Study of the Association of Uterine Perforation and IUD Expulsion With Breastfeeding and Postpartum Timing at IUD Insertion (APEX IUD)—Study Size Estimation to Actuality

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DISCLOSURES

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BACKGROUND

- The Food and Drug Administration required a study to determine the extent to which postpartum timing and breastfeeding at the time of intrauterine device (IUD) insertion practices in the United States (US) are associated with risk of uterine perforation and IUD expulsion (APEX IUD).
- Based on the literature, the cumulative rate of IUD expulsion over 12 months of follow-up in a postpartum cohort is between 87 and 113 per 1,000 women.[1] Uterine perforation, however, is a much more uncommon event: 1.3 cases occur per 1,000 IUD insertions, based on a prospective European cohort of 61,448 women.[2] Therefore, adequate study size to assess uterine perforation was critical for study feasibility.
- Prior to the APEX IUD study, a validation study was conducted to ensure adequate study size, availability of breastfeeding data, and validation of algorithms for outcome variables in 4 US health care systems (3 Kaiser Permanente sites—Northern California, Southern California, and Washington state—and RI in Indiana.[3] The validation study data accrual ended on September 30, 2015.

OBJECTIVE

- We present the approach to estimating study size and the estimated and actual study sizes in the APEX IUD study.

METHODS

- The validation study cohort included women aged ≤ 50 years at IUD insertion with a minimum of 12 months enrollment in the health care system. The postpartum cohort included women who delivered ≤ 52 weeks before the IUD insertion date. The breastfeeding cohort included women in the postpartum cohort who had information on breastfeeding status at the time of IUD insertion (Figure 1).
- The start of patient inclusion in the APEX IUD study varied by site between January 1, 2001, and January 1, 2009, (Figure 2) and was determined by the later of: (1) the date when Mirena was approved; or (2) the date when electronic health records (EHRs) were implemented in the 4 health care systems—KPNC, KPSC, RI, and KPWA.
  - Breastfeeding data became available at varying times for each site (Figure 2).
  - The latest date for a patient to be included in the study population for all sites was April 30, 2018, 2 months before the end date of the data collection (June 30, 2018).
- Projections to estimate APEX IUD study size involved:
  - Including 31 additional months of patient accrual beyond the validation study time frame.
  - Based on the validation study's results, estimating that:
    - 30% would have an IUD inserted within 52 weeks postpartum, and that 90% of those with an IUD insertion within 52 weeks postpartum would have breastfeeding data (percentages from the validation study were projected by site).
- The estimated and actual numbers of women in these categories are presented.

