Analysis of Medicinal Product Utilization Data in the FDA Sentinel System to Inform the Development of a Pregnancy Safety Study Framework

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BACKGROUND

As part of the FDA User Fee Reauthorization Act of 2022, FDA committed to developing a pregnancy safety study framework to optimize the study types (single-arm descriptive, pregnancy registry, or database studies) to assess medicinal product exposure in pregnancy. The framework will leverage estimated magnitude of exposure and study goal (signal identification or evaluation) to optimize the study types to assess safety.

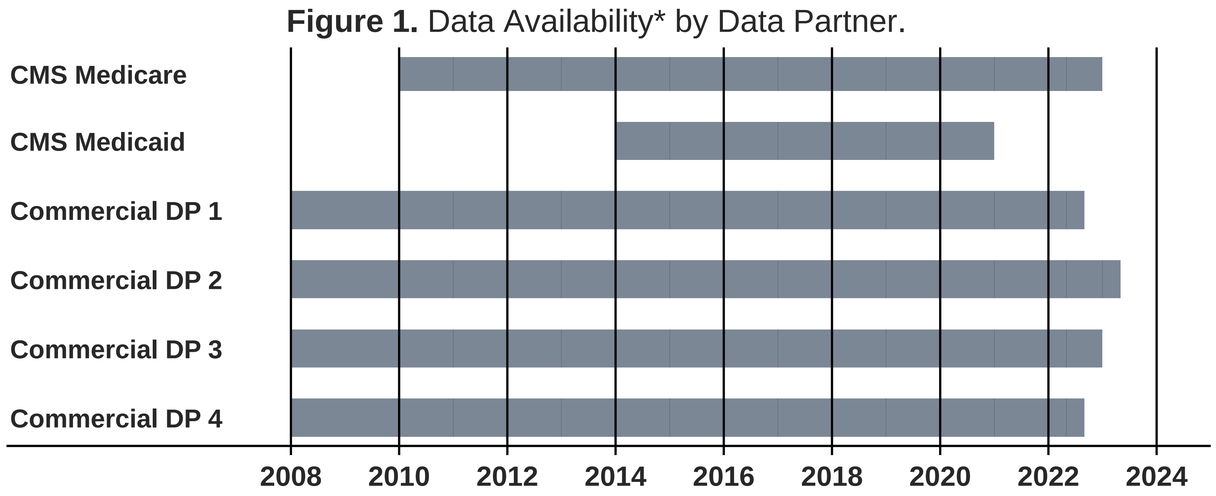
OBJECTIVES

To characterize and describe the magnitude of exposure during pregnancies that ended in live births for medicinal products either (1) with an FDA-issued pregnancy safety postmarketing requirement or commitment, (2) listed on the FDA's Office of Women's Health Pregnancy Registry webpage, or (3) with a pregnancy observational study in ClinicalTrials.gov.

METHODS

Pregnancies ending in live birth delivery among individuals between 10 - 54 years of age in the Sentinel Distributed Database were used to describe the magnitude of exposure during pregnancy. A total of 249 products associated with a postmarketing pregnancy safety study were considered for this analysis. Very low exposure products were excluded from the analysis because they are not likely to be suitable for comparative studies in administrative healthcare data systems that are the focus of the PDUFA VII demonstration projects. A convenience sample of 28 products with pregnancy exposures <2,500 was included to represent low exposure products to inform the framework development. Of the total 72 products included in the final analysis, 44 products had high exposure (≥2,500 pregnancy exposures) and 28 had low (<2,500). The 72 products were grouped into 20 therapeutic classes. The query was distributed to 6 Sentinel Data Partners, including 4 national health insurers, Medicare, and Medicaid. The query included data from January 1, 2008, through January 31, 2023. Data contribution period varied by Data Partner.

Figure 1. Data Availability* by Data Partner.

