Title

Agreement Between Maternal Report and Medical Records During Pregnancy: Medications for Rheumatoid Arthritis and Asthma

Journal

Paediatric and Perinatal Epidemiology, 32(1)

ISSN

0269-5022

Authors

Palmsten, Kristin
Hulugalle, Avanthi
Bandoli, Gretchen
et al.

Publication Date

2018

DOI

10.1111/ppe.12415

Peer reviewed

HHS Public Access

Author manuscript

Paediatr Perinat Epidemiol. Author manuscript; available in PMC 2019 January 01.

Published in final edited form as:

Paediatr Perinat Epidemiol. 2018 January ; 32(1): 68–77. doi:10.1111/ppe.12415.

Agreement Between Maternal Report and Medical Records During Pregnancy: Medications for Rheumatoid Arthritis and Asthma

Kristin Palmsten[a], **Avanthi Hulugalle**[a,b], **Gretchen Bandoli**[a], **Grace M Kuo**[c,d], **Shayda Ansari**[a], **Ronghui Xu**[d,e], and **Christina D. Chambers**[a,d]

[a]School of Medicine, Department of Pediatrics, University of California, San Diego, La Jolla, CA, USA

[b]College of Global Public Health, New York University, New York, NY, USA

[c]Skaggs School of Pharmacy and Pharmaceutical Sciences, Division of Clinical Pharmacy, University of California, San Diego, La Jolla, CA, USA

[d]School of Medicine, Department of Family Medicine and Public Health, University of California, San Diego, La Jolla, CA, USA

[e]Department of Mathematics, University of California, San Diego, La Jolla, CA, USA

Abstract

Background—There are limited data regarding the comparability of medication exposure information during pregnancy from maternal report and medical records, including for rheumatoid arthritis and asthma-related medications.

Methods—This study included pregnant women with rheumatoid arthritis (n=216) and asthma (n=172) enrolled in the MothertoBaby Pregnancy Studies (2009–2014). Women reported types and dates of medications used through semi-structured telephone interviews up to 3 times during pregnancy and once after delivery, and medical records were obtained. We calculated Cohen's kappa coefficients and 95% confidence intervals (CIs) and percent agreement for agreement between report and records.

Results—For rheumatoid arthritis, prednisone was reported most frequently (53%). During pregnancy, kappa coefficients for rheumatoid arthritis medications ranged from 0.32 (95% CI 0.15, 0.50) for ibuprofen, with 84.3% agreement, to 0.90 (95% CI 0.84, 0.96) for etanercept with 95.4% agreement, and was 0.44 (95% CI 0.33, 0.55) for prednisone, with 71.3% agreement. For asthma, albuterol was reported most frequently (77.9%). During pregnancy, kappa coefficients for asthma medications ranged from 0.21 (95% CI 0.08, 0.35) with 64.5% agreement for albuterol to 0.84 (95% CI 0.71, 0.96) for budesonide/formoterol with 96.5% agreement. Where kappas for any use during pregnancy were less than excellent (i.e., ≤0.80), medication use was more frequently captured by report than record.

Corresponding author: Kristin Palmsten, HealthPartners Institute, Mail Stop: 23301A, PO Box 1524, Minneapolis, MN, USA, 55440-1524. Kristin.K.Palmsten@HealthPartners.com.

Conclusions—Agreement was higher for medications typically used continuously than sporadically. Information on medication use from medical records alone may not be adequate when studying the impact of intermittently used medications during pregnancy on perinatal outcomes.

Keywords

asthma; medication; pharmacoepidemiology; pregnancy; rheumatoid arthritis

Introduction

Between 60% and 80% of pregnant women in the United States are dispensed at least one prescription medication and more than 90% use an over-the-counter or prescription medication, excluding vitamins or minerals.[1–3] Observational studies of medication use during pregnancy and risk of adverse obstetric and perinatal outcomes rely on one or more sources of exposure information, including maternal report during pregnancy, maternal report recalled after pregnancy, pharmacy dispensing claims from healthcare utilization databases, and electronic or paper-based medical records.[4–7] Non-differential exposure misclassification tends to bias associations toward the null,[8] which could diminish an association indicative of a harmful medication effect. Several studies have compared medication exposure information from various data sources during pregnancy; however agreement between maternal report and medical records is largely unknown.[9–16] One study compared maternal report with active prescription medications listed in electronic medical records and reported generally higher agreement for medications indicated for chronic conditions compared with sporadically used medications.[13] Although that study presented medications from several classes, the small number of women with certain chronic diseases, including asthma, limited the number of specific medications indicated for the conditions that could be compared.

In this study, we evaluated the comparability of information on medication exposures during pregnancy collected in prospective cohorts from maternal report and medical records. We focused on medications used to treat rheumatoid arthritis and asthma. Because rheumatoid arthritis and asthma are chronic conditions in which both continuously used and sporadically used medications may be taken during pregnancy,[17,18] we were able to evaluate agreement for both types of medication utilization.

Methods

Data sources

This study included pregnant women enrolled in one of two MotherToBaby Pregnancy Studies.[19] The Autoimmune Diseases in Pregnancy Study recruits pregnant women with at least one of several autoimmune diseases and the Asthma Medications in Pregnancy Study recruits pregnant women with asthma. Participants were from the United States and Canada and were self-referred, referred by their healthcare providers, or referred by MotherToBaby, a free counseling service of the Organization of Teratology Information Specialists (OTIS)

that provides evidence-based information regarding medications and other exposures during pregnancy and lactation.