Figure 1. Study Cohort

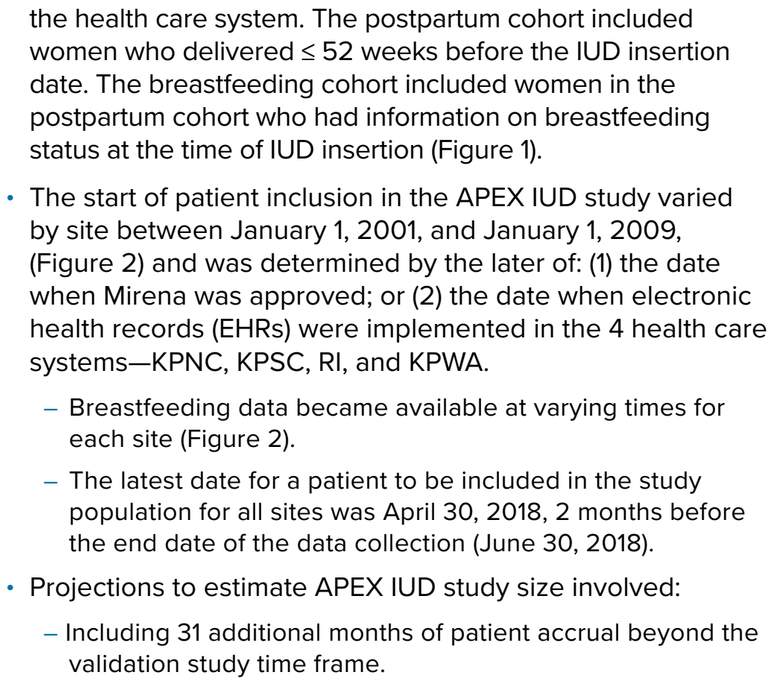
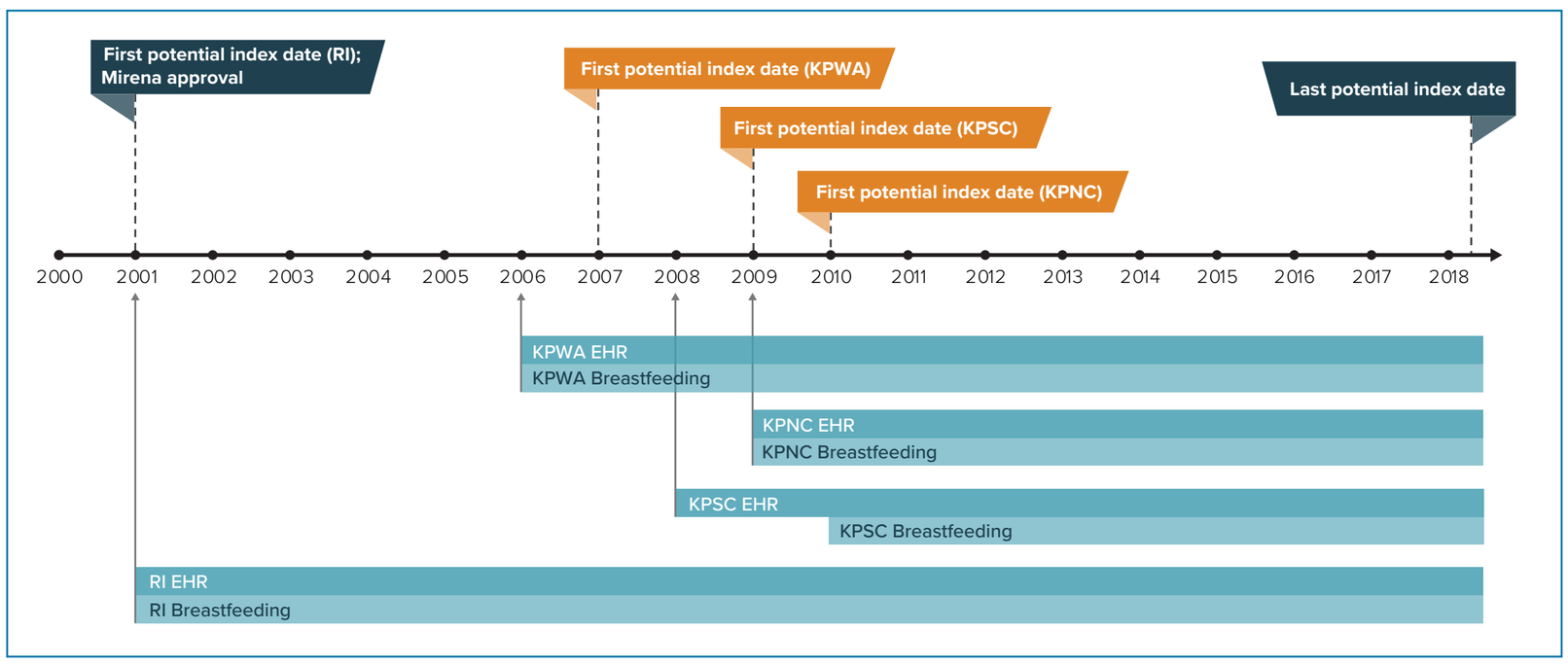


Figure 2. Timeline



RESULTS

- Based on results from the validation study, the projected number of women in the IUD cohort was 264,706. The projected number for those with insertion within 52 weeks postpartum was 79,412 and for those with breastfeeding status available was 71,471 (Figure 3).
- The actual numbers of women who were included were 326,658, 97,824, 93,897, respectively, approximately 25% higher than estimated (see Figure 4).
- The higher than estimated numbers of women were due, in part, to an increase in IUD use during the additional 31 months of data accrual included in the APEX IUD study time frame.

