Landscape analysis of pregnancy exposure registries in low- and middle-income countries
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Abbreviations

APR Antiretroviral Pregnancy Registry
BART Baobab Health Antiretroviral Therapy
CHAMPS Child Health and Mortality Prevention Surveillance Network
CHERISH Children HIV Exposed Uninfected Research to Inform Survival and Health
CLAP/WR Latin American Center for Perinatology/Women’s Health and Reproductive Health
EMA European Medicines Agency
EMBRACE Microbicide Pregnancy Registry of the Microbicide Trials Network
ESC Expert Steering Committee
FDA US Food and Drug Administration
GAIA Global Alignment of Immunization Safety Assessment in pregnancy
HDSS Health and Demographic Surveillance Systems
HER Electronic health records
HICs High income countries
IeDEA International Epidemiology Databases to Evaluate AIDS
JBI Joanna Briggs Institute
LMICs Low- and middle-income countries
MAH market authorization holder
MANGO Measuring Adverse Pregnancy and Newborn Congenital Outcomes
MiMBa Malaria in Mothers and Babies
MNCH Maternal, newborn, and child health
MNHR Maternal Newborn Health Registry
NGOs Non-governmental organizations
NICHD US National Institute of Child Health and Human Development
NIH US National Institute of Health
PAHO Pan American Health Organization
PERs Pregnancy exposure registries
PHDC Provincial Health Data Centre
PIDM WHO Programme for International Drug Monitoring
<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRISMA-ScR</td>
<td>Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews</td>
</tr>
<tr>
<td>RMNCAH</td>
<td>Reproductive, Maternal, Newborn, Child and Adolescent Health</td>
</tr>
<tr>
<td>RSV</td>
<td>Respiratory syncytial virus</td>
</tr>
<tr>
<td>SIP</td>
<td>Sistema Informatico Perinatal</td>
</tr>
<tr>
<td>sSCAN</td>
<td>sub-Saharan African Congenital Anomalies Network</td>
</tr>
<tr>
<td>UBOMI BUHLE</td>
<td>Understanding Birth Outcomes from Mothers and Infants, Building Healthcare by Linking Exposures</td>
</tr>
</tbody>
</table>
Section 1
Executive summary
1.1. Background

Many vaccines and drugs hold the promise of reducing mortality and morbidity among pregnant women and infants living in low- and middle-income countries (LMICs). However, sufficient information on the safety of drugs and vaccines in pregnant women is rarely available at the time of product licensure or approval. To account for this, active safety surveillance efforts are needed during the post-licensure and post-approval phase to assess the safety of drugs and vaccines in pregnant women and their offspring. Pregnancy exposure registries (PER) are used to monitor the safety of vaccines and drugs. PERs are observational studies that systematically collect health information on exposure to medical products such as drugs and vaccines during pregnancy.

While frequently conducted in high income countries (HICs), PERs are much less commonly instituted in LMICs. When they are used in LMIC settings, PERs most often focus on the use of antiretrovirals and antimalarial drugs. Pregnant women in LMICs have unique considerations, including different underlying conditions such as malaria and HIV,[1,2] background rates of clinical outcomes, and access to care, which emphasizes the importance of generating drug and vaccine safety evidence specific to their regions.

New vaccines developed specifically for use by pregnant women, such as those for respiratory syncytial virus (RSV) and Group B Streptococcus, are expected to be approved and available for introduction in LMICs in the near future but prelicensure data on these vaccines will primarily come from HICs. To prepare for new drugs and vaccines and strengthen pharmacovigilance in pregnant populations more generally, better understanding of the presence and characteristics of PERs in LMICs will be important.

1.2. Objectives and methodology

This report summarizes a landscape analysis of PERs and related health data collection platforms and activities in LMICs that systematically record pregnancy exposures to medical products and pregnancy outcomes. This analysis was conducted to better inform how future efforts, such as new vaccine introductions and treatment programs, can support maternal populations in LMICs. The scoping review consisted of a systematic search of the scientific and grey literature published between 2000 and 2022, supplemented by an online survey and interviews with selected key informants. The scoping review protocol follows the Joanna Briggs Institute (JBI) manual for scoping reviews and the search strategy is reported using the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.
1.3. Results

A total of 45 PERs and other systematic data collection resources in LMICs were identified, of whom 36 are currently in operation, organized into six major categories:

Table 1.1. Registry identification by resource category.