Research assistants conducted semi-structured interviews with participants via telephone. Interviewers were trained by standard training documents, one-on-one instruction from the supervisor or previously trained interviewers, and by listening to live interviews. The supervisor provided interviewer feedback through 3-way calling until the supervisor determined that interviewers could conduct interviews alone. Interview evaluation continued throughout data collection. Participants were interviewed up to four times depending on the gestational age at enrollment: at the time of study enrollment, at approximately 24 and 32 weeks' gestation, and after delivery. Interviewers collected data from participants regarding race, ethnicity, socio-economic status (Hollingshead categories based on maternal and paternal education and occupation with possible range from highest=1 to lowest=5)[20], comorbidities and pregnancy outcomes. MotherToBaby Pregnancy Studies aim to collect exposure information on all medications used during pregnancy, not just those used for rheumatoid arthritis and asthma. At the time of enrollment, interviewers used an open-ended prompt to obtain over-the-counter and prescription medication use information such as "Have you taken any over-the-counter medications since your last menstrual period, for example TylenolÒ or TumsÒ?" In addition, women who reported having a specific illness or disease were asked if they took any medication for that condition, e.g., rheumatoid arthritis or asthma. For any medications reported, women were queried for dose and dates of use. During follow-up interviews, women were queried about medication use since their most recent interview and whether they were still using previously reported medications. Furthermore, interviewers administered validated self-assessment questionnaires to measure disease severity including the Health Assessment Questionnaire Disability Index (HAQ-DI; possible range from 0=no disability to 3=completely disabled)[21,22] for women with rheumatoid arthritis and the Pregnancy Asthma Control Test (p-ACT; possible range from 5=poor control to 25= complete control) for women with asthma.[23,24] Obstetrician medical records were requested from all participants. Rheumatologist records were requested from all women who had a rheumatologist visit during pregnancy, and allergist records were requested from all women who had an allergist visit during pregnancy. Records were from paper charts or print outs from electronic medical records. MotherToBaby Pregnancy Studies aim to reconcile discrepancies between maternal report and medical records whenever possible. For the current study, only the maternal report data prior to reconciliation was used.

Study population

Pregnant women with a last menstrual period between 2009 and 2014 were eligible for this study if they reported having rheumatoid arthritis and enrolled in the Autoimmune Diseases in Pregnancy Study or if they reported having asthma and enrolled in the Asthma Medications in Pregnancy Study before gestational week 20 (Online Supplemental Figure 1). Women were excluded who had a spontaneous abortion, were lost to follow up or withdrew, or had an incomplete postpartum interview. Therefore, all women in the study completed at least two interviews, i.e., at enrollment and postpartum. Of the 282 women with rheumatoid arthritis who met the basic inclusion criteria, 39 (14%) were excluded

because medical records had not been released when abstraction for this study began. Due to resource constraints, we randomly sampled 220 women for abstraction. Charts were incomplete or unavailable for four women, and rheumatoid arthritis medication abstraction was completed for 216 women. Of the 216 women, 81% had evidence of visiting a rheumatologist during pregnancy. Nearly all women had obstetrician records available (97%), 74% had rheumatologist records available, and 71% had both records available. Of the 240 women with asthma who met the basic inclusion criteria, 68 (28%) were excluded because medical records had not been released. Asthma medication abstraction was completed for 172 women. Of these women, only 21% had evidence of visiting an allergist during pregnancy and consequently there was a limited number of women with an allergist record available. All women had obstetrician records available and 16% had both obstetrician and allergist records available. Five women were in both the rheumatoid arthritis and asthma sub-cohorts.

Data abstraction

Medication information was abstracted from any available record, i.e., obstetric, specialist, or both, and from any available source within the medical records including ordered medication lists, active medication lists, which rely on patient report or confirmation, and physician's notes. Specifically, medication name and date was abstracted on glucocorticoids, disease-modifying anti-rheumatic drugs, and nonsteroidal anti-inflammatory drugs for the rheumatoid arthritis abstractions and on glucocorticoids (oral and inhaled), short-acting and long-acting beta-agonists, leukotriene modifiers, and other asthma medications for the asthma abstractions using a standardized abstraction database. First, medical records for 10 women with rheumatoid arthritis and 10 women with asthma were independently re-abstracted by a second abstractor, compared for quality control, and used to refine the abstraction form and clarify the protocol. Then, all records were abstracted by one abstractor.

Statistical Analysis

For medications reported by or documented in the medical record for at least 17 women (10% of women in the smaller of the two subcohorts, i.e., asthma), first we calculated Cohen's kappa coefficients (K), which accounts for chance agreement,[25] and 95% confidence intervals (CI) for concordance between maternal report and any type of medical record (obstetrician and/or specialist, i.e., rheumatologist or allergist, record). We classified kappa values ≤0.40 as poor, ≥0.41 and ≤0.60 as moderate, ≥0.61 and ≤0.80 as good, and ≥0.81 as excellent.[26] Also, we calculated percent agreement as the sum of women with agreement between data sources divided by the total number of women. We calculated kappa and percent agreement for the entire pregnancy and within trimesters. In a sensitivity analysis for rheumatoid arthritis, we restricted to the 154 women who had both obstetrician and rheumatologist records and calculated kappas for anytime during pregnancy and during the first trimester using information only from obstetric records and only from rheumatology records, separately. Because of the limited number of women with an allergist record available (n=27), we did not conduct a similar sensitivity analysis for asthma. Next, we examined kappa values and percent agreement for medications reported by at least 100 women according to gestational age at enrollment and maternal characteristics. We chose

