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Economic Evaluation

Postpartum Screening for Type 2 Diabetes in Women With a History of Gestational Diabetes Mellitus: A Cost-Effectiveness Analysis in Singapore

Andrea Cremaschi, PhD, Willem van den Boom, PhD, Nicholas Beng Hui Ng, MMed, Beatrice Franzolini, PhD, Kelvin B. Tan, PhD, Jerry Kok Yen Chan, PhD, Kok Hian Tan, MMed, Yap-Seng Chong, MD, Johan G. Eriksson, DMSc, Maria De Iorio, PhD

ABSTRACT

Objectives: In Singapore, diabetes imposes a huge population health and economic burden. Despite that, there is paucity of evidence on the health economics of screening programs for type 2 diabetes, especially in the context of screening after gestational diabetes (GDM). The objective of this study is to assess cost-effectiveness of universal lifelong screening for type 2 diabetes after GDM, which is supported by current guidelines, compared with elective screening where 54% of mothers with GDM undertake one-off screening. Despite the recommendation for universal lifelong screening, only 54% comply with this in the first postpartum year.

Methods: We perform a cost-effectiveness analysis comparing 5 screening strategies, accounting for lifetime costs to the healthcare system and quality of life for Singapore women diagnosed with GDM. In particular, a hybrid decision model, based on a decision tree and Markov models, is implemented to estimate cost and quality-adjusted life-years (QALY). Probabilities, costs, and utilities are obtained from existing literature, governmental databases, the Growing Up in Singapore Towards Healthy Outcomes birth cohort study, and the National University Hospital.

Results: Compared with elective screening, universal annual screening reduces cost by SG$19.4 million while adding 3.8 thousand QALYs by each annual cohort of pregnant women. Furthermore, annual screening is cost-effective (lower cost and higher QALY) compared with triennial screening. Sensitivity analysis shows that the findings are robust to parameter specifications.

Conclusions: Universal annual screening of women with a history of GDM is cost-effective for reducing diabetes complications compared with strategies with less frequent screening in Singapore.

Keywords: Growing Up in Singapore Towards Healthy Outcomes (GUSTO) birth cohort study, hybrid decision model, lifelong annual screening, Markov model, quality-adjusted life-years.

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Introduction

Type 2 diabetes (T2D) is an increasingly prevalent health problem that afflicts more than half a billion adults worldwide.[1] The International Diabetes Federation predicts that this global prevalence will escalate to 783 million adults by the year 2045.[1] In addition, T2D carries a non-negligible financial burden, costing governments US$1.3 trillion in 2015, which is projected to increase to US$2.3 trillion by 2030.[2] Some of the established risk factors for the development of T2D include age, obesity, hypertension, family history of diabetes, and ethnicity.[3,4] Notably, Asians have a markedly increased predisposition for T2D compared with their Western counterparts, owing to a complex interplay among factors such as genetics, environment, lifestyle, and diet.[5] In turn, diabetes is a major risk factor for cardiovascular and metabolic diseases, which are associated with premature mortality.[3] Early identification of people at risk of development of T2D is a key aspect of prevention given that this may allow earlier implementation of lifestyle interventions.

T2D may remain asymptomatic for a long period of time while its associated complications progress undetected: a window of 4 to 7 years between onset of T2D and clinical diagnosis has been reported.[6,7] For instance, an estimated two-thirds of T2D cases are reportedly asymptomatic at time of diagnosis in England[8] and Denmark.[9] Furthermore, approximately 1 in 2 T2D cases worldwide remains currently undiagnosed.[1,8,10] Therefore, there is an urgent need to implement appropriate screening strategies that may detect glycemic abnormalities at early stages, thus allowing timely and cost-effective interventions for diabetes-related complications, to reduce further morbidity and mortality. However, there are no clear recommendations in relation to lifelong screening for T2D. Several policies suggest screening based on certain risk factors,[3,4] including obesity,[11] age, family history, hypertension, or a sedentary lifestyle. Health economic evaluations

of T2D screening have produced mixed results[12] with universal lifelong screening deemed to be cost-effective in some contexts[13-17] but not in others.[18,19] In contrast, screening based on risk factors for T2D has been found to be cost-effective.[12,20,21]

In Singapore, the prevalence of diabetes is significantly elevated compared with other Southeast Asian countries, standing at 14.9% versus a regional prevalence of 8.7%.[1] Individuals aged 40 years and older are advised to undergo screening for T2D once every 3 years through the subsidized Screen for Life program offered by the Health Promotion Board.[22] In addition, younger adults identified as high-risk individuals are also urged to participate in screenings under the same program. If diagnosed, treatment guidelines in Singapore[23,24] involve firstly lifestyle modification, ie, diet and physical activity. These include optimization of food choices to meet the recommendations suggested by a dietitian specialized in diabetes care, as well as increased physical activity (at least 150 minutes/week of moderate to vigorous aerobic exercise) and gradual weight loss (eg, 5%-10% for obese patients). If lifestyle modification alone is unable to control blood sugar levels, then antidiabetic drugs are administered. If both these treatment options fail, insulin injections may be needed.

This work focuses on gestational diabetes mellitus (GDM) within the Singaporean context given that it is a major risk factor of T2D,[25-27] affecting 15% to 20% of all pregnancies.[28] Nonetheless, health economic analyses of T2D screening for women previously diagnosed with GDM are lacking.[29] GDM arises due to elevated concentrations of placental hormones, which lead to higher insulin resistance and increased glucose concentrations. This is associated with higher rates of complications for both mother and child.[30,31] Importantly, GDM increases the maternal risk of developing T2D.[25-27] Therefore, guidelines, both in Singapore[23,24,32] and elsewhere,[29,33,34] suggest diabetes screening for mothers diagnosed with GDM. The Singapore Ministry of Health (MOH) recommends that a 75-gram 2-hour oral glucose tolerance test (OGTT) should be performed 6 to 12 weeks postpartum, followed by lifelong screening for the development of prediabetes or diabetes at least once every 3 years. Despite that, only 54% of women belonging to this risk group attend the first postpartum diabetes screening in Singapore,[35] with the proportion screened rapidly declining after the first year postpartum.[36] This means that a considerable proportion of the population affected by T2D may go undiagnosed. A similar lack of screening uptake has been reported in other countries.[36-39] As a consequence, women are at risk of delayed diagnosis and delayed interventions, which in turn would lead to increased risk of diabetes-related complications. Therefore, there is an opportunity to improve the uptake of screening for all women previously diagnosed with GDM, at 6 to 12 weeks after delivery and subsequently every 1 to 3 years. For instance, screening uptake can be increased by further shifting screening costs from personal expenses to subsidies from the government. In addition, the number of women going for screening after GDM can be increased through campaigns promoting healthy lifestyles or diabetes awareness.