<table>
<thead>
<tr>
<th>Resource Category</th>
<th>Number identified (number currently active)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy exposure registries</td>
<td>11 (7)</td>
</tr>
<tr>
<td>Health and demographic surveillance systems and other observational cohorts</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Outcomes-based registries</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Maternal condition-based registries</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Manufacturer registries</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Electronic medical record databases and clinical software platforms</td>
<td>6 (6)</td>
</tr>
</tbody>
</table>

These resources cover a wide range of methodologic approaches and areas of focus, ranging from standalone research studies to analyses derived from electronic clinical systems. Pregnancy registries, also known as pregnancy exposure registries, are an essential tool for monitoring the safety of vaccines and other medical products used during pregnancy because they employ rigorous methods purposely designed to analyze the potential relationship between a given drug or vaccine exposure and subsequent clinical outcomes. However, PERs are resource intensive by comparison with other approaches to maternal and infant safety surveillance. Six of the eleven PERs identified in LMICs were designed to study the use of antiretroviral medications in pregnant women. Other resources, including other types of prospective cohorts and outcomes-based registries established in LMICs were also designed around HIV surveillance and treatment more generally, but include embedded studies focused on their pregnant population that capture antenatal exposures and subsequent outcomes.

Several resources exist that are designed primarily to systematically detect and record specified health outcomes, such as birth defects. These surveillance systems are typically structured to conduct broad screening of infants at birth, thus capturing a large number of participants and collecting exposure information retrospectively. These registries are able to evaluate questions regarding rare outcomes more efficiently but may be subject to limitations, such as incomplete recall of exposures or inability to capture early outcomes, including spontaneous abortions or stillbirths.
Other resources in LMICs include Health and Demographic Surveillance Systems (HDSS) and electronic medical record platforms, which are designed to collect a wider set of clinical and epidemiologic data on entire populations in a geographic area or health care system. HDSS’s are located throughout LMICs and are operated by researchers experienced in epidemiologic analyses. These sites usually conduct active surveillance through regular visits to each household within a defined geographic area. This enables populations to be followed longitudinally and typically capture events occurring in both medical facilities as well as the community. This full cohort approach allows the HDSS to estimate population-based incidence rates and relative risks among subgroups compared to the general population. Many HDSS are members of INDEPTH, a collaborative network of sites located throughout Africa, Asia, and Latin America. Participation in this network allows sites to standardize methods and combine data across different regions or countries. Pregnancy exposure studies conducted within the overall operation of the HDSS may require additional data elements (e.g., drug doses and timing, gestational dating), procedural adaptations and additional investment into a system that is often already quite resource intensive. It may be for that reason that only a subset of HDSS sites have published research focused on this issue. However, most of these sites are adaptable by design, and can add maternal pharmacovigilance to their surveillance, given adequate support.

This review identified a number of electronic medical record systems and associated clinical software platforms that have been used for safety surveillance in pregnant populations. In these systems, data collection is performed as part of clinical care and thus pregnancy exposure studies can be accomplished through programming packages that include the extraction and analysis of relevant data. Additional training may be required to ensure that clinical terminology is standardized, and algorithms may need to be developed to fully capture imprecisely defined diagnoses, treatments, and conditions. However, such systems are under expansion in many LMICs, and the addition of maternal pharmacovigilance capabilities would conceivably require only a small incremental investment.

1.4. Conclusions

This review demonstrates that a number of resources presently exist in LMICs that perform active safety surveillance in pregnant populations. These results indicate such systems employ a wide variety of approaches, each with their own set of strengths and challenges, as summarized in the final section of the report. In many cases, successful examples of these resources might be expanded, replicated, or adapted to incorporate new vaccines and medications, particularly if these systems recruit from the general population of pregnant women and use prospective data collection. Comparing results, or even pooling data across multiple studies would be valuable to better evaluate rare events and assess outcome rates across populations. Such efforts would be more feasible with the adoption of harmonized definitions, tools, and protocols, and may be more easily implemented in systems that are supported through public or donor funds. An improved understanding of the current status of maternal pharmacovigilance in LMICs, can help policymakers and researchers better identify and pursue opportunities for ensuring the safety of pregnant women worldwide, including leveraging currently active systems for studies as new interventions are introduced. No or limited information on the safety of medicines during pregnancy can hinder the informed benefit-risk assessment required for clinical and policy decisions about life-saving medicines in women of childbearing age.
Section 2: Introduction
New vaccines and drugs hold the promise of reducing morbidity and mortality among pregnant women and infants living in low- and middle-income countries. However, since pregnant women are actively excluded from most pre-registration clinical trials, safety information for this group is rarely available at the time of a medical product’s licensure or approval.[3,4] Consequently, the safety of drugs and vaccines administered during pregnancy must be evaluated throughout the product’s life cycle, including through active surveillance approaches during the post-licensure or post-authorization phase. Understanding the landscape of critical safety monitoring methods, including pregnancy exposure registries, is therefore important to identify additional safety monitoring preparations that may be needed for product introduction readiness and use. This report provides the results of a scoping review that we conducted to identify and describe PERs and other similar resources operating in LMICs. The information is intended to support global and country decision-making around needs for monitoring the safety of new and existing drug or vaccine products used during pregnancy.

