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A Cost-Effectiveness Study of Antibiotic Drug Delivery System in Chronic Suppurative Otitis Media (CSOM)

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ABSTRACT

Background: Chronic Suppurative Otitis Media (CSOM) is a chronic inflammatory and infectious disease of the middle ear or mastoid cavity that can result in the loss of bodily functions or even death. The higher concentration of CSOM is found in developing nations such as Indonesia, where the population cannot afford treatment. In cases of persistent otorrhea following 3 weeks of treatment with topical ear antibiotics, oral antibiotics may be considered as a second line of treatment. Topical ear antibiotics are insufficiently available at healthcare facilities because they are not included in the Indonesian National List of Essential Medicines (NLEM).

Objectives: The objective of this study was to compare the cost-effectiveness of topical ear antibiotics versus oral antibiotics in the treatment of chronic suppurative otitis media (CSOM).

Methods: This study was a cross-sectional study using retrospective data from medical records and cost assessments at a rural hospital in the Gowa district of South Sulawesi. The effectiveness of the treatments was evaluated based on the frequency of visits to the ENT department, with antibiotic prescriptions and positive otorrhea.

Results: The findings revealed that the Average Cost-Effectiveness Ratio (ACER) for topical ear antibiotics was Rp 161,020, while the ACER for oral antibiotics was Rp 286,968. The Incremental Cost-Effectiveness Ratio (ICER) was determined to be Rp 351, and the Incremental Net Benefit (INB) was positive (Rp 99,857) at threshold Rp 434,500.

Conclusion: Our study found that topical ear antibiotics were more cost-effective than oral antibiotics when considering the INB values based on INA-CBGs, along with fluctuations in cost-effectiveness using sensitivity analysis.

Keywords: cost-effectiveness; CSOM; oral antibiotics; South Sulawesi; topical antibiotics

INTRODUCTION

Chronic Suppurative Otitis Media (CSOM) is a chronic inflammatory and infectious disease of the middle ear or mastoid cavity that can result in the loss of bodily functions or even death.[1] The prevalence of CSOM ranges from 65 to 330 million people worldwide, with a concentration in developing nations where the population lacks the means to pay for treatment.[1] According to WHO stratification, the prevalence of CSOM in Indonesia in 2007 was 5.4%, making Indonesia a country with a very high prevalence that requires attention.[1,2] CSOM is caused by bacterial infections including Pseudomonas aeruginosa (22-44%), Staphylococcus aureus (17-37%), Klebsiella pneumoniae (4-7%), Proteus vulgaris (0.9-3%), and others.[3] Therefore, the therapeutic objective was to eradicate the infection with antipseudomonal agents such as quinolones.[4,5]

Antibiotic treatment for CSOM included various drug delivery systems, such as ofloxacin or ciprofloxacin ear drops with or without topical steroids, and oral medications like ciprofloxacin, levofloxacin, clindamycin, and amoxicillin-clavulanate tablets.[5] Among these, only ciprofloxacin tablets are included on the Indonesian National List of Essential Medicines (NLEM) and have an availability rate of up to 80% in healthcare facilities.[6,7]

In cases of persistent otorrhea following three weeks of treatment with topical antibiotics, oral antibiotics may be considered the second-line option.[4,8] Topical quinolone was more effective than oral quinolone in treating otorrhea because it delivered a higher concentration of the drug to the middle ear.[9–11] The absence of preferred first-line treatments for CSOM in the Indonesian NLEM resulted in insufficient availability and supply at healthcare facilities.[7,12] Research on the availability of essential medicine in Indonesia found that the most common responses for stockouts were that the medicine was not needed (46%), not supplied (38%), substitutable (8%), and due to management difficulties (8%).[7]

The recommended antibiotic prescriptions were a 7-day course of topical ofloxacin (TOX) ear drops at 0.3%, administered as 2 drops three times per day, or oral ciprofloxacin (OCX) tablets at 500 mg, administered as 2 tablets per day. The empirical treatment with topical antibiotics was as effective as combined oral and topical antibiotics, and the inclusion of oral antibiotics did not have any additional beneficial effect.[1,9,13,14]

The prescription of oral antibiotics without consideration of CSOM management frequently resulted in increased costs and diminished treatment efficacy. A study in India revealed a rise in the average cost of antibiotics for CSOM patients from 2012 to 2014, which were INR 1550, INR 2036, and INR 3358, indicating that disease management can reduce the financial burden of treatment.[15] The challenge for pharmacists in Indonesia was ensuring that patients received the most cost-effective treatment.[13,16] The purpose of this study was to compare the cost-effectiveness of topical antibiotics and oral antibiotics in treating patients with CSOM as one of the considerations in selecting or withdrawing medication from the Indonesian NLEM.

