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Predictors of Recall Certainty of Dates of Analgesic Medication Use in Pregnancy

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Abstract

Purpose—Recalled dates of medication use are difficult to validate, particularly for over-the-counter (OTC) medications. We evaluated mothers' recall certainty as an approximation of the accuracy of their recalled exposures.

Methods—We used data from the Slone Epidemiology Center Birth Defects Study collected by retrospective interview of women about pregnancy medication use. For each medication reported, women were asked to report the dates of their use and how certain they were of their reported dates. For this analysis, 32,107 reports from 14,577 analgesic users were categorized as 'high' or 'low' recall certainty if they considered a reported date as exact or estimated, respectively. Patterns of analgesic use, maternal demographics, and health behaviors were explored as predictors of high recall certainty of dates of analgesic use. We used log-binomial regression with the generalized estimating equations extension to account for multiple reports per subject in estimating prevalence ratios (PR) and 95% confidence intervals.

Results—Relative to episodes of short-term routine use (4 times/week for 30 days), high recall certainty was more likely for episodes of a single dose (prescription PR=1.92 (1.61, 2.27); OTC PR=3.65 (3.03, 4.40)) and less likely for episodes of occasional use (prescription PR=0.10 (0.05, 0.18); OTC PR=0.65 (0.53, 0.79)). The association of chronic routine use with high recall certainty was inverse among prescription analgesics and positive among OTC analgesics (prescription PR=0.56 (0.40, 0.80); OTC PR=2.46 (1.92, 3.42)).

Conclusions—Some characteristics that were associated with recall accuracy in previous studies were also associated with recall certainty in this study.

MeSH keywords

mental recall; prescription drugs; non-prescription drugs; abnormalities; drug-induced; pregnant women

INTRODUCTION

In birth defects studies, ascertainment of the timing of exposure during gestation is critically important, since teratogenic effects should generally be confined to the limited period when a given organ undergoes development.¹ However, data on the timing of exposure are difficult to validate for many exposures, and particularly for dates of medication use. In

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medical records, documentation of timing of actual use for most prescription drugs is subject to inaccuracy, while it is scant or non-existent for over-the-counter (OTC) drugs.²

The study participant's recall certainty is a potential tool to assess bias of self-reported exposure measures that are difficult to validate in interview-based studies.³ Our case-control study of birth defects asks women about dates of medication use in pregnancy and employs a memory monitoring approach in which the participant is asked to indicate her recall certainty for all reported dates. Recall certainty may be useful in evaluating associations between birth defects and medication use through sensitivity analyses if recall certainty correlates positively with accuracy of recalled dates of medication use.

As an indirect assessment of this assumption, we sought to explore to what extent subjects' self-reported recall certainty approximates the accuracy of their recalled exposures. Recall certainty is the subjective report of the metacognitive process whereby an individual evaluates the accuracy and relevance of recalled information.⁴ Psychology studies have demonstrated that recall certainty has a moderate positive correlation with recall accuracy for eyewitness events^{5–7} and general knowledge.⁸ We therefore considered whether features of the recalled event that were correlated with recall accuracy in psychology and epidemiology studies were also correlated with recall certainty of dates of medication use in pregnancy. For example, an episode of a single dose of a prescription analgesic may be recalled with greater accuracy than an episode of occasional or regular use because psychology studies have shown that singular events tend to be remembered with greater accuracy.⁹ In drug validation studies, prescription medications are recalled more accurately than OTC medications,^{10–12} and routinely used medications more accurately than occasionally used medications.^{10,12–15} Research for survey methods shows that accuracy of autobiographical memory diminishes with time,^{16,17} which is attributed to interference in memory retrieval by subsequent similar events.⁹ We tested whether recall certainty followed this model by evaluating its association with the number of subsequent episodes of using any analgesic with the same prescription status.

