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Public Safety and Faulty Flood Statistics

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We thank Black (2008) for his thoughtful assembly of diverse perspectives including ours on why another disastrous Mississippi River flood occurred so soon after 1993. We have an update that elucidates and quantifies several key points of his article, particularly that *a*) flood frequency and heights are increasing, *b*) water levels for regulatory “100-year” floods are profoundly underestimated, and *c*) misconceptions about risk confound appropriate responses to flooding.

At many sites in Iowa and Missouri the Flood of 2008 neared or exceeded the record “200-year” or “500-year” levels attained in

1993 [National Weather Service (NWS) 2008; U.S. Army Corps of Engineers (USACE) 2008b], prompting many to wonder how two such events could occur in only 15 years. Defenders of flow-frequency predictions cite their rigorous methods and assure us that improbable outcomes are possible, even two “100-year” floods in consecutive years (U.S. Geological Survey 2005). Such arguments miss the key issue: Are the flood probabilities calculated by USACE (2004, 2008a) credible?

Problems with the USACE (2004, 2008a) probabilities are exemplified by recent flooding at Hannibal, Missouri (Figure 1). The record stage set in 1993 exceeded the calculated 500-year level, whereas 2008 was a 200-year event. In addition, 2001 suffered a 50- to 100-year flood, 1986 and 1996 experienced 25- to 50-year floods, and five more years had 10- to 25-year floods. Are these calculated recurrence intervals reasonable, or is it more likely that the dice, in effect, are loaded?

Statistically, two 200-year floods would likely not occur in an interval < 330 years, but Hannibal has recently had far worse (Figure 1). Two 500-year floods would probably not occur in < 840 years, yet two such floods recently occurred at Canton, Missouri, and Burlington, Iowa. A chi-square statistical test rejects the assumed correctness of the USACE frequencies with 99.9% confidence. The 100-year flood stage at Hannibal should be realistically redefined as a 10-year flood, as reported by Black (2008).

Because floods are becoming more frequent and more severe over much of the Mississippi River basin (Black 2008; Criss and Shock 2001; Remo and Pinter 2007), statistical calculations based on the historical record are not appropriate predictors of future flooding, particularly for extreme events (Klemes 2000). The likelihood of attaining a given flood stage today is not the same as it was a century ago, and besides, the record is far too short to calculate what a 200-year or a 500-year flood might be.

As Black (2008) discussed, calculated flood probabilities are not merely academic. The Federal Emergency Management Agency (FEMA) and the National Flood Insurance Program use these calculations to delimit 100-year flood zones and to set insurance requirements and rates. Understated risk burdens everyone with debt (Crichton 2002; Davidson 2005) and places humans and property at risk from

water that is not only too high but also laden with contaminants and sediment. Unfortunately, erroneous calculations (USACE 2004, 2008a) are being used in the very latest proposals (USACE 2008c) for flood protection and ecosystem restoration. We need to use realistic concepts about flooding in our management plans.

The authors declare they have no competing financial interests.

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REFERENCES

Black H. 2008. Unnatural disaster: human factors in the Mississippi floods. *Environ Health Perspect* 116:A390–A393.
Crichton D. 2002. UK and global insurance responses to flood hazard. *Water Int* 27:119–131.
Criss RE, Shock EL. 2001. Flood enhancement through flood control. *Geology* 29: 875–878.
Davidson B. 2005. How quickly we forget: the National Flood Insurance Program and floodplain development in Missouri. *J Law Policy* 19: 365–395. Available: <http://law.wustl.edu/journal/19/p365Davidson.pdf> [accessed 5 November 2008].
Klemes V. 2000. Tall tales about tales of hydrological distribution. *J Hydrol Eng* 5(3):227–239.
National Weather Service. 2008. Advanced Hydrologic Prediction Service. Available: <http://www.crh.noaa.gov/aahps2/index.php?wfo=lsx/> [accessed 7 November 2008].
Remo JWF, Pinter N. 2007. Retro-modeling the Middle Mississippi River. *J Hydrol* 337:421–435.
USACE (U.S. Army Corps of Engineers). 2004. Upper Mississippi River System Flow Frequency Study: Final Report. Available: <http://www.mvr.usace.army.mil/pdw/pdf/FlowFrequency/flowfreq.htm> [accessed 5 November 2008].
USACE (U.S. Army Corps of Engineers). 2008a. Flow Frequency Query: Upper Mississippi River. Available: http://www2.mvr.usace.army.mil/flow_freq/flow_freq.cfm [accessed 5 November 2008].
USACE (U.S. Army Corps of Engineers). 2008b. Mississippi River at Hannibal, MO. Available: <http://www2.mvr.usace.army.mil/WaterControl/stationinfo2.cfm?sid=HNNM7&fid=HNNM7&dt=S> [accessed July 2008].
USACE 2008c. Upper Mississippi River Comprehensive Plan. Final Report. Rock Island, IL:U.S. Army Corps of Engineers.
U.S. Geological Survey. 2005. Floods: Recurrence intervals and 100-year floods. Available: <http://ga.water.usgs.gov/edu/100yearflood.html> [accessed 5 November 2008].

