U.S. Department of Health and Human Services
Task Force on Research Specific to Pregnant and Lactating Women

Agency Activities: Centers for Disease Control and Prevention

Research

CDC's mission involves fighting disease and promoting public health across populations, including pregnant and lactating women. CDC supports a large portfolio of extramural and intramural research related to pregnant and lactating women, often at the population level. CDC also provides research resources, including health services databases that can be used to develop evidence about public health needs for pregnant and lactating women. In this document we will describe CDC's activities related to identifying and addressing gaps in knowledge and research regarding safe and effective therapies for pregnant and lactating women.

CDC Research Assessing Risk Factors during Pregnancy and Lactation

CDC's National Center on Birth Defects and Developmental Disabilities funds several research centers across the United States to identify risk factors for birth defects and to answer questions about medications taken during pregnancy known jointly as the Centers for Birth Defects Research and Prevention (CBDRP) (https://www.cdc.gov/ncbddd/birthdefects/cbdrp.html). These centers collaborate on two large case-control studies: the National Birth Defects Prevention Study (NBDPS), which includes births from 1997–2011, and the Birth Defects Study To Evaluate Pregnancy exposureS (BD-STEPS), which began with births in 2014. Over the course of 14 years of NBDPS interviews, 43,000 women from 10 states took part in NBDPS, and over 200 scientific papers have been published using these data, with more than 50 about medication exposures. Especially in the field of medications it is important to interview a woman, since only through maternal interview can you establish whether a woman actually took the medication she was prescribed and any over the counter medications she took. Examples of recent publications include:

- A recent study of antibiotic use among pregnant women showed that certain antibiotics may be associated with specific birth defects.
- Data from another CDC study showed that using asthma medication during pregnancy did not increase the risk for most of the birth defects studied, but might increase the risk for some birth defects, such as esophageal atresia (birth defect of the esophagus or food tube), anorectal atresia (birth defect of the anus), and omphalocele (birth defect of the abdominal wall). The most commonly reported asthma medications used during pregnancy were albuterol (2%–3% of women) and fluticasone (about 1% of women). It was difficult to determine whether it was asthma severity or asthma medication use during pregnancy that was related to the increased the risk for these birth defects.

CDC's epidemiological research addresses the impact of occupational and environmental exposures, exposures to medication, and other factors on the health of pregnant women and their offspring. CDC's National Institute for Occupational Safety and Health (NIOSH) works with other CDC Centers and supports several studies to make use of existing cohort data to analyze the long- and short-term effects of occupational exposures on maternal and child health.

Other epidemiological research from CDC documents the use of medication during pregnancy and describes the impact of both medication exposure and disease on developing infants. For example, CDC researchers analyzed a Massachusetts state data system of records of deliveries 1998-2007. They found that women with gestational diabetes had a higher risk than women without GD of serious complications, including preterm birth and macrosomia. In another study, CDC researchers developed a method to identify pregnant women in health insurance databases, and find important information about their pregnancies and their use of antidepressants during pregnancy. Researchers identified nearly 490,000 pregnancies in 2013 health insurance claims data, and found that one in 16 pregnant women filled a prescription for an antidepressant during pregnancy.

The Study to Explore Early Development (SEED) is a multi-year research study funded by CDC. It is currently the largest study in the United States to help identify factors that may put children at risk for autism spectrum disorder (ASD) and other developmental disabilities. Through SEED, CDC is evaluating many possible risk factors that seem to be associated with or related to ASD, including the mother's exposure to certain medications during pregnancy. This information will help to fill knowledge gaps regarding safe and effective therapies for women during pregnancy.

CDC Research Regarding Specific Illnesses and Treatments

CDC supports research on health care delivery, as related to public health interventions. Much of this research is focused on immunizations.

- The Pregnancy Vaccine Effectiveness Network (PREVENT) was established in April 2016 to: i) estimate incidence of influenza and vaccination rates; ii) describe epidemiologic characteristics associated with illness; and iii) estimate influenza vaccine effectiveness in preventing acute respiratory or febrile hospitalizations during pregnancy associated with real-time reverse transcription polymerase chain reaction assay. Study sites include: Australia; Alberta and Ontario, Canada; Israel; Kaiser Permanente, USA.
- CDC is currently funding a study on immunization delivery in obstetrics and gynecology settings, to promote administration of vaccines to women in preconception period and in pregnancy.
- The Internet Panel Survey of Pregnant Women, another CDC effort, is conducted in November and April of each year to monitor vaccination trends in pregnant women, and includes topical questions on current areas of special interest, such as Zika Virus (https://www.cdc.gov/flu/fluvaxview/pregnant-women-nov2013.htm).
- CDC's New Vaccine Surveillance Network conducts surveillance and evaluation activities for acute respiratory illness to assess the burden of currently vaccine-preventable and potentially vaccine-preventable childhood diseases, and to evaluate the impact of new and upcoming vaccines and other strategies. With respect to pregnant women, sites are collecting self-reported data related to influenza vaccination during pregnancy and verifying vaccination status using state registries and medical records. Information is also collected with respect to breastfeeding practices. As part of this, one study site is performing a 3-year cohort study of women and infants to assess how the mother's immune system may help protect infants from illnesses caused by viruses including influenza. (https://www.cdc.gov/surveillance/nvsn)
- Influenza Hospitalization Surveillance Network (FluSurvNet) conducts surveillance for influenza related hospitalizations. FluSurv-NET plans to use data for estimation of influenza vaccine effectiveness among pregnant women using a test negative design (cases are RT-PCR influenza positive and comparison group is RT-PCR influenza negative) during the upcoming 2017-2018 influenza season in the United States.