In this work, we investigated different interventions to reduce the economic and societal burden due to delayed diagnosis with T2D. We explored the cost-effectiveness of a universal and prolonged monitoring strategy for T2D in Singaporean women previously diagnosed of GDM. The existing gap in health economic evaluations in this area,[29] the present context of Singapore waging war against diabetes, and the current economic landscape make this study timely and relevant. We considered various universal screening strategies and evaluated them against a strategy resembling current practice in terms of cost-effectiveness, comparing direct medical costs, average lifetime, and quality-adjusted life-years (QALYs).

Methods

Screening Strategies

Our reference population comprises women who were previously diagnosed with GDM (GDM is defined according to 1999 World Health Organization diagnostic criteria.[40] The same definition was used in the GUSTO cohort study). We considered a variety of screening strategies and their cost-effectiveness. The first strategy was based on current practice where 54% of women with a history of GDM go for screening[35] with that proportion dropping rapidly in subsequent years.[36] In this case, we assumed that 54% of mothers with GDM go for screening in the first year postpartum and do not attend further screening. We refer to this scenario as elective screening. Three other strategies involve universal screening of all mothers with GDM (1) in the first year postpartum, (2) triennially, and (3) every year. For completeness, we also included the strategy with no screening. For all strategies, we used an OGTT as the screening tool of choice for T2D.

Model

We used a hybrid decision model that included (1) an overall decision tree structure for the screening strategies and (2) Markov models for onset of T2D and the evolution of several T2D complications over time. In particular, each intervention corresponded to a branch of the tree, with different rates of diagnosis of T2D and associated treatment. The tree is presented in Figure 1. Broadly speaking, each screening strategy had a different probability of delayed treatment and T2D treatment reduced the probabilities of development of complications. At the leaves of the tree, we report average cost and QALY obtained through Monte Carlo simulations.

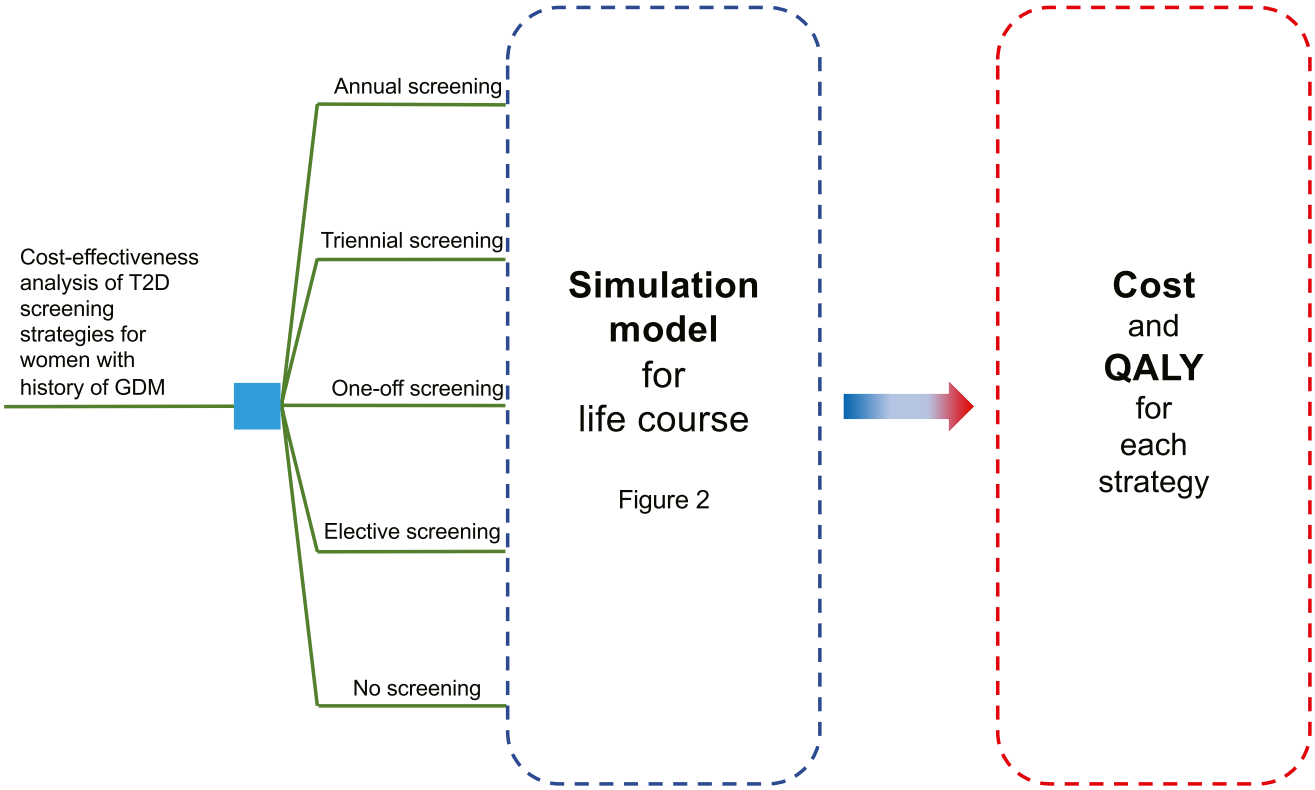
The incidence and progression of each complication was modeled using complication-specific Markov models. In such a model, a set of nodes describes the different possible states of the corresponding complication, whereas the subjects can move through these states according to specific transition probabilities. The set of complications, their disease states, and the possible transitions between them were derived from a recent cost-effectiveness analysis of diabetes screening,[19] which based these Markov models on published literature.[41-44] In particular, we considered the following complications related to the development of T2D and associated states:

- retinopathy: nonproliferative diabetic retinopathy, proliferative diabetic retinopathy, macular edema, blindness
- stroke: stroke, survived stroke, death
- nephropathy: microalbuminuria, macroalbuminuria, end-stage renal disease with medical management, hemodialysis, renal transplant, death
- coronary heart disease: myocardial infarction, post–myocardial infarction, heart failure, death
- foot ulcer: simple ulcer, infected ulcer, minor amputation, major amputation

These complications are common in individuals with T2D and place a major economic burden on the healthcare system. For instance, Singapore has one of the highest diabetes-related lower-extremity amputation rates among all Organization for Economic Cooperation and Development countries.[45]

