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Original Article

Economic Evaluation of Screening Strategies for Thalassaemia Prevention: A Case Study From Thailand

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Abstract

Background: Thalassaemia is a genetic blood disorder endemic in Thailand. Management of severe thalassaemia utilises significant resources posing a substantial socio-economic burden; thus, prevention has been identified as a more sustainable approach to address thalassaemia. This study evaluated the cost-effectiveness and budget impact of various thalassaemia screening strategies in Thailand, including both pre-conception and post-conception approaches.

Methods: A cost-effectiveness analysis (CEA), from the Thai healthcare payer's perspective, was conducted using decision analytic modelling. Decision trees were used to estimate the incremental screening cost per severe thalassaemia birth averted for four main screening strategies compared to "no screening": post-conception screening (Strategy 1), pre-conception screening with targeted deoxyribonucleic acid (DNA) analysis (Strategy 2), pre-conception screening with universal DNA analysis (Strategy 3), and a combination of pre-conception and post-conception screening (Strategy 4). The cost-effectiveness threshold (CET) used was the lifetime cost of managing severe thalassaemia in Thailand. The annual budget impact of the upfront costs of implementing these strategies was also estimated.

Results: Strategies 1, 2, and 4 were cost-saving compared to the threshold of the average lifetime cost of managing severe thalassaemia in Thailand, $21,017. Strategy 4 had the lowest screening cost of $6773 [$4522–$10 066] per severe thalassaemia birth averted. Strategy 2 cost $8977 [$5689–$13 956] per severe thalassaemia birth averted, and Strategy 1 cost $10 474 [$7121–$15 734] per severe thalassaemia birth averted. In contrast, Strategy 3 cost $57 692 [$33 240–$96 123] per severe thalassaemia birth averted and is not cost-saving. The annual budget impact of the upfront costs of implementing thalassaemia screening ranged from $1.30 million to $288.93 million, depending on the strategy adopted and uptake rates.

Conclusion: Post-conception thalassaemia screening is cost-saving in Thailand. Combining pre-conception and post-conception screening strategies may offer even better value for money in the Thai context, but with a higher upfront cost of implementation.

Keywords: Thalassaemia, Pre-conception Screening, Post-conception Screening, Cost-Effectiveness Analysis, Budget Impact Analysis, Thailand

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Background

Haemoglobinopathies are the most common single gene disorders in humans which affect the globin chains of haemoglobin (Hb).[1] Thalassaemia and sickle cell disease make up the majority of haemoglobinopathies,[1,2] and are a major contributor to the global burden of disease.[3] An estimated 7% of the world's population is said to carry thalassaemia traits and 300 000 to 500 000 of babies born annually have severe thalassaemia.[4] This may even be an underestimation as countries with a high burden of thalassaemia and limited resources may be underdiagnosing the condition.[5]

Thalassaemia has been observed to have a higher prevalence in the tropical belt in malaria-endemic regions including South-East Asia, Africa, the Mediterranean, Indian subcontinent, and Middle East regions.[2] Evidence suggests that the high prevalence of these abnormal Hb traits in malaria-endemic regions offers some protection against infection with *Plasmodium falciparum* malaria.[6,7] Notwithstanding, management of severe forms of thalassaemia utilises significant health resources and has socio-economic implications for low- and middle-income countries.[8-10] Cross-border migration has also made thalassaemia increasingly prevalent in non-endemic regions, like North America and Europe, making it a problem of global health concern.[3,7,11,12] The World Health Organization (WHO) has since declared thalassaemia a major threat to public health and countries are intensifying efforts to reduce the disease burden.

In individuals with thalassaemia, there is decreased production of the globin chains in Hb due to genetic mutations, and these genetic mutations are inherited in an autosomal recessive manner.[1] Inheritance of thalassaemia traits from both parents is required for disease manifestation. Individuals who inherit only one abnormal trait are called

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Key Messages

Implications for policy makers

- Post-conception screening, as currently implemented in Thailand, is cost-saving in comparison to "no screening." However, implementing pre-conception screening (using targeted DNA analysis) in addition to post-conception screening may be even more cost-saving for the Thai context and offer better value for money.
- Despite being cost-saving, the annual budget impact of the upfront costs of implementing pre-conception screening, and the combined strategy, is higher than post-conception screening. A phased implementation of these strategies in Thailand could be useful, starting with regions with the highest thalassaemia burden like the Northern and North-East regions.
- Surveillance of thalassaemia prevalence in Thailand must be strengthened as prevalence rates remain highly influential in determining the cost-effectiveness of thalassaemia screening strategies.
- Enhancement of laboratory capacity for thalassaemia screening at all levels of health facilities in Thailand would improve disease prevention and potentially reduce screening costs through economies of scale.

Implications for the public

Thalassaemia is endemic in Thailand, and management of severe forms of the disease poses a substantial socio-economic burden. Previous studies have suggested that prevention may be a more sustainable approach to manage thalassaemia. This study provides evidence to support this assertion, and highlights that preventing thalassaemia, through screening, is a cost-saving approach in Thailand. Thalassaemia screening during pregnancy (prenatal/post-conception screening) offers good value for money. However, screening before pregnancy, as part of family planning services available in Thailand, could be even more cost-saving in reducing the number of severe thalassaemia births. Sustained sensitisation and awareness campaigns to influence behavioural, religious and socio-cultural factors would improve uptake of thalassaemia screening in Thailand and support its cost-effectiveness.

carriers (thalassaemia minor) and are usually asymptomatic. The major clinically relevant types of thalassaemia are α and β-thalassaemia.[1] Haemoglobin E (HbE), a Hb trait unique to South-East Asia, also causes reduced production of β^E-globin chains with mild β-thalassaemia features.[13,14] Severe forms of thalassaemia are Hb Barts (severe α-thalassaemia), homozygous β-thalassaemia and β/HbE thalassaemia, and their clinical features include anaemia, jaundice, hepatosplenomegaly, poor growth, recurrent infections, and major organ dysfunction.[14]

Management options for severe thalassaemia include frequent blood transfusions with/without iron chelation, splenectomy, gene therapy, and haematopoietic stem cell transplantation (HSCT), which is currently the only curative option available.[15] These treatment modalities pose a substantial economic burden, especially in low- and middle-income countries. Moreover, having a chronic disease like thalassaemia also causes psychosocial problems and reduces the quality of life of patients and their families.[16,17] With the high socio-economic burden associated with managing severe thalassaemia, prevention has been identified as a more sustainable approach to tackle the disease.[18,19] Screening strategies for thalassaemia prevention include premarital screening, prenatal screening, neonatal screening, and thalassaemia screening for school-aged children.[20,21]