We also explored whether recall certainty was associated with demographic characteristics and health behaviors. Education was of interest because it was associated with better recall accuracy of medications in some^{10,13,15} but not all studies¹⁸ that investigated this relation. Previous studies of maternal demographics and recall accuracy of medications used in pregnancy provided some evidence that recall accuracy is higher for primiparous women and women age ≥ 30 years, but results were inconsistent.^{10,11} Health behaviors -- pregnancy intention, smoking, and binge drinking -- may indicate lesser or greater attention to medication use, which might affect recall accuracy.¹⁷

To assess predictors of recall certainty of dates, we separately considered prescription and OTC analgesics because use is common in both forms in pregnancy.¹⁹ Data on use and recall certainty were obtained by interview within six months following the completion of the pregnancy.

METHODS

Study Population

The Slone Epidemiology Center Birth Defects Study is an ongoing case-control surveillance project designed to assess the risks of birth defects and pregnancy complications associated with a range of environmental exposures.^{20,21} The study recruits mothers of infants with or without congenital anomalies, who are identified from birth defects registries or birth and tertiary care hospitals at five regional centers: Massachusetts, greater Philadelphia, Pennsylvania; Toronto, Canada; Long Island and upstate New York; and San Diego County,

California. The relevant institutional review boards approved the study protocol, and subjects provide informed consent. Study nurses interview the subjects by phone within six months of pregnancy completion. The standardized computer-assisted interview collects detailed information on maternal medication use and illnesses during pregnancy, demographic characteristics, reproductive history, and health behaviors. Questions on recall certainty of dates were introduced in 1998; since then, >18,000 women have been interviewed.

Outcome: Recall Certainty

In a structured interview, a study nurse asks the participant about medications used, and their dose, frequency, and dates of use. For each reported medication, the participant is asked to report the start date, duration, and stop date, and whether she considered each date to be exact or estimated. *High recall certainty* was defined as a report with an exact start date and either an exact stop date or exact duration. We assumed that all other reports were estimated periods of use, with low recall certainty.

Every drug reported in the Birth Defects Study is defined according to its pharmacologic properties, therapeutic use, and prescription status, based on the American Hospital Formulary Service classification system (American Society of Hospital-System Pharmacists, Bethesda, MD). Analgesics whose prescription status depended on dose were classified as either OTC or prescription according to their reported doses; if dose was not reported, these medications were assumed to be OTC.

Predictors of Recall Certainty

Drug Utilization—Reported frequency and duration of drug use were examined in relation to recall certainty. The open-ended question on frequency of use elicited responses that ranged from < 1 time per month to daily, and alternatively, “single dose.” “Routine” use was defined as ≥ 4 days/week, and “occasional” use was defined as <4 days/week. Duration was also reported in response to an open-ended question, and we dichotomized duration as chronic (>30 days) or short-term (≤ 30 days), to distinguish use for a short-term episode of pain from a more persistent condition.

We evaluated whether recall certainty diminished with time since the event by evaluating when reported drug use ended. Intervals between interview and last use were categorized as long, intermediate, or short, based on use that ended in the first, second, or third trimester, respectively. We also evaluated the association with the number of reports of subsequent episodes of use of an analgesic of the same prescription status to test the theory of interference in memory retrieval.⁹

Demographics and Health Behaviors—The interview elicited information on maternal age, parity, education, pregnancy intention, smoking, and binge drinking. The mother’s pregnancy intention was assessed by the question, “at the time that you became pregnant, did you want to become pregnant then, did you want to wait until later, or did you not want to become pregnant at all?” Participants reported whether they smoked immediately before and during the pregnancy, and the usual number of cigarettes smoked per day. We classified participants as smokers if they reported smoking at least one cigarette per day during the pregnancy. For alcohol, we identified their usual and maximum number of alcoholic drinks per day during the pregnancy, and defined binge drinking during pregnancy as ≥ 4 drinks at once if the mother drank at least once per month.

