHO recommended WTP threshold for a QALY of 1 × per capita GDP (US$46,153). Even if our threshold were half of that recommended by WHO, the intervention would still be highly cost-effective. The PEP group would have higher lifetime costs than the non-PEP group, including those costs resulting from longer survival, but would also have higher lifetime QALYs from the prevention of DM complications.

One strength of this study is that all the parameters were based on local population data,

either from our PEP cohort or from the RAMP-DM data, which eliminates the uncertainty of adapting overseas data to the local population. To validate the model, we compared the observed complication events in the empirical data with the events predicted in the first 5 years from the CEA model. This showed that the probability of developing heart failure could have been overestimated in the model for both the PEP and non-PEP groups but the overall validity of the model was reasonable with overlapping of the 95% CIs for predicted and actual complication rates (Supplemental Table S2).

There were some limitations in our model. The transition probabilities of complications were based on empirical data from the cohort and some of the complication incidence rate s were not significantly different between the PEP and non-PEP groups because the number of cases was small e.g. for ESRD. Also, in order to identify two comparable groups of PEP and non-PEP subjects, we matched two larger groups on several criteria. Although these matched groups were similar in all observed demographic and clinical risk factors at baseline, we cannot exclude differences in unobserved characteristics but we have no reason to think these existed.

PEP was a one-off intervention which aimed to empower patients with knowledge and skills to facilitate their self-management of their chronic condition. There is always uncertainty about the length of any effect of this kind of lifestyle or behaviour change intervention especially if there is no continuing intervention. Assuming that the effect of PEP would be completely gone within a 3-year period (more conservative assumption) the ICER doubled compared with the base case model but was still cost-effective (US$6,675 per QALY gained). When the effect of PEP was assumed to be lifelong (optimistic assumption), the ICER was

less than US$500 per QALY gained. These results indicated that the finding of cost-effectiveness of PEP is robust.

The cost drivers can be seen in the Tornado diagram. The per-subject cost of PEP is the cost which causes the greatest change in ICER, particularly the staff cost component, although none of the cost parameters tested changed the conclusion on the cost effectiveness of PEP. The different NGOs used different types of staff which generated a wide range of costs. At present, we have no information on whether there was any association between the use of more senior and/or more expensive staff and better outcomes and so we cannot present further analyses on these variables at present.

In general, the results show that PEP is probably cost-effective but with a 66% likelihood at the threshold of US$46,153 per QALY. This indicates that there are wide ranges for some parameters used in the model and some sets of estimates result in PEP not being cost-effective. One important set of parameters that contributes to this uncertainty is the hazard ratios for the diabetic complications suffered by the PEP and non-PEP groups. Several of the estimates were not significantly different between the groups and the 95% CIs were wide. The impact of uncertainty on the hazard ratios was also reflected in the cost-effectiveness plane which shows a number of ICERs located in the north-west or south-west quadrant, indicating no benefit for the PEP group compared with the non-PEP group. Future research will be worthwhile to identify any sub-group that is less likely to benefit from PEP, e.g. by sex, or smoking status, and also to see whether there might be an optimum number of PEP sessions to generate an effect on outcomes.

Compare to the three long-term cost-effectiveness studies identified from our systematic

review,[14-16] our PEP programme were different in educational components and educators. Also, unlike our study which applied the observed transition probabilities of the development of complications derived from our empirical data into a long-term model, all three studies applied the observed changes in surrogate outcomes (HbA1c, blood pressure) from RCTs to predict the transition probabilities of diabetic complications. These three studies also found the self-management education programmes were likely to be cost-effective in the long term. Similar to us, Gillett et al.[14] found that their diabetes education and self-management programme (DESMOND) for ongoing and newly diagnosed cases of type 2 diabetes had a 66% (based on trial) to 70% probability of being cost-effective, when compared to usual care.

In conclusion, given the carefully measured cost of PEP and the potentially large benefits, PEP could be highly cost-effective from a societal perspective with ICERs below the WTP threshold of 1 × per capita GDP.

ACKNOWLEDGEMENTS

The authors would like to thank Dr Frank Chan and the staff of the Patient Empowerment Programme team and the Finance Division at the Hospital Authority Head Office, Dr S. V. Lo and the staff of the Statistics & Workforce Planning Department in the Hospital Authority Strategy and Planning Division. We also thank the staff of NGOs, PEP services providers, for their help in completing questionnaires concerning resource use.

