Assessment of Assisted Reproductive Technology Use Questions: Pregnancy Risk Assessment Monitoring System Survey, 2004

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ABSTRACT

Objective. Women who conceive with the assistance of fertility treatments are at increased risk for multiple-gestation pregnancies and accompanying adverse pregnancy outcomes. The Pregnancy Risk Assessment Monitoring System (PRAMS) can be used to assess outcomes associated with fertility treatments, but a previous study suggested that PRAMS questions about fertility treatments overestimated use of assisted reproductive technology (ART) by 2.6 times. These PRAMS ART questions were revised in 2004. We compared prevalence estimates based on revised questions with counts from the National ART Surveillance System (NASS), the standard for describing ART prevalence.

Methods. We compared weighted PRAMS prevalence estimates of births conceived by using ART with corresponding counts from NASS for three states (Florida, Maryland, and Utah) for 2004. We also compared these data by age, parity, plurality, and infant birthweight.

Results. Estimated ART births determined from PRAMS totaled 3,672 (95% confidence interval 2,210, 5,134), compared with 2,939 ART births reported to NASS. PRAMS estimates and NASS counts differed by maternal age ($p=0.02$) and parity ($p<0.01$). For example, PRAMS responses from women aged ≥40 years overestimated ART use by 70% (27.9% vs. 16.5%, $p<0.01$).

Conclusions. Revised PRAMS questions better estimate numbers of ART births than earlier PRAMS questions. PRAMS data are useful to describe behaviors and outcomes associated with ART use.

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Reports of assisted reproductive technology (ART) use in the United States have more than doubled in the past decade; more than 138,000 procedures were reported in 2006.[1] These procedures resulted in 41,343 deliveries of 65,656 infants, comprising an estimated 1.2% of all live births that occurred in 2006 in the U.S. The increased use of ART for conception among people with infertility issues is of interest because of adverse health outcomes reported for ART pregnancies and births. ART has been associated with an increased rate of multiple-gestation pregnancies, which increases risk for preterm delivery, low birthweight (<1,500 grams), infant death, and long-term disability among infant survivors.[2–6] ART has also been linked to low birthweight, preterm delivery, and birth defects among single-gestation pregnancies.[7–11]

Currently, three population-based data sources are available in the U.S. to examine ART prevalence and associated risks: the National ART Surveillance System (NASS), vital records, and the Pregnancy Risk Assessment Monitoring System (PRAMS). Each of these data systems has strengths and limitations. The most well-known source of ART information is NASS, established in response to the Fertility Clinic Success Rate and Certification Act of 1992.[12] NASS is a system in which U.S. providers are mandated by Congress to report data annually to the Centers for Disease Control and Prevention (CDC) for all ART treatments performed and all pregnancies and live births resulting from these treatments.[1] Because of the federal mandate, the reporting level is high (89% in 2004), and NASS is a near complete source of data on ART treatments in the U.S. However, ART providers typically do not provide prenatal care once a pregnancy is established. While NASS providers actively follow up with women to ascertain pregnancy outcomes, they obtain only limited information on pregnancy and perinatal risks and outcomes. Thus, although NASS has complete data on whether a live birth occurred, the date of birth, plurality, and infant birthweights, it lacks data on specific pregnancy complications and prenatal maternal behaviors such as maternal smoking.

A second source of data is vital records.[13] Birth records and fetal death certificates capture information on various maternal medical and behavioral characteristics, pregnancy outcomes, and newborn morbidity and mortality. However, vital records data do not include post-discharge infant care and morbidity. To date, only 19 states have adopted the revised birth certificate that captures data on ART use. Moreover, a recent validity analysis in Massachusetts suggests that the current method of birth certificate reporting based on prenatal care record review likely leads to incomplete data; the sensitivity of ART reporting on the birth certificate was 27%.[14]

The third data source is PRAMS, an ongoing surveillance system maintained by CDC. PRAMS collects state-specific, population-based data on various maternal attitudes and experiences before, during, and shortly after pregnancy.[15] Topics addressed in the PRAMS core questionnaire include barriers to and content of prenatal care, obstetric history, maternal use of alcohol and cigarettes, physical abuse, contraception, economic status, maternal stress, and early infant development and health status. PRAMS offers a unique opportunity to combine vital records data and behavioral survey data. (This surveillance system is further described in the Methods section of this article.)

