Policy Brief

PB

Volume 12

Issue 182 • SEP 2024

Cost-Effectiveness of Cascade Testing for Familial Hypercholesterolemia in Thailand: A Comparative Analysis of Genome Sequencing Methods Across Development Stages

Dimple Butani

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.

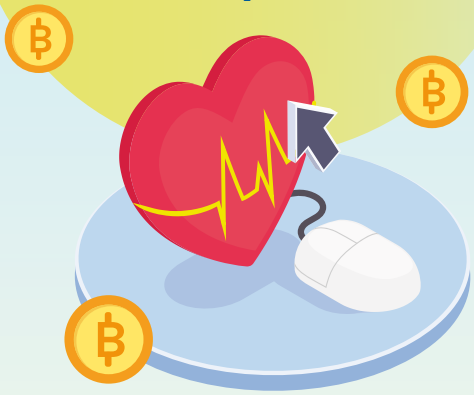
Figure 1

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

Early Economic Evaluation

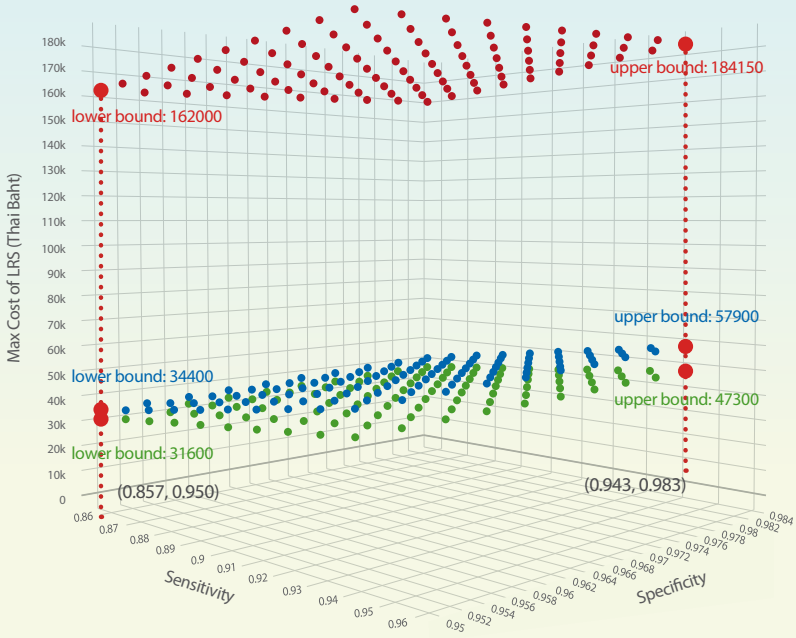
Long-Read Sequencing

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



- Minimally acceptable target
- Acceptable target
- Ideal target

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.

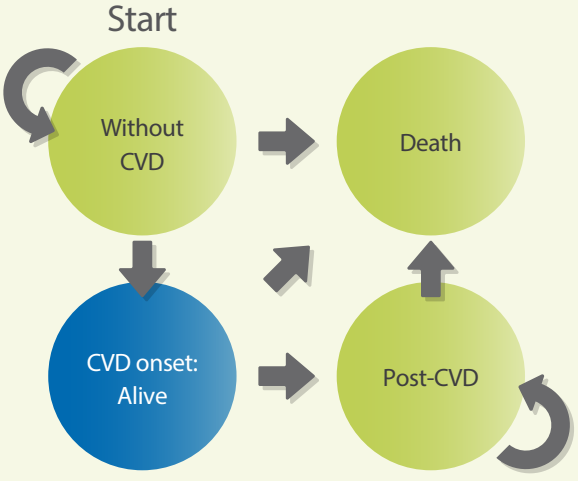


Figure 3

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 Recommendations

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) under Genomics Thailand. The opinions and suggestions expressed in this document are those of the researcher and do not necessarily reflect those of HSRI.

