Rothschild Claire (Orcid ID: 0000-0002-2419-9881)
Dublin Sascha (Orcid ID: 0000-0002-6649-3659)

Full title: Use of a mobile app to capture supplemental health information during pregnancy: implications for clinical research

Short title: Feasibility of mobile apps for pregnancy research

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Authors:

Claire W. Rothschild, SM[1]; Sascha Dublin, MD, PhD[2]; Jeffrey S. Brown, PhD[3,4]; Predrag Klasnja, PhD[2*]; Chayim Herzig-Marx, PhD[3,4]; Juliane S. Reynolds, MPH[3,4]; Zachary Wyner, MPH[3,4†]; Christina Chambers, MPH, PhD[5]; David Martin, MD, MPH[6‡]

Author affiliations:

1. Department of Epidemiology, University of Washington, Seattle, WA
2. Kaiser Permanente Washington Health Research Institute, Seattle, WA
3. Department of Population Medicine, Harvard Medical School, Boston, MA
4. Harvard Pilgrim Health Care Institute, Boston, MA
5. Department of Pediatrics, University of California, San Diego, La Jolla, CA
6. Office of Medical Policy, Center for Drug Evaluation and Research, U.S. Food and Drug Administration

Corresponding author: Sascha Dublin, address: Kaiser Permanent Washington Health Research Institute, 1730 Minor Ave, Suite 1600, Seattle, WA 98101-1466; phone: 206-287-2870, email: Sascha.Dublin@kp.org

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Key words: cell phone, data collection, patient selection, mobile apps, pregnancy, pregnancy research

[*] Current affiliation: School of Information, University of Michigan, Ann Arbor, MI
[†] Current affiliation: Dana-Farber Cancer Institute, Boston, MA
[‡] Current affiliation: Moderna, Cambridge, MA

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Key points:

- Mobile applications ("apps") may be a low-cost and efficient tool for collecting health information from pregnant women for research, but there is little evidence on feasibility or generalizability of app-based data collection methods.
- In this pilot study using a mobile app to collect data from pregnant women, self-reporting of acute health conditions, over-the-counter medication use, and substance use were common, indicating the potential of mobile apps for capturing data not routinely captured via electronic health records.
- Pilot participants were older, more likely to have had Kaiser Permanente healthcare coverage ≥6 months prior to pregnancy, more likely to report White race, and more likely to have depression than a comparison population of pregnant women from the same healthcare system meeting similar eligibility requirements.
- Future app studies should include pre-specified evaluations to assess generalizability of enrolled populations.

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Abstract (word count: 247/250)

Purpose

Mobile applications (“apps”) may be efficient tools for improving the quality of clinical research among pregnant women, but evidence is sparse. We assess the feasibility and generalizability of a mobile app for capturing supplemental data during pregnancy.

Methods

In 2017, we conducted a pilot study of the FDA MyStudies mobile app within a pregnant population identified through Kaiser Permanente Washington (KPWA), an integrated healthcare delivery system. We ascertained health conditions, medications, and substance use through app-based questionnaires. In a post-hoc analysis, we utilized electronic health records (EHR) to summarize sociodemographic and health characteristics of pilot participants and, for comparison, a pregnant population identified using similar methods.

Results

Six percent (64/1,070) of contacted women enrolled in the pilot study. Nearly half (23/53) reported taking medication for headaches and one-fourth for constipation (13/53) and nausea (12/53) each. Few instances (2/92) of over-the-counter medication use were identified in electronic dispensing records. One-quarter to one-third of participants with depression and anxiety/panic, respectively, reported recently discontinuing medications for these conditions. Eighty-eight percent of pilot participants reported White race (95%CI: 81%-95%), versus 67% of the comparison population (N=2,065). More pilot participants filled ≥1 prescription for antianxiety medication (22% [95%CI: 13%-35%]) and antidepressants (19% [95%CI 10%-31%]) pre-pregnancy than the comparison population (10% and 9%, respectively).

Conclusions

Mobile apps may be a feasible tool for capturing health data not routinely available in EHR. Pregnant women willing to use a mobile app for research may differ from the general pregnant population, but confirmation is needed.