METHODS

Study design

The study was designed as a cross-sectional observational study. Retrospective data collection consisted of examining medical records and calculating the costs of treating patients. During the course of the study, ethical approvals were obtained in consideration of the privacy and confidentiality of patients' medical records.

Population and samples

The population of the study consists of CSOM patients from a rural hospital in the Gowa district of South Sulawesi, Indonesia, during January to December 2021. The selection of study participants was based on a non-probability sampling method, specifically utilizing a purposive sampling technique known as total population sampling. This approach allowed for the inclusion of all individuals within the defined population, ensuring comprehensive data collection that reflects the entire group under study.

Patients who met the study's inclusion criteria were primarily diagnosed with CSOM and received treatment with TOX ear drops 0.3% at a dosage of 2 drops three times per day or OCX 500 mg tablets twice per day. Patients receiving an antibiotic combination, undergoing middle ear surgery, or having incomplete medical records were excluded from this study.

Study instruments

The study instrument utilized a simple form to collect patient ID, name, and treatment from the list of visits in the Ear, Nose, and Throat (ENT) Department. The other study instrument used a structured data collection form to extract relevant information from patient medical records. This form included key variables such as patient ID, name, age, gender, date of visit, diagnosis, presence of otorrhea as noted by the physician, prescribed treatment, clinical procedures performed, and the consulting physician's name.

Data collections

This study employed a retrospective data collection approach by reviewing medical records of CSOM patients at a rural hospital in Gowa District, South Sulawesi, Indonesia. We reviewed the number of visits to the ENT Department. After the screening, the complete medical record of patients was identified between TOX and OCX that met the inclusion criteria.

The frequency of patient visits was recorded, and those visits that met the criteria for further review were selected. After screening, the medical records were identified. Because the time evaluation of otorrhea was four weeks or more, we used four weeks (30 days) after the last visit as another episode of CSOM.[17] The final sample consisted of patients who met the inclusion criteria.

The effectiveness of antibiotic therapy was assessed by examining the frequency of subject visits to the ENT department based on two key parameters. The first parameter considered was the absence of recurrence in otorrhea, which served as the baseline evaluation, while the second focused on the prescribing of antibiotics. Follow-up visits determined by the physician were critical treatment variables for both the evaluation of otorrhea and the administration of antibiotics. In the evaluation of otorrhea, patients were categorized as effective if they showed no signs after one week from the first prescription. For antibiotic prescriptions, patients were deemed effective if they received one or more antibiotic prescriptions within one week after the initial visit.

In this study, direct medical expenses, such as antibiotic therapy, non-antibiotic therapy, and clinical procedures, were included in the cost analysis. These costs were derived from the hospital's perspective and represent the amounts billed to the patients for the services rendered during their treatment. The cost-related data were verified with the hospital to ensure accuracy in cost estimation.

Data Analysis

The study determined the Average Cost-Effectiveness Ratio (ACER) for each quadrant, emphasizing that less expensive values were deemed cost-effective.[18] The ACER calculation was provided by Rascati.[18]

$$ACER = \frac{Cost\ of\ Drug}{Effectiveness\ of\ Drug}$$

However, the calculation of the incremental cost-effectiveness ratio (ICER) was only performed in quadrants I and III. Negative ICER or quadrants II and IV values were not deemed cost-effective because they indicated higher costs and lower effectiveness compared to other interventions. The ICER calculation method was described by Rascati.[18]

$$ICER = \frac{Cost\ of\ Drug\ A - Cost\ of\ Drug\ B}{Effectiveness\ of\ Drug\ A - Effectiveness\ of\ Drug\ B}$$

Instead, the incremental net benefit (INB) was used as an alternative cost-effectiveness measure when the results was negative ICER.[19] The positive result of INB meaning the comparator treatment was deemed cost-effective.[20]

$$INB = (Willingness\ to\ Pay \times \Delta Effectiveness) - \Delta Cost$$

Willingness to Pay (WTP) was based on the reasoning provided by the Indonesian Minister of Health, who established the price structure for the Indonesian Case-Based Groups (INA-CBGs) price. This price framework ensured a fixed price to the Badan Penyelenggara Jaminan Sosial (BPJS) Kesehatan as the Indonesian National Health Insurance to pay public who treated for middle ear-related patient procedures. The threshold must be below the Gross Domestic Product (GDP).[18]

