Health state utility values for type 2 diabetes and related complications in East and Southeast Asia: a systematic review and meta-analysis

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Précis

This study derives a reference set of pooled utility and disutility (utility decrement) values for type 2 diabetes and 17 related complications for economic evaluation.

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Abstract

Objectives

East and Southeast Asia has the greatest burden of diabetes in the world. We sought to derive a reference set of utility values for type 2 diabetes without complication, and disutility (utility decrement) values for important diabetes-related complications to better inform economic evaluation.

Methods

A systematic review to identify utility values for diabetes and related complications reported in East and Southeast Asia. We searched MEDLINE (OVID) from inception to 26 May 2020 for utilities values elicited using direct and indirect methods. Identified studies were assessed for quality based on the National Institute of Health and Care Excellence (NICE) guidelines. Utility and disutility estimates were pooled by meta-analyses with sub-group analyses to evaluate differences by nationality and valuation instrument. (PROSPERO: CRD42020191075).

Results

We identified 17 studies for the systematic review from a total of 13,035 studies in the initial search, of which 13 studies met the quality criteria for inclusion in the meta-analyses. The pooled utility value for diabetes without complication was 0.88 (95% CI: 0.83, 0.93), with the pooled utility decrement for associated complications ranging from 0.00 (for excess BMI) to 0.18 (for amputation). The utility values were consistently more conservative than previous estimates derived in Western populations. Utility decrements were comparable for SF-6D and EQ-5D valuation instruments and for Chinese and other Asian groups.

Conclusions

A reference set of pooled disutility and utility values for type 2 diabetes and its complications in East and Southeast Asian populations yielded more conservative estimates than Western populations.

Highlights

What is already known about the topic?

Despite the high prevalence and burden of diabetes in East and Southeast Asia, there lacks a set of utility values for diabetes-related complications to assess quality of life and to conduct economic evaluation in these populations. Utility reference values in other populations have previously been selected based on qualitative analysis alone.

What does the paper add to existing knowledge?

We developed a reference set of pooled disutility and utility values for type 2 diabetes and its related complications for East and Southeast Asia from a systematic review and meta-analysis. We found these populations consistently yielded more conservative values for disutility than previous estimates in Western populations. We also assessed variations due to nationality and valuation instrument.

What insights does the paper provide for informing health care-related decision making?

We propose a reference set of pooled utility values to aid researchers and public health policy makers in conducting health economic analysis and outcomes research for type 2 diabetes and its wide range of complications. Disutility estimates in our East and Southeast Asian population were more conservative than Western populations.

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Introduction

Diabetes is a global health problem. East and Southeast Asia region has the highest burden of diabetes in the world - approximately 247.6 million patients accounting for 53% of the world's total.[1] China has the largest number of people with diabetes for any single country, with a prevalence of 12.8% among adults, corresponding to 129.8 million people in 2017.[2] The prevalence of diabetes was similarly high across East and Southeast Asia, such as Malaysia (17.5%), Korea (14.4%), Singapore (14.2%), Hong Kong (10.3%), Thailand (8.3%), and Japan (7.9%).[1,3-5] Healthcare expenditure on diabetes in East and Southeast Asia totaled USD 162 billion in 2019, of which China and Japan spent USD 109 billion and USD 23.5 billion respectively.[1]

Diabetes leads to a wide range of macrovascular complications (cardiovascular disease, cerebrovascular disease, peripheral vascular disease), and microvascular complications (neuropathy, nephropathy, retinopathy).[6] The impact of diabetes on health-related quality of life (HRQoL) are commonly measured using generic valuation instruments such as the EuroQol five-dimensional (EQ-5D)[7], Short Form-6 dimensions (SF-6D)[8,9], 15-dimensional (15D)[10] questionnaires, and subsequently converted to utilities by means of a tariff. The EQ-5D questionnaire assesses five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression); the SF-6D is derived from the SF-12 or SF-36 questionnaire on eight functional domains (physical functioning, role physical, body pain, general health, vitality, social functioning, role emotional and mental health); and the 15D questionnaire describes fifteen dimensions (mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity). Direct methods of measuring utility are more time consuming and include Standard Gamble (SG) of the risk of death compared to avoidance of the disease state[11], Time-Trade-Off (TTO)[12] for perfect health compared to the disease state, or using a Visual Analogue Scale (VAS)[13] to rate health states on a 0 to 100 visual scale. Although different instruments and valuation methods can produce varying utility values and therefore affect the outcomes of economic evaluation,[14] comparisons of different valuation instruments in patients with type 2 diabetes has not conclusively demonstrated a preference for one particular instrument over others.[15,16]

Despite the high burden of diabetes in East and Southeast Asia and the increasing use of economic evaluation in this region, there lacks a reference set of utility values for comparative assessment of quality of life for diabetes and its related complications in this population. A previous attempt to develop a reference set for diabetes was based on populations in Europe and Australia, with a preferred utility value for each complication selected from a single study.[17] Differences in cultural norms and epidemiology of chronic diseases would lead to expectations that the utility values could differ between the East and Southeast Asian population and other populations.

Cost-effective analyses are growing rapidly in Asia, though non-communicable diseases are under-studied relative to their disease burden.[18] Given the growing burden of diabetes and the increased health care spending in this region, the effective allocation of resources to manage

diabetes is a key public health concern. Generating a robust set of health state utility values for diabetes, that can act as a standardised input in economic evaluation, facilitates rigorous comparisons of different health care interventions in order to establish the most cost-effective care for patients.

To our knowledge, utility values for diabetes and its complications have not been synthesized from multiple studies by meta-analysis. We conducted a systematic review and meta-analysis to pool utility values for each diabetes-related complication, critically assess the studies for quality and discuss the impact of different population groups and valuation instruments on utility values.

Methods

This review was conducted and reported in consonance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the National Institute for Health and Clinical Excellence (NICE) guide for reviews of health state utility values.[19-22] The study protocol was registered with Prospective Register of Systematic Reviews (PROSPERO: CRD42020191075). Approval from an ethics committee was not required as we relied on published data.

Data Sources and Searches

We reviewed economic models in the Mount Hood Diabetes Challenge registry that simulate long-term outcomes among people with type 2 diabetes to identify relevant complications.[23] The twelve models reviewed were the United Kingdom Prospective Diabetes Study Outcomes Model 2 (UKPDS OM2),[24] Chinese Hong Kong Integrated Modeling and Evaluation (CHIME),[25] the Building, Relating, Assessing, and Validating Outcomes (BRAVO),[26] IQVIA CORE Diabetes Model,[27] CDC-RTI Diabetes Cost-effectiveness model,[28] PROSIT Open Source Disease Models for Diabetes Mellitus,[29] Syreon Model,[30] Modelling Integrated Care for Diabetes based on Observational data (MICADO),[31] School for Public Health Research (SPHR),[32] Medical Decision Modelling - Treatment Transitions Model (MDM-TTM),[33] Michigan Model for Diabetes (MMD),[34] and Archimedes Diabetes Model.[35] Relevant complications for diabetes identified from the models were heart failure, myocardial infarction, ischemic heart disease, cardiovascular disease, cerebrovascular disease, peripheral vascular disease, amputation, diabetic foot, nephropathy, end-stage renal disease, retinopathy, blindness, cataract, neuropathy, hypoglycemia, dermatopathy, and excess BMI. The classification and nomenclature of diabetes-related complications is detailed in Appendix S1.

We searched the database MEDLINE (OVID) from inception to 26 May 2020. Detailed search strategy can be found in Appendix S2. We performed an additional search of the reference lists of relevant studies. The search was limited to English and Chinese languages. Our search strategy included diabetes, quality of life, and health utilities including methods of elicitation (indirect using EQ-5D[36] and all its variants, SF-6D[37], and 15D;[10] as well as direct methods of elicitation using SG,[38] TTO,[38] and VAS[39]). We also incorporated search terms from a previous review of type 2 diabetes utility values.[17]

Study Selection

Two reviewers screened the titles and abstracts independently for inclusion. Full texts were retrieved if they met the inclusion criteria and assessed independently by the two reviewers.

Disagreements were resolved by consensus involving a third reviewer. A summary of studies identified, included and excluded are recorded in the PRISMA flow diagram (Figure 1).[40]

We included studies reporting health state utility values among people with type 2 diabetes regardless of age, complications, or treatment status in East and Southeast Asia. There was no restriction on the form of studies (observational or experimental) to be included. Identified studies included those measuring changes in health state utility values of complications before and after interventions, validation of instruments or value sets to assess health-related quality of life in specific countries or regions, and cost-effectiveness analysis incorporated in randomized clinical trials. We excluded all non-human studies and non-original studies, such as editorials, systematic reviews and meta-analysis, protocols, reports, or guidelines. Studies reporting health state but without any estimate of utility value were also excluded.

Data Extraction and Quality Assessment

We included all items stated on the Checklist for Reporting Valuation Studies (CREATE)[41] checklist and National Institute of Health and Care Excellence (NICE) Technical Support Document[20] in our data extraction form (see Appendix S3). Extracted items included study design, participant characteristics, determination of health state utility values, statistical methods, and the utility values. Since there are no agreed reporting standards for health state utility studies, we assessed the quality of the studies using the criteria outlined in the NICE guidance on systematic review of utility values with additional criteria for the inclusion in the meta-analysis (reported uncertainty measurement and appropriateness of tariff used).[20] The quality assessment of included studies is presented in Appendix Table S1.

Data Synthesis and Analysis

We identified the reported utility value of diabetes without complication and pooled the values by meta-analysis. Utility decrements reported for each complication were extracted directly from the included studies. We extracted utility values from the best statistical fitting model where a study presented multiple statistical models. For studies that did not report 95% confidence interval, we estimated the confidence interval around each point estimate based on the reported standard error assuming a normal distribution. Where a study reported multiple disutility values for different severity levels for the same complication, we selected the largest marginal decrement (most severe disutility) for that complication. Utility decrements, with 95% confidence intervals, were pooled in a meta-analysis where multiple studies reported values for the same complication. Estimated utility scores for different health outcomes were calculated using the pooled estimate for type 2 diabetes without any complication as the preferred baseline utility, and then applying the pooled disutility values as the marginal decrement for each respective complication. We compared our pooled utility estimates to a previous set of preferred values selected from studies conducted in Europe and Australia.[17] We performed subgroup analyses by nationality of the participants, and by the valuation instrument used. Random effects models were used for all analyses and heterogeneity among studies assessed by the I^2 statistic. All statistical analyses were conducted in R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria) using the "meta" package.[42]

Results

We identified 13,035 studies in the initial search and screened 105 full-text articles, of which 20 studies were assessed for inclusion (Figure 1). A total of 17 studies (consisting of 42,878 participants) were included in the systematic review with three studies excluded: one did not report utility decrements[43] and two studies only reported utility decrements referenced against other non-diabetes conditions (for example, decrement for diabetic retinopathy relative to ischemic heart disease).[44,45] Background characteristics for each study including setting, methods and tariff are presented in Table 1. We identified studies conducted in China, Hong Kong, Taiwan, Japan, South Korea, Singapore, Thailand and Vietnam. Most studies recruited only type 2 diabetes, one study included a small proportion (6.9%) of type 1 diabetes[46]) and two studies did not explicitly state the type of diabetes.[47,48] Only four studies used direct measurement of health states, either by VAS or TTO. Among the 13 studies (n = 36,950 participants) using indirect health state measurement, nine studies used the EQ-5D instrument and four studies used SF-6D.

All 17 studies had adequate reporting for assessment by the quality assessment criteria (Appendix Table S1). While the overall quality of the studies fulfilled the NICE guidelines, we found seven studies did not address missing data,[46-51] eight studies did not report the tariff used or used a value set mismatched to the local setting,[45,48-50,52,53] and three studies did not report uncertainty measurements around estimates of their utility values.[54-56] The reported utility decrement for each diabetes-related complication from all identified studies are presented in Appendix Table S2. Most studies defined disease states based on patient's self-reported outcomes with only two studies defining complications using established diagnosis codes (see Appendix Table S3 for further details).

We identified a total of 114 measurements of utility decrements for 17 diabetes-relevant complications in our review. The utility values for type 2 diabetes without complications ranged from 0.78 to 1.00 using indirect valuation instruments, and from 72.3 to 76.3 on the visual analogue scale (VAS) (Appendix Table S2). Thirteen studies were included in the meta-analysis to pool utility decrements. Four studies were excluded: three did not report any uncertainty measurements,[54-56] and one did not adjust utility decrements for participant characteristics.[57] Table 2 shows the preferred set of disutility values with 95% confidence intervals for each complication using pooled estimates from meta-analyses. The pooled estimate for type 2 diabetes without complication as a baseline utility value was 0.881 (95% CI: 0.833, 0.929). Amputation had the largest utility decrement of 0.177 (95% CI: 0.291 to 0.063) and excess BMI units had smallest at 0.002 (95% CI: 0.020 to -0.017). Considerable heterogeneity was observed for some complications. Figure 2 illustrates the utility values of each complication using the pooled utility decrements from the single preferred baseline utility value for type 2 diabetes without complication, and also the range of point estimates from all studies.

Compared to previous studies in Europe and Australia, the disutility values in our population were consistently smaller (Figure 3), though the range of point estimates overlapped (Appendix Figure S1). Since most of the included studies were in Greater China, we compared the utility decrements in Chinese and other Asian groups. The utility decrements in Chinese and other Asian populations were similar in magnitude with overlapping confidence intervals for all comparable complications (Appendix Table S4 and Figure S2). EQ-5D was the most commonly used valuation instrument for measuring utility values among the included studies, while SF-6D was available for more than half of the relevant complications. The utility decrements elicited

using EQ-5D and SF-6D were similar for most complications with no significant differences except for cerebrovascular disease and peripheral vascular disease (Appendix Table S5 and Figure S3).

Forest plots of the pooled utility values for type 2 diabetes and each complication are presented in Appendix Figure S4, and by nationality and valuation instrument in Appendix Figures S5 and S6 respectively. We found no obvious publication bias though some complications had too few reported studies to make an assessment (funnel plots are shown in Appendix Figure S7).

Discussion

We conducted a systematic review and meta-analysis of articles reporting utility and disutility values for diabetes and its related complications in East and Southeast Asia. We developed a recommended set of pooled disutility and utility estimates for type 2 diabetes without complication and 17 diabetes-related complications for use in quality of life measurements and economic evaluation. Seventeen studies were included in the systematic review of which 13 met the NICE guidelines in terms of overall quality for inclusion in the meta-analysis. Although there were variations among the studies in terms of participants, choice of valuation instrument and value sets, we found the utility decrements were comparable for Chinese and other Asian populations with no consistent differences between EQ-5D and SF-6D instruments.

The pattern of utility decrements for complications were consistent with a previous review in 2014,[17] which reported amputation having the largest decrement and excess BMI the smallest. Our pooled estimates from studies conducted in East and Southeast Asian populations yielded more conservative values of utility decrements, a finding that was consistent for most complications compared to elicited values in European and Australian populations. For example, diabetes patients with cerebrovascular disease, diabetic foot, neuropathy had utility decrements of 0.09, 0.09, and 0.05 respectively, compared to 0.16, 0.17, 0.08 in Beaudet et al.[17] This could reflect differences in cultural norms, epidemiology of diabetes-related complications, or be attributable to the variations in study country, valuation instrument and tariff. We included studies using either EQ-5D and SF-6D valuation instruments with tariffs adjusted to their local country or region in contrast to previous estimates based solely on EQ-5D with a UK value set.[17] Many of our included studies were published in the last 10 years whereas the main contributing data in earlier studies were conducted decades earlier (CODE-2 and United Kingdom Prospective Diabetes Study).[17] Improvements in the quality of health care and evolutions in the management of complications over time could also contribute to the smaller decrements we observed.

The studies included were mostly conducted in populations with a Chinese majority, such as China, Hong Kong and Taiwan. Despite a considerable Asian population with diabetes among the Indian subcontinent, we did not include this region as we could only identify one study.[58] We found comparable utility decrements for Chinese and other Asian groups with overlapping confidence intervals for all comparable complications. We observed some reductions in heterogeneity of disutility values for diabetes-related complications in the Chinese subgroup, but this was inconsistent, likely due to the small number of studies and hence lacked statistical power.

Although EQ-5D was the most popular elicitation instrument among the identified studies, there was little evidence that the choice of instrument consistently yielded higher or lower utility estimates. We noted considerable heterogeneity in the EQ-5D instrument sub-groups, while there were generally too few studies to assess for SF-6D. Inconsistent application of tariffs likely contributed to the observed heterogeneity. Only half of the studies applied a value set adjusted for their own country or region; five studies did not report the tariff used,[49,50,53,56,57] and three studies used the UK value set to represent Hong Kong, Singapore and Thailand respectively.[48,52,55]

A number of limitations in our study should be noted. There were considerable variations among the included studies that could contribute to the differences in reported disutility values though we applied a random-effects model to account for study heterogeneity. The variables included in the statistical models used to estimate the adjusted utility values or decrements were inconsistent between studies or poorly reported. Most studies recruited only type 2 diabetes, though three studies also included some participants with type 1 diabetes or did not state explicitly.[46-48] Significant heterogeneity was observed for a number of complications, although we conducted subgroup analyses by nationality and valuation instrument to present possible variations. Some studies lacked a baseline utility value for diabetes without complication which prevented estimation of the utility decrement. There are currently no standardized scoring frameworks to assess the quality of the health state utility studies for inclusion. Finally, our study could be prone to selection bias since our search was limited to a single database (MEDLINE) in English and Chinese languages.

