Agreement between paternal self-reported medication use and records from a national prescription database

Short running title: Paternal self-report and prescription agreement

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Key messages:

- Paternal medication use may be of interest in fertility studies and as negative control exposures in pregnancy medication safety studies
- Both self-report and prescription records are reliable sources of information for prescription medication used chronically as there is substantial agreement between them
- There is fair agreement between self-report and prescription records for prescription medication used episodically
- Inaccurate recall, non-compliance, or discontinuation of use may be sources of inconsistency between self-report and prescription records
- If only prescription records are available, medications also available over-the-counter cannot be studied

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Abstract

Purpose: Father's medication use is of interest in fertility studies and as negative control exposures in pregnancy medication safety studies. We sought to compare self-report to prescription records to understand how reliably each of these sources of information may be used.

Methods: We compared self-reported medication use in the 6-months prior to pregnancy from fathers participating in the Norwegian Mother and Child Cohort Study (MoBa) to records of dispensed prescriptions from the Norwegian Prescription Database that overlapped in time. Medications from three main categories were assessed: prescription medications used chronically, prescription medications used episodically, and over-the-counter (OTC)/prescription medications (predominantly obtained without prescription). We calculated agreement between self-report and dispensing records using Cohen's kappa (κ) statistic.

Results: We included 42,848 pregnancies with the father's prescription data available for the nine months before pregnancy. Prescription medications used chronically including antiepileptics, antipsychotics, and antidepressants showed substantial agreement between self-report and prescription records: kappa statistics 0.87, 0.63, and 0.74, respectively. Prescription medications used episodically like anti-infectives, opioids, anxiolytics, and hypnotics and sedatives showed worse agreement: kappa 0.19, 0.32, 0.40, 0.32. OTC/prescription medications like paracetamol and NSAIDs had slight agreement: kappa 0.02 and 0.20.

Conclusions: There is good agreement between paternal self-report and prescription data for prescribed medications used chronically and substantially less for medications used episodically. Suboptimal agreement for episodic medications suggests poor recall (for questionnaires) or false positives due to non-compliance (prescription data). Not surprisingly, use of medications available both with and without a prescription are not well captured using prescription databases alone.

Introduction

Information bias is an important concern for exposure assessment in pharmacoepidemiology. Medication use may be assessed by questionnaire (self-report), prescribing records, and dispensed prescription records. None of these methods of exposure ascertainment is a perfect assessment. Self-report is subject to poor recall; prescribing records are subject to primary non-compliance (unfilled prescription); and dispensed medications are subject to secondary noncompliance (may not be used at all or as directed) (1, 2).

Researchers may be interested in using data from male partners in fertility research or as negative control exposures in studies of maternal medication use in pregnancy. Studying paternal medication use as negative controls can help researchers disentangle the effect of drug from residual confounding by familial genetic or environmental characteristics which are not captured in traditional data sources, e.g. population registers, administrative databases. For example, researchers might estimate the effect of maternal paracetamol use on childhood neurodevelopment, and also paternal paracetamol use. If both maternal and paternal exposure suggests an increased risk of behavioral problems, a possible explanation is that there is residual confounding. Conversely, observing an effect for maternal but not paternal exposure can be interpreted as additional evidence in favor of a causal link for maternal exposure. Thus, for an alternate exposure to be a good negative control, it must be measured with at least the same quality as the exposure of interest (3, 4); otherwise, a null effect for paternal exposure that is due to exposure misclassification hinders the usefulness of the negative control.

The aim of the study was to compare paternal self-report to dispensed prescription records. Since neither is a perfect marker of medication use, we aimed to assess agreement between the two. We compared medications from three main categories where agreement was likely to differ: 1) prescription medication used chronically, 2) prescription medication used episodically, and 3) over-the-counter (OTC)/prescription medications (those predominantly obtained without a prescription). We considered whether agreement between information sources varied according to fathers' characteristics. We hypothesized that agreement would be better for prescription medication used daily than for either episodically-used prescription drugs or OTC/prescription drugs.