A data analysis was performed using the SPSS statistical program. To determine the patients' characteristics, descriptive statistics were employed. The analysis assessed associations between variables and treatment using odds ratios (OR) with 95% confidence intervals (CI). The analysis of the data also consisted of an independent t-test or a Mann-Whitney U-test with a significance level of 0.05, and a normality test was conducted before statistical tests. A sensitivity analysis was conducted to determine the effect on cost-effectiveness when specific variable values were altered while other variable values remained constant.[18] The analysis consisted of estimating the maximum and minimum values for the selected variables.

RESULTS AND DISCUSSION

Subject Characteristic

We found that pharmacoeconomically, TOX was more cost-effective than OCX, as indicated by a positive INB value at a WTP threshold of IDR 434,500. Of the total 68 patients, 12 received TOX therapy, and 56 received OCX therapy. Then, the effectiveness of treatment was evaluated based on two parameters: the ability to eliminate otorrhea as base and the number of antibiotic prescriptions given.

The results showed that a significant difference was only found in the number of antibiotic prescriptions. This finding also indicates that patients in the OCX group received more antibiotics than they should have, which have related to the implementation of prophylactic antibiotics as recommended by WHO in 2004. In addition, the absence of a significant difference between TOX and OCX in terms of improving otorrhea is in line with the meta-analysis conducted by Chong *et al*, while also mentioned that there is some evidence to suggest higher efficacy in topical therapy.[9] On the other hand, our results on cost-effectiveness parameters showed that the use of ACER is sensitive to changes, and the ICER is not alone in determining cost-effectiveness. Therefore, we used the INB approach and results also remained consistent even after being tested through sensitivity analysis on various cost ranges according to INA-CBGs and variations in BPJS contributions.

The proportion of female patients in this study was slightly higher (55.9%) than that of male patients. Most patients were within the 46–65 years age group (47.1%), with a mean age of 48.6 years. The Chi-square test revealed a statistically significant difference in age distribution ($\chi^2(4) = 50.676$; $p < 0.001$), whereas gender distribution showed no significant difference ($\chi^2(1) = 0.941$; $p = 0.332$). This finding is consistent with a study by Rahayu et al. at Sanglah General Hospital, which also reported that individuals aged 46–55 years made up the largest proportion of CSOM cases.[21] Furthermore, these results align with previous literature indicating that middle to older age is a relevant risk factor—likely due to degenerative changes in auditory structures and increased susceptibility to chronic infections during this life stage.[21–23] Additionally, findings by Mediawaty et al., along with a study conducted in Tanzania, support the notion that no significant anatomical or physiological differences exist between male and female ears that could explain gender-based variations in CSOM incidence.[10,24]

Among the 68 patients, the median number of antibiotic prescriptions was two, with an interquartile range (IQR) of two, indicating that 50% of participants received between one and three prescriptions. A total of 22 participants (32.4%) received only one antibiotic prescription. There was a statistically significant difference in the proportion of patients who received just one antibiotic prescription between the TOX (41.7%) and OCX (14.3%) groups (OR = 3.8; 95% CI: 1.1–13.9), suggesting greater prescribing efficiency in the TOX group. In comparison, a study conducted in Ethiopia found the mean number of antibiotic prescriptions among inpatients to be 1.7 ± 1.6, highlighting a similar range of utilization, though in a different clinical context.[25] Additionally, data from pharmacies in Medan reported that ENT specialists were the most frequent prescribers of antibiotics, accounting for 27.5% of all prescriptions, underlining their central role in antimicrobial use in otologic disorders.[26] One possible explanation for the fewer prescriptions in the TOX group lies in the formulation itself. TOX is typically dispensed in a single bottle that allows for multiple administrations without repeat prescriptions, whereas OCX is generally prescribed in fixed regimens requiring separate prescriptions for each course.[27] Furthermore, a study in Depok revealed that physicians often prescribed antibiotics for short durations, which may influence the frequency of antibiotic refills or repeats.[28] Beyond clinical factors, the choice to prescribe antibiotics is frequently influenced by a combination of medical reasoning and non-medical pressures, including fear of complications and parental demand, as demonstrated in a study involving pediatric patients with otitis media in Korea.[29] Taken together with our pharmacoeconomic findings, this prescribing pattern reinforces the interpretation that TOX not only has economic advantages but also may help reduce unnecessary antibiotic exposure, aligning with global efforts toward antibiotic stewardship.