An ART question was first added to PRAMS in 2000. Examination of this initial ART data item indicated that PRAMS respondents in five states likely overreported use of ART to conceive the index pregnancy. The PRAMS estimated that the number of births resulting from ART was 2.6 times higher than the NASS count based on data from the same states and time period.[16] One likely explanation for the discrepancy was that these PRAMS questions lacked specificity on the timing of ART use; thus, some respondents may have reported ART use that occurred many months or years prior to the index pregnancy, even if ART was not the eventual mode of conception. The ART questions were revised in 2004, and different states elected to include the fertility treatment items in their questionnaire. Our analysis attempts to assess and compare estimates of ART use items on the 2004 revision of the PRAMS survey with data from NASS.

METHODS

PRAMS

Thirty states participated in PRAMS in 2004, representing 62% of births in the U.S. that year.[15] We used data from 2004 because the revised questions assessing ART use were implemented that year. The sampling frame for selection for PRAMS participation is derived from the state birth certificate file. Approximately 1,300–3,400 women are sampled in each state per year from the state's birth certificate file, which is a sufficient sample for estimating statewide risk-factor proportions within 3.5% at 95% confidence. Women from some groups, such as mothers of low birthweight infants, are sampled at a higher rate in some states to ensure that adequate data are available for small but high-risk populations. Many states stratify by mother's race or ethnicity as well. Estimated proportions within strata are slightly less precise than statewide estimates, but are typically within 5% at 95% confidence.

Selected women are first contacted by mail two to four months after delivery. If no response is received from repeated mailings, women are contacted and interviewed by telephone. Mothers' responses are linked to extracted birth certificate data items for analysis. Data collection procedures and instruments are standardized to allow comparisons among states, but states can also customize portions of the protocol to tailor procedures to their needs. The standardized data collection methodology is prescribed in CDC's PRAMS Model Protocol, 2009 version.[17]

The specific wording for PRAMS fertility treatment items is presented in Figure 1. The 2000 version (Phase IV, 2000–2003) and the 2004 revision (Phase V, 2004–2008) of the PRAMS questionnaire have the following major differences: (*1*) The Phase V survey contained an item inquiring about the participant's use of *any* medical treatment to aid in conception; the Phase IV survey contained no such item. (*2*) The Phase IV survey included two separate yes/no-response questions describing fertility drug use and ART use, while the Phase V survey included one item inquiring about specific types of fertility treatment from which the respondent could select multiple treatments. (*3*) The Phase V question specified that the participant's response should be based on fertility treatments used during the month of conception; no such instructions were given for the Phase IV item.

The sampling frame for this analysis comprised mother-child pairs included in three PRAMS states (Florida, Maryland, and Utah) during 2004. These states were selected because they chose to include both the general fertility assistance question and the more specific question describing the type of fertility assistance received. Women were included if they indicated that they were trying to conceive at the time they became pregnant, if they responded that they had received medical treatment to help them get pregnant, and if they specified the type of fertility treatment they received (Figure 2). The scope of our analysis was further limited to respondents who reported using ART.

NASS

CDC contracts with Westat, Inc. (Rockville, Maryland) for annual collection of data about ART from all medical centers performing ART procedures in the U.S. and its territories. Data collected include patient demographics, medical history and infertility diagnoses, clinical information pertaining to the ART procedure, and information regarding resulting pregnancies and births. The data file is organized with one record per ART procedure performed; multiple procedures from a single patient are not linked. In 2004, despite the federal mandate, 11% of ART medical centers did not report their 2004 data;[1] however, past internal review of nonreporting medical centers indicates that they are often small practices that went out of business during or shortly after the reporting year and usually treated a relatively small number of patients. Thus, NASS likely captures greater than 90% of all ART treatments in the U.S.

Because the ART surveillance system is organized according to the date of the ART procedure rather than the infant's date of birth, a separate ART data file was created for these analyses. This data file was drawn from two different ART reporting years and comprised (*1*) infants conceived from ART procedures performed in 2003 and born in 2004 (approximately two-thirds of the live-birth deliveries reported to NASS for 2003), and (*2*) infants conceived from ART procedures performed in 2004 and born in 2004 (approximately one-third of live-birth deliveries reported to NASS for 2004).