Our study is an updated systematic review – many of the included studies were published in past 10 years, thus reflecting progress in diabetes management. Previous studies did not conduct any quantitative analysis, and solely relied on qualitative methods to select utility scores.[17] To our knowledge, this is the first meta-analysis of health state utility values for type 2 diabetes and its related complications. The preferred set of utility values is presented with confidence intervals and the range of available estimates to guide sensitivity analyses. We further present the utility values by nationality (Chinese and other Asian groups) and valuation instrument (EQ-5D and SF-6D) to assist the reader in contextualizing their cost-effectiveness analyses. In recent years, a growing number of therapeutic options has become available for patients with type 2 diabetes, while the cost for diabetes medicine has also increased dramatically.[59] With many new therapies in development, there is increasing importance attached to economic evaluation in Asia and elsewhere in determining access to interventions.

Nevertheless, further research work is needed on a number of fronts. For cost-effectiveness modelling purposes, it would be ideal to access the original data in order to apply the appropriate localized tariff for the corresponding EQ-5D or SF-6D instrument. Another area of uncertainty is the impact of the clinical course of disease on quality of life and utility values, particularly as the complication progresses or is treated. The effect on quality of life for patients experiencing multiple complications concurrently also needs future exploration.

Conclusions

We developed a reference set of pooled disutility and utility estimates for diabetes complications in East and Southeast Asia – the region with the world's largest burden of diabetes. Health economics researchers and public health policy makers could use our reference set to conduct

economic analysis of type 2 diabetes. Further research is needed to establish consistent methods and reporting of health state utility valuations including statistical models, study instruments and value sets.

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Table 1. Characteristics of included studies.

Study	Location	Ethnicity (%)	Diabetes type (% type 1)	Setting	n	Age group (mean)	Valuation instrument	Tariff	Statistical method
Jiao et al.[47] (2017)	Hong Kong	Chinese	1 and 2 (Not reported)	Primary and secondary healthcare setting	1275	≥ 18 years (64.84)	SF-6D	Hong Kong [65]	Ordinary least square regression
Lee et al.[64] (2012)	South Korea	Korean	2	Outpatient clinics of 3 university hospitals in South Korea	858	> 20 years (57.7)	EQ-5D	South Korea [66]	Univariate model
Luk et al.[52] (2014)	Hong Kong	Chinese	2	Web-based electronic portal	14826	≥ 18 years (59.2)	EQ-5D and EQ-VAS	UK [67]	Multivariate logistic regression
Pan et al.[68] (2016)	China	Not reported	2	A tertiary hospital in Suzhou, China	289	≥ 18 years (64.9)	EQ-5D	China [69]	Ordinary least square regression
Pan et al.[70] (2018)	China	Chinese	2	Community-based survey in Suzhou, China	913	Not reported (67.7)	EQ-5D	China [71]	Generalized linear regression
Pham et al.[72] (2020)	Vietnam	Vietnamese	2	Outpatient department of a hospital in Hanoi, Vietnam	214	All age included (median: 61.5)	EQ-5D	Vietnam [73]	Multivariate Tobit regression
Quah et al.*[54] (2011)	Singapore	Chinese (73.8) Malay (11.9) Indian (11.3) Other (3.0)	2	Clinical laboratories of 8 SingHealth polyclinics	699	≥ 21 years (63.0)	EQ-5D and EQ-VAS	Singapore [74]	Multiple linear regression model
Sakamaki et al.[75] (2006)	Japan	Not reported	2	Hospital in Saitama Prefecture	220	29-89 years (63.3)	EQ-5D	Japan [76]	Analysis of covariance (ANCOVA) model
Sakthong et al.*[55] (2008)	Thailand	Not reported	2	Outpatients in General Police Hospital in Bangkok, Thailand	303	27-90 years (61.1)	EQ-5D	Japan [77] UK [67,78] US [79]	Mann-Whitney U test
Takahara et al.[46] (2019)	Japan	Japanese	1 and 2 (6.9)	13 medical centers in Japan	4963	Not reported (64)	EQ-5D	Japan [80,81]	Ordinary least square regression
Tan et al.*[57] (2014)	Malaysia	Malay (47.0) Chinese (25.6) Indian (27.5)	2	2 tertiary hospitals in Klang Valley, Malaysia	313	30-78 years (55.7)	15D	Not reported	Mann-Whitney U test

Terauchi et al.[49] (2019)	Japan	Not reported	2	2016 Japan National Health and Wellness Survey (NHWS)	1478	≥ 18 years (63.6)	SF-6D	Not reported	Multivariate analysis on generalized linear models
Tung et al.[50] (2005)	Taiwan	Not reported	2	A community-based survey in Kinmen, Taiwan	406	≥ 30 years (Not reported)	TTO	Not reported	Multiple linear regression model
Venkataraman et al.[48] (2013)	Singapore	Chinese (59.8) Malay (21.4) Indian (18.8)	Not reported	Follow-up examination on participants from four previous cross-sectional surveys from 1982 to 1998	2601	Not reported (48)	SF-6D	UK [82]	Analysis of covariance (ANCOVA) model
Wan et al.[51] (2016)	Hong Kong	Chinese	2	Government-funded primary care outpatient clinics across Hong Kong	1826	≥ 18 years (64.8)	SF-6D	Hong Kong [9,83]	Linear mixed effect models
Zhang et al.[53] (2020)	China	Chinese	2	75 hospitals in 9 cities in China	7081	≥ 18 years (59.6)	EQ-5D and EQ-VAS	Not reported	Ordinary least square regression
Zhang et al.*[56] (2014)	China	Not reported	2	Population-based diabetes survey in urban and rural districts in Qingdao, China	4613	35–74 years (52)	15D	Not reported	Tobit regression model

*Not included in meta-analysis. EQ-5D, EuroQoL-5 dimension; EQ-VAS, EuroQol Visual Analogue Scale; SF-6D, Short Form-6-dimension; TTO, Time-Trade-Off; 15D, 15-dimensional.

Table 2. Preferred (dis)utility values for modelling type 2 diabetes and related complications using pooled estimates from meta-analyses.

Health outcome	(Dis)utility estimates mean (95% CI)	I^2 (%)	Range of candidate values
T2DM without complication	0.881 (0.833, 0.929)	98	0.780, 1.000
Myocardial infarction*	-0.007 (-0.036, 0.022)	-	-
Ischemic heart disease	-0.017 (-0.041, 0.007)	69	-0.040, 0.000
Heart failure*	-0.050 (-0.081, -0.020)	-	-
Cardiovascular disease	-0.029 (-0.036, -0.022)	28	-0.074, -0.008
Cerebrovascular disease	-0.086 (-0.112, -0.060)	76	-0.160, -0.006
Peripheral vascular disease	-0.017 (-0.125, 0.090)	95	-0.070, 0.040
Nephropathy	-0.022 (-0.037, -0.007)	86	-0.080, 0.020
End-stage renal disease	-0.053 (-0.081, -0.025)	0	-0.055, -0.050
Retinopathy	-0.023 (-0.034, -0.011)	48	-0.170, 0.020
Cataract*	-0.016 (-0.031, -0.001)	-	-
Blindness	-0.101 (-0.143, -0.059)	0	-0.113, -0.095
Neuropathy	-0.052 (-0.064, -0.041)	27	-0.063, -0.012
Dermatopathy*	-0.036 (-0.070, -0.002)	-	-
Amputation*	-0.177 (-0.291, -0.063)	-	-
Diabetic foot	-0.094 (-0.133, -0.055)	85	-0.140, -0.030
Hypoglycemia	-0.028 (-0.048, -0.009)	90	-0.040, -0.007
Excess BMI	-0.002 (-0.020, 0.017)	76	-0.030, 0.023

*Single study.

CI, confidence interval; I^2, Heterogeneity statistics; T2DM, type 2 diabetes.

Figure 1. PRISMA flow diagram.

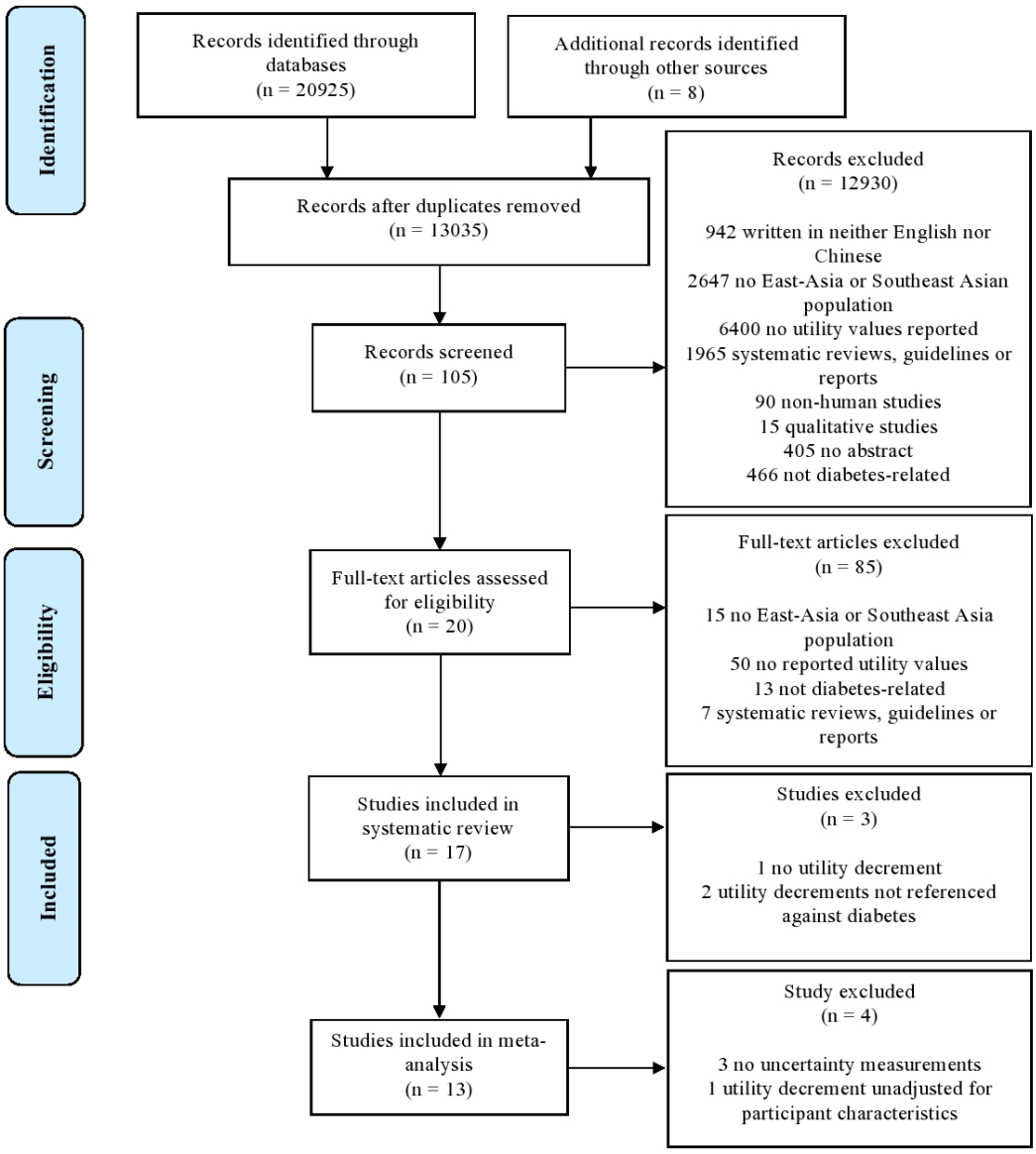
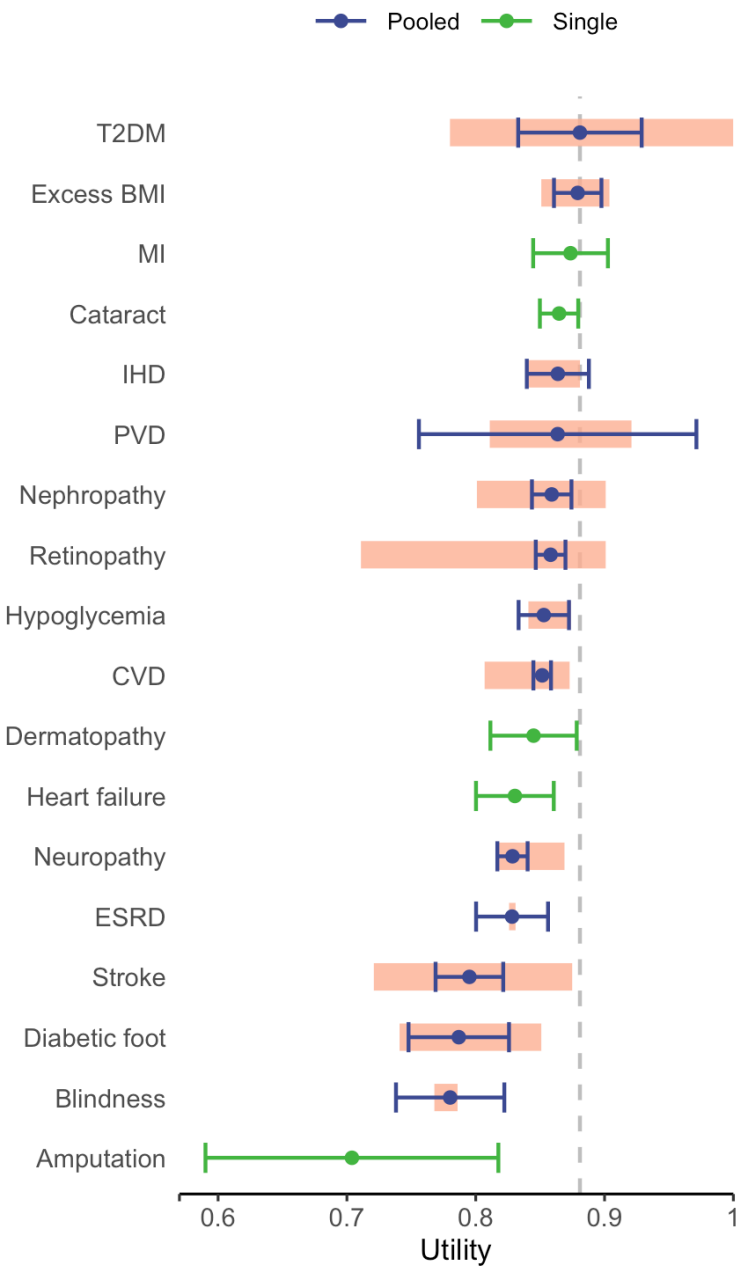
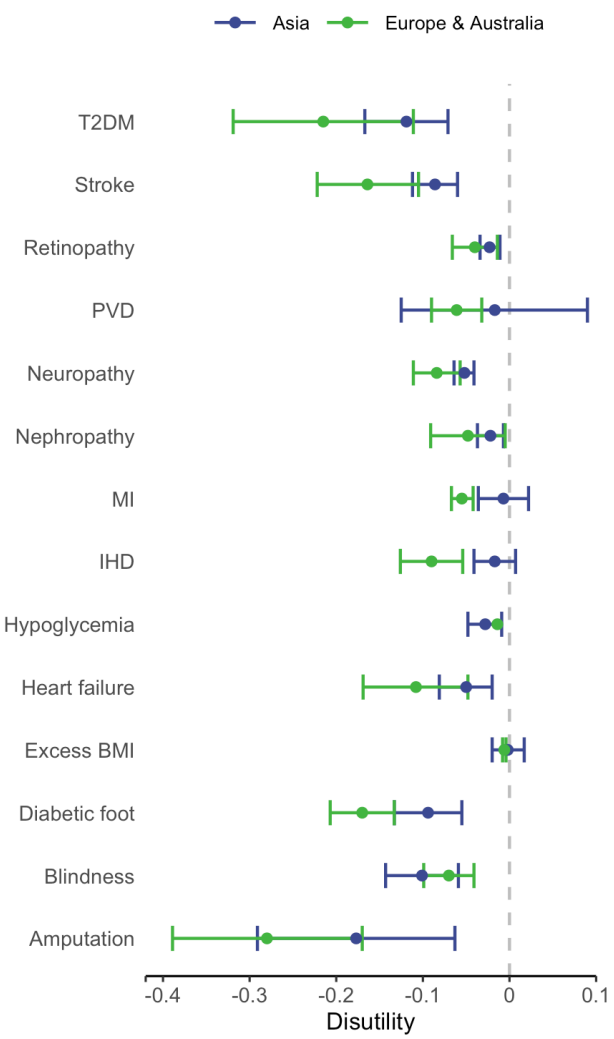


Figure 2. Preferred utility values for modelling type 2 diabetes and related complications.



T2DM, Type 2 diabetes mellitus; BMI, body mass index; MI, myocardial infarction; IHD, ischemic heart disease; PVD, peripheral vascular disease; CVD, cardiovascular disease; ESRD, end-stage renal disease. Utility estimate (dots) and 95% confidence interval (lines). Pink bars represent the range of reported utility values from all included studies.