Premarital screening involves counselling marriageable couples about risks of thalassaemia and providing them with the choice of testing and reconsidering their decision to marry and/or have children based on the test results.[22] In jurisdictions like Thailand where couples are increasingly conceiving without officially getting married,[23] this strategy may function more as pre-conception screening. Couples may or may not seek counselling and testing for thalassaemia once they decide to conceive. Adolescents and school-aged children may also be screened to detect thalassaemia carriers early and possibly influence their choice of future partners to prevent severe thalassaemia births.[24]

In prenatal screening (post-conception screening), thalassaemia screening is done in the first and second trimesters of pregnancy.[21] Based on test results of the couple, testing of the foetus called prenatal diagnosis (PND), may be performed with the option of terminating the pregnancy if identified to have severe thalassaemia.[21] Neonatal screening involves testing of genetic diseases in newborns within 24–48 hours of delivery for early identification and treatment to prevent complications.[21] One critique of neonatal screening is its identification of severe thalassaemia cases after they have already been born, albeit early enough to institute measures to prolong life-expectancy; which questions its sustainability in resource-limited countries.

Thailand, like other South-East Asian countries, has a high burden of thalassaemia. Estimates in 2010 showed that nearly 1% of the 65 million population had severe thalassaemia and 40% were carriers.[25,26] Alpha-thalassaemia is the more prevalent subtype in Thailand with frequencies of 20%–30% compared to 3%–9% for β-thalassaemia.[27] Both forms have higher incidences in Northern Thailand,[27] and approximately 4253 Thai babies are estimated to be born with severe thalassaemia annually.[15,27]

Most treatment options for thalassaemia are available in Thailand,[28] and these have improved the life-expectancy of severe thalassaemic patients. However, studies have revealed that these treatment modalities pose a huge economic burden to the Thai health system. A cost-of-illness study from 2005, taking a societal perspective, found the average annual cost of managing a patient with homozygous β-thalassaemia and β-thalassaemia/Hb E disease in Thailand to be $950, with about 60% attributable to direct medical costs.[29] Similarly, an economic evaluation (EE) conducted in 2008 comparing HSCT to frequent blood transfusions with iron chelation, revealed an incremental cost-effectiveness ratio (ICER) ranging from 80 700 THB ($2374) to 953 000 THB ($28 029)

per quality-adjusted life year (QALY) gained. The Thai government would require about 90 million THB ($2.65 million) annually to provide 200 HSCTs.[15]

Recognising the need to reduce the high burden of thalassaemia in Thailand, the Thai Ministry of Public Health established a "thalassaemia prevention and control" programme in 1992.[27] They additionally developed a national thalassaemia action plan from 2007–2011, and the National Health Security Office (NHSO) also implemented a "thalassaemia prevention and control in pregnancy" programme from 2014–2016.[27,30] The NHSO's programme is a post-conception screening strategy targeted at pregnant couples who register for antenatal care (ANC). It offers the option of terminating pregnancies with severe cases, as abortion is legal in Thailand under conditions which threaten the health of the mother.[31] Thalassaemia screening in Thailand, like other health services, is mainly public-funded.[29]

Generally, evidence on the cost-effectiveness of thalassaemia screening in Thailand is limited. An outcome evaluation conducted in 2018 revealed a marginal decline in the incidence of severe thalassaemia with screening but did not include an EE.[25] Few older studies have evaluated the costs and benefits of thalassaemia screening as has been implemented in specific hospital contexts in Thailand.[32,33] However, these were partial EEs as the costs and benefits of alternative screening strategies were not considered. More recently, studies published in 2025 conducted cost-effectiveness analyses focusing on prenatal (post-conception) screening, suggesting that screening may provide societal cost-savings per case prevented.[34,35] In contrast, evidence on the cost-effectiveness of pre-conception screening in Thailand remains limited.

This study seeks to undertake full cost-effectiveness and budget impact analyses of screening strategies for thalassaemia prevention in Thailand. These include consideration of whether the current screening strategy provides the best value for money in terms of reducing severe thalassaemia births. Which alternative strategies, like pre-conception screening or a combination of pre- and post-conception screening, may be cost-effective? Our findings can contribute to evidence for Thai policy-makers in allocating resources for thalassaemia prevention. Additionally, our models and findings may inform research for haemoglobinopathies in other resource-limited settings to guide policy decisions.

Methods

Cost-Effectiveness Analysis

Screening Strategies

Using decision trees, we conducted cost-effectiveness analysis (CEA) to estimate the incremental screening cost per severe thalassaemia birth averted for four main strategies in Thailand, compared to "no screening." These included (1) post-conception screening (current practice); (2) pre-conception screening with targeted deoxyribonucleic acid (DNA) analysis; (3) pre-conception screening with universal DNA analysis; and (4) a combined strategy of pre-conception screening (with targeted DNA analysis) and post-conception screening.

For Strategy 1 (current practice), the decision tree was based on care pathways observed at Nakhon Pathom hospital, Thailand (Figure 1). This hospital, which works in strategic partnership with the Thalassaemia Research Centre, Mahidol University, serves as a benchmark for thalassaemia diagnosis and treatment in Thailand. Pregnant couples presenting for ANC undergo initial screening using complete blood count (CBC) and dichlorophenolindophenol (DCIP) testing. Those with positive screening results are referred to the thalassaemia clinic for genetic counselling and blood collection for Hb typing using high-performance liquid chromatography or capillary electrophoresis; the woman's blood sample tested first, and the partner's tested only if the woman is identified as a carrier. If both are identified as carriers, confirmatory testing using DNA analysis is performed. Couples classified as high-risk for severe thalassaemia are offered PND at 14 to 16 weeks of pregnancy, with abortion offered by 20 weeks, when severe thalassaemia is confirmed. If couples presented late for their initial ANC visit (after 20 weeks of gestation) and both have abnormal results from CBC and Hb typing, DNA analysis is still performed for documentation and counselling for future pregnancies, but PND and abortion are not offered in accordance with clinical guidelines in Thailand. In our CEA, the decision tree for Strategy 1 starts when pregnant couples are identified as potential carriers after initial screening, and the costs and outcomes of subsequent screening are compared to a scenario where no further tests are performed (Figure 2).