Data analysis and variable definitions

State-specific and combined estimates of ART use among women with a recent live birth in 2004 from PRAMS (Phase V, 2004–2008) and of births resulting from ART ascertained from NASS were compared for Florida, Maryland, and Utah. We calculated weighted estimates from PRAMS data to account for oversampling on infant birthweight in all states and on maternal age and race in Florida, maternal age in Maryland, and maternal education in Utah. Derived weights also account for nonresponse; thus, weighted estimates obtained from PRAMS data are representative of the total birth population for each state. ART item response rates were high: 88.4% in Florida, 87.6% in Maryland, and 83.0% in Utah. Twenty-seven of 31 (87%) Florida clinics, seven of nine (78%) Maryland clinics, and two of three (67%) Utah clinics reported their 2004 data. NASS data were not adjusted for clinic nonresponse.

Differences between the weighted PRAMS prevalence estimates of ART use among women with a live birth and NASS-reported counts of births resulting from ART use were assessed for the three states combined and for each state by maternal age and parity, plurality, and infant birthweight subgroups. Differences were considered statistically significant if the 95% confidence interval (CI) for the PRAMS estimate did not include the NASS count. Chi-square analyses were conducted to determine if differences existed in variable distributions for ART recipients represented in the two data systems. If the global test was suggestive of a difference between the systems (i.e., $p<0.10$), pairwise Chi-square analyses were also conducted; p-values <0.05 were considered statistically significant.

Figure 1. Comparison of PRAMS Phase IV and Phase V questions about fertility treatment

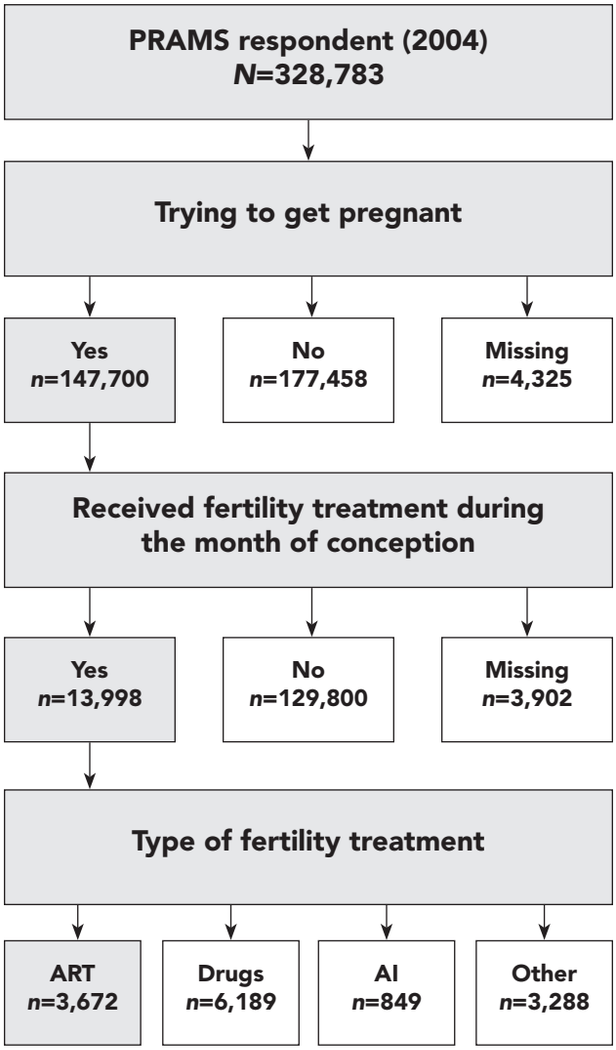
Topic	*Phase IV (2000–2003) questions and response options*	*Phase V (2004–2008) questions and response options*
Pregnancy timing	Thinking back to *just before* you got pregnant, how did you feel about becoming pregnant? Response options: I wanted to be pregnant sooner; I wanted to be pregnant later; I wanted to be pregnant then; I didn't want to be pregnant then or at any time in the future.	Thinking back to *just before* you got pregnant with your *new* baby, how did you feel about becoming pregnant? Check *one* answer. Response options: I wanted to be pregnant sooner; I wanted to be pregnant later; I wanted to be pregnant then; I didn't want to be pregnant then or at any time in the future.
Pregnancy intention	When you got pregnant with your new baby, were you trying to become pregnant? Response options: No; Yes	When you got pregnant with your new baby, were you trying to become pregnant? Response options: No; Yes
Any fertility treatment	NA (question was not asked on the Phase IV questionnaire)	Did you receive treatment from a doctor, nurse, or other health-care worker to help you get pregnant with your new baby? (This may include infertility treatments such as fertility-enhancing drugs or assisted reproductive technology.) Response options: No; Yes
Type of fertility treatment	Did you take any fertility drugs to help you get pregnant with your new baby? (Fertility drugs include Clomid®, Serophene®, Pergonal®, or any other drugs that you may have taken to help you get pregnant.) Response options: No; Yes Did you use any medical procedures (assisted reproductive technology) to help you get pregnant with your new baby? (Assisted reproductive technology procedures include in vitro fertilization [IVF], gamete intrafallopian transfer [GIFT], zygote intrafallopian transfer [ZIFT], embryo transfer, and donor oocytes.) Response options: No; Yes	Did you use any of the following treatments *during the month you got pregnant* with your new baby? Check *all* that apply. Response options: — Fertility-enhancing drugs prescribed by a doctor (fertility drugs include Clomid®, Serophene®, Pergonal®, or other drugs that stimulate ovulation) — Artificial insemination or intrauterine insemination (treatments in which sperm, but NOT eggs, were collected and medically placed into a woman's body) — Assisted reproductive technology (treatments in which BOTH a woman's eggs and a man's sperm were handled in the laboratory, such as in vitro fertilization [IVF], gamete intrafallopian transfer [GIFT], and zygote intrafallopian transfer [ZIFT]).