Researchers

Zhang Yue, Wenjia Chen, Parnnaphat Luksameesate, Dimple Butani, Sutinee Soopairin, Chanthawat Patikorn, Nattanichcha Kulthanachairojana, Pawarut Wongmanovisut, Thanapol Khuharatanachai, Weerapan Khovidhunkit, Poranee Ganokroj, Chanatjit Cheawsamoot, Vorasuk Shotelersuk, Yot Teerawattananon

References

1. Benn M, Watts GF, Tybjaerg-Hansen A, Nordestgaard BG. Familial hypercholesterolemia in the danish general population: prevalence, coronary artery disease, and cholesterol-lowering medication. J Clin Endocrinol Metab. 2012;97(11):3956-64.
2. Ademi Z, Marquina C, Zomer E, Bailey C, Owen A, Pang J, et al. The economic impact of familial hypercholesterolemia on productivity. J Clin Lipidol. 2020;14(6):799-806 e3.
3. Ademi Z, Watts GF, Juniper A, Liew D. A systematic review of economic evaluations of the detection and treatment of familial hypercholesterolemia. Int J Cardiol. 2013;167(6):2391-6.
4. Harada-Shiba M, Arai H, Ishigaki Y, Ishibashi S, Okamura T, Ogura M, et al. Guidelines for Diagnosis and Treatment of Familial Hypercholesterolemia 2017. J Atheroscler Thromb. 2018;25(8):751-70.
5. Goldberg AC, Hopkins PN, Toth PP, Ballantyne CM, Rader DJ, Robinson JG, et al. Familial hypercholesterolemia: screening, diagnosis and management of pediatric and adult patients: clinical guidance from the National Lipid Association Expert Panel on Familial Hypercholesterolemia. J Clin Lipidol. 2011;5(3):133-40.
6. Perez de Isla L, Alonso R, Watts GF, Mata N, Saltijeral Cerezo A, Muñiz O, et al. Attainment of LDL-cholesterol treatment goals in patients with familial hypercholesterolemia: 5-year SAFEHEART registry follow-up. Journal of the American College of Cardiology. 2016;67(11):1278-85.
7. Marquina C, Morton JI, Lloyd M, Abushanab D, Baek Y, Abebe T, et al. Cost-Effectiveness of Screening Strategies for Familial Hypercholesterolaemia: An Updated Systematic Review. Pharmacoeconomics. 2024;42(4):373-92.
8. Meng R, Wei Q, Zhou J, Zhang B, Li C, Shen M. A systematic review of cost-effectiveness analysis of different screening strategies for familial hypercholesterolemia. J Clin Lipidol. 2024;18(1):e21-e32.
9. Ganokroj P, Muanpetch S, Deerochanawong C, Phimphilai M, Leelawattana R, Thongtang N, et al. Gaps in the Care of Subjects with Familial Hypercholesterolemia: Insights from the Thai Familial Hypercholesterolemia Registry. J Atheroscler Thromb. 2023;30(12):1803-16.

If you're interested in receiving the PDF version of the Policy Brief, please sign up at **comm@hitap.net**
Specify your name and email address for delivery.
You can also download other Policy Briefs at https://www.hitap.net/resources/downloads

HITAP Foundation is a research organisation dedicated to studying both the positive and negative impacts of health technologies and policies. Its work supports government health policy decisions, including contributions to the National List of Essential Medicines and the National Health Security Office, as well as evaluations aimed at enhancing public policies.

Contact Information: Head Office : 88/22 Moo 4, 6th Building, 6th Floor, Department of Health, Ministry of Public Health, Tiwanon Road, Taladkwan Subdistrict, Muang Nonthaburi District, Nonthaburi 11000, Thailand

Tel. : +66 2590 4549, +66 2590 4374-5
Fax : +66 2590 4369

E-mail: **comm@hitap.net**
Website: **www.hitap.net**