Author contributions: J.X.L. researched data and wrote the manuscript. S.M.M wrote the manuscript. C.S. and J. C. researched data and contributed to the methods and results of the manuscript. C.K.H.W., W.C.W.W. and C.L.K. L. reviewed and edited the manuscript. W.C.W.W. is the guarantor of this work.

Funding source: This work was supported by Commissioned Study on Enhanced Primary Care (ref: EPC-HKU-1B & EPC-HKU-2).

Conflict of interest: There are no relevant conflicts of interest to disclose.

Reference

1. World Health Organization. Diabetes. Fact sheets. http://www.who.int/mediacentre/factsheets/fs312/en/. Accessed 13 November, 2017.
2. American Diabetes Association. Economic costs of diabetes in the U.S. in 2012. *Diabetes Care.* 2013;36(4):1033-1046.
3. Liebl A, Khunti K, Orozco-Beltran D, Yale JF. Health economic evaluation of type 2 diabetes mellitus: a clinical practice focused review. *Clinical medicine insights Endocrinology and diabetes.* 2015;8:13-19.
4. Powers MA, Bardsley J, Cypress M, et al. Diabetes Self-management Education and Support in Type 2 Diabetes: A Joint Position Statement of the American Diabetes Association, the American Association of Diabetes Educators, and the Academy of Nutrition and Dietetics. *Diabetes Care.* 2015;38(7):1372-1382.
5. Sherifali D, Bai JW, Kenny M, Warren R, Ali MU. Diabetes self-management programmes in older adults: a systematic review and meta-analysis. *Diabet Med.* 2015;32(11):1404-1414.
6. Norris SL, Lau J, Smith SJ, Schmid CH, Engelgau MM. Self-management education for adults with type 2 diabetes: a meta-analysis of the effect on glycemic control. *Diabetes Care.* 2002;25(7):1159-1171.
7. Steinsbekk A, Rygg LO, Lisulo M, Rise MB, Fretheim A. Group based diabetes self-management education compared to routine treatment for people with type 2 diabetes mellitus. A systematic review with meta-analysis. *BMC Health Serv Res.* 2012;12:213.
8. Ellis SE, Speroff T, Dittus RS, Brown A, Pichert JW, Elasy TA. Diabetes patient education: a meta-analysis and meta-regression. *Patient education and counseling.* 2004;52(1):97-105.
9. Lian JX, McGhee SM, Chau J, Wong CKH, Lam CLK, Wong WCW. Systematic review on the cost-effectiveness of self-management education programme for type 2 diabetes mellitus. *Diabetes Res Clin Pr.* 2017;127:21-34.
10. Ritzwoller DP, Sukhanova AS, Glasgow RE, et al. Intervention costs and cost-effectiveness for a multiple-risk-factor diabetes self-management trial for Latinas: economic analysis of inverted exclamation markViva Bien! *Translational behavioral medicine.* 2011;1(3):427-435.
11. Schechter CB, Cohen HW, Shmukler C, Walker EA. Intervention costs and cost-effectiveness of a successful telephonic intervention to promote diabetes control. *Diabetes Care.* 2012;35(11):2156-2160.
12. Ritzwoller DP, Toobert D, Sukhanova A, Glasgow RE. Economic analysis of the Mediterranean Lifestyle Program for postmenopausal women with diabetes. *The Diabetes educator.* 2006;32(5):761-769.
13. Hendrie D, Miller TR, Woodman RJ, Hoti K, Hughes J. Cost-effectiveness of reducing glycaemic episodes through community pharmacy management of patients with type 2 diabetes mellitus. *J Prim Prev.* 2014;35(6):439-449.
14. Gillett M, Dallosso HM, Dixon S, et al. Delivering the diabetes education and self management for ongoing and newly diagnosed (DESMOND) programme for people with newly diagnosed type 2 diabetes: cost effectiveness analysis. *Bmj.* 2010;341(7770):c4093.
15. Prezio EA, Pagan JA, Shuval K, Culica D. The Community Diabetes Education (CoDE) program: cost-effectiveness and health outcomes. *Am J Prev Med.* 2014;47(6):771-779.
16. Mash R, Kroukamp R, Gaziano T, Levitt N. Cost-effectiveness of a diabetes group education program delivered by health promoters with a guiding style in underserved communities in Cape Town, South Africa. *Patient education and counseling.* 2015;98(5):622-626.
17. Handley MA, Shumway M, Schillinger D. Cost-effectiveness of automated telephone self-management support with nurse care management among patients with diabetes. *Ann Fam Med.* 2008;6(6):512-518.
18. Wong CK, Wong WC, Lam CL, et al. Effects of Patient Empowerment Programme (PEP) on clinical outcomes and health service utilization in type 2 diabetes mellitus in primary care: an observational matched cohort study. *PloS one.* 2014;9(5):e95328.