Figure 3. Disutility values for type 2 diabetes and related complications derived in East/Southeast Asia populations compared to Western populations.



T2DM, Type 2 diabetes mellitus; BMI, body mass index; MI, myocardial infarction; IHD, ischemic heart disease; PVD, peripheral vascular disease; CVD, cardiovascular disease.
Disutility values and 95% confidence interval of our pooled estimates from meta-analyses (green) and individual studies cited in Beaudet et al (blue).(Beaudet et al., 2014) Values of T2DM without complication, myocardial infarction, ischemic heart disease, heart failure, cerebrovascular disease, blindness, and amputation were extracted from Clarke et al.(Clarke, Gray, & Holman, 2002) (UK); peripheral vascular disease, neuropathy, and excess BMI were extracted from Bagust and Beale(Bagust & Beale, 2005) (5 European countries); retinopathy was extracted from Fenwick et al.(Fenwick et al., 2012) (Australia); hypoglycemia was extracted from Currie et al.(Currie et al., 2006) (UK). Both our study and Beaudet et al.(Beaudet et al., 2014) identified the same study for cataracts (Lee et al.(Lee et al., 2012) (South Korea)).

Conflict of Interest Disclosures:

The authors reported no conflicts of interest.

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Health state utility values for type 2 diabetes and related complications in East and Southeast Asia: a systematic review and meta-analysis

Supplementary Appendix

S1. Classification and nomenclature of diabetes related complications

- Myocardial infarction
- Ischemic heart disease
    - Angina pectoris
    - Coronary artery disease without cardiac symptom
    - Coronary heart disease
- Heart failure
    - Congestive heart failure
- Cardiovascular disease
    - Heart disease
    - Cardiac symptom
- Cerebrovascular disease
    - Stroke
    - Ischemic stroke
    - Sequela-free cerebrovascular disease
    - Sequelae of stroke
- Peripheral vascular disease
    - Asymptomatic peripheral artery disease
    - Claudication
    - Peripheral arterial disease
- Nephropathy
    - Nephropathy (grade 1/grade 2/grade 3)
    - Overt nephropathy
    - Kidney disease
- End-stage renal disease
    - On dialysis
- Retinopathy
    - Retinopathy (mild/moderate/severe)
    - Non-proliferative diabetic retinopathy
    - Sight-threatening diabetic retinopathy
    - Bilateral diabetic retinopathy
    - Eye disease
    - Proliferative retinopathy without blindness
    - Proliferative diabetic retinopathy
- Cataract
- Blindness
    - Blindness in both eyes
- Neuropathy
    - Peripheral neuropathy
    - Peripheral neuropathy (mild/severe)
    - Symptomatic peripheral neuropathy
    - Decreased sensation
- Dermatopathy
- Amputation
    - Minor amputation

    - Major amputation
- Diabetic foot
    - Lower extremity lesions
    - Foot ulcer/gangrene
- Hypoglycemia
    - Hypoglycemia (more than or equal to once per month)
    - Severe or nocturnal hypoglycemia
    - Symptomatic hypoglycemia
    - Severe hypoglycemia
- Excess BMI

S2. MEDLINE search strategy

1	diabetes mellitus/
2	NIDDM.ti,ab.
3	MODY.ti,ab.
4	(late onset adj diabet$).ti,ab.
5	(maturity onset adj diabet$).ti,ab.
6	(non insulin$ depend$ or noninsulin$ depend$ or non insulin? Depend$ or noninsulin?depend$).ti,ab.
7	(typ$ 2 adj6 diabet$).ti,ab.
8	(typ$ II adj6 diabet$).ti,ab.
9	T2DM.ti,ab.
10	glucose intoleran$.ti,ab.
11	Diabetes Mellitus, Type 2/
12	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13	quality adjusted life.ti,ab.
14	qaly$.ti,ab.
15	qol.ti,ab.
16	quality of life.ti,ab.
17	exp “quality of life”/
18	exp Quality-Adjusted Life Years/
19	Quality adjusted life year$.ti,ab.
20	disability adjusted life.ti,ab.
21	daly$.ti,ab.
22	Health$ year$ equivalent$.ti,ab.
23	exp “Value of Life”/
24	Health-related quality of life.ti,ab.
25	hrqol.ti,ab.
26	hrql.ti,ab.
27	Quality of wellbeing.ti,ab.
28	health utility$ index.ti,ab.
29	HUI.ti,ab.
30	health utility$.ti,ab.
31	(hui or hui1 or hui2 or hui3).ti,ab.
32	disutil$.ti,ab.
33	utility.ti,ab.
34	utility analysis.ti,ab.
35	assessment of quality of life.ti,ab.
36	time trade off.ti,ab.
37	TTO.ti,ab.
38	standard gamble.ti,ab.
39	SG.ti,ab.
40	visual analog$ scale.ti,ab.
41	VAS.ti,ab.
42	rating scale.mp. or rating scale/
43	euroqol.ti,ab.
44	(euroqol 5d or EQ-5D or eq-5d or euroqol).ti,ab.

45 eq$5d.ti,ab.
46 (short form 6d or shortform 6d or sf6d or sf-6d or sf 6d).ti,ab.
47 (willingness adj3 pay).mp.
48 wtp.ti,ab.
49 exp Health Surveys/
50 health assessment questionnaire.ti,ab.
51 exp Health Status/
52 exp Health Status Indicators/
53 Health status.ti,ab.
54 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53
55 obesity/ or body mass/ or body weight/
56 BMI.ti,ab.
57 Body mass index.ti,ab.
58 weight gain/
59 weight gain.ti,ab.
60 (overweight or over weight).ti,ab.
61 obes$.ti,ab.
62 Weight Loss/
63 (weight adj2 (cyc$ or reduc$ or los$ or decreas$)).ti,ab.
64 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63
65 12 and 54 and 64
66 exp Myocardial Infarction/
67 exp Myocardial Ischemia/
68 ami.ti,ab.
69 mi.ti,ab.
70 myocardial infarct$.ti,ab.
71 heart infarction.ti,ab.
72 coronary thrombos$.ti,ab.
73 myomala$.ti,ab.
74 coronary syndrome$.ti,ab.
75 heart attack$.ti,ab.
76 myocardial isch$.ti,ab.
77 post-infarction.ti,ab.
78 Heart infarct$.ti,ab.
79 Nstemi.ti,ab.
80 Unstable coronary.ti,ab.
81 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80
82 12 and 54 and 81
83 Agina Pectoris/
84 angina$.ti,ab.
85 Coronary Disease/
86 Myocardial Ischemia/
87 Myocardial Ischemia.ti,ab.
88 heart muscle ischemia.ti,ab.

89 (coronary adj3 disease$).ti,ab.
90 83 or 84 or 85 or 86 or 87 or 88 or 89
91 12 and 54 and 90
92 Heart Failure/
93 Ventricular Dysfunction/
94 (ventric$ adj6 dysfunction$).ti,ab.
95 (ventric$ adj6 function$).ti,ab.
96 heart failure.ti,ab.
97 cardiac failure.ti,ab.
98 exp Heart Defects, Congenital/
99 (congenital$ adj3 heart).ti,ab.
100 (congenital$ adj3 cardiac).ti,ab.
101 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100
102 12 and 54 and 101
103 Cardiovascular Diseases/
104 cardiovascular disease$.ti,ab.
105 cardiovascular event$.ti,ab.
106 stroke$.ti,ab.
107 cerebrovascular.ti,ab.
108 cva.ti,ab.
109 apoplexy.ti,ab.
110 transient isch$ attack$.ti,ab.
111 TIA.ti,ab.
112 brain infarct$.ti,ab.
113 cerebr$ vascular$.ti,ab.
114 apoplectic.ti,ab.
115 cerebr$ infarct$.ti,ab.
116 ((cerebral or brain or subarachnoid) adj5 (haemorrhage or hemorrhage or haematoma or hematoma or bleed$)).ti,ab.
117 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116
118 12 and 54 and 117
119 peripheral vascular diseases/
120 vascular diseases/
121 intermittent claudication/
122 atherosclerosis/
123 arteriosclerosis/
124 arteriosclerosis obliterans/
125 arterial occlusive diseases/
126 intermittent claudication.ti,ab.
127 ((peripher$ adj3 dis$) or PVD or PAOD or claud$ or dysvascular$).ti,ab.
128 (peripher$ adj3 (occlu$ or arteri$ or vascular)).ti,ab.
129 ((arter$ or vascu$ or vessel or vein$ or venous) adj5 (obstruct$ or occlus$ or lesion? or steno$ or re-stenos$ or restenos$ or isch?em$ or atherosclero$)).ti,ab.
130 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129
131 12 and 54 and 130

132 diabetic nephropathies/
133 albuminuria/
134 proteinuria/
135 renal insufficiency/
136 kidney diseases/
137 diabetic nephrop$.ti,ab.
138 diabetic glomerulo$.ti,ab.
139 renal diabetes.ti,ab.
140 renal insufficiency.ti,ab.
141 kidney disease$.ti,ab.
142 ((diabetic or diabetes) and (renal disease$ or nephron$ or nephrit$ or glomerulo$)).ti,ab.
143 Albuminuria.ti,ab.
144 Microalbuminuria.ti,ab.
145 proteinuria.ti,ab.
146 132 or 133 or 134 or 135 or 136 or 137 or 138 or 139 or 140 or 141 or 142 or 143 or 144 or 145
147 12 and 54 and 146
148 Hemofiltration/
149 Renal Dialysis/
150 renal replacement therapy/
151 renal replacement therapy.ti,ab.
152 (haemodialysis or hemodialysis).ti,ab.
153 (haemofiltration or hemofiltration).ti,ab.
154 (haemodiafiltration or hemodiafitration).ti,ab.
155 dialysis.ti,ab.
156 intradialytic.ti,ab.
157 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156
158 12 and 54 and 157
159 diabetic retinopathy/
160 (diabet$ adj3 retinopath$).ti,ab.
161 (proliferat$ adj3 retinopath$).ti,ab.
162 (diabet$ adj3 maculopath$).ti,ab.
163 159 or 160 or 161 or 162
164 12 and 54 and 163
165 (macula$ adj2 edema).ti,ab.
166 (macula$ adj2 oedema).ti,ab.
167 (DME or DMO or CME CSME).ti,ab.
168 Macular Edema/
169 165 or 166 or 167 or 168
170 12 and 54 and 169
171 ((low or handicap$ or subnormal or impair$ or partial$ or disab$ or disorder$) adj5 (vision or visual$ or sight$)).ti,ab.
172 Vision Disorders/ or Vision, Low/ or Blindness/
173 Visually Impaired Persons/
174 171 or 172 or 173

175 12 and 54 and 174
176 cataract/
177 cataract extraction/
178 capsulorhexis/
179 phacoemulsification/
180 ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj4 lens).ti,ab.
181 ((extract$ or aspirat$ or operat$ or remov$ or surg$ or excis$ or implant$) adj4 cataract$).ti,ab.
182 cataract.ti,ab.
183 176 or 177 or 178 or 179 or 180 or 181 or 182
184 12 and 54 and 183
185 diabetic neuropathy/ or peripheral neuropathy/
186 neuropath$.ti,ab.
187 peripheral nervous system diseases/
188 peripheral$ nervous$ system$ disease$.ti,ab.
189 polyneuropath$.ti,ab.
190 peripheral nerve/
191 exp diabetic neuropathies/
192 diabet$ neuropath$.ti,ab.
193 diabet$ polyneuropath$.ti,ab.
194 foot ulcer/
195 diabetic foot/
196 (diabet$ adj3 ulcer$).ti,ab.
197 (diabet$ adj3 (foot or feet)).ti,ab.
198 (diabet* adj3 wound*).ti,ab.
199 (diabet* and amputat*).ti,ab.
200 (amputat$ adj3 (transfemoral or transtibial or lower limb or lower extremity or above knee or below knee or through knee)).ti,ab.
201 FOOT AMPUTATION/ or KNEE AMPUTATION/ or AMPUTATION/ or BELOW KNEE AMPUTATION/ or ABOVE KNEE AMPUTATION/ or LEG AMPUTATION/ or LIMB AMPUTATION/
202 185 or 186 or 187 or 188 or 189 or 190 or 191 or 192 or 193 or 194 or 195 or 196 or 197 or 198 or 199 or 200 or 201
203 12 and 54 and 202

S3. Data extraction items

Study background information

1. Study Ref ID
2. Authorship
3. Study title
4. Year of publication
5. Name of publication
6. Publication type

Study design

7. Country of respondents
8. Aim of study
9. Study design
10. Study sample size
11. Sampling method
12. Inclusion / exclusion criteria
13. Disease-related health state (selecting and assigning health states to respondents)
14. Details of health state description system (instrument & levels of instrument)
15. Respondent selection and recruitment
16. Response rates
17. Reasons for loss to follow-up
18. Missing data and methods to address
19. Any other potential problems with the study

Participant characteristics*

20. Age
21. Gender
22. Study setting
23. Race
24. Diabetes type

Determination of health state utility values (HUSVs)

25. Method of elicitation of HSUVs – how and who
26. Valuation technique
27. Tariff used
28. Mode of administration
29. Data source
30. Reported HSUV point estimate type (mean / median)
31. Statistical method used
32. HSUVs summary

* For studies including type 1 diabetes patients, only information of those with type 2 diabetes were extracted.

Table S1. Quality assessment of included studies in systematic review

	NICE criteria[1]								
Study	Sample size	Respondent selection & recruitment	Inclusion and exclusion criteria	Response rates to instrument	Completeness of data	Appropriate measure	No other problems	Uncertainty measurement	Appropriate tariff
Jiao et al.[2]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Lee et al.[3]	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Luk et al.[4]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No
Pan et al.[5]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Pan et al.[6]	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Pham et al.[7]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Quah et al.[8]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes
Sakamaki et al.[9]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Sakthong et al.[10]	Yes	Yes	Yes	No	Yes	Yes	Yes	No	No
Takahara et al.[11]	Yes	Yes	No	Yes	No	Yes	Yes	Yes	Yes
Tan et al.[12]	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	No
Terauchi et al.[13]	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No
Tung et al.[14]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No

Venkataraman et al.[15]	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No
Wan et al.[16]	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes
Zhang et al.[17]	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Zhang et al.[18]	Yes	Yes	Yes	Yes	No	Yes	Yes	No	No

Assessment criteria

Sample size:	Is the sample size of the study reported?
Respondent selection & recruitment:	Is the study representative to the population from which they were recruited?
Inclusion/exclusion criteria:	Does the study state out the inclusion and exclusion criteria in recruiting participants?
Response rates to instrument used:	Are response rates reported and if so, are the rates unlikely to be a threat to validity?
Completeness of data	Are the results complete without any missing data?
Appropriateness of measure:	Is the measure used valid in the group of patients?
Any other problems with the study:	Are there no other problems with the study? (e.g. relevance of location/country, patients recruited from, loss to follow-up)
Uncertainty measurement:	Is there any reported uncertainty measurement (e.g. 95% confidence interval, standard error)?
Appropriateness of tariff use:	Is the tariff reported and does it match the study population?

