# META-ANALYSIS: A KEY STATISTICAL METHOD IN CLINICAL RESEARCH THROUGH A REVIEW OF PRETERM BIRTH AND CHILDHOOD WHEEZING DISORDERS

Article Review by Pramod Wable, United Kingdom (M.Sc., Ph.D., in Clinical Research Student of Texila American University) Email: - pjwable@gmail.com

# SOURCE

Been JV, Lugtenberg MJ, Smets E, van Schayck CP, Kramer BW, et al. (2014) Preterm Birth and Childhood Wheezing Disorders: A Systematic Review and Meta-Analysis. PLoS Med 11(1): e1001596. doi:10.1371/journal.pmed.1001596

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# ABSTRACT

Meta-analysis is a statistical approach to combine the data derived from a systematic-review. Therefore, every meta-analysis should be based on an underlying systematic review, but not every systematic review leads to a meta-analysis. Meta-analysis offers a rational and helpful way of dealing with a number of practical difficulties that beset anyone trying to make sense of effectiveness research.

This article review was written after details and critical assessment of the research conducted by Been JV et.al. The researchers undertook meta-analysis and a systematic review investigating risks of asthma/wheezing disorders in children born preterm, including the increasing numbers who, as a result of advances in neonatal care, now survive very preterm birth. The trigger of research was accumulating evidence which implicates early life factors in the aetiology of non-communicable diseases, including asthma/wheezing disorders.

It was evident that preterm birth particularly very preterm birth increases the risk of asthma. Been JV et.al concluded that these is greater need to focus on understanding mechanisms and translate it into preventive actions.

# **KEY WORDS**

Meta-analysis, Systemic Review, Preterm Birth, Asthma, Wheezing, Disorders

# INTRODUCTION

This is a review of the article on, "Preterm Birth and Childhood Wheezing Disorders: A Systematic Review and Meta-Analysis" published in Public Library of Science (PLoC) Medicine on 28 January 2014. This article focuses on the preterm birth and childhood wheezing disorders using the techniques of systemic review and meta-analysis.

This article review begins with a literature review which concisely mentions the current research topic focused in published article. This section also documents related literature and research available in the relevant topic. The literature review section is followed by the article summary.

Further, it briefly analyses the structure of the published article with the different key structural points focusing on contents, alignment and format of the original article. The review also critiques the article through assessing its authority specifying creditability of PLoS Medicine journal in which original article was published and of authors. Further it critiques on currency, accuracy, objectivity, stability and coverage of the published article. This review article analyses the tables, figures and video in detail of their relevance to the actual objective of the research and relevance to the content of the original article before finally evaluating the article's accessibility and credibility. This review article also elaborates the details of any recent advanced related topics to the original research.

The review concludes with the overall impression of the article and its usefulness in the clinical research and any space for the improvement.

#### **REVIEW OF LITERATURE**

Meta-analysis offers a rational and helpful way of dealing with a number of practical difficulties that beset anyone trying to make sense of effectiveness research. Meta-analysis is the use of statistical methods to combine results of individual studies. This allows us to make the best use of all the information we have gathered in our systematic review by increasing the power of the analysis. By statistically combining the results of similar studies we can improve the precision of our estimates of treatment effect, and assess whether treatment effects are similar in similar situations. The decision about whether or not the results of individual studies are similar enough to be combined in a meta-analysis is essential to the validity of the result. (Doi SA, 32008)

Modern statistical meta-analysis does more than just combining the effect sizes of a set of studies using a weighted average. It can test if the outcomes of studies show more variation than expected because sampling of different numbers of research participants. Additionally, study characteristics such as measure instrument used, population sampled, or aspects of the studies' design can be coded and used to reduce variance of the estimator. Thus some methodological weaknesses in studies can be corrected statistically. Meta-analysis allows making the best use of all the information which has gathered in systematic review by increasing the power of the analysis. By statistically combining the results of similar studies it can improve the precision of estimates of treatment effect, and assess whether treatment effects are similar in similar situations. Well conducted meta-analyses allow a more objective appraisal of the evidence than traditional narrative reviews, provide a more precise estimate of a treatment effect, and may explain heterogeneity between the results of individual studies. (Riley RD, 2011)

Other uses of meta-analytic methods include the development of clinical prediction models, where meta-analysis may be used to combine data from different research centers, or even to aggregate existing prediction models.

# **ARTICLE SUMMARY**

The purpose of the research article was to study risks of asthma/wheezing disorders in children born preterm, including the increasing numbers who, as a result of advances in neonatal care, now survive very preterm birth.

The authors of the article used variable and reliable data sources for the research using seven online databases for epidemiological studies investigating the association between preterm birth and asthma/wheezing disorders for period of 1995 to 2013. Additional studies were identified through reference and citation searches, and contacting international experts. In total 42 eligible studies were selected across six continents for the research. Further due to population overlap 12 studies were excluded and final research with help of meta-analysis was conducted on 30 remaining studies involving just over 1.5 million children.