19. Wong CK, Wong WC, Wan EY, Wong WH, Chan FW, Lam CL. Increased number of structured diabetes education attendance was not associated with the improvement in patient-reported health-related quality of life: results from Patient Empowerment Programme (PEP). *Health and quality of life outcomes.* 2015;13:126.
20. Wong CK, Wong WC, Wan YF, Chan AK, Chan FW, Lam CL. Effect of a structured diabetes education programme in primary care on hospitalizations and emergency department visits among people with Type 2 diabetes mellitus: results from the Patient Empowerment Programme. *Diabet Med.* 2016;33(10):1427-1436.
21. Wong CK, Wong WC, Wan YF, Chan AK, Chan FW, Lam CL. Patient Empowerment Programme (PEP) and Risk of Microvascular Diseases Among Patients With Type 2 Diabetes in Primary Care: A Population-Based Propensity-Matched Cohort Study. *Diabetes Care.* 2015;38(8):e116-117.
22. Wong CK, Wong WC, Wan YF, et al. Patient Empowerment Programme in primary care reduced all-cause mortality and cardiovascular diseases in patients with type 2 diabetes mellitus: a population-based propensity-matched cohort study. *Diabetes, obesity & metabolism.* 2015;17(2):128-135.
23. Wong CK, Wong WC, Wan EY, Chan AK, Chan FW, Lam CL. Macrovascular and microvascular disease in obese patients with type 2 diabetes attending structured diabetes education program: a population-based propensity-matched cohort analysis of Patient Empowerment Programme (PEP). *Endocrine.* 2016;53(2):412-422.
24. Wong CK, Lam CL, Wan EY, et al. Evaluation of patient-reported outcomes data in structured diabetes education intervention: 2-year follow-up data of patient empowerment programme. *Endocrine.* 2016;54(2):422-432.
25. Fung CS, Chin WY, Dai DS, et al. Evaluation of the quality of care of a multi-disciplinary risk factor assessment and management programme (RAMP) for diabetic patients. *BMC family practice.* 2012;13:116.
26. Lian J, McGhee SM, So C, et al. Five-year cost-effectiveness of the Patient Empowerment Programme (PEP) for type 2 diabetes mellitus in primary care. *Diabetes, obesity & metabolism.* 2017;19(9):1312-1316.
27. Hong Kong Air Pollution and Health Joint Research Group of the University of Hong Kong and Chinese University of Hong Kong. The provision of service for study of short term health impact and costs due to road traffic-related air pollution 2002; https://www.epd.gov.hk/epd/sites/default/files/epd/english/environmentinhk/air/studyrpts/files/ap_health_impact_02.pdf.
28. Clarke PM, Gray AM, Briggs A, et al. A model to estimate the lifetime health outcomes of patients with Type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS no. 68). *Diabetologia.* 2004;47(10):1747-1759.
29. Fleurence RL, Hollenbeak CS. Rates and probabilities in economic modelling: transformation, translation and appropriate application. *Pharmacoeconomics.* 2007;25(1):3-6.
30. Yang X, So WY, Kong AP, et al. Development and validation of stroke risk equation for Hong Kong Chinese patients with type 2 diabetes: the Hong Kong Diabetes Registry. *Diabetes Care.* 2007;30(1):65-70.
31. Yang X, So WY, Kong AP, et al. Development and validation of a total coronary heart disease risk score in type 2 diabetes mellitus. *Am J Cardiol.* 2008;101(5):596-601.
32. Stevens RJ, Kothari V, Adler AI, Stratton IM, United Kingdom Prospective Diabetes Study G. The UKPDS risk engine: a model for the risk of coronary heart disease in Type II diabetes (UKPDS 56). *Clin Sci (Lond).* 2001;101(6):671-679.
33. Kothari V, Stevens RJ, Adler AI, et al. UKPDS 60: risk of stroke in type 2 diabetes estimated by the UK Prospective Diabetes Study risk engine. *Stroke.* 2002;33(7):1776-1781.
34. Jiao F. *Cost-effectiveness analysis of the multidisciplinary risk assessment and management program for Chinese patients with diabetes mellitus (RAMP-DM) in primary care of the*