We subsequently explored alternative screening strategies, extending screening to a wider population (Figure 2). For Strategy 2 (pre-conception screening with targeted DNA analysis), couples who decide to conceive are initially tested using CBC and Hb typing. If both partners have abnormal results, further testing is conducted using DNA analysis, and couples at high-risk of having a child with severe thalassaemia are counselled to reconsider their decision to conceive. For Strategy 3 (pre-conception screening with universal DNA analysis), couples planning to conceive are screened for thalassaemia using DNA analysis as the first-line test. Finally, Strategy 4 explored how combining pre-conception screening with targeted DNA analysis (Strategy 2) with PND, and an option of abortion, might help reduce severe thalassaemia births in Thailand. Detailed descriptions of all the screening strategies are provided in Table S1 (Supplementary file 1).

Of the three main forms of severe thalassaemia targeted for prevention, this study considered screening only for homozygous β thalassaemia and β/Hb E thalassaemia. As the benefits of screening for Hb Barts (severe α-thalassaemia) are mainly related to preventing severe maternal complications and in-utero foetal deaths, these differ from the outcomes considered in this CEA and were therefore excluded from our analyses.

Study Perspective, Time Horizon, and Discounting

We conducted this CEA from the Thai healthcare payer's perspective. The evaluated screening strategies span a duration of planned or confirmed pregnancy to delivery, with the associated costs and outcomes evaluated also covering this same period; thus, discounting was not applied. However, the threshold for determining the cost-effectiveness of

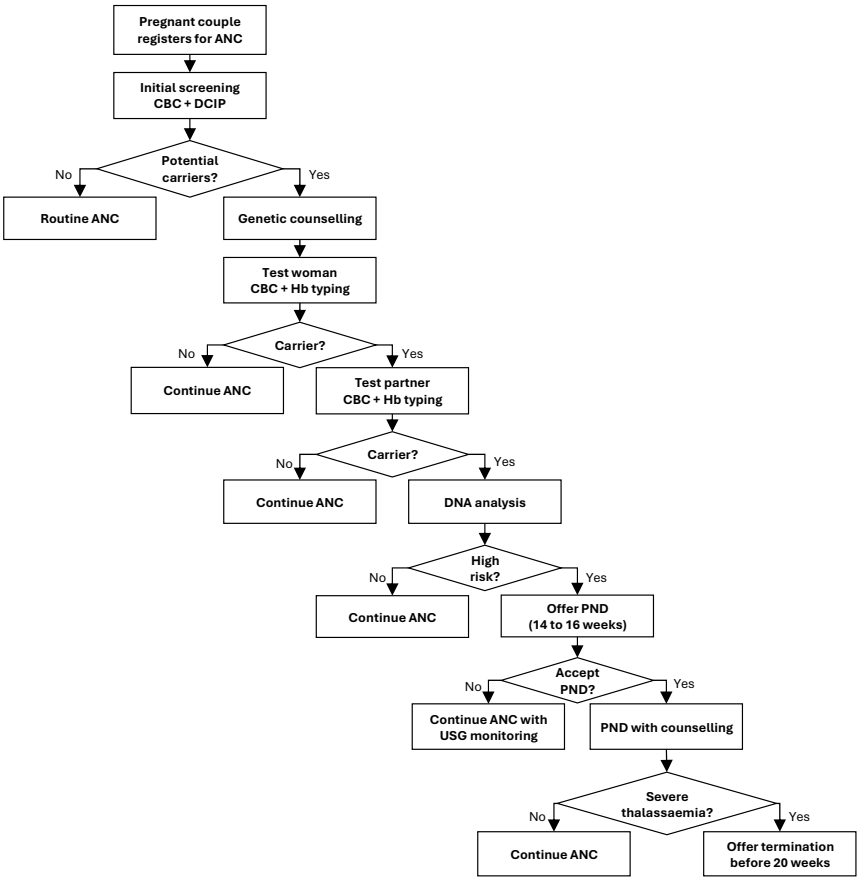

Figure 1. Current Post-conception Screening Process for Thalassemia at the Nakhon Pathom Hospital, Thailand. Abbreviations: ANC, antenatal care; CBC, complete blood count; DCIP, dichlorophenolindophenol; Hb, haemoglobin; DNA, deoxyribonucleic acid; PND, prenatal diagnosis; USG, ultrasonography.

these strategies was the lifetime cost of managing a patient with severe thalassaemia in Thailand. Life-expectancy for severe thalassaemic patients was assumed to be 30 years in this study,[36] and estimation of the present value of the cost-effectiveness threshold (CET) was discounted at 3% annually per guidelines for health technology assessment in Thailand.[37]

Evidence Synthesis and Parameter Selection

Model parameters were informed by a targeted literature review of published and grey literature on thalassaemia epidemiology, prevention, and EEs, with a focus on Thailand. Key parameters, their values, and data sources are summarised in Table 1. Detailed assumptions and justification are provided in Table S2 (Supplementary file 1).

Costs

Based on the study perspective, direct medical costs like costs of CBC and Hb typing, DNA analysis, PND, and abortion were included in this CEA. Cost values were obtained from the NHSO (Table 1).[38] These costs were presented in 2025 THB requiring no inflation. We also presented them in USD at a rate of $1 to 32.50 THB, the exchange rate on July 30, 2025.[39]

Outcomes

The main outcome of interest was the probability of severe thalassaemia birth with and without screening. The ICER for screening compared to "no screening" was calculated as follows:

$$ICER = \frac{C_1 - C_0}{p_1 - p_0}$$

where C_1 and C_0 denote the expected costs under screening and no screening, respectively, and p_1 and p_0 denote the corresponding probabilities of severe thalassaemia births.

Since our evaluation did not measure QALYs, the ICERs could not be compared to Thailand's CET of 160 000 THB per QALY gained. In this context, preventing severe thalassaemia births does not directly result in QALYs gained, which makes QALYs inappropriate outcome measures for this study.[18] Instead, we used an alternative CET based on the lifetime cost of managing severe thalassaemia. This value was derived from a cost-of-illness analysis conducted in Thailand in 2005 for patients with homozygous β-thalassaemia and β/Hb E thalassaemia.[29] All evaluated strategies with estimated ICERs less than the lifetime cost of managing severe thalassaemia were determined to be cost-saving.