It was concluded that there is compelling evidence that preterm birth—particularly every preterm birth—increases the risk of asthma. Given the projected global increases in children surviving preterm births, research now needs to focus on understanding underlying mechanisms, and then to translate these insights into the development of preventive interventions.

The article was core research article with excellent use of systemic review and meta-analysis for the betterment of the medical research and added value to the advance neonatal care and preterm birth.

# **ARTICLE STRUCTURE**

This was an original article based on the research conducted by the Been JV, Lugtenberg MJ, Smets E, van Schayck CP, Kramer BW, et al. The article was structured in following main points.

- 1. Abstract
- 2. Introduction
- 3. Methods
- 4. Results

- 5. Discussion
- 6. Supporting Information
- 7. Acknowledgments
- 8. References

Detail subsections and their relativity to each other helped reader to concentrate and understand the article end research topic clearly. Article was easy to navigate and well written with simple and concise scientific language. The article had contents paragraphed for better and easy understanding for reader. Excellent use, of tables, and figures provided by authors, was done to elaborate research data and discuss results and outcome.

Statistical data generated using data extraction and random-effects meta-analysis methods used in the article to understand research in details.

The article was structured through main bold points as discussed below.

- Point 1 Methods focusing on the eligibility, study selection and data process
- Point 2 Statistical methods using data extraction and meta-analysis
- Point 3 Results focusing on different effects such as study quality, sensitivity etc.
- Point 4 Discussion on study strength, possible interpretations and possible mechanisms
- Point 5 Supporting information

The discussion was developed towards the end of the article. There was no separate section on conclusion included.

References were cited in-text and set out clearly in the literature cited section; 77references were given at the end which was sufficient. However references were not listed in alphabetical order (APA format). The overall article's structure was logically developed, with the use of detail paragraphs helping the reader access the main points more easily. The article was a PDF document.

# ARTICLE CRITIQUE

#### AUTHORITY

PLoS Medicine is the leading open-access medical journal, providing an influential venue for outstanding research and commentary on the major challenges to human health worldwide. It publishes articles relevant to clinicians and policymakers across a range of settings that adhere to

the highest standards of methodology, ethics and reporting and address the major biological, environmental, social, and political determinants of health.

The authors' credibility was established in a number of ways. All the authors were from wellknown universities and have published number of research articles. The author Been JV is from Department of Paediatrics, Maastricht University Medical Centre, Maastricht, Netherlands. (Maastricht University, 2014)

#### ACCURACY

The information in this study was obtained from seven highly recognised databases, citation search and contacting international experts in the research subject. The study was funded and supported by Department of Paediatrics, Maastricht University Medical Centre, Maastricht, Netherlands. Experienced authors of the article made the article accurate and informative. The accuracy was backed up and supported by a comprehensive, recent reference list with these sources cited in-text to support both the literature review and the research itself. The strict editorial and refereeing processes of the PLoS Medicine also contributed to the article's accuracy.

#### CURRENCY

The PLoS Medicine is a peer-reviewed medical journal published under the Creative Commons "by-attribution" license. The article was received by PLoS Medicine on 25 July 2013, accepted on 06 December 2013 and published on 28 January 2014. The research conducted was current, very recent and the article cites up-to-date references in the body of the text ranging from year 1993-2013. All the articles referenced were with latest research performed in preterm birth and neonatal care. Therefore the article is current. (PLoS Medicine, 2014)

#### RELEVANCE

PLoS Medicine (formerly styled PLoS Medicine is a peer-reviewed weekly medical journal covering the full spectrum of the medical sciences. It began operation on October 19, 2004, as the second journal of the PLoS, a non-profit open access publisher. All content in PLoS Medicine is published under the Creative Commons "by-attribution" license. PLoS Medicine applies rigorous editorial and peer review overseen by a team of professional editors and, in the case of research articles, an independent academic editor expert in the field. *PLoS Medicine* is committed to upholding the highest ethical standards in medical publishing, including the management and disclosure of conflicts of interest in reporting, review, and publication (PLoS Medicine, 2014).

# **OBJECTIVITY**

The information in article was objectively developed, well supported with a current research database and with all the latest evidence acknowledged and referenced. The article objective was clearly defined and reflected thorough the content of the article. There was no evidence of bias, a fact that was reinforced by the recognition that the article documents research, which followed the rigorous research processes, and the necessary ethical considerations demanded of such intensely supported research. The sponsors of the research were clearly defined after conclusion of article.