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Purpose

Nearly two-thirds of pregnant women in the U.S. are prescribed at least one medication(1), yet very few medications have high quality evidence for fetal safety.(2, 3) As a result, clinicians and women face challenges when making decisions about treatment during pregnancy.(4) Pregnancy registries, a key source of post-approval safety data, have limitations including low enrollment and possible selection bias.(5) Electronic health records (EHR) are increasingly used to study medication safety, but have limitations including inability to ascertain consumption of filled prescriptions, use of over-the-counter (OTC) medications or illegal substances, and other factors.(6) With 81% smartphone ownership in the U.S., mobile health applications ("apps") present an alternative or supplemental option for data collection to EHR.(7) Understanding how and when app-based data can be used to reduce biases in EHR-based research is critical for leveraging this novel mode of data collection to strengthen pregnancy research.

Several cohort studies among pregnant women have used internet surveys.(8-11) These studies suggest that web-based surveys are feasible for capturing supplemental health information before and during pregnancy.(12, 13) However, these cohorts also indicate that participants willing to participate in web-based research may differ from general pregnant populations in terms of sociodemographics, clinical characteristics, and health behaviors, raising questions about generalizability. Women enrolled in the Danish Snart Gravid cohort were more likely to be primiparae, nonsmokers, and <25 or ≥35 years old relative to all Danish women with contemporaneous births.(14) Participants in the Dutch Pregnancy and Infant Development (PRIDE) cohort who completed web-based questionnaires were more likely to be primiparae and to have higher educational attainment than those who chose to complete paper surveys.(15)

Less is known about the utility of mobile apps for pregnancy research. Mobile apps are distinct from web-based apps in terms of design, usability, and access requirements.(16) Furthermore, nearly 40% of Americans access the internet primarily through a smartphone and 17% have "smartphone-only" internet access, emphasizing the potential role of research tools specifically designed for phone users.(7) It is plausible that both the participants and the data captured via mobile apps may differ from that of web-based research platforms, but evidence is limited. To our knowledge, a single study, the Healthy Pregnancy Research App, has described a pregnant population willing to participate in app-based research data collection.(17)

The Food and Drug Administration (FDA) developed the FDA MyStudies app, an open-source, customizable and reusable mobile data collection platform to capture patient-reported

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data to supplement clinical trial data, electronic health data, or other data sources used for research.(18, 19) In 2017, we conducted a pilot study of the FDA MyStudies app in pregnant women as a "proof-of-concept" in order to assess acceptability, usability, and feasibility of linking mobile app data to EHR data. We describe utility of the FDA MyStudies app pilot study for capturing supplemental data on chronic and acute health conditions, medication use, and other health behaviors during pregnancy. We assess generalizability through a post-hoc, hypothesis-generating analysis in which we describe women who enrolled in the FDA MyStudies app pilot study and, for comparison, a contemporaneous pregnant population from the same healthcare system identified using very similar methods.

Methods

Study population and data collection

The 2017 pilot study was conducted within Kaiser Permanente Washington (KPWA), an integrated healthcare delivery system in the U.S. Eligible participants were identified from the KPWA EHR as currently pregnant and <36 weeks gestational age (identified via estimated delivery date [EDD] recorded in the EHR), 18-45 years old, English-speaking, and enrolled in KPWA for ≥1 month before their estimated last menstrual period (LMP). Women were excluded in the case of possible miscarriage or pregnancy loss recorded in the EHR or if they were insured by Medicaid; the latter exclusion was made in order to ensure completeness of the EHR since Medicaid enrollees may be missing data on prescription fills or healthcare utilization. A random sample of 1,070 eligible patients, stratified by trimester in order to include women at varying stages of pregnancy, was contacted to participate by mail. Study invitations were sent in two waves, in September and October 2017. Recruitment efforts ended when the pre-specified enrollment target of 50 participants was exceeded. Mailed study materials described the aim of the pilot study as assessing medication use during pregnancy. They included an enrollment token that women used to enroll and which allowed investigators to link app data to the EHR. A random subset of 50% received a follow-up phone call as a pre-planned exercise to examine whether this increased enrollment. Participants received no incentives for enrollment.

To enroll in the pilot, women downloaded the app from the Apple App or Google Play stores using an Android or iOS mobile phone and completed an app-based consent process. Participants were then able to complete baseline questionnaires about sociodemographics, pregnancy history, and medical conditions. Patients received additional questionnaires over a 3-month follow-up period. Additional details of the study design are reported elsewhere.(18, 19) The study was approved by the KPWA Institutional Review Board (IRB).

