multivariable analyses. In a fully adjusted model, a previous positive PCR test result (relative risk, 1.52 [95% CI, 1.44-1.60]; $P < .001$) and reported high suspicion of virus exposure (relative risk, 1.23 [95% CI, 1.18-1.28]; $P < .001$) were associated with seroprevalence (Table 2).

Discussion | A 13.7% prevalence of SARS-CoV-2 antibodies in this large cohort study of HCP in the greater NYC area was similar to that among adults randomly tested in New York State (14.0%)[4] but higher than among adults in Los Angeles (4.1%).[5] HCP in a single hospital in Belgium had lower seroprevalence (6.4%), which was significantly associated only with household contact.[6] In this study, high levels of HCP-reported suspicion of virus exposure and prior positive PCR testing results were most strongly associated with seropositivity.

Study limitations include voluntary testing, with only 56% of HCP participating; restriction to the greater NYC area; 7 different assays with variable sensitivity and specificity used; and time between PCR and antibody testing unknown and possibly too short to detect antibody response. Only HCP-reported suspicion of overall exposure was recorded, so distinguishing among community-, home-, and health care–acquired exposures was not possible.

Providing HCP with data about their SARS-CoV-2 virus exposure is important so they can protect themselves, their patients, their colleagues, and their families. High levels of HCP-reported suspicion of virus exposure may be useful as an indication for SARS-CoV-2 testing.

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Accepted for Publication: July 23, 2020.

Published Online: August 6, 2020. doi:10.1001/jama.2020.14765

Author Contributions: Drs Davidson and Chang had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: All authors.
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Obtained funding: Davidson.
Administrative, technical, or material support: Moscola, Jarrett, Farber, Chang, McGinn, Davidson.
Supervision: McGinn, Davidson.

Conflict of Interest Disclosures: None reported.

Funding/Support: This work was supported by grants R24AG064191 from the National Institute on Aging and R01LM012836 from the National Library of Medicine.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Disclaimer: The views expressed in this article are those of the authors and do not represent the views of the National Institutes of Health, the US Department of Health and Human Services, or any other government entity. Dr Davidson is a member of the US Preventive Services Task Force (USPSTF). This article does not represent the views and policies of the USPSTF.

Additional Contributions: We thank the members of the Northwell Health COVID-19 Research Consortium who contributed to this study: Lance B. Becker, MD (North Shore University Hospital/Long Island Jewish Emergency Medical Department, Northwell Health); Dwayne A. Breining, MD, Jacqueline Moline, MD, MSc (Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Northwell Health); Mark J. Butler, PhD, Jennifer Cookingham, MHA, Andrew J. Dominello, BA, Louise Falzon, BA, PGDipInf, Cirrus Foroughi, PhD, Jennifer C. Johnson, MS, MA, Jazmin N. Mogavero, MA, Rachel Monane, BBA, Frank Vicari, BS (Feinstein Institutes for Medical Research, Northwell Health); James M. Crawford, MD, PhD, Sharon S. Fox, BS, Stefan Juretschko, PhD, D(ABMM), Cheryl B. Schleicher, MS-HCA, BA (Northwell Health Laboratories, Northwell Health); Christopher J. Hutchins, Kristen M. McPhillips, MBA, PMP, and Abraham Saraya, MD, MSc (Northwell Health). None of these individuals received any compensation for their contributions.

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Incidence of Malformations After Early Pregnancy Exposure to Modafinil in Sweden and Norway

Modafinil is used to improve wakefulness in adults with excessive sleepiness due to narcolepsy, for fatigue related to multiple sclerosis, and for the treatment of attention-deficit/hyperactivity disorder. In 2018, an interim report from a manufacturer-established pregnancy registry reported a prevalence of 15% for major malformation in infants exposed to modafinil during pregnancy, spurring regulatory bodies to amend product information.[1-3] Recently, a Danish study reported a major malformation rate of 12% (n = 6) among 49 infants exposed to modafinil during early pregnancy compared with 3.9% (n = 32 466) among 828 644 unexposed to modafinil (adjusted odd ratio, 2.7; 95% CI, 1.1-6.9).[4] To add to the emerging evidence, we investigated if modafinil use during early pregnancy was associated with major malformations in Norway and Sweden.