medications reported by at least 100 women to allow for adequate study size after stratification, selecting prednisone among women with rheumatoid arthritis and albuterol among women with asthma. We stratified by enrollment during the first trimester, as enrollment after the first trimester would result in a longer period required for recall of first trimester exposures. We also stratified by risk factors for adverse perinatal outcomes including maternal age >30, primiparity, pre-pregnancy body mass index ≥25 kg/m^2, Health Assessment Questionnaire Disability Index score at the time of study enrollment ≥0.25 (i.e., the median score) for women with rheumatoid arthritis, and Pregnancy Asthma Control Test score at the time of enrollment <20 (i.e., not well controlled asthma) for women with asthma. Finally, in the absence of a gold standard for medication use, we used maternal report as the reference standard, because this information was actively collected at multiple time points during pregnancy, against any type of medical record to calculate sensitivity, specificity, positive predictive value, and negative predictive value and Wilson 95% CIs during pregnancy.

The MotherToBaby Pregnancy Studies were approved by the University of California, San Diego Institutional Review Board and the current study was declared exempt.

Results

The median gestational age at enrollment was 10.7 weeks for women with rheumatoid arthritis and 13.0 weeks for women with asthma (Table 1). Overall, 4.6% of women completed only 2 interviews and 15.7% completed only 3 interviews. The mean maternal age was approximately 32 years, and most women were non-Hispanic white and had high socioeconomic status. On average, women with rheumatoid arthritis had low disease severity and women with asthma had well controlled asthma at enrollment.

The percentage of women with documented medications during pregnancy varied according to maternal report, medical records, or either source for most agents (Table 2). Prednisone was the most frequently used rheumatoid arthritis-related medication according to maternal report (53.2%) and albuterol was the most frequently used asthma-related medication according to maternal report (77.9%). Unlike rheumatoid arthritis-related medications, the frequencies of asthma-related medications were greater according to maternal report than by records.

During pregnancy, kappa coefficients for rheumatoid arthritis medications ranged from 0.32 (95% CI 0.15, 0.50) for ibuprofen to 0.90 (95% CI 0.84, 0.96) for etanercept, and for asthma medications from 0.21 (95% CI 0.08, 0.35) for albuterol to 0.84 (95% CI 0.71, 0.96) for budesonide/formoterol (Table 3). For prednisone, aspirin, fluticasone, fluticasone/salmeterol, and albuterol the number of women who reported medication use during pregnancy but did not have medical record confirmation was more than twice the number of women who had the medication in their medical record only.

Kappa coefficients were lower for medication use during the first trimester compared with use anytime during pregnancy (Table 3). When examining agreement later in pregnancy, precision of estimates for the second and third trimesters were generally lower than for the

first trimester (Supplementary Table 1). Kappas also tended to be lower for the second and third trimesters compared with the entire pregnancy. One exception was prednisone among women with asthma, for which second and third trimester kappas were similar to the entire pregnancy. Notably, kappas for disease modifying antirheumatic drugs decreased in the second and third trimesters compared with the first trimester. Furthermore, the number of women with maternal report for a disease modifying antirheumatic drug with no medical record confirmation generally decreased after the first trimester, whereas the number of women with use according to their medical record only increased.

For women with rheumatoid arthritis who had both types of records available, agreement between maternal report and obstetrician records for medication use anytime during pregnancy and during the first trimester was similar to agreement with rheumatologist records with the exception of sulfasalazine anytime during pregnancy (Supplementary Table 2; K=0.55 (95% CI 0.29, 0.80) for obstetrician records and K=0.85 (95% CI 0.71, 0.99) for rheumatologist records).

Kappas for prednisone among women with rheumatoid arthritis were slightly higher among women with higher disease severity (0.46 (95% CI 0.31, 0.60)) than women with lower severity (0.35 (95% CI 0.17, 0.53)) and were consistent across other maternal characteristics (Table 4). Kappa values for albuterol among women with asthma were slightly higher among women older than 30 years (0.25, (95% CI 0.08, 0.42)) than women 30 years and younger (0.14, (95% CI −0.08, 0.37)) and among women who were overweight or obese (0.29 (95% CI 0.09, 0.48)) compared with women who were not (0.14 (95% CI −0.05, 0.33)).

Using maternal report as the reference, sensitivities ranged from 37.5% (95% CI 22.9%, 54.8%) for ibuprofen to 96.2% (95% CI 89.4%, 98.7%) for etanercept and specificities ranged from 89.1% (95% CI 81.5%, 93.8%) for prednisone to 97.9% (95% CI 94.8%, 99.2%) for sulfasalazine for rheumatoid arthritis medications (Table 5). Sensitivities ranged from 33.3% (95% CI 17.2%, 54.6%) for fluticasone to 81.8% (95% CI 61.5%, 92.7%) for budesonide/formoterol and specificities ranged from 63.2% (95% CI 47.3%, 76.6%) for albuterol to 100% (95% CI 97.5%, 100%) for fluticasone for asthma medications.