Methods

The Norwegian Mother and Child Cohort Study (MoBa)

The Norwegian Mother and Child Cohort Study (MoBa) is a population-based pregnancy cohort conducted by the Norwegian Institute of Public Health (5, 6). Pregnant women from Norway received a postal invitation around pregnancy week 17 from 1999-2008. Of those invited, 40.6% consented to participate and male partners participated in about 68% of pregnancies. Male partners were invited to participate via mailed questionnaire. The cohort includes 114 500 children, 95 200 mothers and 77 260 fathers. Follow-up is conducted by questionnaires at regular intervals and is ongoing. Some of the information in MoBa is obtained from the Medical Birth Registry of Norway (MBRN). MBRN is a nationwide registry that is based on compulsory notification of every birth or late abortion from 12 weeks of gestation onwards in Norway.

We received the 9th version of the MoBa quality assured data from October 2015. We used the father's questionnaire (QF) to collect fathers' self-reported medication use in the six months before pregnancy. Fathers reported medicines used at any time during the six-month window and for how long (<1 week, 1week-1month, >1 month). Reported medicines were previously coded in MoBa using the World Health Organization's Anatomical Therapeutic Chemical (ATC) classification system. We obtained the gestational age at delivery from MBRN data, which we used to calculate the start and end of the 6-month pre-pregnancy period. Paternal characteristics including education, smoking, physical illness, and history of major depression were obtained from the QF. For some characteristics, however, the QF was less complete. These characteristics were obtained from MBRN (age, marital status) or the first maternal questionnaire (Q1; BMI, calculated as kg/m^2 from father's height and weight, income), based on completeness of the data.

The Norwegian Prescription Database (NorPD)

Since January 2004, all pharmacies in Norway are obliged to send data to the Norwegian Institute of Public Health on prescribed medications dispensed in ambulatory care. NorPD data from January 2004 to December 2008 were linked to fathers in MoBa by an encrypted personal identity number. For fathers participating in MoBa who filled a prescription at any time from 2004-2008, we received the date of dispensing of each prescription coded as the days difference from the date of birth and detailed information on medications dispensed.

We defined binary exposure variables for each medication ATC group of interest, based on prescriptions dispensed in the nine months prior to pregnancy, whose supply overlapped (by at least one day) with

the six-month pre-pregnancy period. We calculated the days' supply for each prescription as the number of defined daily doses (DDDs) dispensed. When the DDD was missing (1%), it was re-coded as 1 DDD.

Medication groups studied

We selected representative medications from three main groups: 1) prescription medication used chronically (antiepileptics, ATC-code N03; antidepressants, N06A; and antipsychotics, N05A), 2) prescription medication used episodically (systemic anti-infectives, J; opioids, N02A; anxiolytics, N05B; and hypnotics/sedatives, N05C) and 3) OTC/prescription medications where some formulations and package sizes require a prescription (paracetamol, N02BE01; NSAIDs, M01A).

Study population

The study population included fathers who completed the QF, were successfully linked to the NorPD and had a gestational age of 20-44 completed weeks available in the MBRN. We excluded fathers where the nine-months before pregnancy were not entirely covered by the NorPD data to ensure complete capture of prescriptions that overlapped with the six months before pregnancy. We randomly selected one pregnancy per father who met the above criteria, as men could participate in MoBa with their partner more than once.

Statistical analysis

We described the sociodemographic characteristics of included fathers and compared them to the overall MoBa sample. We calculated the prevalence of paternal medication use in the six-months prior to pregnancy according to paternal report (MoBa) and dispensed medications (NorPD). We calculated agreement between self-report and dispensing records using Cohen's Kappa statistic and 95% confidence intervals (CIs). We used the categories defined by Landis and Koch to describe the level of agreement: 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1 almost perfect (7). To assess whether there are differences in quality of reporting based on paternal characteristics, we compared the kappa statistics across categories of smoking, depression, age, and education.

