

### In Utero Smoking Exposure Warrants Further Investigation

**D**'Onofrio et al<sup>1</sup> present data from a large Swedish population-based study testing the association between fetal exposure to maternal smoking during pregnancy and later offspring criminality, using unexposed siblings as controls. Their results suggest that the observed association between nicotine exposure and offspring criminality is accounted for by differences in familial background factors rather than the exposure per se. These observations should not, however, be interpreted as negating the numerous studies that have shown long-term adverse effects of prenatal nicotine exposure. First, in utero exposure to smoking has been associated with a range of problems, from complications during pregnancy and low birth weight, to conduct and other behavioral problems in childhood and adolescence, and ultimately drug and alcohol use and addiction. Only a small percentage of these offspring, however, commit crimes and by focusing solely on incarceration as an outcome, D'Onofrio et al may have been examining a different subgroup. It is unclear whether they would have found similar effects in the same cohort had they examined other psychiatric, behavioral, or developmental outcomes. D'Onofrio et al also note that the observed effects may be driven by unmeasured parental psychopathology. Yet, a number of groups who have directly assessed the parental psychiatric state have found that offspring outcomes are not confounded by parental diagnostic variables or by maternal postnatal smoking.<sup>2,3</sup> Finally, there is a body of animal literature,<sup>4-7</sup> now being supplemented with human imaging,<sup>8,9</sup> that documents physiological and behavioral abnormalities resulting from in utero nicotine exposure and that cannot be fully attributed to familial background effects.

The article was clear and scholarly in the citation of methodologic limitations and implications for future research. However, we would further underscore that the findings therein should not be taken to imply that in utero exposures are merely a proxy for other familial factors and therefore not warranting continued investigation. To the contrary, the translation of epidemiologic observations into testing using animal genetic and neuroimaging methods is necessary to target mechanisms underlying transmission of prenatal

risks. This type of translational epidemiology is now beginning to happen in psychiatry.

Ardesheer Talati, PhD  
Myrna M. Weissman, PhD

**Author Affiliations:** Department of Psychiatry, Columbia University, New York, New York.

**Correspondence:** Dr Talati, Department of Psychiatry, Columbia University, 1051 Riverside Dr, Unit 24, New York, NY 10032 (at2071@columbia.edu).

**Financial Disclosure:** In the past 5 years, Dr Weissman received investigator-initiated grants from GlaxoSmithKline, Eli Lilly and Company, and the Josiah Macy Foundation. These are no longer active and ended in 2007. She currently receives royalties from Oxford University Press, Perseus Press, the American Psychiatric Association Press, and MultiHealth Systems.

**Funding/Support:** This work was supported in part by grant R01 MH36197 ("Children at High and at Low Risk for Depression," Dr Weissman, principal investigator) from the National Institute of Mental Health (NIMH), including a supplement from the National Institute on Drug Abuse (NIDA). Dr Weissman receives research funding from the NIMH, the NIDA, the National Alliance for Research on Schizophrenia and Depression, the Sackler Foundation, the Templeton Foundation, and the Interstitial Cystitis Association. Dr Talati receives research support from the Research Foundation for Mental Hygiene, Inc.

**Role of the Sponsors:** Neither the NIMH nor the NIDA were involved in the preparation of this letter.

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