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Cost-Effectiveness Analysis Of Biomarker-Based And Risk-Based Screening In Early Detection Of Preeclampsia: Systematic Review

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Abstract

Preeclampsia is one of the leading causes of maternal morbidity and mortality, especially in developing countries. Evaluation of the cost-effectiveness of first-trimester screening is essential to ensure accurate and efficient interventions. The objective of this review is to examine and compare the cost-effectiveness between biomarker-based preeclampsia screening and maternal risk-based screening in the first trimester of pregnancy. This study used a systematic review method based on the PRISMA guidelines. Articles searched through PubMed and ScienceDirect with a range of 2020–2025. Quality assessment using the CHEERS Checklist. Five studies were included in this review. All studies show that first-trimester preeclampsia screening is a cost-effective, even cost-saving strategy, especially when combined with early aspirin. Biomarker-based screening and risk algorithms are more cost-efficient than conventional screening. These results can be the basis for the formulation of maternal health policies in Indonesia. Preeclampsia, first trimester screening, cost-effectiveness, biomarkers.

Keywords: Biomarkers, Cost-Effectiveness, Preeclampsia, First Trimester Screening.

INTRODUCTION

Preeclampsia is still one of the main causes of maternal and perinatal morbidity and mortality in the world, especially in developing countries. According to the World Health Organization (WHO), 2011, preeclampsia and eclampsia are responsible for about 10–15% of all maternal deaths in the world. This disease is characterized by new hypertension that appears after 20 weeks of gestation accompanied by organ dysfunction, and can lead to premature birth and long-term health problems for both mother and baby (Duley, 2009). This condition is characterized by increased blood pressure and organ dysfunction that can worsen rapidly, especially if it occurs before 37 weeks gestational age or known as preterm preeclampsia (Gillon, et al., 2014; Duley, 2009). Early interventions such as low-dose aspirin have been shown to reduce the incidence of preeclampsia, especially if started before 16 weeks of pregnancy (Rolnik, et al., 2017). Therefore, early screening in the first trimester is essential to identify high-risk pregnant women who can benefit most from such preventive therapies.

A variety of approaches have been developed to conduct preeclampsia risk screening, ranging from standard maternal characteristics-based methods recommended by clinical guidelines such as NICE, to predictive models that integrate biomarkers and other biochemical parameters. Although biomarker-based approaches and predictive algorithms are considered to be more clinically accurate, their higher implementation costs raise questions regarding their efficiency and feasibility in the context of different health systems (Chappell, et al., 2021; Magee, et al., 2014). Cost-effectiveness analysis (CEA) is important to assess whether the intervention provides added value in economic and clinical aspects.

However, studies on CEA preeclampsia screening are still limited and results vary between countries, depending on the economic model used, the price of the intervention unit, and local epidemiological parameters. Most of the research was conducted in high-income countries and has not been systematically studied in terms of direct comparisons between the two main approaches to screening, namely biomarker-based and risk-based screening. This leaves a research gap, especially in understanding which strategies are the most cost-efficient in different healthcare settings.

This study offers novelty through the preparation of a systematic review of recent cost-effectiveness analysis studies that compare the two main interventions of first-trimester preeclampsia screening. By integrating evidence from different countries and reviewing the economic approaches used, the study is expected to answer the question of whether the biomarker-based screening approach is really economically feasible compared to conventional methods.
The purpose of this study was to examine and compare the cost-effectiveness between biomarker-based preeclampsia screening and standard maternal characteristics-based screening in the first trimester of pregnancy, with a systematic review approach to the current literature for the 2020–2025 period.

RESEARCH METHODS

Study Design

This article uses a systematic literature review research design that aims to analyze, review, and analyze the cost-effectiveness of preeclampsia screening in the first trimester, especially with a biomarker-based screening approach compared to risk-based screening. The formulation of the research questions is formulated in the PICO table below.