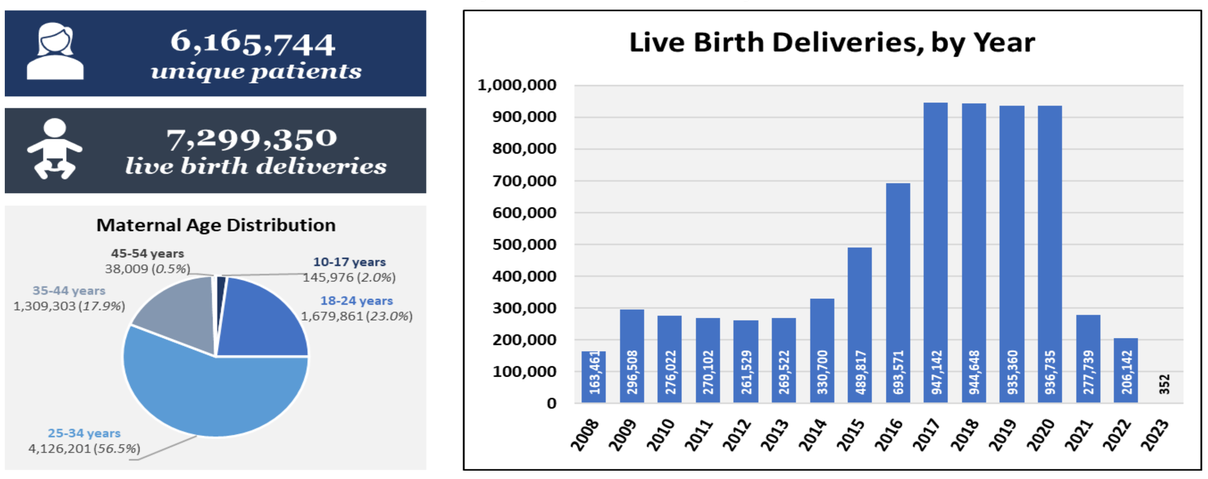


* Data prior to January 1, 2008, not utilized; dates are current as of August 4, 2023, query distribution
CMS: Centers for Medicare and Medicaid Services; DP: Data Partner

RESULTS

7.3M live births were contributed by 6.2M individuals over the 15-year query period. The 25 to 34 years old maternal age group generated 57% of all live birth deliveries.

Figure 2. Characterization of Live Birth Deliveries in the Sentinel Distributed Database: January 1, 2008 – January 31, 2023.



The overall exposure during pregnancy for the 72 medicinal products was low. One-third of products had evidence of exposure in < 1,000 pregnancies and 60% in < 10,000 pregnancies during the 15-year query period. Only 4 medicinal products had evidence of exposure in >100,000 pregnancies. These 4 products were on the market for more than 20 years as they were first approved prior to 2002.

Figure 3. Total Number of Exposed Pregnancies from 2008-2023 for each of the 72 Products from the Convenience Sample.

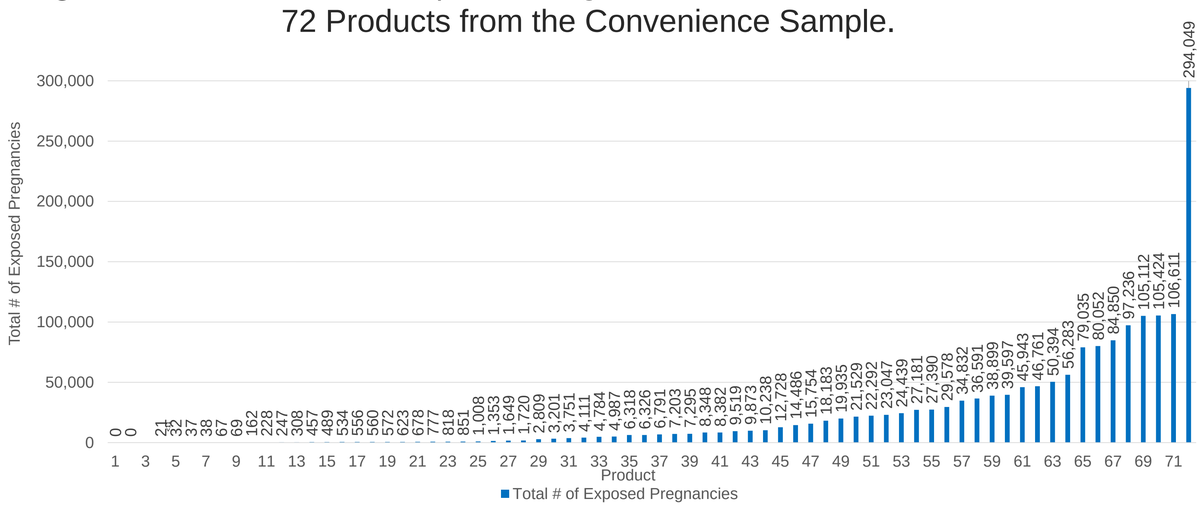


Table 1. Length of Time Utilization Data Contributed to the Analysis.