Methods | All singleton pregnancies resulting in live births in the nationwide medical birth registers in Norway (2005-2017) and Sweden (2006-2016) were identified and linked to their respective prescribed drug registers (containing data on medication dispensed at pharmacies) and national patient registers (containing data on diagnoses made during hospital-based specialist care). We excluded pregnancies with missing gestational age and those resulting in infants born with chromosomal anomalies (*International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* [*ICD-10*] codes Q90-Q99).

Exposure to modafinil (Anatomical Therapeutic Chemical code N06BA07) during the first trimester was defined as 1 or more filled prescriptions within the 30 days before the date of last menstrual period and the end of the first trimester (day 97 of gestation). A secondary exposure definition was 1 or more filled prescriptions during the first trimester. Unexposed pregnant women had no filled prescriptions of modafinil during the year before the last menstrual period to the end of the first trimester.

Characteristics of women, including maternal age at delivery, prepregnancy body mass index, and smoking during early pregnancy, were reported along with diagnoses recorded during the year before the last menstrual period to the end of the first trimester, and filled prescriptions during the 90 days before the last menstrual period to the end of the first trimester.

Major malformations were identified by *ICD-10* codes.[5] The number and percentage of cases of malformations after exposure or without exposure to modafinil was reported. Crude risk ratios and 2-sided Wald 95% CIs were calculated using SAS version 9.4 (SAS Institute Inc). This study was approved by research ethics committees in Norway and Sweden; register-based studies are exempt from informed consent.

Results | In a cohort of 1 917 605 pregnancies (744 311 in Norway and 1 173 294 in Sweden), 133 (0.007%; 38 in Norway and 95

Table. Characteristics by Modafinil Exposure Status During Pregnancy in Norway (2005-2017) and Sweden (2006-2016)

Characteristics	Exposed to modafinil[a]	Unexposed to modafinil[b]
Pregnant women, No. (%)	133 (0.007)	1 917 472 (99.993)
Maternal age, mean (SD), y	31.2 (5.0)	30.6 (5.2)
BMI prior to pregnancy		
Mean (SD)[c]	26.4 (5.8)	24.6 (4.7)
No. (%)		
<25[c]	52 (39.1)	909 093 (47.4)
≥25[c]	59 (44.4)	531 324 (27.7)
Missing	22 (16.5)	477 055 (24.9)
Smoking during early pregnancy, No. (%)		
No	104 (78.2)	1 629 482 (85.0)
Yes	23 (17.3)	134 169 (7.0)
Missing	6 (4.5)	153 821 (8.0)
Maternal comorbidities, No. (%)		
Multiple sclerosis (*ICD-10* code G35)	29 (21.8)	2303 (0.1)
Narcolepsy (*ICD-10* code G47.4)	23 (17.3)	97 (<0.1)
ADHD (*ICD-10* code F90.0)	6 (4.5)	6605 (0.3)
Mental or behavioral disorder[d]	31 (23.3)	69 760 (3.6)
Maternal medications, No. (%)		
Known teratogens[e]	3 (2.3)	7923 (0.4)
Potential teratogens[f]	11 (8.3)	135 152 (7.0)
Analgesics (ATC code N02)	30 (22.6)	113 598 (5.9)
Antiepileptics (ATC code N03)	24 (18.0)	11 920 (0.6)
Psycholeptics (ATC code N05)[g]	21 (15.8)	58 729 (3.1)
Psychoanaleptics (ATC code N06)[h]	35 (26.3)	72 714 (3.8)
Multiple sclerosis treatment[i]	15 (11.3)	804 (<0.1)
Infant major malformation, No. (%)	3 (2.6)	40 697 (2.1)

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; ATC, Anatomical Therapeutic Chemical; BMI, body mass index; *ICD-10, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*.

[a] Defined as 1 or more filled modafinil prescriptions within the 30 days before the date of the last menstrual period to the end of the first trimester.

[b] Defined as no filled modafinil prescriptions within the year prior to the date of the last menstrual period to the end of the first trimester.

