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Uncovering Exposures Responsible for Birth Season – Disease Effects: A Global Study

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Abstract

Birth month and climate impact lifetime disease risk while the underlying exposures remain largely elusive. We seek to uncover distal risk factors underlying these relationships by probing the relationship between global exposure variance and disease risk variance by birth season. This study utilizes Electronic Health Record data from six sites representing ten and a half million individuals and three countries (USA, South Korea and Taiwan). Three of these sites are OHDSI collaborators. We obtained birth month – disease risk curves from each site in a case-control manner. Next, we correlated each birth month – disease risk curve with each exposure. A meta-analysis was then performed of correlations across sites. This allowed us to identify the most significant birth month – exposure relationships supported by all six sites while adjusting for multiplicity. We also successfully distinguish relative age effects (a cultural effect) from environmental exposures. Attention Deficit Hyperactivity Disorder was the only identified relative age association. Our methods identified several culprit exposures that correspond well with the literature in the field. We will discuss these findings at our talk.

Introduction

The relationship between seasonality, climate, and disease has been studied for millennia. Geographic location alters our exposure to climate factors generally [1], but also our exposure to a plethora of environmental factors. We previously constructed an algorithm, called SeaWAS for Season-Wide Association Study, to systematically

investigate birth month - disease dependencies across all diseases having sufficient prevalence in Electronic Health Records (EHRs) [2]. In all of our analyses, birth month serves as a proxy for birth seasonality. We conducted our initial SeaWAS study using data from the New York City (NYC) climate. Novel cardiovascular disease findings where then subsequently replicated at Mount Sinai Hospital [3].

In this study, we investigate the relationship between developmental stages (first, second, third trimester, perinatal or pregnancy-wide) and seasonal environmental exposures (climate, pollution, flu) for birth month – disease relationships. We also delineate birth month – disease relationships due to differences in school cutoff dates across sites indicating the effect of relative age on human health and disease. Because of the diversity of diseases associated with birth month or season, different mechanisms and exposures are likely to be involved depending on the particular disease implicated. We present results obtained using data from six distinct institutions, over three countries, spanning five cities, and four distinct climates. We identify risk factors involved in birth season associations.

Methods

Our birth season – disease (SeaWAS: Season-Wide Association Study) algorithm conforms to the Common Data Model (CDM) adopted by the Observational Health Data Sciences and Informatics (OHDSI) consortium [4]. We provided the SeaWAS code to each of our collaborators, who ran it locally on their EHRs using OHDSI-formatted R scripts. Permission was obtained from each institution's local Institutional Review Board (IRB).

Culture vs. Climate/Pollution Effects

Importantly, two different types of effects can manifest themselves in variance in disease risk by birth month. The first is cultural/sociological related to the timing of school start-dates and the second is related to variance in pollution, climate factors (e.g., sunlight) that vary seasonally. These two types of birth month effects are important as both can result in changes in disease risk. For cultural effects of birth month, we investigate relative age effects [5]. We define relative age as an individual's age relative to the individual's peers in the same school grade. Relative age in school provides a competitive advantage for certain children with regards to sports performance [5]. This can result in changes in disease risk as children involved in sports are likely to experience more physical trauma (e.g., head trauma in football). Also children younger then their peers are more likely to be victims of bullying, which can alter neurological development via direct trauma (e.g., concussion) or indirect trauma (e.g., depression). It is important to separate and distinguish these cultural effects from other climate/pollution driven birth season effects.

Conclusion

This comprehensive study of factors involved in birth month – disease risk used data from over 10 million patients, three countries, two continents, and five climates. We were able to distinguish the cultural effect of relative age from seasonal environmental exposures that both affect birth month – disease dependencies. We were also able to identify both the seasonal environmental exposure and the stage that resulted in increased disease risk. Several important findings were noted and will be discussed at the talk.

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