#### STABILITY

The article was a source of research work studying preterm birth and childhood wheezing. The article carefully demonstrated conducted research with the data generated during the research. The article was based on the current research, clinical trials recently conducted and backed up with practical evidences published in the recent research; therefore it's stable. The stability of the article can also be judged with the help of the authors and their creditability, expertise and work history. The PLoS Medicine and its creditability also makes article stable.

#### ANALYSIS OF GRAPH/IMAGE/TABLE

There were 3 tables and 7 figures were used to elaborate the research work in this article. All tables and figures were clearly titled and linked within the text; detail analysis of each of them is given below. Overall tables and figures were clearly defined and compliment the entire original article.

- Table 1 (pages 4 and 5) –The table explained, Characteristics of included studies: the actual cohort studies.
- Table 2 (pages 6 and 7) Table 2 shown, Characteristics of included studies: case control and cross-sectional studies.
- Table 3 (page 8) Table 3 tabulated, Meta-regression analysis according to study characteristics.
- Figure 1 (page3) Figure 1 shown flowchart outlining study selection.
- Figure 2 (page 8) Figure 2 shown, Meta-analysis of unadjusted association between preterm birth and childhood wheezing disorders.
- Figure 3 (page 9) Figure 3shown, Meta-analysis of adjusted association between preterm birth and childhood wheezing disorders.

- Figure 4 (page 10) Figure 4 described, Meta-analysis of adjusted dose-response association between gestational age (per week increase) and childhood wheezing disorders.
- Figure 5 (page 11) Figure 5, Meta-analysis of association between very preterm birth and childhood wheezing disorders. (A) unadjusted effect estimates; (B) adjusted effect estimates. Subgroups taken from individual studies noted in parentheses.
- Figure 6 (page 12) Figure 6 explained, Meta-analysis of association between moderately preterm birth and childhood wheezing disorders. (A) unadjusted effect estimates; (B) adjusted effect estimates. Subgroups taken from individual studies noted in parentheses.
- Figure 7 (page 13) Figure 7 described, Funnel plots for studies reporting unadjusted and adjusted association measures. (A) unadjusted association measures; (B) adjusted association measures.

# **RECENT ADVANCES RELATED TO THE TOPIC**

# There were few recent researches conducted on maternal smoking during pregnancy, prematurity and recurrent wheezing in early childhood. An example is discussed below.

In 2012, Robison RG et.al conducted a study to evaluate the interactive effects of maternal smoking and prematurity upon the development of early childhood wheezing.

For this prospective study, researchers evaluated 1,448 children with smoke exposure data from a prospective urban birth cohort in Boston. Maternal antenatal and postnatal exposure was determined from standardized questionnaires. Gestational age was assessed by the first day of the last menstrual period and early prenatal ultrasound (preterm < 37 weeks gestation). Wheezing episodes were determined from medical record extraction of well and ill/unscheduled visits. The primary outcome was recurrent wheezing, defined as  $\geq$  4 episodes of physician documented wheezing. Logistic regression models and zero inflated negative binomial regression (for number of episodes of wheeze) assessed the independent and joint association of prematurity and maternal antenatal smoking on recurrent wheeze, controlling for relevant covariates. It demonstrated an interaction between maternal smoking during pregnancy and prematurity on childhood wheezing in this urban, multiethnic birth cohort.

Another study was conducted in 2013 by Joshi S et.al, to assess for exercise-induced bronchoconstriction in 8- to 12-year-old children who had chronic lung disease (CLD) in infancy, and to evaluate the response of bronchoconstriction to bronchodilation with albuterol in comparison with preterm and term controls. Ninety-two children, including 29 with CLD, 33 born preterm at  $\leq$ 32 weeks' gestation, and 30 born at term, underwent lung spirometry before and after cycle ergometry testing and after post-exercise bronchodilation with albuterol.

School-age children who had CLD in infancy had significant exercise-induced bronchoconstriction that responded significantly to bronchodilation. Reversible exercise-induced bronchoconstriction is common in children who experienced CLD in infancy and should be actively assessed for and treated.

#### CONCLUSION

The research discussed in the original article "Preterm Birth and Childhood Wheezing Disorders: A Systematic Review and Meta-Analysis" was with clear objective and a true research. The content, structure, strengths and limitations of the article were analysed and critiqued. The article has contributed to the literature in terms of its valuable research of preterm birth and neonatal care. The article was very good reference information based on the practical and current research.

The article expressed detail picture and true data on preterm birth and childhood wheezing disorders using the data available from various sources and performing meta-analysis with systemic review. The article was very well written and had all the necessary sections to discuss the detail research conducted and outcome obtained. Tables and figures included in the article were accurate, and clear for understanding. It was very useful and informative article for the academic and healthcare researchers.

It is suggested that a conclusion section highlighting key conclusions would be useful in the article. For future research wide range of outcomes and physiological conditions would be useful to include in the research to show more explicit results of neonatal disorders.

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