Using self-report as the primary reference standard, we calculated the validity of prescription records of medication use. We calculated the sensitivity, specificity, positive predictive value, and negative predictive value of at least one dispensed prescription and two or more during the exposure window. Since prescription medications used episodically are more likely to be subject to poor recall than

prescription medication used chronically, we also examined the prescription as the reference standard for the seven prescription medication groups. The sensitivity and specificity of self-report correspond to the PPV and NPV, respectively, where self-report is the reference standard.

Analyses were carried out in SAS Version 9.4 (SAS Institute Inc., Cary, NC, United States).

Ethics

The establishment and data collection in MoBa has obtained a licence from the Norwegian Data Inspectorate and approval from The Regional Committee for Medical Research Ethics. The current study was approved by The Regional Committee for Medical Research Ethics (Region South-East).

Results

There were 46,104 pregnancies among 42,848 fathers with the father's prescription data from NorPD available for the 9 months before pregnancy (**Figure**). Around 40% of pregnancies with participating fathers were excluded from the study because they entered MoBa before the establishment of NorPD in 2004. Fathers in the sample were similar to fathers of all MoBa pregnancies; however, there were fewer missing data points for variables like father's weight, height, and education in Q1 among the partners of participating fathers (results not shown). Fathers in the study sample were mostly married or cohabiting, infrequently obese, and a high proportion reported smoking in the 6-months prior to pregnancy (**Table 1**).

(Table 1 here)

Among the medications considered, prevalence of use based on prescription dispensing records was higher than self-report, with the exceptions of paracetamol (**Table 2**). The difference was particularly large for anti-infective medications (2.33% based on paternal report versus 12.1% based on dispensed medications). Of the fathers with a prescription for a medication used chronically, 50-81% reported use in the questionnaire. Of the fathers with a prescription for a medication used episodically, 13-30% reported use in the questionnaire; while of the OTC/prescription medications reported in the questionnaire between 2% (paracetamol) and 31% (NSAIDs) were also recorded in the prescription registry.

Prescription medications used on a daily basis such as antiepileptic medications, antipsychotics, and antidepressants showed good agreement between self-report and prescription records (**Table 2**). Prescription medications used episodically like anti-infectives, opioids, anxiolytics, hypnotics and sedatives showed lower levels of agreement than chronically used medications. Anti-infectives, typically used for acute conditions, had poorer agreement than other episodically used prescription medications. Medications available over-the-counter like paracetamol and NSAIDs had slight agreement.

(Table 2 here)

Paternal characteristics affected agreement between self-report and prescription records to different extents and in some cases, in different directions (**Table 3**). Depression was associated with lower agreement for anti-infective medication but higher agreement for antidepressants. Higher education improved agreement for both antipsychotic and anti-infective medications. Smoking was associated with lower agreement for antidepressants.

(Table 3 here)

Considering self-report as the reference standard, we found high specificity and moderate to high sensitivity for at least one prescription, and lower but still substantial sensitivity with the requirement of two prescriptions for medications used on a daily basis (**Table 4**). Antiepileptics (74%) and antidepressants (68%) were the medication groups most often filled more than once. The positive predictive value (PPV) varied considerably based on one prescription, and was highest for antiepileptic medications at 81.5% and lowest for antipsychotics at 49.7%. For medications used episodically, there was high specificity for one prescription, with the exception of anti-infectives, and moderate sensitivity. The requirement of at least two dispensed prescriptions strongly impacted the sensitivity for episodically used medications. The PPV for anti-infectives was particularly low compared to other episodically used medication groups examined. For medications available over-the-counter, there was very low sensitivity for one or more prescriptions and almost no sensitivity for paracetamol. When we considered the prescription record to be the reference standard for both chronic and episodically used prescription medications, sensitivity of recall is enhanced for prescriptions filled more than once in the 6-months prior to pregnancy. However, specificity of self-report was high regardless of the number of fills.