PRAMS = Pregnancy Risk Assessment Monitoring System

NA = not applicable

PRAMS is based on maternal state of residence; NASS residency data are also based on maternal state of residence, but in cases of missing residency (2.5% in 2004), residency was assumed to be the same as the state in which the ART occurred. PRAMS estimates of maternal age, parity, and plurality were captured from the state-specific birth certificate files; NASS maternal data are based on ART provider records. Maternal age was categorized as <30, 30–34, 35–39, and ≥40 years; parity was grouped as 0, 1, and ≥2. Plurality was described as singleton, twin, or triplet. PRAMS captures data on multiple births only up to triplets; therefore, delivery information captured by NASS was also limited to gestations of order three or fewer.

Figure 2. Flow chart describing respondent inclusion criteria for arrival at analytic sample, PRAMS (Phase V), 2004



PRAMS = Pregnancy Risk Assessment Monitoring System
ART = assisted reproductive technology
AI = artificial insemination or intrauterine insemination

PRAMS estimates of birthweight were also derived from the birth certificate. Birthweight and date of birth data in NASS were collected by active follow-up with ART patients (85%) or their obstetric providers (15%). Birthweight distributions among ART infants born in 2004 are presented by plurality of birth (singleton vs. multiple). All analyses were performed using SAS®-Callable SUDAAN® release 10.0.[18]

RESULTS

Weighted estimates indicated that more than 147,000 PRAMS respondents in Florida, Maryland, and Utah in 2004 reported that they were trying to conceive prior to their most recent pregnancy. Nearly 14,000 (9.5%) respondents also indicated that they had received some type of fertility assistance for their most recent pregnancy. Fewer than 1.0% of women who indicated that they had received any fertility assistance reported that they wanted to become pregnant later or did not want to become pregnant at the time they conceived (data not shown). No respondents who indicated that they had used ART the month they got pregnant reported wanting to become pregnant later or never.

The weighted estimate based on PRAMS respondents indicates that 3,672 (95% CI 2,210, 5,134) women who were residents of the three states and gave birth in 2004 had conceived using ART (Table 1). During the same period, NASS reported that 2,939 women from these states had received ART therapies resulting in a live birth. This difference of 733 women resulted in a ratio of approximately 1.3 (PRAMS:NASS). Overall, the difference between PRAMS prevalence estimates and NASS counts of ART use in 2004 was not statistically significant, as the PRAMS confidence limit included the NASS count.

However, statistically significant differences in reporting of ART use were apparent by certain maternal and infant characteristics (Table 2). For example, ART use was reported 1.7 times more often among PRAMS respondents aged ≥40 years compared with their counterparts represented in NASS (27.9% vs. 16.5%, $p<0.01$). The overall distribution of parity differed among PRAMS respondents compared with NASS respondents ($p<0.01$). Compared with counts derived from NASS data, fewer nulliparous women reported ART in PRAMS ($p=0.02$), while more women with one previous birth ($p=0.03$) or two or more previous births ($p<0.01$) reported ART in PRAMS. ART use was reported 40% less frequently among PRAMS respondents delivering low birthweight infants compared with NASS counts (11.9% vs. 21.1%, $p=0.05$). However, this finding was not statistically significant for singleton deliveries. Further, PRAMS estimates of ART use did not differ from NASS counts for maternal state of residence, plurality, and birthweight among singletons.