Table I. Subject Characteristics

Characteristic	Subject (n = 68)
Ages	
>65 year	2 (2.9%)
46-65 year	32 (47.1%)
26-45 year	21(30.9%)
12-25 year	12 (17.6%)
0-11 year	1 (1.5%)
Gender (Female)	38 (55.9%)
Antibiotic Prescriptions (1 prescription)	22 (32.4%)
History of Antibiotic Use	13 (19.1%)
Evidence-based Antibiotic	60 (88.2%)
Follow-Up	55 (80.9%)

Among the 68 patients, 13 participants (19.1%) reported a history of antibiotic use. Interestingly, a significantly higher proportion of patients in the TOX group (58.3%) reported previous antibiotic use compared to the OCX group (26.8%) (OR = 4.3; 95% CI: 1.1–16.9). This suggests that topical therapy was often initiated after prior treatments—possibly systemic antibiotics—had failed to resolve recurrent otorrhea. Studies have shown that recurrent CSOM may be associated with suboptimal prior therapies, including the use of systemic antibiotics alone or non-antibiotic ear drops, which are inadequate to eliminate persistent infections.[3] Furthermore, concerns over ototoxicity—especially related to topical aminoglycosides—have led some physicians to prefer systemic antibiotics despite WHO's recommendation favoring topical agents in uncomplicated cases.[1,9,17]

In terms of treatment practices, 60 out of 68 prescriptions (88.2%) in this study were aligned with clinical guidelines, indicating a generally high level of evidence-based prescribing. Additionally, follow-up evaluations were completed for 55 patients (80.9%), reflecting substantial post-treatment monitoring compliance. However, antibiotic exposure itself remains a critical concern, as extensive literature shows that repeated or inappropriate antibiotic use contributes significantly to resistance development.[9,26,30] For instance, a study in Depok, Indonesia, found that 72.3% of antibiotic prescriptions were irrational concerning the duration of therapy, but in CSOM were 100% because the duration of therapy.[28] This finding is consistent with a broader review across Chinese hospitals, which identified prior drug exposure—particularly involving prolonged or incorrect antibiotic use—as a key driver of resistance in healthcare settings.[30] Reinforcing this, a more recent study by Kusumawardani et al. in Depok demonstrated that irrational prescribing practices remain prevalent, even after the implementation of accreditation systems, particularly related to therapy duration and drug selection.[31] Collectively, these findings underscore the urgent need for robust antimicrobial stewardship interventions and guideline dissemination in both primary and secondary care settings to ensure rational antibiotic use and mitigate the risk of resistance.

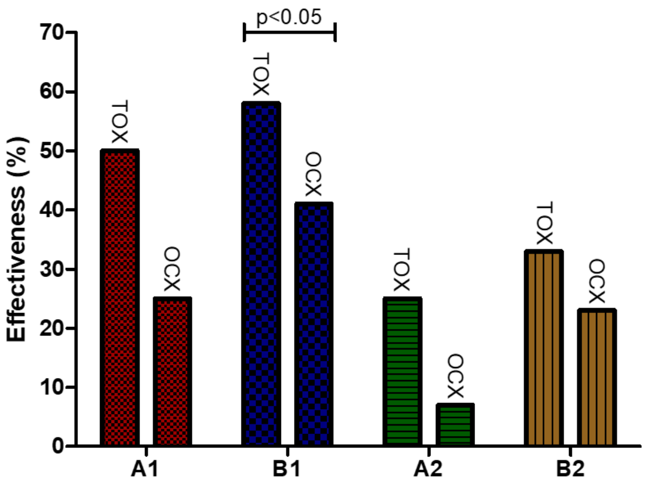

Figure 1. Effectiveness of antibiotics; A1 positive otorrhea (base); B1 antibiotic prescription; A2 positive otorrhea with uncertain value; B2 antibiotic prescription with uncertain value

