


The Global Burden of Cholesteatoma: A Systematic Review and Meta-analysis

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Abstract

Objective. This systematic review and meta-analysis sought to estimate the global and World Health Organization (WHO) regional prevalence and burden of cholesteatoma.

Data Sources. PubMed, APA PsycINFO, the Cochrane Library, Embase, and WHO International Clinical Trials Registry Platform (ICTRP) from 2010 to 2025.

Review Methods. Teams of independent reviewers assessed each study for inclusion. Studies reporting primary data on cholesteatoma prevalence, recurrence, or its impact were included. The primary outcome was the global prevalence, whereas secondary outcomes were regional prevalence and recidivism rates, treatment, and complications. A random-effects meta-analysis was used to pool data, and study quality and publication bias were assessed. This study was registered with PROSPERO (CRD42024533132).

Results. Forty-six eligible studies were included in the meta-analysis. The pooled global prevalence of cholesteatoma was estimated at 4.02 per 1000 persons (95% CI 1.79-7.10). By the WHO regions, the pooled prevalence of cholesteatoma in the Western Pacific Region, European Region, South East Asian Region, Region of the Americas, and African Region was estimated at 5.73 per 1000 persons (95% CI 1.00-13.87), 2.32 per 1000 persons (95% CI 2.23-2.42), 3.30 per 1000 persons (95% CI 2.65-4.11), 0.06 per 1000 persons (95% CI 0.00-0.00), and 7.32 per 1000 persons (95% CI 2.77-13.96), respectively. The prevalence of hearing loss in cholesteatoma was estimated at 75.68 per 100 cases (95% CI 59.02-89.24).

Conclusion. This meta-analysis is the first to systematically quantify global and regional cholesteatoma prevalence,

complications, and treatment approaches, highlighting regional disparities and informing public health strategies and policy globally.

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Cholesteatoma, a seemingly benign yet insidious condition, poses a significant threat to global health, with its destructive potential often underestimated until severe complications arise. The condition's potential for irreversible hearing loss, facial paralysis, and intracranial complications makes it a critical concern for otolaryngologists and audiologists, who must balance the need for effective treatment with the risk of surgical complications.

Cholesteatoma is a benign, keratinized squamous epithelial lesion that can affect different areas of the temporal bone,¹ especially the middle ear cleft, and is either acquired or congenital.² Cholesteatoma is characterized by bone erosion, which results in persistent otorrhea and hypoacusis.³ Globally, cholesteatoma poses a significant threat to hearing, balance,⁴ and overall quality of life (QOL).⁵ Despite its severity, cholesteatoma remains a neglected and under-reported condition,^{6,7} particularly in low- and middle-income countries where access to ear and hearing care is limited.

The burden of cholesteatoma is influenced by a complex interplay of patient-related factors (such as age and genetic predisposition),^{8,9} disease-related factors (such as size and extent of the cholesteatoma),¹⁰ and socioeconomic factors (such as access to healthcare and education),¹¹ which can ultimately affect the severity of symptoms, QOL, and treatment outcomes.

The World Health Organization (WHO)¹² has identified the African Region as one of the most vulnerable to ear and hearing disorders, including cholesteatoma. The region's high burden of infectious diseases, limited access to healthcare services, and inadequate sanitation and hygiene infrastructure create a perfect storm for the development and progression of cholesteatoma.

Despite the likelihood of a high burden of cholesteatoma in the African Region, there is a glaring lack of comprehensive global prevalence data to inform decision-making and policy development. Most available data are based on hospital-based studies, which may not accurately reflect the true burden of the disease in any region. Furthermore, the few available studies have methodological limitations, including small sample sizes, poor study design, and inadequate diagnostic criteria. This lack of reliable data hinders the development of effective prevention and control strategies, ultimately perpetuating the cycle of neglect and neglect of ear and hearing disorders across the globe.

This systematic review and meta-analysis aims to bridge the existing knowledge gap by quantifying the global and regional prevalence, complications, and select treatment approaches for cholesteatoma, economic implications, and

QOL associated with the disease, thereby informing evidence-based healthcare policy, optimizing resource allocation, and guiding future research agendas.

Methods

Search Strategy and Selection Criteria

To provide evidence on the global burden of cholesteatoma, we embarked on a systematic review and meta-analysis of existing literature. An international collaborative was created. We prospectively registered our protocol with PROSPERO (CRD42024533132). We followed the PRISMA reporting guidelines in this study.¹³

We searched for relevant studies that were published from January 01, 2010, to March 31, 2025, across multiple databases, including PubMed, CINAHL, the Cochrane Library, Embase, and WHO International Clinical Trials Registry Platform (ICTRP). To ensure comprehensive coverage, we searched the gray literature, reference lists of included studies, and conducted manual searching for eligible articles. We contacted field experts for data on relevant studies they are aware of or involved with that were either not published or captured from the electronic databases. The search was conducted using a combination of MeSH search terms and keywords relating to cholesteatoma (Supplemental File S1, available online).

For this systematic review and meta-analysis, we included studies involving patients clinically or radiologically diagnosed with cholesteatomas that provide original data on the prevalence, complications, and recidivism rate of cholesteatoma. These studies can be observational, randomized controlled trials, those involving humans of all ages, sexes, and conducted in any healthcare setting or with data extracted from registries/national databases. We included studies conducted globally without any geographical restrictions.