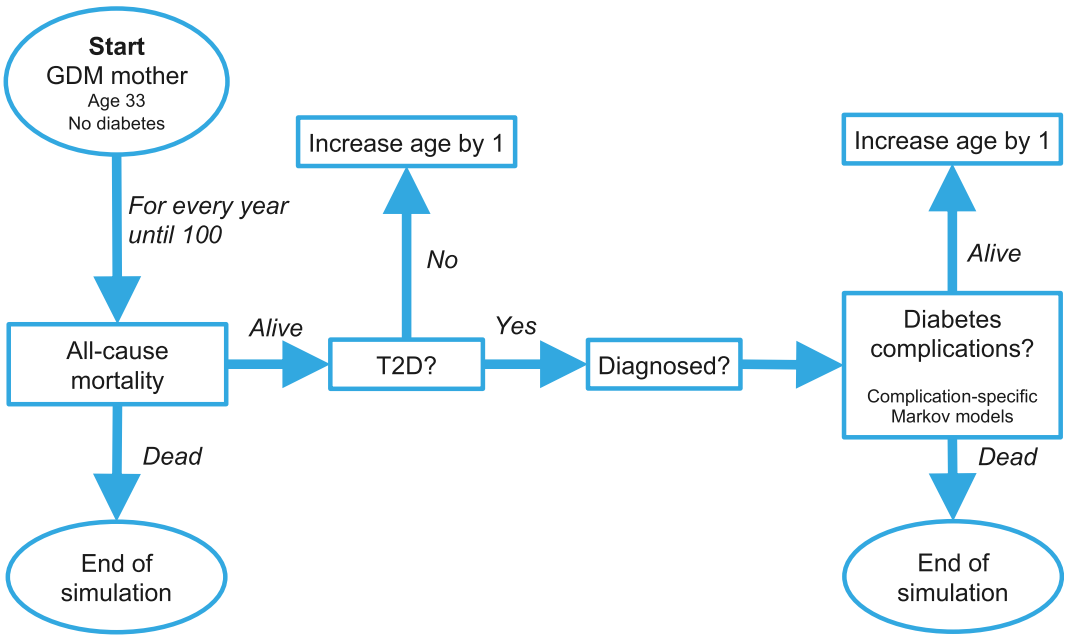
A graphical representation of the possible transitions in the Markov models is presented in Appendix 1 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101048. Each model had an absorbent state, such as death, from which no further progression is possible. In addition to the complication-specific Markov models, each annual cycle carried an age-specific probability of all-cause mortality, capturing death due to causes other than T2D complications.

Figure 1. Decision tree structure of the hybrid decision model.



GDM indicates gestational diabetes; QALY, quality-adjusted life-year; T2D, type 2 diabetes.

Figure 2. Schematic representation of the simulation model. Probability of transition is specific to each screening strategy.



GDM indicates gestational diabetes; T2D, type 2 diabetes.

The simulation model, displayed schematically in Figure 2, is used to evaluate average costs and QALY associated with each intervention, by simulating the life course of women diagnosed with GDM from delivery to either death or 100 years (whichever occurs first). In each annual cycle, the women had a probability of dying from any cause and, if not, developing T2D. The screening strategy determined at which years T2D screening took place. In addition, we assumed the detection of T2D based on symptoms, such that any complication due to undiagnosed T2D resulted in a T2D diagnosis in the same year. Furthermore, in the absence of lifelong screening, we assumed that T2D was diagnosed at the latest 6 years after T2D onset, based on existing evidence.[7] We assumed that T2D diagnosis came with T2D treatment, given that it has been reported that 97.4% of Singaporeans with diabetes receive treatment.[46] The life trajectories in the simulation model started at delivery at 33 years of age, which is the average age of women with GDM in the Growing Up in Singapore Towards Healthy Outcomes (GUSTO) cohort.[47] See Section B.5 of Appendix 2 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101048 for the probabilities used in the model for each screening strategy. Future costs, life-years, and QALY were discounted at 3%. The code used for the analyses is included in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101048. Each simulation of the model in Figure 2 started with a woman of age 33 years diagnosed of GDM and without T2D and proceeded as outlined below.

While age ≤ 100 years and alive:
Start of annual cycle: simulate whether death due to all-cause mortality occurs.

- If death, **stop.**
- Else, check for presence of T2D.
    - If no T2D, simulate whether T2D develops.
        - If no T2D, increase age by 1 and **start** a new cycle.
        - If T2D, check if it is diagnosed.*
            - If T2D is diagnosed, simulate complication-specific Markov models for diagnosed T2D (*treated*).†
            - If T2D is not diagnosed, simulate complication-specific Markov models for undiagnosed T2D (*untreated*).†
    - If T2D, check if it is diagnosed.*
        - If T2D is diagnosed, simulate complication-specific Markov models for diagnosed T2D (*treated*).†
        - If T2D is not diagnosed, simulate complication-specific Markov models for undiagnosed T2D (*untreated*).†
- Else, check for presence of T2D.
    - If no T2D, simulate whether T2D develops.
        - If no T2D, increase age by 1 and **start** a new cycle.
        - If T2D, check if it is diagnosed.*

End

*Depending on the screening strategy, this can happen in the same annual cycle or delayed up to a maximum of 6 years of remaining undiagnosed; ie, after 6 years from onset, we assume that T2D is diagnosed.[7]

†See Appendix Tables 4 to 8 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101048.

Probabilities

The probabilities in the simulation model were based on findings from GUSTO and available literature. The Singapore Department of Statistics provided sex- and age-specific probabilities of all-cause mortality.[48] The annual probability of T2D onset was estimated from (1) GUSTO,[47] which provided T2D status up to 8 years postpartum, and (2) literature on T2D incidence after GDM beyond 8 years.[36] This implies that the resulting probability varied with age.

The incidence of complications for treated T2D was based on studies conducted in Singapore,[49-51] except for the incidence of diabetic foot ulcers, which was from the United Kingdom.[52] For untreated T2D, the incidence rates of complications are generally higher due to poorer glycemic control. To derive probabilities of complications with untreated T2D from those with treated T2D, we considered relative risks derived from a recent cost-effectiveness analysis of diabetes screening.[19]

Probabilities of progression of complications, including progression to death, were derived from publicly available sources, most of which were specific to the Singaporean context.[53-59] All probabilities and how they were derived from GUSTO and available literature are presented in Appendix 2 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101048.