In this study, oral ciprofloxacin (OCX) was the most frequently prescribed treatment, accounting for 82.4% of the total sample. This finding aligns with previous studies that reported a high tendency to prescribe systemic antibiotics in CSOM cases, particularly in outpatient settings in Indonesia and low-resource countries.[21,32,33] However, the effectiveness analysis (Figure 1) demonstrated that topical ofloxacin (TOX) yielded higher clinical success rates across multiple subgroups (25%–58%) compared to OCX (7%–41%), albeit with variability. This variability highlights the uncertainty inherent in treatment response parameters, further emphasizing the need for individualized therapy selection. The reduced effectiveness of OCX can be attributed to its limited bioavailability at the infection site, microbial resistance, mucosal scarring, and poor vascularization of the middle ear mucosa.[3,17] Furthermore, in cases where the tympanic membrane perforation is small or where thick mucopurulent discharge is present, the entry of topical agents into the middle ear may also be compromised, potentially reducing TOX efficacy in certain cases.[17]

Cost-Effectiveness Study

Although no significant difference was observed in the resolution of otorrhea between TOX and OCX groups (Figure 1), the number of antibiotic prescriptions differed significantly, with OCX patients receiving more prescriptions. This pattern may stem from physicians' concerns about recurrence or intermittent ear discharge (particularly due to water exposure), [23] coupled with the widespread but inappropriate practice of prolonging topical antibiotics post-resolution. Notably, while WHO in 2004 endorsed prophylactic antibiotic use,[1] recent evidence from Mittal et al no longer supports this recommendation.[3] The implications of these prescription patterns are not limited to clinical outcomes but extend to pharmacoeconomic consequences, as shown in Tables

II and III. OCX treatment incurred higher overall costs, including medication and consultation expenses, contributing to its unfavorable cost-effectiveness profile compared to TOX. The mean cost difference was statistically significant (p<0.05), which directly affected the Average Cost-Effectiveness Ratio (ACER) and Incremental Net Benefit (INB) values, both favoring TOX.

There was a correlation between the difference in antibiotic therapy obtained and the cost of antibiotics (Table II). Similarly, a study found that the antibiotic prescription made a significant difference.[34] Interestingly, cost comparisons further revealed that ototopical drops such as TOX are priced higher than ophthalmic drops, despite sharing similar production processes and sterility standards.[35] However, various factors—such as limited regulatory control, opaque pricing structures, and brand-name dominance—have driven up the price of ototopical formulations beyond justified manufacturing costs.[27] These findings underline how prescribing practices and drug formulation choices, when misaligned with pharmacoeconomic rationale, can inadvertently burden healthcare systems. Therefore, promoting evidence-based prescribing and greater pricing transparency is essential, not only to improve CSOM outcomes but also to support sustainable antibiotic use in primary and secondary care.

Table II. Cost of CSOM

Cost	TOX Median (IQR)	OCX Median (IQR)	p-Value
Antibiotics	Rp43010 (0)	Rp3048 (3556)	<0.05[a]
Non-Antibiotics	Rp3930 (13520)	Rp16300 (19068)	<0.05[a]
Clinical Procedures	Rp37500 (28125)	Rp55000 (54374)	<0.05[a]

a Mann-Whitney U-Test

Chronic Suppurative Otitis Media (CSOM) is often accompanied by symptoms of upper respiratory tract infection (URTI), such as cough, sore throat, and nasal congestion. The WHO has long recognized the link between URTI and otitis media, emphasizing the importance of addressing concurrent respiratory symptoms to prevent middle ear complications.[1] This clinical connection is further supported by Hassooni et al., who demonstrated both microbiological and symptomatic correlations between URTI and CSOM, reinforcing the need for comprehensive symptom management in these patients.[36] In our study, several non-antibiotic medications were prescribed to manage accompanying symptoms, including methylprednisolone (MP), pseudoephedrine HCl combined with triprolidine HCl, ambroxol, cetirizine, nonsteroidal anti-inflammatory drugs (NSAIDs), and multivitamins.