Comment

Main findings

In this study of pregnant women with rheumatoid arthritis and asthma, prevalence estimates of medication use differed depending on the information source used and were highest when both maternal report and medical records were utilized. Agreement between maternal report and medical records for medication exposure anytime during pregnancy varied depending on the type of medication. Agreement according to kappa coefficients was excellent for biologic and non-biologic disease-modifying antirheumatic drugs and for inhaled glucocorticoid/long-acting beta-agonist combination medications. Agreement was good for montelukast, a leukotriene receptor antagonist, and only moderate for prednisone, an oral glucocorticoid, inhaled glucocorticoids, and aspirin. Agreement was poor for ibuprofen, a nonsteroidal anti-inflammatory drug, and albuterol, a short-acting beta-agonist, which are used on an as-needed basis. For all medications with less than excellent agreement at any

time in pregnancy or the first trimester, regardless of whether they were rheumatoid arthritis or asthma medications, the exposure was captured more frequently by report than by records. Furthermore, agreement for prednisone among women with rheumatoid arthritis and albuterol among women with asthma did not differ greatly according to gestational timing of enrollment and was non-differential with respect to the risk factors for adverse perinatal outcomes that were evaluated.

Interpretation

Trimester-specific kappa values were generally lower than kappas for use anytime during pregnancy, which reflects in part the shorter time interval for agreement. Lower kappas for disease modifying antirheumatic drugs in the second and third trimesters compared with the first trimester may be due to discontinuation of these medications that was not reflected in the medical record. Sensitive time periods are typically of interest when studying the adverse effects of medication use during pregnancy, as opposed to the entire pregnancy.[27] Therefore, reconciliation between maternal report and medical records, or other data collection methods, such as daily journals or mobile apps, may be needed when studying outcomes with narrow etiologically-relevant gestational windows.

Agreement for rheumatoid arthritis medications was similar when considering only obstetrician records or only rheumatologist records with the exception of sulfasalazine use anytime during pregnancy, which had higher agreement between report and rheumatologist records compared with obstetrician records. The generally similar agreement for rheumatoid arthritis medications suggests that obstetrician records may be used in lieu of rheumatologist records to capture rheumatoid arthritis-related medication use during pregnancy.

Sensitivities for medication use anytime during pregnancy were near 80% or greater for disease modifying anti-rheumatic drugs and for inhaled glucocorticoid/long-acting beta agonist combination medications, suggesting that any use of these medications during pregnancy according to maternal report will frequently be captured by medical records. However, positive maternal reports of montelukast and the intermittently used medications were not captured well by records. Specificities were near 90% or greater for all medications except for albuterol, suggesting that few women who do not report any use of these medications during pregnancy will be identified as using these medications from their medical records. In contrast, around 40% of women who did not report any albuterol during pregnancy were identified as having used albuterol during pregnancy according to records. We do not have a gold standard for medication exposure; however, exposure misclassification from medical records and prospective maternal report would be expected to be non-differential with respect to perinatal outcomes. Consequently, such misclassification would tend to bias results towards the null and could hide a harmful effect. Conversely, exposure misclassification from retrospective maternal report, as is commonly used in retrospective case-control studies, could be either non-differential or differential with respect to perinatal outcomes, and therefore could bias results in either direction.

Previous studies comparing sources of medication use during pregnancy, most often comparing pharmacy dispensing information with maternal report, for a range of medications reported that agreement tended to be higher for medications that are typically

used continuously than for medications that may be used occasionally.[9–14,16] There is potential for correlated errors between maternal report and medical records, e.g., under-reporting medication use during a study interview and to a health care provider, whereas, correlated errors between prescription drug registers and maternal report seem less plausible. Nevertheless, in accordance with the prior studies, we also found that agreement tended to be higher for continuously versus sporadically used medications, regardless of whether they were rheumatoid arthritis or asthma medications. In the previous study by Sarangarm and colleagues that compared active prescription medications from electronic medical records with maternal interview, the medications reported by study participants were mostly different from those in our study. That study reported a higher kappa value for albuterol (0.74 (95% CI 0.54–0.94)), although only 15 women used albuterol according to at least one of the sources.[13] It is possible that the higher kappa for albuterol in the Sarangarm et al study reflects more consistent use of rescue inhalers than women in the current study, who had well-controlled asthma on average.

Maternal report of medication use may differ from medical records for many reasons, including incomplete records, inaccurately recorded medications, out-of-date medication lists, and illegible notes. From the perspective of the patient, discordance may arise from primary non-adherence (i.e., not filling a prescribed medication), discontinuing a medication, taking a medication differently than prescribed (e.g., delaying initiation until after the first trimester), taking a medication provided by family members or friends that was not prescribed for the individual, and inaccurately recalling medication use.[13,28] Regarding occasionally used medications for indications other than rheumatoid arthritis or asthma, i.e., aspirin, ibuprofen, and prednisone, discordance between maternal report and medical record may arise from use that is not captured in the record for other indications. Specifically, a provider may not query about occasionally-used medications for indications other than rheumatoid arthritis or asthma or for those prescribed by another provider.

Limitations of the data

The major limitation of this study was that we did not have a true gold-standard reflective of actual medication use because both maternal report and medical records are expected to have inaccuracies and missing information. Individuals with more frequent health care encounters may be more likely to have accurate medication use information in their medical records because of more opportunities for health care providers to update medication use records.

