Indonesian Journal of Global Health Research
Volume 7 Number 6, December 2025
e-ISSN 2715-1972; p-ISSN 2714-9749
http://jurnal.globalhealthsciencegroup.com/index.php/IJGHR

INTEGRATING DRUG-RELATED PROBLEMS IDENTIFICATION AND INA-CBGS COST GAP ANALYSIS IN HEMORRHAGIC STROKE PATIENTS WITH HYPERTENSION: A PCNE-BASED SYSTEMATIC REVIEW

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ABSTRACT
Hemorrhagic stroke with comorbid hypertension is a complex clinical condition with a high economic burden. In the National Health Insurance (JKN) financing system, INA-CBG package rates often do not reflect the actual costs incurred by hospitals. One potential factor contributing to this cost gap is Drug-Related Problems (DRPs), which include incorrect dosing, drug interactions, and inappropriate therapy.Objective to assess the impact of DRPs on the cost gap between INA-CBG tariffs and actual costs of hemorrhagic stroke care with hypertension, as well as to evaluate the effectiveness of the PCNE method in identifying DRPs. Following PRISMA guidelines, a literature search was conducted on PubMed, ScienceDirect, ProQuest, and Google Scholar (2020–2025) using keywords related to hemorrhagic stroke, hypertension, cost-effectiveness, INA-CBGs, and PCNE. Primary studies analyzing DRPs and/or comparing actual costs with INA-CBGs tariffs in hemorrhagic stroke patients were included. The data were synthesized narratively, focusing on types of DRPs, application of PCNE, and cost gaps. Of 195 articles, 11 were included in the synthesis, with 3 highly relevant. DRPs (eg, inappropriate drug selection) were detected in over 60% of cases using PCNE, leading to increased costs. The gap between actual costs and INA-CBGs tariffs reached up to IDR 8 million. DRPs are significant determinants of cost inefficiency in the care of hemorrhagic stroke patients with hypertension. Systematic implementation of the PCNE method integrated with pharmacoeconomic evaluation is recommended to support the sustainability of JKN. This study suggests tariff adjustments for INA-CBGs and an expanded role for pharmacists.

Keywords: DRP; hemorrhagic stroke; hypertension; INA-CBGs; PCNE; pharmacoeconomics

How to cite (in APA style)
Ariawan, D. S., Nugraha, D. P., Ayu, F. D., Ningrum, V. D. A., & Julaeha, J. (2025). Integrating Drug-Related Problems Identification and INA-CBGs Cost Gap Analysis in Hemorrhagic Stroke Patients with Hypertension: A PCNE-Based Systematic Review. Indonesian Journal of Global Health Research, 7(6), 1–10. https://doi.org/10.37287/ijghr.v7i6.151.

INTRODUCTION

Hemorrhagic stroke is an acute neurological disease with high mortality and morbidity rates, accounting for approximately 29% of all stroke cases but responsible for 50% of the global disability burden (DALYs) (World Stroke Organization, 2025). In Indonesia, stroke is the third largest catastrophic disease within the National Health Insurance (JKN) system, with treatment costs reaching IDR 5.2 trillion in 2023 (Ministry of Health, 2023). Hypertension, as a major risk factor, increases clinical complexity and the risk of Drug-Related Problems (DRPs), such as inappropriate dosing or drug interactions, which can worsen clinical outcomes and increase treatment costs.

The JKN financing system uses INA-CBGs tariffs based on a prospective payment system; However, these rates often do not reflect actual costs, especially in hemorrhagic stroke cases with comorbid hypertension. Studies have shown a gap between real costs and INA-CBGs tariffs up to IDR 8.5 million in type C hospitals (Kaban et al., 2023). DRPs, such as polypharmacy or antihypertensive therapy failure, contribute to increased length of stay (LOS) and costs (Bhusal et al., 2025). The Pharmaceutical Care Network Europe (PCNE) method has proven effective in identifying DRPs, with detection rates up to 60% (Chen et al., 2020; Wenny et al., 2025), yet its integration with pharmacoeconomic analysis remains limited.