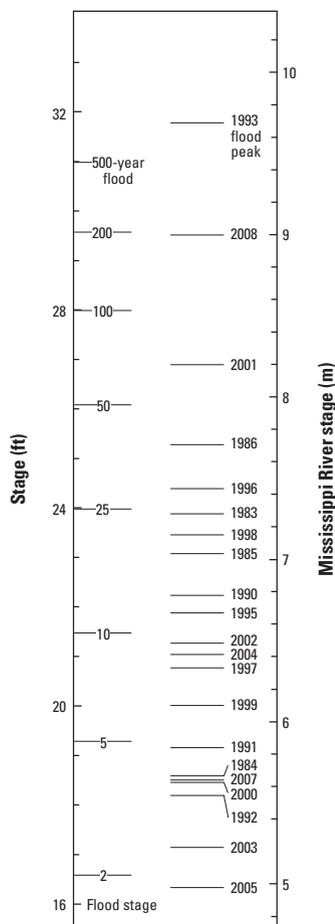


Figure 1. Mississippi River flood levels recorded at Hannibal over the last 25 years [right (NWS 2008; USACE 2008b)] compared with the theoretical stages for 2-year to 500-year floods [left (USACE 2004, 2008a)].

Longer Rodent Bioassay Fails to Address 2-Year Bioassay's Flaws

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In their commentary, Huff et al. (2008) proposed that exposing experimental animals to test substances *in utero* and for 30 months or until their natural deaths increases the sensitivity of bioassays, avoids false negative results, and strengthens the value and validity of results. Instead, longer exposure results in increased numbers of spontaneously arising tumors, as well as increased cost and animal suffering, while failing to address the bioassay's fundamental flaws.

Although it is troubling when the bioassay produces false negative results, a far

more pervasive problem is that of false positives. In our analysis of > 500 National Toxicology Program (NTP) bioassays [People for the Ethical Treatment of Animals (PETA) 2006], we found that more than half of the substances evaluated (259) produced evidence of carcinogenicity in at least one group of animals, but only about one-third of these (89) were subsequently classified as known or probable human carcinogens by the NTP itself. Even fewer of the substances, 40 and 16, respectively, were classified as carcinogens by the U.S. Environmental Protection Agency (EPA) and the International Agency for Research on Cancer (IARC) (PETA 2006). This high false-positive rate is thought to be largely an indirect effect of increased cell proliferation in response to cell injury and death caused by the near toxic doses of test substances used in the bioassay (Gaylor 2005). Species-specific modes of action operating in rats or mice but not in humans, such as those mediated by 2 μ -globulin, peroxisomes, and thyroid-stimulating hormone, also contribute to the high rate of false positives (Cohen 2004).

Huff et al. (2008) asserted that one of the “well-accepted observations” upon which the “relevance of experimental bioassays to humans” rests is that “findings from independently conducted bioassays on the same chemicals are consistent.” In fact, in a comparison of 121 bioassays from the NTP database with those in the published scientific literature, Gottmann et al. (2001) found that the studies produced consistent results only 57% of the time.