We excluded studies with irrelevant or unreliable data. In this systematic review and meta-analysis, we define studies with unreliable data as those with data that cannot be verified or validated due to issues like missing or incomplete data, lack of transparency, or unreported methodology. These include case reports, editorials, studies with unclear data, and studies with noncomparable outcomes. Reviews were also excluded. No language restrictions were applied to the search, ensuring the inclusion of relevant studies published in all languages. Studies published in non-English languages were translated using a web-based translation tool (Google Translate) to facilitate inclusion and data extraction. We conducted the final search on April 05, 2025.

Data Collection

Data extraction and quality appraisal were conducted independently by multiple authors, utilizing standardized forms to record various outcomes. Title and abstract screening, as well as full-text review, were conducted in duplicate. To ensure accuracy, screening results were

cross-validated in groups of four. Discrepancies were resolved through consensus. A standardized data extraction form was used to collect data on study characteristics (identifier, design, setting, and population), outcomes (prevalence, incidence, recidivism, and complications), and quantitative results. We operationally defined recidivism as the presence of residual or recurrent cholesteatoma,¹⁴ reflecting persistent or re-emergent disease activity. The methodological quality of included studies was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Tool (Supplemental File S2, available online).

Data Analysis

The pooled prevalence of cholesteatoma was calculated using the inverse variance random-effects model, with the restricted maximum-likelihood method used to estimate the between-study variance. The Freeman-Tukey double arcsine transformation was used for variance stabilization. Heterogeneity was quantified and tested using the I^2 statistic and chi-square test statistic, respectively. The prevalence is presented per 1000 persons with 95% confidence intervals (CIs). Sensitivity analysis was performed to determine if any one study influenced the pooled prevalence estimate. For outcomes with at least 10 studies, publication bias was assessed using a funnel plot. In instances where data were stratified by patient or ear, our meta-analysis was conducted accordingly, with cholesteatoma patients or affected ears serving as the respective units of analysis. Data were analyzed using the R “meta” package.

Given the variability in study methodologies and data presentations, a narrative approach was employed to describe the socioeconomic status (SES) and QOL outcomes. This approach involved a qualitative synthesis of the findings, highlighting key patterns, themes, and differences observed in the studies. The narrative presentation allowed for detailed examination of the diverse findings across studies. It provided context and depth to the understanding of variables that could not be analyzed quantitatively, highlighting areas of agreement and discrepancy.

Complication outcomes, including hearing loss, facial nerve palsy, and intracranial complications, were derived from pre-operative data. In contrast, QOL outcomes were based on postoperative data, consistent with the prevailing literature, which predominantly focuses on postsurgical QOL assessments. Our study employed a population-specific approach to analyze cholesteatoma-related complications. Hearing loss outcomes were evaluated exclusively among patients from the general population. Facial nerve palsy and intracranial complications, however, were assessed across both general population cohorts and high-risk populations, which comprised patients with severe or advanced disease. Separate analyses were conducted for each population group to ensure accurate and unbiased outcome estimates.

Results

The literature search identified 2510 records, of which 474 were duplicates and thus removed. We subsequently screened 2036 titles and abstracts, followed by a detailed review of 168 full-text articles. We contacted 14 authors, four of whom responded but did not provide the requisite information. Data from three unpublished studies from field experts were received and included in our meta-analysis. This process resulted in the selection of 51 studies for the systematic review, and 46 of these studies were ultimately included in our meta-analysis (**Figure 1**).

The included studies represented a global distribution, spanning six WHO regions. Specifically, the regional breakdown consisted of 6 studies from African Region (AFRO),¹⁵⁻¹⁷ 5 from Region of the Americas (AMRO),¹⁸⁻²² 5 from Eastern Mediterranean Region (EMRO),²³⁻²⁷ 17 from the European Region (EURO),^{9,28-42} 7 from the South-East Asia Region (SEARO),^{35,39,43-47} and 6 from the Western Pacific Region (WPRO).⁴⁸⁻⁵² The studies examined various facets of cholesteatoma, with findings on prevalence (10 studies),^{9,22,36,46,50-52} recidivism (15 studies),^{16,18,20,21,30,31,35,37-40,42,53,54} hearing loss (13 studies),^{15,22-26,28,29,34,35,44,45,47} facial nerve palsy (14 studies),^{22-25,27-29,34,35,43-45,47,48} intracranial complications (12 studies),^{22-25,27,29,34,35,43-45,47} canal wall-down (CWD; 15 studies),^{16,17,19,21,32,33,38-42,49,53,55,56} and canal wall-up (CWU; 13 studies).^{16,17,19,21,32,33,38-40,49,53,55,56}

Global and Regional Prevalence

Table 1 shows the characteristics of studies included in the prevalence meta-analysis. The overall pooled prevalence of cholesteatoma was reported by ten studies with 28,988,533 participants and estimated at 4.02 per 1000 persons (95% CI 1.79-7.10). High heterogeneity was observed among the studies ($P < .001$; $I^2 = 99.9\%$) (**Figure 2**).

