

Drinking or Smoking While Breastfeeding and Later Cognition in Children

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abstract

BACKGROUND AND OBJECTIVES: Although prenatal alcohol and nicotine exposure are associated with reduced cognition in children, associations between consumption of alcohol during lactation and cognition have not been examined. We aimed to examine whether drinking or smoking while breastfeeding lowers children's cognitive scores. We hypothesized that increased drinking or smoking would be associated with dose-dependent cognitive reductions.

METHODS: Data were sourced from Growing Up in Australia: The Longitudinal Study of Australian Children. Participants were 5107 Australian infants recruited in 2004 and assessed every 2 years. Multivariable linear regression analyses assessed relationships between drinking and smoking habits of breastfeeding mothers and children's Matrix Reasoning, Peabody Picture Vocabulary Test–Third Edition and Who Am I? scores at later waves.

RESULTS: Increased or riskier wave 1 maternal alcohol consumption was associated with reductions in Matrix Reasoning scores at age 6 to 7 years in children who had been breastfed ($B = -0.11$; $SE = 0.03$; 95% confidence interval: -0.18 to -0.04 ; $P = .01$). This relationship was not evident in infants who had never breastfed ($B = -0.02$; $SE = 0.10$; 95% confidence interval = -0.20 to 0.17 ; $P = .87$). Smoking during lactation was not associated with any outcome variable.

CONCLUSIONS: Exposing infants to alcohol through breastmilk may cause dose-dependent reductions in their cognitive abilities. This reduction was observed at age 6 to 7 years but was not sustained at age 10 to 11 years. Although the relationship is small, it may be clinically significant when mothers consume alcohol regularly or binge drink. Further analyses will assess relationships between alcohol consumption or tobacco smoking during lactation and academic, developmental, physical, and behavioral outcomes in children.



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Mr Gibson conceptualized the research topic, designed the analyses, conducted all analyses, and drafted the initial manuscript; Prof Porter assisted in the design of the analyses; and all authors reviewed and revised the manuscript and approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Although alcohol is a known teratogen, studies of maternal alcohol use during breastfeeding and infants' basic developmental scores have produced mixed results. No previous study has assessed the impact of maternal drinking or smoking on cognitive outcomes in the child.

WHAT THIS STUDY ADDS: This is the first study to directly examine cognitive outcomes in relation to lactational alcohol and nicotine exposure. Increased or riskier maternal alcohol consumption while breastfeeding was associated with reduced abstract reasoning ability in the child at age 6 to 7 years.

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Although teratogenic effects of alcohol are well documented,¹⁻⁴ cognitive risks of alcohol and breastfeeding are unknown.⁵ Likewise, although tobacco smoking during pregnancy is associated with reductions in childhood cognition,⁶ cognitive effects from smoking tobacco during lactation have not been researched. Because alcohol⁷ and nicotine⁸ are available in breastmilk after maternal intake, understanding whether smoking tobacco or drinking alcohol during lactation impacts children's cognitive abilities is important.

Although the World Health Organization recommends avoiding alcohol and drugs while breastfeeding,⁹ 12% to 83%^{5,10-16} of breastfeeding women report consuming alcohol and 7% to 16%^{11,17} report smoking tobacco. These may be underestimates because people often underreport alcohol drinking habits.¹⁸ Older maternal age, increased education, and longer breastfeeding duration are associated with increased alcohol consumption during lactation.¹¹ Conversely, younger maternal age, lower education, and decreased income are associated with increased tobacco smoking.¹⁹

Breastfeeding women report drinking alcohol because of the lack of harmful evidence²⁰ and a mistaken²¹ belief that alcohol is a galactagogue.²⁰ Alcohol passes quickly through to breastmilk at similar concentrations to maternal blood alcohol concentration²² and reduces milk production.²¹ Although drinking alcohol immediately after feeding minimizes ethanol exposure,²³ not all women use this technique,^{16,20} and unpredictable infant feeding can mar such attempts.²⁰ Expressing and discarding "contaminated" breastmilk does not reduce ethanol concentration because this is related to maternal blood alcohol concentration.⁷

Nicotine also passes quickly through to breastmilk, in which concentrations may be higher than maternal serum concentrations.⁸ Nicotine is associated with reduced milk production and changes in breastmilk composition and taste.²⁴ Breastfeeding women report that despite a belief that maternal tobacco smoking is harmful to infants, difficulties curbing addictive behaviors interfere with its cessation.²⁵

Studies in which alcohol consumption or tobacco smoking during lactation are assessed are limited, and conductors of rat studies generally expose dams to larger alcohol quantities than consumed by human mothers. Despite this, available research suggests that alcohol exposure through breastmilk may have negative cognitive consequences for offspring. Research of dams intoxicated while pregnant and lactating found reduced learning in pups.²⁶ This may be because of prenatal exposure alone, however, because Gray et al²⁷ found no decline when alcohol was only given during lactation. Likewise, dam offspring who consumed alcohol while pregnant and nursing had reduced hippocampal neurons,²⁸ cerebellar neurons,²⁹ and increased cerebral cortex cell apoptosis and necrosis.³⁰ Similar neuronal loss and decreased myelination in pup cerebellums was also found after only lactational exposure.³¹

Human research has largely been focused on disrupted infant sleeping and feeding patterns.^{5,32} The authors of a case study from 1978,³³ however, described an infant who developed a pseudo-Cushing syndrome after high maternal alcohol consumption during lactation but not pregnancy. Symptoms abated after alcohol cessation. Whereas Little et al^{34,35} found reduced psychomotor scores at 1 year in infants whose mothers drank alcohol while breastfeeding, the authors of more recent studies found no reduction in developmental scores.¹⁶

Rat studies of nicotine intake during lactation have revealed reversible hypothyroidism in offspring.^{36,37} Although hypothyroidism is associated with cognitive deficits in humans,³⁸ Gaworski et al³⁹ found that pups exposed to nicotine during pregnancy and lactation had intact learning and memory.³⁹ In a study of dams exposed to nicotine during pregnancy and lactation, offspring had delayed muscarinic receptor development.⁴⁰ Because decreased acetylcholine transmission is associated with cognitive decline,⁴¹ this could potentially impact cognitive development.