Data Analysis

The episode of medication use was the unit of analysis. Because many participants reported multiple episodes of use, the outcomes could be correlated within a participant. We accounted for this correlation by using the generalized estimating equations extension of the log-binomial regression model with an exchangeable correlation structure for all regression analyses.²² Prevalence ratios (PRs) and 95% confidence intervals (95% CIs) were estimated for all predictors of recall certainty. Based on prior evidence that recall of medication use differs by prescription status,^{10–12} we performed separate analyses for recall of prescription and OTC analgesics.

Reports of routine use were sufficiently numerous to allow a comparison of chronic (>30 days) duration versus short-term (≤30 days) within that category, whereas reports of occasional use were less common. Therefore, we combined frequency and duration to create four categories: single dose; occasional; short-term, routine; and chronic, routine. The most common mode of use, short-term routine, was the reference category. Both interval since last use and number of subsequent episodes were retained in the same model, with indicators for intermediate and short intervals and indicators for the number of subsequent reports (1, 2, 3).

We also analyzed all features of drug use stratified by maternal demographic characteristics to evaluate the potential for confounding and effect-measure modification. Because stratum-specific estimates did not vary appreciably and adjusted estimates did not differ from the crude estimates by ≥10%, we report the crude estimates.

We examined medical factors and health behaviors, including whether the infant had a malformation (yes, no); the total number of medications reported during pregnancy, excluding vitamins (1–4, 5–7, 8–10, ≥11); whether the pregnancy was intended (yes, no); any smoking in pregnancy (yes, no); any binge drinking in pregnancy (yes, no). Medical factors and health behaviors were adjusted for age (<20, 20–24, 25–29, 30–34, 35–39, ≥40). Analyses were performed in SAS version 9.1 (SAS Institute, Cary, NC).

RESULTS

Study Sample

The sample included 14,577 mothers who were interviewed between 1998 and 2009 and reported 32,107 episodes of analgesic use in pregnancy (2,982 prescription, 29,125 OTC). Interviews occurred 2.5 to 6.0 months postpartum (median = 4.9). Excluded were 213 women who reported only analgesics that were either illegal or not commercially available in the US or Canada, were topical products, or who had incomplete information on frequency or duration of use. An additional 383 women were excluded due to incomplete information on age, education, parity, drinking or smoking habits, date of last menstrual period, or date when they first suspected they were pregnant. The excluded participants did not differ from the sample with respect to likelihood of reporting high recall certainty.

Participants were predominantly between the ages of 25–39 and married; due to the nature of the BDS design, most were mothers of infants with a birth defect (Table 1). Higher education was common, with 54.4% of participants having education beyond high school. The majority of participants reported ≥2 episodes of analgesic use; nearly all (98.0%) reported use of OTC, and 14.0% reported use of prescription analgesics. There were 1,724 (5.3%) reports that were assumed to be OTC because dose was not reported, and the analgesic's prescription status depended on its dose (e.g., ibuprofen).

Drug Utilization

Participants reported high recall certainty for 480 (16.1%) of 2,982 reports of prescription analgesic use, and for 707 (2.4%) of 29,125 reports of OTC analgesic use (Table 2). Short-term, routine use was the most common pattern for both prescription and OTC reports; for routinely-used analgesics, the association of chronic use with self-rated accuracy depended on prescription status (prescription: chronic, routine use versus short-term, routine use, PR=0.56, 95% CI: 0.40, 0.80; OTC reports: chronic, routine use versus short-term, routine use, PR=2.56, 95% CI: 1.92, 3.42).

Subsequent episodes of OTC analgesic use and recall certainty were inversely associated, with a linear dose-response trend, adjusted for interval since last use (3 subsequent OTC analgesics versus none PR=0.51, 95% CI: 0.36, 0.74; P -trend <0.0001). These results were essentially unchanged when we confined the analysis to participants who reported 3 OTC analgesics (data not shown). There was no inverse association between subsequent episodes of prescription analgesic use and recall certainty (3 subsequent prescription analgesics versus none PR=1.16, 95% CI: 0.80, 1.71; P -trend=0.78). Participants who recalled the largest number of medications of any kind were more likely to report dates with high self-rated accuracy (11 total medications versus 4, prescription PR=1.41, 95% CI: 1.01, 1.97; OTC PR=1.35, 95% CI: 1.07, 1.70).

