

Response by the ISUOG Safety Committee to *JAMA Pediatrics* publication ‘Association of prenatal ultrasonography and autism spectrum disorder’

London, 12 February 2018

In this modest sized retrospective case–control study¹, the authors find that children with autism spectrum disorder (ASD) were exposed to a shorter duration of prenatal ultrasound and lower-energy scans. They find that the mean depth of penetration of the ultrasound beam is greater in those that developed ASD compared to in healthy children.

There are several substantial limitations of the study that should be mentioned ‘up front’. The authors do not tell us what their primary outcome was, in other words what was the key comparison that they wanted to make, nor do they tell us the power of the study to find an effect. In this context, the authors present a new, hitherto unknown and in the paper undefined, index of ultrasound exposure: the time-weighted mean depth of ultrasound. However, it is important to bear in mind that depth of penetration of ultrasound is not a measure of ultrasound exposure, it simply tells us how deep the ultrasound beam is. So, for example, in more obese women the depth of penetration would be greater and, indeed in this study, there is a greater proportion of women with moderately high body mass index (BMI) in the ASD group compared to those with developmental delay. We do not know what the average BMI is in the groups as these data are not presented: this information would help us to understand if the mean depth was simply a reflection of physical characteristics of the women being scanned.

The most meaningful interpretation of these data should include consideration of the ultrasound safety indices, in particular the thermal index and mean duration of ultrasound. It is very reassuring that there was no relationship between ASD and duration of ultrasound exposure or thermal index: these indices, in a drug study, are equivalent to the duration of taking the drug and its dose, not how far the tablet had to travel to get to the stomach.

A further methodological concern is that the authors present multiple comparisons. In doing so, they fall foul of the first law of statistics: if you want to find a positive answer, keep analysing the problem in many different ways and you will finally come up with one by chance. In most research, this practice is adjusted for but it is not in this study.

In summary, despite many limitations, this paper does not suggest that ultrasound exposure is associated with ASD. In fact, its findings are very reassuring. It suggests that, among many other comparisons, children with ASD had slightly shorter scans during fetal life with lower exposure; and a slightly greater depth of ultrasound, well within normal clinical parameters, was used during scanning.

What it definitely does not tell us is that ultrasound causes autism. We, as the Safety Committee of a major international group of clinicians, physicists and safety experts believe that it is crucial for studies to be correctly performed and interpreted. It is beholden to authors and reputable journals to adhere to the highest scientific and statistical standards, particularly when broadcasting important health messages that may affect many millions of women. Barely two decades ago, Dr Andrew Wakefield’s small cohort study in *The Lancet* suggested that the measles, mumps and rubella (MMR) vaccination caused autism. The statistical analysis was flawed, he was wrong and the resulting harm was incalculable.

ISUOG Safety Committee:

Christoph Lees (Chair), Jacques Abramowicz, Christoph Brezinka, Karel Marsal, Kjell Salvesen, Ragnar Sande, Caroline Shaw, Gail ter Haar.

Reference

1. Rosman NP, Vassar R, Doros G, DeRosa J, Froman A, DiMauro A, Santiago S, Abbott J. Association of Prenatal Ultrasonography and Autism Spectrum Disorder. *JAMA Pediatrics* 2018