A commonly used method to assess post-approval safety of drugs and vaccines in pregnant women and their offspring is through a pregnancy exposure registry. A PER is an observational study that systematically collects health information on exposure to medical products such as drugs and vaccines during pregnancy.[5] PERs, particularly in high-income countries, are commonly used throughout the post-marketing phase of drugs and vaccines.[6,7] PERs have been less frequently used in LMICs, due to a number of unique challenges, including limited access to the interventions under evaluation, insufficient data collection resources and infrastructure, and the capacity to link these data sources together.[4] Nevertheless, pregnancy exposure registries have been established in LMICs, and include those set up to evaluate drugs or vaccines of particular relevance for their populations, such as for malaria and HIV treatment and COVID-19 prevention.[8–10]

An improved understanding of the presence and nature of PERs in LMICs can better inform how future public health efforts in their maternal populations, such as new vaccine introductions and treatment programs, can be supported. While most research assessing the global status of drug and vaccine safety monitoring in pregnancy has focused on HICs,[6] one recent study focused on identifying existing maternal, newborn, and child health (MNCH) data collection systems in LMICs that could be used for active safety surveillance of vaccines used during pregnancy.[11] In contrast to these broader surveillance systems, PERs focus on active data collection specifically related to medical product exposures during pregnancy and pregnancy safety outcomes, and may be conducted by private as well as public agencies. Leveraging existing resources for the collection and use of data should better inform maternal immunization and maternal and neonatal in LMICs.

We conducted the scoping review detailed in the following sections to address this need for an improved understanding of PERs and other similar resources operating in LMICs. In this landscape report, we identify and describe our findings on existing PERs and other resources and discuss where gaps exist that may need to be addressed for introduction and implementation readiness.
Section 3

Methods
The methods for this landscape analysis have been published.[12] Briefly, a scoping review was conducted to identify pregnancy exposure registries, databases and other routinely collected health data that systematically record exposures to medical products during pregnancy and maternal and infant outcomes in LMICs. This review consisted of a systematic search of the scientific and grey literature and was supplemented by an online survey and interviews with selected key informants, as needed.

This scoping review followed the Joanna Briggs Institute (JBI) manual for scoping reviews, and the search strategy is reported using the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist.[13,14] This protocol was registered with the Open Science Framework.[15] The scoping review start and end dates were July 1, 2022 and June 30, 2023, respectively.

### 3.1. Eligibility criteria

For the literature search, the following eligibility criteria for selection were developed:

#### 3.1.1. Inclusion criteria

1. Publications and documents published or produced from January 2000 to the present, to ensure that identified registries possess features that are more relevant to current scientific and technological conditions; online sources were accessed.
2. Populations studied are located entirely or at least partially in LMICs.[16]
3. Reference to prospective and retrospective electronic or combined paper-electronic data collection systems including demographic national registers in LMICs.
4. Reference to prospective and retrospective cohort studies, with no restrictions regarding age range (other than women of childbearing age [i.e., 15-49 years of age]) or underlying conditions other than pregnancy, such as heart disease or epilepsy.
5. Reference to systems that collect data on exposure to one or more drugs or vaccines during pregnancy.
6. Reference to systems that collect data on pregnancy outcomes, including delivery, post-partum, and neonatal (may include an extended time frame to include birth defects detected later).