Table 1. Framework of PICO Studies

Components	Explanation
P (Population/Patient)	First trimester pregnant women
I (Intervention)	Biomarker-based preeclampsia screening (e.g., FMF algorithm)
C (Comparison)	Routine risk-based screening (standard care/NICE guideline-based screening)
O (Outcome)	Cost-effectiveness, service cost savings, prevention of preeclampsia and/or improvement of QALY (Quality-Adjusted Life Years)

Search Strategy

The details of the literature search strategy used in this article are to determine the selection of studies based on eligibility assessments, synthesis data, and extraction data, using a systematic search approach from several leading databases such as PubMed, Scopus, and ScienceDirect. The search process is carried out by utilizing Boolean operators and predefined keywords. Keywords used include: ("preeclampsia" OR "pre-eclampsia") AND ("cost-effectiveness" OR "economic evaluation" OR "cost-benefit analysis") AND ("first trimester screening" OR "biomarker-based screening" OR "risk-based screening"). The time range for publication of literature is limited from 2020 to 2025 to ensure the relevance and up-to-date of the study.

Eligibility Criteria

The inclusion criteria in this study are research articles that evaluate the cost-effectiveness of preeclampsia screening in the first trimester, studies that compare biomarker-based screening with maternal risk-based screening, studies that use cost-effectiveness analysis methods, articles written in English and available in full-text form, studies conducted in healthcare settings such as hospitals, antenatal clinics, or systems national health. Meanwhile, exclusion criteria include review, editorial, opinion, or case report studies without empirical economic data, studies that only discuss preeclampsia screening without including economic analysis, articles that cannot be accessed in full-text, and studies outside the 2020–2025 range.

Literature Selection

The literature that has been found is selected using the Preferred Reporting Items for Systematic Reviews and Meta-analysis or PRISMA method depicted in the flow diagram in figure 1. Based on the PRISMA diagram method that has been implemented, the results were obtained from a total of 201 literature

identified from two databases (PubMed and ScienceDirect), 21 of which were excluded due to data duplication, with 175 articles not in accordance with the inclusion and exclusion criteria based on titles, keywords, and abstracts. So that a total of 5 articles were obtained that will be used as a *reference for literature review*.

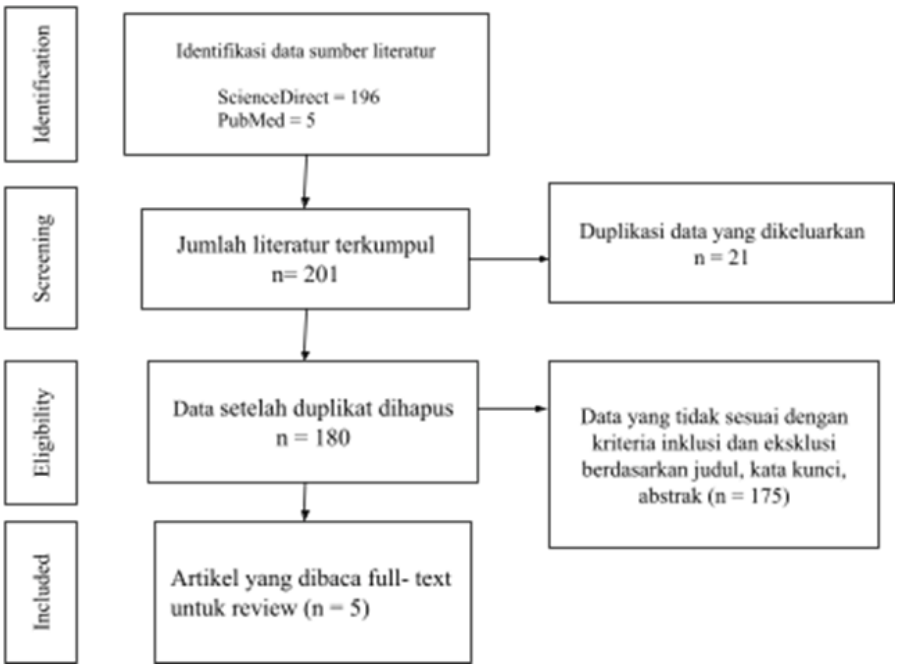

Figure 1. PRISMA Flow Diagram

Synthesis of Data

The synthesis process in this study was carried out by comparing literature that has met the inclusion and exclusion criteria, with reference to the research objectives. Then, the CHEERS Checklist (*Consolidated Health Economic Evaluation Reporting Standards*) was used to assess the quality of literature sources.