Hospital Authority. (Thesis). Hong Kong: Family Medicine and Primary Care, The University of Hong Kong (Pokfulam, Hong Kong); 2016.
35. Hong Kong SAR Department of Health. *In-depth cost-effectiveness study of the Multi-disciplinary Risk Factor Assessment and Management Programme (RAMP) of the Hospital Authority* Hong Kong 2017.
36. Lam CL, Brazier J, McGhee SM. Valuation of the SF-6D Health States Is Feasible, Acceptable, Reliable, and Valid in a Chinese Population. *Value Health.* 2008;11(2):295-303.
37. McGhee SM, Brazier J, Lam CL, et al. Quality-adjusted life years: population-specific measurement of the quality component. *Hong Kong medical journal = Xianggang yi xue za zhi / Hong Kong Academy of Medicine.* 2011;17 Suppl 6:17-21.
38. Jiao F, Wong CKH, Gangwani R, Tan KCB, Tang SCW, Lam CLK. Health-related quality of life and health preference of Chinese patients with diabetes mellitus managed in primary care and secondary care setting: decrements associated with individual complication and number of complications. *Health and quality of life outcomes.* 2017;15(1):125.
39. HKSAR Census and Statistics Department. Annual Report on the Consumer Price Index (2017 Edition). 2018; https://www.censtatd.gov.hk/hkstat/sub/sp270.jsp?productCode=B1060002. Accessed 21 June 2018.
40. World Health Organization. *Macroeconomics and health: investing in health for economic development. Report of the Commission on Macroeconomics and Health: Executive Summary.* Geneva: Switzerland: WorldHealth Organization;2001.
41. HKSAR Census and Statistics Department. Gross Domestic Product (Quarterly) (First Quarter 2018). 2018; https://www.statistics.gov.hk/pub/B10300012018QQ01B0100.pdf. Accessed 21 June 2018.
42. Hutubessy R, Chisholm D, Edejer TT. Generalized cost-effectiveness analysis for national-level priority-setting in the health sector. *Cost Eff Resour Alloc.* 2003;1(1):8.
43. Augustovski F, Colantonio LD, Galante J, et al. Measuring the Benefits of Healthcare: DALYs and QALYs - Does the Choice of Measure Matter? A Case Study of Two Preventive Interventions. *Int J Health Policy Manag.* 2017;7(2):120-136.

Tables

Figures

Supplemental material

Table 1. Parameters on effectiveness in CEA model

Parameters	Base-case	Range for one-way sensitivity analysis	Sources of the tested range	Distribution for probabilistic sensitivity
Annual transition probabilities of DM complications				
PEP group (Male)				
AMI	0.332%	NA	NA	NA
Other IHD	0.795%	NA	NA	NA
Heart failure events	0.406%	NA	NA	NA
Stroke events	0.706%	NA	NA	NA
STDR events	0.129%	NA	NA	NA
ESRD events	0.359%	NA	NA	NA
PEP group (Female)				
AMI	0.178%	NA	NA	NA
Other IHD	0.520%	NA	NA	NA
Heart failure events	0.246%	NA	NA	NA
Stroke events	0.606%	NA	NA	NA
STDR events	0.065%	NA	NA	NA
ESRD events	0.147%	NA	NA	NA
Non-PEP group (Male)				
AMI	0.384%	NA	NA	NA
Other IHD	0.774%	NA	NA	NA
Heart failure events	0.383%	NA	NA	NA
Stroke events	0.900%	NA	NA	NA
STDR events	0.097%	NA	NA	NA
ESRD events	0.281%	NA	NA	NA
Non-PEP group (Female)				
AMI	0.234%	NA	NA	NA
Other IHD	0.516%	NA	NA	NA
Heart failure events	0.409%	NA	NA	NA
Stroke events	0.652%	NA	NA	NA
STDR events	0.090%	NA	NA	NA
ESRD events	0.214%	NA	NA	NA
Sex specific hazard ration for age on incidence rate				
PEP group (Male)				
AMI	1.047	NA	NA	NA
Other IHD	1.030	NA	NA	NA
Heart failure events	1.114	NA	NA	NA
Stroke events	1.052	NA	NA	NA
STDR events	0.933	NA	NA	NA
ESRD events	1.104	NA	NA	NA
PEP group (Female)				