Costing

Discounted costs were aggregated across the years in the simulation model. Only direct healthcare costs related to diabetes were considered, ie, the cost of screening, of treating T2D, and of treating complications. Strategies involving more frequent screening have a higher cost of T2D testing and treatment and a lower cost of complications.

Screenings were assumed to include a primary care visit and an OGTT. The cost of the OGTT used for T2D screening was derived from billing data of the National University Hospital, Singapore, whereas the primary care visit was costed based on MOH data. In the event of T2D diagnosis through screening, the cost of a confirmatory OGTT was included in the analysis.[32] For T2D treatment excluding complications, an estimate of the average cost was provided by MOH. Finally, costs of specific Markov disease states were provided by Singapore-specific burden of disease studies on diabetes complications[60-63] and MOH's list of fee benchmarks[64] complemented by information from experts.

All costs were expressed in constant Singaporean dollar values[65] with 2022 as base year using healthcare-specific inflation data from the Singapore Consumer Price Index. Amounts are reported in Singapore dollars. We provide a description of all costs and their sources in Appendix 3 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101048.

QALYs

Similar to costs, the QALYs of each simulated lifetime were evaluated as the sum of the discounted QALY weights, ie, health-related quality of life, associated with the health state of each annual cycle in the model. The healthy state without T2D was assigned a QALY weight of 1. Weights for other health states were obtained by transforming the values in Kaur et al[19] to the Singaporean context. Whenever multiple T2D complications were present simultaneously, the corresponding QALY weight was computed as the minimum of the single-condition weights.

For the health states in the simulation model, Kaur et al[19] provided QALY weights based on a Thailand value set. Such valuations of health states can vary substantially between countries, and thus, it is important to use country-specific value sets for estimating utility.[66,67] Therefore, we transform the Thai weights to adapt them to the Singaporean context. In particular, QALY weights from Singapore[68] and Thailand[69] are available for the set of health states included in the EuroQoL Quality of Life Questionnaire with 5 dimensions and 3-level scale (EQ-5D-3L). A linear

Table 1. Health outcomes and lifetime costs for T2D after GDM per 6500 individuals by screening strategy.

Outcome/cost	Screening strategy				
	Never	Elective	One-off	Triennial	Annual
Life-years (thousand)	161.0	161.0	161.0	161.7	162.0
QALYs (thousand)	128.3	128.4	128.5	130.9	132.2
Total cost (million SG$)	200.6	200.3	200.0	182.0	180.9
Disaggregated costs					
Screening cost (million SG$)	0.0	0.6	1.1	6.7	17.8
T2D treatment cost (million SG$)	32.9	33.0	33.2	37.2	39.2
Retinopathy treatment cost (million SG$)	31.3	31.1	30.9	26.3	23.9
Stroke treatment cost (million SG$)	6.5	6.5	6.5	6.4	6.4
Nephropathy treatment cost (million SG$)	58.9	58.5	58.2	48.9	44.0
Coronary heart disease treatment cost (million SG$)	3.2	3.2	3.2	3.1	3.1
Foot ulcer treatment cost (million SG$)	67.9	67.4	67.0	53.4	46.5

Note. Costs are expressed in 2022 Singapore dollars.
GDM indicates gestational diabetes mellitus; QALY, quality-adjusted life-year; SG$, Singapore dollars; T2D, type 2 diabetes.

regression of the Singaporean weights onto the Thai weights provided the calibration curve:

Singaporean weight = 1.12 × Thai weight − 0.23

As a result, the Singaporean weights were lower than the Thai weights, which is in line with previous work on how Singaporeans and Thai value health.[66] In particular, in a comparison among 7 Asian countries, Singaporeans were found to be the most sensitive to changes in the severity of health states, as opposed to Thai nationals who were ranked second least sensitive (after Koreans). Moreover, the Singapore population prioritized the effect of changes in anxiety/depression health states.[66] We applied the transformation to the QALY weights provided in Table S1 of Kaur et al[19] to obtain the QALY weights used in this analysis. The QALY weights are listed in Appendix 4 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101048.

Sensitivity Analysis

We performed deterministic one-way sensitivity analyses and a probabilistic sensitivity analysis to account for parameter uncertainty. For the probabilistic sensitivity analysis, distributions were derived for all parameters from their sensitivity ranges. In particular, we assigned beta distributions to the probabilities and gamma distributions to the costs, the disutilities (ie, 1 minus the QALY weight), and the log of the relative risks, as suggested by Briggs et al.[70] The parameters for such distributions were set in such a way that the 2.5% and 97.5% percentiles of the distribution corresponded to the limits of the sensitivity range. Monte Carlo estimates of the cost-effectiveness acceptability curves were computed from 1000 simulations where all parameters are varied simultaneously. See Appendix 5 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101048 for further details on the sensitivity analyses.

Results

Base Case Cost-Effectiveness

In the GUSTO cohort, 19% of the pregnant women (n = 201) had GDM. Therefore, we reported results per 6500 cases of GDM, which is approximately 19% of the annual number of births in Singapore. We summarized the outcomes for the base case in Table 1. For completeness, we reported results per individual in Table 2. We do not report incremental cost-effectiveness ratios (ICERs) (ratio of cost and QALY differences) in the tables given that additional screening was always a dominating intervention, ie, yielding lower cost and higher QALY, compared with less frequent screening.

Screening for T2D was cost-effective with annual screening being preferred among all strategies: annual screening versus triennial screening increased QALY by 1.3 thousand and reduced costs by SG$1.0 million. Annual screening compared with the strategy of 54% undergoing elective screening increased QALY by 3.8 thousand while reducing cost by SG$19.4 million.

Health outcomes improved with additional screening. The improvement was more pronounced in terms of QALY than in terms of life-years. This suggests that the effectiveness of screening and associated lower rates of T2D complications derived more from improved health-related quality of life than from an extension in lifespan.

With regard to cost, increased rates of screening resulted in (1) higher screening costs and (2) lower T2D-related expenses, due to fewer complications, despite an increase in T2D diagnoses and associated T2D treatment. The reductions in T2D-related cost were larger than the increases in screening costs. As a result, strategies with more frequent screening were cost-saving measures compared with strategies with less frequent screening.

The number of diagnoses and complications is presented in Table 3. In terms of number of T2D diagnoses through screening, 141 mothers with GDM out of 6500 are diagnosed if all are screened in the first year postpartum. Lifelong screening leads to much higher numbers: triennial screening results in 3843 diagnoses and annual screening in 5403 diagnoses.