(Table 4 here)

Discussion

Agreement between fathers self-report of medication used in the six months before pregnancy in the MoBa Study and records of dispensed prescriptions in the NorPD varied greatly by medication type. Chronically used psychotropic medications tended to have high agreement, particularly antiepileptic medication. Thus, researchers focusing on chronically used prescription medication could use either data source with confidence. Among the medications considered, prevalence of use based on prescription records was mostly higher than self-report which may be due to a combination of non-compliance, discontinuation, and poor recall of medications used months earlier, but we are unable to determine which of these is the greatest contributor to exposure misclassification in these data.

This is the first study to compare self-report and prescription records of medication use among fathers participating in a birth cohort study. Prior studies have carried out similar designs for assessing the quality of maternal medication reporting in the context of a prospective pregnancy cohort. Skurtveit *et al.* assessed the validity of prescription records for opioids, antidepressants and benzodiazepines (BZD) compared to self-report of use during pregnancy in mothers participating in MoBa (8). Sensitivity of medication use as recorded in NorPD for the pregnancy period was highest for antidepressants (66.9%) and BZD-antiepileptics (100%) and lowest for BZD-anxiolytics (44.8%) and BZD-hypnotics (27.8%). Expansion of the time windows for dispensed medications in the NorPD to include one and two months before pregnancy in order to not miss relevant prescriptions led to higher sensitivity, but lower specificity for all classes of medications. For opioids, sensitivity increased from 48.8% to 53.6%, while specificity decreased from 98.7 to 97.6%. For antidepressants and BZD-anxiolytics, specificity decreased for both from 99.7 to 99.4%. Compared to quality of maternal self-report, sensitivity was slightly higher for opioids and antidepressants among the MoBa fathers and specificity was similarly high when considering only prescriptions dispensed during pregnancy. This comparison implies that the quality of information from fathers is similar to information from mothers for these medications. We similarly found higher prevalence of prescription medication use based on prescription records compared to self-report; the opposite was true for OTC/prescription medications.

Sundermann *et al.* compared self-report to daily diaries to assess the validity of maternal recall of early pregnancy medication exposures for NSAIDs and SSRIs among 318 women in the Right from the Start Study (9). Compared to diary, the sensitivity, specificity and kappa for recall of SSRI antidepressants was

77.8%, 99.0%, and 0.79, respectively. We found even higher sensitivity and specificity for a single prescription, considering self-report as the reference standard with a similar kappa agreement statistic (0.74). Since these authors were able to assess prescription and non-prescription medication use, they found higher agreement between the two sources of information for NSAIDs (0.41 versus 0.20).

Though neither self-report nor prescription records are prefect reference standards, when timing of use is important, self-report is a better choice as prescription dispensing records may give poor information on correct timing of use, particularly for episodically used medications. Selecting self-report as the reference standard is reasonable for prescribed medications as prescriptions may be filled but not used, and the only option for OTC/prescription medication. Father's questionnaire was completed at pregnancy week 17, therefore, the time from use to assessment ranged between 4 and 10 months.

The validity of self-report or prescription medication, however, varies depending on the medication and how it is used (chronically or episodically). Anti-infectives may be considered somewhat distinct from the other examples of episodically used prescribed medications because they are used for acute rather than chronic conditions. Using self-report to assess paternal anti-infective use may be problematic. For anti-infectives, the prescription record may be a better reference standard since the short course of treatment is likely to be forgotten months later when interview occurs. For medications available over-the-counter, there was very low sensitivity for one or more prescriptions and almost no sensitivity for paracetamol, suggesting self-report data sources are the only appropriate option when investigating paternal use of these medications.

For studies where only self-report is available, the data show that agreement for prescription medication used episodically was slight to fair. Anti-infectives may be most likely to suffer from poor recall; sensitivity of self-report was very low when considering the prescription as the reference standard at 13% compared to 20-30% for other group 2 medications. Self-report appears to be of sufficient quality for prescription medications used chronically and is the only good option for OTC/prescription medications. For studies relying on prescription records, it is not recommended to do studies on medications available OTC, particularly for paracetamol.