Human studies in which relationships between tobacco smoking during lactation and childhood developmental outcomes are assessed are scant.^{42,43} Women who smoke may have infants of lower birth weight⁴⁴ and wean infants earlier.⁴⁵ Because low birth weight⁴⁶ and shorter breastfeeding duration⁴⁷ are associated with decreased cognition, these factors alone could reduce infant cognition. Laurberg et al⁴⁸ found that smoking tobacco while lactating caused dose-dependent reductions in milk iodine content and increased children's risk of iodine deficiency. Although iodine deficiency could theoretically result in cognitive impairment,⁴⁹ this was not examined.⁴⁸

In the context of available research, our aim in the current study was to assess whether drinking alcohol or smoking tobacco during lactation adversely impacts cognitive outcomes in children. It was hypothesized that alcohol and nicotine use would result in lower cognitive scores in a dose-dependent manner independent of pregnancy use.

METHODS

Ethics

Ethics approval was obtained from Macquarie University Human Research Ethics Committee.

Study Design and Data Source

Data were sourced from Growing Up in Australia: The Longitudinal Study of Australian Children (LSAC). Detailed information regarding LSAC can be found on the LSAC Web site.⁵⁰ Briefly, LSAC is a longitudinal study of Australian children and their families, conducted by the Australian Government Department of Social Services, the Australian Institute of Family Studies, and the Australian Bureau of Statistics. The researchers aim to examine impacts of social and cultural variables on a range of physical and psychological health and developmental outcomes.⁵¹

Study Cohort

Two cohorts (B and K) were recruited into LSAC at wave 1 in 2004. Cohort K was not included in current analyses because the children were 4 to 5 years old at recruitment. Cohort B comprised 5107 infants and caregivers who were managed over time every 2 years. Demographic, lifestyle, cognitive, academic, and developmental variables were collected at each of the 6 waves available for data analyses^{52,53}; further recruitment details are available in LSAC Technical Paper No. 1.⁵⁴

Breastfeeding

Caregivers were asked whether infants were being breastfed at wave 1 and whether they had ever been breastfed.⁵⁵ This allowed stratification into wave 1 breastfeeding infants and infants who had been breastfed at any time.

Predictor Variables

Mothers were asked a modified version of the Alcohol Use Disorders Identification Test Alcohol Consumption Questions (AUDIT-C)^{56,57} at wave 1 (Table 1). Respondents who answered “never” to question 1 were assigned a score of 0 for

question 2. Scores were summed to create a total score (range: 1–19). Higher scores indicated increased or riskier alcohol consumption. Pregnancy alcohol was recorded retrospectively (Table 1). The average number of days pregnant mothers drank alcohol per week was calculated by averaging trimester results. Mothers were asked how many cigarettes they smoked on average per day at wave 1 and how many cigarettes they smoked on average per day during pregnancy.⁵⁵

Outcome Variables

Outcome variables were as follows:

- Transformed scores from an adapted Peabody Picture Vocabulary Test–Third Edition (PPVT-III)^{58,59} (waves 3, 4 and 5). Higher scores indicated increased vocabulary.
- Raw scores from the Matrix Reasoning (MR) subtest of the Wechsler Intelligence Scale for Children–Fourth Edition⁶⁰ (waves 4, 5 and 6). Higher scores indicated increased nonverbal reasoning.
- Raw scores from the Who Am I? test (WAI),^{59,61,62} with 1 change to item 11⁶³ (wave 3). Higher scores indicated increases in cognitive processes underlying early literacy and numeracy.

Control Variables

Infant sex was controlled for because of postulated sex differences in cognitive abilities.⁶⁴ Infant and maternal age were included because maternal age is associated with alcohol and cigarette use during lactation,^{11,19} and cognition varies with age.⁶⁵ Because women who smoke tend to have lower birth weight infants⁴⁴ and lower birth weight is associated with poorer cognition,⁴⁶ birth weight was also included as a control variable. Breastfeeding duration was controlled for because

earlier weaning is associated with lowered cognition⁴⁷ as well as maternal tobacco smoking.⁴⁵

Combined household income and maternal education were included because both are associated with tobacco smoking and alcohol consumption during lactation^{11,19} as well as cognitive outcomes.⁶⁶ Learning difficulties (delay relative to peers in the context of a medical condition) and brain injuries (concussion and/or internal head injury requiring medical attention) were included as control variables because both can alter cognitive profiles.^{67,68} The primary language spoken at home was only included for the adapted PPVT-III and WAI analyses because both are language reliant.

Statistical Analyses

Data were analyzed by using IBM SPSS version 24 (IBM SPSS Statistics, IBM Corporation). Missing data from all included variables were imputed by using multiple imputation (MI). To reduce estimate bias, arithmetically derived variables were calculated after MI of individual items.⁶⁹ Thirty imputations were used because the highest proportion of missing data for any variable was 30% (Supplemental Information). When missing data are <50%, matching the imputation number to missing data percentage increases efficiency and replicability of data.⁷⁰ Imputations were constrained to variable ranges where applicable and were not rounded to integers to reduce estimate bias.⁷¹ Skewed independent variables were not transformed before MI because this can produce poorer estimates.⁷²

Multivariable linear regression analyses were performed including each of the predictor and control variables. Multicollinearity was assessed by using the variance inflation factor (VIF). A VIF <10 was

TABLE 1 Frequencies for Each of the Responses and Missing Data for Categorical Predictor, Control, and Outcome Variables Before Data Imputation (*N* = 5107)