Sensitivity Analyses

One-way sensitivity analyses are presented in Appendix 5 in Supplemental Materials found at https://doi.org/10.1016/j.vhri.2024.101048. The 3 most influential parameters were the cost of the OGTT test, the probability of developing T2D, and the relative risk of developing a foot ulcer for untreated versus treated T2D. Varying

(1) the probability of developing T2D
(2) the relative risks of developing a foot ulcer or nephropathy

Table 2. Health outcomes and lifetime costs for T2D after GDM per individual by screening strategy.

Outcome/cost	Screening strategy				
	Never	Elective	One-off	Triennial	Annual
Life-years	24.76	24.77	24.77	24.87	24.93
QALYs	19.74	19.76	19.77	20.15	20.34
Total cost (SG$)	30 858	30 809	30 768	27 997	27 837
Disaggregated costs					
Screening cost (SG$)	0	90	166	1028	2744
T2D treatment cost (SG$)	5055	5080	5101	5718	6038
Retinopathy treatment cost (SG$)	4812	4783	4759	4046	3674
Stroke treatment cost (SG$)	996	996	996	986	982
Nephropathy treatment cost (SG$)	9056	8997	8946	7516	6767
Coronary heart disease treatment cost (SG$)	494	494	493	482	477
Foot ulcer treatment cost (SG$)	10 445	10 370	10 307	8221	7155

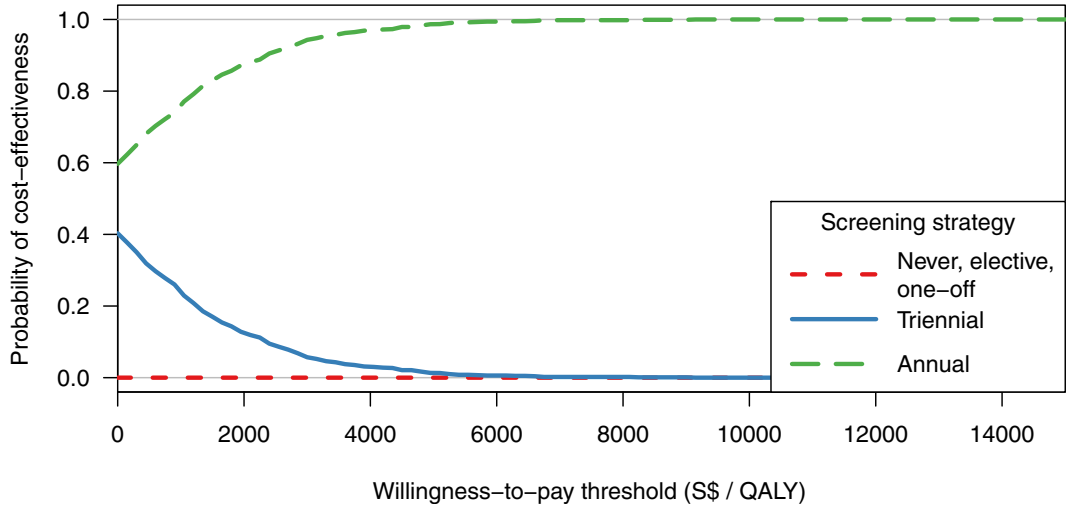
Note. Costs are expressed in 2022 Singapore dollars.
GDM indicates gestational diabetes mellitus; QALY, quality-adjusted life-year; T2D, type 2 diabetes, SG$, Singapore dollars.

Table 3. Number of diagnoses and complications after GDM per 6500 individuals by screening strategy.

Outcome	Screening strategy				
	Never	Elective	One-off	Triennial	Annual
No. diagnosed by screening	0	76	141	3843	5403
Cases of retinopathy	3990	3986	3983	3659	3508
Cases of stroke	1084	1085	1085	1084	1084
Cases of nephropathy	3668	3664	3660	3324	3166
Cases of myocardial infarction	1921	1920	1920	1898	1889
Cases of foot ulcer	2622	2616	2611	2225	2042

GDM indicates gestational diabetes mellitus.

Figure 3. Cost-effectiveness acceptability curves. No screening (never), elective screening, and universal one-off screening had identical CEACs that were equal to zero everywhere.



CEAC indicates cost-effectiveness acceptability curve. QALY indicates quality-adjusted life-year.

(3) cost of the OGTT, foot ulcer, or nephropathy within a 20% (30% for costs) range from base case resulted in a cost increase, instead of reduction, for annual screening compared with triennial screening. Still, the corresponding ICER of annual versus triennial screening did not exceed SG$2000/QALY, which is well below willingness-to-pay (WTP) thresholds that are typically used in Singaporean cost-effectiveness analyses (in the range SG$50 000-SG$70 000/QALY[71-73]). A higher probability of T2D or a higher relative risk of complications corresponded to a lower ICER whereas a higher cost of a test increased the ICER.

For the probabilistic sensitivity analysis, the cost-effectiveness acceptability curves in Figure 3 show that annual screening was incrementally cost-effective in all 1000 Monte Carlo simulations for WTP thresholds above SG$9000, which is consistent with the base case analysis. For WTP thresholds below SG$9000, triennial screening was most cost-effective in some simulations. In contrast, no screening, elective screening, and universal one-off screening were never more cost-effective than the other interventions.

Discussion

In Singapore, the prevalence of T2D is significantly elevated compared with other Southeast Asian countries.[1] This work focuses on GDM in Singapore, given its significant role as a major risk factor for T2D among women. In particular, we evaluated the cost-effectiveness of strategies for T2D screening after GDM.

Universal annual screening was a dominating strategy compared with strategies with less frequent screening given that it increased QALY while reducing cost, which suggests that annual screening is the optimal strategy for Singapore. Moreover, under commonly used WTP threshold, annual screening was consistently the cost-effective choice in sensitivity analyses when varying costs, QALY weights, and other input parameters, with the ICER of annual versus triennial screening always below SG$2000/QALY. In the probabilistic sensitivity analysis, no screening, elective screening, and universal one-off screening in the first year after pregnancy were never the optimal strategy compared with lifelong (ie, triennial or annual) screening. The findings are consistent with cost-effectiveness analyses of periodical T2D screening based on risk factors.[12,20,21] For instance, Gillies et al[20] and Nagy et al[21] report an ICER for risk-based screening versus no screening of £14 150/QALY and €3630/QALY, respectively.