A significant difference was observed in the cost of non-antibiotic therapies between the TOX and OCX groups. As shown in Table II, patients receiving OCX incurred higher non-antibiotic costs, which may reflect the presence of more severe or persistent accompanying symptoms requiring additional treatment. This finding aligns with Hadiningsih's analysis, which demonstrated that the cost of treatment increases substantially when more than two medications are prescribed, a common occurrence in polypharmacy scenarios.[34] Effective management of non-antibiotic symptoms is crucial, as it contributes to the resolution of otorrhea and helps prevent recurrence, supporting a more holistic treatment approach. Furthermore, the clinical procedure costs differed significantly between groups. The OCX group recorded higher costs, primarily due to the inclusion of ear cleaning and tampon placement procedures, which were not commonly performed in the TOX group. According to Hadiningsih, such procedural differences often stem from variability in physician practice and institutional protocols, both of which can significantly impact cost outcomes.[34] Notably, in our study, the tampon procedure appeared to obstruct access to the middle ear and was thus deemed unnecessary for TOX administration. This finding highlights the importance of rationalizing procedural interventions to avoid unnecessary costs and potential therapeutic inefficiencies.

According to Table III, the difference in ACER between TOX and OCX was Rp125,948, with TOX showing a lower value. This indicates that TOX was more cost-effective than OCX. While the ICER suggested an increase in cost when switching from OCX to TOX, the ICER value alone could not definitively determine cost-effectiveness. To overcome this limitation, the Incremental Net Benefit (INB) approach was employed. The INB value of +Rp99,857, calculated at a Willingness to Pay (WTP) threshold of Rp434,500, demonstrated that TOX was more cost-effective than OCX. Previous studies have supported the superior cost-effectiveness of topical antibiotics. Parmar et al. found that topical monotherapy was more cost-effective than combination therapy involving both topical and oral antibiotics in the management of CSOM.[37] Likewise, Van Dongen et al. showed that topical antibiotics were more economically advantageous than oral therapies in the treatment of acute otorrhea in children with tympanostomy tubes.[38] Collectively, these findings suggest that topical antibiotics are generally more cost-effective than oral antibiotics, regardless of variations in disease conditions or treatment populations.

Table III. Cost-Effectiveness

Antibiotics	Total Cost Median (Rp)	Base Effectiveness (%)	ACER (Rp)	WTP (Rp)	ΔE (%)	ΔC (Rp)	ICER (Rp)	INB (Rp)
TOX	80510	50	161020	434500	25	8768	351	+99857
OCX	71742	25	286968					

Note: ACER = Average Cost-Effectiveness Ratio; WTP = Willingness to Pay; E= effectiveness; C= cost; ICER= Incremental Cost-Effectiveness Ration; INB= Incremental Net Benefit

Due to parameter uncertainty in pharmacoeconomic analysis, a one-way sensitivity analysis was conducted to evaluate the robustness of the findings. As noted by Rascati, both cost and effectiveness parameters can influence cost-effectiveness outcomes.[18] In our analysis (Table IV), variations in the cost parameter did not significantly affect the results. However, changes in the effectiveness parameter had a substantial impact. Notably, when TOX and OCX were assumed to have equivalent effectiveness (25%), TOX yielded a higher ACER than OCX. This highlights the critical importance of accurate and context-specific clinical effectiveness estimates when interpreting pharmacoeconomic conclusions.

Table IV. Sensitivity Analysis (ACER)

Variables	Value Effectiveness = % Cost = Rp	ACER		
		TOX (Rp000)	OCX (Rp000)	TOX – OCX (Rp000)
Effectiveness				
TOX	25	322	287	35
	58	139	287	-148
OCX	7	161	1025	-867
	41	161	175	-14
Cost				
TOX	32000	139	287	-148
	50000	175	287	-112
OCX	100	161	279	-118
	800	161	313	-152
Corticosteroids	200	161	279	-118
	600	161	308	-147
Pseudoephedrine + Triprolidine	1000	161	283	-122
	2000	161	321	-160
Vitamin	650	161	287	-126
	850	161	287	-126
Mucolytics	100	161	287	-126
	500	161	291	-130
Antihistamines	100	161	281	-120
	1200	161	295	-134
NSAID’s	200	161	287	-126
	1000	161	293	-132
Ear Cleaning	10000	108	154	-46
	50000	186	337	-151
Ear Tampon	10000	161	264	-103
	50000	161	388	-227

However, when the minimum effectiveness of TOX (25%) and OCX (7%) was considered in the sensitivity analysis, it showed no impact on cost-effectiveness. When the effectiveness of TOX fell to 25%, it was no longer more cost-effective than OCX. In the meta-analysis conducted by Chong et al., the probability of topical antibiotic effectiveness falling below that of oral antibiotics was low or nonexistent due to the limited amount of low-quality evidence available to examine whether topical or oral antibiotics were more effective.[9] Therefore, the calculation of ACER was not a clear method to determine cost-effectiveness in this case.