DISCUSSION

The validity of PRAMS questions for estimating ART births has improved since the 2004 (Phase V) revision. The wording of a previous Phase IV question appeared to be associated with substantial and significant over-

Table 1. Resident live births resulting from use of ART treatments in Florida, Maryland, and Utah: PRAMS (Phase V) and NASS, 2004

	PRAMS			NASS		
Characteristic	*Weighted estimate* N	*SE*	*95% CI*	*Count* N	*Difference (PRAMS – NASS)*	*Ratio (PRAMS/ NASS)*
Maternal state of residency						
Florida	2,089[a]	686	744, 3,434	1,531	558	1.4
Maryland	1,169	265	640, 1,698	1,152	17	1.0
Utah	414[a]	125	169, 659	256	158	1.6
Total	3,672	746	2,210, 5,134	2,939	733	1.3
Maternal age (in years)						
<30	381[b]	159	69, 693	437	−56	0.9
30–34	1,271	445	400, 2,143	1,060	211	1.2
35–39	997	396	221, 1,773	957	40	1.0
≥40	1,023	426	188, 1,858	485	538	2.1
Previous births (parity)						
0	1,888	523	863, 2,913	2,111	−233	0.9
1	1,114	420	291, 1,937	604	510	1.8
≥2	670[a]	335	13, 1,327	223	447	3.0
Plurality						
Singleton	2,762	679	1,431, 4,093	2,081	681	1.3
Twin	866	312	254, 1,478	805	61	1.1
Triplet	44[b]	22	1, 87	53	−9	0.8
Infant birthweight—all infants (in grams)						
<1,500	171[a]	46	81, 261	109	62	1.6
1,500–2,499	437	68	304, 570	612	−175	0.7
≥2,500	3,064	742	1,610, 4,518	2,182	882	1.4
Infant birthweight—singletons (in grams)						
<1,500	64	32	1, 127	25	39	2.6
1,500–2,499	182	46	92, 276	169	13	1.1
≥2,500	2,516	677	1,189, 3,843	1,865	651	1.4

[a]Unweighted $n<30$

[b]Unweighted $n<20$

ART = assisted reproductive technology

PRAMS = Pregnancy Risk Assessment Monitoring System

NASS = National ART Surveillance System

SE = standard error

CI = confidence interval

reporting, as the PRAMS estimate of ART conception based on this question was 2.6 times higher than expected, compared with the standard NASS count.[16] In contrast, the estimate reported here based on the revised question was much closer to the NASS standard.

Overreporting of ART use in PRAMS may still exist for some groups, including older women and women with no prior pregnancies. However, our ability to assess subgroup differences was limited because of small numbers. The noted discrepancies in ART data may result from some PRAMS respondents' broad understanding of what constitutes ART vs. the specific procedures considered to be ART. However, we scanned text fields associated with reporting of "other" fertility treatments for possible misclassification on PRAMS but failed to find any obviously erroneous data. Additionally, despite revised questions, some women may still report ART from a previous birth as opposed to their most recent pregnancy. However, Phase V PRAMS introduced changes in wording of the question about type of fertility assistance and added a specific time for the reproductive assistance (i.e., "during the month you got pregnant"). This modification, along with the addition of a question asking whether the

Table 2. Distribution of maternal sociodemographic and pregnancy characteristics and infant birthweight among recipients of ART in Florida, Maryland, and Utah: PRAMS (Phase V) and NASS, 2004