Generalizability

This study only considered women who were specifically recruited and enrolled because of their diagnosis. It is possible that women who enroll in a study regardless of their diagnoses or medication use would report their medication use with less accuracy. Furthermore, women were primarily non-Hispanic white, had relatively high socio-economic status and older maternal age. The results may not generalize to other populations if accuracy of maternal report or medical record information varies by demographic factors.

Women in this study reported medication use in response to open-ended prompts as opposed to a structured query using an exhaustive list of specific medications. Prevalence of

medication use according to maternal report and agreement between maternal report and medical records may have been higher had women been queried about specific rheumatoid arthritis and asthma medications. Sources of medication information in records was variable across women and included ordered medication lists, active medication lists, which rely on patient report, and physicians' notes. Variability in medication reconciliation practice (reconciling discrepancies between patient report and medical record) among individual clinics was unavailable but could contribute to different levels of medication agreement. Agreement between maternal report and records may be higher in settings where active medication lists are consistently reviewed and reconciled at each visit.

Conclusions

In this study, rheumatoid arthritis and asthma medications with moderate or poor agreement between maternal report and medical records included medications that may be used intermittently, and maternal report only was more frequent than medical record information only for the use of these medications anytime during pregnancy and in the first trimester. These findings suggest that information on medication use from medical records alone may not be adequate when studying the impact of intermittently used medications during sensitive gestational windows on perinatal outcomes. If maternal report of medication use is not available, then bias analysis could be used to account for exposure misclassification.[29]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

MotherToBaby Pregnacy Studies are or have been funded by research grants from AbbVie, Amgen, Apotex, Barr, Bristol-Myers Squibb (BMS), Par, Kali, Sandoz, Teva, Roche/Genetech, GSK, UCB, Pfizer, Janssen, Celgene, Takeda, Sanofi-Aventis / Genzyme and by a grant from the Agency for Healthcare Research and Quality (R18HS018474, CD Chambers).

K Palmsten is supported by a career development award from the *Eunice Kennedy Shriver* National Institute of Child Health & Human Development, National Institutes of Health (K99HD082412). G Bandoli is supported by the National Institutes of Health, Grant TL1TR001443.

The funders had no role in the study design, in the data collection, in the analysis and interpretation of data, in the writing of the report, or in the decision to submit the article for publication.

References

1. Andrade SE, Gurwitz JH, Davis RL, Chan KA, Finkelstein JA, Fortman K, et al. Prescription drug use in pregnancy. American Journal of Obstetrics and Gynecology. 2004; 191:398–407. [PubMed: 15343213]
2. Mitchell AA, Gilboa SM, Werler MM, Kelley KE, Louik C, Hernandez-Diaz S, et al. Medication use during pregnancy, with particular focus on prescription drugs: 1976-2008. American Journal of Obstetrics and Gynecology. 2011; 205:51.e1–51.e8. [PubMed: 21514558]
3. Palmsten K, Hernandez-Diaz S, Chambers CD, Mogun H, Lai S, Gilmer TP, et al. The Most Commonly Dispensed Prescription Medications Among Pregnant Women Enrolled in the U.S. Medicaid Program. Obstetrics and Gynecology. 2015; 126:465–473. [PubMed: 26244530]
4. Chambers CD, Johnson DL, Robinson LK, Braddock SR, Xu R, Lopez-Jimenez J, et al. Birth outcomes in women who have taken leflunomide during pregnancy. Arthritis and Rheumatism. 2010; 62:1494–1503. [PubMed: 20131283]