Huff et al. (2008) cited questions about the safety of aspartame raised by 3-year bioassays conducted by the Ramazzini Foundation to support their conclusions. Although they noted that the European Food Safety Authority (EFSA) and the U.S. Food and Drug Administration (FDA) dispute these studies’ conclusions, the EFSA’s Committee on Carcinogenicity (COC) (2006) observed that

In view of the inadequacies in design of the [Ramazzini Foundation] study and the use of rats with a high concurrent infection rate, the COC considered that no valid conclusions could be derived from it.

Further, the COC noted that groups of animals fed aspartame had lower body weights and thus lived longer, which may have compromised the results by leading to an apparent increase in spontaneously arising tumors. Considering that lower body weights are typically observed among animals in the bioassay’s experimental groups, this is likely to generally confound the interpretation of longer bioassays.

We must stress that animals suffer during the bioassay: They live in the barren, stressful conditions of the laboratory—often including daily forced feeding or inhalation—and many also suffer from exposure to near toxic doses of test substances. These exposures often produce lethargy, anemia, diarrhea, weight loss, and other symptoms of sickness and distress. The proposal of Huff et al. (2008) to extend the length of the bioassay would obviously result in a proportional increase in this suffering.

Further, extending the bioassay runs counter to current trends in regulatory testing. Concern for the suffering of animals has caused regulatory agencies to review the usefulness of long-term studies, resulting in elimination of the 1-year dog toxicity test (U.S. EPA 2007) and an international effort to replace the two-generation reproductive toxicity test (Cooper et al. 2006). Huff et al.’s proposal thus clearly represents a step backward for toxicological science.

According to the NTP’s own estimates, each bioassay requires 5 years to plan, conduct, and evaluate; 860 animals to be killed; and \$2–\$4 million. As a result, the NTP has conducted an average of only 12 bioassays/year over the past several decades. Considering that humans are thought to be exposed to approximately 80,000 environmental toxicants (Ward et al. 2003), it would take more than 32 millenia, 68 million animals, and \$160 billion to test them all at this rate. Once again, extending the length of the bioassay would only increase these already ridiculous numbers.

The time has clearly come for antiquated animal tests such as the bioassay to be abandoned in favor of modern, human-relevant methods such as epidemiologic studies, high-throughput *in vitro* methods, and computational toxicology.

The authors are employed by People for the Ethical Treatment of Animals, an animal advocacy organization.

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REFERENCES

- COC (Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment). 2006. Statement on a Carcinogenicity Study of Aspartame by the European Ramazzini Foundation. Available: <http://www.advisorybodies.doh.gov.uk/pdfs/aspart.pdf> [accessed 7 November 2008].
- Cohen SM. 2004. Human carcinogenic risk evaluation: an alternative approach to the two-year rodent bioassay. *Toxicol Sci* 80:225–229.
- Cooper RL, Lamb JC, Barlow SM, Bentley K, Brady AM, Doerrner NG, et al. 2006. A tiered approach to life stages

testing for agricultural chemical safety assessment. *Critical Rev Toxicol* 36:69–98.

Gaylor DW. 2005. Are tumor incidence rates from chronic bioassays telling us what we need to know about carcinogens? *Regul Toxicol Pharmacol* 41:128–133.

Gottmann E, Kramer S, Pfahringer B, Helma C. 2001. Data quality in predictive toxicology: reproducibility of rodent carcinogenicity experiments. *Environ Health Perspect* 109:509–514.

Huff J, Jacobson MF, Davis DL. 2008. The limits of 2-year bioassay exposure regimens for identifying chemical carcinogens. *Environ Health Perspect* 116:1439–1442.

PETA. 2006. Wasted Money, Wasted Lives: A Layperson’s Guide to the Problems with Rodent Cancer Studies and the National Toxicology Program. Norfolk, VA: People for the Ethical Treatment of Animals. Available: [http://www.stopanimaltests.com/pdfs/Wasted\\$\\$\\$_.pdf](http://www.stopanimaltests.com/pdfs/Wasted$$$_.pdf) [accessed 5 November 2008].