CDC also has supported behavioral and educational intervention research in pregnant and lactating women. Examples include:

- CDC is working with scientists from an NIH clinical research network to support a clinical trial of a brief screening and educational intervention to prevent CMV infection;
- As many as one in five pregnant women experience depression, which poses significant, ongoing risks for both the woman and her child. Researchers are now evaluating the efficacy of their low-cost, comprehensive intervention for these women in the "real-world" setting of obstetric/gynecology clinics, where referrals and consultations and access to appropriate levels of psychiatric care are offered in conjunction with pregnancy-related clinical services.

CDC supports a range of efforts relating to opioid use during pregnancy:

- In a systematic review of previous studies on opioid use during pregnancy and risk for birth defects, CDC researchers found that use of opioids during pregnancy may be linked to various birth defects such as oral clefts, congenital heart defects, and clubfoot. However, many of the studies reviewed had issues with study methods and quality.
- Opioid use during pregnancy can also lead to neonatal abstinence syndrome (NAS). CDC is supporting two pilot projects to better understand the incidence, severity, and long-term developmental and educational outcomes associated with NAS.
- CDC is tracking trends in prescription opioid use among pregnant and reproductive aged women to monitor the opioid epidemic and progress towards the goal of reducing opioid use in these populations.

CDC's Zika Pregnancy and Birth Defects Task Force conducts research and implements programs to reduce the risk and impact of Zika virus infection in pregnant women, infants, and children. Data are used to update recommendations for clinical care, plan for services for pregnant women, their infants and families affected by Zika, and improve prevention of Zika infection during pregnancy.

- CDC established the US Zika Pregnancy and Infant Registries, which are enhanced national surveillance efforts coordinated by CDC in collaboration with state, tribal, territorial, and local health departments to monitor the effect of Zika virus infection during pregnancy on fetal and infant outcomes.
- Additionally, enhanced surveillance of pregnant women with Zika in Colombia has been established in collaboration with Colombia's Instituto Nacional de Salud.
- CDC also collaborates with Colombia's INS on a cohort study to identify risk factors for Zika virus transmission; the full spectrum of adverse maternal, fetal, and infant health outcomes associated with Zika virus infection; and risk factors for occurrence of these outcomes.
- Since activation of CDC's Zika Virus Response, the Pregnancy and Birth Defects Task Force has conducted more than 300 clinical outreach presentations, and released more than 35 scientific publications, 13 clinical guidance updates, and 10 Health Alert Network (HAN) Advisories.

CDC Research to Improve Outcomes around the World

CDC's Center for Global Health, along with other CDC programs, is conducting research to improve pregnancy outcomes around the world. Examples include:

- CDC-supported scientists are implementing point-of-care systems to speed identification and treatment of HIV-positive women in Zambia;
- In South Africa, CDC-supported researchers are aiming to eliminate mother-to-child transmission of HIV infection through a multifaceted approach, including early identification of

infection; early and sustained antiretroviral therapy to HIV-positive pregnant women; promoting the involvement of male partners in treatment, especially to improve adherence; and rapid and repeated HIV testing in infants.

- In Kenya, CDC supports an influenza vaccine demonstration project, using an Inactivated Influenza Vaccine (IIV) already licensed in Kenya to vaccinate pregnant women in a high HIV prevalence and malaria-endemic setting in western Kenya. CDC has multiple efforts to expand the use of seasonal influenza vaccines in countries outside the US, and many of these efforts target pregnant women.
- In Morocco, CDC is supporting efforts to enhance surveillance for severe acute respiratory disease among pregnant women.
- CDC and NIH are supporting a large, randomized placebo-controlled trial in Thailand, where 6 percent to 7 percent of adults are chronically infected with hepatitis B virus (HBV). Researchers will test the safety and efficacy of a short course of antiviral therapy to prevent pregnant women with HBV from passing the infection along to their babies. CDC is also supporting a randomized controlled clinical trial among HIV-HBV co-infected women in China. This study will test the safety of tenofovir during pregnancy with regards to the infant bone mineral density, as well as other potential toxicities.