Table 2. CHEERS Scoring

Author	Year	Research Description	Score	Quality
Beernink et al.	2021	PT-PE screening in the Netherlands	56/56	Very Good
Nzelu et al.	2023	FMF algorithm + aspirin vs NICE guideline-based screening	52/56	Very Good
van Montfort et al.	2020	Risk-based preeclampsia detection care	48/56	Good
Violago & Quinio	2022	Screening + aspirin (ASA) in private hospital setting	48/56	Good

Mewes et al.	2020	Health economic model of biomarker-based screening (Germany & Switzerland)	54/56	Very Good

RESULTS AND DISCUSSION

The results of the five articles reviewed showed that preeclampsia screening in the first trimester, especially when combined with interventions in the form of low-dose aspirin administration early in pregnancy, tended to show cost-effective and even cost-saving results in various health systems. These studies use a variety of methodological approaches, ranging from economic modeling, before-after cohorts, to retrospective observations.

Table 3. Summary of Article Results

Author (Year)	Country / Population	Study Design	Intervention (Setting & Sample)	Comparator	Economic Outcome	CEA Conclusion
Mewes et al. (2020)	Germany & Switzerland / Pregnant women	Health economic modelling	First trimester biomarker-based screening	No screening (baseline)	ICER per PE case prevented (€14; WTP > €4,200); cost-saving in Switzerland	Cost-effective (Germany) and cost-saving (Switzerland)
Nzelu et al. (2023)	United Kingdom / 5,957 pregnancies	Retrospective observational + model	FMF algorithm + aspirin prophylaxis	NICE risk-based screening	ICER per QALY; cost-saving (£9.06 per patient); QALY gain 0.00006	Cost-saving and more effective
Violago & Quinio (2023)	Philippines / 1,916 pregnant women	Descriptive economic analysis	First trimester screening (FTS) + early aspirin	No screening / no aspirin	Cost: ₱9,993; savings ₱53,000–69,000 per patient	Highly cost-saving
Beernink et al. (2022)	Netherlands / National population	Cost-effectiveness modelling	First trimester biomarker-based screening	Routine maternal risk-based screening	€4 million savings/year; 228 PE cases prevented	Dominant (cost-saving and more effective)
van Montfort et al. (2021)	Netherlands / 3,425 women (2 cohorts)	Before–after cohort study	Risk-based care using first trimester prediction algorithm	Care-as-usual	Savings €2,766 per patient; no decrease in quality of life	Cost-effective

DISCUSSION

The study of Mewes et al. (2020) in Germany and Switzerland used a simulation-based health economics model to project the cost and effectiveness of PE screening using biomarkers compared to maternal characteristics-based screening. The results show that the biomarker-based approach is cost-saving in Switzerland and cost-effective in Germany if the WTP (willingness to pay) threshold is > €4,200. The economic outcome used is ICER per case of preventable preeclampsia. Research carried out by Beernink et al. (2022) using model simulations and located in the Netherlands, showed that biomarker-based screening for preeclampsia could prevent 228 cases of preeclampsia per year, with savings of €4 million. Research conducted by Violago & Quinio (2023) shows that the combination of FTS (first trimester screening) and early aspirin savings PHP53,000-69,000/patient taking into account the out of pocket cost of the patient. s

A study conducted by Nzelu et al. (2023), showed that biomarker + aspirin-based screening (FMF) resulted in a favorable ICER with a QALY gain of 0.00006 and saved £9.06 per patient. Meanwhile, van Montfort et al. (2021) conducted a risk-based care study based on risk prediction in the first trimester reduced the incidence of perinatal outcomes in nullipara and resulted in savings of €2,766 per patient.

Comparison Of Studies Between Countries

Based on the five studies reviewed, all of them consistently show that preeclampsia (PE) screening in the first trimester, especially when accompanied by early aspirin administration in high-risk pregnant women, is a strategy that is not only cost-effective but in some cases also cost-saving. Although each study used a different design and approach to economic analysis—such as economic simulation models, observational retrospective studies, and before-after cohort field trials—the results still support the effectiveness of screening and early intervention policies in reducing the cost burden of PE complications, both at the individual level and the health system as a whole.