U.S. EPA. 2007. Pesticides; Data Requirements for Conventional Chemicals; Final Rule. Fed Reg 72:60934–60988. Available: <http://edocket.access.gpo.gov/2007/pdf/E7-20826.pdf> [accessed 5 November 2008].

Ward EM, Schulte PA, Bayard S, Blair A, Brandt-Rauf P, Butler MA, et al. 2003. Priorities for development of research methods in occupational cancer. *Environ Health Perspect* 111:1–12.

Longer Rodent Bioassay: Huff et al. Respond

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We appreciate and sympathize with Manuppello and Willett’s concerns about the inappropriate use of animals in research. Significant advances in animal protection have been secured in the United States through standards that have been promulgated, and we hope that further progress will be made.

Drugs are developed today often using methods that evaluate impacts *in vitro* and take advantage of innovations in three-dimensional structure-activity modeling. Still, because *in vitro* and theoretical methods are imperfect and because relying on them alone could result in considerable harm to humans, drugs and other chemicals are studied—and are required to be studied—in animals before being tested on humans or introduced into the human environment.

Epidemiologic studies, high-throughput *in vitro* methods, and computational toxicology would be preferable to animal research if they provided sensitive, accurate measures of human risk. Unfortunately, epidemiology studies are insufficiently sensitive, *in vitro* methods are insufficiently predictive, and computational toxicology is insufficiently developed. Ideally, government would provide much greater funding to further develop those and other technologies to expedite less expensive and more accurate means of risk assessments and reduce the need for animal bioassays.

The fact that positive animal bioassays have not always been mirrored in positive human findings provides an ethical public policy challenge. If we must wait for human evidence of cancer before acting to prevent future cases, then we are conducting

experiments on unwitting subjects without controls—especially if animal evidence already indicated a risk.

Current standards for concluding that an agent is a human carcinogen require statistically significant proof of sufficient numbers of cases of cancer in humans with measured or estimated exposures. Human cancers can take up to several decades to become evident in populations. Surveillance of the workplace and general environmental monitoring are not being widely conducted at this time. The last national survey of workplace carcinogens was conducted in the last century, and no new survey is planned at this time. Furthermore, except in cases where the cancer risks are enormous, such as tobacco smoking and workplace exposure to asbestos, linking a chemical outside the workplace, for example, in the diet, air, or water, to human cancers is virtually impossible.

In fact, the 2.5- to 3-year bioassays of the European Ramazzini Foundation of Oncology and Environmental Sciences on toluene, benzene, radiation, and aspartame (Soffritti et al. 2004, 2007) consistently indicate that the results of 2-year studies—the normal length of rat studies—underpredict potency/carcinogenicity and that true lifetime studies more accurately reflect cumulative impacts.

In addition, the paradigm-busting work of researchers on transgenerational effects, male-mediated teratogenesis, and the general critical impact of early developmental windows all strengthen the case for regarding 2-year postnatal bioassays as incomplete indications of toxicity/carcinogenicity (e.g., Dolinoy et al. 2007; Newbold

and McLachlan 1982; Sonne et al. 2008; Swan et al. 2006).

In our commentary (Huff et al. 2008) we indicated that 2-year results tend to be biased toward the null hypothesis. In no way do we state or imply that a positive finding in a 2-year assay would be negated by a longer test, nor do we indicate the contrary, that the absence of a positive finding in a 2-year assay should be construed as proof that there is no impact.

The current typical bioassay has served society well, but it does have several flaws: It cannot provide adequate prediction for the growing proportion of the population that is now living well into their eighties and nineties; it is not designed to evaluate the impact of prenatal exposures on later life; rodents are not a perfect model for humans; and countless animals must be sacrificed to obtain admittedly imperfect results.

By focusing improved bioassays on high-volume chemicals for which there are *a priori* grounds for concern, current approaches promise to yield the greatest good with the least harm. Simultaneously, more research must be done to identify fast, sensitive, accurate, and economical means of identifying chemicals that might be harmful to humans.

M.F.J. is employed by an advocacy organization that supports stronger testing requirements for chemicals in food. The other authors declare they have no competing financial interests.