[c] Calculated as weight in kilograms divided by height in meters squared.

[d] All *ICD-10* chapter F diagnoses.

[e] Includes retinoids, angiotensin-converting enzyme inhibitors, vitamin K antagonist, valproic acid, lithium, carbamazepine, oxcarbazepine, phenytoin, phenobarbital, and methotrexate.

[f] Includes danazol, progestins, methimazole, propylthiouracil, corticosteroids, and fluconazole.

[g] Includes barbiturates and benzodiazepines.

[h] Includes antidepressants; modafinil was excluded.

[i] Includes interferon beta, glatiramer acetate, fingolimod, dimethyl fumarate, teriflunomide, peginterferon beta-1a, natalizumab, and fampridine.

in Sweden) were exposed to modafinil during early pregnancy. Compared with pregnant women who had not taken modafinil, pregnant women who had taken modafinil were more often overweight or obese and had higher rates of smoking and diagnoses of narcolepsy, multiple sclerosis, and attention-deficit/hyperactivity disorder (**Table**).

Overall, the rate of major malformations in the unexposed group was 2.1% (n = 40 697). There were 3 modafinil-exposed infants diagnosed as having a major malformation, resulting in a prevalence rate of 2.6% and a crude risk ratio of 1.06 (95% CI, 0.35-3.26). When restricted to only filled prescriptions during the first trimester, 75 pregnancies were exposed and 1 modafinil-exposed infant was diagnosed as having a major malformation (risk ratio, 0.44; 95% CI, 0.06-3.10).

Discussion | In this study, modafinil use during early pregnancy was not significantly associated with increased risk of major malformations. The combined Norwegian and Swedish study population had a similar proportion of modafinil-exposed pregnancies compared with the Danish study, allowing for more than double the number of exposed infants to be followed up. However, the 95% CIs estimated in this study overlap with those from the Danish study and allow for the possibility of a greater than 3-fold risk as previously reported.[4]

The limitations include that filled prescriptions were used as a proxy for medication use; any nonuse of modafinil would bias the results toward the null. Overall, the absolute number of exposed infants and malformations was low, hindering rigorous analyses accounting for potential confounding factors.

These results illustrate the need to focus on performing large and sufficiently powered studies for drug safety in pregnancy research, preferably from several countries, when exposures and outcomes are rare.[6]

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Accepted for Publication: May 20, 2020.

Author Contributions: Mr Karlsson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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Obtained funding: Kieler, Furu.
Administrative, technical, or material support: Cesta, Kieler.
Supervision: Kieler, Furu.

Conflict of Interest Disclosures: None reported.

Funding/Support: This study was funded by NordForsk as part of the Nordic Pregnancy Drug Safety Studies project No. 83539 and by the Research Council of Norway as part of the International Pregnancy Drug Safety Studies project No. 273366. All funding was awarded to Dr Furu.

Role of the Funder/Sponsor: The funders/sponsors had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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COMMENT & RESPONSE

Reducing Vasopressor Exposure in Patients With Vasodilatory Hypotension

To the Editor A clinical trial by Dr Lamontagne and colleagues showed that reducing exposure to vasopressors through a lower mean arterial pressure (MAP) target during resuscitation in older patients with vasodilatory hypotension decreased 90-day mortality, although it did not reach statistical significance.[1] Three large randomized clinical trials also showed that early goal-directed therapy did not improve outcomes in patients with septic shock.[2-4]

Several aspects of the trial need clarification.

Although the study targeted a MAP of 60 to 65 mm Hg, the median blood pressure was 66.7 mm Hg, with an interquartile range of 64.5 to 69.8 mm Hg. Therefore, it does not appear that the target blood pressure was met.

Blood pressure should not be the only guide during hemodynamic resuscitation; parameters such as tissue perfusion should also be used.

Almost 20% of the patients did not have sepsis, and the causes of their hypotension were not known; 29% of patients had sepsis but without shock, and the reason for needing vasopressors in this group is not clear.

The study included patients with vasodilatory hypotension and adequate fluid resuscitation or ongoing fluid resuscitation. If the patients had vasodilatory hypotension, why was