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Feasibility of app-based data as a supplemental data source for pregnancy research

We present descriptive summaries of pilot participants' self-reported acute and chronic health conditions, medication use, and substance use including use of alcohol and marijuana (legal in Washington State). To assess chronic health conditions, women were asked to select all conditions that she had been told she had by a doctor or other healthcare provider. For acute conditions, participants were asked about specific symptoms and conditions during pregnancy. Women were next asked about medication use for each reported chronic and acute condition. For chronic conditions, women were asked at baseline if they had stopped medications for the condition in the past year or, in recurrent questionnaires, since the last time she answered the question in the app. Details are provided in the Supplementary Material. For all analyses, we used a complete case approach and included all available data from both baseline and recurrent questionnaires.

For common OTC and prescription medications, we categorized participant reports of medication use as either self-reported only or as identified through both self-report and EHR dispensing records. We captured dispensing records occurring prior to study enrollment (110 days for chronic and 30 days for acute conditions) through study completion to ensure complete ascertainment of dispensed medications. Since women were enrolled at a variety of gestational ages and may have responded to multiple questionnaires over follow-up, summary statistics represent neither incidences or prevalences, but rather illustrate participants' willingness to respond to specific topics and response patterns for the purposes of hypothesis generation.

Generalizability of mobile app pilot participants

To assess generalizability, it would be ideal to directly compare pilot participants to women who declined participation. However, the KPWA IRB determined that women who declined participation could not be directly studied for ethical reasons. We attempted to identify an appropriate comparator population by applying the original inclusion/exclusion criteria to the KPWA EHR to identify pregnant women who could have been eligible for participation, but extending the allowable time window for the EDD from March 2017 to June 2018 to obtain a larger sample. (Eligible women contacted to participate had EDDs from October 2017 to July 2018.) Women who enrolled in the pilot were excluded, resulting in an EHR population of pregnant women who met eligibility criteria, including women who declined participation and those who were never approached. To improve completeness of data about pre-pregnancy

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characteristics, we removed from both populations women covered by KPWA for <6 months pre-pregnancy for this descriptive comparison.

Using EHR data, we summarized sociodemographic and clinical characteristics before and during pregnancy. To assess medication use, we first retrieved all EHR pharmacy dispensing records occurring during and in the 6 months prior to pregnancy and then categorized each identified medication by therapeutic class (additional details are included in the Supplementary Material). Beginning of pregnancy was identified as the last menstrual period, calculated by subtracting 280 days from the estimated delivery date recorded in the EHR. We calculated 95% confidence intervals (CI) for estimates in the pilot participant sample based on distributions appropriate to variable type (Normal, Poisson, and binomial for continuous, count, and binary variables, respectively, and Sison Glaz simultaneous confidence intervals for categorical variables(20)). Because the comparator population comprised all eligible pregnant women not enrolled in the MyStudies pilot, estimates for this group are not subject to sampling error and therefore we did not calculate CIs for these estimates. We identified characteristics in which the pilot sample might have differed from the comparator population by determining if the comparator population estimate fell within the CI of the pilot sample.

Results

Overall, 6% (64/1,070) of women contacted to participate downloaded the MyStudies app and provided informed consent to enroll in the pilot study, hereafter referred to as pilot participants. Among women who received a phone call, 8% enrolled (versus 4% who were contacted only by mail). Completion of app-based questionnaires ranged from 91% (58/64) for the chronic health conditions survey to 61% (39/64) for questions related to use of alcohol, marijuana or cannabis, and other recreational drugs (Figure 1).

Among 48 participants who completed an app-based sociodemographic questionnaire, mean maternal age was 33.5 years old (range: 23-43), with 81% (39/48) reporting White race and 94% (45/48) having a 4-year college degree or higher educational attainment (data not shown). Anxiety or panic attacks and depression were the most commonly reported chronic health conditions reported by participants in the app-based questionnaires, with one-third (19/58) of pilot participants reporting anxiety or panic attacks and 28% (16/58) reporting depression at least once during the pilot (Table 1). Nearly one-fifth (11/58) of participants reported antianxiety medication use during pregnancy, while one-third of those with anxiety (6/19) reported medication discontinuation in the past year. Twelve percent (7/58) of all

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participants reported using antidepressants during pregnancy, with one-quarter of women with depression (12/28) reporting antidepressant discontinuation in the past year. Over half of pilot participants reported experiencing nausea (38/53), cold-like symptoms (35/53), constipation (34/53), headaches (34/53), and sleeping problems (28/53) during pregnancy. Nearly half of all participants (23/53) reported using medications for headaches, 25% (13/53) for constipation, and 23% (12/53) for pregnancy-related nausea. Most episodes of self-reported use of common prescription medications were corroborated through EHR dispensing records (Table 2). Dispensing records for OTC medication use were uncommon, with 2 occurrences of concordance among 92 total reported instances of OTC medication use.