5. Broussard CS, Rasmussen SA, Reefhuis J, Friedman JM, Jann MW, Riehle-Colarusso T, et al. Maternal treatment with opioid analgesics and risk for birth defects. American Journal of Obstetrics and Gynecology. 2011; 204:314.e1–314.e11. [PubMed: 21345403]
6. Palmsten K, Hernandez-Diaz S, Huybrechts KF, Williams PL, Michels KB, Achtyes ED, et al. Use of antidepressants near delivery and risk of postpartum hemorrhage: cohort study of low income women in the United States. BMJ. 2013; 347:f4877. [PubMed: 23965506]
7. Petersen I, Sammon CJ, McCrea RL, Osborn DP, Evans SJ, Cowen PJ, et al. Risks associated with antipsychotic treatment in pregnancy: Comparative cohort studies based on electronic health records. Schizophrenia Research. 2016; 176:349–356. [PubMed: 27484686]
8. Rothman, KJ., Greenland, S., Lash, TL. Validity in epidemiologic studies. In: Rothman, KJ.Greenland, S., Lash, TL., editors. Modern Epidemiology. 3rd. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2008. p. 139-142.
9. de Jong-van den Berg LT, Waardenburg CM, Haaijer-Ruskamp FM, Dukes MN, Wesseling H. Drug use in pregnancy: a comparative appraisal of data collecting methods. European Journal of Clinical Pharmacology. 1993; 45:9–14. [PubMed: 8405037]
10. Olesen C, Sondergaard C, Thrane N, Nielsen GL, de Jong-van den Berg L, Olsen J, et al. Do pregnant women report use of dispensed medications? Epidemiology. 2001; 12:497–501. [PubMed: 11505166]
11. Stephansson O, Granath F, Svensson T, Haglund B, Ekbom A, Kieler H. Drug use during pregnancy in Sweden - assessed by the Prescribed Drug Register and the Medical Birth Register. Clinical Epidemiology. 2011; 3:43–50. [PubMed: 21386973]
12. Espnes MG, Bjorge T, Engeland A. Comparison of recorded medication use in the Medical Birth Registry of Norway with prescribed medicines registered in the Norwegian Prescription Database. Pharmacoepidemiology and Drug Safety. 2011; 20:243–248. [PubMed: 21351305]
13. Sarangarm P, Young B, Rayburn W, Jaiswal P, Dodd M, Phelan S, et al. Agreement between self-report and prescription data in medical records for pregnant women. Birth Defects Research. Part A, Clinical and Molecular Teratology. 2012; 94:153–161. [PubMed: 22253196]
14. van Gelder MM, van Rooij IA, de Walle HE, Roeleveld N, Bakker MK. Maternal recall of prescription medication use during pregnancy using a paper-based questionnaire: a validation study in the Netherlands. Drug Safety. 2013; 36:43–54. [PubMed: 23315295]
15. Skurtveit S, Selmer R, Tverdal A, Furu K, Nystad W, Handal M. Drug exposure: inclusion of dispensed drugs before pregnancy may lead to underestimation of risk associations. Journal of Clinical Epidemiology. 2013; 66:964–972. [PubMed: 23800534]
16. Pisa FE, Casetta A, Clagnan E, Michelesio E, Vecchi Brumatti L, Barbone F. Medication use during pregnancy, gestational age and date of delivery: agreement between maternal self-reports and health database information in a cohort. BMC Pregnancy and Childbirth. 2015; 15:310. [PubMed: 26608022]
17. Ostensen M, Forger F. Management of RA medications in pregnant patients. Nature Reviews Rheumatology. 2009; 5:382–390. [PubMed: 19506586]
18. Namazy JA, Schatz M. The safety of asthma medications during pregnancy: an update for clinicians. Therapeutic Advances in Respiratory Disease. 2014; 8:103–110. [PubMed: 25034020]
19. Bharti B, Lee SJ, Lindsay SP, Wingard DL, Jones KL, Lemus H, et al. Disease Severity and Pregnancy Outcomes in Women with Rheumatoid Arthritis: Results from the Organization of Teratology Information Specialists Autoimmune Diseases in Pregnancy Project. The Journal of Rheumatology. 2015; 42:1376–1382. [PubMed: 25877497]
20. Hollingshead, AB. Unpublished Working Paper. Yale University; New Haven, CT: 1975. Four factor index of social status. https://artlesstanzim.files.wordpress.com/2014/05/hollinghead-four-factors-2.pdf
21. Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis and Rheumatism. 1980; 23:137–145. [PubMed: 7362664]
22. Bruce B, Fries JF. The Stanford Health Assessment Questionnaire: dimensions and practical applications. Health and Quality of Life Outcomes. 2003; 1:20. [PubMed: 12831398]

23. Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA, et al. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. The Journal of Allergy and Clinical Immunology. 2006; 117:549–556. [PubMed: 16522452]

24. Palmsten K, Schatz M, Chan PH, Johnson DL, Chambers CD. Validation of the Pregnancy Asthma Control Test. The Journal of Allergy and Clinical Immunology. In Practice. 2016; 4:310–315 e11. [PubMed: 26776373]

25. Maclure M, Willett WC. Misinterpretation and misuse of the kappa statistic. American Journal of Epidemiology. 1987; 126:161–169. [PubMed: 3300279]

26. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977; 33:159–174. [PubMed: 843571]

27. Obican S, Scialli AR. Teratogenic exposures. American Journal of Medical Genetics. Part C, Seminars in Medical Genetics. 2011; 157C:150–169.

28. Petersen EE, Rasmussen SA, Daniel KL, Yazdy MM, Honein MA. Prescription medication borrowing and sharing among women of reproductive age. J Womens Health (Larchmt). 2008; 17:1073–1080. [PubMed: 18774892]

29. Fox MP, Lash TL, Greenland S. A method to automate probabilistic sensitivity analyses of misclassified binary variables. International Journal of Epidemiology. 2005; 34:1370–1376. [PubMed: 16172102]

Table 1

Maternal and pregnancy characteristics from 388 women enrolled in MotherToBaby Pregnancy Studies, 2009–2014.

Characteristics	Rheumatoid Arthritis N=216	Asthma N=172
Gestational Week at Enrollment, median (IQ Range)	10.7 (7.1)	13.0 (6.9)
Maternal Age, mean (SD)	32.6 (4.3)	32.5 (5.0)
Completed only 2 Interviews	14 (6.5)	4 (2.3)
Completed only 3 interviews	33 (15.3)	28 (16.3)
Race/Ethnicity, n (%)		
Non-Hispanic White	171 (79.2)	144 (83.7)
Other	25 (11.6)	18 (10.5)
Missing	20 (9.3)	10 (5.8)
Socioeconomic Status[a], n (%)		
1 or 2	165 (76.4)	143 (83.1)
3, 4, or 5	47 (21.8)	29 (16.9)
Missing	4 (1.9)	0
Primiparous, n (%)	101 (46.8)	104 (60.5)
Multifetal Gestation, n (%)	14 (6.5)	8 (4.7)
Pre-pregnancy Body Mass Index mg/kg^2, n (%)		
<25	135 (62.5)	84 (48.8)
25–29.9	46 (21.3)	51 (29.7)
≥30	35 (16.2)	37 (21.5)
Health Assessment Disability Index Score at Enrollment, mean (SD)	0.5 (0.6)	NA
Pregnancy Asthma Control Test Score at Enrollment, mean (SD)[b]	NA	20.6 (4.0)
Gestational Age at Delivery (weeks), mean (SD)	38.4 (2.3)	39.0 (2.6)

Abbreviations: IQ, interquartile; NA, not applicable; SD, standard deviation.