The hybrid decision model used has several merits. First, many parameters were derived from Singaporean data, which makes the findings more relevant. For instance, QALY weights were based on a Singapore-specific value set.[68] The simulation model was able to account for many possible different scenarios of T2D progression, allowing, for instance, for time-varying T2D susceptibility and multiple diabetes complications simultaneously, given that it is realistic.

Our analysis has limitations. We did not consider screening for prediabetes or alternatives to the OGTT used for screening, such as using fasting glucose or glycated hemoglobin.[12,17,19] We obtained the time between onset of T2D and its diagnosis from previous findings,[7] estimating 6 years' delay. However, this value is obtained with data collected between 1991 and 2010 and might not be a realistic estimate of the time between onset of T2D and its diagnosis. Analogously, the computations for the rates of onset of complications for untreated T2D were partly based on the UK Prospective Diabetes Study[19,74] (1977-1997). Furthermore, the Markov models contain many arguably unrealistic simplifications. For instance, complications develop and progress independently from each other in the simulation model, and most probabilities were assumed to be constant across time and age. Nevertheless, the findings seemed to be robust to changes in these probabilities. Moreover, such Markov models and their simplifications are common in health economic analyses of T2D screening,[17,19,21] although more involved models have been developed.[75] Another limitation is that some probabilities were derived from countries other than Singapore, but again our findings did not change substantially in sensitivity analyses. In addition, we assumed 100% screening compliance in some strategies, which might not be feasible in practice. Finally, we considered only healthcare-related costs and thus omitted others costs such a productivity loss, eg, as a result of T2D complications. Still, our study highlights the importance of more comprehensive interventions after GDM and, more in general, the need for cost-effectiveness evaluations of diabetes prevention programs.

Author Disclosures

Author disclosure forms can be accessed below in the Supplemental Material section.

Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.vhri.2024.101048.

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Author Affiliations: School of Science and Technology, IE University, Madrid, Spain (Cremaschi); Institute for Human Development and Potential (IHDP), Agency for Science, Technology and Research (A*STAR), Singapore, Singapore (van den Boom, Chong, Eriksson, De Iorio); Department of Paediatrics, National University Hospital, Singapore, Singapore (Ng); Bocconi Institute for Data Science and Analytics, Bocconi University, Milan, Italy (Franzolini); Ministry of Health, Singapore, Singapore (K.B. Tan); Saw Swee Hock School of Public Health, National University of Singapore, Singapore, Singapore (K.B. Tan); Department of Reproductive Medicine, KK Women's and Children's Hospital, Singapore, Singapore (Chan); Duke-NUS Medical School, Singapore, Singapore (Chan, K.H. Tan); Department of Maternal Fetal Medicine, KK Women's and Children's Hospital, Singapore, Singapore (K.H. Tan); Department of Obstetrics and Gynaecology, National University of Singapore, Singapore, Singapore (Chong, Eriksson); Department of Paediatrics, National University of Singapore, Singapore, Singapore (De Iorio).

Correspondence: Willem van den Boom, PhD, Institute for Human Development and Potential (IHDP), Agency for Science, Technology and Research (A*STAR), 30 Medical Drive, Singapore 117609, Republic of Singapore. Email: Willem_van_den_Boom@sics.a-star.edu.sg

Author Contributions: *Concept and design:* Eriksson, De Iorio
Acquisition of data: Cremaschi, van den Boom, Ng, Franzolini, K.B. Tan, Chan, K.H. Tan, Chong, Eriksson, De Iorio
Analysis and interpretation of data: Cremaschi, van den Boom, De Iorio
Drafting of the manuscript: Cremaschi, van den Boom, Ng
Critical revision of the paper for important intellectual content: Cremaschi, van den Boom, Ng, Franzolini, K.B. Tan, Chan, K.H. Tan, Chong, Eriksson, De Iorio
Statistical analysis: Cremaschi, van den Boom, Franzolini, De Iorio
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REFERENCES

