Supplemental Folate and the Relationship Between Traffic-Related Air Pollution and Livebirth Among Women Undergoing Assisted Reproduction

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Traffic-related air pollution has been linked to higher risks of infertility and miscarriage. We evaluated whether folate intake modified the relationship between air pollution and livebirth among women using assisted reproductive technology (ART). Our study included 304 women (513 cycles) presenting to a fertility center in Boston, Massachusetts (2005–2015). Diet and supplements were assessed by food frequency questionnaire. Spatiotemporal models estimated residence-based daily nitrogen dioxide (NO2), ozone, fine particulate, and black carbon concentrations in the 3 months before ART. We used generalized linear mixed models with interaction terms to evaluate whether the associations between air pollutants and livebirth were modified by folate intake, adjusting for age, body mass index, race, smoking, education, infertility diagnosis, and ART cycle year. Supplemental folate intake significantly modified the association of NO2 exposure and livebirth ($P = 0.01$). Among women with supplemental folate intakes of $<800 \mu g$/day, the odds of livebirth were 24% (95% confidence interval: 2, 42) lower for every 20-parts-per-billion increase in NO2 exposure. There was no association among women with intakes of $\geq 800 \mu g$/day. There was no effect modification of folate on the associations between other air pollutants and livebirth. High supplemental folate intake might protect against the adverse reproductive consequences of traffic-related air pollution.

Abbreviations: ART, assisted reproductive technology; BC, black carbon; BMI, body mass index; EARTH, Environment and Reproductive Health; IQR, interquartile range; PM$_{2.5}$, particulate matter with an aerodynamic diameter equal to or less than 2.5 $\mu$m; NO2, nitrogen dioxide; O$_3$, ozone; TRAP, traffic-related air pollution.

Editor’s note: An invited commentary on this article appears on page 1605.

There is increasing evidence that exposure to traffic-related air pollution (TRAP) is related to lower fecundity and fertility among women attempting to conceive spontaneously and through assisted reproductive technology (ART) (1, 2). In previous studies, women residing closer to major roadways were shown to have a higher risk of infertility (3), longer time to pregnancy (4), higher risk of spontaneous abortion (5), and reduced likelihood of livebirth following ART (6). Moreover, higher exposure to nitrogen dioxide (NO2), a marker of TRAP (7, 8), was linked to lower census-tract level livebirth rates (9), decreased fecundability (10), and lower probability of implantation (11), pregnancy (12), and livebirth (13) following ART.

In addition, there is growing acceptance that nutrients, such as folic acid, might be related to enhanced reproductive success among women (14) and could reduce the toxicity of environmental pollutants (15). A high intake of folic acid has been related to lower risk of infertility (16), shorter time to pregnancy (17), lower risk of pregnancy loss (18), and better outcomes of ART (19–21). Furthermore, a high folic acid intake has been shown to attenuate the associations of certain reproductive toxicants such as bisphenols and phthalates (22, 23), pesticides (24, 25), and arsenic (26) on various health outcomes. Emerging evidence also suggests that folate intake, as measured by dietary folate equivalents (as well as other methyl donors), might mute the association between TRAP
and risk of birth defects (27) and that folic acid intake (from diet and supplements) could attenuate the association between TRAP on risk of autism (28).

Although the specific underlying biological pathways through which TRAP exposure and folic acid intake could affect female fertility are unknown, it is hypothesized that both are involved in the induction of epigenetic changes, including alterations in DNA methylation (29–31), as well as the generation of oxidative stress and inflammation (32, 33). Therefore, we hypothesized that folate, in particular folic acid from supplements (due to the higher bioavailability of folate in this form), might attenuate the adverse reproductive consequences of air pollution exposure on likelihood of livebirth following ART.

METHODS

Study population

Study subjects were recruited into the Environment and Reproductive Health (EARTH) Study starting in November 2004 from patients presenting at the Massachusetts General Hospital Fertility Center. All women aged 18–46 years were eligible, and approximately 60% of those contacted participated. Upon enrollment, all participants provided their residential address. Women were followed through their infertility treatment until discontinuation or livebirth. Women received financial incentives for participation: $100 for the entry visit, $50 for baseline assessment (introduced in 2007), bringing our final sample size to 513 ART cycles from 304 women. For the analysis of black women, we excluded 127 cycles from women who did not complete a dietary assessment (introduced in 2007), bringing our final sample size to 386 ART cycles from 254 women. The EARTH Study was approved by the Human Studies Institutional Review Boards of Massachusetts General Hospital and the Harvard T.H. Chan School of Public Health. All study participants signed an informed consent after the study procedures were explained by trained study staff.