Table S2. (Dis)utility values by health outcome

Health outcome	Method of Elicitation	Score for diabetes without complication	Mean (dis)utility values (95% CI)	p-value
Heart failure				
Lee et al.[3]	EQ-5D	NR	-0.0505 (-0.081, -0.020)	0.001
Myocardial infarction				
Lee et al.[3]	EQ-5D	NR	-0.0073 (-0.036, 0.022)	0.624
Ischemic heart disease				
Lee et al.[3]	EQ-5D	NR	-0.0266 (-0.049, -0.004)	0.02
Quah et al.[8]	EQ-5D	0.91	-0.05 (NR)	<0.01
Takahara et al.[11]	EQ-5D	0.936	0 (-0.012, 0.012)	NR
Cardiovascular disease				
Luk et al.[4]	EQ-5D	NR	-0.034 (-0.042, -0.026)	<0.001
Pan et al.[5]	EQ-5D	0.956	-0.074 (-0.112, -0.036)	<0.05
Pan et al.[6]	EQ-5D	NR	-0.008 (-0.016, -0.001)	0.003
Pham et al.[7]	EQ-5D	1.00	-0.05 (-0.14, 0.04)	NR
Sakthong et al.[10] (Japan)	EQ-5D	NR	-0.1 (NR)	NR
Sakthong et al.[10] (UK)	EQ-5D	NR	-0.13 (NR)	NR
Sakthong et al.[10] (US)	EQ-5D	NR	-0.1 (NR)	NR
Takahara et al.[11]	EQ-5D	0.936[P]	-0.031 (-0.055, -0.007)	<0.05
Zhang et al.[17]	EQ-5D	0.92	-0.028 (-0.038, -0.018)	<0.001
Jiao et al.[2]	SF-6D	0.882[P]	-0.017 (-0.042, 0.008)	0.19
Terauchi et al.[13]	SF-6D	NR	-0.02 (-0.03, -0.002)	NR
Wan et al.[16]	SF-6D	NR	-0.026 (-0.043, -0.009)	<0.05
Tan et al.[12]	15D	NR	-0.116 (NR)	NR
Zhang et al.[18]	15D	NR	-0.01 (NR)	0.001
Luk et al.[4]	EQ-VAS	NR	-1.88 (-2.593, -1.167)	<0.001
Zhang et al.[17]	EQ-VAS	73.5	-1.013 (-1.924, -0.102)	0.029
Cerebrovascular disease				
Lee et al.[3]	EQ-5D	NR	-0.0761 (-0.102, -0.050)	<0.001
Pan et al.[5]	EQ-5D	0.956	-0.16 (-0.22, -0.1)	<0.05
Quah et al.[8]	EQ-5D	0.91	-0.07 (NR)	<0.05
Takahara et al.[11] (Sequela-free cerebrovascular disease)	EQ-5D	0.936[P]	-0.006 (-0.024, 0.012)	NR
Takahara et al.[11] (Sequelae of stroke)	EQ-5D	0.936[P]	-0.098 (-0.133, -0.063)	<0.01

Zhang et al.[17]	EQ-5D	0.92	-0.101 (-0.113, -0.089)	<0.001
Jiao et al.[2]	SF-6D	0.882[P]	-0.042 (-0.072, -0.012)	0.005
Venkataraman et al.[15]	SF-6D	0.78	-0.04 (-0.118, 0.038)	NR
Zhang et al.[17]	EQ-VAS	73.5	-3.34 (-4.451, -2.229)	<0.001
Peripheral vascular disease				
Quah et al.[8]	EQ-5D	0.91	-0.08 (NR)	<0.05
Takahara et al.[11] (Asymptomatic peripheral artery disease)	EQ-5D	0.936[P]	0.001 (-0.017, 0.019)	NR
Takahara et al.[11] (Claudication)	EQ-5D	0.936[P]	-0.07 (-0.080, -0.060)	<0.01
Venkataraman et al.[15]	SF-6D	0.78	0.04 (-0.005, 0.085)	NR
Amputation				
Takahara et al.[11] (Minor amputation)	EQ-5D	0.936[P]	0.002 (-0.069, 0.073)	NR
Takahara et al.[11] (Major amputation)	EQ-5D	0.936[P]	-0.177 (-0.291, -0.063)	<0.01
Diabetic foot				
Pan et al.[6]	EQ-5D	NR	-0.07 (-0.085, -0.055)	<0.001
Sakamaki et al.[9]	EQ-5D	0.884	-0.03 (-0.12, 0.06)	NR
Takahara et al.[11]	EQ-5D	0.936[P]	-0.14 (-0.207, -0.073)	<0.01
Zhang et al.[17]	EQ-5D	0.92	-0.118 (-0.136, -0.100)	<0.001
Sakamaki et al.[9]	EQ-VAS	76.3	-5.7 (-15.4, 4)	NR
Zhang et al.[17]	EQ-VAS	73.5	-4.26 (-6.102, -2.418)	<0.001
Nephropathy				
Lee et al.[3]	EQ-5D	NR	-0.0044 (-0.037, 0.028)	0.794
Luk et al.[4]	EQ-5D	NR	-0.014 (-0.020, -0.008)	<0.001
Pan et al.[6]	EQ-5D	NR	-0.003 (-0.013, 0.008)	0.594
Pham et al.[7]	EQ-5D	1.00	-0.08 (-0.23, 0.07)	NR
Sakamaki et al.[9]	EQ-5D	0.884	-0.06 (-0.17, 0.05)	NR
Sakthong et al.[10] (Japan)	EQ-5D	NR	-0.07 (NR)	NR
Sakthong et al.[10] (UK)	EQ-5D	NR	-0.1 (NR)	NR
Sakthong et al.[10] (US)	EQ-5D	NR	-0.07 (NR)	NR
Takahara et al.[11]	EQ-5D	0.936[P]	-0.017 (-0.031, -0.003)	<0.05
Zhang et al.[17]	EQ-5D	0.92	-0.058 (-0.070, -0.046)	<0.001
Jiao et al.[2]	SF-6D	0.882	-0.011 (-0.029, 0.006)	0.194
Venkataraman et al.[15] (Grade 1)	SF-6D	0.78	0.02 (-0.015, 0.055)	NR
Venkataraman et al.[15] (Grade 2)	SF-6D	0.78	-0.03 (-0.065, 0.005)	NR
Venkataraman et al.[15] (Grade 3)	SF-6D	0.78	-0.04 (-0.079, -0.001)	NR
Zhang et al.[18]	15D	NR	-0.02 (NR)	0.001

Luk et al.[4]	EQ-VAS	NR	-1.105 (-1.711, -0.499)	<0.001
Sakamaki et al.[9]	EQ-VAS	76.3	-15.6 (-27.2, -4)	NR
Zhang et al.[17]	EQ-VAS	73.5	-3.283 (-4.394, -2.172)	<0.001
End-stage renal disease				
Takahara et al.[11]	EQ-5D	0.936[P]	-0.05 (-0.091, -0.009)	<0.05
Jiao et al.[2]	SF-6D	0.882	-0.055 (-0.093, -0.017)	0.004
Retinopathy				
Lee et al.[3]	EQ-5D	NR	-0.0217 (-0.040, -0.003)	0.019
Pan et al.[5]	EQ-5D	0.956	-0.016 (-0.045, 0.013)	NR
Pan et al.[6] (Unilateral retinopathy)	EQ-5D	NR	-0.013 (-0.029, 0.005)	0.372
Pan et al.[6] (Bilateral retinopathy)	EQ-5D	NR	-0.019 (-0.037, -0.002)	0.009
Pham et al.[7]	EQ-5D	1.00	-0.17 (-0.37, 0.03)	NR
Quah et al.[8]	EQ-5D	0.91	-0.04 (NR)	<0.05
Sakamaki et al.[9]	EQ-5D	0.884	-0.01 (-0.08, 0.06)	NR
Takahara et al.[11]	EQ-5D	0.936[P]	-0.003 (-0.019, 0.013)	NR
Zhang et al.[17]	EQ-5D	0.92	-0.022 (-0.032, -0.012)	<0.001
Jiao et al.[2] (Non-proliferative diabetic retinopathy)	SF-6D	0.882[P]	0.004 (-0.024, 0.032)	0.769
Jiao et al.[2] (Sight threatening diabetic retinopathy)	SF-6D	0.882[P]	-0.043 (-0.075, -0.01)	0.01
Venkataraman et al.[15] (Mild)	SF-6D	0.78	0.02 (-0.041, 0.081)	NR
Venkataraman et al.[15] (Moderate)	SF-6D	0.78	-0.01 (-0.051, 0.031)	NR
Venkataraman et al.[15] (Severe)	SF-6D	0.78	-0.03 (-0.065, 0.005)	NR
Zhang et al.[18]	15D	NR	-0.011 (NR)	<0.001
Sakamaki et al.[9]	EQ-VAS	76.3	-5.5 (-12.4, 1.2)	NR
Zhang et al.[17]	EQ-VAS	73.5	-2.191 (-3.095, -1.287)	<0.001
Tung et al.[14] (Non-proliferative diabetic retinopathy)	TTO	NR	-0.063 (-0.096, -0.031)	0.0002
Tung et al.[14] (Proliferative diabetic retinopathy)	TTO	NR	-0.104 (-0.17, -0.039)	0.002
Blindness				
Takahara et al.[11]	EQ-5D	0.936[P]	-0.095 (-0.146, -0.044)	<0.01
Tung et al.[14]	TTO	NR	-0.113 (-0.188, -0.039)	0.003
Cataract				
Lee et al.[3]	EQ-5D	NR	-0.0162 (-0.031, -0.001)	0.034

Neuropathy				
Luk et al.[4]	EQ-5D	NR	-0.063 (-0.077, -0.049)	<0.001
Pan et al.[5]	EQ-5D	0.956	-0.057 (-0.088, -0.027)	<0.05
Quah et al.[8]	EQ-5D	0.91	-0.05 (NR)	<0.01
Sakamaki et al.[9]	EQ-5D	0.884	-0.02 (-0.08, 0.04)	NR
Takahara et al.[11] (Symptomatic peripheral neuropathy)	EQ-5D	0.936[¶]	-0.044 (-0.056, -0.032)	<0.01
Takahara et al.[11] (Decreased sensation)	EQ-5D	0.936[¶]	-0.012 (-0.022, -0.002)	<0.05
Venkataraman et al.[15] (Mild peripheral neuropathy)	SF-6D	0.78	-0.02 (-0.059, 0.019)	NR
Venkataraman et al.[15] (Severe peripheral neuropathy)	SF-6D	0.78	-0.06 (-0.125, 0.005)	NR
Luk et al.[4]	EQ-VAS	NR	-1.547 (-2.821, -0.273)	0.017
Quah et al.[8]	EQ-VAS	72.3	-3.3 (NR)	<0.05
Sakamaki et al.[9]	EQ-VAS	76.3	-2.3 (-8.5, 3.9)	NR
Hypoglycemia				
Luk et al.[4]	EQ-5D	NR	-0.04 (-0.050, -0.030)	<0.001
Takahara et al.[11]	EQ-5D	0.936[¶]	-0.025 (-0.049, -0.001)	<0.05
Zhang et al.[17] (Symptomatic hypoglycemia)	EQ-5D	0.92	-0.007 (-0.011, -0.003)	<0.001
Zhang et al.[17] (Severe hypoglycemia)	EQ-5D	0.92	-0.008 (-0.016, -0.00016)	0.049
Terauchi et al.[13]	SF-6D	NR	-0.04 (-0.06, -0.03)	NR
Luk et al.[4]	EQ-VAS	NR	-2.585 (-3.579, -1.591)	<0.001
Zhang et al.[17] (Symptomatic hypoglycemia)	EQ-VAS	73.5	-0.281 (-0.667, 0.105)	0.153
Zhang et al.[17] (Severe hypoglycemia)	EQ-VAS	73.5	-1.507 (-2.285, -0.729)	<0.001
Dermatopathy				
Pan et al.[5]	EQ-5D	0.956	-0.036 (-0.070, -0.003)	<0.05
Excess BMI				
Lee et al.[3] (BMI: ≥25 kg/m^2)	EQ-5D	NR	0.0229 (-0.002, 0.047)	0.068
Luk et al.[4] (BMI: ≥25 kg/m^2)	EQ-5D	NR	-0.007 (-0.013, -0.001)	0.023
Takahara et al.[11]	EQ-5D	0.936[¶]	0.001 (-0.005, 0.007)	NR

(BMI: 25-30 kg/m^2 VS <25 kg/m^2)				
Takahara et al.[11] (BMI: 30-35 kg/m^2 VS <25 kg/m^2)	EQ-5D	0.936⁋	-0.006 (-0.018, 0.006)	NR
Takahara et al.[11] (BMI: ≥35 kg/m^2 VS <25 kg/m^2)	EQ-5D	0.936⁋	-0.03 (-0.052, -0.008)	<0.01
Luk et al.[4] (BMI: ≥25 kg/m^2)	EQ-VAS	NR	-0.534 (-1.108, 0.040)	0.068
Tung et al.[14] (BMI: ≥25 kg/m^2 VS <25 kg/m^2)	TTO	NR	0.013 (-0.012, 0.038)	0.32

NR, Not reported. EQ-5D, EuroQoL-5 dimension; SF-6D, Short Form-6-dimension; 15D, 15-dimensional; EQ-VAS, EuroQol Visual Analogue Scale; TTO, Time-Trade-Off.

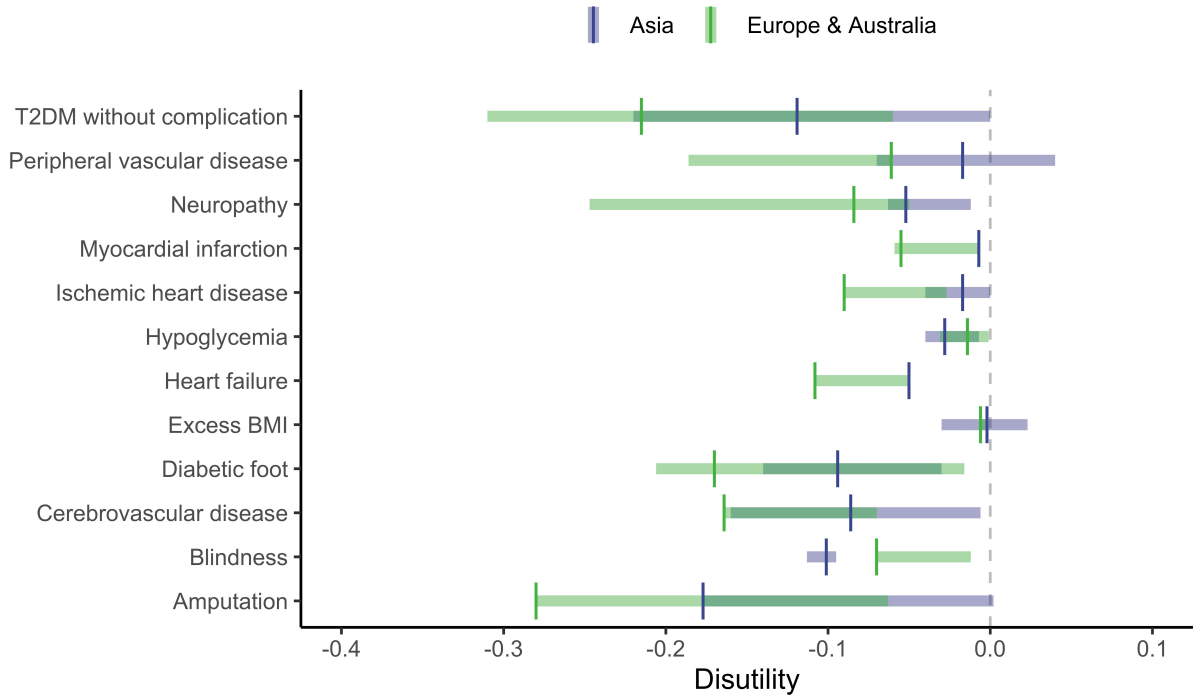
⁋ Population include both type 1 and 2 diabetes

Table S3. ICD-9-CM, ICPC-2 codes for diabetes-related complications in included studies

Study	Disease	ICPC-2 Codes	ICD-9-CM Codes
Jiao et al.[2] (2017)	Heart disease	K74-K77	410.00-410.92, 411.0-411.89; 412; 413.0-413.9; 414.0-414.9, 428.0-428.9, 798.1-798.9
	Stroke	K89-K91	430; 431;432.0-432.9; 433.00-433.91; 434.00-434.91; 435.0-435.9; 436; 437.0-437.9; 438.0-438.9
	NPDR / pre-PDR	F83	249.5, 250.5; 362.01; 362.03-362.06; 365; 366.41
	STDR	NA	362.02; 362.07
	Diabetic retinopathy	NA	250.40-250.43; 249.40-249.41; 585.1-585.4; 585.9; 791.0
	ESRD	NA	585.5-585.6; 586
Lee et al.[3] (2012)	Myocardial infarction, angina pectoris, congestive heart failure, ischemic stroke, cataract, retinopathy, nephropathy	NA	NA
Luk et al.[4] (2014)	Nephropathy, retinopathy, sensory neuropathy, cardiovascular disease	NA	NA
Pan et al.[5] (2016)	Retinopathy, Neuropathy, Heart disease, cerebrovascular disease	NA	NA
Pan et al.[6] (2018)	Heart disease, diabetic foot, nephropathy, retinopathy	NA	NA
Pham et al.[7] (2020)	Heart disease, nephropathy, retinopathy	NA	NA
Quah et al.[8] (2011)	Stroke, Ischemic heart disease, peripheral neuropathy, eye disease, peripheral vascular disease	NA	NA
Sakamaki et al.[9] (2006)	Neuropathy, retinopathy, nephropathy, lower extremity lesions	NA	NA
Sakthong et al.[10] (2008)	Neuropathy, retinopathy, nephropathy, cardiovascular diseases	NA	NA
Takahara et al.[11] (2018)	They had their own definitions of complication categories and other symptoms (please refer to study)		
Tan et al.[12] (2014)	Cardiovascular disease	NA	NA
Terauchi et al.[13] (2019)	Cardiovascular disease, hypoglycaemia	NA	NA
Tung et al.[14] (2004)	Diabetic retinopathy	Definition by diabetic retinopathy disease severity scale	

Venkataraman et al.[15] (2013)	Retinopathy, peripheral neuropathy, peripheral arterial disease, nephropathy	Definition stated in study	Coronary heart disease, stroke (self-reported)
Wan et al.[16] (2016)	Chronic kidney disease	Estimated glomerular filtration rate <60 mL/min/1.73 m^2	
	Hypertension	K86, K87	NA
	History of CVD event	K74-K76 (coronary heart diseases) K77 (heart failure) K89-K91 (Stroke)	410.x, 411.x-414.x, 798.x (coronary heart diseases) 428.x (heart failure) 430.x-438.x (stroke)
Zhang et al.[17] (2020)	Hypertension, cardiovascular disease, hyperlipidemia, stroke, retinopathy, neuropathy, nephropathy, diabetic foot, symptomatic hypoglycaemia, severe hypoglycaemia	NA	NA
Zhang et al.[18] (2014)	Kidney disease, Eye disease, cardiovascular disease, hypertension, dyslipidemia	NA	NA

Figure S1. Disutility values for diabetes and related complications derived in East/Southeast Asia populations compared to Western populations



Disutility values are represented by horizontal bars (range of candidate values). Values from our meta-analyses (Asian) and individual studies cited in Beaudet et al.[19] (Western). Values of T2DM without complication, myocardial infarction, ischemic heart disease, heart failure, cerebrovascular disease, blindness, and amputation were extracted from Clarke et al.[20] (UK); peripheral vascular disease, neuropathy, and excess BMI were extracted from Bagust and Beale[21] (5 European countries); retinopathy was extracted from Fenwick et al.[22] (Australia); hypoglycemia was extracted from Currie et al.[23] (UK). Both our study and Beaudet et al.[19] identified the same study for cataracts (Lee et al.[3] (South Korea)).