AMI	1.089	NA	NA	NA
Other IHD	1.048	NA	NA	NA
Heart failure events	1.124	NA	NA	NA
Stroke events	1.089	NA	NA	NA
STDR events	0.994	NA	NA	NA
ESRD events	1.109	NA	NA	NA
Non-PEP group (Male)				
AMI	1.067	NA	NA	NA
Other IHD	1.031	NA	NA	NA
Heart failure events	1.108	NA	NA	NA
Stroke events	1.079	NA	NA	NA
STDR events	0.991	NA	NA	NA
ESRD events	1.122	NA	NA	NA
Non-PEP group (Female)				
AMI	1.096	NA	NA	NA
Other IHD	1.057	NA	NA	NA
Heart failure events	1.129	NA	NA	NA
Stroke events	1.080	NA	NA	NA
STDR events	0.968	NA	NA	NA
ESRD events	1.097	NA	NA	NA
Effectiveness of PEP				
Male				
Hazard ratio of AMI	0.858	(0.627, 1.173)	95% CI	Log-normal distribution
Hazard ratio of other IHD	1.027	(0.831, 1.269)		
Hazard ratio of heart failure	1.061	(0.788, 1.428)		
Hazard ratio of stroke	0.799	(0.647, 0.988)		
Hazard ratio of STDR	1.308	(0.748, 2.287)		
Hazard ratio of ESRD	1.338	(0.957, 1.870)		
Female				
Hazard ratio of AMI	0.746	(0.521, 1.068)	95% CI	Log-normal distribution
Hazard ratio of other IHD	1.001	(0.799, 1.254)		
Hazard ratio of heart failure	0.610	(0.455, 0.817)		
Hazard ratio of stroke	0.929	(0.757, 1.140)		
Hazard ratio of STDR	0.747	(0.413, 1.353)		
Hazard ratio of ESRD	0.693	(0.471, 1.022)		
Health utility decrements				
Utility of DM subjects without complications	0.883	(0.778, 0.989)	95% CI	Normal distribution
Female	-0.024	(-0.041, -0.007)		
AMI	-0.017	(-0.042, 0.008)		
Other IHD	-0.017	(-0.042, 0.008)		
Heart failure	-0.017	(-0.042, 0.008)		
Stroke	-0.042	(-0.072, -0.012)		

ESRD	-0.055	(-0.093, -0.017)
STDR	-0.043	(-0.075, -0.010)

AMI= Acute Myocardial Infarction; IHD= Ischaemic Heart Disease; STDR=Sight Threatening Diabetic Retinopathy; ESRD= End Stage Renal Disease; CI= confidence interval; QALYs= quality-adjusted life-years; NA=Not applicable;

Table 2. Parameters on cost in CEA model

Parameters	Base-case	Range for one-way sensitivity analysis	Sources of the tested range	Distribution for probabilistic sensitivity
Discount rate				
Discount on both cost and QALYs	3.5%	(0%, 5%)		NA
Cost, US$				
Cost of PEP (societal perspective)	276	(213, 332)	Minimum and maximum among clusters, except for extreme cases	Uniform distribution
Cost of PEP (extreme case) †	276	(138, 553)		
NGO resource cost	98	(48, 155)		
NGO setup cost	5	(1, 13)		
Staff	77	(43, 97)		
Staff (extreme case)	77	(0, 289)		
Venue rental	5	(0, 14)		
Equipment	1	(0, 2)		
Other operating expenses	10	(2, 55)		
Cost to the community	14	(3, 51)		
Cost to subjects	105	(95, 118)		
Public cost multipliers				
Baseline cost‡, US$	1650	NA	NA	NA
Age – 63	1.02	NA	NA	NA
Female	1.01	NA	NA	NA
New complication				
AMI	4.50	(3.50, 5.79)	95% CI	Log-normal distribution
other IHD	2.88	(2.47, 3.37)		
Heart failure	4.56	(3.77, 5.51)		
Stroke	7.04	(6.22, 7.97)		
STDR	1.52	(1.13, 2.05)		
ESRD	9.24	(7.29, 11.71)		
Existing complications				
AMI	2.01	(1.44, 2.82)	95% CI	Log-normal distribution
other IHD	1.33	(1.17, 1.51)		
Heart failure	2.10	(1.74, 2.53)		
Stroke	2.43	(2.20, 2.69)		
STDR	1.22	(0.99, 1.50)		
ESRD	2.56	(1.95, 3.37)		
Private cost multipliers				
Baseline cost§, US$	218	NA	NA	NA
Age – 65	0.97	NA	NA	NA