Developed countries such as Germany, the Netherlands, Switzerland, and the United Kingdom have shown concrete results that biomarker-based screening, which combines maternal clinical data with biochemical and/or ultrasound indicators, can significantly identify pregnant women at high risk of PE more accurately than traditional methods that rely solely on the mother's medical history or age. The integration of these biomarkers allows for early detection of risks, so that preventive interventions such as low-dose aspirin can be given before 16 weeks of pregnancy—a critical phase in placental formation. This intervention has been shown to reduce the incidence of PE, especially the preterm PE type which has the highest morbidity and management costs. In addition, with the decrease in the incidence of PE, additional costs for intensive care of mothers and premature babies, emergency measures such as cesarean delivery, and extended hospitalizations can be significantly reduced.

The study from the Philippines provides an additional dimension that is particularly relevant for developing countries. In a healthcare system where financing is still dominated by out-of-pocket payments, cost-effectiveness is a key consideration in clinical and policy decision-making. The fact that an investment of less than ₱10,000 for screening and aspirin can prevent the cost of treatment of PE complications ranging from ₱100,000 to ₱150,000 proves that even with budget constraints, this strategy remains economically profitable. This sends a strong signal that similar interventions can be tailored and implemented in the Indonesian health system, especially in private hospitals and government facilities with the support of BPJS Kesehatan.

Furthermore, this cross-country comparison shows that the successful implementation of screening and early intervention depends not only on medical technology, but also on the readiness of the health system, including training of medical personnel, the provision of laboratory infrastructure for biomarkers, and integration into antenatal care service protocols. Flexible risk-algorithm-based implementation—for example by adopting approaches such as FMF (Fetal Medicine Foundation) or its local adaptation—can be a transitional solution to more comprehensive screening. In the context of Indonesia, where maternal and infant mortality rates are still high and preeclampsia is one of the main contributors, the adoption of this strategy not only has financial implications, but also has the potential to save lives and improve long-term quality of life.

Implications For Maternal Health Policy In Indonesia

The results of this review provide important implications for the maternal health care system in Indonesia. Currently, preeclampsia risk screening in antenatal services in Indonesia is still simple, focusing on the history of hypertension, maternal age, and blood pressure. There has been no integration of predictive approaches based on biomarkers or risk algorithms in primary service systems such as health centers. In fact,

based on WHO data, preeclampsia is a significant cause of maternal and neonatal deaths, and poses a large economic burden due to intensive care and long-term complications (WHO, 2022).

Therefore, the results of international studies that have been proven to be effective and economically efficient can be the cornerstone in national health policy advocacy. The integration of risk screening using algorithm-based predictive tools or biomarkers can be considered for inclusion in the Minimum Service Standards (SPM) of pregnant women, especially in areas with a high prevalence of preeclampsia. In addition, the administration of low-dose aspirin as a low-cost but high-impact intervention can be gradually adopted, in line with the WHO recommendation (2022) which states that aspirin is one of the preventive interventions that has been proven to reduce the incidence of preeclampsia in high-risk mothers.

However, the implementation of this strategy requires health system readiness, including training of health workers, the provision of basic laboratory facilities, and the widespread availability of aspirin. Policy support from the Ministry of Health, integration with BPJS Kesehatan, and regional-based pilot projects can be the first step before replication nationally.

CONCLUSION

This systematic review demonstrates that first-trimester preeclampsia screening, particularly biomarker-based approaches and risk prediction algorithms combined with early low-dose aspirin, consistently proves cost-effective across diverse healthcare settings including Germany, Switzerland, the Netherlands, UK, and the Philippines. All five reviewed studies report favorable economic outcomes, with some showing substantial cost savings (e.g., €4 million annually in the Netherlands, ₱53,000-69,000 per patient in the Philippines) and improved clinical results such as QALY gains and reduced preterm preeclampsia cases. These findings highlight the superior efficiency of advanced screening over conventional maternal risk-based methods.

However, limitations include methodological heterogeneity across studies, varying economic models, and limited generalizability to low-resource settings like Indonesia due to differences in healthcare infrastructure and cost structures. Future research should prioritize local adaptation studies and real-world implementation analyses in developing countries. Practically, these results advocate integrating biomarker-enhanced screening into Indonesia's antenatal care protocols, supported by BPJS Kesehatan, to optimize maternal health resource allocation while reducing preeclampsia-related morbidity and economic burden.

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