Only direct medical costs were extracted for the CET, based on our study perspective, to allow for comparability. These included costs for drugs, medical materials, blood transfusions, diagnostic investigations, routine services, and operations. The average annual cost was $562.76 (22 634.21 THB) in 2005 ($1 to 40.22 THB), ranging from $224.90 (9045.48 THB) at the regional hospitals with lower levels

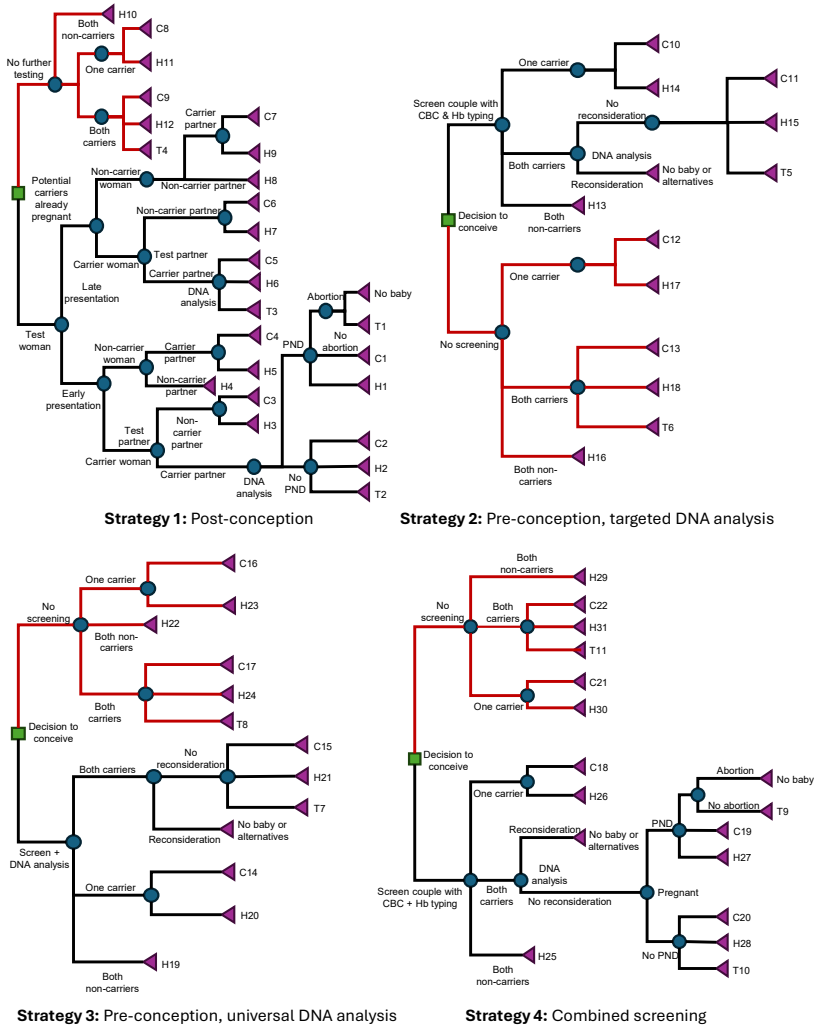

Figure 2. Decision Trees Describing Thalassaemia Screening Strategies Compared to Scenarios Where "No Screening" Is Performed (red branches). Triangles (leaves) represent birth outcomes, with H indicating a healthy (non-carrier) baby, C a carrier baby, and T a baby with severe thalassaemia (primary outcome of interest). The numbers after each of these outcomes are unique identifiers for that particular outcome in each arm. Abbreviations: CBC, complete blood count; Hb, haemoglobin; DNA, deoxyribonucleic acid; PND, prenatal diagnosis.

of care to $782.70 (31 480.19 THB) at hospitals with higher levels of care.[29] These costs were inflated to 2024 values using Thai gross domestic product deflators from the World Bank,[46] and projected over a 30-year period, corresponding to the expected lifespan of patients with β/Hb E thalassaemia,[47] at an annual discount rate of 3%. The discounted costs were then summed to obtain the lifetime cost of managing severe thalassaemia, which was used as the CET for this analysis. This amounted to 683 041.13 THB, ranging from 272 968.85 THB under lower levels of care to 949 989.85 THB under higher levels of care.

In addition to ICERs, we calculated a benefit-cost ratio (BCR), which compares the costs saved through screening (ie, lifetime cost of managing a patient with severe thalassaemia), denoted as L, to the screening cost per severe thalassaemia birth averted:

$$BCR = \frac{L}{ICER}$$

A BCR greater than 1 indicates that the benefits of screening are likely to exceed the costs, a BCR of 1 indicates a break-even point, and a BCR less than 1 indicates that costs are likely to outweigh benefits.[48]

Sensitivity analysis

We conducted deterministic sensitivity analyses (DSA), probabilistic sensitivity analyses (PSA), and scenario analyses to assess parameter uncertainty. In the univariate DSA, each parameter was varied individually between its minimum and maximum values while all other parameters were held constant, and the absolute change in the ICER value was examined. For this study, the 2.5th and 97.5th percentile values obtained from the parameter distributions were assigned as the minimum and maximum values, respectively (Supplementary file 1, Table S3). The parameter uncertainties which caused the greatest absolute change in the ICER values were ranked in descending order and presented as tornado diagrams. Threshold analyses were also performed to identify the critical parameter values at which these strategies became or stopped being cost-saving. Probabilities of healthy (non-carrier), carrier, or severe thalassaemia babies were excluded from the sensitivity analyses, as they are determined by