#### 3.1.2. Exclusion criteria

1. Editorials, opinion pieces, promotional literature.
2. Guidelines or guidance documents.
3. Reference to non-allopathic (e.g., traditional, homeopathic, or naturopathic) interventions.
3.2. Search strategy and information sources

Using an iterative process, a strategy was developed for a search in PubMed incorporating controlled vocabulary/ Medical Subject Headings and free text (Appendix 6.1). A LMIC filter was applied to focus results to the geographic regions of interest. An independent information specialist peer reviewed the strategy using the PRESS Checklist. [17] After finalizing in PubMed, the strategy was translated to Embase, CINAHL, and WHO’s Global Index Medicus. Reference lists of potentially relevant records and articles were also reviewed.

Additionally, a grey literature search was conducted, including Google Scholar search and relevant websites, such as industry and professional organizations, associations and alliances; selected Ministries of Health (including regulatory agencies and pharmacovigilance centers) in LMICs; and selected HIC organizations, academic and other non-governmental groups. The final search strategies are provided in Section 6.1.

3.3. Study selection and data extraction

Records retrieved by the search strategy were downloaded to EndNote Version 9.3.3 (Clarivate) for de-duplication and then uploaded to review management software (Covidence) for screening. Each title and abstract was screened by two independent reviewer authors to determine eligibility and categorized into categories (Yes, Maybe, No). Disagreements between reviewers, including uncertainties regarding eligible titles and abstracts, were resolved by a third reviewer. After screening, full-text reviews by two reviewers were then conducted to select records for data extraction. An adapted version of the PRISMA flow diagram was constructed to summarize record disposition.[14] Key information regarding the registries from the selected full-text articles and grey literature was recorded using a pilot-tested data extraction form (Section 6.2) and entered into an electronic database (Smartsheet).
3.4. Informant Survey and Interviews

An online survey was sent to experts and key informants to identify additional resources in LMICs that may not have been captured, or to provide additional detail for resources that were already identified. Key informants were identified for semi-structured interviews when additional information about the registries was needed. Responses were recorded in an electronic database for analysis. The survey instrument was developed (Section 6.3) and initially shared by members of the WHO Pharmacovigilance Team with counterparts at the WHO regional offices. The survey was delivered on July 7, 2022, to all members of the WHO Programme for International Drug Monitoring (PIDM),[18] which included over 350 contacts from Pharmacovigilance Center and National Regulatory Authorities from over 155 countries. The survey was also sent to members of the WHO Expert Steering Committee (ESC) on Safety Surveillance in Pregnancy in LMICs.

3.5. Data analysis

Identified resources were summarized in tables according to relevant characteristics, including methodology, geographic coverage, exposures and outcomes captured, and citations. The selected PERs were further evaluated based on additional questions (strengths, weaknesses, ability to add new interventions, and ability to combine data with other systems), and the quality of the existing registries. Geographic coverage was assessed using maps.

3.6. Consultation

A multi-disciplinary technical working group was established to provide assistance and guidance throughout the course of this review, and the protocol and results were reviewed by an Expert Steering Committee on Safety Surveillance in Pregnancy in LMICs, established by WHO. Feedback from both groups were incorporated to produce this final document.
4.1. Search Results

A total of 9,016 records were identified in our search, with 7,526 records remaining after de-duplication. These 7,526 records were imported for title and abstract screening (Figure 4.1). Through screening, an additional 11 duplicates were identified. Of the remaining 7,515 records, 396 were selected for full-text review, and 156 of those met eligibility criteria for data extraction. The reasons for exclusion during full-text review, listed in Section 3, included 78 publications with the wrong study design, 50 records where information on drug or vaccine exposures was not collected, and 45 records where studies were conducted in the wrong setting (e.g., did not include a substantial number of participants from a LMIC). An additional 47 records, publications, and other sources were identified through review of reference lists, websites, the online survey, and informant interviews, resulting in a total of 203 records with relevant information. Given that multiple records could contribute to describing a single “resource” (PER or similar data collection system), the selected 203 records yielded 45 resources that met our criteria for inclusion in the analysis.

Figure 4.1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of records screened and included.[14]
These 203 records also included descriptions of 45 research studies that were conducted as stand-alone analyses of retrospectively collected clinical data to evaluate the occurrence of maternal and/or infant outcomes following exposure to drugs or vaccines during pregnancy. Typically designed to be time-limited, these were generally not intended for ongoing surveillance and therefore only limited information was collected. These studies are summarized in Section 6.4.1. In addition to the searches of literature databases, grey literature, and internet resources, the survey yielded a total of 18 unique individuals submitted 21 responses, and after excluding duplicates and negative responses, and results were incorporated into the resource review above. A summary of these results is provided in Section 6.4.2.