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REFERENCES

- Dolinoy DC, Huang D, Jirtle RL. 2007. Maternal nutrient supplementation counteracts bisphenol A-induced DNA hypomethylation in early development. *Proc Natl Acad Sci USA* 104:13056–13061.
- Huff J, Jacobson MF, Davis DL. 2008. The limits of 2-year bioassay exposure regimens for identifying chemical carcinogens. *Environ Health Perspect* 116:1439–1442.
- Newbold RR, McLachlan JA. 1982. Vaginal adenosis and adenocarcinoma in mice exposed prenatally or neonatally to diethylstilbestrol. *Cancer Res* 42:2003–2011.
- Soffritti M, Belpoggi F, Padovani M, Lauriola M, Degli Esposti D, Minardi F. 2004. Life-time carcinogenicity bioassays of toluene given by stomach tube to Sprague-Dawley rats. *Eur J Oncol* 9:91–102.
- Soffritti M, Belpoggi F, Tibaldi E, Esposti DD, Lauriola M. 2007. Life-span exposure to low doses of aspartame beginning during prenatal life increases cancer effects in rats. *Environ Health Perspect* 115:1293–1297.
- Sonne SB, Kristensen DM, Novotny GW, Olesen IA, Nielsen JE, Skakkebaek NE, et al. 2008. Testicular dysgenesis syndrome and the origin of carcinoma in situ testis. *Int J Androl* 31(2):275–287.
- Swan SH. 2006. Prenatal phthalate exposure and anogenital distance in male infants. *Environ Health Perspect* 114:A88–A89.

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ERRATA

A typographical error on page A480 of the November Focus article ["Linking TB and the Environment: An Overlooked Mitigation Strategy," *Environ Health Perspect* 116:A478–A485 (2008)] misidentified DOTS as a 66-month treatment regimen. DOTS is actually a 6-month regimen. *EHP* regrets the error.

Brauer et al. [*Environ Health Perspect* 116:680–686 (2008)] identified several minor errors in their recent publication. First, in the "Results" section of the abstract, the values given for low full-term birth weight (LBW) were incorrect; "Residence within 50 m of highways was associated with ... a 22% (95% CI, 0.81–1.87) increase in LBW." There were also inconsistencies in the description and application of missing data rules across all pollutants (Tables 3–7); the description of these rules in the text (bottom of p. 681) should read "For both approaches, a subject was considered missing if there was a gap of > 5 consecutive days in air monitoring data or if there were > 10 missing days within the term of the pregnancy."

In Tables 2, 3, and 5, results for the small-for-gestational-age (SGA) outcome were presented for births restricted to gestational periods of ≥ 37 weeks, and not for the full cohort; in Tables 2, 3, 5, and 7, coding errors in the application of birth weight and gestational period cutoffs resulted in slight differences in the number of cases of SGA and preterm births; and in Tables 5 and 6, one road proximity measure was not labeled correctly: < 150 m from a major road/highway was actually 50–150 m from a major road/highway.

Correcting these errors results in small changes in the numbers of subjects included in specific analyses and slight differences in odds ratios (ORs) but does not alter our overall findings. The corrected tables are presented below.

The authors apologize for the errors.

Table 2. Prevalence of SGA, LBW and pre-term birth in the cohort ($n = 70,249$).

Outcome	No. (%)
SGA (< 10th percentile)	7,217 (10.3)
LBW (< 2,500 g at ≥ 37 weeks ^a)	897 (1.3)
Gestation < 37 weeks	3,748 (5.3)
Gestation < 35 weeks	1,247 (1.8)
Gestation < 30 weeks	241 (0.3)

^a $n = 66,501$ births at full (≥ 37 weeks) term.

Table 3. Crude and adjusted ORs^a for SGA.