Most (85%, 33/39) participants reported using alcohol before pregnancy, with 18% (7/39) reporting alcohol use at least once during pregnancy. Marijuana/cannabis use was reported by 26% (10/39) before and 5% (2/39) during pregnancy (Table 3). Several women reported use of cigarettes (2%, 1/47), e-cigarettes (2%, 1/45), or other recreational drugs (3%, 1/39) during pregnancy.

For the purposes of assessing generalizability relative to the KPWA EHR population, we present EHR data on sociodemographic and clinical characteristics of 58/64 (91%) pilot participants who were covered by KPWA for ≥6 months prior to pregnancy (Table 4). An additional 2,664 women who would have met eligibility criteria for the pilot study were identified from the KPWA EHR, of whom 2065 (78%) were KPWA members ≥6 months pre-pregnancy. Among these 58 pilot participants, median gestational age at study enrollment was 21.1 weeks (mean 21.3, interquartile range 15.4-26.9). Relative to the EHR population, pilot participants were older [mean age 33 (95%CI 32.4-34.0), compared to 31 years], with a higher proportion of White participants (88% [95%CI 81-95] vs. 67%) and a similar proportion Hispanic (7% [95%CI 2%-17%] vs. 8%) (Table 4). Depression diagnoses were more prevalent among pilot participants (34% [95%CI 22%-48%]) relative to the EHR population (20%). A higher proportion of pilot participants filled at least 1 prescription for antianxiety medication (22% [95%CI 13%-35%]) and antidepressants (19% [95%CI 10%-31%]) within 6 months pre-pregnancy, versus the EHR population (10% and 9%, respectively). Pilot participants had higher outpatient healthcare utilization in the 6 months prior to pregnancy, with a mean of 5.1 outpatient visits (95%CI 4.5-5.7) compared to the EHR population's mean 3.1 outpatient visits. The groups appeared comparable in terms of body mass index; selected comorbidities; and pre-pregnancy emergency department utilization.

Conclusions

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Findings from this pilot study suggest that mobile apps may be a useful tool for supplementing EHR and other existing data sources for clinical research, and may be particularly important for capturing information on acute conditions of pregnancy for which women often do not seek medical care but self-treat with OTC medications.(21) Here, we find a substantial proportion of pregnant women reporting and taking medication for acute conditions such as colds, constipation, nausea, and headaches, data which are infrequently captured in EHR.(22) EHR capture of substance use is similarly poor: alcohol use, for example, is typically identified only through recorded diagnoses for alcohol use disorders.(23) Here, alcohol use disorders were identified via the EHR for no pilot participants with ≥6 months KPWA coverage and only 1% of the EHR population. By contrast, nearly one-fifth of pilot respondents reported consuming alcohol at least once during pregnancy, an exposure that may be relevant for studies of medication safety. Participants also seemed willing to self-report sensitive health behaviors, with several reports of marijuana or cannabis use, which is legal for recreational use in Washington State.

Our results also suggest utility of mobile apps for improved ascertainment of prescription medication use during pregnancy. While most reported prescription medication use was also identified in dispensing records, we found that a substantial proportion of women with chronic conditions – from one-quarter of women experiencing depression to one-third experiencing anxiety or panic attacks – reported recently discontinuing medication use for these conditions. Evidence on concordance between self-reported and EHR medication use in pregnant populations is mixed, with several studies finding moderate to poor adherence to psychotropic medications during pregnancy (24, 25). Here, a formal analysis of concordance between self-report and dispensed medications, including interviewing women to resolve apparent discrepancies, was not practical given the small sample size. However, the findings of common self-reported discontinuation of medications for anxiety and depression suggest that mobile apps could be useful for reducing misclassification of specific prescription medications. This may be of particular concern if pregnant populations are more likely than the general population to “self-discontinue” medications over concern for fetal safety without informing their healthcare provider.