Variable	<i>N</i> (%)
Sex of child	
Male	2608 (51.1)
Female	2499 (48.9)
Missing	0 (0.0)
Wave 1 child still breastfeeding	
Yes	2007 (39.3)
No	3096 (60.6)
Missing	4 (0.1)
Child was breastfed at any time	
Yes	4685 (91.7)
No	418 (8.2)
Missing	4 (0.1)
Mother's trimester 1 d per wk drinking alcohol	
0 or occasional	3934 (77)
1	141 (2.8)
2	85 (1.7)
3	32 (0.6)
4	17 (0.3)
5	12 (0.2)
6	5 (0.1)
7	4 (0.1)
Missing	877 (17.2)
Mother's trimester 2 d per wk drinking alcohol	
0 or occasional	3823 (74.9)
1	206 (4.0)
2	118 (2.3)
3	48 (0.9)
4	19 (0.4)
5	9 (0.2)
6	5 (0.1)
7	3 (0.1)
Missing	876 (17.2)
Mother's trimester 3 d per wk drinking alcohol	
0 or occasional	3802 (74.4)
1	190 (3.7)
2	133 (2.6)
3	54 (1.1)
4	24 (0.5)
5	14 (0.3)
6	6 (0.1)
7	5 (0.1)
Missing	879 (17.2)
Pregnancy: average No. drinks on drinking d	
0 or none	2597 (50.9)
1 or 2	1560 (30.5)
3 or 4	56 (1.1)
5 or 6	7 (0.1)
7–10	3 (0.1)
11 or more	5 (0.1)
Missing	879 (17.2)
Mother's level of education	
Never attended or still attending school	4 (0.1)
≤Year 8	83 (1.6)
Year 9 or Eq	161 (3.2)
Year 10 or Eq	820 (16.1)
Year 11 or Eq	539 (10.6)
Year 12 or Eq	1813 (35.5)
Bachelor degree	998 (19.5)
Graduate diploma or certificate	319 (6.2)
Postgraduate degree	361 (7.1)
Missing	9 (0.2)

considered acceptable.⁷³ Analyses were conducted separately for each outcome variable at each wave. Only data from biological mothers were included. Infants still being breastfed at wave 1 and infants who had been breastfed at any time were analyzed separately. The Benjamini and Hochberg⁷⁴ procedure was used to correct for type I error ($\alpha = .05$). This procedure is superior to the Bonferroni correction in preserving power.⁷⁴

RESULTS

Descriptive Statistics

Full descriptive statistics of all variables before MI are shown in Tables 1 and 2.

Power Analyses

Sixteen female caregivers who were not biological mothers were excluded after MI. This left 2009 breastfed infants and 4679 infants who had been breastfed at some time. Power analyses revealed that with 2009 subjects, 99.57% (14 independent variables) and 99.49% (15 independent variables) power was achieved to detect a small effect size (Cohen's $d = 0.2$, $\alpha = .05$). A sample size of 4679 provided >99% power to detect an effect size of Cohen's $d = 0.2$ ($\alpha = .05$), with 14 or 15 independent variables.^{75,76}

Wave 1 Maternal Alcohol Consumption (Before MI)

Modified AUDIT-C scores of wave 1 breastfeeding mothers (mean = 5.55; SD = 2.46; 95% confidence interval [CI]: 5.42 to 5.68) were lower than scores for mothers who were not breastfeeding (mean = 6.13; SD = 2.72; 95% CI: 6.02 to 6.24; $P < .001$; Cohen's $d = 0.22$). There was no statistically significant difference in modified AUDIT-C scores between

TABLE 1 Continued

Variable	N (%)
Combined family income (Australian dollars)	
≥\$2400 per wk or ≥\$124 800 per y	384 (7.5)
\$2200–\$2399 per wk or \$114 400–\$124 799 per y	106 (2.1)
\$2000–\$2199 per wk or \$104 000–\$114 399 per y	158 (3.1)
\$1500–\$1999 per wk or \$78 000–\$103 999 per y	674 (13.2)
\$1000–\$1499 per wk or \$52 000–\$77 999 per y	1295 (25.4)
\$800–\$999 per wk or \$41 600–\$51 999 per y	685 (13.4)
\$700–\$799 per wk or \$36 400–\$41 599 per y	367 (7.2)
\$600–\$699 per wk or \$31 200–\$36 399 per y	287 (5.6)
\$500–\$599 per wk or \$26 000–\$31 199 per y	266 (5.2)
\$400–\$499 per wk or \$20 800–\$25 999 per y	273 (5.3)
\$300–\$399 per wk or \$15 600–\$20 799 per y	231 (4.5)
\$200–\$299 per wk or \$10 400–\$15 599 per y	78 (1.5)
\$100–\$199 per wk or \$5200–\$10 399 per y	17 (0.3)
\$50–\$99 per wk or \$2600–\$5199 per y	7 (0.1)
\$1–\$49 per wk or \$1–\$2599 per y	1 (<0.1)
Nil income	2 (<0.1)
Negative income	4 (0.1)
Missing	272 (5.3)
Mother's frequency of drinking alcohol (modified AUDIT-C question 1)	
Never	387 (7.6)
Not in the last y	414 (8.1)
Monthly or less	1234 (24.2)
2–3 times a mo	582 (11.4)
Once a wk	590 (11.6)
2–3 times a wk	604 (11.8)
4–6 times a wk	303 (5.9)
Every d	91 (1.8)
Missing	902 (17.7)
Mother's average No. drinks when drinking (modified AUDIT-C question 2)	
0	387 (7.6)
1 or 2	2484 (48.6)
3 or 4	611 (12.0)
5 or 6	184 (3.6)
7–10	64 (1.3)
≥11	17 (0.3)
Missing	1360 (26.6)
Mother's frequency of drinking ≥5 drinks in 1 sitting (modified AUDIT-C question 3)	
Not in the last y	2879 (56.4)
Monthly or less	1022 (20.0)
2 or 3 times a mo	148 (2.9)
Once a wk	95 (1.9)
2–3 times a wk	46 (0.9)
4–6 times a wk	7 (0.1)
Every d	1 (0.1)
Missing	909 (17.8)
Head injury wave 3 ^a	
Yes	7 (0.1)
No	4379 (85.7)
Missing	721 (14.1)
Head injury wave 4 ^a	
Yes	19 (0.4)
No	4223 (82.7)
Missing	865 (16.9)
Head injury wave 5 ^a	
Yes	24 (0.5)
No	4024 (78.8)
Missing	1059 (20.7)
Head injury wave 6 ^a	
Yes	28 (0.5)
No	3670 (71.9)

mothers who had breastfed ($n = 3443$; mean = 5.90; SD = 2.60; 95% CI: 5.81 to 5.99) and had never breastfed their infants (mean = 5.81; SD = 3.04; 95% CI: 5.50 to 6.13; $P = .60$; Cohen's $d = 0.03$).

