Cohort effects explain the increase in autism diagnosis: an identifiability problem of the age-period-cohort model

From Stefan N Hansen* and Erik T Parner

Section for Biostatistics, Department of Public Health, Aarhus University

*Corresponding author. stefanh@biostat.au.dk

Keyes et al.1 used an age-period-cohort model in an effort to disentangle time trends in autism to distinguish effects attributable to age, period and cohort, respectively. It is well known, in particular in the statistical literature, that the age-period-cohort model suffers from

Conflict of interest: None declared.

References

10. Coyne DW. The health-related quality of life was not improved by targeting higher hemoglobin in the Normal Hematocrit Trial. Kidney Int 2012;82:235–41.
an identifiability issue\(^2\) since the date of diagnosis is the sum of the date of birth and the age at diagnosis. This issue is often resolved by using a constraint-based approach. However, any such constraint cannot be validated from data itself\(^2\) and thus has to come from prior knowledge.

In their original paper, the authors of Keyes et al. used the constraint that the age-effect should be constant between ages 8 and 12 years, based on the observed rates in their data being approximately constant after age 8. However, the observed rate as a function of age does not depict the age-effect. In a letter to the editor, Spiers\(^3\) questioned their choice of constraint and pointed out that in the statistical literature it is known that even a slight inconsistency between the constraint and reality can have a large impact on estimated effects. In a response to Spiers,\(^4\) the authors of Keyes et al. however argued that ‘there is substantial evidence that diagnoses are more common among 3- and 4-year-old children than older children, thus a simple constraint that diagnosis is constant after the age of 8 years allowed us to parsimoniously model the data without assuming that period- and cohort-effects are nonlinear variation from overall drift’. Whereas it is true that the authors of Keyes et al. assume nothing about the period- and cohort-effects, what is missing is still an exploration of how sensitive their estimated age-, period- and cohort-effects are to the constraint imposed on the age-effect. The purpose of this letter is to illustrate, on the same data as Keyes et al.,\(^1\) that even a small change in their constraint can yield very different conclusions.

Below we repeat, in the left-hand graph of Figure 1, the estimated age-, period- and cohort-effects that appeared in the original paper: that is, under the constraint of a constant age-effect between ages 8 and 12 years. The authors of Keyes et al. concluded that the prevalence increase is driven mainly by a cohort-effect. The right-hand graph shows the estimated age-, period- and cohort-effects still consistent with the observed autism rates but under a minor change in that constraint. Instead of assuming a constant age-effect between ages 8 and 12, we have used the constraint that the age-effect is linear with a slightly negative slope, i.e. this constraint is very close to the constraint of a constant age-effect between ages 8 and 12. From these results it appears that the prevalence increase was driven mainly by a period-effect.

Since the two constraints used in Figure 1 are almost identical, it is our impression that the estimated age-, period- and cohort-effects are very sensitive to the assumptions made. We acknowledge that the authors of Keyes et al. did perform some sensitivity analyses of their results, as the authors write that ‘for these data we carefully examined the graphical trends in the data, estimated models with varying assumptions…’. However, there are still reasonable constraints that the authors failed to explore, as seen in Figure 1. The same sensitivity to specific constraints was also observed when we applied an age-period-cohort analysis for autism diagnoses in Denmark among children born in the same period with similar follow-up. The huge difference in conclusion with very similar constraints illustrates the limitations of the age-period-cohort model.

### References