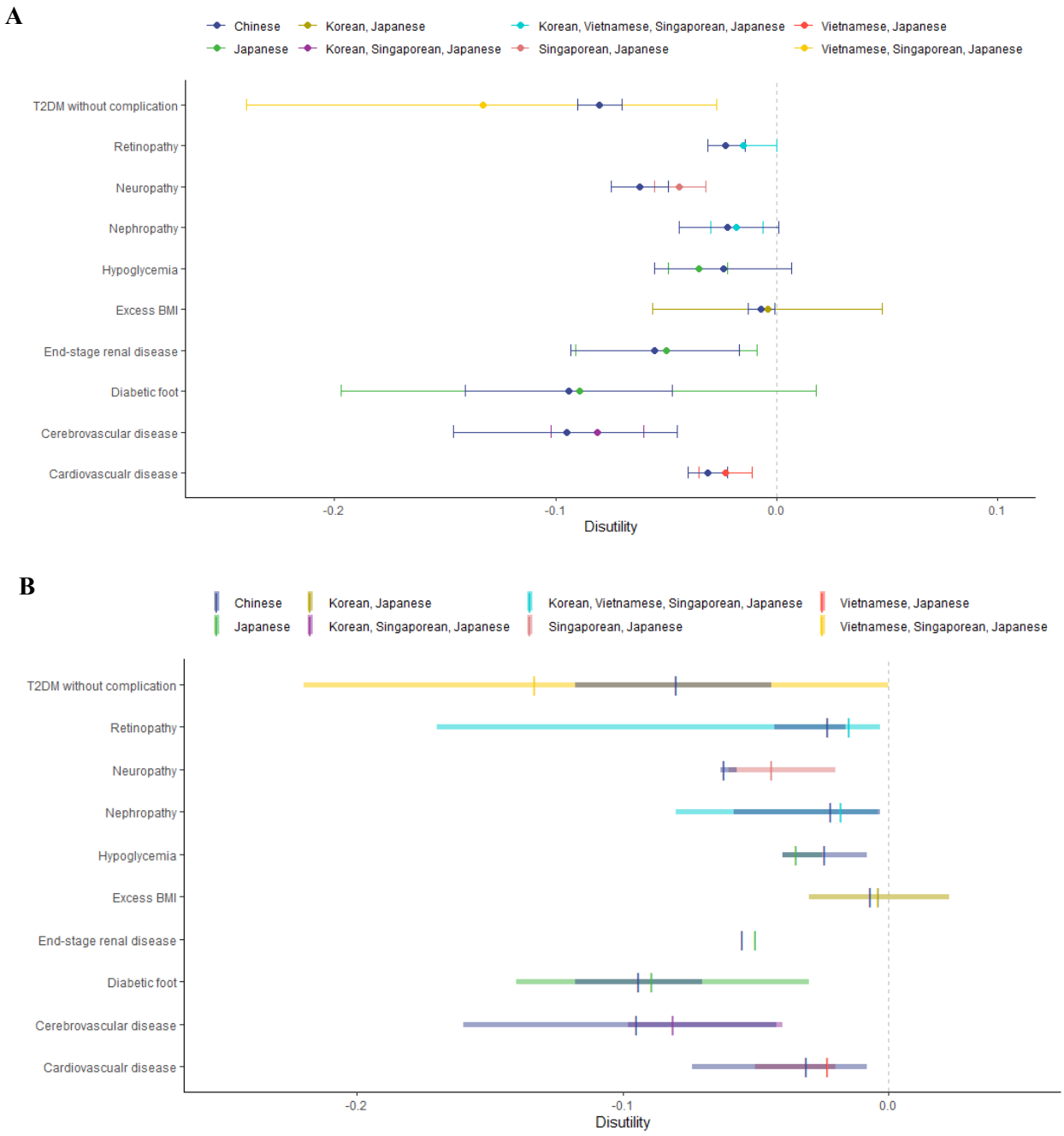
Table S4. Mean (dis)utility values by nationality of participants using pooled estimates from meta-analyses

Health outcome	Chinese		Other Asian Groups	
	(Dis)utility estimates, mean (95% CI)	I^2 (%)	(Dis)utility estimates, mean (95% CI)	I^2 (%)
T2DM without complication	0.92 (0.910, 0.930)	0	0.867 (0.760, 0.973)	99
Myocardial infarction	-	-	-0.007 (-0.036, 0.022)*	-
Ischemic heart disease	-	-	-0.017 (-0.041, 0.007)	69
Heart failure	-	-	-0.05 (-0.081, -0.020)*	-
Cardiovascular disease	-0.031 (-0.040, -0.022)	46	-0.023 (-0.035, -0.011)	0
Cerebrovascular disease	-0.095 (-0.146, -0.045)	89	-0.081 (-0.102, -0.060)	4
Peripheral vascular disease	-	-	-0.017 (-0.125, 0.090)	95
Nephropathy	-0.022 (-0.044, 0.001)	95	-0.018 (-0.030, -0.006)	0
End-stage renal disease	-0.055 (-0.093, -0.017)	-	-0.05 (-0.091, -0.009)	-
Retinopathy	-0.023 (-0.031, -0.014)	0	-0.015 (-0.031, 0.000)	30
Cataract	-	-	-0.016 (-0.031, -0.001)*	-
Blindness	-	-	-0.095 (-0.146, -0.044)	-
Neuropathy	-0.062 (-0.075, -0.049)	0	-0.044 (-0.055, -0.032)	0
Dermatopathy	-0.036 (-0.070, -0.002)*	-	-	-
Amputation	-	-	-0.177 (-0.291, -0.063)*	-
Diabetic foot	-0.094 (-0.141, -0.047)	94	-0.089 (-0.197, 0.018)	73
Hypoglycemia	-0.024 (-0.055, 0.007)	96	-0.035 (-0.049, -0.022)	10
Excess BMI	-0.007 (-0.013, -0.001)	-	-0.004 (-0.056, 0.048)	90

* Single study.

T2DM, type 2 diabetes; CI, confidence interval; I^2, Heterogeneity statistic.

Figure S2. Disutility values by nationality



(A) 95% confidence intervals of pooled values, and (B) ranges of candidate values by nationality.

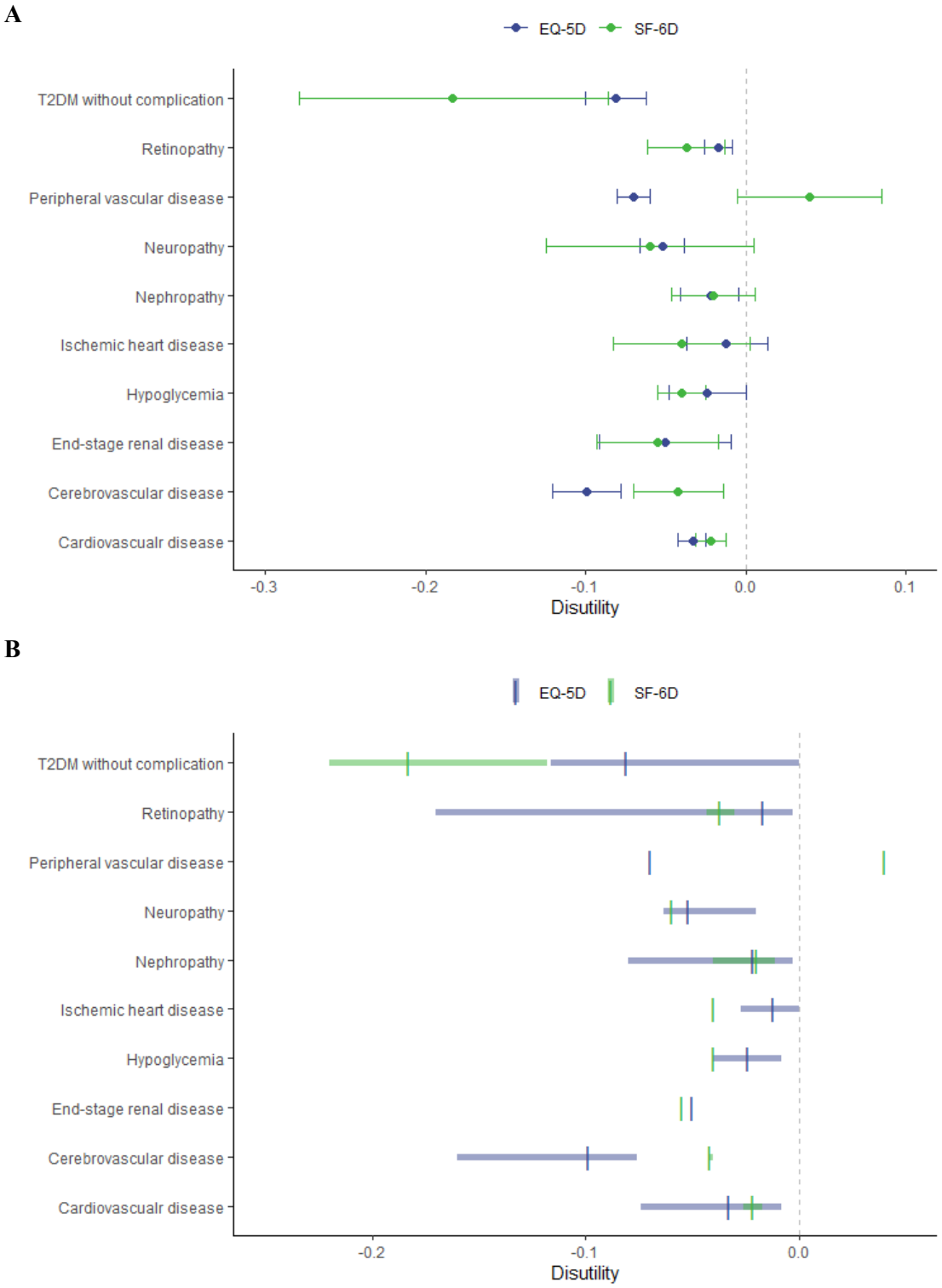
Table S5. Mean (dis)utility values by valuation instruments using pooled estimates from meta-analyses

Health outcome	EQ-5D		SF-6D	
	(Dis)utility estimates, mean (95% CI)	I^2 (%)	(Dis)utility estimates, mean (95% CI)	I^2 (%)
T2DM without complication	0.919 (0.900, 0.938)	90	0.817 (0.721, 0.914)	71
Myocardial infarction	-0.007 (-0.036, 0.022)*	-	-	-
Ischemic heart disease	-0.012 (-0.037, 0.014)	77	-0.040 (-0.083, 0.003)	-
Heart failure	-0.05 (-0.081, -0.020)*	-	-	-
Cardiovascular disease	-0.033 (-0.042, -0.025)	30	-0.022 (-0.031, -0.012)	0
Cerebrovascular disease	-0.099 (-0.121, -0.078)	57	-0.042 (-0.070, -0.014)	0
Peripheral vascular disease	-0.07 (-0.080, -0.060)	-	0.040 (-0.005, 0.085)	-
Nephropathy	-0.022 (-0.041, -0.004)	89	-0.020 (-0.046, 0.006)	43
End-stage renal disease	-0.05 (-0.091, -0.009)	-	-0.055 (-0.093, -0.017)	-
Retinopathy	-0.017 (-0.026, -0.008)	24	-0.037 (-0.061, -0.013)	0
Cataract	-0.016 (-0.031, -0.001)*	-	-	-
Blindness	-0.095 (-0.146, -0.044)	-	-	-
Neuropathy	-0.052 (-0.066, -0.038)	45	-0.060 (-0.125, 0.005)	-
Dermatopathy	-0.036 (-0.070, -0.002)*	-	-	-
Amputation	-0.177 (-0.291, -0.063)*	-	-	-
Diabetic foot	-0.094 (-0.133, -0.055)	85	-	-
Hypoglycemia	-0.024 (-0.048, 0.000)	92	-0.040 (-0.055, -0.025)	-
Excess BMI	-0.006 (-0.028, 0.017)	80	-	-

* Single study.

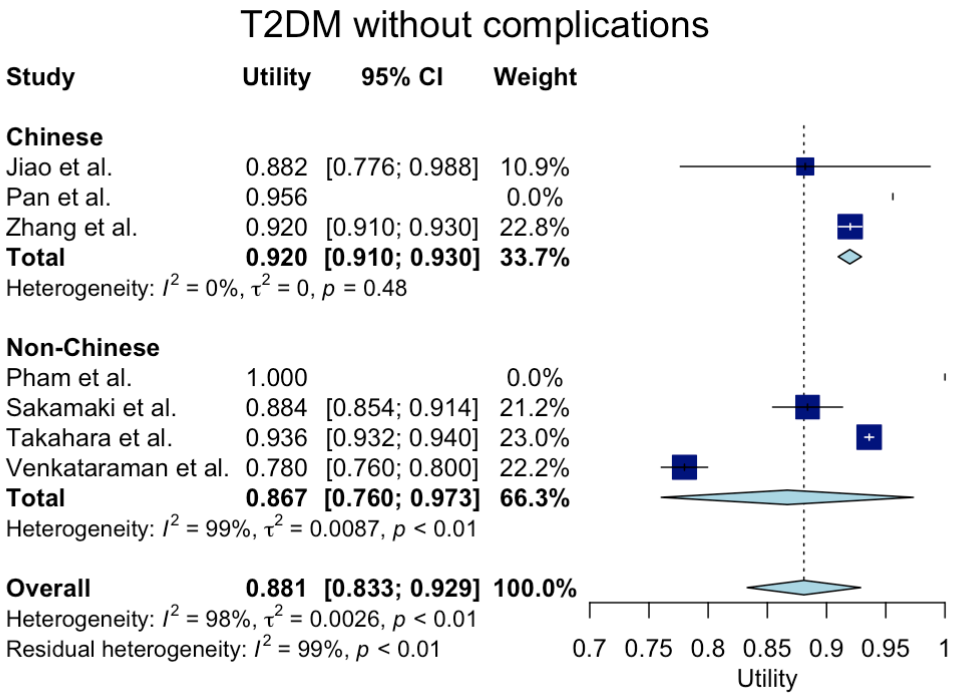
T2DM, type 2 diabetes; CI, confidence interval; I^2, Heterogeneity statistic.

Figure S3. Disutility values by valuation instrument



(A) 95% confidence intervals of pooled values, and (B) ranges of candidate values by valuation instrument.

Figure S4. Forest plots of baseline utility value for diabetes without complication by nationality and by instrument.