This study aims to evaluate the impact of DRPs on cost efficiency in the care of hemorrhagic stroke patients with comorbid hypertension at AN-NISA Hospital Tangerang through a PRISMA-based systematic review. By integrating comparative analyzes of actual costs and INA-CBGs tariffs with DRP identification using the PCNE method, this study offers novel insights to support optimization of pharmacological therapy and value-based health policy reform. The results are expected to provide evidence-based recommendations for INA-CBG tariff adjustments, improved hospital resource efficiency, and support for JKN sustainability.

METHOD

Study Design

This study employs a systematic review method to identify, evaluate, and synthesize scientific evidence on the influence of Drug-Related Problems (DRPs) on cost efficiency in the care of hemorrhagic stroke patients with comorbid hypertension. The review adopts a qualitative narrative approach based on the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. All references were managed using Mendeley reference manager to ensure citation consistency and eliminate duplicates.

Literature Search Strategy

A systematic search was conducted across four major scientific databases: PubMed, ScienceDirect, ProQuest, and Google Scholar, covering the period from January 2020 to May 2025. Keywords were formulated using Boolean operators ("AND" and "OR") with the following strings: "hemorrhagic stroke" AND "hypertension" AND "cost effectiveness" AND "PCNE" AND "INA-CBGs". Variations included: "hemorrhagic stroke", "hypertension", "real costs", "cost effectiveness", "Pharmaceutical Care Network Europe". Searches were limited to articles published in Indonesian or English with full-text availability. The search and article selection followed the PICOS framework (Population, Intervention, Comparator, Outcome, Study Design) to ensure relevance and quality of evidence analyzed. Inclusion Criteria, articles were included if they met the following criteria: Primary research (quantitative, observational, economic evaluation, or pharmaceutical intervention), analyzed hemorrhagic stroke patients (with or without comorbid hypertension), provided data on healthcare costs (actual costs or INA-CBGs tariffs), mentioned or analyzed Drug-Related Problems (DRPs), either descriptively or classified (PCNE or other methods). Available in full-text and published between 2020 and 2025.

Exclusion Criteria articles were excluded if they were narrative reviews, editorials, commentaries, or opinion surveys, they did not explicitly specify hemorrhagic stroke as the stroke type., they lacked information on service costs, INA-CBGs tariffs, or DRPs, they were duplicates or unavailable in full-text format, they were not available in Indonesian or English.

This review was not restricted to a single study design, given the complexity of the topic that requires a multidisciplinary approach.

Article Selection

The selection process consisted of three stages: (1) screening titles and abstracts, (2) full-text assessment, and (3) data extraction. Articles meeting inclusion criteria were evaluated based on study design, population, DRP classification methods, cost outcomes, and relevance to INA-CBGs.

Search Result Overview

A literature search across four major databases—PubMed, ScienceDirect, ProQuest, and Google Scholar—was conducted to identify relevant studies addressing hemorrhagic stroke, hypertension, cost of care (cost-effectiveness), INA-CBGs, and identification of Drug-Related Problems (DRPs) using the PCNE approach over the period 2019–2025. Search results indicated that topics individually such as "hemorrhagic stroke," "hypertension," and "cost effectiveness" returned thousands to hundreds of thousands of articles in all databases. However, when combined with INA-CBGs and PCNE, the number of available articles drastically decreases.