Air pollution exposures

The residential address of each woman was geocoded using ArcGIS and linked to validated spatiotemporal models for each air pollutant. Daily concentrations of particulate matter with an aerodynamic diameter equal to or less than 2.5 μm (PM_{2.5}) and NO_{2} were both modeled using satellite remote sensing data in combination with land-use terms (35, 36). Daily ozone (O_{3}) models additionally included chemical transport models, O_{3} vertical profiles, meteorological variables, and other atmospheric compounds (37). Daily BC exposure was estimated at the address using ambient BC measurements from over 300 monitors in Massachusetts, Rhode Island, and southern New Hampshire (38). For each pollutant, we averaged daily estimated concentrations from 3 months prior to the start of the ART cycle to represent a women’s average air pollution exposure. This time window also roughly corresponds to the proposed window of follicular development (39). Distance to major roadways (meters) was determined using the ESRI StreetPro 2007 data layer. We selected US Census feature class codes to include A1, A2, or A3 road segments.

Dietary assessment

Dietary folate intake was assessed using a validated food frequency questionnaire (40). Participants were asked to report how often they consumed 131 food items during the previous year. Multivitamin and supplement users were asked to specify the brand, the dose, and frequency of use. Nutrient intakes were estimated by summing the nutrient contribution of all foods and supplements. Nutrient contents were obtained from the US Department of Agriculture, with additional information from manufacturers (41). Folate intake with this questionnaire has been validated against dietary records (r = 0.77 (42) and plasma (r = 0.54) folate concentrations. We dichotomized total and supplemental folate intake by taking into consideration the distribution of intake in our population as well as clinically relevant cutoffs such as 400 μg/day (the recommended daily amount (RDA), 800 μg/day (2 times the RDA), and 1,000 μg/day (the tolerable upper intake level). The cutoff closest to the 75th percentile of intake in our population was used for dichotomization.

Outcome assessment

For fresh ART cycles, patients underwent luteal-phase gonadotropin-releasing hormone agonist protocol, follicular-phase gonadotropin-releasing hormone agonist/thalidomide protocol, or gonadotropin-releasing hormone-antagonist protocol, as clinically indicated. During stimulation, patients were monitored for serum estradiol, follicle size, and endometrial thickness. Human chorionic gonadotropin was administered approximately 36 hours before scheduled oocyte retrieval to induce oocyte maturation. Following retrieval, oocytes were fertilized using conventional insemination or intracytoplasmic sperm injection. For cryo-thaw or donor-egg recipient cycles, patients underwent endometrial preparation protocols. Following embryo transfer, all clinical outcomes were assessed identically for fresh, cryo-thaw, and donor-egg recipient cycles. Successful implantation was defined as a serum β-human chorionic gonadotropin level >6 mIU/mL (approximately 17 days after egg retrieval), clinical pregnancy as an intratubal pregnancy confirmed on the 6-week ultrasound, and livebirth as the birth of a neonate of ≥24 weeks’ gestation.

Covariate assessment

At enrollment, height and weight were measured to calculate body mass index (BMI; weight (kg)/height(m)^2). Participants completed a take-home questionnaire regarding lifestyle factors, reproductive health, and medical history. Census-tract level, median family income in the past 12 months (in 2011
inflation-adjusted dollars) was calculated from the American Community Survey 2007–2010. The alternate Healthy Eating Index 2010 (aHEI-2010) was calculated as a measure of a healthy diet (45). Clinical information including infertility diagnosis (diminished ovarian reserve, endometriosis, male factor, ovulatory, tubal, uterine, and unexplained) and protocol type was abstracted from electronic medical records.