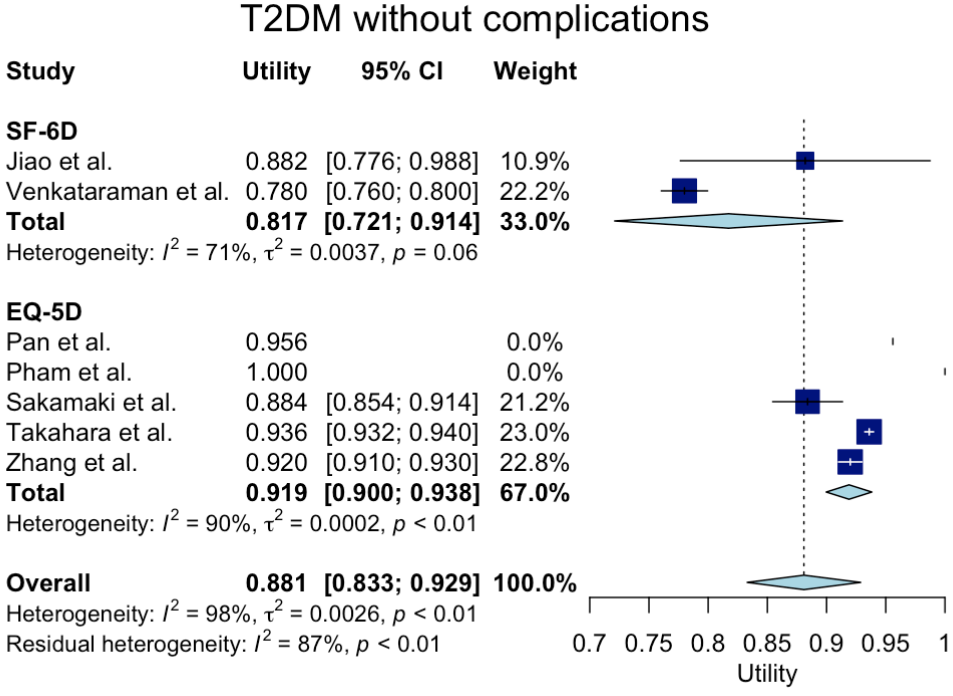
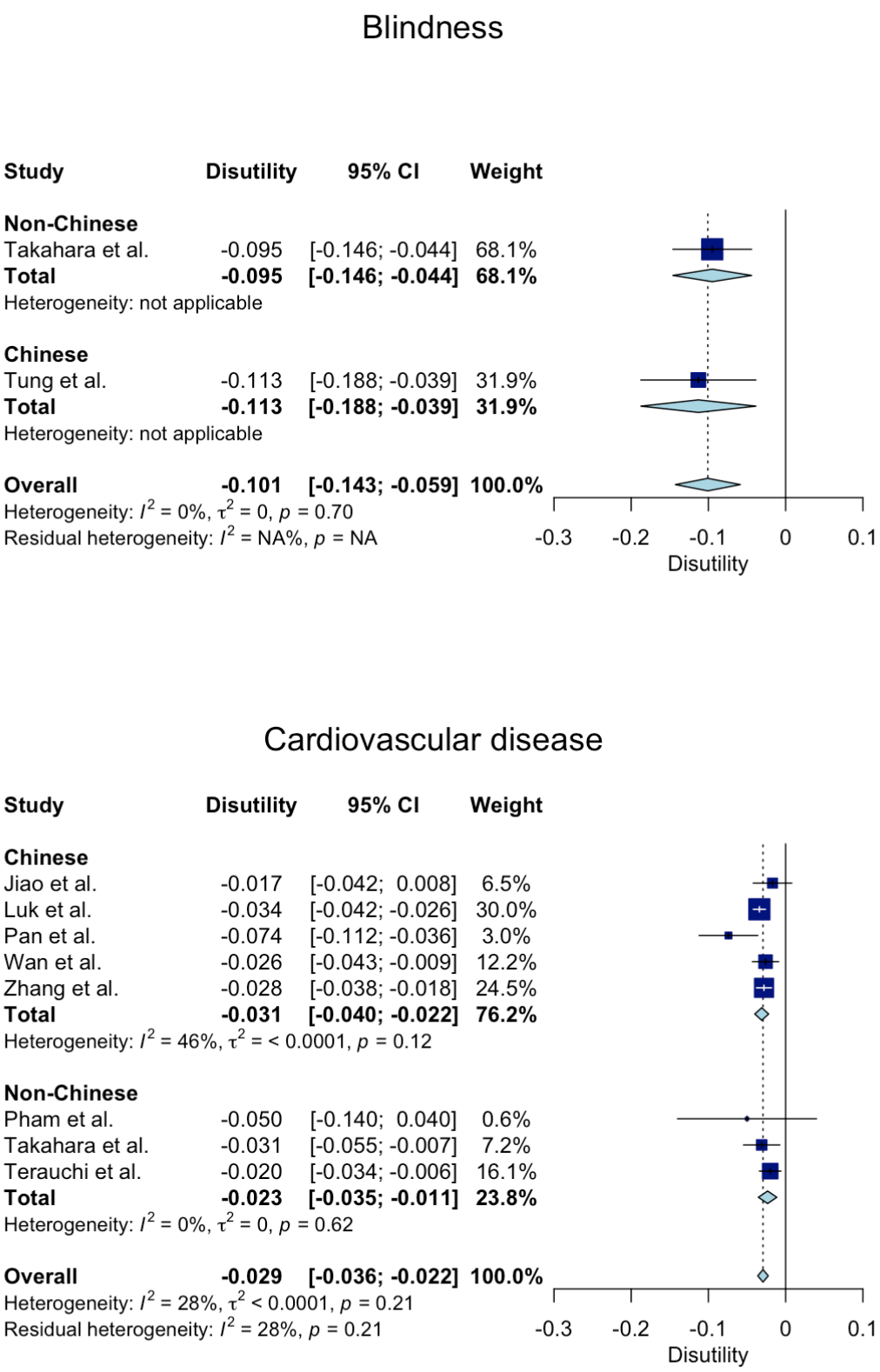
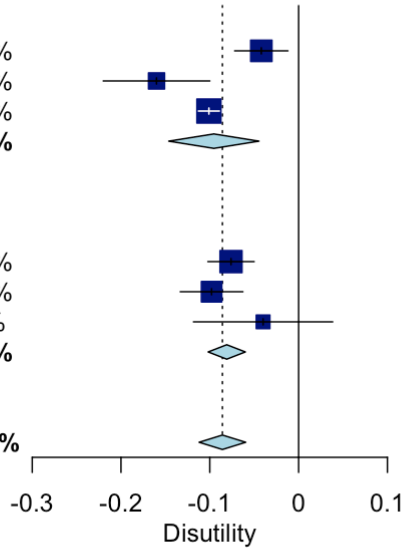


Figure S5. Forest plots of disutility values by nationality of participants



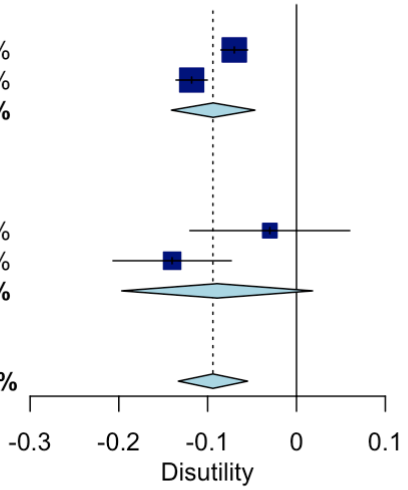
Cerebrovascular disease

Study	Disutility	95% CI	Weight
Chinese			
Jiao et al.	-0.042	[-0.072; -0.012]	19.1%
Pan et al.	-0.160	[-0.220; -0.100]	10.9%
Zhang et al.	-0.101	[-0.113; -0.089]	24.3%
Total	**-0.095**	**[-0.146; -0.045]**	**54.4%**
Heterogeneity: I^2 = 89%, τ^2 = 0.0017, p < 0.01			
Non-Chinese			
Lee et al.	-0.076	[-0.102; -0.050]	20.4%
Takahara et al.	-0.098	[-0.133; -0.063]	17.5%
Venkataraman et al.	-0.040	[-0.118; 0.038]	7.8%
Total	**-0.081**	**[-0.102; -0.060]**	**45.6%**
Heterogeneity: I^2 = 4%, τ^2 = < 0.0001, p = 0.35			
Overall	**-0.086**	**[-0.112; -0.060]**	**100.0%**
Heterogeneity: I^2 = 76%, τ^2 = 0.0007, p < 0.01			
Residual heterogeneity: I^2 = 80%, p < 0.01			



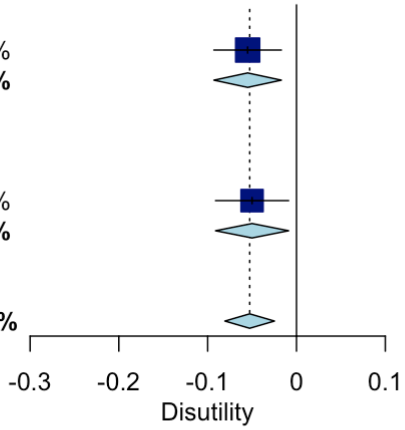
Diabetic foot

Study	Disutility	95% CI	Weight
Chinese			
Pan et al.	-0.070	[-0.085; -0.055]	35.2%
Zhang et al.	-0.118	[-0.136; -0.100]	34.5%
Total	**-0.094**	**[-0.141; -0.047]**	**69.7%**
Heterogeneity: I^2 = 94%, τ^2 = 0.0011, p < 0.01			
Non-Chinese			
Sakamaki et al.	-0.030	[-0.120; 0.060]	12.5%
Takahara et al.	-0.140	[-0.207; -0.073]	17.8%
Total	**-0.089**	**[-0.197; 0.018]**	**30.3%**
Heterogeneity: I^2 = 73%, τ^2 = 0.0044, p = 0.05			
Overall	**-0.094**	**[-0.133; -0.055]**	**100.0%**
Heterogeneity: I^2 = 85%, τ^2 = 0.0011, p < 0.01			
Residual heterogeneity: I^2 = 90%, p < 0.01			



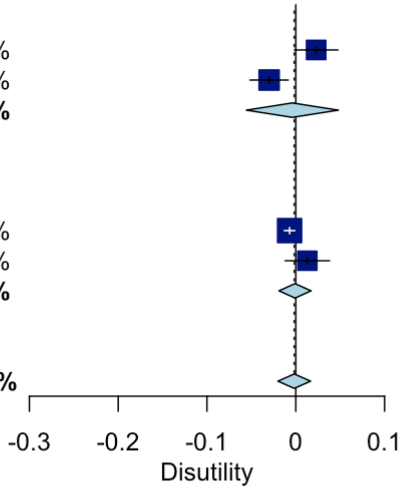
End-stage renal disease

Study	Disutility	95% CI	Weight
Chinese			
Jiao et al.	-0.055	[-0.093; -0.017]	54.0%
Total	**-0.055**	**[-0.093; -0.017]**	**54.0%**
Heterogeneity: not applicable			
Non-Chinese			
Takahara et al.	-0.050	[-0.091; -0.009]	46.0%
Total	**-0.050**	**[-0.091; -0.009]**	**46.0%**
Heterogeneity: not applicable			
Overall	**-0.053**	**[-0.081; -0.025]**	**100.0%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.86			
Residual heterogeneity: I^2 = NA%, p = NA			



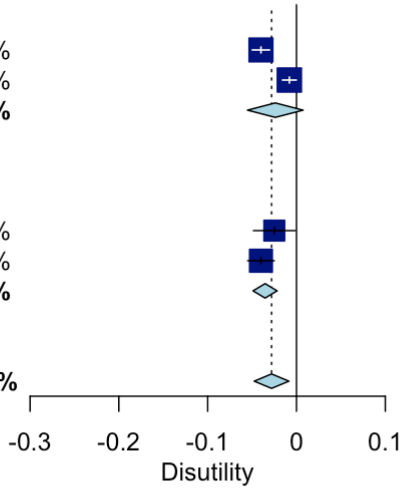
Excess BMI

Study	Disutility	95% CI	Weight
Non-Chinese			
Lee et al.	0.023	[-0.002; 0.047]	21.6%
Takahara et al.	-0.030	[-0.052; -0.008]	23.6%
Total	**-0.004**	**[-0.056; 0.048]**	**45.1%**
Heterogeneity: I^2 = 90%, τ^2 = 0.0013, p < 0.01			
Chinese			
Luk et al.	-0.007	[-0.013; -0.001]	33.6%
Tung et al.	0.013	[-0.012; 0.038]	21.2%
Total	**-0.001**	**[-0.019; 0.017]**	**54.9%**
Heterogeneity: I^2 = 57%, τ^2 = 0.0001, p = 0.13			
Overall	**-0.002**	**[-0.020; 0.017]**	**100.0%**
Heterogeneity: I^2 = 76%, τ^2 = 0.0003, p < 0.01			
Residual heterogeneity: I^2 = 84%, p < 0.01			



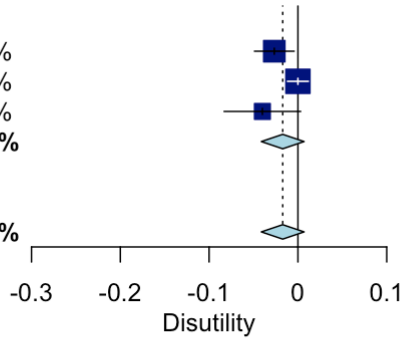
Hypoglycemia

Study	Disutility	95% CI	Weight
Chinese			
Luk et al.	-0.040	[-0.050; -0.030]	27.0%
Zhang et al.	-0.008	[-0.016; 0.000]	27.7%
Total	**-0.024**	**[-0.055; 0.007]**	**54.8%**
Heterogeneity: I^2 = 96%, τ^2 = 0.0005, p < 0.01			
Non-Chinese			
Takahara et al.	-0.025	[-0.049; -0.001]	20.4%
Terauchi et al.	-0.040	[-0.055; -0.025]	24.8%
Total	**-0.035**	**[-0.049; -0.022]**	**45.2%**
Heterogeneity: I^2 = 10%, τ^2 = < 0.0001, p = 0.29			
Overall	**-0.028**	**[-0.048; -0.009]**	**100.0%**
Heterogeneity: I^2 = 90%, τ^2 = 0.0003, p < 0.01			
Residual heterogeneity: I^2 = 92%, p < 0.01			



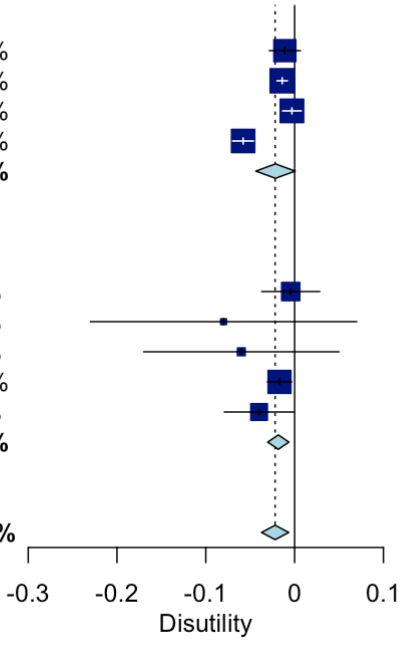
Ischemic heart disease

Study	Disutility	95% CI	Weight
Non-Chinese			
Lee et al.	-0.027	[-0.049; -0.004]	35.4%
Takahara et al.	0.000	[-0.012; 0.012]	45.3%
Venkataraman et al.	-0.040	[-0.083; 0.003]	19.3%
Total	**-0.017**	**[-0.041; 0.007]**	**100.0%**
Heterogeneity: I^2 = 69%, τ^2 = 0.0003, p = 0.04			
Overall	**-0.017**	**[-0.041; 0.007]**	**100.0%**
Heterogeneity: I^2 = 69%, τ^2 = 0.0003, p = 0.04			
Residual heterogeneity: I^2 = 69%, p = 0.04			



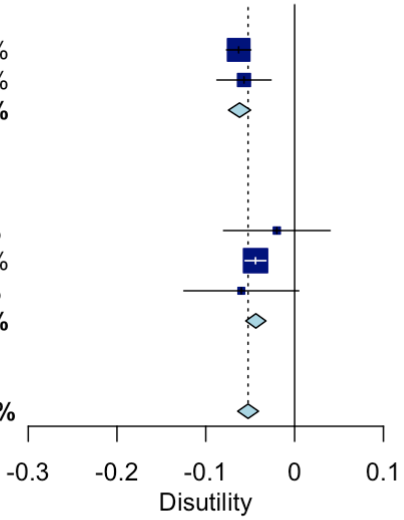
Nephropathy

Study	Disutility	95% CI	Weight
Chinese			
Jiao et al.	-0.011	[-0.028; 0.007]	14.3%
Luk et al.	-0.014	[-0.020; -0.008]	17.2%
Pan et al.	-0.003	[-0.013; 0.007]	16.3%
Zhang et al.	-0.058	[-0.070; -0.046]	16.0%
Total	**-0.022**	**[-0.044; 0.001]**	**63.8%**
Heterogeneity: I^2 = 95%, τ^2 = 0.0005, p < 0.01			
Non-Chinese			
Lee et al.	-0.004	[-0.037; 0.028]	9.8%
Pham et al.	-0.080	[-0.230; 0.070]	1.0%
Sakamaki et al.	-0.060	[-0.170; 0.050]	1.8%
Takahara et al.	-0.017	[-0.031; -0.003]	15.5%
Venkataraman et al.	-0.040	[-0.079; -0.001]	8.2%
Total	**-0.018**	**[-0.030; -0.006]**	**36.2%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.54			
Overall	**-0.022**	**[-0.037; -0.007]**	**100.0%**
Heterogeneity: I^2 = 86%, τ^2 = 0.0003, p < 0.01			
Residual heterogeneity: I^2 = 88%, p < 0.01			



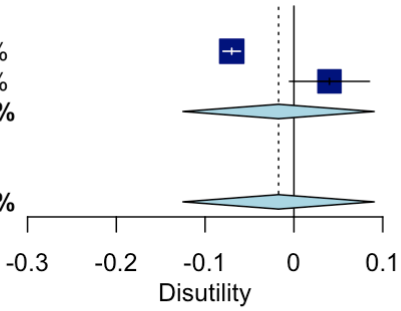
Neuropathy

Study	Disutility	95% CI	Weight
Chinese			
Luk et al.	-0.063	[-0.077; -0.049]	37.4%
Pan et al.	-0.057	[-0.088; -0.027]	12.4%
Total	**-0.062**	**[-0.075; -0.049]**	**49.9%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.73			
Non-Chinese			
Sakamaki et al.	-0.020	[-0.080; 0.040]	3.6%
Takahara et al.	-0.044	[-0.056; -0.032]	43.3%
Venkataraman et al.	-0.060	[-0.125; 0.005]	3.2%
Total	**-0.044**	**[-0.055; -0.032]**	**50.1%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.66			
Overall	**-0.052**	**[-0.064; -0.041]**	**100.0%**
Heterogeneity: I^2 = 27%, τ^2 < 0.0001, p = 0.24			
Residual heterogeneity: I^2 = 0%, p = 0.81			