[a]Calculated using Hollingshead categories based on maternal and paternal education and occupation; Possible Range: 1, highest to 5, lowest

[b]Missing for 6 women.

Table 2

Frequencies of rheumatoid arthritis and asthma-related medications according to maternal report, medical records, or either source.

Medication	Medication Class	Maternal Report n (%)	Medical Record[a] n (%)	Maternal Report or Medical Record n (%)
Rheumatoid Arthritis, n=216				
Prednisone	Oral Glucocorticoid	115 (53.2)	75 (34.7)	126 (58.3)
Hydroxychloroquine	Oral Non-biologic DMARD	52 (24.1)	59 (27.3)	62 (28.7)
Sulfasalazine	Oral Non-biologic DMARD	22 (10.2)	23 (10.7)	26 (12.0)
Etanercept	Injectable Biologic DMARD	79 (36.6)	83 (38.4)	86 (39.8)
Adalimumab	Injectable Biologic DMARD	38 (17.6)	39 (18.1)	43 (19.9)
Ibuprofen	Oral NSAID	32 (14.8)	26 (12.0)	46 (21.3)
Aspirin	Oral NSAID	28 (13.0)	19 (8.8)	35 (16.2)
Asthma, n=172				
Prednisone	Oral Glucocorticoid	24 (14.0)	17 (9.9)	29 (16.9)
Fluticasone	Inhaled Glucocorticoid	21 (12.2)	7 (4.1)	21 (12.2)
Budesonide	Inhaled Glucocorticoid	19 (11.1)	17 (9.9)	25 (14.5)
Fluticasone/salmeterol	Inhaled Glucocorticoid/LABA	52 (30.2)	44 (25.6)	54 (31.4)
Budesonide/formoterol	Inhaled Glucocorticoid/LABA	22 (12.8)	20 (11.6)	24 (14.0)
Albuterol	Inhaled SABA	134 (77.9)	101 (58.7)	148 (86.1)
Montelukast	Oral Leukotriene Receptor Antagonist	26 (15.1)	21 (12.2)	31 (18.0)

Abbreviations: DMARD, disease-modifying antirheumatic drug; LABA, long-acting beta-agonist; SABA, short-acting beta-agonist; NSAID, nonsteroidal anti-inflammatory drug.

[a]Any medical record, i.e., obstetrician or rheumatologist record for rheumatoid arthritis and obstetrician or allergist record for asthma.

Paediatr Perinat Epidemiol. Author manuscript; available in PMC 2019 January 01.

Table 3

Agreement between maternal report and medical record for rheumatoid arthritis and asthma medications, according to gestational period.

Medication	Anytime During Pregnancy				First Trimester			
	K (95% CI)	% Agreement[a]	Maternal Report Only, n[b]	Medical Record Only, n[c]	K (95% CI)	% Agreement[a]	Maternal Report Only, n[b]	Medical Record Only, n[c]
Rheumatoid Arthritis, n=216								
Prednisone	0.44 (0.33, 0.55)	71.3	51	11	0.24 (0.12, 0.36)	69.0	56	11
Hydroxychloroquine	0.84 (0.76, 0.93)	94.0	3	10	0.66 (0.54, 0.79)	89.4	10	13
Sulfasalazine	0.83 (0.70, 0.95)	96.8	3	4	0.69 (0.49, 0.88)	95.8	5	4
Adalimumab	0.86 (0.77, 0.95)	95.8	4	5	0.74 (0.61, 0.88)	94.0	7	6
Etanercept	0.90 (0.84, 0.96)	95.4	3	7	0.71 (0.61, 0.81)	88.0	13	13
Ibuprofen	0.32 (0.15, 0.50)	84.3	20	14	0.21 (0.02, 0.40)	87.5	20	7
Aspirin	0.45 (0.27, 0.64)	89.4	16	7	0.22 (0.02, 0.43)	89.8	18	4
Asthma, n=172								
Prednisone	0.53 (0.34, 0.73)	90.1	12	5	0.24 (−0.06, 0.54)	93.6	8	3
Fluticasone	0.47 (0.24, 0.69)	91.9	14	0	0.12 (−0.11, 0.34)	92.4	12	1
Budesonide	0.57 (0.36, 0.77)	91.9	8	6	0.45 (0.15, 0.75)	94.8	7	2
Fluticasone/salmeterol	0.83 (0.73, 0.92)	93.0	10	2	0.47 (0.30, 0.63)	83.7	20	8
Budesonide/formoterol	0.84 (0.71, 0.96)	96.5	4	2	0.45 (0.18, 0.72)	93.6	10	1
Albuterol	0.21 (0.08, 0.35)	64.5	47	14	0.06 (−0.06, 0.18)	48.8	71	17
Montelukast	0.63 (0.46, 0.80)	91.3	10	5	0.28 (0.06, 0.50)	87.2	13	9

Abbreviation: K, kappa; CI, confidence interval.

[a]The number of women who reported the medication and had the medication in any of their medical records plus the number of women who did not report the medication and did not have the medication in any of their medical records divided by the total number of women.