### 4.2. Resource Location and Categorization

The resources selected for further analysis were distributed across several LMICs, as demonstrated in Figure 4.2. More than one resource was identified in some countries; conversely, some resources were found to operate in multiple countries.

As resources were examined, they were grouped into categories based on broad characteristics, as summarized in Table 4.1.

Each of these resource categories are described in further detail below.

**Table 4.1.** Categorization of the pregnancy exposure registries and other resources identified through study methods.

<table>
<thead>
<tr>
<th>Resource Category</th>
<th>Brief Description</th>
<th>Number of Resources (Number currently active)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pregnancy exposure registries</td>
<td>Self-designated PERs with prospective enrollment and a stated aim to record exposures and outcomes</td>
<td>11 (7)</td>
</tr>
<tr>
<td>Health and demographic surveillance systems and other observational cohorts</td>
<td>Population-based cohorts with prospective collection of clinical and epidemiologic data</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Outcomes-based registries</td>
<td>Registries that focus on outcomes, such as birth defects</td>
<td>7 (7)</td>
</tr>
<tr>
<td>Maternal condition-based registries</td>
<td>Registries that enroll pregnant women with specific underlying health conditions</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Manufacturer registries</td>
<td>Registries established by a drug or vaccine manufacturer, often for regulatory purposes</td>
<td>8 (6)</td>
</tr>
<tr>
<td>Electronic medical record databases and clinical software platforms</td>
<td>Electronic platforms that prospectively record clinical information within a health care institution or system</td>
<td>6 (6)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td><strong>45 (36)</strong></td>
</tr>
</tbody>
</table>
For the literature search, the following eligibility criteria for selection were developed:

### 4.2.1. Pregnancy exposure registries

Resources included in this category are typically referred to as “pregnancy exposure registries,” defined as prospective observational cohorts focused on the enrollment and follow-up of pregnant women who receive one or more specific drug(s) or vaccine(s) of interest. [5] Enrollment of pregnant women typically occurs before exposure to the drug or vaccine of interest. If recruitment into a PER occurs after exposure to the medical product, entry into the cohort must at least occur before any pregnancy outcomes are known, and an unexposed or non-pregnant population may be enrolled for comparison. In these systems, women are followed to the end of their pregnancy or longer in order to collect health outcome information on the mothers and their infants. Data are systematically collected on maternal exposures to medical product(s) of interest, maternal sociodemographic and health characteristics, and health events from pregnancy to outcomes for the woman and child. These resources can be used to calculate the rate of specific health events and may or may not include a reference population to provide comparison rates of health events.
4.2.2. Health and Demographic Surveillance Systems and other Observational cohorts

A number of population-based cohorts identified in this analysis did not meet all criteria to be considered as PERs but are capable of conducting maternal pharmacovigilance evaluations. Many resources in this category are designated as health and demographic surveillance systems (HDSS), and a majority of HDSS’s are members of the INDEPTH, a network of research sites that maintains a common set of standards for data collection. [19] These sites and the other cohorts in this group are conducted in geographically-defined area(s) in which residents are followed longitudinally and clinical and epidemiologic data are collected prospectively at regular intervals. They monitor a defined population, of which pregnant women are a subset, and usually record aspects of overall health care rather than focus on exposure to specific drugs or vaccines.

Observational cohorts are included in this group if the resource published analyses examining drug or vaccine exposures during pregnancy and reported obstetric and neonatal outcomes.

4.2.3. Outcomes-based registries

Outcomes-based registries focus on the detection and recording of specific outcomes, such as congenital malformations. They may be focused on a particular geography or a specific population. In most cases, enrollment in an outcomes-based registry occurs at the time of delivery or birth. Therefore, exposure information is collected retrospectively. Some registries may assess infants in a single visit while others follow infants to monitor outcomes for up to six weeks. In addition, some registries may enroll unaffected infants to serve as a comparison group.