Wave 1 Maternal Tobacco Smoking (Before MI)

Breastfeeding wave 1 mothers smoked fewer cigarettes on average per day (mean = 1.06; SD = 3.67; 95% CI: 0.77 to 1.25) than women who were not breastfeeding (mean = 2.84; SD = 5.97; 95% CI: 2.64 to 3.04; $P < .001$; Cohen's $d = 0.37$). Mothers whose infants had been breastfed at some time, smoked fewer cigarettes on average per day (mean = 1.85; SD = 4.87; 95% CI: 1.69 to 2.01) than mothers whose infants had never breastfed (mean = 5.00; SD = 8.02; 95% CI: 4.43 to 5.57; $P < .001$; Cohen's $d = 0.47$).

Missing Data

Little's missing completely at random test revealed that data were not missing completely at random, $P < .001$. Previous LSAC analysis revealed that more poorly educated caregivers tended to drop out of the study,⁷⁷ suggesting that missing data were related to independent variables and suitable for MI.⁷⁸

Linear Regression: MR Scores

Full wave 5 to 6 results are available in Supplemental Table 5.

Infants Breastfeeding at Wave 1

Models explained 1% to 19%, 1% to 26%, and 2% to 14% of variance, respectively, across waves for each imputation. Older wave 4 child age was associated with increased wave 4 MR scores. Increased and/or riskier maternal alcohol consumption while breastfeeding was associated with decreased wave 4 MR scores. This was no longer statistically significant, however, after multiple comparison

TABLE 1 Continued

Variable	N (%)
Missing	1409 (27.6)
Learning difficulty wave 3	
Yes	84 (1.6)
No	4302 (84.2)
Missing	721 (14.1)
Learning difficulty wave 4	
Yes	25 (0.5)
No	4217 (82.6)
Missing	865 (16.9)
Learning difficulty wave 5	
Yes	92 (1.8)
No	3955 (77.4)
Missing	1060 (20.8)
Learning difficulty wave 6	
Yes	107 (2.1)
No	3670 (71.9)
Missing	1409 (27.6)

^a Head injuries noted at earlier waves were automatically recorded at all later waves.

TABLE 2 Means, SDs, Ranges, and Missing Data for Quantitative Predictor, Control, and Outcome Variables Before Data Imputation (N = 5107)

Variable	Mean (SD)	Range	Missing Data N (%)
Child's birth wt, g	3410.15 (568.83)	382.00–5440.00	35 (0.7)
Child's age wave 1, y	0.77 (0.21)	0.33–1.59	0 (0)
Child's age wave 3, y	4.88 (0.25)	4.16–5.84	721 (14)
Child's age wave 4, y	6.91 (0.29)	6.16–7.92	865 (17)
Child's age wave 5, y	8.99 (0.32)	8.08–9.84	1022 (20)
Child's age wave 6, y	11.01 (0.33)	10.08–11.84	1343 (26)
Mother's age wave 1, y	31.48 (5.47)	15.66–63.92	7 (0.1)
Average daily cigarettes while pregnant	1.19 (3.81)	0.00–55.00	1041 (20)
Mother's average daily cigarettes wave 1	2.09 (5.25)	0.00–40.0	823 (16)
WAI score wave 3	26.94 (7.10)	1.00–43.00	910 (18)
Adapted PPVT-III score wave 3	65.16 (5.99)	34.00–85.00	841 (17)
Adapted PPVT-III score wave 4	74.43 (5.15)	36.00–92.00	922 (18)
Adapted PPVT-III score wave 5	79.10 (4.83)	52.00–106.00	1093 (21)
MR score wave 4	14.00 (4.67)	3.00–30.00	927 (18)
MR score wave 5	19.55 (4.83)	1.00–32.00	1107 (22)
MR score wave 6	22.08 (5.07)	1.00–33.00	1509 (30)
Breastfeeding duration, d	228.89 (202.88)	0.00–1157	583 (11)

adjustment. No other statistically significant relationships were observed. Full results are shown in Table 3.

Infants Who Had Been Breastfed at Any Time

Models explained 2% to 16%, 3% to 25%, and 2% to 14% of variance, respectively, across waves for each imputation. Increased MR wave 4 scores were predicted by increased wave 4 child age. Increased or riskier maternal alcohol consumption was associated with decreased wave 4 MR

scores. This relationship remained statistically significant after multiple comparison adjustments. At wave 5, only older wave 5 child age was associated with increased wave 5 MR scores. At wave 6, learning difficulties predicted lower wave 6 MR scores. Full results are shown in Table 4.

Infants Who Had Never Been Breastfed

When assessing infants who had never breastfed, only modified AUDIT-C scores were included as a

predictor to maximize power. With 1 independent variable, a sample size of 412 provided 80% power to detect a small effect size (Cohen's $d = 0.2$; $\alpha = .05$).^{75,76} The model accounted for <0.001% variance, and modified AUDIT-C scores weren't associated with wave 4 MR scores (B = -0.02 ; SE = 0.10; 95% CI = -0.20 to 0.17; $P = .87$).

Linear Regression: WAI Scores

Full results are available in Supplemental Table 6.

Infants Breastfeeding at Wave 1

The model explained 7% to 41% of variance across imputations. Older wave 3 child age was associated with increased WAI scores. Learning difficulties were also associated with decreased WAI scores. There was no association between maternal alcohol consumption or tobacco smoking and WAI scores.

Infants Who Had Been Breastfed at Any Time

The model explained 9% to 41% of variance across imputations. Older wave 3 child age predicted higher WAI scores. Learning difficulties predicted lower WAI scores. No other variables were statistically significant.

Linear Regression: Adapted PPVT-III Scores

Full results are available in Supplemental Table 7.

Infants Breastfeeding at Wave 1

Models explained 4% to 17%, 2% to 15%, and 1% to 25% of variance, respectively, across waves for each imputation. Learning difficulties were associated with lower wave 3–adapted PPVT-III scores. Older wave 4 child age was associated with higher wave 4 scores. No other variables were statistically significant.

