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Random and Systematic Bias in Population Oral Health Research: an introduction

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Bias in population oral health research is a form of systematic error that can affect scientific investigations and distort inference (i.e under or over confidence in an estimate). A biased study loses validity in relation to the degree of the bias. While some study designs are more prone to bias, its presence is universal. It is difficult to completely eliminate bias; in the process of attempting to do so, new bias may be introduced or a study may be rendered less generalizable. The goals are to therefore minimize bias and for investigators and readers to comprehend its residual effects, limiting misinterpretation and misuse of data. In the four papers that follow, we seek to contribute to the discourse around random and systematic bias in population oral health research through the lens of case controlled studies, longitudinal studies and genomics re search. The papers formed the basis of a symposium entitled *'Random and Systematic Bias in Population Oral Health Research'* at the 98th General Session of the International Association of Dental Research held March 2020 in Washington DC, United States.

Using tangible examples, the collected authors describe the intractable role of bias in population oral health research; how to minimise, identify and articulate; demonstrate the increasingly sophisticated techniques for addressing measurement error and bias in population oral health research, including specific statistical software and codes; and discuss the implications of addressing (or not addressing) bias in population oral health research at an international level, including the role of advocacy and engaging with oral health policymakers to both minimize bias and to increase comprehension of its residual effects that may lead to misinformed policy. Mittinty describes simple methods for conducting sensitivity analysis for unmeasured confounders in his paper entitled 'Estimating Bias Due to Unmeasured Confounding in Oral Health Epidemiology', with examples provided through case studies and vignettes. He explains how confounding arises when variables are associated with both exposure and outcome but are not on the causal pathway. Because unmeasured confounders can have a cumulative effect, can make associations seem bigger when the true effect is smaller (or vice-versa) or can make associations appear negative when they are actually positive, understanding and accounting for confounding is essential. Duran and colleagues, in their paper entitled 'Quantitative Bias Analysis of misclassification in case-control studies: an example with Human Papillomavirus and Oropharyngeal Cancer', describe how an implausible association between oral sex practice and oropharyngeal cancer was explained by biases in the data (mediator misclassification). Using sensitivity and specificity estimates of a diagnostic test from a meta-analysis, the authors emphasised the importance of widespread adoption of quantitative bias analysis in oral health research. Celleste and colleagues' paper entitled 'Bias in population oral health research: longitudinal studies' provides an overview of key issues related to selection bias, time-varying confounders, solutions to bias and challenges in longitudinal studies in dental research. Selection bias is described as distortions in estimates due to losses of follow-up or use of specific population groups. This kind of bias can be understood conceptually through directed acyclic graphs, collider bias or missing data theory. Time-varying confounding is when an exposure varies over time and is affected by past exposure of other time-varying covariates. Information that is missing in this way might be informed by other variables or managed through multiple imputation or inverse probability weighting. However, the best solution is to prevent losses to follow-up in the first place. Agler and Divaris, in their paper 'Sources of bias in genomics research of oral and dental traits', describe how generation of genome-wide association (GWAS) data is prone to many sources of random and systematic error, including type I and II errors, population stratification and heterogeneity, selection bias, adjustment for heritable covariates, appropriate reference panels for imputation, and gene annotation. They describe how the lack of diversity of populations (data to date is mainly European) is problematic from multiple standpoints, ranging from biological to social.

The papers are a valuable contribution to the literature on the role of bias in population oral health research across a range of study designs commonly used in the field. The far-reaching influence of bias in our everyday research lives, from both epidemiological and pragmatic perspectives, and the multi-faceted positive or adverse effects on oral health policy this might have, provide an important clarion call for addressing unmeasured random and systematic error in our analytical and study design processes moving forward.

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