CDC Surveillance and Data Collection Efforts

In addition to supporting research directly, CDC supports surveys and large-scale data collection efforts, and these resources can be used by independent researchers to conduct studies applicable to pregnant and lactating women. Key efforts in this area include:

- CDC's Pregnancy Risk Assessment Monitoring System (PRAMS) {https://www.cdc.gov/prams/index.htm }. PRAMS collects state-specific, population-based data on maternal attitudes and experiences before, during, and shortly after pregnancy. PRAMS surveillance currently covers about 83% of all U.S. births. PRAMS provides data not available from other sources. These data can be used to identify groups of women and infants at high risk for health problems, to monitor changes in health status, and to measure progress towards goals in improving the health of mothers and infants. PRAMS data are used by researchers to investigate emerging issues and by state and local governments to plan and review programs and policies aimed at reducing health problems among mothers and babies. PRAMS includes core questions asked in every state and optional questions available to states and localities. Core PRAMS questions cover areas including flu shots; gestational diabetes; preeclampsia; depression; tobacco use; alcohol use; violence; breastfeeding; and infant sleep positions. Optional questions expand available information about breastfeeding; vitamin use; other vaccines; medication for thyroid, epilepsy, and mental health conditions; and substance use and abuse, among other topics.
- Maternity Practices in Infant Nutrition and Care (mPINC) Survey: CDC has developed and supported the mPINC survey since 2007. Every other year, all facilities in the United States that provide maternity care are invited to participate. Nationwide, 82% of facilities contribute data on practices and policies in seven dimensions of medical and nursing care that support breastfeeding. https://www.cdc.gov/breastfeeding/data/mpinc/index.htm
- The Truven Health MarketScan database, which includes healthcare claims and encounters, admission and discharge data, and beneficiary enrollment data, is used to estimate cost and rates of healthcare utilization associated with vaccine administrations, including tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccination, and vaccine preventable

diseases, including Hepatitis B virus, tetanus, pertussis, and influenza-like illnesses, among privately and publicly insured pregnant women.

Through the National Center for Health Statistics, CDC spearheads the development of new questions and methods to obtain key information about public health issues related to maternal health, pregnancy, and breastfeeding. CDC is developing new questions for NCHS surveys and the National Vital Statistics to better capture contemporary practices in breastfeeding, and to rigorously test new questions to ensure their validity and reliability. Other examples include:

- National Vital Statistics System – information on whether the mother breastfed her newborn prior to discharge from the hospital is available from birth certificates for varying numbers of states from 2009 on (48 states and the District of Columbia for 2016) https://www.cdc.gov/nchs/data_access/vitalstatsonline.htm. These data can be analyzed by numerous maternal (e.g., age, education, race) and infant (gestational age, NICU admission, birthweight) characteristics. A recent study assessing the quality of this and other new items from the birth certificate found high agreement between breastfeeding data reported on the birth certificate and information recorded in hospital medical records https://www.cdc.gov/nchs/data/nvsr/nvsr62/nvsr62_02.pdf.
- The National Health and Nutrition Examination Survey (NHANES) is a program of studies designed to assess the health and nutritional status of adults and children in the United States. The survey is unique in that it combines interviews and physical examinations. Data from NHANES has been used for studies of pregnant women and nutrition and exposures (https://www.cdc.gov/nchs/nhanes/index.htm).
- The National Survey of Family Growth (NSFG) is a household-based, nationally representative survey of reproductive aged women and men (https://www.cdc.gov/nchs/nsfg/index.htm). Since 1973, the survey has included questions on breastfeeding initiation and duration, as part of the full pregnancy and birth history collected from all female respondents. These data on breastfeeding can be analyzed in the context of other survey information including pregnancy intendedness, contraception, marital/cohabitation history, reproductive health, and use of related health services.
- The National Health Interview Survey (NHIS) is a population-based national household survey. CDC has included questions to determine influenza vaccination among women pregnant during the influenza season, and is working to develop new questions to determine tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap) vaccination during pregnancy among women having live births in the past 12 months. Since July 2001, breastfeeding questions were included on the NIS to assess the population's breastfeeding practices. The parent or guardian is asked about breastfeeding, formula feeding, and first time feeding of something other than breast milk or formula (https://www.cdc.gov/breastfeeding/data/nis_data/index.htm). These data help to inform CDC's Breastfeeding Report Card (https://www.cdc.gov/breastfeeding/data/reportcard.htm) , which is released every other year.