TABLE 3 Infants Being Breastfed at Wave 1: Regression Coefficients, SEs, CIs, *P* Values, and Adjusted *P* Values for Each Predictor and Control Variable for Wave 4 MR Scores (*n* = 2009)

Variable ^a	B Coefficient	SE	95% CI	<i>P</i>	Adjusted <i>P</i> ^b
Intercept	3.98	3.02	−1.96 to 9.92	.19	N/A
Child's age wave 4	1.64	0.40	0.85 to 2.44	<.001	<.001
Mother's modified AUDIT-C score wave 1 ^c	−0.12	0.06	−0.23 to −0.01	.03	.22
Child's birth wt	<0.001	<0.001	−0.001 to <0.001	.12	.48
Pregnancy: average d per wk drinking alcohol	0.28	0.19	−0.09 to 0.65	.14	.48
Pregnancy: average No. drinks	0.27	0.25	−0.23 to 0.76	.30	.72
Learning difficulty wave 4	−1.72	1.67	−5.10 to 1.66	.31	.72
Combined family income	−0.04	0.05	−0.14 to 0.05	.36	.73
Mother's age wave 1	0.02	0.02	−0.03 to 0.06	.44	.77
Average daily cigarettes while pregnant	−0.05	0.08	−0.20 to 0.10	.53	.81
Head injury wave 4	0.93	1.65	−2.40 to 4.25	.58	.81
Child's sex	−0.08	0.22	−0.52 to 0.36	.72	.81
Breastfeeding duration	<0.001	<0.001	<0.001 to <0.001	.72	.81
Mother's level of education	0.02	0.08	−0.14 to 0.19	.77	.81
Mother's average daily cigarettes wave 1 ^d	0.01	0.06	−0.10 to 0.13	.81	.81

N/A, not applicable.

^a VIF <10 for all variables.

^b Benjamini-Hochberg method.

^c Unadjusted B = −0.045; SE = 0.05; 95% CI: −0.14 to 0.05; *P* = .35.

^d Unadjusted B = −0.02; SE = 0.03; 95% CI: −0.08 to 0.04; *P* = .49.

TABLE 4 Infants Who Had Been Breastfed at Any Time: Regression Coefficients, SEs, CIs, *P* Values, and Adjusted *P* Values for Each Predictor and Control Variable for Wave 4 MR Scores (*n* = 4679)

Variable ^a	B Coefficient	SE	95% CI	<i>P</i>	Adjusted <i>P</i> ^b
Intercept	2.88	2.14	−1.32 to 7.09	.18	N/A
Child's age wave 4	1.83	0.29	1.27 to 2.40	<.001	<.001
Mother's modified AUDIT-C score wave 1 ^c	−0.11	0.03	−0.18 to −0.04	.001	.01
Average daily cigarettes while pregnant	−0.05	0.03	−0.12 to 0.02	.13	.46
Pregnancy: average d per wk drinking alcohol	0.19	0.14	−0.08 to 0.46	.16	.46
Child's birth wt	<0.001	<0.001	<0.001 to <0.001	.17	.46
Pregnancy: average No. drinks	0.22	0.17	−0.12 to 0.55	.21	.48
Learning difficulty wave 4	−1.51	1.55	−4.66 to 1.64	.34	.54
Mother's age wave 1	−0.01	0.02	−0.04 to 0.02	.35	.54
Combined family income	−0.03	0.03	−0.09 to 0.04	.38	.54
Mother's average daily cigarettes wave 1 ^d	0.02	0.03	−0.03 to 0.07	.39	.54
Breastfeeding duration	<0.001	<0.001	<0.001 to 0.001	.48	.61
Mother's level of education	0.04	0.06	−0.08 to 0.15	.54	.63
Head injury wave 4	0.86	1.56	−2.31 to 4.02	.59	.63
Child's sex	−0.05	0.15	−0.33 to 0.24	.76	.76

N/A, not applicable.

^a VIF <10 for all variables.

^b Benjamini-Hochberg method.

^c Unadjusted B = −0.07; SE = 0.03; 95% CI: −0.12 to 0.01; *P* = .03.

^d Unadjusted B = −0.01; SE = 0.02; 95% CI: −0.04 to 0.02; *P* = .50.

Infants Who Had Been Breastfed at Any Time

Models explained 3% to 13%, 2% to 14%, and 2% to 18% of variance, respectively, across waves for each imputation. Learning difficulties were associated with lower wave 3–adapted PPVT-III scores. Older wave 3 child age was associated with higher wave 4 scores. Other variables were not statistically significant.

DISCUSSION

This is the first study in which associations between alcohol exposure through breastmilk and cognition in children are examined. Greater or riskier maternal alcohol intake was associated with decreased nonverbal reasoning at 6 to 7 years in a dose-dependent manner. This was independent of prenatal alcohol consumption, sex,

child and maternal age, income, birth weight, breastfeeding duration, learning delay, head injury, and pregnancy and breastfeeding tobacco smoking. Although this relationship was found in wave 1 breastfeeding children, with multiple comparison adjustment it was no longer statistically significant. In children who had been breastfed at any time, however, this

association remained statistically significant after adjustment.

There was no relationship between maternal alcohol consumption and MR scores in infants who had never breastfed. This suggests that alcohol exposure through breastmilk was responsible for cognitive reductions in breastfed infants rather than psychosocial or environmental factors surrounding maternal alcohol consumption. This supports the suggestion that alcohol exposure through breastmilk can reduce cognition in children.

No relationship between maternal tobacco smoking and MR scores was found in wave 1 breastfed infants or infants who had been breastfed at any time at any wave. Likewise, no associations were observed between maternal alcohol or cigarette use and adapted PPVT-III or WAI scores for either group at any wave. The suggestion that smoking tobacco during lactation reduces cognition in children was not supported.

Although no directly comparable previous research exists, Little et al³⁴ found reduced developmental scores in children of mothers who drank while breastfeeding. The authors of a case study of a breastfed infant who developed a pseudo-Cushing syndrome also found that symptoms abated once maternal alcohol was ceased. Because the infant had no prenatal alcohol exposure, this suggests that alcohol exposure through breastmilk can directly impact children's development.³³ Additionally, prenatal alcohol exposure is more consistently associated with executive dysfunction than language or numeracy impairments.⁴ This is consistent with the observed reductions in MR scores but not the language- or numeracy-based measures.