Demographics and Health Behaviors

Higher education, particularly graduate school education, was positively associated with recall certainty (17 years versus 12 years, prescription PR=1.76; 95% CI: 1.26, 2.45; OTC PR=1.32; 95% CI: 1.01, 1.73). The participant's age was not associated with recall certainty of dates of OTC analgesics, but younger age was inversely associated with recall certainty of dates of prescription analgesics (19 years versus 25–29 years, PR=0.60, 95% CI: 0.36, 0.99, P -trend=0.0002). Pregnancy intention was associated with high recall certainty (prescription PR=1.25, 95% CI: 1.02, 1.53; OTC PR=1.33, 95% CI: 1.11, 1.59). Having an infant with a birth defect was not appreciably associated with recall certainty (prescription PR=1.14, 95% CI: 0.93, 1.40; OTC PR=1.13, 95% CI: 0.95, 1.34). Smoking in pregnancy was inversely associated with recall certainty (prescription PR=0.71, 95% CI: 0.57, 0.89; OTC PR=0.84, 95% CI: 0.67, 1.05). Binge-drinking in pregnancy was positively but marginally associated with recall certainty of dates of prescription analgesic use only (PR=1.26, 95% CI: 1.00, 1.59).

DISCUSSION

We examined whether recall certainty of reported dates of analgesic use in pregnancy was associated with certain features of the recalled event that were correlated with validity in prior psychology and epidemiology studies. We found that high recall certainty was associated with many of these features, including more frequent use, fewer subsequent episodes of use, and prescription status, suggesting it may indeed be a marker of the actual validity of self-reported timing of analgesic medications use in pregnancy.

Compared with dates of short-term routine use, dates of occasional use were less likely to have high recall certainty, and the date of a single dose was more likely to have high recall certainty. These findings are consistent with drug validation studies that have found better recall accuracy for routine use than occasional use,^{10,12–15} and with a study of recalled medical office visits that found better recall accuracy for singular events than for repetitive events.²³ They are also consistent with an established theory in the psychology of autobiographical memory.^{9,24,25} We expected that routine use of an analgesic for >30 days would be associated with better recall certainty relative to routine use for 30 days because

a longer episode of use would be more important and thus be remembered with greater accuracy.²⁶ This was true for reports of OTC analgesic use, but not for reports of prescription analgesic use. It is possible that the central nervous system effects of prescription analgesics (e.g., drowsiness) may explain why chronic, routine users of that form of analgesics (e.g., codeine) had less recall certainty.

Also, studies have found that accuracy was better for prescription than for OTC drugs.^{10–12} For this reason, we presented results stratified by prescription status. We found that recall certainty of dates of OTC analgesics tended to be lower if there were a number of subsequent episodes of OTC analgesic use, consistent with psychology theory that subsequent, similar events interfere with recall.⁹

We also hypothesized that factors associated with a healthy lifestyle, such as pregnancy intention and higher education, would be associated with greater attention to medication use in pregnancy. In general, these results showed only modest associations or no association, with the exception of higher recall certainty of dates of prescription analgesic use in women who completed at least a college education. The positive association between education and recall certainty is consistent with results from some but not all prior studies of education and recall accuracy of medication use. In one study, high education was associated with better recall, eight years later, of use of any medications during pregnancy,¹⁰ but it did not examine education in relation to recall of dates. College education was associated with better recall of the use of estrogens^{13,15} and single-use prescription non-steroidal anti-inflammatory drugs (NSAIDs),¹⁵ but not with recall of repetitive-use prescription NSAIDs¹⁵ or antidepressants.¹⁸ We found that smoking was inversely associated with recall certainty, in agreement with our hypothesis that smokers generally have a less healthful lifestyle and thus, are less likely to pay close attention to the use of medications in pregnancy. The evidence for an association of current smoking and recall accuracy of prescription medications is inconsistent, with inverse associations reported for recall accuracy of post-menopausal estrogens,^{13,15} but not for recall accuracy of NSAIDs.¹⁵ The result that mothers age <20 were less likely to recall dates of prescription analgesic use with high recall certainty was also in agreement with our hypothesis.