**Statistical analysis**

Descriptive statistics were calculated comparing the bottom and top quartiles of estimated NO2 exposure stratified by supplemental folate intake (<800 μg/day vs. ≥800 μg/day). To test whether the associations between air pollutants and livebirth were modified by folate intake, multivariate mixed-effects logistic regression models with a subject-specific random effect and a product of the continuous air pollutant and dichotomized folate intake were used, because they can account for within-person correlations in outcomes (46). Each air pollutant was modeled as a continuous exposure, and effect sizes are reported in interquartile range (IQR) increments. Distance to major roadways was modeled per 250-m increment. Additional models were fitted, including a product of the continuous air pollutant and continuous folate intake. An interaction term was considered suggestive when the P value was <0.10. Results are presented as the multiplicative change in odds of livebirth (95% confidence interval) per IQR increase in the air pollutant or predicted probabilities of livebirth at the average value of continuous covariates and the most common value of categorical covariates (47).

We also evaluated evidence of additive interaction by placing women into one of 4 categories based on air pollution exposure (< or ≥ median) and folate intake. Generalized estimating equations with binomial distribution and log link function were used to assess the combined effect of air pollution and folate intake on the risk of livebirth. The relative excess risk due to interaction was calculated as RR11−RR10−RR01 + 1 and confidence bounds were estimated using approximate variance estimators (48).

Intermediate ART endpoints were investigated only if an interaction was detected between folate, the pollutant, and livebirth to minimize multiple testing and type 1 error. We used generalized linear mixed models with random intercepts and normal (for peak estradiol and endometrial thickness), Poisson (for oocyte counts), or binomial (for implantation, clinical pregnancy, and pregnancy loss) distribution. Pregnancy loss, including therapeutic abortions (all of which were performed due to life-threatening abnormalities), was examined only among cycles with successful implantation (n = 290 cycles). Confounding was evaluated using prior knowledge and descriptive statistics from our cohort through the use of directed acyclic graphs (49). Variables retained in the final multivariable models were maternal age (continuous), race (white, other), BMI (continuous), smoking status (ever, never), educational level (less than graduate degree, graduate degree), initial infertility diagnosis (female, male, unexplained), and year of ART cycle (continuous). Multivariable models were also fitted with further adjustment for the other pollutants and without adjustment for infertility diagnosis (due to concerns that it might be a downstream consequence of exposure). Several sensitivity analyses were conducted, including restricting our analyses to noncurrent smokers (n = 501 cycles,

98%), autologous fresh ART cycles (n = 427 cycles, 83%), cycles with embryo transfer (n = 468, 91%), cycles with prospective diet (n = 495, 96%), first in-study ART cycles (n = 304 cycles, 59%), first ART cycles at Massachusetts General Hospital (n = 235, 46%), and nulligravid women (n = 300, 58%).

**RESULTS**

Among the 304 women in our analysis, the mean age was 35.2 (standard deviation, 4.0) years and BMI was 24.3 (standard deviation, 4.4). The majority of women were white (83%), had a college education or higher (91%), had never smoked (72%), and had unexplained infertility at baseline (38%). During the study period, the median estimated air pollution concentrations in the 3 months prior to ART were 22.9 (10th–90th percentile, 5.3–47.1) parts per billion for NO2, 34.2 (10th–90th percentile, 19.9–50.2) parts per billion for O3, 8.5 (10th–90th percentile, 6.8–10.9) μg/m3 for PM2.5, and 0.49 (10th–90th percentile, 0.36–0.76) μg/m3 for BC. The median distance to A1–A3 roadways was 107.8 (10th–90th percentile, 3.7–414.1) m. The correlations between pollutants were modest (Web Table 1, available at https://academic.oup.com/aje), with the highest magnitude observed for NO2 and BC (r = 0.39). Ozone had weak inverse correlations with NO2 (r = −0.13) and BC (r = −0.22).

Women in this cohort were high consumers of total and supplemental folate, with median intakes of 1,100 (range, 187–2,675) μg/day and 571 (range, 0–2,400) μg/day, respectively. Only 16% of our women consumed <400 μg/day and 20% of women consumed ≥1,000 μg/day of supplemental folate, which precluded a meaningful evaluation of these cutoffs. A total of 468 (91%) of the initiated cycles had at least 1 embryo transferred, with 290 (57%) resulting in implantation, 257 (50%) in clinical pregnancy, and 206 (40%) in livebirth (Web Figure 1). Women contributed an average of 1.7 ART cycles (range, 1–6).