Clinical Practice Information and Recommendations

CDC does not directly support clinical care, but the agency creates materials that can help inform health care systems, patients, and providers. Although these services and materials cover a variety of areas, several are focused on or include information related to pregnancy and lactation.

CDC's Treating for Two initiative, which involves collaboration with a range of partners and other federal agencies, is designed to address the need for clinical information. Treating for Two is working to expand and accelerate research to fill knowledge gaps; evaluate available evidence to facilitate reliable guidance; and deliver up-to-date information to support decision making among prescribers, pharmacists and consumers (https://www.cdc.gov/pregnancy/meds/treatingfortwo/index.html).

- Through a small business grant, CDC is testing whether delivering information through mobile devices can improve knowledge and communication of data on drug safety to pregnant women.
- CDC, in collaboration with the March of Dimes and RTI, conducted a research project to triangulate findings from formative research with women (recently pregnant or planning pregnancy), prescribers, and pharmacists to develop an understanding of shared challenges and opportunities in improving medication safety during pregnancy.

The *U.S. Medical Eligibility Criteria for Contraceptive Use, 2016* are evidence-based, clinical guidelines provide information for healthcare providers on the safety of contraceptive methods for women with certain characteristics or medical conditions, including pregnancy and breastfeeding (https://www.cdc.gov/reproductivehealth/contraception/mmwr/mec/summary.html).

Environmental exposure information for providers is another important area for CDC:

- The Prenatal Assessment of Environmental Risk (PEAR) is an online environmental exposure assessment toolkit to help provider identify and assist patients to lower environmental exposure risk.
- Pediatrics Environmental Health Specialty Units are a source of medical information providing advice on the prevention, diagnosis, management and treatment of environmentally-related health effects in adults and children;
- CDC provides guidelines for identifying and managing lead exposure in pregnant and lactating women (https://www.cdc.gov/nceh/lead/publications/leadandpregnancy2010.pdf).

The Advisory Committee on Immunization Practices (ACIP) develops recommendations on the use of vaccines, including for pregnant women (https://www.cdc.gov/vaccines/acip/index.html).

CDC supports evidence-based strategies in hospitals to help women who choose to breastfeed start and continue breastfeeding, by promoting the Ten Steps to Successful Breastfeeding (Ten Steps), a set of practices outlined by the WHO/UNICEF Baby-Friendly Hospital Initiative (BFHI) that have been shown to support breastfeeding mothers and infants.

CDC Health Information for International Travelers (the Yellow Book) provides recommendations to clinicians advising travelers who are pregnant or breastfeeding. (https://wwwnc.cdc.gov/travel/yellowbook/2018/advising-travelers-with-specific-needs/pregnant-travelers and https://wwwnc.cdc.gov/travel/yellowbook/2018/international-travel-with-infants-children/travel-and-breastfeeding)

Communications

CDC focuses its communications efforts on public health professionals and the general public, although health care providers are also an important audience. CDC's website provides a broad array of consumer information on issues relevant for pregnant and lactating women, including:

- Gestational diabetes (https://www.cdc.gov/pregnancy/diabetes-gestational.html)

- Zika (https://www.cdc.gov/zika/reporting/pregnancy-outcomes.html)
- Infections (https://www.cdc.gov/ncbddd/birthdefects/infographics/prevent2protect/index.html)
- Folic acid (https://www.cdc.gov/ncbddd/folicacid/index.html)
- Preventing birth defects (https://www.cdc.gov/ncbddd/birthdefects/prevention.html)
- Safe medication use in pregnancy (https://www.cdc.gov/treatingfortwo)
- Pregnancy and opioid pain medication (https://www.cdc.gov/drugoverdose/pdf/pregnancy_opioid_pain_factsheet-a.pdf)
- International travel (https://wwwnc.cdc.gov/travel/page/pregnant-travelers) and special information for pregnant women on all international travel destination pages (www.cdc.gov/travel)
- Listeriosis (https://www.cdc.gov/listeria/risk-groups/pregnant-women.html)
- Blood pressure (https://www.cdc.gov/bloodpressure/about.htm)and
- Breastfeeding (https://www.cdc.gov/breastfeeding/)

Other Collaborative Efforts

In addition to efforts noted above, CDC participates in the Federal Interagency Forum on Child and Family Statistics, an interagency group designed to improve both the quality and use of data on children and families by investigating questions of data quality, data measurement, and data integration and by coordinating the development and use of statistical data bases among Federal agencies (http://childstats.gov).

CDC co-chairs the Federal Interagency Breastfeeding Work Group, an interagency group designed to increase sharing of information and expertise, prevent duplication, and increase collaboration on projects and initiatives with mutual goals. This work group has also collaborated with the Federal SIDS/SUIDS Work Group in order to mutually promote safe sleep and the safe implementation of maternity practices supportive of breastfeeding.