We were not able to perform a validation study and measure agreement, in large part because the timing of actual use of most prescription drugs is not documented in medical records, and use of OTC medications themselves is rarely if ever recorded systematically. A feasible validation study would recruit pregnant women, collect real-time reports of their medication use, and later interview them to collect information on recalled timing of exposure and recall certainty. However, the real-time report could itself improve both retrospective accuracy and certainty. Because it is likely that recall certainty is not a perfect correlate of recall accuracy, our results should not be interpreted as a validation study. Results from the few studies that have examined the validity of recall certainty suggest that recall certainty is modestly associated with recall accuracy.^{5–7} A physical activity study that validated self-rated recall against a real-time accelerometer reading found that participants reporting high self-rated accuracy had higher recall accuracy of moderate activity, but not other forms of activity.²⁷ Recall certainty of dates of smoking cessation lapses showed poor agreement with the timing of real-time reports.²⁸

Several additional limitations to our study also deserve mention. This study analyzed recall certainty of the dates for analgesic use only, and the results may not be generalizable to other classes of drugs. In particular, the low prevalence of recall certainty of OTC analgesics was likely due to attributes of these drugs, i.e., that they are used occasionally to relieve mild symptoms that resolve quickly and tend to recur. Therefore, we expect this low prevalence of recall certainty would be unlikely to apply to all OTC drugs. Further, certain

indications for the analgesics – e.g., migraine headache, cold or influenza – may have affected both characteristics of use and recall certainty. When data on the predictors and the outcome are collected in the same interview, as they were in our study, dependent misclassification may induce a bias in the results away from the null.²⁹

Our study has several strengths for examining correlates of recall certainty. Data were collected via standardized interview that was designed to improve the completeness of reporting exposures in pregnancy.³⁰ The large study sample included variation in drug use and maternal characteristics and behavior, providing considerable statistical power. Also, data were collected and available on details of drug use, allowing OTC and prescription drugs, and their frequency, duration, and number, to be considered in analyses.

Maximizing the accuracy of exposure and exposure timing is critical for studying the association of maternal medications in pregnancy and risk of birth defects. We were motivated to undertake this study because the lack of a gold standard for medication use, and particularly for timing of use in pregnancy, makes proxy approaches to estimate validity necessary. Many studies of prenatal medication exposure and risk of birth defects will continue to rely on participant recall, as will other studies of rare outcomes and exposures that lack complete, accurate documentation. Our data suggest that ascertainment of recall certainty in such studies will provide a useful tool for assessing validity.

One very practical application is in a probabilistic sensitivity analysis of exposure misclassification.³¹ This method quantifies the likely impact on the effect estimate and confidence interval from exposure misclassification, using ranges for misclassification values selected by the investigator to simulate the data that would have been observed under perfect exposure classification. Observations with high recall certainty would be assigned a lower probability of exposure misclassification and those with low recall certainty would conversely be assigned a higher probability of such misclassification, thereby improving the estimated impact of exposure misclassification on the study results. If a study does not collect data on recall certainty, the investigators may choose to vary the misclassification values with a variable that our data show is a strong correlate of recall certainty, e.g., single dose versus short-term, routine use of OTC analgesics.

Another application of recall certainty to a sensitivity analysis would be to confine the analysis to the exposed group of study subjects with high recall certainty, which may produce a less biased effect estimate if the exposure misclassification is non-differential with respect to the outcome.^{32,33} (We found no evidence of differential misclassification of analgesics with respect to birth defects as an outcome, since birth defect status was not associated with high recall certainty).