Table 1.
Number of Articles Based on Keyword Combinations in Four Databases (2020–2025)

Keyword search	Pubmed	Science Direct	Proquest	Google Scholar
Hemorrhagic stroke (2020-2025)	3,829	42,857	4.4470	17,100
Hypertension (2020-2025)	149,763	295,931	683,082	963,000
INA-CBGs (2020–2025)	6	39	46	1,730
Cost effectiveness (2020-2025)	41,455	651,871	1,825,904	17,800
PCNE (2020–2025)	75	96	718	2350
Hemorrhagic stroke AND hypertension AND cost effectiveness (2020–2025)	1	2,929	6,206	17,100
Hemorrhagic stroke AND hypertension AND PCNE (2020–2025)	0	0	7	93
Hemorrhagic stroke AND hypertension AND cost effectiveness AND PCNE(2020–2025)	0	0	6	86
Hemorrhagic stroke AND hypertension AND INA-CBGs AND cost effectiveness AND PCNE (2020–2025)	0	0	0	3

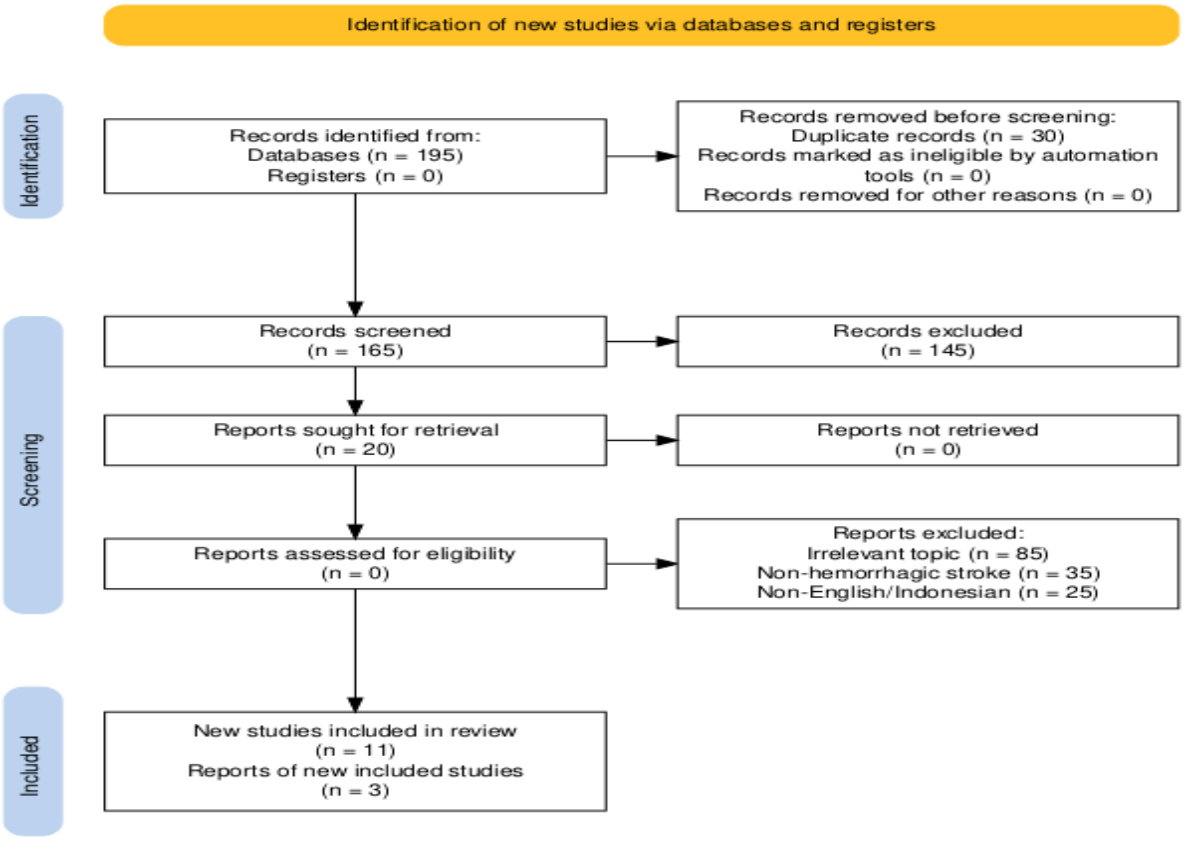

Figure 1. PRISMA flow diagram outlining the study selection process for inclusion in the systematic review, adapted from PRISMA 2020 guidelines.