Investigators assessing the use of antipsychotic medication in fathers may benefit from requiring two or more filled prescriptions, as there was a large improvement in the PPV without a substantial decrease in the sensitivity of exposure assessment, compared to self-report. However, a single dispensed prescription may capture an exposure with sufficient specificity for antiepileptic and antidepressant

medication. For opioids, anxiolytics, and hypnotics prescription medications used episodically but for recurrent conditions requiring at least two prescriptions strongly increased the PPV but came at a large cost to sensitivity.

The availability of augmented administrative claims data bases, large birth cohort, prescription- and birth registries will enable more studies using data on paternal medication in fertility research or as negative control exposures in safety studies of maternal medication use in pregnancy. Understanding the possible impact of exposure misclassification in the context of a paternal negative control exposure study is vital to proper interpretation of the effect estimates.

Fathers who were included in this study were similar to all fathers participating in the MoBa study. However, participating fathers were more likely to be older and married, as was found for mothers (10) and may have more access to resources than the general population in terms of education and income, as we see for most research participants. However, age was not found to have any important influence on agreement, and education had moderate association with antipsychotic and anti-infective use. Therefore, we may have slightly overestimated agreement for these medications in MoBa.

One of the strengths of the study was that we had two high-quality sources of information on medication use to compare. The father's questionnaire asked about the presence of medical conditions and immediately following that, asked about medication use. Although the medication use was not sought in direct association with indications, as was done for mothers, the close proximity of questions on health conditions and medication use likely improved recall (2). The Norwegian Prescription Database contains a complete record of prescriptions dispensed in Norway.

We assessed several questions that are of practical importance to researchers. We addressed the questions of whether and when to use claims data, i.e. records of dispensed prescriptions, and when might it be appropriate to restrict to two or more prescriptions to enhance specificity.

In conclusion, there is good agreement between paternal self-report and prescription data for prescribed medications used chronically and substantially less for medications used episodically. Not surprisingly, OTC/prescription NSAIDs and paracetamol are not well captured in prescription databases. Rigorous assessment of data quality and completeness is recommended regardless of data source. The results of this study may be used to inform future bias analyses, as well as to determine whether the results of a negative control study using paternal exposure can be interpreted as expected, given observed data quality.

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Conflict of Interest

Jacqueline Cohen has received salary support from a research grant from GlaxoSmithKline for unrelated work. Sonia Hernández-Díaz received research funding from GlaxoSmithKline, Eli Lilly, and Pfizer for unrelated work; salary support from the North American AED Pregnancy Registry; and consulted for UCB, Teva, and Boehringer-Ingelheim.

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Tables

Table 1. Characteristics of fathers in the study sample

Table 2. Agreement between paternal self-reported use of medication in the Norwegian Mother and Child cohort study (MoBa) and dispensed prescriptions from the Norwegian Prescription Database (NorPD) in the 6 months prior to pregnancy

Table 3. Variation in agreement by fathers' characteristics, κ (95% CI)

Table 4. Validity of prescription records (NorPD) compared to fathers' self-reported use (MoBa)

Table 5. Validity of fathers' self-reported use of prescription medication (MoBa) compared to prescription records (NorPD), by number of prescriptions

Table 1. Characteristics of fathers in the study sample

	Study Sample (n=42 848)	
Characteristic[a]	N	percent
Father's Age		
<30	11417	26.7
30 - 34 years	16691	39.0
≥35	14697	34.3
Missing	43	0.1
Marital Status		
Married / Co-habitant	41446	96.7
Other	1402	3.3
Father's BMI		
<25 (normal or underweight)	18227	42.5
25-<30 (overweight)	18541	43.3
≥30 (obese)	4230	9.9
Missing	1850	4.3
Father's Income[b]		
<300 000 NOK (<42 000 USD)	10318	24.1
300-399 999 NOK (42-55 999 USD)	13697	32.0
400-499 999 NOK (56-69 999 USD)	7979	18.6
> 500 000 NOK (>70 000 USD)	8068	18.8
Missing	2786	6.5
Father's Education[c]		
Less than 4-year college	18755	43.8
Started or completed university	11259	26.3
Post-graduate education	11159	26.0
Missing	1675	3.9
Father's Smoking[d]		
No	30541	71.3
Yes	11802	27.5
Missing	505	1.2
Self-reported physical illness		
Pain condition	12995	30.3
Epilepsy	135	0.32
Migraine/headaches	2101	4.9
Diabetes	387	0.9
CVD or Hypertension	1493	3.5
History of major depression[e]	4950	11.7