Table 1. Costs, Probabilities, and Other Variables Used in the Analyses

Category	Variable	Value	Range	Source
Costs in 2025 THB (USD)	Cost of CBC	120 ($3.69)	-	[38]
	Cost of Hb typing	270 ($8.31)	-	[38]
	Cost of DNA analysis	3000 ($92.31)	-	[38]
	Cost of PND (sample collection + DNA analysis)	5500 ($169.23)	-	[38]
	Cost of abortion	3000 ($92.31)	-	[38]
Probabilities	Prevalence of β/HbE thalassaemia trait in men in Thailand	0.16	0.13–0.18	[40]
	Prevalence of β/HbE thalassaemia trait in women (pregnant and non-pregnant) in Thailand	0.16	-	[40-42]
	Prevalence of β/HbE thalassaemia trait in either partner in Thailand	0.27	-	Calculated using Punnett square[44]
	Prevalence of β/HbE thalassaemia trait in both partners in Thailand	0.03	-	Calculated using Punnett square[44]
	Probability of couples receiving post-conception screening early (before 20 weeks' gestation) in Thailand	0.80	-	Assumption
	Probability of high-risk couples agreeing to PND	0.58	0.29–0.87	[25]
	Probability of couples with a severe thalassaemic foetus agreeing to an abortion	0.67	0.35–1.00	[25]
	Probability of carrier couples reconsidering their decision to conceive (pre-conception screening)	0.50	-	Assumption
	Probability of a severe thalassaemic baby, given both parents are carriers	0.25	-	Estimated from Mendelian pattern of inheritance[43]
	Probability of a carrier baby, given either or both parents are carriers	0.50	-	Estimated from Mendelian pattern of inheritance[43]
	Probability of a healthy baby depending on carrier status of both parents	Varies between 0.25, 0.50, and 1	-	Estimated from Mendelian pattern of inheritance[43]
Other variables	Average annual births in Thailand over three years (2022, 2023, 2024), rounded to the nearest 100 000	500 000	-	[45]
	Average Thai population in the reproductive age group (18–45 years) in 2024	25 529 914	-	[45]

Abbreviations: CBC, complete blood count; Hb, haemoglobin; DNA, deoxyribonucleic acid; PND, prenatal diagnosis; HbE, haemoglobin E.

Mendelian pattern of inheritance.[43]

PSA was then conducted to assess joint uncertainty across all parameters. Costs, constrained to be positive, were assigned gamma distributions, with standard deviations set at 20% of their mean values due to lack of empirical variance data. Probabilities were assigned beta distributions, while partner thalassaemia carrier status followed Dirichlet distributions, implemented as conditional beta distributions for computational convenience.[49] A Monte Carlo simulation with 10 000 iterations was performed, and results were presented using cost-effectiveness planes. It should be noted that some randomly sampled prevalence values from Dirichlet distributions exceeded a total probability of one, affecting computations in the DSA. These parameters were excluded from DSA but retained in PSA.[50] All the parameters used in the sensitivity analyses, with their distributions, lower and upper bound values, are presented in Supplementary file 1, Table S3.

We estimated the uncertainty around the BCRs under three different scenarios: the lower, average, and higher lifetime costs of managing a patient with severe thalassaemia in Thailand. In each scenario, we used the ICER uncertainties from the PSA simulations. Finally, we ran separate scenario analyses to explore the effect of thalassaemia prevalence rates in Thailand on the ICERs, and to identify the prevalence thresholds at which strategies became or ceased to be cost-saving.

Budget Impact Analysis

For the cost-saving strategies, a budget impact analysis (BIA) was conducted from the perspective of the NHSO to estimate the upfront costs of implementing thalassaemia screening strategies over a one-year horizon. These were calculated as the screening cost per couple, for each strategy, multiplied by the eligible population. For Strategy 1 (post-conception screening), the annual number of births (2022–2024 average) served as a surrogate for the eligible population,[45] with an estimated 50% requiring definitive thalassaemia testing. For the pre-conception strategy, the target population included Thai individuals aged 18-45,[45] modelled as couple units. To account for varying levels of programme adoption, our analysis evaluated the annual budget impact across three uptake scenarios: 25%, 50%, and 75%. Detailed justifications for these assumptions are provided in Table S4 (Supplementary file 1).

Software and Reproducibility

All analyses were conducted in R version 4.4.3, using the "*rdecision*" package.[51] All R codes are available at https://github.com/PhyllisTenkorang/Econ_model_Thalassaemia.git.

Results

Cost-Effectiveness Analysis

In the baseline analysis, the ICERs for thalassaemia screening compared to "no screening" were 220 132.36 THB ($6773.30), 291 750.00 THB ($8976.92) and 340 414.76 THB ($10 474.30) per severe thalassaemia birth averted for Strategy 4 (combination screening), Strategy 2 (pre-conception screening with targeted DNA analysis), and Strategy 1 (current post-conception screening), respectively (Table 2). All three ICERs were substantially lower than the lifetime cost of managing a patient with severe thalassaemia, 683 041.13 THB ($21 016.65), suggesting that these strategies are cost-saving. In contrast, the ICER for Strategy 3 (pre-conception screening with universal DNA analysis) was 1 875 000 THB ($57 692.31) per severe thalassaemia birth averted, almost three times the lifetime cost of managing severe thalassaemia; implying that it is not cost-saving.

Sensitivity Analysis

Univariate DSA showed that the costs of initial screening, ie, CBC and Hb typing costs for Strategies 1, 2 & 4, and the DNA analysis cost for Strategy 3, were the most sensitive parameters which caused the greatest absolute changes in the ICER values (Supplementary file 1, Figure S1).

Threshold analysis (Supplementary file 1, Table S5) suggested that, for Strategy 2, thalassaemia screening may not be cost-saving when the probability of couples reconsidering their decision to conceive falls below 0.22. In contrast, Strategy 3 may become cost-saving only if the cost of DNA analysis is less than or equal to 2185.73 THB per couple. At the current cost, this strategy remains unlikely to be cost-saving even if all high-risk couples reconsider their decision to conceive.

PSA revealed that the probabilities of the strategies being cost-saving, based on 10 000 iterations, were 100% [range: 14% to 100%], 100% [range: 39% to 100%], 0% [range: 0% to 1%], and 100% [range 86% to 100%] for Strategies 1, 2, 3, and 4, respectively (Figure 3). These ranges of probabilities were estimated by determining the proportion of PSA simulations below the lower, average, and higher lifetime costs of managing a patient with severe thalassaemia in Thailand (CETs). The 95% uncertainty intervals for the ICERs, and the BCR using the average lifetime management cost, are also presented in Table 2. Table S6 (Supplementary file 1) shows all the uncertainty intervals for the BCRs using the lower, average, and higher lifetime costs of managing severe thalassaemia.

In addition, scenario analyses revealed that at prevalence rates below 10% for β/Hb E thalassaemia carriers in Thailand, Strategies 1 and 2 may not be cost-saving from our models. For Strategy 4, the prevalence rate threshold is lower at 8.5%. In contrast, Strategy 3 may become cost-saving at prevalence rates above 27%.

