



ORIGINAL ARTICLE

Meta-analysis of prevalence of wheezing and recurrent wheezing in infants

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Abstract

Background: Wheezing affects children's quality of life, and is related with asthma in childhood. Although prevalence of wheezing has been previously studied in several countries, there is no reference of worldwide prevalence in infants. The aim of this meta-analysis is to estimate the prevalence of wheezing and recurrent wheezing in infants aged up to two years, and compare the prevalence across world regions.

Methods: Literature search was conducted in MEDLINE and SCOPUS databases, looking for observational studies published up to June 2016, including as keywords "prevalence" or "epidemiology" combined with "wheeze", "wheezing" or "asthma symptoms" and "infant" or "preschool". Fast*Pro software and random effects Bayesian model were used. Heterogeneity was estimated using I^2 statistic, and sensitivity analyses were performed.

Results: We identified 109 studies after duplicates were removed. After exclusions, 14 studies were included in the meta-analysis. Prevalence of wheezing and recurrent wheezing were 36.06% (95% CI 35.17–36.96), and 17.41% (95% CI 16.74–18.09), respectively. In European countries, prevalence of wheezing was 30.68% (95% CI 28.97–32.45), and 12.35% (95% CI 11.27–13.47) for recurrent wheezing. Prevalence of wheezing and recurrent wheezing in Latin America were higher, 40.55% (95% CI 39.40–41.71), and 19.27% (95% CI 18.44–20.11), respectively. In Africa, prevalence of wheezing was 15.97% (95% CI 14.05–18.00). Low or no heterogeneity was found in all cases.

Conclusions: More than one third of infants suffer from wheezing and almost one fifth from recurrent wheezing, being these illnesses especially prevalent in Latin American countries, pointing out an important public health problem.

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Introduction

Wheezing in infants not only affects children's quality of life,¹ but is related to the development of asthma childhood.² Several risk factors, such as viral respiratory infections,³ prenatal and postnatal tobacco smoke exposure,⁴ familial history of asthma,⁵ or pollution⁶ have been previously identified.

Prevalence of asthma and wheezing in schoolchildren and adolescents has been studied in the past. The International Study of Asthma and Allergies in Childhood (ISAAC) found highest prevalence of wheezing in children in United Kingdom, Oceania and Latin American countries.⁷ In Phase III of the same study, increasing trends were found in countries which showed lower prevalence in Phase I, while in the Oceanian countries decreasing trends were found.⁸

More recently, the International Study of Wheezing in Infants (Estudio Internacional de Sibilancias en Lactantes in Spanish, or EISL), a multicentre study in European and Latin American countries, was conducted to determine the prevalence, severity and risk factors for wheezing in infants.⁹

However, no previous studies about the worldwide prevalence of wheezing in infants have been conducted. Therefore, the aim of this meta-analysis is to estimate the prevalence of wheezing and recurrent wheezing in infants aged up to two years, and compare the prevalence across different world regions.

Materials and methods

This meta-analysis has been conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement,¹⁰ and its protocol has been registered in PROSPERO (reference CRD42016039446).

Search strategy and selection criteria

The literature search was performed in MEDLINE and SCOPUS databases, looking for observational studies published up to June 2016.

Search terms were "prevalence" or "epidemiology" (title), combined with "wheeze", "wheezing" or "asthma symptoms" (title), and "infant" or "preschool" (topic). The search terms were combined with Boolean search function "and". No language filters were used.

Studies were included in the meta-analysis if they met the following criteria: (1) Original community-based studies; (2) Participants aged up to two years; (3) Wheezing and/or recurrent wheezing were defined; (4) Provided original data on the prevalence of wheezing and/or recurrent wheezing.

The search was complemented by reviewing the references of the selected articles to identify additional studies. In those cases that we could not have technical access, we requested the article through the Public University of Navarre library to other institutions. Two researchers (I.A.A. and H.N.) conducted the search and evaluate the studies, resolving the discrepancies by discussion.

After excluding duplicates, 109 articles were found. Reviews, pool studies, studies which did not provide wheezing cases, or its study population was older than two years

were excluded. Abstracts and non-published studies were also excluded.

Studies quality was assessed using the Quality Assessment Tool for Observational and Cross-Sectional Studies, developed by the National Heart, Lung and Blood Institute (NHLBI).¹¹ We assigned one point to positive answers, and zero points to negative answers, calculating the percentage. Low, medium and high quality studies were those which scored less than 50%, between 50% and 75%, and more than 75%, respectively. Low quality studies were removed from the analysis.

Data extraction

Two researchers (I.A.A. and H.N.) conducted the data extraction, resolving the differences by consulting another researcher (F.G.G.). The following data were recorded from each article: (1) Author's name and year of publication; (2) Country where the study was conducted; (3) Definition of wheezing and/or recurrent wheezing; (4) Age range; (5) Number of participants in the study; (6) Wheezing and/or recurrent wheezing cases.

Quantitative analysis (meta-analysis)

Separate meta-analyses were conducted for wheezing and recurrent wheezing in infants. Besides, we conducted additional meta-analyses for world regions (Europe, Latin America and Africa). Fast*Pro software was used to make the calculations. We used a random effects Bayesian model, showing 95% credibility intervals (95% CI).

In Bayesian analysis, credibility intervals are different from confidence intervals of the frequentist statistics. 95% credible interval means that the probability that the real value is in the range of the 95%, according to our initial belief and the observed data. However, a 95% confidence interval indicates that in many repeated samples, 95% of the intervals will show a true value.

Sensitivity analyses were performed, replicating the results after excluding studies with the lowest and highest prevalence, to study the robustness of the analysis and the influence of the removed study.

To estimate the heterogeneity, I^2 statistic was used, estimating the percentage of total variability between studies explained by heterogeneity.¹²

The risk of publication bias was assessed graphically by a funnel plot.

Although no wheezing definition was specified, Dela Bianca et al.,¹⁸ Ferreira et al.²³ and Moraes et al.²⁴ used the written questionnaire from the EISL study, considering wheezing definitions from this questionnaire.¹³ Bueso et al.¹⁷ provided data from both Honduras and El Salvador EISL studies, which were separately included in this meta-analysis. Recurrent wheezing was defined as three or more episodes of wheezing by all the studies.

Results

We identified 148 studies (94 in MEDLINE and 54 in SCOPUS). After duplicates were removed, we reviewed 109 studies. We excluded 59 studies whose title and/or abstract were

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