Across both strata of supplemental folate intake, women in the highest quartile of estimated NO2 exposure had lower BMI (95% confidence interval: 2.4% (95% confidence interval: 2.4–4.0%)). Variants of the NO2 and livebirth association by smoking status (ever, never) were evaluated by folate intake, multivariate mixed-effects logistic regression models with a subject-specific random effect and a product of the continuous air pollutant and dichotomized folate intake were used, because they can account for within-person correlations in outcomes (46). Each air pollutant was modeled as a continuous exposure, and effect sizes are reported in interquartile range (IQR) increments. Distance to major roadways was modeled per 250-m increment. Additional models were fitted, including a product of the continuous air pollutant and continuous folate intake. An interaction term was considered suggestive when the P value was <0.10. Results are presented as the multiplicative change in odds of livebirth (95% confidence interval) per IQR increase in the air pollutant or predicted probabilities of livebirth at the average value of continuous covariates and the most common value of categorical covariates (47).

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<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Women Who Consumed &lt;800 μg/day of Supplemental Folate (n = 173)</th>
<th>Women Who Consumed ≥800 μg/day of Supplemental Folate (n = 131)</th>
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<tr>
<td></td>
<td>NO₂ Quartile 1 (n = 44)</td>
<td>NO₂ Quartile 4 (n = 47)</td>
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<tr>
<td>Estimated NO₂ exposure, ppb</td>
<td>Mean (SD)</td>
<td>No.</td>
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<tr>
<td>Age, years</td>
<td>35.1 (4.0)</td>
<td>35.0 (4.1)</td>
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<td>White race</td>
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<td>40 85.1</td>
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<tr>
<td>BMI^a</td>
<td>25.5 (5.2)</td>
<td>23.9 (4.1)</td>
</tr>
<tr>
<td>Smoking status</td>
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<tr>
<td>Never</td>
<td>32 72.7</td>
<td>32 68.1</td>
</tr>
<tr>
<td>Former</td>
<td>9 20.5</td>
<td>14 29.8</td>
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<td>Current</td>
<td>3 6.8</td>
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<td>Educational level</td>
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<tr>
<td>High school or less</td>
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<td>4 8.5</td>
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<tr>
<td>College</td>
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<tr>
<td>Graduate school</td>
<td>26 59.1</td>
<td>30 63.8</td>
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<tr>
<td>Distance to A1–A3 roadway, m</td>
<td>279.7 (337.3)</td>
<td>129.4 (105.1)</td>
</tr>
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<td>Census tract median income, $</td>
<td>105,327 (31,418)</td>
<td>95,474 (45,496)</td>
</tr>
<tr>
<td>Total calories, kcal/day</td>
<td>1,877.0 (625.8)</td>
<td>1,834.3 (609.0)</td>
</tr>
<tr>
<td>Total folate, μg/day</td>
<td>797.5 (291.0)</td>
<td>808.9 (308.3)</td>
</tr>
<tr>
<td>Food folate, μg/day</td>
<td>459.1 (202.7)</td>
<td>483.6 (168.4)</td>
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<tr>
<td>Supplemental folate, μg/day</td>
<td>338.4 (194.2)</td>
<td>325.3 (218.8)</td>
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<tr>
<td>Alcohol intake, g/day</td>
<td>9.0 (14.3)</td>
<td>12.3 (13.3)</td>
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<tr>
<td>aHEI-2010 score</td>
<td>62.9 (11.0)</td>
<td>68.0 (10.1)</td>
</tr>
<tr>
<td>Duration of pregnancy attempt, months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤12</td>
<td>8 18.2</td>
<td>20 42.6</td>
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<tr>
<td>13–24</td>
<td>25 56.8</td>
<td>21 44.7</td>
</tr>
<tr>
<td>≥24</td>
<td>11 25.0</td>
<td>6 12.8</td>
</tr>
<tr>
<td>Previous IVF cycle at MGH</td>
<td>13 29.6</td>
<td>5 10.6</td>
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<tr>
<td>Nulligravid</td>
<td>27 61.4</td>
<td>31 66.0</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>38 86.4</td>
<td>42 89.4</td>
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Table 1.