According to Figure 2, the sensitivity analysis demonstrated a wide response range within Rp0 to Rp500,000. This range was selected to reflect possible out-of-pocket expenditures or insurance reimbursements in Indonesian healthcare settings. At the lower threshold of INA-CBGs pricing, cost-effectiveness was unaffected; however, when the Willingness to Pay (WTP) dropped below Rp35,702, the Incremental Net Benefit (INB) turned negative, suggesting a potential shift in cost-effectiveness in favor of OCX. This critical threshold closely resembles the minimum individual contribution to the BPJS Kesehatan scheme (Rp42,000), which—after government subsidies—requires only Rp35,000 from the public. Policymakers should encourage public participation in the national insurance system rather than allowing individuals to self-pay for healthcare without insurance coverage. Thus, even marginal policy adjustments in healthcare should been pushing, can significantly impact pharmacoeconomic decisions.

Given these findings, the role of pharmacists becomes vital in evaluating and adjusting treatment plans based on dynamic pricing and reimbursement models. Pharmacists are uniquely positioned to monitor drug costs, ensure formulary adherence, and educate patients on optimal regimens—contributing directly to reducing healthcare.[16] The outcomes of the INB-based sensitivity analysis reaffirm the importance of integrating economic parameters such as INA-CBGs and BPJS premiums into therapeutic decision-making processes.

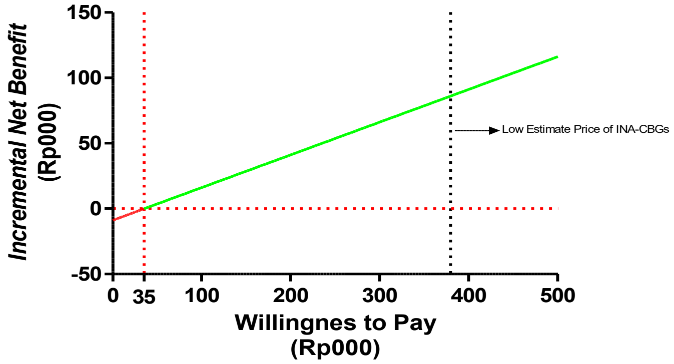

Figure 2. Sensitivity Analysis using INB

This study is not without limitations. The retrospective observational design raises concerns regarding ascertainment and selection bias. The relatively small number of patients receiving TOX (n=12) limits statistical power and increases susceptibility to type II error in comparative effectiveness analyses. Moreover, the study's geographic confinement to a rural Indonesian facility restricts the generalizability of the clinical and economic findings to urban or alternative health system contexts. The absence of microbiological culture data impairs interpretation of antibiotic-specific efficacy, while the exclusion of indirect and societal costs narrows the scope of the economic evaluation. Additionally, the lack of randomization and absence of adjustment for confounding variables such as comorbidities or concurrent medications may introduce residual bias. Nevertheless, these limitations are mitigated by the application of a comprehensive pharmacoeconomic framework, the use of complete-case analysis, and the integration of real-world cost components relevant to policy and practice in the Indonesian healthcare setting.

CONCLUSION

In summary, the study concluded that topical antibiotics were more cost-effective than oral antibiotics in treating CSOM, considering INB values based on INA-CBGs prices, while also accounting for changes in cost-effectiveness. We recommend further multicenter studies from urban and rural areas, prospective studies with larger sample sizes, and longer follow-ups that include patient-reported outcomes (quality of life) to strengthen the findings.

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STATEMENT OF ETHICS

Ethical Approval Number 1998/UN4.14.1/TP.01.02/2023 from the Healthy Research Ethics Committee, Faculty of Public Health, Hasanuddin University, approved on 13 February 2023.

STATEMENT ON AI USE IN MANUSCRIPT PREPARATION

We declare that in the preparation of this manuscript, we utilized several AI tools, such as Grammarly and editGPT, to improve the readability of the manuscript. However, all authors remained fully involved in the research design, data analysis, and interpretation of results. All scientific content writing was done entirely by the authors. All authors have read, reviewed, and ensured the accuracy and integrity of the manuscript content in its entirety. All authors are fully responsible for the scientific content and integrity of this manuscript.

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