Despite the potential of mobile apps as a supplemental data source, low enrollment in this pilot study (6% of contacted women) raises concerns about generalizability. We find that such women may differ in sociodemographic and clinical characteristics from their pregnant counterparts in the source population. Notably, pilot participants were older than the EHR population. The Healthy Pregnancy Research Program enrolled older women relative to national

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estimates of age at first pregnancy.(17) However, a study conducted within two German university hospitals found that younger pregnant women were more likely than older women to use consumer-focused pregnancy apps.(26) These mixed findings may be explained by the fact that women willing to use a research app may differ from users of consumer-focused pregnancy apps.(26) Women who participated in our pilot study were also more likely to have been covered by KPWA for at least 6 months pre-pregnancy and had higher pre-pregnancy outpatient healthcare utilization, suggesting that patients who are more invested in a healthcare system may be more willing to participate in research. Unlike the Healthy Pregnancy Research Program which enrolled a similar proportion of White participants to national averages, a higher proportion of our pilot participants were White compared with our EHR population.(17) The proportion with Hispanic ethnicity did not differ. Possible explanations for the observed differences by race include differences in willingness to participate in research generally, unmeasured differences in socioeconomic status, and sampling variability.

We also found that depression diagnosis and filling of antianxiety and antidepressant medications were higher among pilot participants. We hypothesize this was driven by increased interest in the study among women using medications. Two studies of consumer health app users found higher app use among women who felt the app was relevant to their own health conditions, behaviors, or goals.(27, 28) In the FDA MyStudies pilot study, recruitment materials described the study as focused on medication use during pregnancy, and recruitment phone calls revealed that some eligible women did not initially enroll because they believed the study would only be interested in recruiting women taking medications.

Our study has a number of strengths. We report on data captured through a novel data collection platform, the FDA MyStudies app. Linkages with KPWA EHR data allowed us to describe patterns of concordance between self-reported use and dispensed medications. Although we could not directly compare women who accepted versus declined participation in the pilot study for ethical reasons, we were able to identify and describe a well-defined population of women from the same healthcare system who would have been eligible to participate, using similar methods as the pilot study.

Our study also has several limitations. While the small sample size is appropriate for a proof-of-concept pilot study, it did not allow for precise estimation of prevalence of self-reported health conditions or medication use during pregnancy, nor for a formal assessment of concordance of self-reported medication use with EHR medication data. Non-response to the app-based surveys was high, particularly for several questionnaires related to substance use. It is plausible that participants engaging in stigmatized behaviors may be less likely to respond,

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which would result in underestimates of substance use from app-based data. Non-response may also be influenced by the order in which questionnaires were administered, with higher non-response observed in later questionnaires. While 19 participants who completed qualitative "exit" interviews generally reported high levels of comfort navigating the app, several commented that logging back into the app was time-consuming (possibly due to participants choosing to enable an optional passcode protection). We would expect resulting non-response to be non-differential with respect to outcomes of interest, but additional research is warranted. Also, a pre-specified plan to assess generalizability of the enrolled sample was not included in the pilot. While we observed some suggestive differences between app participants and the EHR population, crude differences between groups should be interpreted with caution due to the lack of adjustment for possible confounders and small samples. We were also not able to empirically assess generalizability, such as by estimating well-characterized exposure-outcome relationships among pilot participants.(14)

Mobile apps have great potential to improve evidence on medication? safety during pregnancy, but studies relying on mobile apps could have limited generalizability if participation rates are low. Use of recruitment materials that are carefully designed to appeal to the broader target population may also be a promising strategy for increasing enrollment. Research studies utilizing apps could also improve inference by incorporating assessments of generalizability at multiple points in the research continuum. In the design phase, real-time identification of low participation among specific groups could be used to iteratively refine enrollment and retention strategies. Pre-specified efforts to identify characteristics of non-participants may also allow reweighting of the final enrolled sample to better reflect characteristics of the population of interest.(29) Participation in a mobile app for research is affected by many factors, including method of study recruitment, financial or other incentives for participation, smartphone ownership, and willingness to participate in research, as well as interest in engaging with an app. Any of these steps could affect generalizability. Future research is required to disentangle factors that influence participation as well as to establish best practices in participant recruitment and retention in app-based research.

Conflict of Interest

The authors have no conflicts of interest to declare.