[a]From Medical Birth Registry of Norway (MBRN; age, marital status), maternal questionnaire (Q1; BMI, calculated as kg/m^2 from father's height and weight, income), and paternal questionnaire (QF; education, smoking, physical illness, history of major depression)

[b]Translation to USD an average of exchange rates from 1999-2008 (1 NOK=0.14 USD), rounded to the nearest thousand

[c]Less than 4-year college: secondary education, vocational training, post-secondary (1-3 years); Started or completed university: up to and including 4 years; Post-graduate education: higher education over 4 years (fathers report)

[d]During the 6 months before pregnancy (as reported by father)

[e]Based on Kendler's History of Major Depression scale. Reported having had 3 or more of the following symptoms for 2 weeks simultaneously (n=632 missing): Felt depressed, sad; Had problems with appetite or eaten too; Been bothered by feeling weak or lack of energy; Blamed yourself and felt worthless; Had problems with concentration or had problems making decisions

Table 2. Agreement between paternal self-reported use of medication in the Norwegian Mother and Child cohort study (MoBa) and dispensed prescriptions from the Norwegian Prescription Database (NorPD) in the 6 months prior to pregnancy

Medication category [ATC code]	Neither	MoBa only	NorPD only	Both	Self-report (MoBa)		Dispensed medications (NorPD)		Agreement	
	n	n	n	N	n	% (95% CI)	n	% (95% CI)	κ (95% CI)	Range[a]
Group 1: Prescription medication used chronically										
Antiepileptics [N03]	42590	15	45	198	213	0.50 (0.43-0.56)	243	0.57 (0.50-0.64)	0.87 (0.83-0.90)	Almost perfect
Antipsychotics [NO5A]	42671	12	83	82	94	0.22 (0.18-0.26)	165	0.39 (0.33-0.44)	0.63 (0.56-0.70)	Substantial
Antidepressants [N06A]	42110	34	271	433	467	1.09 (0.99-1.19)	704	1.64 (1.52-1.76)	0.74 (0.71-0.76)	Substantial
Group 2: Prescription medication used episodically										
Anti-infectives for systemic use [J]	37332	325	4518	673	998	2.33 (2.19-2.47)	5191	12.1 (11.8-12.4)	0.19 (0.17-0.20)	Slight
Opioids [N02A]	40872	309	1269	398	707	1.65 (1.53-1.77)	1667	3.89 (3.71-4.07)	0.32 (0.29-0.34)	Fair
Anxiolytics [N05B]	42460	65	225	98	163	0.38 (0.32-0.44)	323	0.75 (0.67-0.84)	0.40 (0.35-0.46)	Fair
Hypnotics and sedatives [N05C]	42295	62	386	105	167	0.39 (0.33-0.45)	491	1.15 (1.05-1.25)	0.32 (0.27-0.36)	Fair
Group 3: OTC/prescription medication										
NSAIDs [M01A]	36345	2217	3280	1006	3223	7.52 (7.27-7.77)	4286	10.0 (9.72-10.3)	0.20 (0.19-0.21)	Slight
Paracetamol [N02BE01]	36200	6289	230	129	6418	15.0 (14.6-15.3)	359	0.84 (0.75-0.92)	0.02 (0.02-0.03)	Slight

[a]Subdivisions by Landis and Koch: < 0 no agreement , 0–0.20 as slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, 0.81–1 almost perfect

Table 3. Variation in agreement by father's characteristics, κ (95% CI)