At the WHO regional levels, the highest pooled prevalence of cholesteatoma was estimated at 7.32 per 1000 persons (95% CI: 2.77-13.96; 23,253 participants; 3 studies; $I^2 = 96.4\%$) for African Region; followed by 5.73 per 1000 persons (95% CI: 1.00-13.87; 126,189 participants; 3 studies; $I^2 = 99.5\%$) for Western Pacific Region, and 3.30 per 1000 persons (95% CI: 2.65-4.11; 25,147 participants; 1 study) for South East Asian Region. The lowest prevalence was estimated at 0.06 per 1000 persons (95% CI: 0.00-0.00; 27,870,522 participants; 1 study) for the Americas and followed by 2.32 per 1000 persons (95% CI: 2.23-2.42; 943,422 participants; 2 studies; $I^2 = 0\%$) for the European Region (**Figures 3 and 4**).

Complications of Cholesteatoma

Hearing Loss

The pooled prevalence of hearing loss among patients with cholesteatoma was 75.68 per 100 persons (95% CI 59.02-

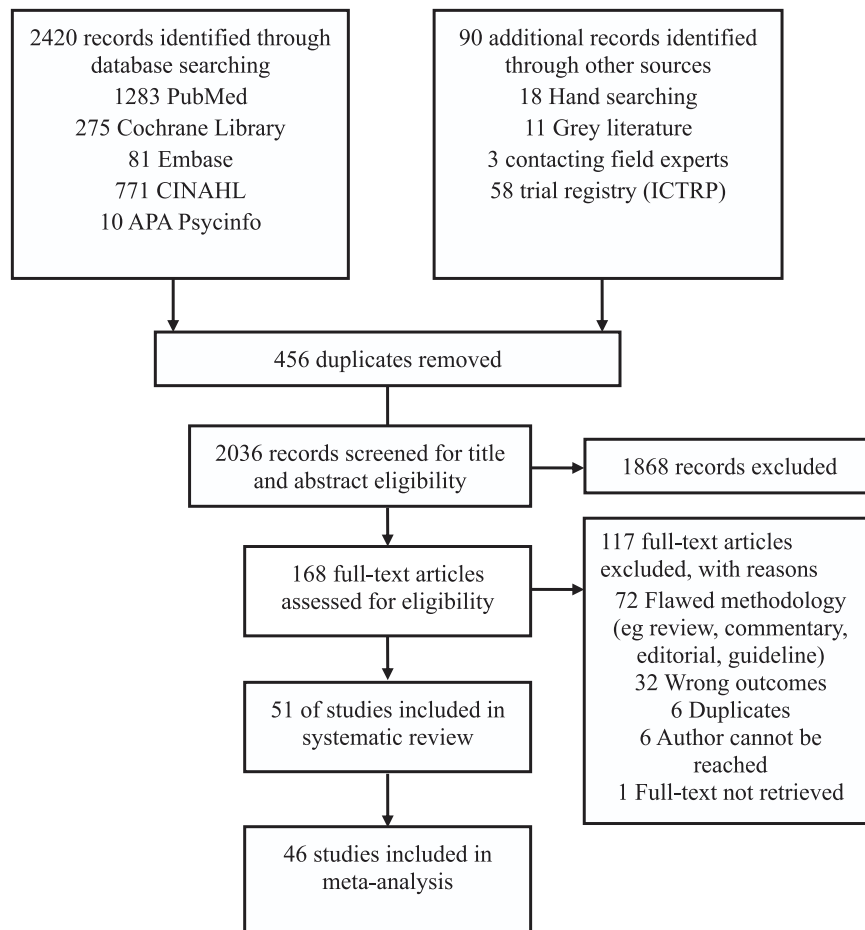


Figure 1. Study selection.

89.24; 2773 participants; 13 studies). High heterogeneity was observed among the studies ($P < .001$; $I^2 = 98.9\%$).

Facial Nerve Palsy

The pooled prevalence of facial nerve palsy among patients with cholesteatoma from the general population was 3.22% (95% CI 1.31-5.79; 3358 participants), with significant heterogeneity observed across studies ($P = 90.3\%$, $P < .001$). In contrast, the pooled prevalence among high-risk population (patients with severe or advanced disease) was substantially higher, at 40.18% (95% CI 26.38-54.77; 863 participants), with considerable heterogeneity also evident ($P = 84.3\%$, $P < .001$).

Intracranial Complications

The pooled prevalence of intracranial complications among patients with cholesteatoma from the general population was 9.09% (95% CI 3.18-17.39; 3084 participants), with substantial heterogeneity observed across studies ($P = 95.6\%$, $P < .001$). A significantly higher pooled prevalence was found among high-risk populations at 14.37% (95% CI 2.23-33.06; 855 participants), with considerable heterogeneity also evident ($P = 93.4\%$, $P < .001$) (Supplemental Figures S3-S5, available online).

Type of Mastoidectomy

The pooled proportion of cholesteatoma patients undergoing CWD procedure was estimated at 17.44 per 100 patients (95% CI 8.24-29.11; 19,225 participants; 7 studies; $I^2 = 95.4\%$). The pooled proportion of cholesteatoma ears undergoing CWD procedure was estimated at 33.65 per 100 ears (95% CI 9.65-63.09; 2044 ears; 8 studies; $P < .001$, $I^2 = 99.0\%$).