<table>
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<tr>
<th>Characteristic</th>
<th>NO2 Quantile 1 (n = 32)</th>
<th>NO2 Quantile 4 (n = 29)</th>
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<tr>
<td>Infertility diagnosis</td>
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<td>Mean (SD) No. %</td>
</tr>
<tr>
<td>Male factor</td>
<td>13 29.6</td>
<td>7 21.9</td>
</tr>
<tr>
<td>Female</td>
<td>15 36.4</td>
<td>7 24.1</td>
</tr>
<tr>
<td>Unexplained</td>
<td>16 36.2</td>
<td>12 41.4</td>
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<tr>
<td>Protocol</td>
<td>9 28.1</td>
<td>2 6.9</td>
</tr>
<tr>
<td>Antagonist or luteal phase agonist</td>
<td>20 65.9</td>
<td>24 82.8</td>
</tr>
<tr>
<td>Antagonist or cryo-thaw cycle</td>
<td>29 65.9</td>
<td>3 9.4</td>
</tr>
</tbody>
</table>

Abbreviations: aHEI-2010, alternate Health Eating Index 2010; ART, assisted reproductive technology; BMI, body mass index; IVF, in vitro fertilization; MGH, Massachusetts General Hospital; NO2, nitrogen dioxide; ppb, parts per billion; SD, standard deviation.

**Discussion**

In our prospective cohort study of women undergoing ART, intake of supplemental folate modified the relationship of estimated NO2 exposure with probability of livebirth. Specifically, there was a lower likelihood of livebirth with increasing estimated exposure to NO2 3 months prior to ART among women consuming <800 μg/day of supplemental folate; however, estimated NO2 exposure was unrelated to livebirth among women with higher intake. The negative association of estimated NO2 on livebirth among women with low supplemental folate intake was driven primarily by a higher risk of pregnancy loss with increasing NO2 exposure. We found no evidence of an interaction with total or supplemental folate intake on the relationships between estimated O3, PM2.5, BC, and distance to A1–A3 roadways and livebirth (Figure 1).

When evaluating the models for additive interaction, we found that women with higher estimated exposure to NO2, PM2.5, O3, and BC and low supplemental folate intake had the lowest risk of livebirth compared with women with lower exposure to those pollutants and high supplemental folate intake (Web Table 2). However, only for NO2 did the effect estimate suggest a departure from expected interaction (relative excess risk due to interaction: −0.36, 95% confidence interval: −0.82, 0.09).

There was no evidence of effect modification of supplemental folate on the associations between estimated NO2 and estradiol levels, endometrial thickness, or total or mature oocyte yield (Web Table 3). We observed a weak interaction between supplemental folate, estimated NO2, and odds of implantation and clinical pregnancy, but the effect estimate of estimated NO2 on these outcomes, while stronger among women with supplemental folate intakes <800 μg/day, was not significant (Figure 3). Supplemental folate intake did modify the association between estimated NO2 and pregnancy loss (P = 0.06). The odds ratio for pregnancy loss was 1.54 (95% confidence interval: 1.00, 2.37) per 20-parts-per-billion increase in estimated NO2 among women with intakes <800 μg/day. There was no association among women with intakes of ≥800 μg/day.

The effect modification of folate on the relationship between estimated NO2 and livebirth remained similar when analyses were restricted to cycles from noncurrent smokers, fresh autologous cycles, cycles with embryo transfer, cycles with prospective diet, first-in-study cycles, first cycles at Massachusetts General Hospital, and nulligravid women (Web Table 4). Results were also similar after coadjustment for the other pollutants (Web Table 5) and without adjustment for infertility diagnosis (data not shown).

**DISCUSSION**

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While this is, to our knowledge, the first time that an interaction between NO2 and supplemental folate has been investigated in a study focused on fertility, previous studies have observed a similar interaction of TRAP, and specifically NO2 exposure, with folate intake during pregnancy on risk of birth defects (27) and autism (28). In the National Birth Defects Prevention Study, a greater than additive interaction between exposure to NO2 and folate intake was observed during pregnancy.
was observed for methyl donor intakes of methionine, choline, vitamin B6, and folate with NO2 exposure and odds of perimembranous ventricular septal defect (27). In the Childhood Autism Risk from Genetics and the Environment study, women with low folic acid intake (<800 μg) who were exposed to higher levels of air pollution (e.g., near-roadway pollution, NO2, PM10, and PM2.5) during the first trimester had a higher risk of having a baby with autism compared with women with high folic acid intake who were exposed to lower air pollution levels (28).