Characteristic	*PRAMS (Weighted n=3,672) Weighted percent (95% CI)*	*NASS (n=2,939) Percent*	*P-value (χ^2)*	*Difference (PRAMS – NASS)*	*Ratio (PRAMS/ NASS)*
Maternal state of residency			0.28		
Florida	56.9 (38.6, 73.4)[a]	52.1		4.8	1.1
Maryland	31.8 (18.8, 48.6)	39.2		−7.4	0.8
Utah	11.3 (5.7, 21.0)[a]	8.7		2.6	1.3
Maternal age (in years)			0.02		
<30	10.4 (4.4, 22.7)[b]	14.9	0.24	−4.5	0.7
30–34	34.6 (18.5, 55.2)	36.1	0.81	−1.5	1.0
35–39	27.2 (13.0, 48.1)	32.6	0.34	−5.4	0.8
≥40	27.9 (13.1, 49.6)	16.5	<0.01	11.4	1.7
Previous births (parity)			<0.01		
0	51.4 (32.2, 70.3)	71.9	0.02	−20.4	0.7
1	30.3 (15.3, 51.2)	20.6	0.03	9.8	1.5
≥2	18.2 (7.1, 39.5)[a]	7.6	<0.01	10.7	2.4
Plurality			0.60		
Singleton	75.2 (57.0, 87.4)	70.8		4.4	1.1
Twin	23.6 (11.6, 42.0)	27.4		−3.8	0.9
Triplet	1.2 (0.4, 3.4)[b]	1.8		−0.6	0.7
Infant birthweight—all infants (in grams)			0.08		
<1,500	4.7 (2.4, 8.7)[a]	3.8	0.64	0.9	1.2
1,500–2,499	11.9 (7.3, 18.9)	21.1	0.05	−9.2	0.6
≥2,500	83.4 (74.5, 86.7)	75.2	0.34	8.3	1.1
Infant birthweight—singletons (in grams)			0.52		
<1,500	2.3 (0.8, 6.7)	1.2		1.1	1.9
1,500–2,499	6.6 (3.4, 12.6)	8.2		−1.6	0.8
≥2,500	91.1 (83.7, 95.3)	90.6		0.5	1.0

[a]Unweighted $n<30$

[b]Unweighted $n<20$

ART = assisted reproductive technology

PRAMS = Pregnancy Risk Assessment Monitoring System

NASS = National ART Surveillance System

CI = confidence interval

respondent received *any* type of fertility assistance, may have improved the respondents' comprehension of the question, thereby improving the accuracy of ART reporting. The importance of question construction, testing, and validation must be stressed for others using this or a similar methodology.[19]

Strengths and limitations

The presentation of prevalence data, coupled with the distributions of the variables under consideration, is a strength of this analysis. The prevalence data enable readers to assess whether PRAMS overestimates or underestimates ART use among various subgroups, and the distributions show *how* the differences in estimates are distributed. One limitation we note is that PRAMS and NASS are not linked data systems; thus, different ART cycles are possibly represented in the two surveillance systems. However, great care was taken to ensure that the data used were similar regarding the delivery date, maternal state of residence, and demographic and pregnancy-related characteristics of the women selected for inclusion. Despite these steps, this analysis is ultimately limited to a comparison of ART prevalence estimates from the two systems and is not a true validation study. Although we cannot be certain that the increase in agreement of PRAMS ART estimates with NASS counts was due to revision of the ART questions, the population under study probably did not change sufficiently during four years to result in the observed improvement in agreement between the two systems.

Another potential limitation of this analysis is the exclusion of stillbirths, fetal deaths, and abortions from the PRAMS sampling frame. If ART resulted in an increased risk of congenital anomalies or other defects inconsistent with life, this exclusion would also alter the validity of our findings because these losses would not be included in the PRAMS sample. However, at least two studies have shown that spontaneous abortion rates are not higher among ART users compared with the general population of pregnant women if maternal age is considered.[20,21] Another limitation was the small analytic sample size, which was limited to states that included type of fertility treatment on their PRAMS survey; this limited sample resulted in highly variable estimates with large standard errors. Continued assessment of the validity of PRAMS questions about ART use is needed, particularly as more states add the questions and as types and availability of infertility therapies increase and improve. Data may also be pooled over multiple years to increase the sample size, thereby reducing the standard errors around the PRAMS estimates.

CONCLUSIONS

Revised PRAMS questions provide a better estimate of ART births compared with earlier versions. Findings in this study suggest that information on ART use may be obtained by maternal retrospective report; however, estimates may be less reliable for certain population subgroups, such as women aged ≥40 years and those who have previously given birth. Current vital statistics data collection protocol involves using only the prenatal care record to ascertain ART use to conceive; however, these findings as well as a previous report by Zhang et al. suggest that maternal report may be a better method of collecting data on ART for the birth certificate,[14] and improved quality of the data available on the birth certificate has important implications for research and surveillance. Furthermore, the ART items on PRAMS could be easily adapted to a range of other instruments. Finally, PRAMS includes items describing maternal prenatal care behaviors, infant care practices, and environmental factors, and may be a useful tool to study these topics as they relate to pregnancy outcomes and infant health among users of ART.

The findings and conclusions found in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. This study was exempt from Institutional Review Board approval.

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