4.2.4. Maternal condition-based registries

Resources in this category are based on enrolling pregnant women who have specific health conditions such as epilepsy, HIV infection, cardiac disease, or coagulopathy. These registries focus on exposure to medications associated with these disorders and usually assess outcomes in the infants such as congenital malformations over a limited period of time. Maternal outcomes related to the health condition of interest can also be included.
4.2.5. Manufacturer-initiated registries

Resources included in this category are registries funded and owned by the manufacturer or market authorization holder (MAH) of a drug or vaccine used in pregnant women. Such registries can be operated by a contract research organization, an academic group, or the manufacturer themselves. The US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) recommend that manufacturers establish surveillance efforts, such as pregnancy registries, for medical products on the market that are likely to be used during pregnancy or by women of childbearing age.[20,21] These registries are often established to meet a regulatory commitment or requirement for post-licensure safety monitoring, contribute to benefit-risk assessments, support product labeling, and inform guidance for regulators, health care providers, and the public throughout a medical product’s life-cycle. Pregnant women exposed intentionally or unintentionally to the medical product of interest are typically identified passively through sporadic reporting from recipients or care providers, although there may be outreach to potential participants. Once identified, there is usually active follow-up of participants to record information about health outcomes in the mother and infants. These registries are typically based in HICs but accept reports from other regions. While these data are generally not made available to the public, the US FDA maintains a list providing contact information for manufacturer registries that operate in the United States.[22]

4.2.6. Electronic health records databases and clinical software platforms

Electronic health records (EHR) databases and clinical software platforms typically collect and record clinical information prospectively on patients within a health care system. Using records linkage across time and various health and administrative databases comes with the advantage of identifying large numbers of pregnant women exposed to particular vaccines and other medicines, as well as their pregnancy outcomes. In these situations, pregnant women and their infants are usually a subset of the population, although some EHR’s may be specifically deployed in targeted maternal and newborn clinics. EHR systems are included in this report if a LMIC site has published a study or report on drug or vaccine exposures during pregnancy and their subsequent outcomes. For the purposes of this report, other resources, such as insurance claims databases have been included in this category.

The following sections report on findings, organized into the identified six categories.
4.3. Pregnancy exposure registries

Among the resources identified in this report, twelve self-identified as PERs or otherwise possessed typical characteristics of PERs (Table 4.2). While such classically designed PERs focusing on LMIC populations were found in multiple continents, the majority were located in sub-Saharan Africa (Figure 4.2), and most are currently active. Many PERs have been in operation for fewer than five years with some notable exceptions. Specifically, the Antiretroviral Pregnancy Registry (APR) and the Microbicide Pregnancy Registry of the Microbicide Trials Network (EMBRACE), have operated for over 10 years. Most PERs are funded through public or donor sources and are run by academic or non-governmental organizations (NGOs).

The majority of registries focus on antiretroviral drug exposures, but also include systems created to evaluate exposures to antimalarials. More recently, COVID-19 therapeutics and vaccines are the focus of PERs. Geographic coverage ranged from single hospitals to multi-national, with a similarly broad range in sample size from less than 500 to more than 25,000 participants accumulated over time. Some registries, such as the Measuring Adverse Pregnancy and Newborn Congenital Outcomes (MANGO) registry and the Malaria in Mothers and Babies (MiMBa) Pregnancy Registry, enroll a comparison group such as non-pregnant women of childbearing age. Others, such as the Understanding Birth Outcomes from Mothers and Infants, Building Healthcare by Linking Exposures (UBOMI BUHLE) registry and the Children HIV Exposed Uninfected Research to Inform Survival and Health (CHERISH) registry, enroll only pregnant women, but follow participants both exposed and unexposed to the interventions of interest.

The amount of detail provided in the available publications and other reports varied, but most registries were sufficiently described as encompassing a full range of obstetric and neonatal outcomes. A significant proportion follow the infants through the neonatal period only, with a focus on major congenital anomalies that can be detected in that timeframe. Infants are followed through one year (or potentially even more) in a few studies, however, to follow growth and development, as well as detect late-appearing birth defects.
Table 4.2. Pregnancy exposure registries.