Approximately 48.76% (95% CI 32.72%-64.93%) of cholesteatoma patients underwent the CWU procedure, based on data from 188,819 participants across 6 studies. However, there was significant heterogeneity between studies ($P = 98.3\%$). The same procedure was performed on an estimated 42.07% (95% CI 20.06%-65.82%) of cholesteatoma-affected ears, based on data from 2044 ears across 7 studies. This result was statistically significant ($P < .001$), but there was substantial heterogeneity between studies ($P = 96.8\%$) (Supplemental Figures S6 and S7, available online).

Recidivism

Patient-level analysis showed the pooled proportion of cholesteatoma patients who had recidivistic cholesteatoma was estimated to be 16.20% (95% CI 9.91%-23.63%).

Table 1. Characteristics of Studies Included in Prevalence Meta-analysis

Study	Time period of data collection in months	Country	WHO region	Study design	Sex	Ages	Sample size	Cases
Spilsbury et al ⁵¹ a	288	Australia	Western Pacific	Retrospective	Males, females	Children	45,980	460
Benson and Mwaniri ⁵⁰	30	Australia	Western Pacific Region	Cross-sectional	Males, females	All ages	444	4
Djurhuus et al ³⁶	42	Denmark	European Region	Retrospective	Males, females	All ages	441,041	1039
Chung et al ⁴⁶	36	South Korea	South East Asian Region	Cross-sectional	Males, females	>4 y of age	25,147	83
Kuo et al ⁵	120	Taiwan	Western Pacific Region	Retrospective	Males, females	All ages	79,765	133
Lee et al ²²	9	United States	Region of the Americas	Cross-sectional	Males, females	Children (mean age 9.9 y)	27,870,522	1552
Unpublished data 1, 2024	72	South Africa	African Region	Retrospective	Males, females	All ages	1632	16
Unpublished data 2, 2024	22	Zambia	African Region	Retrospective	Both	All ages	9124	27
Unpublished data 3, 2024	48	South Africa	African Region	Retrospective	Males, females	All ages	12,497	138
Wilson et al ⁹	48	United Kingdom	European Region	Retrospective	Males, females	40-69 y	502,408	1151

^aPopulation was among children who underwent a ventilation tube insertion (VTI). Cases were defined as occurrence at least 6 months after the first VTI.

This finding was based on a comprehensive data set of 26,141 participants from 9 studies. However, a high degree of heterogeneity was observed between studies ($P < .001$, $I^2 = 95.8\%$), indicating significant variability in the results. Our analysis of 778 ears across six studies revealed a substantial proportion of recidivistic cholesteatoma. The pooled proportion of ears with recurrent or persistent disease was estimated to be 19.29% (95% CI 13.50%-25.81%). This finding was highly significant ($P < .001$). Although moderate heterogeneity was observed between studies ($I^2 = 69.8\%$, $P = .005$), our results suggest a notable burden of recidivistic cholesteatoma in the affected population (Supplemental Figure S8, available online).

SES and Cholesteatoma

Observational studies conducted in South East Asian Region have revealed a significant association between socioeconomic deprivation and the development of cholesteatoma. A case series of 100 patients identified poverty, illiteracy, overcrowding, and poor living conditions (including residence in slums with earthen floors and frequent exposure to contaminated water sources) as key determinants of disease etiology.⁴³ The increased incidence of cholesteatoma in disadvantaged populations has been attributed to compromised hygiene, malnutrition, and impaired immune function.²³

Consistent with these findings, a study conducted in the African Region among 57 children with cholesteatoma found that all patients belonged to lower socioeconomic strata, with 77% living below the poverty line (annual household income < \$4500).¹⁶ Similarly, a large-scale study involving 1552 pediatric cases in the Americas observed an inverse relationship between SES and disease complications, with children from lower-income families exhibiting a higher frequency of acute mastoiditis and subperiosteal abscess compared to their higher-income counterparts.²² Notably, multivariate analysis revealed that children in the lowest income quartile were at increased risk of developing acute mastoiditis (odds ratio [OR] 1.87, 95% CI 1.15-3.03) and subperiosteal abscess (OR 6.75, 95% CI 2.22-20.56), while those in the second income quartile were less likely to undergo ossicular chain surgery (OR 0.31, 95% CI 0.13-0.72).