Although current analyses found an association between increased or

riskier alcohol consumption while breastfeeding and MR scores, the mechanism is unclear. Consistent with animal models, ethanol in breastmilk may interfere with normal brain development.²⁸⁻³¹ Increased cerebral cortex apoptosis and necrosis,³⁰ for example, may disrupt higher order executive skills relied on in reasoning tasks. Likewise, decreased myelination³¹ could reduce the processing speed needed to problem solve quickly. Alternatively, reduced cognition may be secondary to changes in feeding and sleeping.^{5,32} Alterations in nutritional intake and sleep patterns may modify brain development or cause behavioral changes that reduce exposure to enriching stimuli.

The relationship between increased alcohol exposure through breastmilk and decreased cognition was not evident at waves 5 to 6. Because older age also ceased to be predictive of wave 6 MR scores, the effects of age and alcohol may be mediated by factors such as increased education. Because learning difficulties were associated with lower wave 6 MR scores, alcohol may also indirectly alter cognition by contributing to developmental disorders in older children.

Interestingly, despite known teratogenic effects,^{1,3} no association between prenatal alcohol exposure and children's cognition was observed. This may be related to the small quantities and infrequency of prenatal alcohol consumption. Furthermore, prenatal binge drinking of alcohol was not recorded and has been associated with reduced cognition in children.² The size of the observed relationship between alcohol exposure through breastmilk and cognition was also small, and clinical implications may be limited unless mothers drink large quantities or frequently

binge drink. Additionally, given this small effect, the sample size of infants who had never breastfed may have been too small to detect a relationship, despite attempts to maximize power.

There are several other limitations. The frequency and quantity of milk consumed by infants was not recorded, nor was the timing of alcohol consumption or the amount of ethanol in breastmilk. The impact of this is unknown, however, because not all women time their alcohol consumption to limit alcohol exposure, and unpredictable infant feeding patterns can interfere with timing attempts.²⁰

Although wave 1 alcohol consumption was recorded contemporaneously, pregnancy alcohol measures were retrospective. Although both are likely to be underestimates,¹⁸ retrospective measures may be even less accurate. Furthermore, measures of wave 1 and pregnancy alcohol differed, preventing direct comparisons.

Cognitive measures available from LSAC were limited. A more comprehensive assessment of cognition including executive functioning, processing speed, learning and memory, visuospatial abilities, and basic as well as complex attention would have been beneficial.

CONCLUSIONS

Increased or riskier maternal alcohol consumption during lactation was associated with dose-dependent reductions in abstract reasoning at age 6 to 7 years. This relationship was not observed in infants who had never breastfed, suggesting a direct relationship between alcohol exposure through

breastmilk and decreased cognition. The association was not evident at ages 8 to 11 years, which may relate to increased education in older children. Alternatively, because learning difficulties predicted lower MR scores at ages 10 to 11 years, alcohol may be associated with developmental disorders that contribute to these difficulties. Further analyses of LSAC data are planned to assess this possibility as well as relationships between alcohol exposure through breastmilk and academic, physical, and behavioral outcomes in children. Future research should also be focused on direct measures of alcohol in breastmilk and use

more comprehensive cognitive assessments.

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ABBREVIATIONS

AUDIT-C: Alcohol Use Disorders Identification Test Alcohol Consumption Questions
CI: confidence interval
LSAC: Growing Up in Australia, The Longitudinal Study of Australian Children
MI: multiple imputation
MR: Matrix Reasoning
PPVT-III: Peabody Picture Vocabulary Test—Third Edition
VIF: variance inflation factor
WAI: Who Am I? test

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REFERENCES

1. Popova S, Lange S, Probst C, Gmel G, Rehm J. Estimation of national, regional, and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: a systematic review and meta-analysis. *Lancet Glob Health*. 2017;5(3):e290–e299
2. Bailey BN, Delaney-Black V, Covington CY, et al. Prenatal exposure to binge drinking and cognitive and behavioral outcomes at age 7 years. *Am J Obstet Gynecol*. 2004;191(3):1037–1043
3. Lange S, Probst C, Gmel G, Rehm J, Burd L, Popova S. Global prevalence of fetal alcohol spectrum disorder among children and youth: a systematic review and meta-analysis. *JAMA Pediatr*. 2017;171(10):948–956
4. Kodituwakku PW. Neurocognitive profile in children with fetal alcohol spectrum disorders. *Dev Disabil Res Rev*. 2009;15(3):218–224
5. Haastrup MB, Pottegård A, Damkier P. Alcohol and breastfeeding. *Basic Clin Pharmacol Toxicol*. 2014;114(2):168–173
6. Batty GD, Der G, Deary IJ. Effect of maternal smoking during pregnancy on offspring's cognitive ability: empirical evidence for complete confounding in the US national longitudinal survey of youth. *Pediatrics*. 2006;118(3):943–950
7. Lawton ME. Alcohol in breast milk. *Aust N Z J Obstet Gynaecol*. 1985;25(1):71–73
8. Luck W, Nau H. Nicotine and cotinine concentrations in serum and milk of nursing smokers. *Br J Clin Pharmacol*. 1984;18(1):9–15
9. World Health Organization. *Guidelines for the Identification and Management of Substance Use and Substance Use Disorders in Pregnancy*. Geneva, Switzerland: World Health Organization; 2014
10. Lange S, Quere M, Shield K, Rehm J, Popova S. Alcohol use and self-perceived mental health status among pregnant and breastfeeding women in Canada: a secondary data analysis. *BJOG*. 2016;123(6):900–909
11. Maloney E, Hutchinson D, Burns L, Mattick RP, Black E. Prevalence and predictors of alcohol use in pregnancy and breastfeeding among Australian women. *Birth*. 2011;38(1):3–9
12. Giglia RC, Binns CW. Patterns of alcohol intake of pregnant and lactating women in Perth, Australia. *Drug Alcohol Rev*. 2007;26(5):493–500
13. Popova S, Lange S, Rehm J. Twenty percent of breastfeeding women in Canada consume alcohol. *J Obstet Gynaecol Can*. 2013;35(8):695–696
14. Nascimento AL, de Souza AF, de Amorim AC, Leitão MB, Maio R, Burgos MG. Alcohol intake in lactating women assisted in a University Hospital. *Rev Paul Pediatr*. 2013;31(2):198–204
15. Breslow RA, Falk DE, Fein SB, Grummer-Strawn LM. Alcohol consumption among breastfeeding women. *Breastfeed Med*. 2007;2(3):152–157
16. Wilson J, Tay RY, McCormack C, et al. Alcohol consumption by breastfeeding mothers: frequency, correlates and