Female	1.30	NA	NA	NA
Macrovascular complications				
Heart disease	2.34	(1.21, 4.52)	95% CI	Log-normal distribution
Stroke	1.52	(0.68, 3.38)		
Microvascular complications				
STDR	2.08	(0.91, 4.74)		
ESRD	1.93	(0.79, 4.73)		

AMI= Acute Myocardial Infarction; IHD= Ischaemic Heart Disease; STDR=Sight Threatening Diabetic Retinopathy; ESRD= End Stage Renal Disease; CI= confidence interval; QALYs= quality-adjusted life-years; NA=Not applicable;

† extreme case – from half of the base cost up to double the cost

‡ for a male patient with diabetes, age 63 with no complication

§ for a male patient with diabetes, age 65 with no complication

Table 3. Cost-effectiveness of PEP versus Non-PEP (from societal perspective)

	Cost† (US$) (a)	QALY† (b)	Incremental cost (US$) (c)	Incremental QALYs (d)	ICER (US$) (c) / (d)
Base case 5-year intervention effect					
No PEP	30,423	10.06			
- public health service cost	27,315				
- private health service cost	3,108				
PEP	30,621	10.12	197	0.06	3,290
- PEP programme cost	276				
- public health service cost	27,227				
- private health service cost	3,118				
Scenario analysis 3-year intervention effect					
No PEP	30,423	10.06			
- public health service cost	27,315				
- private health service cost	3,108				
PEP	30,690	10.10	267	0.04	6,675
- PEP programme cost	276				
- public health service cost	27,298				
- private health service cost	3,116				
Scenario analysis lifelong effect					
No PEP	30,423	10.06			
- public health service cost	27,315				
- private health service cost	3,108				
PEP	30,538	10.30	115	0.24	478
- PEP programme cost	276				
- public health service cost	27,126				
- private health service cost	3,135				