Another sensitivity analysis has been employed in this same dataset, which used an algorithm to categorize participants by their likelihood of exposure in a given temporal window, using the reported duration of use as well as the precision of reported start and stop dates.³³ Recall certainty as defined in the present analysis, i.e., self-rated reporting of exact start and stop dates, could be incorporated into the aforementioned algorithm as a further sensitivity analysis. This approach would be similar to confining the exposed group to those with high recall certainty, i.e., exact start and stop dates.

In conclusion, we found that recall certainty was correlated with certain features of the recalled event, in agreement with studies of predictors of recall accuracy. Recall certainty may have utility in performing sensitivity analyses. Further research to validate recall certainty as a marker for validity is needed to confirm our conclusions.

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Abbreviations and Acronyms

OTC	over-the-counter
PR	prevalence ratio
95% CI	95% confidence interval

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Key Points

1. In interview-based studies where exposures are difficult to validate, the study participant's recall certainty is a promising tool to assess bias in exposure measurement.
2. Recall certainty of dates of analgesic use in pregnancy was associated with certain features of the recalled event that were correlated with validity in prior psychology and epidemiology studies, including frequency of use, number of subsequent events, and prescription status.
3. Further study is warranted to assess the performance of recall certainty as a marker of validity of recalled dates of medication use in pregnancy.

Table 1

Characteristics of 14,577 study participants who reported any analgesic use during pregnancy: Slone Birth Defects Study, USA, 1998 – 2009.

Characteristic	Number (%)
Sociodemographic	
Age:	
19 y	981 (6.7)
20 – 24 y	2,096 (14.4)
25 – 29 y	3,726 (25.6)
30 – 34 y	4,832 (33.1)
35 – 39 y	2,436 (16.7)
40 y	506 (3.5)
Married or living as married	13,001 (89.2)
Parous before index pregnancy	8,504 (58.3)
Infant had malformation	9,422 (64.6)
Educational attainment [*] :	
< 12 y	2,496 (20.9)
12 y	2,962 (24.8)
13 – 15 y	3,302 (27.6)
16 y	3,206 (26.8)
Health behavior in pregnancy	
Pregnancy was intended	9,066 (62.2)
Binge drinking (4 drinks at once)	1,828 (12.5)
Smoking	2,846 (19.5)
Illness and medications during pregnancy	
Health conditions associated with pregnancy, median (IQR)	4 (2–6)
Medications used, median (IQR)	5 (3–8)
Analgesics used, prescription and OTC combined	
1	5,527 (37.9)
2	4,401 (30.2)
3	2,521 (17.3)
4	2,078 (14.6)
Used 1 prescription analgesic	2,041 (14.0)
Used 1 over-the-counter analgesic	14,287 (98.0)

^{*} Among 11,966 women age 24 y.

IQR, Interquartile range; OTC, over-the-counter.

Table 2

Predictors of recall certainty of the dates of analgesic use during pregnancy, stratified by prescription status: 32,107 episodes from 14,577 participants in the Slone Birth Defects Study, USA, 1998–2009.