- infant outcomes. *Drug Alcohol Rev.* 2017;36(5):667–676
17. Demirci JR, Sereika SM, Bogen D. Prevalence and predictors of early breastfeeding among late preterm mother-infant dyads. *Breastfeed Med.* 2013;8(3):277–285
 18. Livingston M, Callinan S. Underreporting in alcohol surveys: whose drinking is underestimated? *J Stud Alcohol Drugs.* 2015;76(1):158–164
 19. Gaffney KF. Postpartum smoking relapse and becoming a mother. *J Nurs Scholarsh.* 2006;38(1):26–30
 20. Giglia RC, Binns CW. Alcohol and breastfeeding: what do Australian mothers know? *Asia Pac J Clin Nutr.* 2007;16(suppl 1):473–477
 21. Mennella JA, Pepino MY, Teff KL. Acute alcohol consumption disrupts the hormonal milieu of lactating women. *J Clin Endocrinol Metab.* 2005;90(4):1979–1985
 22. Kesäniemi YA. Ethanol and acetaldehyde in the milk and peripheral blood of lactating women after ethanol administration. *J Obstet Gynaecol Br Commonw.* 1974;81(1):84–86
 23. Ho E, Collantes A, Kapur BM, Moretti M, Koren G. Alcohol and breast feeding: calculation of time to zero level in milk. *Biol Neonate.* 2001;80(3):219–222
 24. Napierala M, Mazela J, Merritt TA, Florek E. Tobacco smoking and breastfeeding: effect on the lactation process, breast milk composition and infant development. A critical review. *Environ Res.* 2016;151:321–338
 25. Goldade K, Nichter M, Nichter M, Adrian S, Tesler L, Muramoto M. Breastfeeding and smoking among low-income women: results of a longitudinal qualitative study. *Birth.* 2008;35(3):230–240
 26. Museridze DP, Tsaishvili TS, Svanidze IK, Khanayeva Z. Disorders in memory and learning in offspring of alcoholized female rats, and a possibility for correction of these changes. *Neurophysiology.* 2008;40(2):115–120
 27. Gray SL, Potts FL, Means LW. Failure of neonatal ethanol exposure to impair maze acquisition in rats. *IRCS Med Sci.* 1981;9:16
 28. González-Burgos I, Alejandre-Gómez M, Olvera-Cortés ME, Pérez-Vega MI, Evans S, Feria-Velasco A. Prenatal-through-postnatal exposure to moderate levels of ethanol leads to damage on the hippocampal CA1 field of juvenile rats: a stereology and Golgi study. *Neurosci Res.* 2006;56(4):400–408
 29. Borges S, Lewis PD. A study of alcohol effects on the brain during gestation and lactation. *Teratology.* 1982;25(3):283–289
 30. Climent E, Pascual M, Renau-Piqueras J, Guerri C. Ethanol exposure enhances cell death in the developing cerebral cortex: role of brain-derived neurotrophic factor and its signaling pathways. *J Neurosci Res.* 2002;68(2):213–225
 31. Hekmatpanah J, Haghghat N, Adams CR. Alcohol consumption by nursing rats and its effect on the cerebellum of the offspring. *Alcohol Alcohol.* 1994;29(5):535–547
 32. Giglia R, Binns C. Alcohol and lactation: a systematic review. *Nutr Diet.* 2006;63(2):103–116
 33. Binkiewicz A, Robinson MJ, Senior B. Pseudo-Cushing syndrome caused by alcohol in breast milk. *J Pediatr.* 1978;93(6):965–967
 34. Little RE, Anderson KW, Ervin CH, Worthington-Roberts B, Clarren SK. Maternal alcohol use during breastfeeding and infant mental and motor development at one year. *N Engl J Med.* 1989;321(7):425–430
 35. Little RE, Northstone K, Golding J; ALSPAC Study Team. Alcohol, breastfeeding, and development at 18 months. *Pediatrics.* 2002;109(5). Available at: www.pediatrics.org/cgi/content/full/109/5/e72
 36. de Oliveira E, de Moura EG, Santos-Silva AP, et al. Neonatal hypothyroidism caused by maternal nicotine exposure is reversed by higher T3 transfer by milk after nicotine withdraw. *Food Chem Toxicol.* 2011;49(9):2068–2073
 37. Oliveira E, Moura EG, Santos-Silva AP, et al. Short- and long-term effects of maternal nicotine exposure during lactation on body adiposity, lipid profile, and thyroid function of rat offspring. *J Endocrinol.* 2009;202(3):397–405
 38. Wekking EM, Appelhof BC, Fliers E, et al. Cognitive functioning and well-being in euthyroid patients on thyroxine replacement therapy for primary hypothyroidism. *Eur J Endocrinol.* 2005;153(6):747–753
 39. Gaworski CL, Carmines EL, Faqi AS, Rajendran N. In utero and lactation exposure of rats to 1R4F reference cigarette mainstream smoke: effect on prenatal and postnatal development. *Toxicol Sci.* 2004;79(1):157–169
 40. Zhu J, Takita M, Konishi Y, Sudo M, Muramatsu I. Chronic nicotine treatment delays the developmental increase in brain muscarinic receptors in rat neonate. *Brain Res.* 1996;732(1–2):257–260
 41. Sirviö J. Strategies that support declining cholinergic neurotransmission in Alzheimer's disease patients. *Gerontology.* 1999;45(suppl 1):3–14
 42. Banderali G, Martelli A, Landi M, et al. Short and long term health effects of parental tobacco smoking during pregnancy and lactation: a descriptive review. *J Transl Med.* 2015;13:327
 43. Primo CC, Ruela PB, Brotto LD, Garcia TR, Lima EF. Effects of maternal nicotine on breastfeeding infants. *Rev Paul Pediatr.* 2013;31(3):392–397
 44. Jaddoe VW, Troe EJW, Hofman A, et al. Active and passive maternal smoking during pregnancy and the risks of low birthweight and preterm birth: the Generation R Study. *Paediatr Perinat Epidemiol.* 2008;22(2):162–171
 45. Horta BL, Kramer MS, Platt RW. Maternal smoking and the risk of early weaning: a meta-analysis. *Am J Public Health.* 2001;91(2):304–307
 46. Aarnoudse-Moens CSH, Weisglas-Kuperus N, van Goudoever JB, Oosterlaan J. Meta-analysis of neurobehavioral outcomes in very preterm and/or very low birth weight children. *Pediatrics.* 2009;124(2):717–728
 47. Bernard JY, Armand M, Peyre H, et al; EDEN Mother-Child Cohort Study Group (Etude des Déterminants Pré- et Postnatals Précoces du Développement et de la Santé de l'Enfant). Breastfeeding, polyunsaturated fatty acid levels in colostrum and child intelligence quotient at age 5-6 years. *J Pediatr.* 2017;183:43–50.e3