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Tables

Table 1. Self-reported chronic and acute health conditions during pregnancy

Panel A. Chronic health conditions (N=58)	**Reported condition** n (% of total sample)	**Reported medication use for condition during pregnancy** n (% of total sample)	**Discontinued medication use for condition in the past year** n (% of those with condition)
Anxiety or panic attacks	19 (33%)	11 (19%)	6/19 (32%)
Depression	16 (28%)	7 (12%)	4/16 (25%)
Migraine	7 (12%)	1 (2%)	1/7 (14%)
Asthma	3 (5%)	3 (5%)	1/3 (33%)
Hypothyroidism	2 (3%)	2 (3%)	0/2 (0%)
Panel B. Acute health conditions (N=53)			
Cold-like symptoms	35 (66%)	9 (17%)	
Fever	5 (9%)	0 (0%)	
Constipation	34 (64%)	13 (25%)	
Gastroenteritis	17 (32%)	4 (8%)	
Headaches	34 (64%)	23 (43%)	
Pregnancy-related nausea	38 (72%)	12 (23%)	
Sleeping problems	28 (53%)	5 (9%)	
Allergies (indoor or outdoor)	10 (19%)	8 (15%)	
Urinary tract infection	3 (6%)	3 (6%)	
Vaginal yeast infection	3 (6%)	3 (6%)	

Notes: Percentages of participants reporting a condition and using a medication for the condition are calculated out of the total number of distinct participants in the analysis. Row percentages for medication discontinuation are calculated out of the total number of women reporting the specific health condition. Panel A: analysis includes 58 pilot participants who completed either a baseline medical condition history or recurrent current medical condition information survey at least once. Panel B: analysis includes 53 pilot participants who completed either a baseline questionnaire on short-term illness history during pregnancy or a recurrent survey on recent short term illnesses. Women were defined as reporting the condition, reporting medication use, and reporting medication discontinuation if they ever responded “yes” to corresponding items in any completed surveys (either at baseline or during follow-up).

Table 2. Self-reported use of common OTC and prescription medications with corresponding KPWA dispensing records

Medication (condition)	Patient-reported only n	Both patient report and KPWA EHR dispensing record n
Panel A. Over-the-counter (OTC) medications		
Acetaminophen	22	1
Ranitidine	9	1
Tums	10	0
Unisom	7	0
Ibuprofen	3	0
Docusate	5	0
Panel B. Prescription medications		
Sertraline	2	8
Ondansetron	0	5
Levothyroxine	0	2
Fluticasone	0	1
Nitrofurantoin	0	1

Notes: Women were asked to report chronic and acute health conditions at baseline and via recurrent surveys. Participants who reported health conditions were asked about medication use for each condition, as well as if they had recently stopped taking medication for the condition. Analysis comprises all medications reported as being currently used by pilot participants, as identified through responses to two baseline surveys (one on medical conditions history [58 completed surveys among 58 participants] and one on short term illness history [54 completed surveys among 53 participants] during pregnancy) and two recurrent surveys (on current medical conditions [106 completed surveys among 39 participants] and recent short term illnesses [92 completed surveys among 36 participants]). For medications for chronic conditions, EHR dispensing records were included spanning 110 days prior to the participant's app start date until the app's closing date; for acute conditions, the time span was 30 days prior to app start date until the app's closing date.

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Table 3. Self-reported substance use before and during pregnancy

Substance use:	*N*	Before pregnancy n (%)	At least once during pregnancy n (%)
Alcohol	39	33 (85)	7 (18)
Cigarettes	47	2 (4)	1 (2)
E-cigarettes	45	2 (4)	1 (2)
Marijuana or cannabis	39	10 (26)	2 (5)
Other recreational drugs	39	1 (3)	1 (3)

Notes: Sample sizes are the number of distinct participants who responded to either a baseline or recurrent questionnaire on use of the specific substance at least once during the pilot study. Substance use before pregnancy was captured in a single baseline questionnaire, in which participants were asked, “did you [use specific substance, e.g. “smoke cigarettes”] before becoming pregnant?” Substance use during pregnancy was captured both in the baseline questionnaire by the question, “have you [smoked cigarettes] since you became pregnant?” and during recurrent questionnaires on current exposures during pregnancy using the question, “have you [smoked cigarettes] since you last answered this question in this app?”. Women who completed the current exposure questionnaire multiple times are defined based on all reported data. Use of “other recreational drugs” was assessed by asking women about use of “recreational or ‘street’ drugs.”