<table>
<thead>
<tr>
<th>Resource Name</th>
<th>Countries</th>
<th>Focus</th>
<th>Time period</th>
<th>Funding source and implementing organization</th>
<th>Coverage and sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHERISH (Children HIV Exposed Uninfected Research to Inform Survival and Health)</td>
<td>South Africa, Kenya</td>
<td>Antiretrovirals</td>
<td>2020-present</td>
<td>US NIH, implementing organization Stellenbosch University, Cape Town</td>
<td>Provincial, 1,800 total</td>
</tr>
<tr>
<td>C-VIPER (COVID-19 Vaccines International Pregnancy Exposure Registry) and PIPER (Pregnancy International Pregnancy Exposure Registry)</td>
<td>Global, based in the United States, Uganda, Kenya, Tanzania, South Africa</td>
<td>Antiretrovirals</td>
<td>2020-present (C-VIPER) or 2022-present (PIPER)</td>
<td>Manufacturer, implementing organization Commercial</td>
<td>Global, C-VIPER: 8,172 (target 6,000), PIPER: 1,220 (target 10,000)</td>
</tr>
<tr>
<td>MANGO (Measuring Adverse Pregnancy and Newborn Congenital Outcomes)</td>
<td>Kenya (western)</td>
<td>Antiretrovirals</td>
<td>2020-present</td>
<td>Manufacturer, implementing organization Commercial</td>
<td>368 (target 2000)</td>
</tr>
<tr>
<td>MIMba (Malaria in Mothers and Babies) Pregnancy Registry</td>
<td>Kenya, Burkina Faso</td>
<td>Antimalarials</td>
<td>2020-present</td>
<td>Public, implementing organization Liverpool School of Tropical Medicine</td>
<td>Multi-district, 15,000</td>
</tr>
<tr>
<td>PIWEB (Pregnancy, Infant and Child Exposure to Birth Defects)</td>
<td>South Africa (3 provinces)</td>
<td>Antiretrovirals</td>
<td>2013-2017 (KwaZulu Natal site), 2016-present (Western Cape site)</td>
<td>Bill &amp; Melinda Gates Foundation (PIWEB), Public, implementing organization The Reproductive Health and HIV Institute (MRHI) and University of Cape Town</td>
<td>Provincial, 766,000 as of 2020, Multi-provincial, 16,000 per year, 55,000 cumulative to date</td>
</tr>
<tr>
<td>REPRESENT (Xiamen Registry of Pregnant Women and Offspring)</td>
<td>China (Xiamen)</td>
<td>None specified</td>
<td>2008-present</td>
<td>Public, implementing organization Xiamen Health Commission, Xiamen Health and Medical Big Data Center, Chinese Evidence-based Medicine Center, Xichuan University</td>
<td>Provincial, 766,000 as of 2020</td>
</tr>
<tr>
<td>UBONI BUNLE (Understanding Birth Outcomes from Mothers and Infants, Building Healthcare by Linking Exposures) National Pregnancy Exposure Registry</td>
<td>South Africa (3 provinces)</td>
<td>Antiretrovirals</td>
<td>2020-present</td>
<td>Bill &amp; Melinda Gates Foundation (CVD), Public, implementing organization Wits Reproductive Health and HIV Institute (MRHI) and University of Cape Town</td>
<td>Provincial, 766,000 as of 2020, Multi-provincial, 16,000 per year, 55,000 cumulative to date</td>
</tr>
</tbody>
</table>

**Design and eligibility and duration of follow-up**
- Prospective: Pregnant women with known HIV status at 24–36 weeks estimated gestational age, Follow-up of children to 3–5 years.
- Maternal Outcomes: Infant and under 3-year-survival, infant and under 1-year-all-cause and infectious-cause hospitalization, growth and neurodevelopmental outcomes at 3–5 years of age.
- Maternal outcomes: Severely low birth weight, neonatal death, neonatal encephalopathy, neonatal infections, neonatal acute kidney injury, preterm birth, respiratory distress in the newborn, small for gestational age, stillbirth, or COVID-19; infant weight, length, developmental milestones through 1 year of age.

**Comparison groups:**
- Prospective and retrospective: Pregnant women exposed to COVID-19 drugs.
- Prospective: Pregnant women exposed to COVID-19 and not exposed (PIPER) to COVID-19 vaccines.
- Retrospective: Pregnant women exposed to COVID-19 drugs

**References**
- [23]
- [10,24–26]
- [29,30]
- [31,32]
- [33–35]
- [36–40]
<table>
<thead>
<tr>
<th>Resource Name</th>
<th>Countries</th>
<th>Focus</th>
<th>Time period</th>
<th>Funding source and Implementing organization</th>
<th>References</th>
</tr>
</thead>
</table>
| Efavirenz in Pregnancy Registry                   | South Africa                                  | Antiretrovirals  | 2006-2008            | Funding source: N/A
Implementing organization: Frere Hospital, East London, South Africa                                                                                 | [41]       |
| EMBRACE Microbicide Pregnancy Registry (Microbicide Trials Network (MTN-016)) | Malawi, South Africa, Uganda, Zimbabwe | Microbicides and antiretrovirals | 2008–2020 | Funding source: Public
Implementing organization: HIV Prevention Trials Network                                                                                           | [42–45]   |
| POISE (Pregnancy Outcomes in the Era of Universal Antiretroviral Treatment in sub-Saharan Africa) associated registry | Malawi                                           | Antiretrovirals  | 2016-2017            | Funding source: US NIH
Implementing organization: Johns Hopkins University                                                                                               | [46]       |
| WHO Pregnancy Registry                             | Multinational (Kenya, Uganda, Tanzania, Ghana, Brazil [Rondonia]) | None specified  | 2010-2012            | Funding source: WHO
Implementing organization: WHO                                                                                                                        | [9,47]     |