1. International Diabetes Federation. *IDF Diabetes Atlas. 10th ed. International Diabetes Federation*. 2021.
2. Bommer C, Sagalova V, Heesemann E, et al. Global economic burden of diabetes in adults: projections from 2015 to 2030. *Diabetes Care*. 2018;41(5):963–970.
3. National Institute for Health and Care Excellence. Type 2 diabetes: prevention in people at high risk. NICE. https://www.nice.org.uk/guidance/ph38; 2017. Accessed December 8, 2023.
4. National Institute for Health and Care Excellence. *Obesity: Identification, Assessment and Management*. London, England: NICE; 2023.
5. Ma RC, Chan JC. Type 2 diabetes in East Asians: similarities and differences with populations in Europe and the United States. *Ann N Y Acad Sci*. 2013;1281(1):64–91.
6. Harris MI, Klein R, Welborn TA, Knuiman MW. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. *Diabetes Care*. 1992;15(7):815–819.
7. Porta M, Curletto G, Cipullo D, et al. Estimating the delay between onset and diagnosis of type 2 diabetes from the time course of retinopathy prevalence. *Diabetes Care*. 2014;37(6):1668–1674.
8. Ogurtsova K, Guariguata L, Barengo NC, et al. IDF Diabetes Atlas: global estimates of undiagnosed diabetes in adults for 2021. *Diabetes Res Clin Pract*. 2022;183:109118.
9. Gedebjerg A, Almdal TP, Berencsi K, et al. Prevalence of micro- and macrovascular diabetes complications at time of type 2 diabetes diagnosis and associated clinical characteristics: a cross-sectional baseline study of 6958 patients in the Danish DD2 cohort. *J Diabetes Complications*. 2018;32(1):34–40.
10. Beagley J, Guariguata L, Weil C, Motala AA. Global estimates of undiagnosed diabetes in adults. *Diabetes Res Clin Pract*. 2014;103(2):150–160.
11. US Preventive Services Task Force, Davidson KW, Barry MJ, et al. Screening for prediabetes and type 2 diabetes: US Preventive Services Task Force recommendation statement. *JAMA*. 2021;326(8):736–743.
12. Einarson TR, Bereza BG, Acs A, Jensen R. Systematic literature review of the health economic implications of early detection by screening populations at risk for type 2 diabetes. *Curr Med Res Opin*. 2017;33(2):331–358.
13. Toi PL, Wu O, Thavorncharoensap M, et al. Economic evaluation of population-based type 2 diabetes mellitus screening at different healthcare settings in Vietnam. *PLoS One*. 2021;16(12):e0261231.
14. CDC Diabetes Cost-Effectiveness Study Group. The cost-effectiveness of screening for type 2 diabetes. *JAMA*. 1998;280(20):1757–1763.
15. Chen TH, Yen MF, Tung TH. A computer simulation model for cost-effectiveness analysis of mass screening for type 2 diabetes mellitus. *Diabetes Res Clin Pract*. 2001;54(suppl 1):S37–S42.
16. Kahn R, Alperin P, Eddy D, et al. Age at initiation and frequency of screening to detect type 2 diabetes: a cost-effectiveness analysis. *Lancet*. 2010;375(9723):1365–1374.
17. Schaufler TM, Wolff M. Cost effectiveness of preventive screening programmes for type 2 diabetes mellitus in Germany. *Appl Health Econ Health Policy*. 2010;8(3):191–202.
18. Hoerger TJ, Harris R, Hicks KA, Donahue K, Sorensen S, Engelgau M. Screening for type 2 diabetes mellitus: a cost-effectiveness analysis. *Ann Intern Med*. 2004;140(9):689–699.
19. Kaur G, Chauhan AS, Prinja S, et al. Cost-effectiveness of population-based screening for diabetes and hypertension in India: an economic modelling study. *Lancet Public Health*. 2022;7(1):e65–e73.
20. Gillies CL, Lambert PC, Abrams KR, et al. Different strategies for screening and prevention of type 2 diabetes in adults: cost effectiveness analysis. *BMJ*. 2008;336(7654):1180–1185.
21. Nagy B, Zsolyom A, Nagyjanosi L, et al. Cost-effectiveness of a risk-based secondary screening programme of type 2 diabetes. *Diabetes Metab Res Rev*. 2016;32(7):710–729.
22. HealthHub. Let's BEAT diabetes. Ministry of Health, Singapore. https://www.healthhub.sg/programmes/diabetes-mellitus. Accessed December 8, 2023.
23. Ministry of Health. MOH clinical practice guidelines on diabetes mellitus. Ministry of Health, Singapore. https://www.moh.gov.sg/hpp/doctors/guidelines/guidelinedetails/cpgmed_diabetes_mellitus; 2014. Accessed December 8, 2023.
24. Goh SY, Ang SB, Bee YM, et al. Ministry of Health clinical practice guidelines: diabetes mellitus. *Singapore Med J*. 2014;55(6):334–347.
25. Scott DA, Loveman E, McIntyre L, Waugh N. Screening for gestational diabetes: a systematic review and economic evaluation. *Health Technol Assess*. 2002;6(11):1–161.
26. Irgens HU, Reisaeter L, Irgens LM, Lie RT. Long term mortality of mothers and fathers after pre-eclampsia: population based cohort study. *BMJ*. 2001;323(7323):1213–1217.
27. The Guideline Development Group. Management of diabetes from preconception to the postnatal period: summary of NICE guidance. *BMJ*. 2008;336(7646):714–717.
28. Lim W. Gestational diabetes mellitus: what is it and how does it affect you and your baby? HealthXchange.sg, SingHealth. https://www.healthxchange.sg/diabetes/essential-guide-diabetes/gestational-diabetes-mellitus-what-how-affect-you-baby. Accessed December 8, 2023.
29. Metzger BE, Buchanan TA, Coustan DR, et al. Summary and recommendations of the Fifth International Workshop-Conference on Gestational Diabetes Mellitus. *Diabetes Care*. 2007;30(suppl 2):S251–S260.
30. Zhang CH, Liu XY, Zhan YW, Zhang L, Huang YJ, Zhou H. Effects of prepregnancy body mass index and gestational weight gain on pregnancy outcomes. *Asia Pac J Public Health*. 2015;27(6):620–630.
31. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. *Diabetes Care*. 2002;25(10):1862–1868.
32. Agency for Care Effectiveness (ACE). Gestational diabetes mellitus – an update on screening, diagnosis, and follow-up. Ministry of Health Singapore. https://www.ace-hta.gov.sg/healthcare-professionals/ace-clinical-guidances-(acgs)/details/gestational-diabetes-mellitus-an-update-on-screening-diagnosis-and-follow-up; 2022. Accessed December 8, 2023.
33. National Institute for Health and Care Excellence. *Diabetes in Pregnancy: Management from Preconception to the Postnatal Period*. London, England: NICE; 2020.
34. ElSayed NA, Aleppo G, Aroda VR, et al. Management of diabetes in pregnancy: standards of care in diabetes–2023. *Diabetes Care*. 2023;46(suppl 1):S254–S266.
35. Sunny SH, Malhotra R, Ang SB, et al. Facilitators and barriers to post-partum diabetes screening among mothers with a history of gestational diabetes mellitus–a qualitative study from Singapore. *Front Endocrinol*. 2020;11:602.
36. Daly B, Toulis KA, Thomas N, et al. Increased risk of ischemic heart disease, hypertension, and type 2 diabetes in women with previous gestational diabetes mellitus, a target group in general practice for preventive interventions: a population-based cohort study. *PLoS Med*. 2018;15(1):e1002488.
37. Kim C, Tabaei BP, Burke R, et al. Missed opportunities for type 2 diabetes mellitus screening among women with a history of gestational diabetes mellitus. *Am J Public Health*. 2006;96(9):1643–1648.
38. Chang Y, Chen X, Cui H, Zhang Z, Cheng L. Follow-up of postpartum women with gestational diabetes mellitus (GDM). *Diabetes Res Clin Pract*. 2014;106(2):236–240.
39. Paez KA, Eggleston EM, Griffey SJ, et al. Understanding why some women with a history of gestational diabetes do not get tested for diabetes. *Womens Health Issues*. 2014;24(4):e373–e379.
40. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med*. 1998;15(7):539–553.
41. Aoki N, Dunn K, Fukui T, Beck JR, Schull WJ, Li HK. Cost-effectiveness analysis of telemedicine to evaluate diabetic retinopathy in a prison population. *Diabetes Care*. 2004;27(5):1095–1101.
42. Cheng Q, Lazzarini PA, Gibb M, et al. A cost-effectiveness analysis of optimal care for diabetic foot ulcers in Australia. *Int Wound J*. 2017;14(4):616–628.
43. Adler AI, Stevens RJ, Manley SE, et al. Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). *Kidney Int*. 2003;63(1):225–232.
44. Rachapelle S, Legood R, Alavi Y, et al. The cost-utility of telemedicine to screen for diabetic retinopathy in India. *Ophthalmology*. 2013;120(3):566–573.
45. Ang Y, Yap CW, Saxena N, Lin L-K, Heng BH. Diabetes-related lower extremity amputations in Singapore. *Proc Singapore Healthc*. 2017;26(2):76–80.
46. Tan KB, Tan WS, Bilger M, Ho CWL. Monitoring and evaluating progress towards universal health coverage in Singapore. *PLoS Med*. 2014;11(9):e1001695.