The literature selection process followed the PRISMA 2020 guidelines, with article searches across the PubMed, ScienceDirect, ProQuest, and Google Scholar databases covering January 2020 to May 2025. The keywords used included "hemorrhagic stroke," "hypertension," "cost effectiveness," "PCNE," and "INA-CBGs." From 195 initially identified articles, 30 duplicates were removed, leaving 165 articles for title and abstract screening. Of these, 145 were excluded due to irrelevant topics (n=85), non-hemorrhagic stroke focus (n=35), or being published in languages other than English or Indonesian (n=25). After evaluating 20 full-text articles, 9 were further excluded because they were not specific to hemorrhagic stroke (n=3), did not contain INA-CBGs or cost data (n=3), or lacked PCNE/DRP analysis (n=3). Ultimately, 11 articles were included in the qualitative synthesis, with three considered highly relevant: Wenny et al. (2024), Mahardika et al. (2024), and Setiani et al. (2021).

Among the relevant studies, Wenny et al. (2024) conducted an observational study at Tanjungpura University Hospital, Pontianak, identifying Drug-Related Problems (DRPs) in stroke patients with hypertension using the PCNE V9.00 classification. They found a high prevalence of DRPs such as inappropriate drug selection (46.2%) and incorrect dosing (30.8%), with potential drug interactions as a key factor. However, this study did not analyze service costs or INA-CBGs cost gaps. Mahardika et al. (2024) performed a PRISMA-based systematic review analyzing healthcare costs in Indonesia, reporting average cost differences between actual expenses and INA-CBGs tariffs ranging from IDR 110,000 to IDR 8,000,000, particularly for patients with complex diseases like stroke. This study, however, did not include DRP analysis or PCNE use. Setiani et al. (2021) evaluated costs specifically for hemorrhagic stroke patients in Indonesia, finding an average cost difference of IDR 1,900,000 compared to ischemic stroke based on INA-CBGs tariffs, but they did not analyze DRPs or employ PCNE classification.

Additional supporting studies provided context but had limitations in direct relevance. For example, Budiyanti et al. (2024) and Chen et al. (2020) used PCNE to identify DRPs but were not specific to hemorrhagic stroke or INA-CBGs. Bhusal et al. (2025) reported DRP prevalence in stroke using non-PCNE classifications. Kusumawardani et al. (2020) and Priya et al. (2021) discussed DRPs in hypertension, while Girotra et al. (2020) and Siskou et al. (2023) analyzed stroke costs outside the Indonesian setting, limiting their applicability to INA-CBGs.

The literature synthesis highlighted several key findings. DRPs such as inappropriate drug selection and drug interactions are prevalent among stroke patients with hypertension, with some studies reporting prevalence up to 91.9% (Bhusal et al., 2025). The PCNE method has proven effective for DRP identification (Wenny et al., 2024; Budiyanti et al., 2024). There is a significant cost gap between actual service costs and INA-CBGs tariffs in hemorrhagic stroke cases, with differences reported up to IDR 8,000,000 (Mahardika et al., 2024) and IDR 1,900,000 (Setiani et al., 2021), often driven by treatment complexity and comorbidities. Notably, no study has yet integrated PCNE-based DRP analysis with INA-CBGs cost evaluation in hemorrhagic stroke, indicating a critical gap for future research.

Quality Appraisal

Each included study was assessed for methodological quality using standardized tools. Observational and cross-sectional studies were evaluated with the Newcastle-Ottawa Scale (NOS), while systematic reviews were assessed using the Joanna Briggs Institute (JBI) critical appraisal checklist. Studies were rated based on selection, comparability, and outcome/reporting quality. All assessments were performed independently based on full-text content available in the included studies. Any unclear criteria were scored conservatively to avoid overestimation. Only studies scoring moderate to high quality were included in the final synthesis.