Quality of Life

Hearing preservation and restoration are critical factors in determining QOL outcomes.⁵⁷ However, disease recurrence rates and surgical complications influence QOL outcomes. Patients with cholesteatoma compared to those without were 1.69 times (95% CI = 1.21-2.36, $P = 0.002$) more likely to suffer from depressive disorders.⁵ Analyzing the postoperative health-related quality of life (HRQoL) for three techniques—exclusively transcanal technique (ETC), combined transcanal transmastoidal technique (TCM), and CWD surgery with obliteration—the ETC group compared to TCM and CWD had a lower restriction in HRQOL.⁵⁸

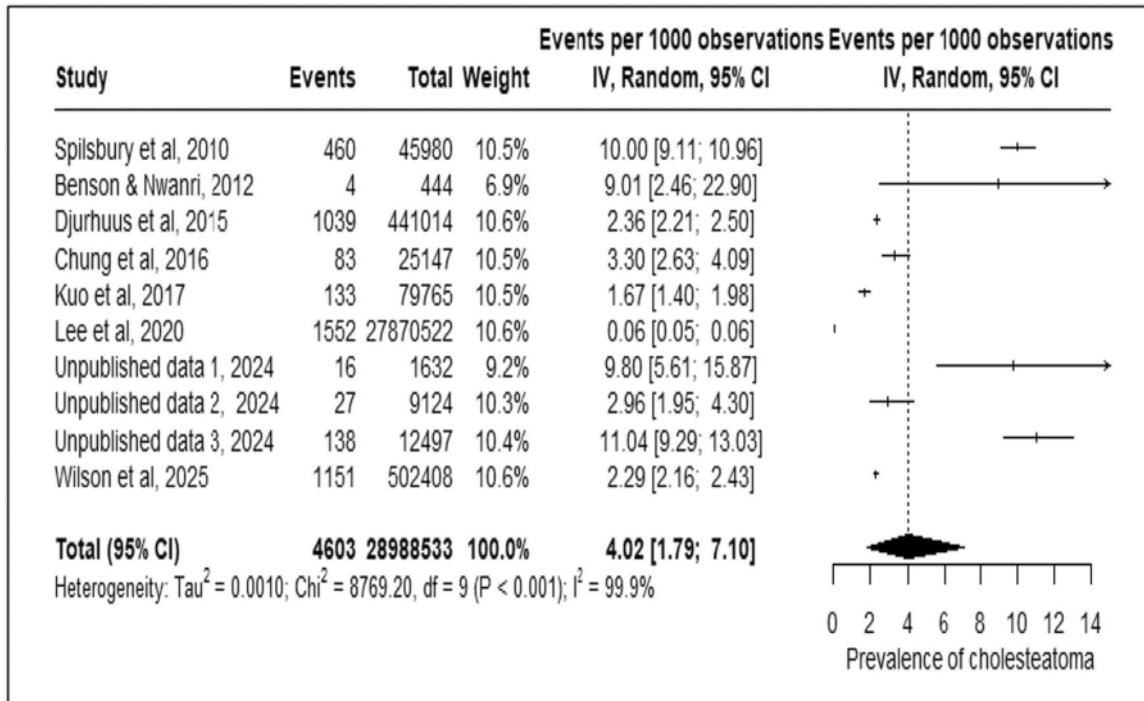


Figure 2. Forest plot for the prevalence of cholesteatoma.

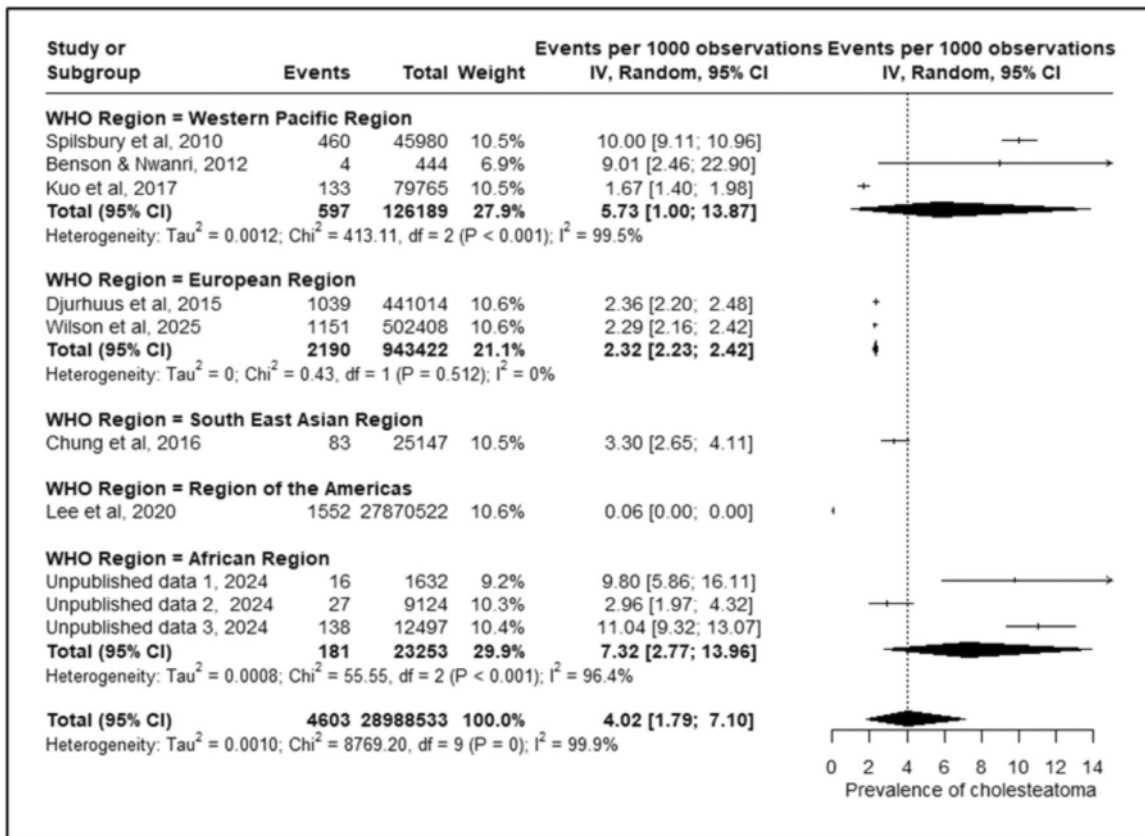


Figure 3. Subgroup analysis by World Health Organization (WHO) region.