[b]The number of women who reported the medication but did not have the medication in any of their medical records.

[c]The number of women with the medication in any of their medical records who did not report the medication.

Table 4

Kappa values for prednisone among women with rheumatoid arthritis and albuterol among women with asthma by maternal characteristics.

Characteristics	N (%)	K (95% CI)	% Agreement
Rheumatoid Arthritis, n=216			
Enrollment During 1st Trimester	100 (46.3)	0.45 (0.30, 0.60)	38.4
Enrollment After 1st Trimester	116 (53.7)	0.42 (0.25, 0.58)	32.9
Maternal Age ≤30	71 (32.9)	0.40 (0.20, 0.59)	22.7
Maternal Age >30	145 (67.1)	0.46 (0.32, 0.59)	48.6
Primiparous	101 (46.8)	0.44 (0.29, 0.60)	33.3
Multiparous	115 (53.2)	0.43 (0.28, 0.59)	38.0
Body Mass Index of <25 kg/m2	135 (62.5)	0.43 (0.29, 0.56)	44.0
Body Mass Index of ≥25 kg/m2	81 (37.5)	0.45 (0.27, 0.64)	27.3
Health Assessment Disability Index Score at Enrollment <0.25	99 (45.8)	0.35 (0.17, 0.53)	32.4
Health Assessment Disability Index Score at Enrollment ≥0.25	117 (54.2)	0.46 (0.31, 0.60)	38.9
Asthma, n=172			
Enrollment During 1st Trimester	108 (62.8)	0.27 (0.02, 0.51)	25.6
Enrollment After 1st Trimester	64 (37.2)	0.19 (0.02, 0.35)	39.0
Maternal Age ≤30	59 (34.3)	0.14 (−0.08, 0.37)	20.9
Maternal Age >30	113 (65.7)	0.25 (0.08, 0.42)	43.6
Primiparous	104 (60.5)	0.22 (0.04, 0.40)	40.1
Multiparous	68 (39.5)	0.20 (−0.01, 0.41)	24.4
Body Mass Index of <25 kg/m2	84 (48.8)	0.14 (−0.05, 0.33)	29.7
Body Mass Index of ≥25 kg/m2	88 (51.2)	0.29 (0.09, 0.48)	34.9
Asthma Control Test Score at Enrollment <20	49 (28.5)	0.12 (−0.09, 0.33)	19.8
Asthma Control Test Score at Enrollment ≥20	117 (68.0)	0.17 (0.00, 0.34)	41.3

Abbreviation: K, kappa; CI, confidence interval.

Table 5

Sensitivity, specificity, positive predictive value, and negative predictive value for rheumatoid arthritis and asthma medications with maternal report as the reference.

Medication	Sensitivity % (95% CI)	Specificity % (95% CI)	Positive Predictive % Value (95% CI)	Negative Predictive % Value (95% CI)
Rheumatoid Arthritis, n=216				
Prednisone	55.7 (46.5, 64.4)	89.1 (81.5, 93.8)	85.3 (75.6, 91.6)	63.8 (55.6, 71.3)
Hydroxychloroquine	94.2 (84.4, 98.0)	93.9 (89.1, 96.7)	83.1 (71.5, 90.5)	98.1 (94.5, 99.4)
Sulfasalazine	86.4 (66.7, 95.3)	97.9 (94.8, 99.2)	82.6 (62.9, 93.0)	98.5 (95.5, 99.5)
Etanercept	96.2 (89.4, 98.7)	94.9 (89.8, 97.5)	91.6 (83.6, 95.9)	97.7 (93.6, 99.2)
Adalimumab	89.5 (75.9, 95.8)	97.2 (93.6, 98.8)	87.2 (73.3, 94.4)	97.7 (94.3, 99.1)
Ibuprofen	37.5 (22.9, 54.8)	92.4 (87.6, 95.4)	10.5 (6.9, 15.7)	89.5 (84.3, 93.1)
Aspirin	42.9 (26.5, 60.9)	96.3 (92.5, 98.2)	63.2 (41.0, 80.9)	91.9 (87.2, 94.9)
Asthma, n=172				
Prednisone	50.0 (31.4, 68.6)	96.6 (92.3, 98.6)	70.6 (46.9, 86.7)	92.3 (87.0, 95.5)
Fluticasone	33.3 (17.2, 54.6)	100 (97.5, 100)	100 (64.6, 100)	91.5 (86.3, 94.9)
Budesonide	57.9 (36.3, 76.9)	96.1 (91.7, 98.2)	64.7 (41.3, 82.7)	94.8 (90.2, 97.4)
Fluticasone/salmeterol	80.8 (68.1, 89.2)	98.3 (94.1, 99.5)	95.5 (84.9, 98.7)	92.2 (86.2, 95.7)
Budesonide/formoterol	81.8 (61.5, 92.7)	98.7 (95.3, 99.6)	90.0 (69.9, 97.2)	97.4 (93.4, 99.0)
Albuterol	64.9 (56.5, 72.5)	63.2 (47.3, 76.6)	86.1 (78.1, 91.6)	33.8 (23.9, 45.4)
Montelukast	61.5 (42.5, 77.6)	96.6 (92.2, 98.5)	76.2 (54.9, 89.4)	93.4 (88.2, 96.4)

Abbreviation: CI, confidence interval.