RESULT

Based on a literature synthesis, PCNE-based DRPs, such as inappropriate drug selection and drug interactions, impact the cost-efficiency of care for hemorrhagic stroke patients with hypertension in Indonesia. The cost gap between INA-CBGs rates and actual costs is significant, with a difference of up to IDR 8,000,000, influenced by the complexity of therapy and DRPs. The use of PCNE can improve DRP identification, but its application in pharmacoeconomic analysis is still limited.

Although DRP classification has been widely used in clinical practice, its integration into healthcare financing policies remains very limited. This study reinforces the crucial role of clinical pharmacists in detecting and preventing DRPs early in hospitalization, particularly in patients with high comorbidities such as hypertension and hemorrhagic stroke. The PCNE approach not only aids in problem classification but can also be used as a tool for monitoring and justifying costs for more complex patient care.

Furthermore, given the finding that the difference between actual costs and INA-CBGs can reach up to IDR 8 million, PCNE-based DRP data can be used as a basis for healthcare facilities to propose revisions to INA-CBG rates. This strategy can strengthen hospitals' positions in tariff negotiations and improve resource efficiency. This integration of clinical and economic data is a step toward a more equitable and sustainable *value-based healthcare model for Indonesia's National Health Insurance (JKN) system.*

Table 2.
Characteristics of Studies Related to DRP and INA-CBGs in Hemorrhagic Stroke Patients with Hypertension Comorbidity

No	Researcher & Year	Types of research	Research Design	Data source	PCNE / DRP Indicator	Research methods	Difference between Real Costs and INA-CBGs
1	Mahardika et al., 2024	Systematic Review	Retrospective (10 primary studies)	Medical records, hospital fees, INA-CBGs	Not using PCNE	PRISMA review, cost analysis	Average negative difference: IDR 110 thousand – IDR 8 million
2	Setiani et al., 2021	Cost of Inventory Evaluation (COI)	Cross-sectional	Hospital data & medical records	Not mentioned	Regression analysis, T-test, ANOVA	Ischemic: IDR 4.6M; Hemorrhagic: Rp. 6.5M; difference: IDR 1.9M
3	Wenny et al., 2024	Observational	Cross-sectional, retrospective	Medical records of stroke patients with a history of hypertension (January-December 2023)	PCNE V9.00: Drug selection (C1.4), dose selection (C3.1, C3.2, C3.3, C3.4)	Retrospective data collection, identification of DRPs based on literature (Stockley's Drug Interaction, ISO, Pharmacotherapy Handbook), univariate analysis with Microsoft Excel	Not analyzed

Table 3.
Risk of Bias Assessment of Included Studies

Study	Study Type	Tool Used	Selection (★)	Comparability (★)	Outcome/ Reporting (★)	Total Score (Max 9)	Risk Level
Bhusal et al., 2025	Observational	NOS	★★★	★★	★★	7	High
Budiyanti et al., 2024	Observational	NOS	★★	★	★	4	Low
Chen et al., 2020	Observational	NOS	★★★	★	★★	6	Moderate
Girotra et al., 2020	Cost Study (USA	NOS	★★	★	★★	5	Moderate
Kusumawardani et al., 2020	Cross-sectional	NOS	★★	★	★★	5	Moderate
Mahardika et al., 2024	Systematic Review	JBI				10	High
Murgiati et al., 2024	Drug Utilization Study	NOS	★★	★	★★	5	Moderate
Priya et al., 2021	Observational	NOS	★★★	★★	★★	7	High
Setiani et al., 2021	Cross-sectional	NOS	★★	★	★★	5	Moderate
Siskou et al., 2023	Economic Evaluation (Greece)	NOS	★★	★★	★★	6	Moderate
Wenny et al., 2024	Observational (Cross-sectional)	NOS	★★★	★	★★	6	Moderate

Overall, the risk of bias across studies was acceptable, with most included articles rated as moderate to high quality. No study was excluded based on risk of bias, but their quality levels were considered in the interpretation of findings.