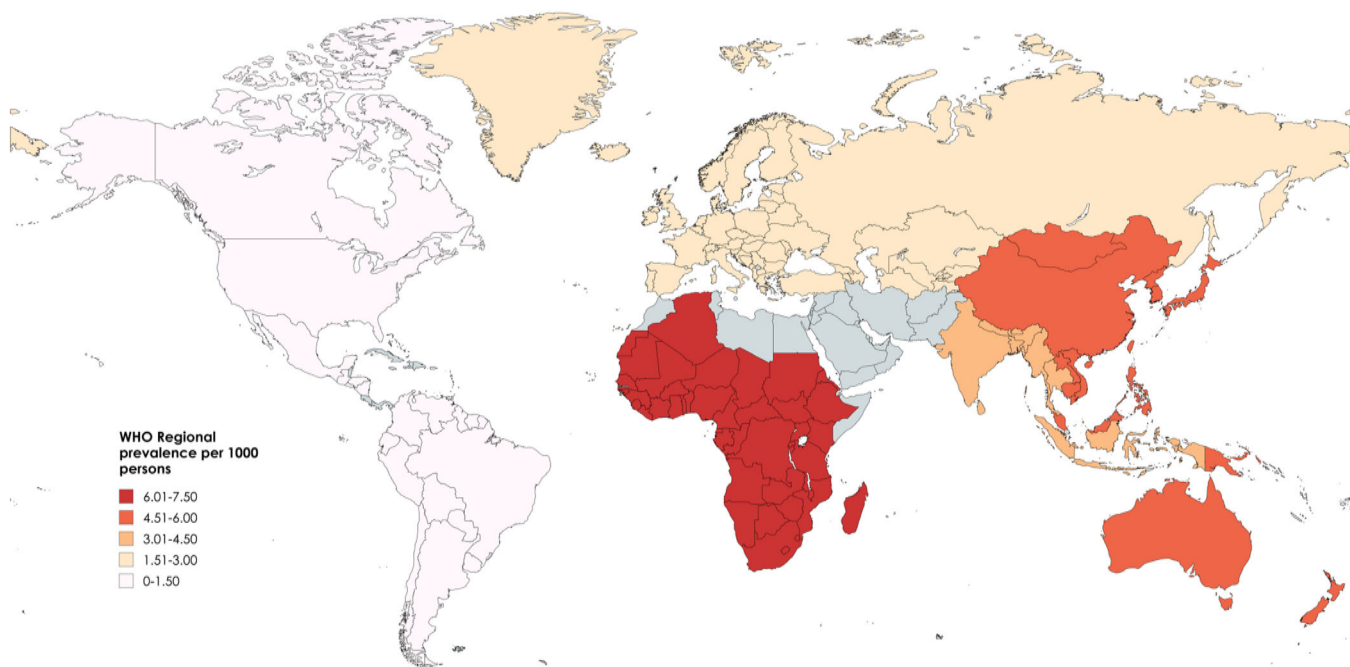


Figure 4. World Health Organization (WHO) regional burden of cholesteatoma.

Using the Chronic Otitis Media Questionnaire-12 (COMQ-12), there was no significant difference in the QOL after cholesteatoma surgery using either the CWU or CWD procedures.⁵⁹ Similarly for patients that had either microscopic or transcanal endoscopic ear surgery (TEES) surgeries, a preoperative and postoperative assessment using the Zurich Chronic Middle Ear Inventory (ZCMEI-21) for both surgical technique and intraoperative staging of the cholesteatoma (ChOLE classification) showed no significant difference in the HRQol.⁶⁰

Sensitivity Analysis

To assess the robustness of the findings, we conducted sensitivity analyses excluding studies with (high risk of bias/outliers/unpublished data). The sensitivity analysis found that the pooled prevalence ranged between 3.40 and 4.85 per 1000 (**Table 2**). The results of the sensitivity analysis showed that the overall effect estimate remained relatively stable, with minimal change in effect size when specific studies were excluded.

Risk of Bias

To assess publication bias, we constructed a funnel plot using the Freeman-Tukey double arcsine transformed proportion. The Freeman-Tukey double arcsine transformation was applied to stabilize the variance of the proportions. The transformed proportions were then plotted against the standard error of each study. Funnel plots (Supplemental Figures S9-S12, available online) show the distribution of studies around the pooled estimate. Visual inspection of the plots suggests asymmetry, indicating publication bias.