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Table 4. Characteristics of FDA MyStudies App Participants and a Comparison EHR Pregnant Population

	Pilot Participants (N=58)		EHR Population (N=2065)
	n (%) or mean	(95% CI)	n (%) or mean
Sociodemographic characteristics			
Age (at LMP, in years)	33	(32.4-34.0)	31
Age category (at LMP, in years)			
18-24	0 (0%)	(0-14%)	272 (13%)
25-29	8 (14%)	(2-28%)	499 (24%)
30-34	30 (52%)	(40-66%)	803 (39%)
35-39	19 (33%)	(21-47%)	415 (20%)
≥40	1 (2%)	(0-16%)	76 (4%)
Race			
White	51 (88%)	(81-95%)	1390 (67%)
Black/African American	0 (0%)	(0-7%)	132 (6%)
Asian	4 (7%)	(0-14%)	230 (11%)
American Indian/Alaskan Native	1 (2%)	(0-9%)	16 (0.7%)
Native Hawaiian/Pacific Islander	0 (0%)	(0-7%)	29 (1%)
Multiple races	1 (2%)	(0-9%)	110 (5%)
Other	1 (2%)	(0-9%)	92 (4%)
Unknown or not reported	0 (0%)	(0-7%)	66 (3%)
Hispanic ethnicity[a]	4 (7%)	(2-17%)	154 (8%)
KPWA coverage			
Duration of pre-pregnancy KPWA coverage (months)	24	(19-28)	24
Covered ≥12 months pre-pregnancy	52 (90%)	(79-96%)	1787 (87%)
Covered for entirety of pregnancy	55 (95%)	(86-99%)	1907 (92%)
Clinical characteristics			
BMI (kg/m^2)[b]	26.5	(24.8-28.2)	26.8
Comorbid conditions before or during pregnancy			
Anxiety[c]	19 (33%)	(21-46%)	474 (23%)
Depression[c]	20 (34%)	(22-48%)	417 (20%)
Hypertension[d]	0 (0%)	(0-6%)	17 (0.8%)
Diabetes[d]	0 (0%)	(0-6%)	27 (1%)
Alcohol use disorder[c]	0 (0%)	(0-6%)	28 (1%)
Healthcare utilization before and during pregnancy			

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Outpatient visits in 6 months prior to pregnancy	5.1	(4.5 – 5.7)	3.1
Emergency department visits in 6 months prior to pregnancy	0.05	(0.01 – 0.15)	0.09
Medication use before and during pregnancy			
≥1 prescription medication fills in the 6 months prior to pregnancy			
Antianxiety medication	13 (22%)	(13-35%)	198 (10%)
Antidepressant	11 (19%)	(10-31%)	185 (9%)
Antihypertensive	0 (0%)	(0-6%)	0 (0%)
Opioid	9 (16%)	(7-27%)	254 (12%)
Proton pump inhibitor	1 (2%)	(0-9%)	33 (2%)
Asthma	2 (3%)	(0.4-12%)	72 (3%)
Sleep medication	0 (0%)	(0-6%)	10 (0.5%)
≥1 prescription medication fills during pregnancy			
Antianxiety medication	12 (21%)	(11-33%)	173 (8%)
Antidepressant	8 (14%)	(6-25%)	147 (7%)
Antihypertensive	1 (2%)	(0-9%)	32 (2%)
Opioid	7 (12%)	(5-23%)	291 (14%)
Proton pump inhibitor	1 (2%)	(0-9%)	26 (1%)
Asthma	2 (3%)	(0.4-12%)	114 (6%)
Sleep medication	0 (0%)	(0-6%)	12 (0.6%)

LMP = last menstrual period

Notes: 95% confidence intervals for binary variables were calculated using the binomial exact method with estimates bounded by 0, 1, and one-sided 97.5% intervals provided for estimated proportions of 0 (0/58); simultaneous confidence intervals for factor variables (age, race) were estimated using the method proposed by Sison and Glaz; for continuous variables, 95% confidence intervals were constructed using the Wald method assuming Normality; for count variables (number of outpatient and ED visits), exact 95% confidence intervals of means were constructed specifying a Poisson distribution. Confidence intervals are not provided for the EHR population, as this group represents the entirety of the pregnant population. [a]n=1995 in EHR population due to 70 observations with unknown ethnicity; [b]n=1963 in EHR population due to missing values; BMI captured at the most recent pre-pregnancy visit with complete data on height and weight or at the earliest visit during pregnancy (if pre-pregnancy BMI not available); [c]Depression, anxiety and alcohol use disorders were assessed during the 1 year prior to the LMP through delivery; [d]Chronic (non-gestational) hypertension and diabetes were assessed during the 2 years prior to the LMP; codes were reviewed through 140 days post-LMP to capture chronic hypertension and diabetes but excluding gestational hypertension and diabetes. Prescription medications assessed for each reported condition are provided in the Supplementary Material.