[†]Discounted at 3.5% per year

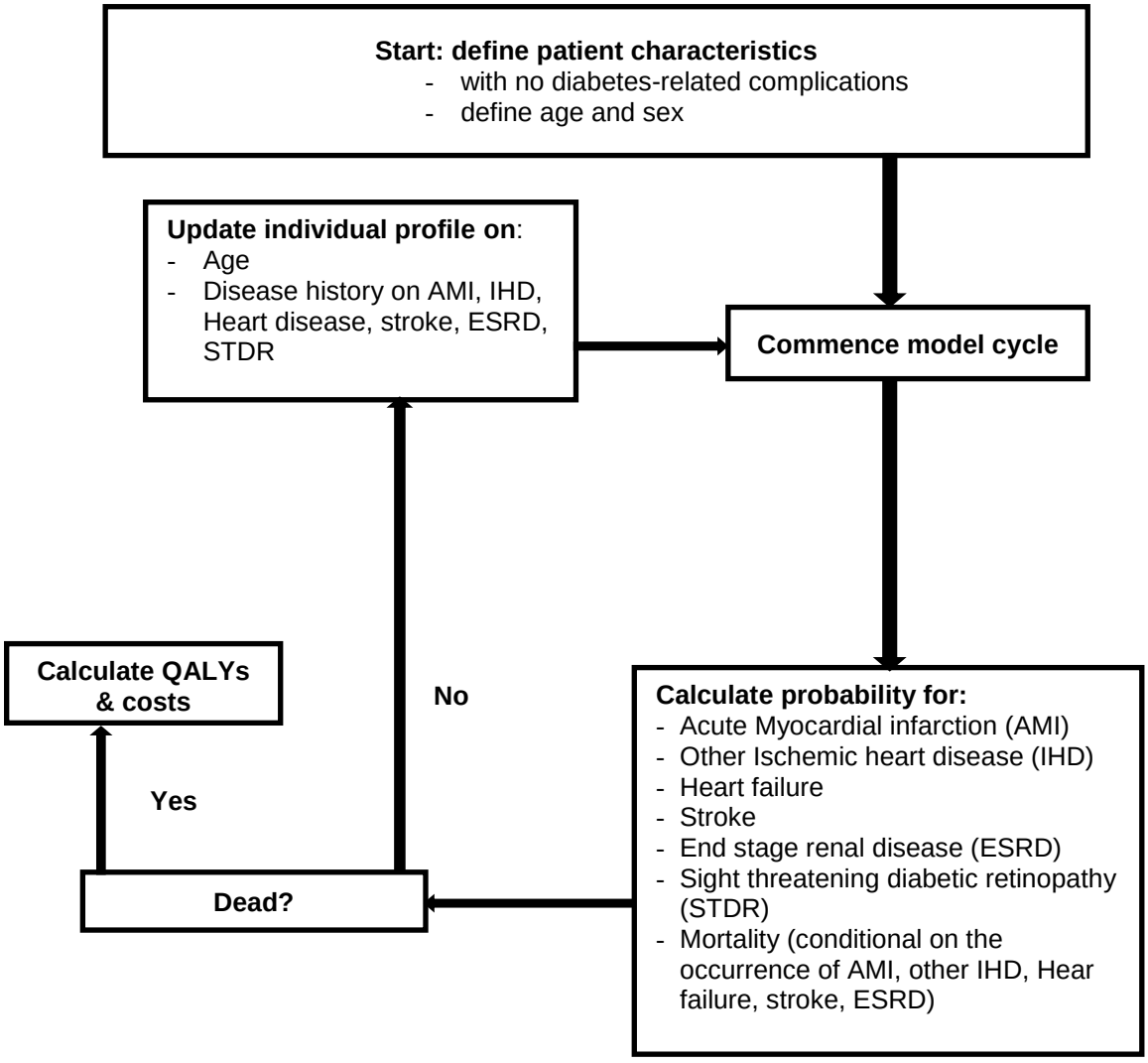

Figure 1. Structure of long-term CEA Model

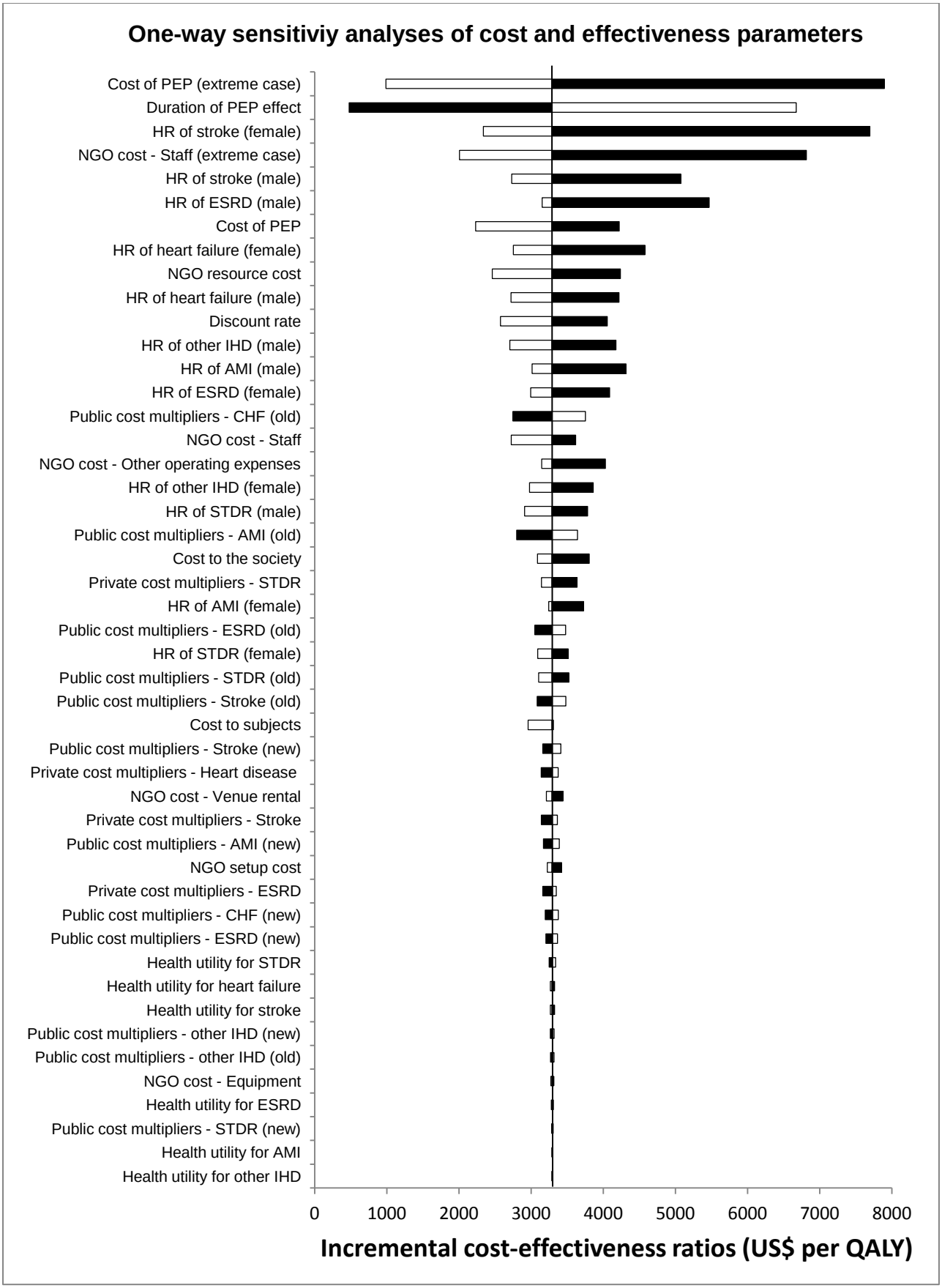