Figure 3. Process for Study Size Estimation

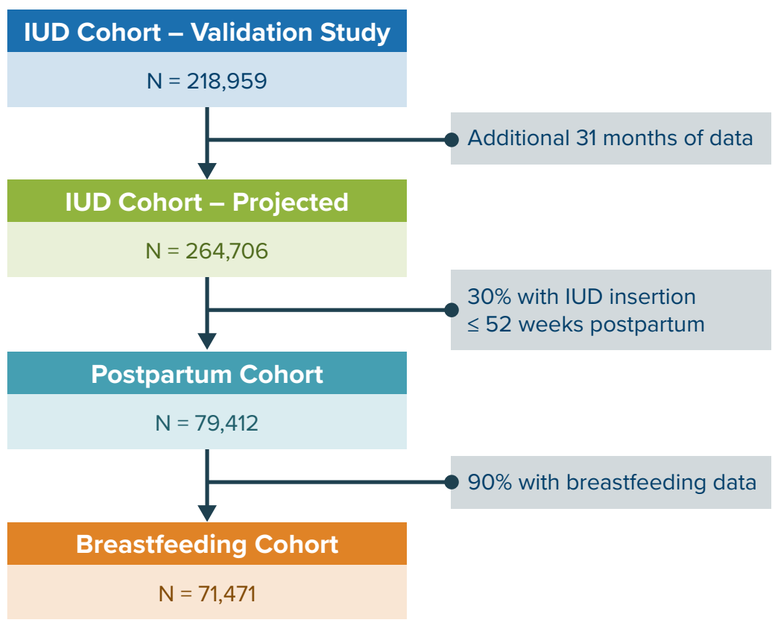
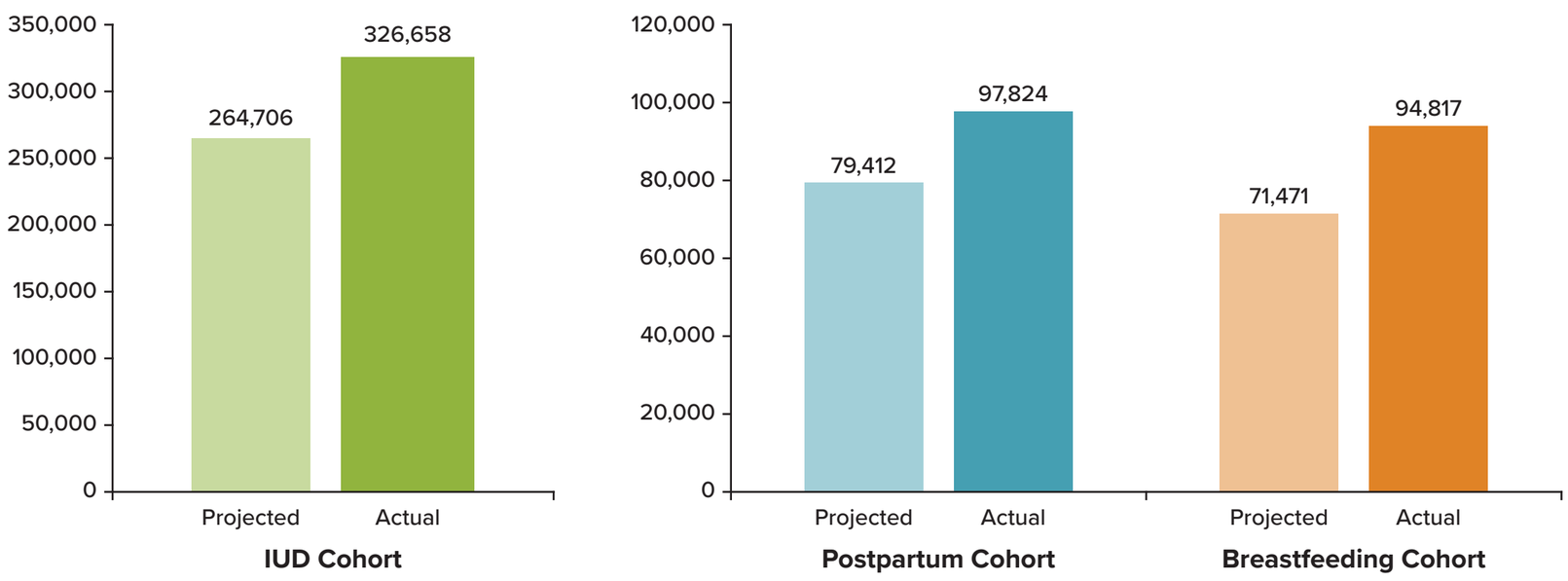


Figure 4. Projected and Actual Numbers of Women in the APEX IUD Study



[a] Data loss includes incomplete data and trimming during analysis.
Note: Data for first insertion only.

DISCUSSION AND CONCLUSIONS

- The actual numbers of women in the APEX IUD study were higher than estimated based on our projections from the validation study.
- Accounting for greater than linear increase in use of IUDs over time, rather than a linear increase, could have improved the projections.
- The projections correctly indicated that the study would be feasible.

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