Budget Impact Analysis

For Strategy 1 (post-conception screening), the estimated annual budget impact of upfront implementation costs increases from about 42 million THB at 25% uptake to about

Table 2. Cost-Effectiveness Analysis Results

Outcomes	Strategy 1: Post-conception	Strategy 2: Pre-conception With Targeted DNA Analysis	Strategy 3: Pre-conception With Universal DNA Analysis	Strategy 4: Combined Strategy
Cost of screening per couple in THB (USD)	677.30 [489.87–899.27] ($20.84 [$15.07–$27.67])	933.60 [646.45–1266.23] ($28.73 [$19.89–$38.96])	6000.00 [3870.96–8524.48] ($184.62 [$119.11–$262.29])	978.16 [688.61–1320.78] ($30.10 [$21.19–$40.64])
Cost of "no screening"	0.00	0.00	0.00	0.00
Probability of severe thalassaemia birth with screening	0.0044	0.0032	0.0032	0.0020
Probability of severe thalassaemia birth without screening	0.0064	0.0064	0.0064	0.0064
Proportion of severe thalassaemia births averted with screening	0.0020 [0.0013–0.0028]	0.0032 [0.0022–0.0044]	0.0032 [0.0022–0.0044]	0.0044 [0.0032–0.0059]
Incremental screening cost per severe thalassaemia birth averted in THB (USD)	340 414.76 [231 424.56–511 350.71] ($10 474.30 [$7120.76–$15 733.87])	291 750.00 [184 897.60–453 567.43] ($8976.92 [$5689.16–$13 955.92])	1 875 000.00 [1 080 308.71–3 123 987.68] ($57 692.31 [$33 240.27–$96 122.70])	220 132.36 [146 971.65–327 140.25] ($6773.30 [$4522.20–$10 065.85])
Benefit-Cost Ratio (using the average lifetime cost of managing severe thalassaemia)	2.01 [1.34–2.95]	2.34 [1.51–3.69]	0.36 [0.22–0.63]	3.10 [2.09–4.65]

Abbreviation: DNA, deoxyribonucleic acid.

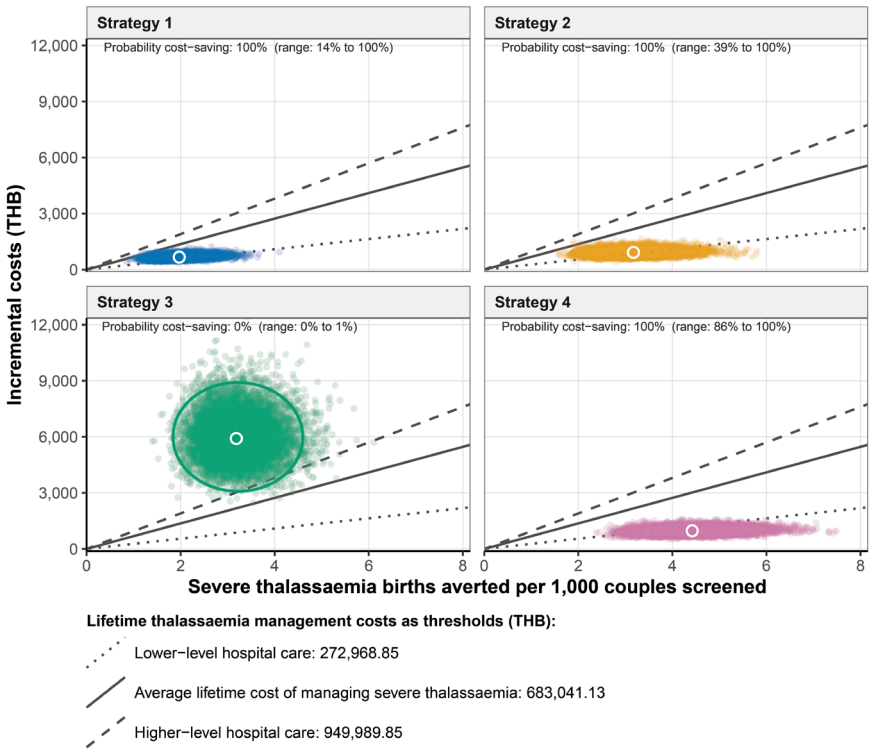

Figure 3. Probabilistic Sensitivity Analyses for the Cost-effectiveness Analyses of Thalassaemia Screening Strategies in Thailand. The cost-effectiveness plane shows incremental costs (THB) against the number of severe thalassaemia births averted per 1000 couples screened. Each small, coloured point represents one iteration of the Monte Carlo simulation for the respective strategy. Large white points indicate the median estimates, and ellipses show the 95% uncertainty regions. Points below the threshold lines represent the cost-saving iterations. The probability of being cost-saving is calculated as the proportion of Monte Carlo iterations in which the ICERs falls below the lifetime costs of managing severe thalassaemia in Thailand. Abbreviation: ICERs, incremental cost-effectiveness ratios.

127 million THB at 75% uptake (Table 3). Strategy 1 has the lowest annual budget impact because it targets a relatively smaller population and has the lowest screening cost per couple. In contrast, Strategy 4 (combined strategy) has the highest budget impact, with upfront costs of implementation exceeding 9 billion THB at 75% uptake (Table 3).

Discussion

This study evaluated the cost-effectiveness and annual budget impact of the current thalassaemia screening strategy in Thailand as well as alternative strategies which may be implemented. Our model findings add to the limited evidence available for Thai policy-makers in allocating resources for thalassaemia prevention. In our study, post-conception screening (Strategy 1; current), pre-conception screening with targeted DNA analysis (Strategy 2) and the combination strategy (Strategy 4) have been estimated to be cost-saving in Thailand compared to "no screening." The annual budget impact of their upfront implementation costs was estimated to range from 42.33 million THB ($1.30 million) to 9.39 billion THB ($288.93 million) depending on the strategy adopted and uptake rates.