DISCUSSION

Impact of Drug-Related Problems (DRPs) on Cost Efficiency in Hemorrhagic Stroke with Hypertension

Drug-Related Problems (DRPs), including inappropriate drug selection, dosing errors, and potential drug interactions, are critical contributors to cost inefficiencies in managing hemorrhagic stroke with hypertensive comorbidity. Wenny et al. (2024) demonstrated that DRPs, particularly involving drug interactions, prolonged the length of stay (LOS) and increased treatment complexity, leading to substantial healthcare costs. Although the study highlighted clinical implications, it lacked quantitative pharmacoeconomic analysis, leaving a gap in the understanding of the financial burden attributed to DRPs.

Empirical studies by Mahardika et al. (2024) and Setiani et al. (2021) further support that therapeutic complexity—particularly when managing comorbid hypertension—drives the cost gap between actual hospital expenditures and INA-CBG reimbursement rates. Kusumawardani et al. (2020) found that DRPs in hypertensive patients can inflate treatment costs by up to 23%. The application of the PCNE classification system has proven effective in identifying these inefficiencies, especially with the high prevalence of DRP categories C1 (drug selection) and C3 (dosing) in stroke populations.

The Relevance of PCNE Classification in the Indonesian Health System

PCNE version 9.00 has been validated for its accuracy and sensitivity in detecting DRPs in complex patient populations. Studies by Budiyanti et al. (2024) and Wenny et al. (2024) confirmed its applicability in Indonesian clinical settings, particularly in capturing DRPs such as therapy duplication (C1.3) and contraindications (C1.2). However, the use of PCNE remains limited to DRP identification without integration into broader pharmacoeconomic evaluation or reimbursement frameworks like INA-CBGs.

This review identified a significant research gap: no studies have systematically integrated PCNE-based DRP analysis with a comprehensive evaluation of the cost gap under the INA-CBGs system. Saldanha et al. (2020) reported that 15.5% of DRPs in general hospitals were due to irrational therapy duration and high-cost medications, leading to cost increases of 18–22%. These findings underscore the urgent need for integrated analytical models combining PCNE classification with cost-effectiveness frameworks under Indonesia's national health insurance (JKN) policy.

A recent international study by Abushanab et al. (2023) in Qatar projected an annual economic benefit of USD 621,106 resulting from clinical pharmacist interventions across 852 cases in a tertiary hospital. The interventions—most commonly involving anti-infective agents, cardiovascular drugs, and prophylactic agents—effectively reduced adverse drug events (ADEs), generating substantial cost avoidance. This study validates the economic utility of pharmacist-led DRP management and supports the incorporation of such roles in cost-containment strategies within hospital systems.

Cost Gap in INA-CBGs and Policy Implications

Comparative analysis between real costs and INA-CBGs tariffs revealed a significant disparity—up to IDR 8 million per case (Mahardika et al., 2024). Key contributing factors include the use of high-cost medications (eg, newer antihypertensive agents), intensive interventions due to unresolved DRPs, and extended hospital stays due to suboptimal therapy. International evidence supports strategic investment in clinical pharmacy services. Simonetti et al. (2024) demonstrated a return on investment (ROI) of 1:24.2 through DRP prevention. Similarly, Abdul-Ghaffar et al. (2022) found that 100% of cardiovascular patients with complex comorbidities experienced at least one DRP, reinforcing the clinical and economic value of pharmacist involvement in therapy management.

CONCLUSION

This review highlights that DRPs substantially contribute to cost inefficiencies in the management of hemorrhagic stroke with comorbid hypertension. The current INA-CBGs tariff system often underestimates the real costs of care, especially in complex cases. The PCNE classification is an effective tool to identify and monitor DRPs but remains underutilized in economic evaluations.

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