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Birth Order and Myopia: What are the Messages to Readers?

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Over the past few years, there has been considerable interest in whether life influences, other than the well-documented factors of education^{1,2} and more recently time outdoors,^{3,4} could contribute to the world-wide increase in the prevalence of myopia⁵. An article, led by Guggenheim, published in this issue⁶ deals with one of these factors, namely birth order. The authors are to be congratulated for their achievement in assembling a large number of study subjects from four independent studies, to assess the association between birth order and myopia.

Previous studies have suggested that first-born children are more likely to be myopic than their siblings⁷; however, the studies were significantly limited by small sample size and constraints in methodology. This new paper analyzes data from four separate epidemiological studies, each of which shows the same direction of effect, and hence provides evidence of consistency of an association between birth order and myopia. However, due to the fact that these four studies were not designed to specifically address this issue, there are some methodological limitations. Two of the four studies used cycloplegic refraction, the gold standard for assessing myopia in children and young adults, and while their independent results are suggestive of an association, neither of these two studies showed statistically significant associations of birth order and myopia. Results from the studies with the largest sample sizes did show a statistically significant association, but neither used cycloplegia and, therefore, may have misclassified myopia.

Limitations aside, this new report does provide incremental evidence for an association. To arrive at a definitive conclusion about an association of birth order with myopia would require further studies with large sample sizes and the use of gold standard methodology, preferably in multiple population groups and where multiple siblings in the same family participated. But, as is often the case, insight about disease associations from epidemiologic studies sometimes depends on studies of less than perfect design. Therefore, consistency in evidence is important to provide confidence in the findings, which is what this paper delivers.

In the absence of additional, specially designed studies, what further can be gleaned from this report? If first-born status is a risk indicator, it can be argued that the potential public

health implications are limited, given that birth order itself is not a modifiable factor. Moreover, the effect size of birth order on myopia, or the magnitude of the odds ratios for being myopic if first-born, is relatively low. In other words, not all first-borns will get myopia, and many people with later birth order will also develop myopia. Compared with the known secular increase in the prevalence of myopia that has occurred in East and Southeast Asia, where it has doubled or tripled since the end of the Second World War⁸, the risk of myopia associated with first-born status is very modest. The reported magnitude of association of myopia with birth order is similarly small relative to the very high prevalence of myopia in boys attending Orthodox Jewish schools in Israel compared to the prevalence in the rest of the school population⁹. In the current paper, Guggenheim and co-authors sensibly resist the temptation to over-emphasize their findings by not suggesting that the small effects of birth order they have observed could explain the increased prevalence of myopia in East and Southeast Asia, or even the differences in prevalence observed between closely matched urban and rural areas^{10,11}.

On the other hand, with the demographic changes taking place in much of the world, the relative prevalence of only children and first-born children is increasing. In turn, the attributable risk associated with first-born status will increase in importance and this provides a good reason to follow up this finding. One critical issue to be addressed is that there are long-standing and strong positive associations of myopia with education, as noted previously, and there is a substantial literature linking birth order and educational achievement, suggesting, despite considerable potential confounding, that early born children achieve more highly than their later-born siblings.^{12,13} Therefore, it is possible that a link between myopia and birth order could be confounded by level of educational achievement. While the authors of the current study adjusted for variables that were associated with both birth order and myopia, including near work and intelligence, none of the four studies completely addressed this potential confounding issue.

If effects of birth order independent of education are demonstrated, consideration of other factors influenced by birth order could provide important clues to help elucidate potential mechanisms underlying myopia development. For example, any differences between birth order and parental health, their education and other exposure profiles, familial characteristics, as well as antenatal, perinatal and postnatal environments to which children are exposed, could hint at possible pathways which could influence the development of myopia. Along these lines, the authors⁶ note the relationships between birth order and low birth weight, catch up growth, insulin resistance and obesity, and suggest that these associations could be linked to the involvement of glucagon and insulin in the control of eye growth pathways in experimental myopia¹⁴. However, this link has only been clearly demonstrated in chickens.

In summary, the authors have documented consistent trends towards a higher prevalence of myopia in first-born children. Given the global trend towards smaller family size, birth order might become more important in the etiology of myopia in the future, and deserves further study. How this factor interacts with environmental risk factors for myopia such as education and time outdoors, as well as with the recently documented genetic associations of a number of single nucleotide polymorphisms (SNPs) of small effect with myopia,^{15,16}

remains to be established. It is important to note that the interactions could be extremely complex, involving a range of biological, social and cultural factors, and in fact a recent study from Taiwan has shown complex interactive modulation of learning achievement in adolescents by birth order, gender and parental education.¹⁷

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