Policy Brief

PB

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Cost-Effectiveness of Cascade Testing for Familial Hypercholesterolemia in Thailand:

A Comparative Analysis of Genome Sequencing Methods Across Development Stages

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Key Takeaways

Genetic Disorder

Familial Hypercholesterolemia is a common genetic disorder that significantly increases the risk of cardiovascular disease (CVD).

Underdiagnosis

Less than 7% of FH cases are diagnosed globally; early detection can prevent CVD.

Study Aim

To evaluate the cost-effectiveness of different FH cascade genetic in Thailand and guide policy on integrating genetic testing into universal health benefit package.

Understanding Familial Hypercholesterolemia

What is FH?

FH is a genetic disorder causing high low density level (LDL) cholesterol (LDL–C) levels from birth, leading to an elevated risk of CVD and early mortality. It is primarily due to mutations in the LDLR genes.

Prevalence

FH affects about **1 in 500** people globally (0.2%). In Thailand, the prevalence is higher at 0.9%.

Health Impact

Without treatment, individuals with FH face a **10–20 times** higher risk of CVD and a 100 times increased risk of early death compared to the general population. Early detection is crucial.

Economic Burden

FH significantly impacts healthcare costs due to CVD. Despite the potential for prevention, less than **7%** of FH cases are diagnosed worldwide.

Study Objectives

1 **Evaluate the cost-effectiveness of cascade genetic testing using Whole Exome Sequencing (WES) and Long-Read Sequencingat (LRS) different stages of market development.**

Conventional Economic Evaluation

Develop a conventional cost-effectiveness analysis (CEA) model to assess the value for money of Whole Exome Sequence with (WES).

Early Stage Economic Evaluation

Determine Target Product Profile (TPP) for Long-Read Sequencing with (LRS), and its potential cost-effectiveness compared to standard lipid testing.

2 **Test the relevance and applicability of newly developed Precision Medicine Reference Case (PM-RC).**

Population: Individuals in Thailand aged 35 or older with elevated cholesterol levels (>189 mg/dL) and without prior diagnoses of FH or CVD.
Intervention: Genetic cascade testing using (WES) and (LRS).
Comparator: Opportunistic lipid testing (standard of care).
Outcome: Conventional Economic Evaluation (EE): Incremental Cost-Effectiveness Ratio (ICER) for WES. Early EE: Target Product Profile with (TPP) for LRS.

Results

Conventional Economic Evaluation

Whole Exome Sequencing Cascade Testing

Cost-effective with an ICER of **89,619 THB per Quality-Adjusted Life Year (QALY)**, below Thailand's willingness-to-pay (WTP) threshold of **160,000 THB**.

Outcomes

WES cascade screening would **prevent 16 CVD cases** per 100 people screened, resulting in **51 additional life years** and **209 QALYs** per 100 people.

One-way Sensitivity Analysis

Key variables include the number of relatives contacted and their uptake. If only one relative is contacted or if the uptake rate is less than **10%**, WES screening is not cost-effective.

Probabilistic Sensitivity Analysis

Shows a 77.8% likelihood of cost-effectiveness at the Thai WTP threshold, increasing to **95.1%** and **99.95%** at 1-and 3-times Thailand's GDP, respectively.

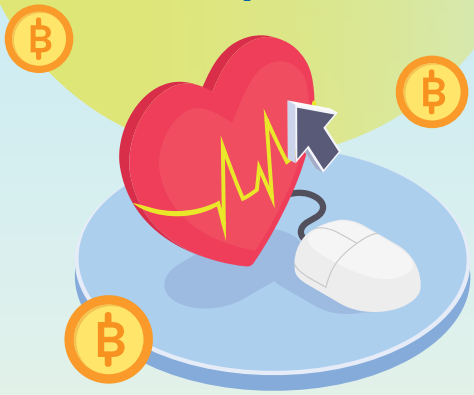
Figure 1

Cost-effectiveness acceptability curve of WES genetic testing vs standard of care

Early Economic Evaluation

Long-Read Sequencing

To be cost-effective at the Thai WTP threshold, the maximum cost package was 173,134 THB.