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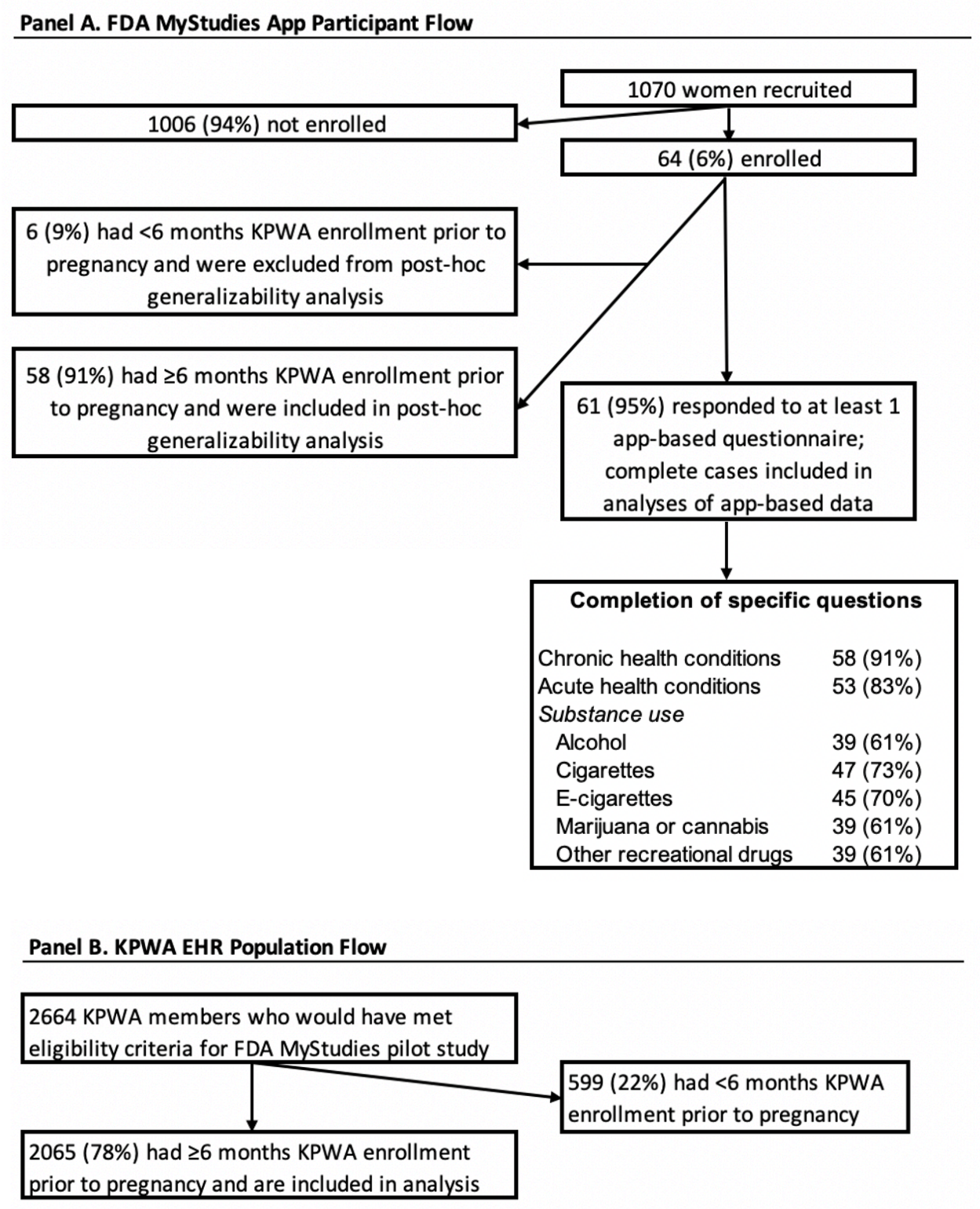
Figure 1. Study Flow



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