Number of years of contributed data	Time period of first approval	Number of products
0-6	After 12/31/2015	11
7-13	Between 02/01/2009 – 12/31/2015	11
14-15	Before 02/01/2009	50

Figure 4. Total Number of Exposed Pregnancies for Products Contributing 0 to 6 Years of Utilization Data to the Analysis from the Convenience Sample.

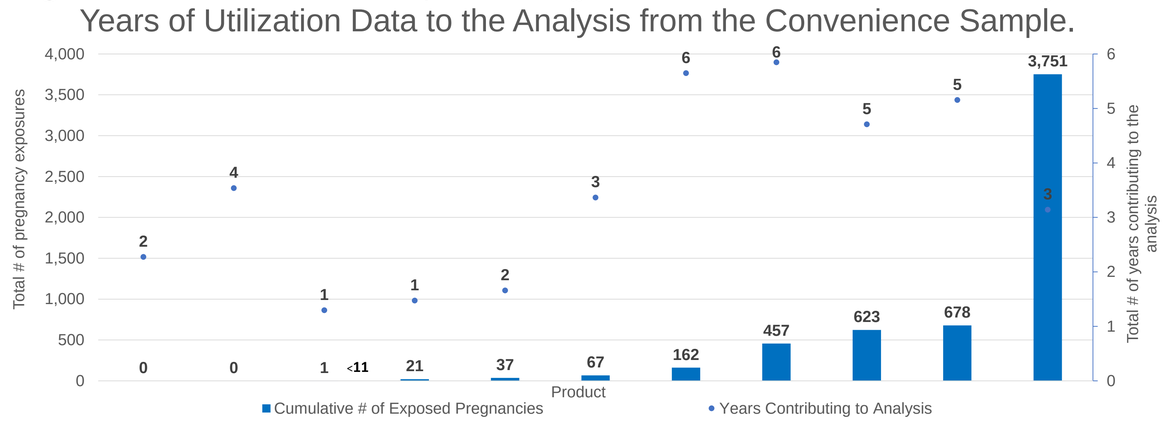


Figure 5. Total Number of Exposed Pregnancies for Products Contributing 7 to 13 Years of Utilization Data to the Analysis from the Convenience Sample.