Exposure (entire pregnancy)	SGA cases (n)	Crude OR (95% CI)	Adjusted ^b OR (95% CI)
NO-IDW (10 $\mu\text{g}/\text{m}^3$)	7,215	1.02 (1.00–1.05)	1.05 (1.02–1.08)
NO-LUR (10 $\mu\text{g}/\text{m}^3$)	7,023	1.03 (1.01–1.05)	1.03 (1.00–1.05)
NO ₂ -IDW (10 $\mu\text{g}/\text{m}^3$)	7,215	1.12 (1.08–1.16)	1.14 (1.09–1.18)
NO ₂ -LUR (10 $\mu\text{g}/\text{m}^3$)	7,023	1.04 (0.99–1.10)	0.98 (0.93–1.04)
CO-IDW (100 $\mu\text{g}/\text{m}^3$)	5,779	1.04 (1.01–1.06)	1.06 (1.03–1.08)
PM _{2.5} -IDW (1 $\mu\text{g}/\text{m}^3$)	5,818	1.01 (0.97–1.05)	1.06 (1.00–1.12)
PM _{2.5} -LUR (1 $\mu\text{g}/\text{m}^3$)	7,023	1.03 (1.02–1.05)	1.01 (1.00–1.03)
BC-LUR (10 ⁻⁵ /m)	7,023	1.03 (1.01–1.05)	1.01 (0.99–1.03)
PM ₁₀ -IDW (1 $\mu\text{g}/\text{m}^3$)	7,217	1.02 (1.00–1.04)	1.03 (1.00–1.07)
SO ₂ -IDW (1 $\mu\text{g}/\text{m}^3$)	7,138	1.00 (0.99–1.02)	1.01 (1.00–1.02)

BC, black carbon.

^aORs per standardized increases (indicated in parentheses), roughly corresponding to interquartile range. ^bAdjusted for infant sex, First Nations status, parity, maternal age, maternal smoking during pregnancy, month-year of birth, income (quintile-census), maternal education (quartile-census).

Table 4. Crude and adjusted ORs^a for LBW at full (≥ 37 weeks) term.

Exposure (entire pregnancy)	LBW cases (n)	Crude OR (95% CI)	Adjusted ^b OR (95% CI)
NO-IDW (10 $\mu\text{g}/\text{m}^3$)	897	1.02 (0.96–1.09)	1.03 (0.96–1.11)
NO-LUR (10 $\mu\text{g}/\text{m}^3$)	877	1.03 (0.97–1.09)	1.02 (0.95–1.08)
NO ₂ -IDW (10 $\mu\text{g}/\text{m}^3$)	897	1.11 (1.02–1.22)	1.10 (1.00–1.22)
NO ₂ -LUR (10 $\mu\text{g}/\text{m}^3$)	877	1.02 (0.89–1.18)	0.93 (0.80–1.08)
CO-IDW (100 $\mu\text{g}/\text{m}^3$)	730	1.03 (0.97–1.09)	1.03 (0.96–1.11)
PM _{2.5} -IDW (1 $\mu\text{g}/\text{m}^3$)	724	0.96 (0.87–1.07)	1.00 (0.85–1.17)
PM _{2.5} -LUR (1 $\mu\text{g}/\text{m}^3$)	877	1.05 (1.02–1.09)	1.03 (0.99–1.07)
BC-LUR (10 ⁻⁵ /m)	877	1.03 (0.97–1.09)	1.01 (0.95–1.07)
PM ₁₀ -IDW (1 $\mu\text{g}/\text{m}^3$)	897	1.01 (0.95–1.08)	1.04 (0.95–1.13)
SO ₂ -IDW (1 $\mu\text{g}/\text{m}^3$)	891	0.99 (0.96–1.02)	0.98 (0.96–1.01)

BC, black carbon.

^aORs per standardized increases (indicated in parentheses), roughly corresponding to interquartile range. ^bAdjusted for infant sex, First Nations status, parity, maternal age, maternal smoking during pregnancy, month-year of birth, income (quintile-census), maternal education (quartile-census).

Table 5. Crude and adjusted ORs for SGA and road proximity.