Characteristic	Group 1: Prescription medication used chronically			Group 2: Prescription medication used episodically				Group 3: OTC/prescription medication	
	Antiepileptics	Antidepressants	Antipsychotics	Anti-infectives	Opioids	Anxiolytics	Hypnotics and sedatives	NSAIDs	Paracetamol
Smoking									
Yes	0.81 (0.74-0.88)	0.68 (0.64-0.73)[a]	0.54 (0.43-0.65)	0.17 (0.15-0.20)	0.36 (0.31-0.40)	0.40 (0.32-0.48)	0.34 (0.27-0.41)	0.17 (0.14-0.19)	0.02 (0.01-0.03)
No	0.89 (0.86-0.93)	0.78 (0.75-0.82)[a]	0.71 (0.62-0.78)	0.19 (0.18-0.21)	0.30 (0.27-0.33)	0.41 (0.33-0.48)	0.30 (0.23-0.36)	0.21 (0.20-0.23)	0.02 (0.02-0.03)
Depression									
Yes	0.84 (0.77-0.90)	0.76 (0.72-0.80)[a]	0.71 (0.62-0.79)	0.15 (0.12-0.18)[a]	0.36 (0.30-0.42)	0.50 (0.42-0.58)	0.40 (0.32-0.47)	0.21 (0.18-0.25)	0.02 (0.00-0.04)
No	0.88 (0.84-0.92)	0.68 (0.63-0.73)[a]	0.53 (0.42-0.64)	0.19 (0.18-0.21)[a]	0.31 (0.29-0.34)	0.33 (0.25-0.40)	0.25 (0.19-0.31)	0.20 (0.18-0.21)	0.02 (0.02-0.03)
Age									
≤30	0.87 (0.81-0.93)	0.71 (0.64-0.78)	0.53 (0.37-0.68)	0.20 (0.18-0.23)	0.34 (0.29-0.39)	0.36 (0.25-0.47)	0.33 (0.23-0.43)	0.19 (0.16-0.21)	0.02 (0.01-0.03)
30-34	0.92 (0.88-0.97)	0.76 (0.71-0.80)	0.75 (0.65-0.85)	0.19 (0.17-0.22)	0.30 (0.25-0.33)	0.43 (0.33-0.53)	0.33 (0.24-0.41)	0.19 (0.17-0.21)	0.02 (0.01-0.02)[a]
≥35	0.83 (0.77-0.89)	0.73 (0.69-0.77)	0.60 (0.49-0.70)	0.16 (0.14-0.18)	0.33 (0.29-0.37)	0.40 (0.32-0.48)	0.30 (0.23-0.36)	0.22 (0.19-0.24)	0.03 (0.02-0.05)[a]
Education[b]									
Low	0.80 (0.75-0.86)[a]	0.69 (0.64-0.73)[a]	0.54 (0.45-0.64)[a]	0.14 (0.12-0.16)[a]	0.34 (0.31-0.37)[a]	0.40 (0.33-0.47)	0.37 (0.30-0.43)	0.21 (0.19-0.23)	0.03 (0.02-0.04)[a]
Medium	0.93 (0.88-0.98)[a]	0.81 (0.76-0.87)[a]	0.78 (0.65-0.90)[a]	0.21 (0.18-0.24)[a]	0.32 (0.27-0.37)[a]	0.38 (0.26-0.50)	0.27 (0.17-0.37)	0.20 (0.18-0.23)	0.02 (0.01-0.03)
High	0.94 (0.89-0.99)[a]	0.79 (0.73-0.85)[a]	0.79 (0.66-0.92)[a]	0.23 (0.21-0.26)[a]	0.26 (0.21-0.32)[a]	0.44 (0.31-0.57)	0.23 (0.14-0.32)	0.17 (0.14-0.20)	0.01 (0.00-0.02)[a]

NSAIDS: Non-steroidal anti-inflammatory drugs

[a]Differences between groups (at least 2 of three category variables) suggested by non-overlapping 95% confidence intervals