48. Laurberg P, Nøhr SB, Pedersen KM, Fuglsang E. Iodine nutrition in breast-fed infants is impaired by maternal smoking. *J Clin Endocrinol Metab.* 2004;89(1):181–187
49. Benton D. The influence of dietary status on the cognitive performance of children. *Mol Nutr Food Res.* 2010;54(4):457–470
50. Growing Up in Australia. Publications. Available at: www.growingupinaustralia.gov.au/pubs/index.html. Accessed October 6, 2017
51. Sanson A, Nicholson J, Ungerer J, et al. *Introducing the Longitudinal Study of Australian Children. LSAC Discussion Paper No. 1.* Melbourne, Australia: Australian Institute of Family Studies; 2002
52. Australian Institute of Family Studies. The longitudinal study of Australian children: frequently asked questions. Available at: www.growingupinaustralia.gov.au/about/faq.html. Accessed October 12, 2016
53. Australian Institute of Family Studies. *Longitudinal Study of Australian Children Data User Guide – November 2015.* Melbourne, Australia: Australian Institute of Family Studies; 2015
54. Soloff C, Lawrence D, Johnstone R. *LSAC Technical Paper No. 1: Sample Design.* Melbourne, Australia: Australian Institute of Family Studies; 2005
55. Growing Up in Australia. Wave 1 release labelled study questionnaires. Available at: <https://data.growingupinaustralia.gov.au/studyqns/wave1qns/index.html>. Accessed October 6, 2017
56. Babor TF, Higgins-Biddle JC, Saunders JB, Monteiro MG; World Health Organization. *AUDIT: The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Health Care.* 2nd ed. Geneva, Switzerland: World Health Organization; 2001
57. Bush K, Kivlahan DR, McDonell MB, Fihn SD, Bradley KA. The AUDIT alcohol consumption questions (AUDIT-C): an effective brief screening test for problem drinking. Ambulatory Care Quality Improvement Project (ACQUIP). Alcohol use disorders identification test. *Arch Intern Med.* 1998;158(16):1789–1795
58. Dunn LM, Dunn LM. *PPVT-III: Peabody Picture Vocabulary Test.* Circle Pines, MN: American Guidance Service; 1997
59. Rothman S. *Report on Adapted PPVT-III and Who Am I?* Melbourne, Australia: Australian Council for Educational Research; 2005
60. Wechsler D, Kaplan E, Fein D, et al. *Wechsler Intelligence Scale for Children: Fourth Edition (WISC-IV).* San Antonio, TX: Pearson; 2003
61. Australian Council for Educational Research (ACER). *Who Am I?* Camberwell, VIC, Australia: Australian Council for Educational Research; 1999
62. De Lemos M. *Patterns of Young Children's Development: An International Comparison of Development as Assessed by Who Am I?* Hull, Canada: Applied Research Branch, Human Resources Development Canada; 2002
63. Rothman S. *Who Am I? Supplementary Information.* Melbourne, Australia: Australian Council for Educational Research; 2007:1–9
64. Hyde JS, McKinley NM. Gender differences in cognition: results from meta-analyses. In: Caplan PJ, Crawford M, Hyde JS, Richardson JTE, eds. *Counterpoints: Cognition, Memory, and Language. Gender Differences in Human Cognition.* New York, NY: Oxford University Press; 1997:30–51
65. Verhaeghen P, Salthouse TA. Meta-analyses of age-cognition relations in adulthood: estimates of linear and nonlinear age effects and structural models. *Psychol Bull.* 1997;122(3):231–249
66. Tong S, Baghurst P, Vimpani G, McMichael A. Socioeconomic position, maternal IQ, home environment, and cognitive development. *J Pediatr.* 2007;151(3):284–288, 288.e1
67. van Heugten CM, Hendriksen J, Rasquin S, Dijcks B, Jaeken D, Vles JHS. Long-term neuropsychological performance in a cohort of children and adolescents after severe paediatric traumatic brain injury. *Brain Inj.* 2006;20(9):895–903
68. Semrud-Clikeman M. Neuropsychological aspects for evaluating learning disabilities. *J Learn Disabil.* 2005;38(6):563–568
69. Eekhout I, de Vet HC, Twisk JW, Brand JP, de Boer MR, Heymans MW. Missing data in a multi-item instrument were best handled by multiple imputation at the item score level. *J Clin Epidemiol.* 2014;67(3):335–342
70. von Hippel PT. The number of imputations should increase quadratically with the fraction of missing information. 2016. Available at: <https://arxiv.org/ftp/arxiv/papers/1608/1608.05406.pdf>. Accessed September 7, 2017
71. Rodwell L, Lee KJ, Romaniuk H, Carlin JB. Comparison of methods for imputing limited-range variables: a simulation study. *BMC Med Res Methodol.* 2014;14:57
72. von Hippel PT. Should a normal imputation model be modified to impute skewed variables? *Sociol Methods Res.* 2013;42(1):105–138
73. O'Brien RM. A caution regarding rules of thumb for variance inflation factors. *Qual Quant.* 2007;41(5):673–690
74. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc B.* 1995;57(1):289–300
75. Faul F, Erdfelder E, Buchner A, Lang A-G. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. *Behav Res Methods.* 2009;41(4):1149–1160
76. Faul F, Erdfelder E, Lang A-G, Buchner A. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behav Res Methods.* 2007;39(2):175–191
77. Baxter JA. *Employment Characteristics and Transitions of Mothers in the Longitudinal Study of Australian Children.* Canberra, Australia: Department of Social Services; 2013
78. Sterne JA, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ.* 2009;338:b2393