Uncertainty Analysis: The maximum cost package for LRS ranged from:

Minimum Acceptable Target:	Acceptable Target:	Ideal Target:
162,000 THB (minimum sensitivity and specificity).	**34,400** THB to **57,900** THB	**31,600** THB to **47,300** THB

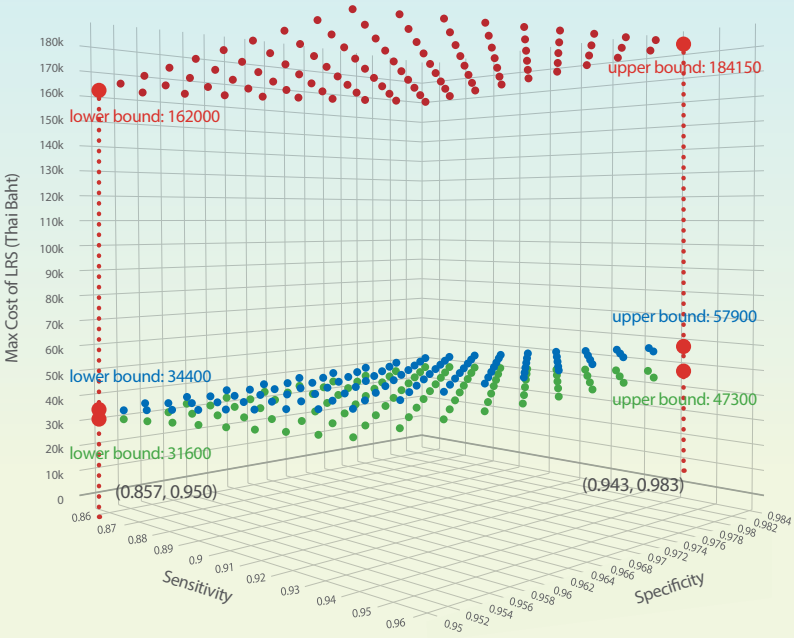


Figure 2

Uncertainty analysis for LRS accuracy. The figure shows results indicating the maximum cost package of LRS (z-axis) associated with different specificity (y-axis) and sensitivity (x-axis) combinations in the range provided by the technology developers.

Methodology

Approach:

Hybrid decision tree and Markov model reflecting Thai clinical practices.

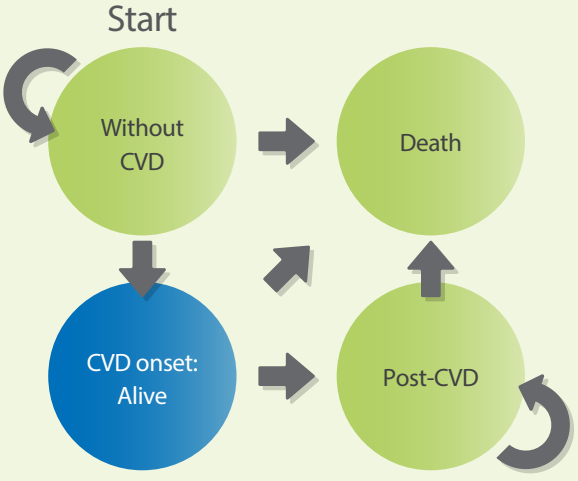


Figure 3

Markov Model to simulate CVD progression

Cohort:

Thai individuals aged 35+ with elevated cholesterol and no prior diagnoses or CVD.

Comparator & Intervention:

Opportunistic lipid testing (SoC) versus WES and LRS.

Data Sources:

Thai FH registry, local hospitals, literature, and expert opinions.

Method:

For conventional EE, ICER was assessed at the Thai WTP of 160,000 THB with sensitivity analyses. For early EE, TPPs were developed using a reversed CEA approach. Uncertainty in TPPs was assessed through probabilistic analysis and scenario analysis.

Recommendations & Conclusion

Innovative Study

First global evaluation of FH cascade testing using both conventional and early-stage economic evaluations.

Last Key Recomendations

For both conventional and early EE, the compliance with PM-RC was more than 60%, making it relevant and applicable to other countries.

Value

FH cascade testing is cost-effective at Thailand's WTP threshold.

Investing in FH cascade genetic screening is a cost-effective strategy that can improve early diagnosis and management of FH, ultimately reducing CVD risk and healthcare costs in Thailand.

Research Details

This policy brief is part of the research project titled "Development of reference case for economic evaluation on precision medicine for health insurance reimbursement in Thailand" funded by the Health Systems Research Institute (HSRI). The opinions and suggestions expressed in this document are those of the researcher and do not necessarily reflect those of HSRI.

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