47. Soh SE, Tint MT, Gluckman PD, et al. Cohort profile: growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort study. *Int J Epidemiol*. 2014;43(5):1401–1409.
48. Singapore Department of Statistics. Complete life tables for Singapore resident population, 2021-2022. https://www.singstat.gov.sg/-/media/files/publications/population/lifetable21-22.ashx; 2023. Accessed December 8, 2023.
49. Tan S, Wong LY, Toh MPH. Incipient albuminuria in persons with newly diagnosed type 2 diabetes mellitus: a 5-year retrospective cohort study. *Ann Acad Med Singap*. 2018;47(12):502–508.
50. Seng JJB, Kwan YH, Lee VSY, et al. Differential health care use, diabetes-related Complications, and mortality among five unique classes of patients with type 2 diabetes in Singapore: a latent class analysis of 71,125 patients. *Diabetes Care*. 2020;43(5):1048–1056.
51. Neelam K, Aung KCY, Ang K, Tavintharan S, Sum CF, Lim SC. Association of triglyceride glucose index with prevalence and incidence of diabetic retinopathy in a Singaporean population. *Clin Ophthalmol*. 2023;17:445–454.
52. Crawford F, McCowan C, Dimitrov BD, et al. The risk of foot ulceration in people with diabetes screened in community settings: findings from a cohort study. *Q J M*. 2011;104(5):403–410.
53. Aziz Z, Lin WK, Nather A, Huak CY. Predictive factors for lower extremity amputations in diabetic foot infections. *Diabet Foot Ankle*. 2011;2(1):7463.
54. Sun Y, Lee SH, Heng BH, Chin VS. 5-year survival and rehospitalization due to stroke recurrence among patients with hemorrhagic or ischemic strokes in Singapore. *BMC Neurol*. 2013;13(1):133.
55. Ang YG, Heng BH, Saxena N, Liew STA, Chong PN. Annual all-cause mortality rate for patients with diabetic kidney disease in Singapore. *J Clin Transl Endocrinol*. 2016;4:1–6.
56. Yeo KK, Zheng H, Chow KY, et al. Comparative analysis of recurrent events after presentation with an index myocardial infarction or ischaemic stroke. *Eur Heart J Qual Care Clin Outcomes*. 2017;3(3):234–242.
57. Yap J, Chia SY, Lim FY, et al. The Singapore heart failure risk score: prediction of survival in Southeast Asian patients. *Ann Acad Med Singap*. 2019;48(3):86–94.
58. National Registry of Diseases Office. *Singapore Myocardial Infarction Registry Annual Report 2020*. Singapore: Health Promotion Board; 2022. https://nrdo.gov.sg/docs/librariesprovider3/default-document-library/smir-web-report-2020.pdf. Accessed October 21, 2024.
59. Live On. *Statistics Information Booklet*. Singapore: National Organ Transplant Unit; 2023. https://www.liveon.gov.sg/docs/info_booklets/LiveOn_stats.pdf. Accessed October 21, 2024.
60. Zhang X, Low S, Kumari N, et al. Direct medical cost associated with diabetic retinopathy severity in type 2 diabetes in Singapore. *PLoS One*. 2017;12(7):e0180949.
61. Ng CS, Toh MP, Ng J, Ko Y. Direct medical cost of stroke in Singapore. *Int J Stroke*. 2015;10(suppl):A100:75-82.
62. Lo ZJ, Surendra NK, Saxena A, Car J. Clinical and economic burden of diabetic foot ulcers: a 5-year longitudinal multi-ethnic cohort study from the tropics. *Int Wound J*. 2021;18(3):375–386.
63. Lim GJ, Liu YL, Low S, et al. Medical costs associated with severity of chronic kidney disease in type 2 diabetes mellitus in Singapore. *Ann Acad Med Singap*. 2020;49(10):731–741.
64. Ministry of Health. List of Fee Benchmarks (With Effect From 14 June 2023). https://www.moh.gov.sg/cost-financing/hospital-bills-and-fee-benchmarks-search-result/; 2023. Accessed December 5, 2023.
65. Kumaranayake L. The real and the nominal? Making inflationary adjustments to cost and other economic data. *Health Policy Plan*. 2000;15(2):230–234.
66. Wang P, Liu GG, Jo MW, et al. Valuation of EQ-5D-5L health states: a comparison of seven Asian populations. *Expert Rev Pharmacoecon Outcomes Res*. 2019;19(4):445–451.
67. Yang Z, Purba FD, Shafie AA, et al. Do health preferences differ among Asian populations? A comparison of EQ-5D-5L discrete choice experiments data from 11 Asian studies. *Qual Life Res*. 2022;31(7):2175–2187.
68. Luo N, Wang P, Thumboo J, Lim YW, Vrijhoef HJ. Valuation of EQ-5D-3L health states in Singapore: modeling of time trade-off values for 80 empirically observed health states. *Pharmacoeconomics*. 2014;32(5):495–507.
69. Tongsiri S, Cairns J. Estimating population-based values for EQ-5D health states in Thailand. *Value Health*. 2011;14(8):1142–1145.
70. Briggs AH, Claxton K, Sculpher MJ. *Decision Modelling for Health Economic Evaluation*. Oxford, England: Oxford University Press; 2006.
71. Chen PY, Finkelstein EA, Ng MJ, et al. Incremental cost-effectiveness analysis of gestational diabetes mellitus screening strategies in Singapore. *Asia Pac J Public Health*. 2016;28(1):15–25.
72. Ni W, Kunz WG, Goyal M, Ng YL, Tan K, De Silva DA. Lifetime quality of life and cost consequences of delays in endovascular treatment for acute ischaemic stroke: a cost-effectiveness analysis from a Singapore healthcare perspective. *BMJ Open*. 2020;10(9):e036517.
73. Chootipongchaivat S, Wong XY, Ten Haaf K, et al. Cost-effectiveness analysis of breast cancer screening using mammography in Singapore: a modeling study. *Cancer Epidemiol Biomarkers Prev*. 2021;30(4):653–660.
74. Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ*. 2000;321(7258):405–412.
75. Eddy DM, Schlessinger L. Archimedes: a trial-validated model of diabetes. *Diabetes Care*. 2003;26(11):3093–3101.