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The risk of congenital malformations in infants exposed in the first trimester to smoking cessation pharmacotherapies: A multi-national cohort study.

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Abstract

Background and Aims: The pharmacotherapies varenicline, nicotine replacement therapy (NRT) and bupropion are the most effective smoking cessation strategy, but prior studies had inadequate statistical power to elucidate their potential teratogenic effects. This multi-national study assessed the risk of major congenital malformations (MCM) associated with exposure to these pharmacotherapies in the first trimester.

Design and Methods: We linked records of all pregnancies resulting in birth (2003-2020) in New South Wales (NSW) Australia, New Zealand, Norway and Sweden to pharmaceutical dispensing, in/outpatient care, and death data. We identified women using varenicline, NRT or bupropion in the first 13 weeks of pregnancy. We identified any and body-system MCMs from infant's records within 18 months of birth. We compared with infants born to mothers who smoked without using pharmacotherapy. To date, we have calculated crude relative risks (RR, 95% confidence interval [CI]) for NSW, Norway and Sweden. Next, we will include New Zealand data, apply propensity score matching and meta-analyse adjusted RRs.

Results: In NSW, 1540; 658 and 296 infants were exposed to varenicline, NRT and bupropion, respectively. In Norway/Sweden, 558; 64 and 118 infants were exposed, respectively. Crude analyses showed no differences in the risk of any MCM for varenicline (NSW 0.85 [0.64-1.12]; Norway/Sweden 1.03 [0.67-1.58]), NRT (NSW 1.04 [0.72-1.53]), bupropion (NSW 1.10 [0.63-1.92]). For varenicline, cardiac MCM risks were 0.62 [0.29-1.29] (NSW), 1.46 [0.84-2.57] (Norway/Sweden). NSW data yielded RR 0.70 [0.36-1.35] for varenicline and limb MCMs; 1.48 [0.87-2.51] for varenicline and genitourinary MCMs; 2.27 [1.26-4.11] for NRT and cardiac MCMs; and 1.10 [0.49-2.45] for NRT and limb MCMs.

Conclusions: Unadjusted estimates show no increased risk of reported MCMs but are imprecise. Pooled estimates will provide more robust evidence on the safety of smoking cessation pharmacotherapies during pregnancy.

Impact: This evidence will support informed decision-making and optimise outcomes for pregnant women wanting to stop smoking.