Peripheral vascular disease

Study	Disutility	95% CI	Weight
Non-Chinese			
Takahara et al.	-0.070	[-0.080; -0.060]	52.1%
Venkataraman et al.	0.040	[-0.005; 0.085]	47.9%
Total	**-0.017**	**[-0.125; 0.090]**	**100.0%**
Heterogeneity: I^2 = 95%, τ^2 = 0.0058, p < 0.01			
Overall	**-0.017**	**[-0.125; 0.090]**	**100.0%**
Heterogeneity: I^2 = 95%, τ^2 = 0.0058, p < 0.01			
Residual heterogeneity: I^2 = 95%, p < 0.01			



Retinopathy

Study	Disutility	95% CI	Weight
Chinese			
Jiao et al.	-0.043	[-0.076; -0.010]	8.8%
Pan et al.	-0.019	[-0.036; -0.002]	17.5%
Tung et al.	-0.104	[-0.169; -0.038]	2.8%
Zhang et al.	-0.022	[-0.032; -0.012]	24.2%
Total	**-0.030**	**[-0.048; -0.012]**	**53.4%**
Heterogeneity: I^2 = 60%, τ^2 = 0.0002, p = 0.06			
Non-Chinese			
Lee et al.	-0.022	[-0.040; -0.003]	16.9%
Pham et al.	-0.170	[-0.370; 0.030]	0.3%
Sakamaki et al.	-0.010	[-0.080; 0.060]	2.5%
Takahara et al.	-0.003	[-0.019; 0.013]	19.0%
Venkataraman et al.	-0.030	[-0.065; 0.005]	7.8%
Total	**-0.015**	**[-0.031; 0.000]**	**46.6%**
Heterogeneity: I^2 = 30%, τ^2 = < 0.0001, p = 0.22			
Overall	**-0.023**	**[-0.034; -0.011]**	**100.0%**
Heterogeneity: I^2 = 48%, τ^2 = 0.0001, p = 0.05			
Residual heterogeneity: I^2 = 47%, p = 0.07			

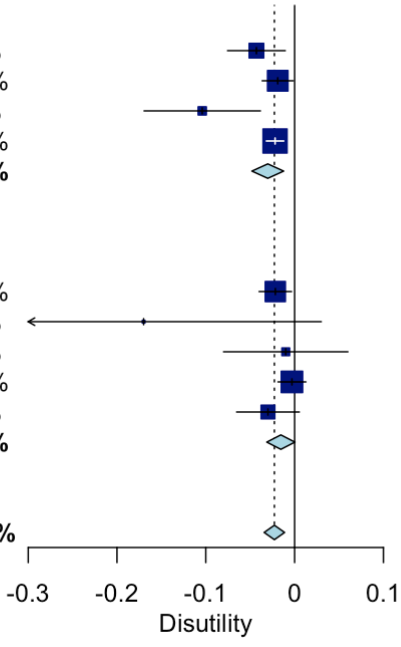
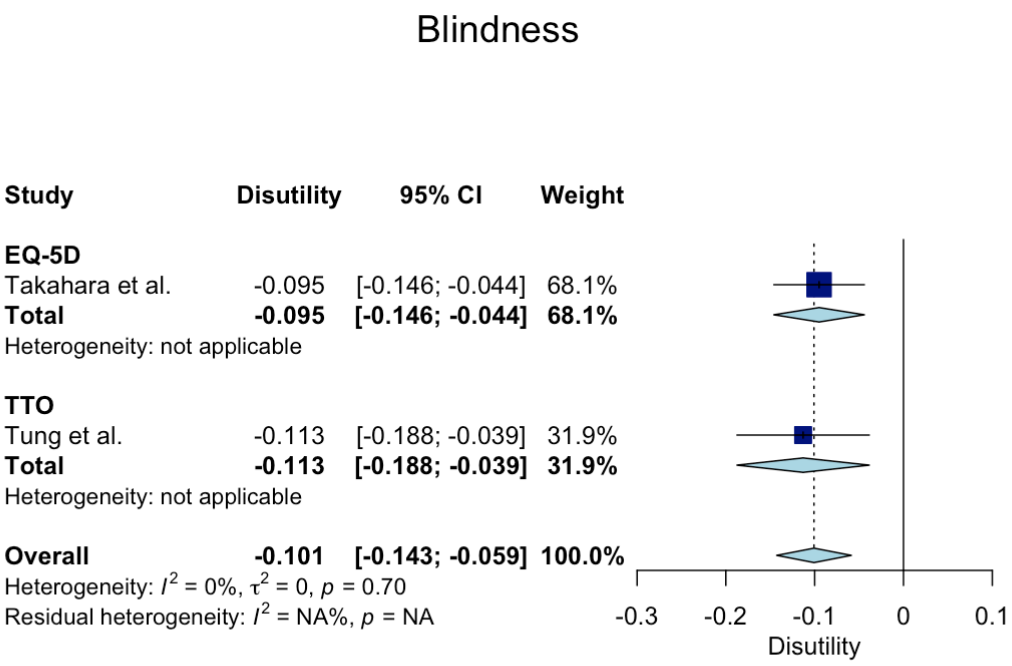
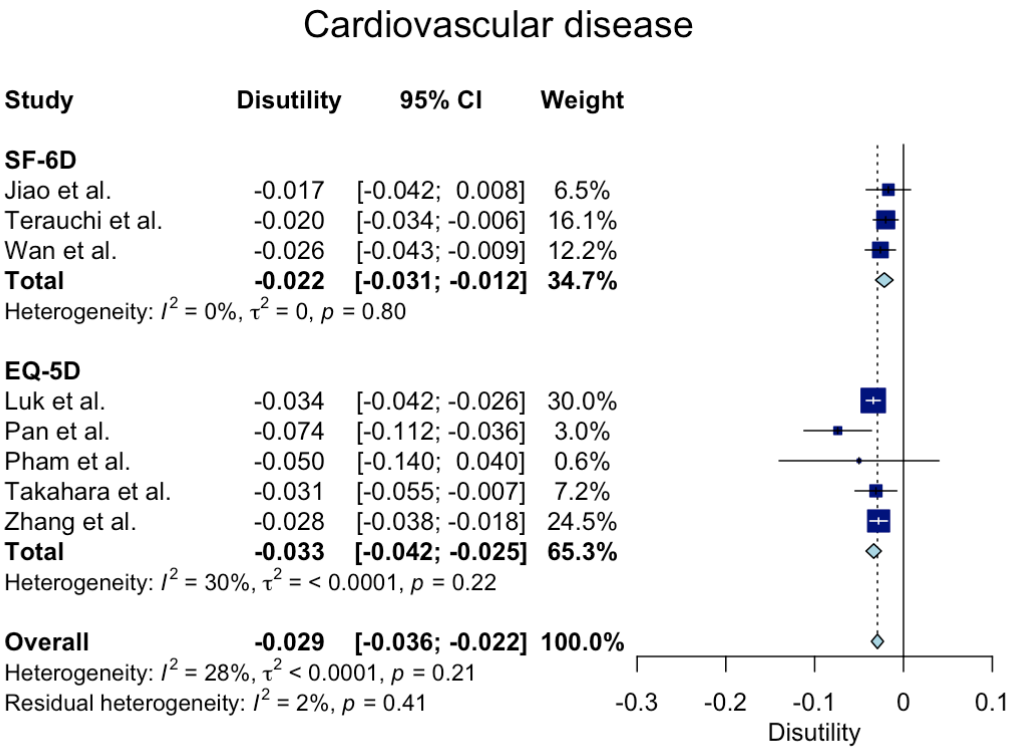
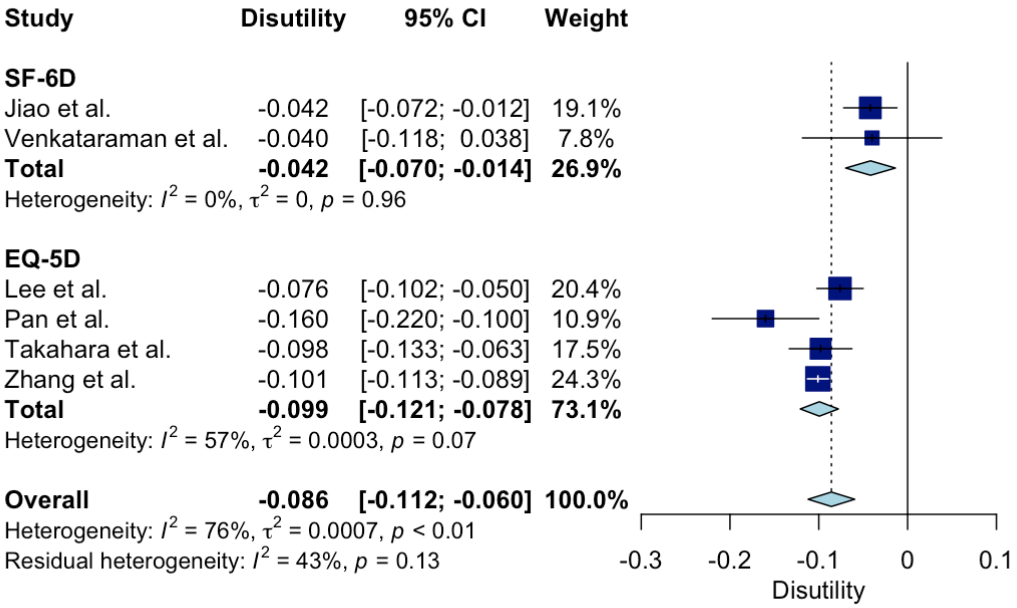


Figure S6. Forest plots of disutility values by valuation instrument.

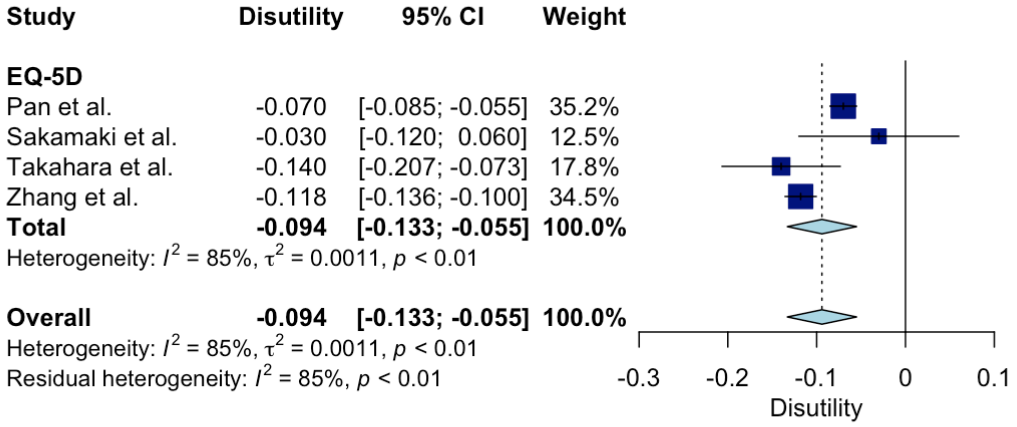




Cerebrovascular disease



Diabetic foot

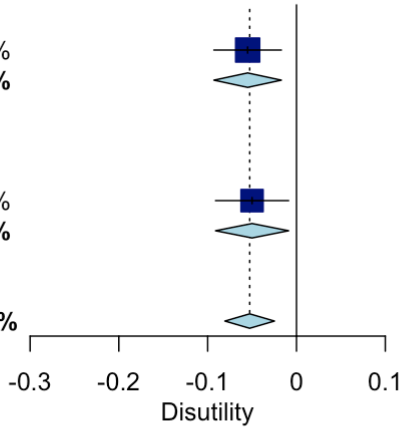


End-stage renal disease

Study	Disutility	95% CI	Weight
SF-6D			
Jiao et al.	-0.055	[-0.093; -0.017]	54.0%
Total	**-0.055**	**[-0.093; -0.017]**	**54.0%**
Heterogeneity: not applicable			
EQ-5D			
Takahara et al.	-0.050	[-0.091; -0.009]	46.0%
Total	**-0.050**	**[-0.091; -0.009]**	**46.0%**
Heterogeneity: not applicable			
Overall	**-0.053**	**[-0.081; -0.025]**	**100.0%**

Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.86

Residual heterogeneity: I^2 = NA%, p = NA

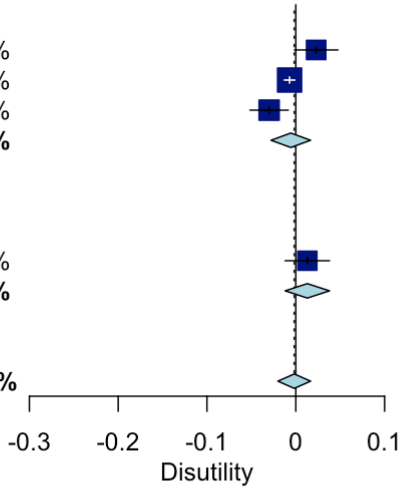


Excess BMI

Study	Disutility	95% CI	Weight
EQ-5D			
Lee et al.	0.023	[-0.002; 0.047]	21.6%
Luk et al.	-0.007	[-0.013; -0.001]	33.6%
Takahara et al.	-0.030	[-0.052; -0.008]	23.6%
Total	**-0.006**	**[-0.028; 0.017]**	**78.8%**
TTO			
Tung et al.	0.013	[-0.012; 0.038]	21.2%
Total	**0.013**	**[-0.012; 0.038]**	**21.2%**
Heterogeneity: not applicable			
Overall	**-0.002**	**[-0.020; 0.017]**	**100.0%**

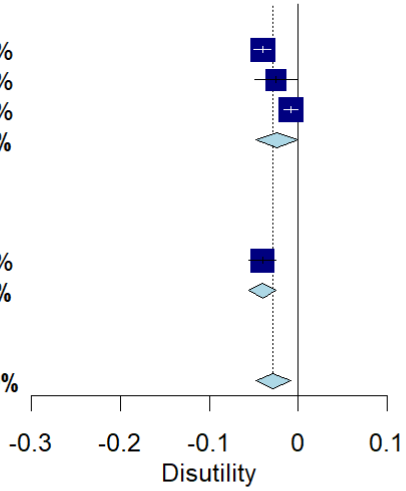
Heterogeneity: I^2 = 76%, τ^2 = 0.0003, p < 0.01

Residual heterogeneity: I^2 = 80%, p < 0.01



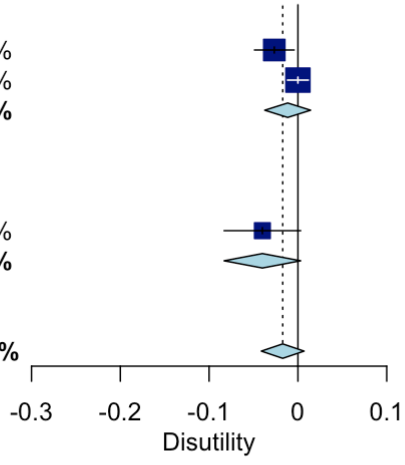
Hypoglycemia

Study	Disutility	95% CI	Weight
EQ-5D			
Luk et al.	-0.040	[-0.050; -0.030]	27.0%
Takahara et al.	-0.025	[-0.049; -0.001]	20.4%
Zhang et al.	-0.008	[-0.016; 0.000]	27.7%
Total	**-0.024**	**[-0.048; 0.000]**	**75.2%**
Heterogeneity: I^2 = 92%, τ^2 = 0.0004, p < 0.01			
SF-6D			
Terauchi et al.	-0.040	[-0.055; -0.025]	24.8%
Total	**-0.040**	**[-0.055; -0.025]**	**24.8%**
Heterogeneity: not applicable			
Overall	**-0.028**	**[-0.048; -0.009]**	**100.0%**
Heterogeneity: I^2 = 90%, τ^2 = 0.0003, p < 0.01			
Residual heterogeneity: I^2 = 92%, p < 0.01			



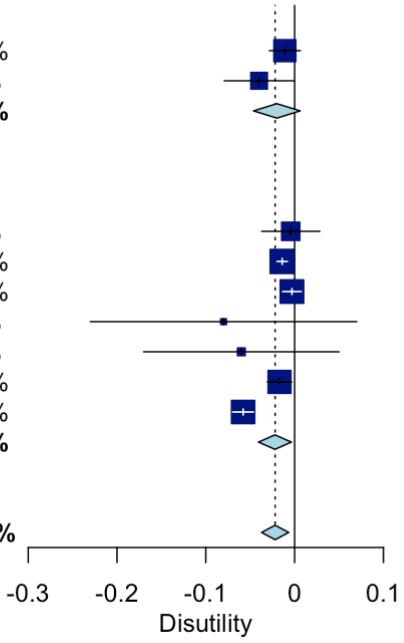
Ischemic heart disease

Study	Disutility	95% CI	Weight
EQ-5D			
Lee et al.	-0.027	[-0.049; -0.004]	35.4%
Takahara et al.	0.000	[-0.012; 0.012]	45.3%
Total	**-0.012**	**[-0.037; 0.014]**	**80.7%**
Heterogeneity: I^2 = 77%, τ^2 = 0.0003, p = 0.04			
SF-6D			
Venkataraman et al.	-0.040	[-0.083; 0.003]	19.3%
Total	**-0.040**	**[-0.083; 0.003]**	**19.3%**
Heterogeneity: not applicable			
Overall	**-0.017**	**[-0.041; 0.007]**	**100.0%**
Heterogeneity: I^2 = 69%, τ^2 = 0.0003, p = 0.04			
Residual heterogeneity: I^2 = 77%, p = 0.04			