Figure 2. Tornado diagram for one-way sensitivity analyses

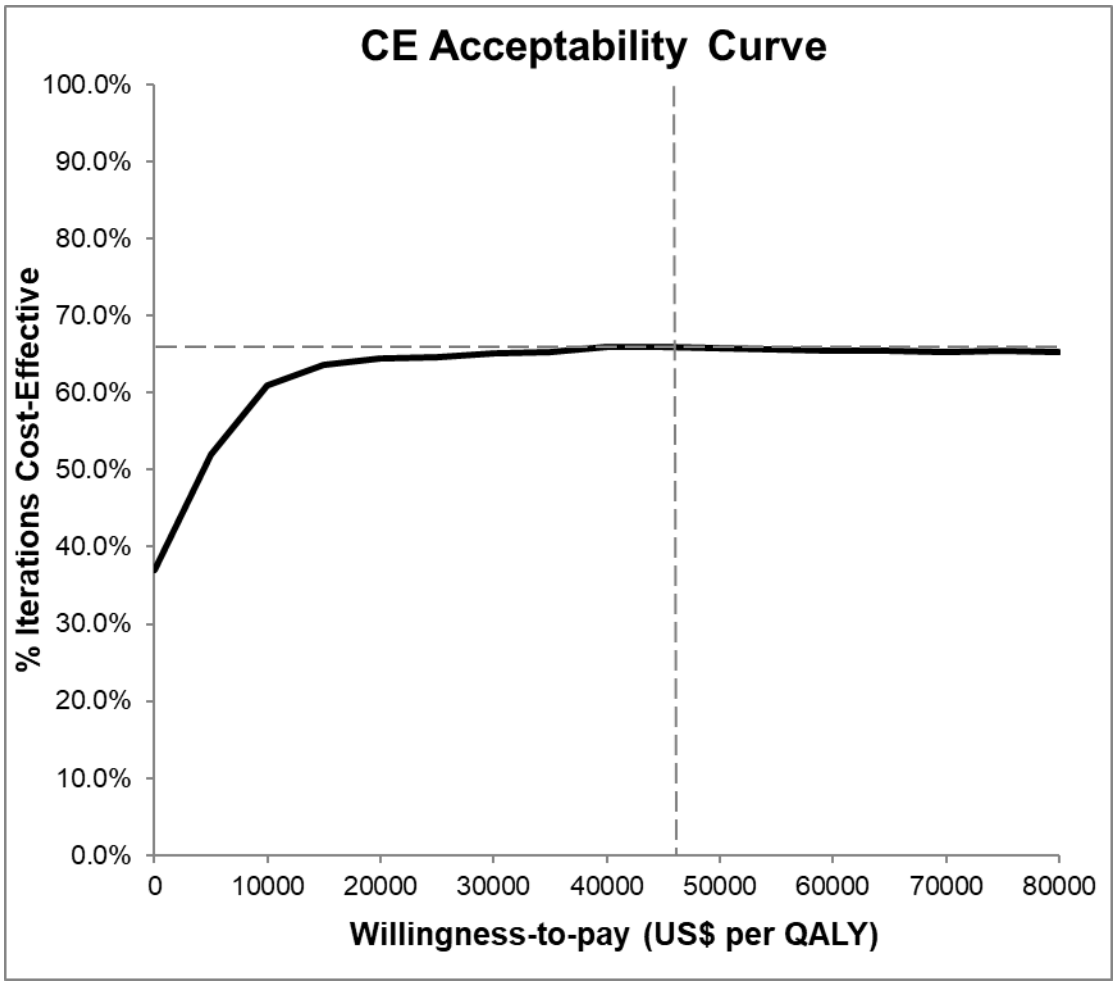

Figure 3. Cost-effectiveness acceptability curve