Although the consistency of our findings with previous studies suggests that they might represent a true biological interaction, it was not possible to discern the underlying biological mechanisms. There are two leading hypotheses, however, based on mechanistic studies in humans. The first is that higher short- and long-term exposure to ambient TRAP decreases DNA

![Figure 1](https://academic.oup.com/aje/article-abstract/188/9/1595/5523269)
methylated in peripheral blood leukocytes as well as the placenta (31, 50–52), and this might adversely affect early embryo development and pregnancy maintenance (29). Because dietary folate is a key source of the one carbon group used to methylate DNA (53), adequate folate intake could protect against DNA hypomethylation. A recent intervention study further supports this hypothesis, showing that, among healthy adults receiving a B-vitamin supplement, the association between a 2-hour controlled exposure to PM2.5 and DNA methylation was attenuated (32), which has been implicated in a full spectrum of reproductive functions (55). Due to folic acid’s antioxidant properties (33), this could also explain the attenuated association we observed between NO₂ and livebirth in women with high supplemental folate intake.

Similar to previous studies, our data suggest that supplemental folate intake is preferable to food folate in the context of counteracting the negative reproductive consequences of NO₂ exposure. This could be because natural food folate has a lower proportion of folate that is absorbed and available for metabolic reactions and/or storage compared with folic acid, due to food folate’s limited release from the food matrix, its destruction within the gastrointestinal tract, and/or incomplete hydrolysis of glutamates (56). Second, even in the context of a fortified food supply, it is difficult to consume high levels of folate from diet alone. Therefore, the stronger associations we observed with supplemental folate could be driven by wider intakes and greater absorption, which combined allow for more extreme comparisons.

Of note, while most previous studies on TRAP and fertility have consistently found an adverse link, the majority of women in these studies also likely had supplemental folate intakes well below 800 µg/day, where we observed an adverse association between NO₂ and livebirth. For example, the expected percentage of women taking folic acid before conception is <25% among pregnancy cohorts in Europe (57–59) and <33% in the United States (60). Even among highly motivated women planning pregnancy, such as those enrolled in the Longitudinal Investigation of Fertility and the Environment Study, only 63% were taking a multivitamin, 22% were taking a prenatal vitamin, and 4% were taking a folic acid supplement (61). Given that the standard amount of folic acid in multivitamins is 400 µg/day—up to 600–800 µg/day in prenatal vitamins—even with higher rates of supplementation (such as in the EARTH Study where 92% of women took either a prenatal or folic acid supplement), few women would be expected to have supplemental folate intakes >800 µg/day.

Our study has several limitations. For the air pollutants, we used residence-based ambient air pollution exposures as a proxy of personal exposure. Furthermore, we lacked information on the women’s work addresses or their time-activity patterns, which might have improved exposure assessment. We also did not
update a woman’s address over the follow-up period. However, the spatiotemporal models of air pollution that we used are validated and specific to the woman’s home address, which is important for pollutants with small-scale spatial variation such as NO₂ (62). Given that most women in our study resided at the same address as their male partner, it is also difficult to rule out the possibility that male exposure to TRAP could partially or fully explain the associations. Dietary assessment by food frequency questionnaire is also subject to measurement error; however, we used a questionnaire known to relate well to biomarker levels (43, 63). Due to the prospective nature of our study, measurement error of both air pollution and folate would most likely be nondifferential with respect to the outcomes and result in an attenuation of the observed associations. Our analysis included only women undergoing ART at a single academic medical center in Massachusetts. While this benefitted our analysis by limiting confounding across regions and treatment centers, the air pollution concentrations were generally low and thus it is unclear how generalizable our results are to women undergoing ART worldwide. Due to our relatively small sample size, it is possible that small but clinically meaningful interactions could have been missed. While residual confounding could still be explaining associations, unlike many other pregnancy cohorts, supplemental folate intake was not correlated with measures of socioeconomic status or healthy diet in this population. Strengths of our study include its prospective design and complete follow-up of participants, the comprehensive adjustment for confounding variables, and a wide range of folate intake.

In conclusion, we found that intake of supplemental folate of ≥800 μg/day appeared to attenuate the adverse association between estimated NO₂ exposure and probability of livebirth following ART. Given that women have little control over their daily air pollution exposures, our findings provide potentially valuable guidance as to an individual-level dietary change that could ameliorate some of the negative reproductive consequences of TRAP exposure. In conjunction with the broader literature, which has observed interactions between folate and environmental exposures (22–26), such as TRAP (27, 28), on reproductive outcomes, our findings provide further support for research investigating interactions between nutrients and environmental exposures on reproductive outcomes.

Acknowledgments

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References