[b]Low, Less than 4-year college; Medium, Started or completed university; High, Post-graduate education

Table 4. Validity of prescription records (NorPD) using to fathers' self-reported use (MoBa) as reference standard

Medication category	MoBa, n	1+ Rx						2+ Rx					
		NorPD, n	Both, n	Se (95% CI)	Sp (95% CI)	PPV (95% CI)[a]	NPV (95% CI)[b]	NorPD, n	Both, n	Se (95% CI)	Sp (95% CI)	PPV (95% CI)[a]	NPV (95% CI)[b]
Group 1: Prescription medication used chronically													
Antiepileptics	213	243	198	93.0 (88.7-96.0)	99.9 (99.9-99.9)	81.5 (76.0-86.2)	100 (99.9-100)	179	162	76.1 (69.7-81.6)	100 (99.9-100)	90.5 (85.2-94.4)	99.9 (99.8-99.9)
Antipsychotics	94	165	82	87.2 (78.8-93.2)	99.8 (99.8-99.8)	49.7 (41.8-57.6)	100 (100-100)	79	63	67.0 (56.6-76.4)	100 (99.9-100)	79.7 (69.2-88.0)	99.9 (99.9-100)
Antidepressants	467	704	433	92.7 (90.0-94.9)	99.4 (99.3-99.4)	61.5 (57.8-65.1)	99.9 (99.9-99.9)	477	361	77.3 (73.2-81.0)	99.7 (99.7-99.8)	75.7 (71.6-79.5)	99.7 (99.7-99.8)
Group 2: Prescription medication used episodically													
Anti-infectives	998	5191	673	67.4 (64.4-70.3)	89.2 (88.9-89.5)	13.0 (12.1-13.9)	99.1 (99.0-99.2)	1124	257	25.8 (23.1-28.6)	97.9 (97.8-98.1)	22.9 (20.4-25.4)	98.2 (98.1-98.3)
Opioids	707	1667	398	56.3 (52.5-60.0)	97.0 (96.8-97.1)	23.9 (21.8-26.0)	99.2 (99.2-99.3)	363	181	25.6 (22.4-29.0)	99.6 (99.5-99.6)	49.9 (44.6-55.1)	98.8 (98.7-98.9)
Anxiolytics	163	323	98	60.1 (52.2-67.7)	99.5 (99.4-99.5)	30.0 (25.4-35.7)	99.8 (99.8-99.9)	113	59	36.2 (28.8-44.1)	99.9 (99.8-99.9)	52.2 (42.6-61.7)	99.8 (99.7-99.8)
Hypnotics and sedatives	167	491	105	69.9 (55.1-70.2)	99.1 (99.0-99.2)	21.4 (17.8-25.3)	99.9 (99.8-99.9)	160	65	38.9 (31.5-46.8)	99.8 (99.7-99.8)	40.6 (32.9-48.7)	99.8 (99.7-99.8)
Group 3. OTC/prescription medication													
NSAIDs	3223	4286	1006	31.2 (29.6-32.8)	91.7 (91.4-92.0)	23.5 (22.2-24.8)	94.3 (94.0-94.5)	1014	433	13.4 (12.3-14.7)	98.5 (98.4-98.6)	42.7 (39.6-45.8)	93.3 (93.1-93.6)
Paracetamol	6418	359	129	2.01 (1.68-2.38)	99.4 (99.3-99.4)	35.9 (31.0-41.1)	85.2 (84-9-85.5)	50	24	0.37 (0.24-0.56)	99.9 (99.9-100)	48.0 (33.7-62.6)	85.1 (84.7-85.4)

Abbreviations: MoBa, Norwegian Mother and Child cohort study; NorPD, Norwegian Prescription Database; NPV, negative predictive value; PPV, positive predictive value; Rx, dispensed prescription; Se, sensitivity; Sp, specificity

[a]Equivalent to the sensitivity of prescription record using self-report as the reference standard

[b]Equivalent to the specificity of prescription record using self-report as the reference standard