The most appropriate method to conduct EEs of screening strategies for genetic diseases, including thalassaemia, is not clear.[18] Recommended outcomes for EEs like cost per QALY gained or DALY averted are typically not presented for these evaluations because DALYs averted for preventing severe thalassaemia births may be substantial whereas no QALYs

Table 3. Budget Impact Analysis Results for Cost-Saving Strategies

Outcome	Strategy 1: Post-conception	Strategy 2: Pre-conception, Targeted DNA Analysis	Strategy 4: Combined Strategy
Cost of screening per couple in THB (USD)	677.30 ($20.84)	933.60 ($28.73)	978.16 ($30.10)
Total eligible population (rounded to the nearest 100 000)	250 000	12 800 000	12 800 000
Annual budget impact of upfront costs with 25% uptake in THB (USD)	42 331 250 ($1 302 500)	2 987 520 000 ($91 923 692)	3 130 112 000 ($96 311 138)
Annual budget impact of upfront costs with 50% uptake in THB (USD)	84 662 500 ($2 605 000)	5 975 040 000 ($183 847 385)	6 260 224 000 ($192 622 277)
Annual budget impact of upfront costs with 75% uptake in THB (USD)	126 993 750 ($3 907 500)	8 962 560 000 ($275 771 077)	9 390 336 000 ($288 933 415)

Abbreviation: DNA, deoxyribonucleic acid.

can be said to have been gained since birth was avoided.[18] This introduces potential bias and raises ethical issues when interpreting results. Furthermore, the decision of whether to include the effects of pregnancy-related screening on the mother and/or unborn foetus, introduces additional complexities.[52] Outcomes which compare screening cost per severe case averted to lifetime treatment costs of managing severe thalassaemia are thus generally acceptable,[18] and EEs of thalassaemia screening in Israel, Iran, Hong Kong, and Sri Lanka have used this approach.[53]

Various studies have estimated screening to be cost-saving compared to treating thalassaemia.[20,32,33,54-58] These studies assessed cost-effectiveness of screening by comparing programme costs of implementing thalassaemia screening over a period, and the number of severe cases averted, to the treatment costs saved by averting these cases. None, except the study in Sri Lanka,[20] compared an implemented screening strategy to potential alternative strategies.

In Israel, prenatal screening was estimated to cost $67 369 per severe thalassaemia case averted with a BCR of 4.22 to 6.01.[57] In Iran, a CEA using a hybrid decision tree-Markov model to estimate the cost of premarital screening and lifetime cost of managing severe thalassaemia, reported screening cost of $32 624 per severe case averted with a BCR of 4.19.[55] In 2003, an evaluation of prenatal screening for severe thalassaemia in Chiang Mai reported a BCR of 20.6 compared to treatment.[33] This study reported low initial screening costs for couples (250 THB) without the costs of confirmatory tests, possibly accounting for the high BCR. In addition, recent studies support the cost-effectiveness of prenatal (post-conception) thalassaemia screening in Thailand, showing that simultaneous couple screening (mean corpuscular volume/mean corpuscular hemoglobin + DCIP followed by Hb typing, if both are positive) is the most efficient protocol,[34] and that genetic testing can achieve societal cost-savings of about $490 per severe case prevented.[35] While these studies focus exclusively on post-conception screening, our study extends the analysis by including alternative pre-conception strategies.

The above examples signify that regardless of the strategy chosen, thalassaemia screening appears to be cost-saving. The extent of how cost-saving it is seemingly depends on the CEA methods employed. With the conservative life-expectancy for severe thalassaemic patients chosen for our study (30 years), implying an equally conservative lifetime cost of treatment, the BCRs estimated from our models are lower than what is reported in the literature; thalassaemia screening in Thailand may probably be more cost-saving than what we have estimated.

Although the CET used in this EE represents a pragmatic way to interpret the ICERs, there are critiques with its choice. The study population used in the cost-of-illness analysis highlighted a proportion of β/Hb E thalassaemia to homozygous β-thalassaemia of 10:1, which was higher than that in the general population (5:1) at the time.[29] Therefore, these results may not have been completely representative of the Thai population. HSCT costs were also not captured in the analysis possibly due to its limited availability in Thailand. Regardless, the study presented a comprehensive cost-of-illness analysis for severe thalassaemia treatment in Thailand, viable for interpreting the ICERs in our models.

Pre-conception screening with targeted DNA analysis (Strategy 2) was found to be cost-saving in this study. When combined with post-conception screening, it is even more cost-saving. However, this finding is heavily dependent on the assumption that 50% of high-risk couples will reconsider their decision to conceive as this strategy is yet to be implemented in Thailand. Though studies from the US have reported reconsideration rates of about 60% after genetic testing,[59,60] the true value in the Thai context should be obtained by piloting pre-conception screening before implementation on a large-scale. Regions with the highest burden of thalassaemia in Thailand, like the Northern and North-East regions, could be targeted for this pilot implementation. This may be warranted as pre-conception screening utilises a population-based approach with the eligible population larger than that in post-conception screening, accruing higher upfront implementation costs ($91.92 million to $288.93 million). Depending on the setting under which it is implemented, it may attract additional programmatic costs which may also affect its potential cost-effectiveness and affordability.

Thalassaemia screening for school-aged children in Thailand was not included in this CEA as this strategy requires them to recall their carrier status in future and prompt their partners for testing, if needed, before they conceive. The decision choices from this strategy are more complex and cannot be adequately captured with decision trees. Dynamic models assessing the impact of screening may be a better methodology to evaluate the effects of screening school-aged children as has been done in UAE and India.[61,62] This was out of the scope of this study but could be considered in future modelling studies for thalassaemia prevention in Thailand.

Practical Implications

Though assumed to be widely available in our model, post-conception screening services may not be equitably distributed throughout Thailand.[63] Lower-level facilities may not have the capacity to undertake all the necessary tests in this strategy.[64,65] There may be potential delays in referring patients to higher facilities and interruption of timely interventions to prevent severe thalassaemia births. To improve implementation, laboratory capacity should be enhanced in these lower-level facilities with proper co-ordination between hospitals to ensure seamless thalassaemia screening services in Thailand.

The Thai government could leverage public acceptability of its successful family planning programme to facilitate implementation of pre-conception screening.[66,67] Close to 80% of Thai women aged 15–49 years are reported to use some form of contraception.[68] Pre-conception screening services could equally be made available through avenues that provide family planning in Thailand to encourage screening uptake.

