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## Age, Period, and Cohort Effects in Perinatal Epidemiology: Implications and Considerations

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In this issue of *Paediatric and Perinatal Epidemiology*, Margerison-Zilko presents evidence regarding age, period, and cohort effects on term small for gestational age (SGA) births in the US from 1989 to 2010.<sup>1</sup> Age–period–cohort (APC) analysis is an informative and increasingly utilised methodology to provide a nuanced understanding of time trends in health outcomes. In this commentary, we evaluate the results through the lens of ongoing controversies in APC modelling strategies, and reflect on the public health implications of the temporal trends in SGA in the US with regard to race and ethnic disparities in health.

Before commenting on the specific methodological approach used by Margerison-Zilko, it is important to set APC analysis in historical context. The powerful way in which many health outcomes aggregate by birth cohort has been recognised for almost a century,<sup>2,3</sup> but it was not until the 1970s that rigorous attempts at statistical approaches to estimating age, period, and cohort effects began to proliferate.<sup>4</sup> It was no sooner that statistical approaches began to be implemented that criticisms of each approach were launched.<sup>5</sup> Fundamentally, the controversy revolves around the inability to separate the linear effects of age, period, and birth cohort (cohort = period–age); logically, it is impossible for any individual to advance in age without moving forward in time, and thus impossible to vary one of the three parameters while holding two constant. In fact, the interpretation of ‘unique’ effects of age, period, and cohort while holding each other constant requires, in and of itself, metaphysically impossible inference (i.e. what if humans had the ability to retain a birth year and current age, but could move in a time machine a decade away?<sup>6</sup> Of course, a solution to this interesting problem will be dealt within the depths of quantum mechanics and theory of relativity in years to come!). Given these limitations, APC analysis has typically been confined to graphical depiction of data that provide some additional nuance to examination of time trends.

APC methods achieved resurgence in the last decade, due in part to the proliferation of new methods to estimate the model, including but certainly not limited to the intrinsic estimator

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(IE) approach used by Margerison-Zilko.<sup>7</sup> The IE is essentially a principal components regression approach to APC analysis, and achieves model identification, similar to almost all methods, by forcing constraints on the linear components of age, period, and cohort coefficients. Lately, this model, like many before it, has begun to receive criticism,<sup>8</sup> and the debate about the meaning of age, period, and cohort effects has renewed.

Debates about the validity of statistical assumptions across data structures will persist as long as researchers are interested in APC effects. No model will be valid in all situations. There are many health outcomes that have non-linear age, period, and cohort effects (including, for example, obesity<sup>9</sup>), interactions across time and age, and other structures for which a formulaic application of a particular statistical model may be inappropriate. APC modelling is most informative when testing a specific theory or hypothesis,<sup>9</sup> when specific a priori information can inform the model and interpretation, or when effects are strong and robust thus consistent across modelling approaches with varying assumptions and constraints.

The results of Margerison-Zilko demonstrate robustness across both an IE approach and a hierarchical APC (random-effects) model, and while the consistency itself does not validate the estimates provided (both could be biased), it does provide at least some additional confidence in the observed trends. Results indicate robust disparities in term SGA with offspring of non-Hispanic Black women consistently at higher risk, and further, that SGA is increasing among non-Hispanic Black women in the US born after 1970; no such increases were seen for other racial/ethnic groups. It is concerning that there is little explanation for the observed cohort effects in term SGA births, hampering interpretability and mechanisms for action. Margerison-Zilko suggests that the results are hypothesis generating, and that a combination of social and economic factors that have influenced African-American women to a greater degree than other racial/ethnic groups likely underlie the results. To that end, then, these results add to the profound and vast literature on the continuing inequalities in adverse perinatal outcomes, inequities that continue to persist, and if we believe, the results of Margerison-Zilko, may be growing.

Birth outcomes among African-American women in the US continue to evidence stark disparities, and these disparities may be growing among women in more recently born cohorts for term SGA.<sup>1</sup> African-American women in the US are more likely to experience a number of adverse perinatal outcomes such as preterm delivery,<sup>10,11</sup> placental abruption,<sup>12,13</sup> preeclampsia,<sup>14</sup> and stillbirth,<sup>15</sup> and a host of other conditions. These disparities persist after rigorous account for observed measures of socio-economic characteristics and pregnancy health behaviours. Substantial data have indicated that African-American women in the US experience poorer birth outcomes as they age due to the cumulative stress of disadvantage,<sup>16</sup> though this explanation is unlikely to completely account for observed differences. Better understanding and addressing these inequities is a critical public health goal.

Margerison-Zilko also notes that among African-American women, the risk of term SGA births is growing in more recently born cohorts. Common risk factors such as smoking and pregnancy complications cannot explain this finding, as Margerison-Zilko states that

decreases in term birthweight persist within strata of these factors, and there is little evidence to suggest that these factors are increasing in prevalence among African-American women in more recent cohorts.<sup>1</sup> Substantially increasing evidence indicates that a potentially important area of research in health disparities is the pervasive effects of structural as well as interpersonal discrimination. Discrimination – defined as the unequal treatment of certain groups on the basis of some socially signified characteristic – can occur at multiple levels, ranging from interpersonal (e.g. being called a racial epithet) to institutional (e.g. policies that segregate schools on the basis of race). Existing evidence documents that interpersonal discrimination due to race is a risk factor for morbidity and mortality among African-Americans,<sup>17</sup> and that structural discrimination – which refers to societal-level conditions that constrain individuals' opportunities, resources, and well-being based on race – is evident across a wide variety of important life domains, including hiring and employment practices, wages, promotions, job control, housing, credit, and consumer markets. Despite the pervasiveness of structural discrimination, most research has focused on interpersonal discrimination, as structural discrimination is often ubiquitous, and thus variation is unable to be quantified.

Structural forms of discrimination are a plausible and yet un-researched potential driver of the effects observed here. For example, women of Arab-American descent delivering in the US in the 6 months after 9/11 had worse birth outcomes compared to Arab-American women prior to 9/11 as well as women of other ethnic backgrounds at the same time.<sup>18</sup> There is little potential explanation for such a result except perhaps stress due to a suddenly marginalised social status. There is also emerging evidence that state-level variation in historical policies and laws influence health among African-Americans, but not among Caucasians.<sup>19,20</sup> Taken together, we suggest that a concerted effort to measure, quantify and examine exposures that affect African-Americans to a particularly salient degree may be good candidates for further research on the growing disparity in SGA. This requires diligence and creativity in looking beyond standard measures of socio-economic status and health behaviours to the broad and pervasive ways in which legacies of discrimination and exploitation continue to potentially exert and influence on the health of Americans.

So what new lessons does an age–period–cohort modelling inform us of temporal changes in term SGA births in the US? Certainly, it suggests that a renewed and explicit focus on social and contextual drivers of adverse birth outcomes has never been more imperative. The rates of SGA among African-American women in the US remain unacceptably high, and this robust data indicate that there are still more drivers of disparities that relate to variation across birth cohorts that are left to be uncovered and intervened upon. Methodologically, APC analyses moving forward should be hypothesis driven, informed by theory and data about changing social, cultural and environmental factors that create variation over time and across cohort. Further, rigorous APC analysis should extensively rely on modelling the descriptive data; examine sensitivities to departures from the underlying assumptions about data structure. While debates about sound vs. unsound methodological approaches to APC analysis will undoubtedly remain a firestorm of debate in the literature, as well it should, the results of well-executed age–period–cohort analyses remain critical in shaping our understanding of long-lasting and population-level drivers of critically important health indicators.

## Biographies

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