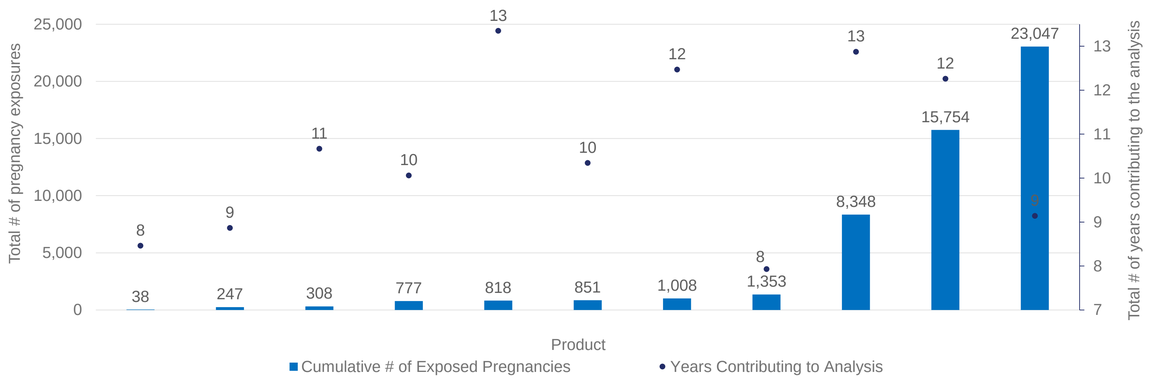
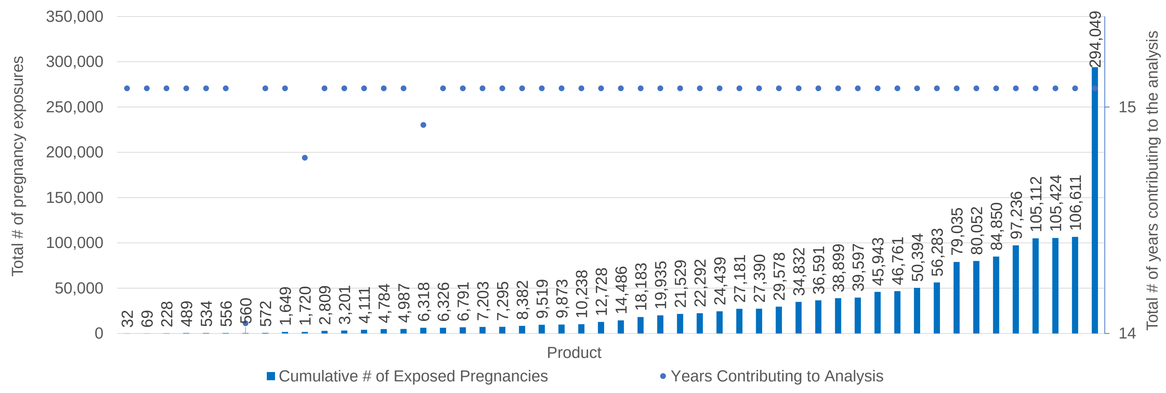
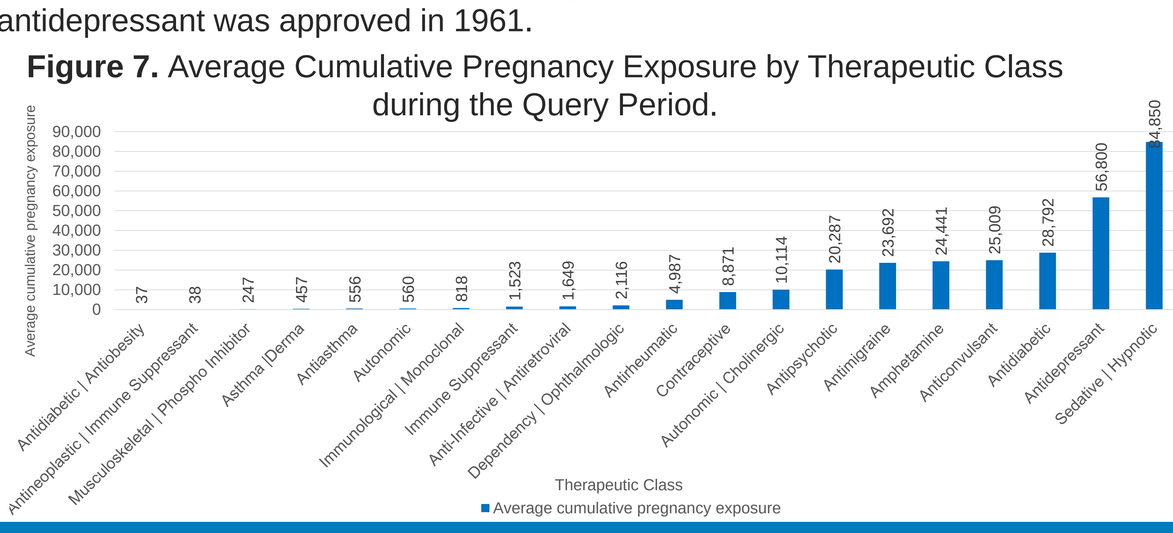


Figure 6. Total Number of Exposed Pregnancies for Products Contributing 14 to 15 Years of Utilization Data to the Analysis from the Convenience Sample.



The therapeutic classes with the highest average number of exposed pregnancies were sedatives/hypnotics (84,850) and antidepressants (56,800). The oldest sedative/hypnotic included in this query was approved in 1992 and the oldest antidepressant was approved in 1961.

Figure 7. Average Cumulative Pregnancy Exposure by Therapeutic Class during the Query Period.



CONCLUSION

- Utilization of the 72 products from the convenience sample during pregnancy was low, especially among those approved after 2008.
- 80% of the products included in this preliminary analysis had 10 or more years of utilization data in Sentinel to characterize their use during pregnancy.
- Sedative/hypnotic and antidepressant products showed the highest exposure during pregnancy.
- The oldest sedative/hypnotic included in this query was approved in 1992 and the oldest antidepressant was approved in 1961.

LIMITATIONS/NEXT STEPS

- The product exposure characterization during pregnancy among live birth deliveries will be updated to include products that were excluded from this convenience sample.
- Year of approval, disease, and product related factors will be further explored to inform observed patterns of utilization.
- Product exposure by trimester of pregnancy will be described.

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- The contents are those of the authors and do not necessarily represent the official views of, nor and endorsement, by FDA/HHS, or the U.S. Government.
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