Thalassaemia prevalence rates remain highly influential in CEA of its screening strategies.[69] Our models suggested that screening may not be cost-saving with low thalassaemia prevalence rates in Thailand (<10%). The model for Strategy 3 further indicated that its high upfront costs may be justified

with thalassaemia prevalence rates above 27% in Thailand. These findings signal the need for robust surveillance on thalassaemia prevalence if these CEA models are to be improved in future for better informed policy decisions. As highlighted in Iran, tailoring thalassaemia screening to local prevalence rates may represent more efficient use of resources.[55]

Migrant Populations and Thalassaemia in Thailand

There are peculiar challenges with thalassaemia management for minority groups, like the migrant population, in Thailand.[70] There has been an increase in the number of migrant workers coming to Thailand from Cambodia, Laos People's Democratic Republic, and Myanmar due to activities of the Association of South-East Asian Nations Economic Community.[71,72] Found to have an equally high thalassaemia burden as the Thai population, these migrant populations have genetic traits peculiar to their countries of origin and possibly uncommon in Thailand creating diagnostic and screening challenges.[71,73] Substantial out-of-pocket payments, low utilisation of healthcare and cultural factors have also been cited as barriers to thalassaemia screening for migrant populations in Thailand.[70]

To fully address the burden of thalassaemia and ensure health equity for migrant populations in Thailand, a recommendation may be to restructure the migrant health insurance scheme established by the Thai government.[74] Pooling multiple sources of funds through taxes, reduced premiums and partnerships with private insurance schemes could be explored. Stakeholder engagement with representative migrant groups could also be undertaken to ensure better alignment of the migrant scheme with the needs of the target population.

Ethical and Social Issues

EEs are based on utilitarian principles which favour the most cost-effective interventions to maximise population health.[75] However, in thalassaemia screening, there are major steps that draw on the autonomy of individuals in deciding whether they want to be screened, accept PND/abortion or reconsider their decision to conceive/marry. Thus, even though this EE suggests that thalassaemia screening in Thailand is cost-saving, its implications require a measured consideration of what this means for individual autonomy.

Our findings draw out important ethical considerations. For example, should Thailand emulate Iran and North Cyprus[55,76] and make thalassaemia screening mandatory before provision of ANC services? That would probably facilitate rapid reduction in severe thalassaemia births and maximise population health. Or should they focus on increased public sensitisation and hope that behavioural, socio-cultural and religious factors are positive enough to encourage individuals to voluntarily screen for thalassaemia? This would preserve individual autonomy but may mean it will take a significantly longer time, if ever, to reduce the thalassaemia burden in Thailand. The latter may be more attractive and signifies the need for increased public sensitisation about thalassaemia to accelerate screening uptake.

Religious and community leaders have been instrumental in the popularity of contraception services in Thailand and could equally act as "positive influencers" to promote thalassaemia screening.[67] However, there is a potential for religion to also complicate the adoption of thalassaemia screening in Thailand as previous studies from Iran, Bangladesh, and UK have indicated that some individuals believe they deserve to have thalassaemic children based on their religion.[77-79] The role of religion in facilitating or hindering the acceptance of various thalassaemia screening strategies in Thailand must therefore be comprehensively explored.

Finally, by comparing ICERs to the lifetime cost of managing severe thalassaemia, are implicit assumptions being made that investments in abortion and reconsideration of decision to conceive may be better than improving management of severe thalassaemia? Considering the sustained efforts by the Thai government to improve the life-expectancy of patients with severe thalassaemia, there may be deliberations around prioritisation of screening. However, these assertations are not the focus of this study but by undertaking this EE, we have provided a framework making explicit use of available evidence to support decisions for thalassaemia screening in Thailand. This health economic framework can help promote accountability in the decision-making process for Thai policy-makers.

Study Strengths and Limitations

Overall, this study is a valuable addition to the limited evidence on cost-effectiveness and affordability of thalassaemia screening strategies in Thailand. We undertook an EE comparing relevant alternatives to "no screening" using decision analytic modelling. To our knowledge, this study is the first of its kind for thalassaemia prevention in Thailand and provides a foundation for future studies on the subject. By being explicit in our methodology, similar methods could also be reproduced for haemoglobinopathies in other resource-limited settings.

However, our study has some limitations. The use of decision trees limited our assessment of the complex dynamics of behavioural factors on the cost-effectiveness of these screening strategies. This may potentially affect the inferences made from our models. Qualitative studies exploring how behavioural, religious and socio-cultural factors affect implementation of thalassaemia screening in Thailand will be useful to complement the EE undertaken in this study. Future studies could also use disease dynamic modelling to investigate the influence of these factors on the cost-effectiveness of different thalassaemia screening strategies in Thailand in the long-term.

The assumptions made in estimating the budget impact may also result in significant over/underestimation. Regardless, by presenting different scenarios for the BIA, we provide useful ranges to help fiscal planning. Proper monitoring and evaluation systems must be established to track the number of couples who are routinely screened for thalassaemia as this will be highly useful to improve future BIAs of these screening strategies. The establishment of the national perinatal registry portal in Thailand is highly commendable,[80] but widespread

accessibility to its data could enhance transparency.

Lastly, by not comparing the ICERs in this study to Thailand's CET, the inferences made from our models do not address opportunity costs of investing in thalassaemia screening in Thailand. Notwithstanding, these strategies improve health and are cost-saving in the long-term without opportunity costs. The broader community of health economists need to arrive at a consensus regarding standardised methods for conducting EEs of screening strategies for genetic diseases and determine more appropriate CETs for these evaluations. This will be particularly useful for EEs targeting screening for Hb Barts (severe α-thalassaemia), where maternal benefits are more complex to evaluate.

Conclusion

We have estimated that post-conception screening, pre-conception screening with targeted DNA analysis and the combination strategies are cost-saving compared to "no screening" in Thailand. Despite high upfront implementation costs, thalassaemia screening is cost-saving in the long-term by reducing severe thalassaemia births and total management costs. These findings add to the limited evidence available to Thai policy-makers on the value thalassaemia screening offers for money. Future studies exploring behavioural, religious and socio-cultural factors that affect thalassaemia screening will enrich the evidence provided through this EE.

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Disclosure of artificial intelligence (AI) use

Not applicable.

Ethical issues

Not applicable, as this study used secondary data from published sources and did not involve human participants or identifiable individual-level data.

Conflicts of interest

Authors declare that they have no conflicts of interest.

Authors' contributions

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Writing–original draft: Phyllis Tenkorang.
Writing–review & editing: Phrutsamon Wongnak, Benjaporn Kiatpakdee, Kittiphong Paiboonsukwong, Na'ima Nasir, Caesar Atuire, Chris Painter, and Wirichada Pan-ngum.

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Supplementary files

Supplementary file 1 contains Tables S1-S6 and Figure S1.

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