Discussion

Cholesteatoma, a chronic and potentially debilitating condition, poses a significant burden on individuals and healthcare systems worldwide. Our analysis reveals a high prevalence of hearing loss among patients with cholesteatoma, affecting approximately 75.68% of individuals, with a high degree of consistency across studies. Furthermore, our findings indicate that the global prevalence of cholesteatoma is estimated to be 4.02 per 1000 individuals, underscoring the need for increased awareness and improved management strategies. This review synthesizes the available evidence on the global burden of cholesteatoma, providing insights into the prevalence, complications, and consequences of this condition, and informing strategies for prevention, and treatment.

Type of Mastoidectomy

The primary objectives of surgical intervention for cholesteatoma are multifaceted, encompassing complete disease eradication, prevention of recurrence, enhancement of auditory function, and optimization of patient QOL, while mitigating the risk of future complications. Nevertheless, the choice between CWD and CWU mastoidectomy approaches remains a subject of ongoing debate, underscoring the complexity and nuance inherent to cholesteatoma management.⁶¹ The CWU mastoidectomy approach preserves the posterior bony external auditory canal wall, thereby maintaining the native anatomical structure and function of the ear. In contrast, CWD mastoidectomy involves the removal of the posterior canal wall, creating a larger cavity that facilitates enhanced access and surveillance.^{62,63} CWU is often associated with improved audiological outcomes and reduced postoperative maintenance requirements, including

Table 2. Sensitivity Analysis Showing the Pooled Prevalences When Omitting Any One Study

Analysis	Prevalence per 1000 persons	95% CI
Omitting Spilsbury et al ⁵¹	3.47	(1.37; 6.45)
Omitting Benson and Mwanri ⁵⁰	3.79	(1.60; 6.90)
Omitting Djurhuus et al ³⁶	4.27	(1.75; 7.83)
Omitting Chung et al ⁴⁶	4.14	(1.64; 7.69)
Omitting Kuo et al ⁵	4.39	(1.86; 7.91)
Omitting Lee et al ²²	4.85	(2.62; 7.73)
Omitting Unpublished data 1, 2024	3.58	(1.44; 6.62)
Omitting Unpublished data 2, 2024	4.18	(1.68; 7.73)
Omitting Unpublished data 3, 2024	3.40	(1.38; 6.25)
Omitting Wilson et al ⁹	4.28	(1.76; 7.84)
Pooled estimate	4.02	(1.79; 7.10)

less frequent cleaning and fewer water restrictions.^{62,63} Conversely, CWD may offer superior disease clearance, but is potentially offset by increased risks of complications, such as vestibular dysfunction and hearing aid intolerance, as well as a greater need for regular cavity maintenance.⁶⁴

Hearing Loss in Cholesteatoma

Our analysis demonstrated a significant burden of hearing loss in patients with cholesteatoma, primarily mediated by the destructive potential of cholesteatoma on the middle ear ossicles.^{65,66} Consistent with existing data, our findings revealed that cholesteatomas are predominantly associated with conductive hearing loss, characterized by impaired sound conduction through the outer and middle ear. This auditory deficit arises from compromised mechanical transmission of sound energy via the ossicular chain. In exceptional cases, cholesteatoma extension into the inner ear can precipitate sensorineural hearing loss, highlighting the potential for variable audiological sequelae depending on the extent of disease progression.⁶⁷ By prioritizing hearing preservation, healthcare providers can mitigate the long-term consequences of cholesteatoma on auditory health and QOL. Early intervention is key to minimizing hearing loss and optimizing treatment results.

Intracranial Complications

This review further affirmed that intracranial complications arising from cholesteatoma are predominantly attributable to the condition's osteolytic properties, facilitating the contiguous spread of infection from the temporal bone to intracranial structures. This can precipitate severe complications, including meningitis,^{27,47} cerebral abscess formation,⁴⁷ and lateral sinus thrombosis.^{27,47} Notably, intracerebral abscesses represent a particularly common and clinically significant sequela, resulting from the direct extension of middle ear infection through areas of osseous destruction, ultimately leading to focal suppuration within the brain parenchyma.

Facial Nerve Palsy

Facial nerve compromise in cholesteatoma arises from multifactorial pathophysiology, including osteolytic processes, compressive neuropathy secondary to edema, and enzymatic degradation mediated by the cholesteatoma matrix. Surgical intervention, encompassing decompression and eradication of the disease process, is frequently necessitated to address facial nerve dysfunction. Notably, our meta-analysis revealed a pooled prevalence of facial nerve palsy of 3.22% (95% CI 1.31-5.79), consistent with the reported incidence ranges of 1% to 3.4% in case series.^{68,69}

Low SES and Cholesteatoma

The intersection of poverty and cholesteatoma highlights significant healthcare disparities. Limited access to medical care in low-income settings can lead to delayed diagnosis and treatment of cholesteatoma, resulting in increased complications and morbidity. In resource-constrained environments, the burden of chronic otorrhea and hearing loss can further exacerbate social and economic challenges. Public health initiatives aimed at improving access to ear, nose, and throat (ENT) services and promoting awareness of ear disease can help mitigate these disparities. Moreover, addressing systemic barriers to healthcare access is crucial for reducing the impact of cholesteatoma in impoverished communities. By understanding these dynamics, healthcare providers can develop targeted interventions to improve outcomes and reduce the burden of this condition on vulnerable populations. Effective management of cholesteatoma in these settings requires a multifaceted approach that includes both medical treatment and socioeconomic support. Community-based programs can play a vital role in early detection and management.