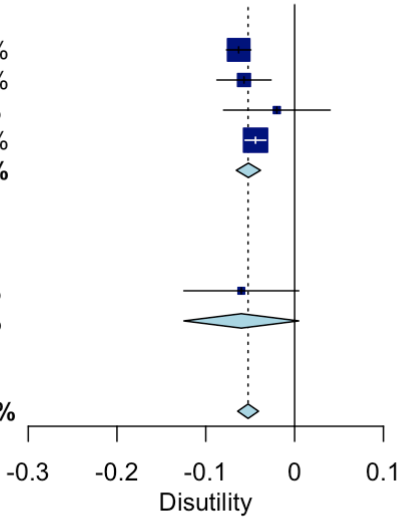
Nephropathy

Study	Disutility	95% CI	Weight
SF-6D			
Jiao et al.	-0.011	[-0.028; 0.007]	14.3%
Venkataraman et al.	-0.040	[-0.079; -0.001]	8.2%
Total	**-0.020**	**[-0.046; 0.006]**	**22.5%**
Heterogeneity: I^2 = 43%, τ^2 = 0.0002, p = 0.19			
EQ-5D			
Lee et al.	-0.004	[-0.037; 0.028]	9.8%
Luk et al.	-0.014	[-0.020; -0.008]	17.2%
Pan et al.	-0.003	[-0.013; 0.007]	16.3%
Pham et al.	-0.080	[-0.230; 0.070]	1.0%
Sakamaki et al.	-0.060	[-0.170; 0.050]	1.8%
Takahara et al.	-0.017	[-0.031; -0.003]	15.5%
Zhang et al.	-0.058	[-0.070; -0.046]	16.0%
Total	**-0.022**	**[-0.041; -0.004]**	**77.5%**
Heterogeneity: I^2 = 89%, τ^2 = 0.0004, p < 0.01			
Overall	**-0.022**	**[-0.037; -0.007]**	**100.0%**
Heterogeneity: I^2 = 86%, τ^2 = 0.0003, p < 0.01			
Residual heterogeneity: I^2 = 88%, p < 0.01			



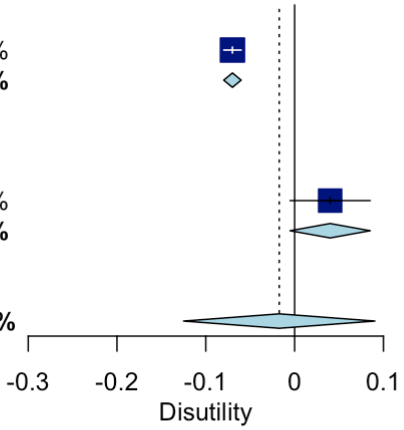
Neuropathy

Study	Disutility	95% CI	Weight
EQ-5D			
Luk et al.	-0.063	[-0.077; -0.049]	37.4%
Pan et al.	-0.057	[-0.088; -0.027]	12.4%
Sakamaki et al.	-0.020	[-0.080; 0.040]	3.6%
Takahara et al.	-0.044	[-0.056; -0.032]	43.3%
Total	**-0.052**	**[-0.066; -0.038]**	**96.8%**
Heterogeneity: I^2 = 45%, τ^2 = < 0.0001, p = 0.14			
SF-6D			
Venkataraman et al.	-0.060	[-0.125; 0.005]	3.2%
Total	**-0.060**	**[-0.125; 0.005]**	**3.2%**
Heterogeneity: not applicable			
Overall	**-0.052**	**[-0.064; -0.041]**	**100.0%**
Heterogeneity: I^2 = 27%, τ^2 < 0.0001, p = 0.24			
Residual heterogeneity: I^2 = 45%, p = 0.14			



Peripheral vascular disease

Study	Disutility	95% CI	Weight
EQ-5D			
Takahara et al.	-0.070	[-0.080; -0.060]	52.1%
Total	**-0.070**	**[-0.080; -0.060]**	**52.1%**
Heterogeneity: not applicable			
SF-6D			
Venkataraman et al.	0.040	[-0.005; 0.085]	47.9%
Total	**0.040**	**[-0.005; 0.085]**	**47.9%**
Heterogeneity: not applicable			
Overall	**-0.017**	**[-0.125; 0.090]**	**100.0%**
Heterogeneity: I^2 = 95%, τ^2 = 0.0058, p < 0.01			
Residual heterogeneity: I^2 = NA%, p = NA			



Retinopathy

Study	Disutility	95% CI	Weight
SF-6D			
Jiao et al.	-0.043	[-0.076; -0.010]	8.8%
Venkataraman et al.	-0.030	[-0.065; 0.005]	7.8%
Total	**-0.037**	**[-0.061; -0.013]**	**16.6%**
Heterogeneity: I^2 = 0%, τ^2 = 0, p = 0.60			
EQ-5D			
Lee et al.	-0.022	[-0.040; -0.003]	16.9%
Pan et al.	-0.019	[-0.036; -0.002]	17.5%
Pham et al.	-0.170	[-0.370; 0.030]	0.3%
Sakamaki et al.	-0.010	[-0.080; 0.060]	2.5%
Takahara et al.	-0.003	[-0.019; 0.013]	19.0%
Zhang et al.	-0.022	[-0.032; -0.012]	24.2%
Total	**-0.017**	**[-0.026; -0.008]**	**80.6%**
Heterogeneity: I^2 = 24%, τ^2 = < 0.0001, p = 0.25			
TTO			
Tung et al.	-0.104	[-0.169; -0.038]	2.8%
Total	**-0.104**	**[-0.169; -0.038]**	**2.8%**
Heterogeneity: not applicable			
Overall	**-0.023**	**[-0.034; -0.011]**	**100.0%**
Heterogeneity: I^2 = 48%, τ^2 = 0.0001, p = 0.05			
Residual heterogeneity: I^2 = 13%, p = 0.33			

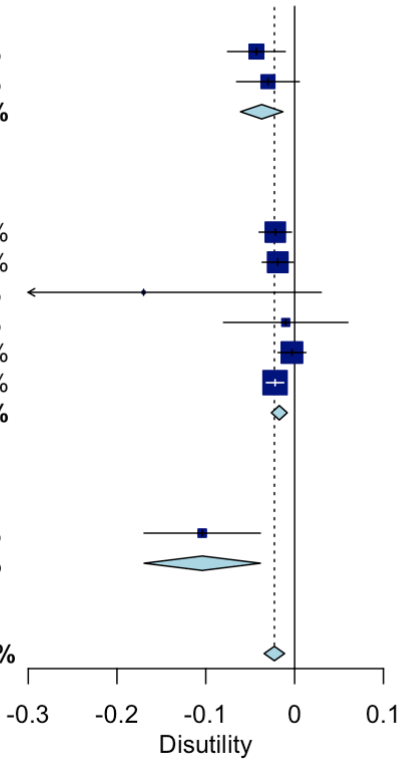
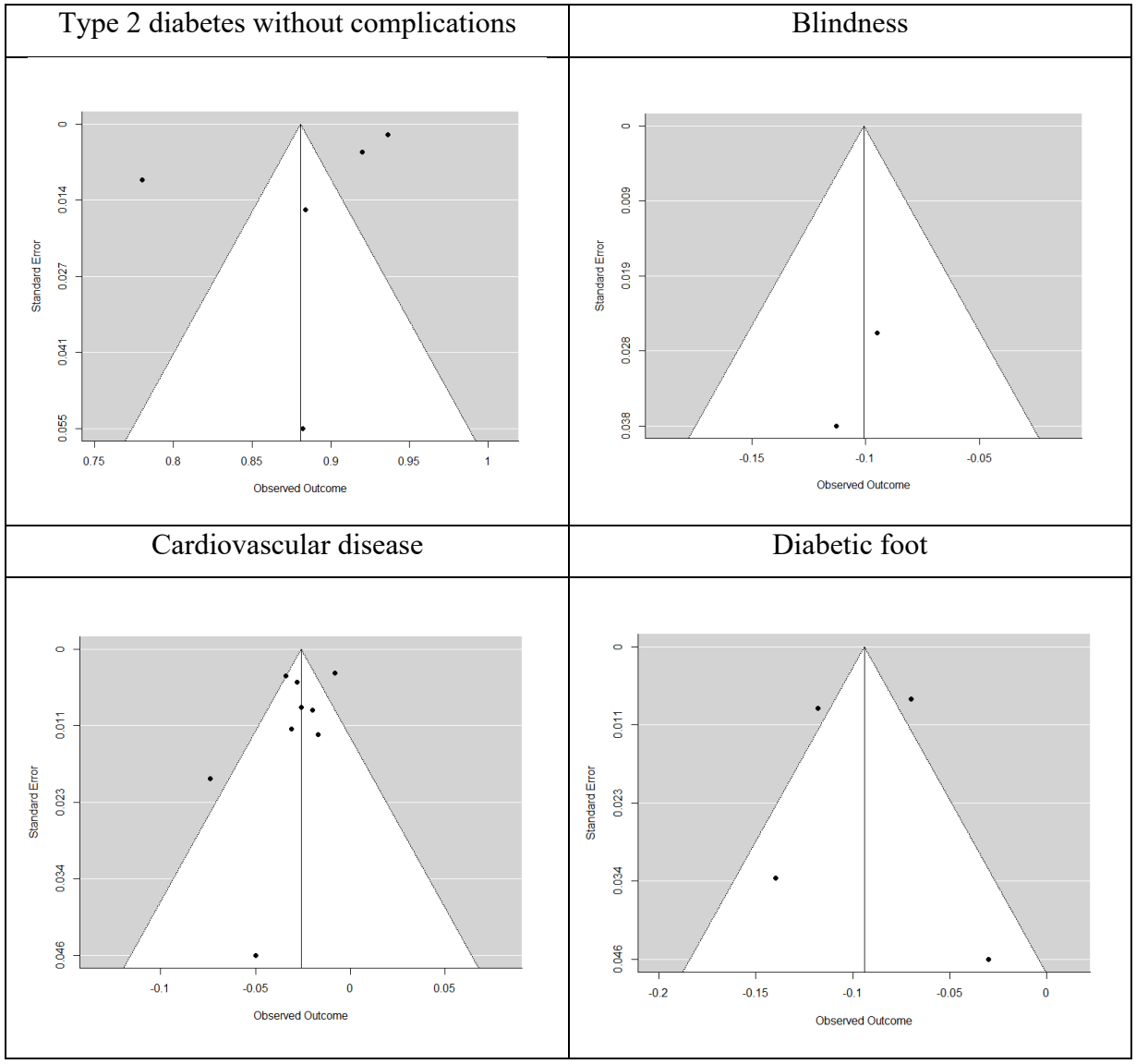
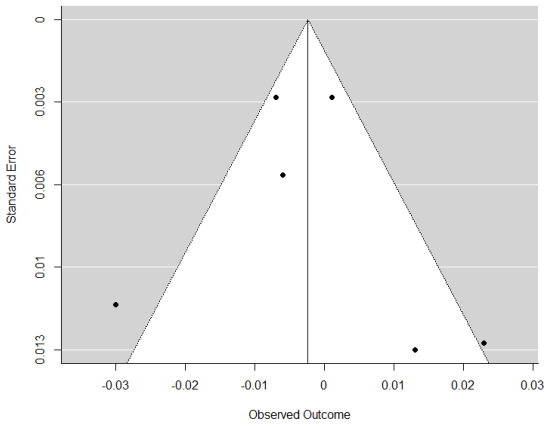
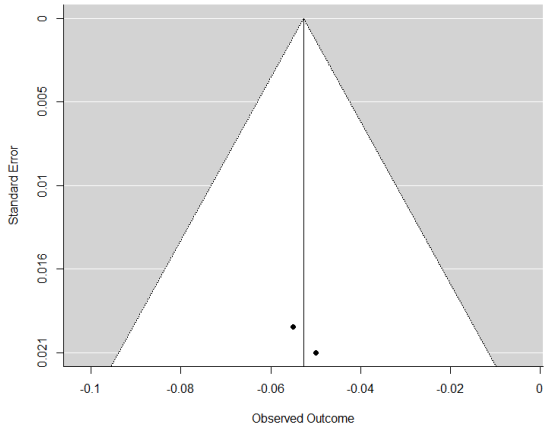
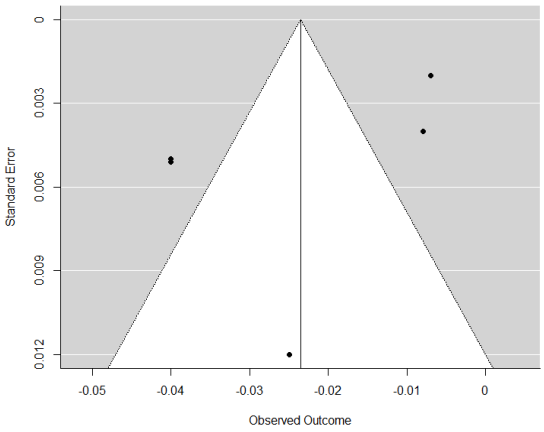
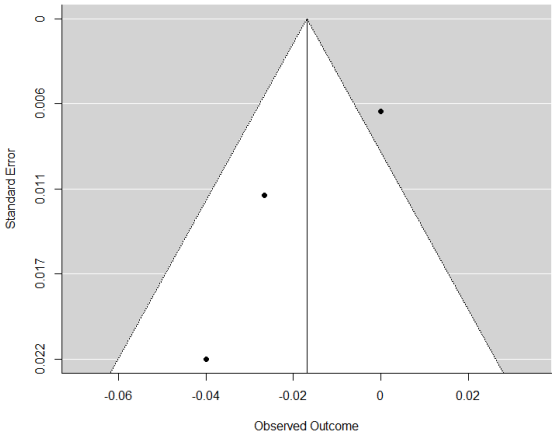
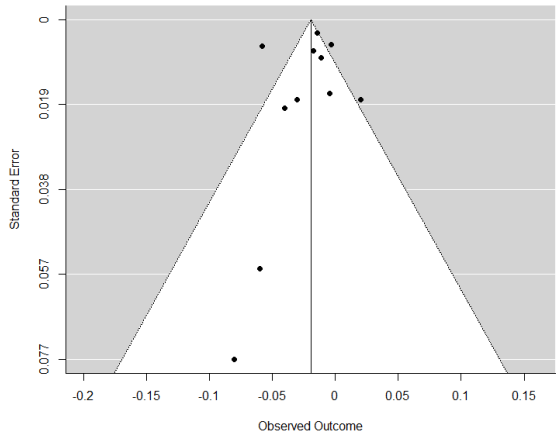
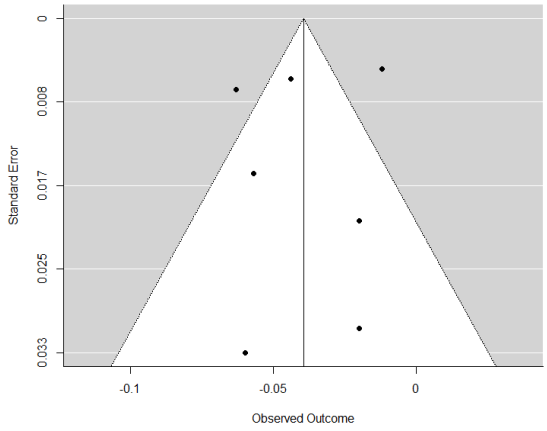
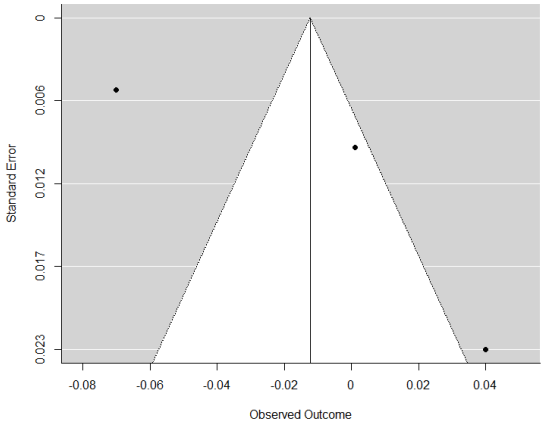
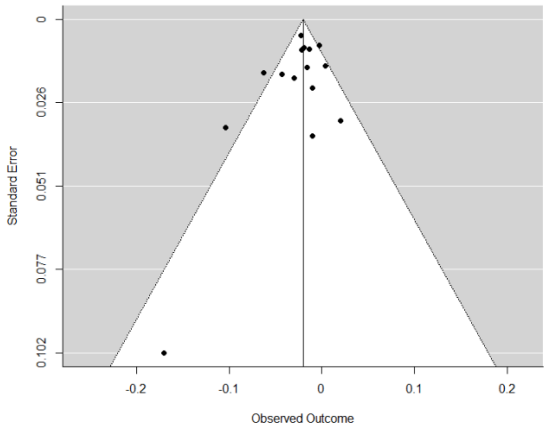


Figure S7. Funnel plots of disutility values by complication



Excess BMI	End-stage renal disease
	
Hypoglycemia	**Ischemic heart disease**
	

Nephropathy	Neuropathy
	
Peripheral vascular disease	**Retinopathy**
	

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