	Prescription Analgesics		Over-the-Counter Analgesics	
	High [*] /Total	PR (95% CI) [†]	High/Total	PR (95% CI) [†]
Total Reports	480/2,982	--	707/29,125	--
Characteristics of use				
Single dose	214/635	1.92 (1.61, 2.27)	258/3,456	3.65 (3.03, 4.40)
Short-term, routine	235/1,449	1.00 (ref)	221/11,242	1.00 (ref)
Chronic, routine	25/312	0.56 (0.40, 0.80)	69/1,317	2.56 (1.92, 3.42)
Occasional	6/586	0.10 (0.05, 0.18)	159/13,110	0.65 (0.53, 0.79)
Interval since last use [‡] :				
Long	219/1,521	1.00 (ref)	269/13,038	1.00 (ref)
Intermediate	107/547	1.44 (1.17, 1.78)	112/3,531	1.21 (0.95, 1.54)
Short	154/913	1.19 (0.98, 1.46)	326/12,549	1.02 (0.86, 1.22)
Subsequent use [‡] :				
None	326/1,715	1.00 (ref)	421/13,864	1.00 (ref)
1	100/502	0.99 (0.84, 1.18)	164/8,140	0.69 (0.58, 0.82)
2	26/172	0.92 (0.69, 1.23)	75/3,822	0.67 (0.53, 0.86)
3	28/113	1.16 (0.80, 1.71)	47/2,575	0.51 (0.36, 0.74)
Stop date < 1 month following date when pregnancy was suspected [§]				
Yes	44/548	0.51 (0.37, 0.70)	73/6,730	0.38 (0.28, 0.49)
No	175/973	1.00 (ref)	196/6,308	1.00 (ref)
Total number of medications:				
1 – 4	43/376	1.00 (ref)	196/8,607	1.00 (ref)
5 – 7	115/751	1.34 (0.95, 1.89)	188/9,486	0.88 (0.71, 1.08)
8 – 10	132/678	1.64 (1.17, 2.31)	157/5,740	1.19 (0.95, 1.49)
11	190/1,117	1.41 (1.01, 1.97)	166/5,292	1.35 (1.07, 1.70)
Characteristics of Mother and Infant				
Age				
< 20 y	20/219	0.60 (0.36, 0.99)	54/1,928	1.23 (0.89, 1.71)
20 – 24 y	69/559	0.80 (0.59, 1.09)	89/4,148	0.91 (0.69, 1.19)
25 – 29 y	117/778	1.00 (ref)	179/7,457	1.00 (ref)
30 – 34 y	172/846	1.24 (0.97, 1.58)	212/9,723	0.91 (0.73, 1.13)
35 – 39 y	82/470	1.11 (0.83, 1.49)	143/4,891	1.18 (0.92, 1.51)
40 y	20/110	1.29 (0.80, 2.06)	30/978	1.30 (0.87, 1.93)
Parity [¶]				
Primiparous	203/1,200	1.00 (ref)	323/12,401	1.00 (ref)
Multiparous	277/1,782	0.85 (0.70, 1.03)	384/16,724	0.88 (0.74, 1.04)
Education [#]				
12 y	73/610	1.00 (ref)	97/4,625	1.00 (ref)

	Prescription Analgesics		Over-the-Counter Analgesics	
	High [*] /Total	PR (95% CI) [†]	High/Total	PR (95% CI) [†]
13 – 15 y	107/659	1.46 (1.07, 2.00)	154/6,051	1.22 (0.94, 1.60)
16 y	109/523	1.65 (1.19, 2.82)	162/6,816	1.10 (0.84, 1.45)
17 y	118/527	1.76 (1.26, 2.45)	177/6,473	1.32 (1.01, 1.73)
Infant had birth defect [¶]				
Yes	339/2,010	1.14 (0.93, 1.40)	478/18,713	1.13 (0.95, 1.34)
No	141/972	1.00 (ref)	229/10,412	1.00 (ref)
Health Behaviors in Pregnancy				
Binge drinking [¶]				
Yes	90/475	1.26 (1.00, 1.59)	105/4,100	1.06 (0.84, 1.33)
No	390/2,507	1.00 (ref)	602/25,025	1.00 (ref)
Smoking [¶]				
Yes	118/999	0.71 (0.57, 0.89)	126/5,994	0.84 (0.67, 1.05)
No	362/1,983	1.00 (ref)	581/23,131	1.00 (ref)
Pregnancy was intended [¶]				
Yes	307/1,645	1.25 (1.02, 1.53)	476/17,866	1.33 (1.11, 1.59)
No	173/1,337	1.00 (ref)	231/11,259	1.00 (ref)

^{*} High recall certainty, report that recalled dates were exact.

[†] PR: prevalence ratio; 95% CI: 95% confidence interval; unadjusted except where noted.

[‡] Interval since last use was classified according to the trimester when the episode of analgesic use ended. Interval since last use and subsequent use were retained in the same model.

[§] Analysis of reports with stop dates in 1st trimester.

[¶] PR and 95% CI are adjusted for age.

[#] In 11,966 Women age ≥ 24 years; PR and 95% CI are adjusted for age and parity.