Quality of Life

Cholesteatoma's impact on QOL is multifaceted, affecting physical, emotional, and social aspects. Patients often experience anxiety, depression, and reduced social

interaction. Successful surgical intervention improves QOL, but outcomes vary depending on disease severity.

Our sensitivity analyses indicate that the results of the review are generally robust to different assumptions and exclusions. However, the findings should be interpreted with caution due to the limited number of studies, heterogeneity, and other limitations.

Strengths

To our knowledge, this systematic review and meta-analysis presents the most current and comprehensive evidence on the global burden of cholesteatoma, focusing on patient-centered outcomes. Leveraging the largest available data sets and incorporating substantial new data, as well as a large number of outcome events not captured in previous analyses, our study provides the most precise estimates to date of key outcomes, thereby informing a more accurate understanding of this condition.

This systematic review and meta-analysis has several methodological strengths. Firstly, we formulated focused review questions. We also developed and registered a protocol a priori. A well-established tool (JBI) was used to appraise the included studies. Appraisal was conducted independently by two reviewers who were not involved in any of the included studies, with discrepancies resolved by a third independent reviewer. We contacted authors of published studies for clarity or additional data where relevant data required for inclusion were missing.

Limitations

While our study provides valuable insights into the burden of cholesteatoma, it has several limitations. The scarcity of studies from certain regions, such as the EMRO, hindered our ability to accurately estimate regional prevalence for all regions. Furthermore, many studies either omitted or failed to report outcomes for specific subgroups of interest, limiting our power to detect clinically meaningful subgroup effects. Additionally, despite our intention to report on long-term QOL and functional outcomes, none of the included studies provided these data, highlighting a notable evidence gap. Also, our funnel plots suggested evidence of publication bias evidenced by the plots' asymmetry. Smaller studies with negative or nonsignificant results appear to be underrepresented. The presence of publication bias may result to an overestimation of the true effect size. We acknowledge this limitation and interpret the results with caution. Future studies should aim at addressing this by including more unpublished data or engaging with robust methodologies that account for potential publication bias.

Implications

The findings of this systematic review and meta-analysis on the global burden of cholesteatoma have far-reaching implications for public health policy and clinical practice. Our analysis reveals a disproportionate burden

of cholesteatoma in the AFRO, where the prevalence was highest, highlighting an urgent need for targeted interventions and resource allocation. Conversely, the complete absence of prevalence data from the EMRO underscores a critical gap in our understanding of the disease burden in this region.

The high prevalence of hearing loss associated with cholesteatoma is a pressing concern, given its potential to exacerbate disability and impact QOL. Our estimated global prevalence of 4.02 cases per 1000 persons provides a crucial benchmark for policymakers and healthcare providers. Furthermore, our analysis of complications reveals a substantial burden of recidivistic cholesteatoma, hearing loss, facial nerve palsy, and intracranial complications, which underscores the need for improved diagnosis, treatment, and follow-up care.

These findings collectively emphasize the importance of strengthening healthcare systems, enhancing disease surveillance, and promoting evidence-based management strategies to mitigate the global burden of cholesteatoma and its associated complications. The lack of data from certain regions and the high prevalence of complications highlight the need for further research and investment in global ear and hearing health.

Recommendations

Despite extensive studies on cholesteatoma, significant knowledge gaps persist, hindering the development of effective treatments and interventions. This review highlights the key areas where further research is needed to address these gaps. The scarcity of comprehensive studies providing accurate global prevalence estimates highlights the need for more extensive research. Further research is needed to elucidate the link between cholesteatoma and socioeconomic deprivation. Elucidating the mechanisms underlying cholesteatoma formation and progression is a critical research priority. Specifically, the precise mechanisms governing cholesteatoma development, including the role of hyperproliferative stratified squamous epithelium, remain unclear. Unraveling these mechanisms can inform the development of targeted interventions. The interplay between epithelial and mesenchymal components in cholesteatoma growth and development warrants further exploration. Variability in reporting outcomes and results across studies hinders comparison and synthesis of data. Standardizing reporting protocols can facilitate more effective data analysis and interpretation. The absence of universally accepted classification systems for cholesteatoma subtypes and stages complicates diagnosis and treatment. Developing standardized classification systems can enhance diagnostic accuracy and inform treatment decisions. Ongoing debates surrounding the most effective surgical techniques and approaches for cholesteatoma management underscore the need for further research. Comparative studies can help establish evidence-based guidelines for surgical interventions. The limited research

on non-surgical treatments and their efficacy in managing cholesteatoma highlights an area ripe for investigation.

Ongoing assessment of emerging evidence is crucial for characterizing shifts in epidemiological trends, informing evidence-based medical guidelines, and supporting informed clinical decision-making. The results of this systematic review offer a foundation for shaping public health policy and guiding individualized cholesteatoma management strategies.

Author Contributions

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
Supplemental Material

Additional supporting information is available in the online version of the article.

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