Measure	No. of SGA cases (% of total subjects)	Crude OR (95% CI)	Adjusted ^a OR (95% CI)
< 150 m highway ^b or < 50 major road ^c	1,374 (1.96)	1.04 (0.98–1.11)	1.02 (0.96–1.08)
< 50 m highway	176 (0.25)	1.25 (1.07–1.47)	1.21 (1.03–1.42)
50–150 m highway	404 (0.57)	0.95 (0.86–1.06)	0.92 (0.83–1.03)
< 50 m major road	841 (1.20)	1.06 (0.98–1.14)	1.04 (0.97–1.13)
50–150 m major road	1,592 (2.27)	1.05 (0.99–1.11)	1.04 (0.98–1.10)

^aAdjusted for infant sex, First Nations status, parity, maternal age, maternal smoking during pregnancy, month-year of birth, income (quintile-census), maternal education (quartile-census). ^bDMTI type 1 and 2 road (expressway: 114,000 vehicles/day; principal highway: 21,000 vehicles/day). ^cDMTI type 3 and 4 road (secondary highway: 18,000 vehicles/day; major road: 15,000 vehicles/day).

Table 6. Crude and adjusted odds ratios for LBW at full term and road proximity.

Measure	No. of LBW cases (% of total subjects)	Crude OR (95% CI)	Adjusted ^a OR (95% CI)
< 150 m highway ^b or < 50 major road ^c	169 (0.25)	1.03 (0.87–1.22)	0.99 (0.84–1.18)
< 50 m highway	24 (0.04)	1.37 (0.91–2.07)	1.28 (0.85–1.93)
50–150 m highway	55 (0.08)	1.05 (0.80–1.39)	1.01 (0.77–1.33)
< 50 m major road	100 (0.15)	1.00 (0.81–1.24)	0.99 (0.80–1.22)
50–150 m major road	184 (0.28)	0.95 (0.81–1.12)	0.94 (0.80–1.10)

^aAdjusted for infant sex, First Nations status, parity, maternal age, maternal smoking during pregnancy, month-year of birth, income (quintile-census), maternal education (quartile-census). ^bDMTI type 1 and 2 road (expressway: 114,000 vehicles/day; principal highway: 21,000 vehicles/day). ^cDMTI type 3 and 4 road (secondary highway: 18,000 vehicles/day; major road: 15,000 vehicles/day).

Table 7. Crude and adjusted ORs^a for preterm births < 30 weeks.

Exposure (entire pregnancy)	Cases (n)	Crude OR (95% CI)	Adjusted ^b OR (95% CI)
NO-IDW (10 $\mu\text{g}/\text{m}^3$)	241	1.15 (1.03–1.28)	1.18 (1.03–1.35)
NO-LUR (10 $\mu\text{g}/\text{m}^3$)	235	1.09 (0.98–1.21)	1.06 (0.94–1.19)
NO ₂ -IDW (10 $\mu\text{g}/\text{m}^3$)	241	1.12 (0.94–1.33)	1.10 (0.91–1.34)
NO ₂ -LUR (10 $\mu\text{g}/\text{m}^3$)	235	1.15 (0.88–1.50)	1.09 (0.82–1.45)
CO-IDW (100 $\mu\text{g}/\text{m}^3$)	192	1.06 (0.94–1.19)	1.04 (0.91–1.20)
PM _{2.5} -IDW (1 $\mu\text{g}/\text{m}^3$)	200	1.22 (1.01–1.48)	2.01 (1.38–2.92)
PM _{2.5} -LUR (1 $\mu\text{g}/\text{m}^3$)	235	1.07 (0.99–1.14)	1.05 (0.97–1.13)
BC-LUR (10 ⁻⁵ /m)	235	1.02 (0.92–1.14)	1.00 (0.90–1.11)
PM ₁₀ -IDW (1 $\mu\text{g}/\text{m}^3$)	241	1.17 (1.04–1.32)	1.18 (1.01–1.38)
SO ₂ -IDW (1 $\mu\text{g}/\text{m}^3$)	238	1.02 (0.97–1.07)	1.01 (0.95–1.06)

BC, black carbon.

^aORs per standardized increases (in parentheses), roughly corresponding to interquartile range. ^bAdjusted for infant sex, First Nations status, parity, maternal age, maternal smoking during pregnancy, month-year of birth, income (quintile-census), maternal education (quartile-census).