Pregnancy exposure registries are among the stronger study designs identified in this scoping review. Key features include systematic, prospective data collection; a focus on pregnant populations; and an emphasis on particular exposures of interest. Pregnancy registries have numerous advantages (Table 4.3). By enrolling women before outcomes are known, the prospective approach of pregnancy registries avoids recall and reporting biases of both patients and providers, allows for the systematic recording of concomitant diseases and medications, and can use standardized methods and procedures to assess outcomes, including methods for gestational dating and ensuring the collection of details regarding the dose and timing of exposures to drugs or vaccines. The availability of both numerator and denominator data allows calculations of baseline rates of events (including AEFIs), and disease incidence in vaccinated and unvaccinated populations. Enrollment of a comparator group can be a valuable feature of a PER that allows for better estimation of risk. A comparator group could be pregnant women who are not exposed to the drug or vaccine. Due to the observational nature of PERs, analytical methods must account for potential biases in comparisons between exposed and unexposed groups.

Pregnancy registries can have limitations. Because reporting for some pregnancy registries is generally voluntary, prospectively reported pregnancies may lead to reporting bias toward high-risk pregnancies. Women who consent to take part in a study may have different characteristics from those who do not consent, introducing selection bias. Moreover, abnormal outcomes are more likely to be reported than normal outcomes. Enrollment of women limited to those who attend antenatal care may bias results and diminish the generalizability of findings. Late disclosure of pregnancy and late initiation of antenatal care limit information regarding the first trimester of pregnancy, gestational age dating, and early pregnancy loss. Home births and migration increase the potential for loss to follow-up, which may bias results. Finally, few pregnancy registries follow the health of children beyond the newborn period.
Table 4.3. Strengths and limitations of selected currently active pregnancy exposure registries (PERs) with available information.

<table>
<thead>
<tr>
<th>Resource</th>
<th>Strengths</th>
<th>Limitations and challenges</th>
</tr>
</thead>
</table>
| **Category-wide attributes** | • Systematic, prospective data collection  
• Purposely designed to capture relevant details of drug or vaccine exposures  
• Usually includes a comparator group and may be able to make statistical inferences | • Resource intensive  
• If voluntary recruitment, may bias toward high-risk  
• Few PER’s follow children beyond newborn |
| **C-VIPER** | • Global, including LMIC; rapid enrollment; multilingual;  
• Not resource-intensive  
• Social media targets young women of child-bearing age (WOCBA)  
• Includes unexposed comparator cohort | • Voluntary online recruitment through social media and word of mouth requires access and resources that may limit generalizability, particularly in LMICs |
| **MANGO** | • Partnership between Kenyan and US academic groups  
• Second largest national referral hospital in Kenya  
• One of the largest HIV programs in sub-Saharan Africa (AMPATH) | • None reported |
| **MiMBa** | • Prospective, focused on antimalarials, particularly a comparison between older and newer treatments (quine versus ACTs)  
• Also includes unexposed pregnant women for comparison  
• Good capture of first trimester exposures  
• Works with HDSS sites  
• Able to add new interventions (e.g., COVID-19 vaccine) | • Conducted in sentinel sites in two countries, limiting generalizability; however, the anticipated large size may mitigate this concern |
| **UBOMI BUHLE** | • Operating in three provinces  
• Linked to multiple electronic health record and other clinical databases  
• Merged and built from prior registries | • None reported |
| **Xiamen REPRESENT** | • Large population-based registry created by linking multiple data platforms.  
• Antenatal and facility-based electronic medical record databases can capture exposures and early outcomes, while a maternal and child health database can capture longer-term outcomes | • None reported |
4.4. Health and Demographic Surveillance Systems and other Observational cohorts

A number of health and demographic surveillance systems (HDSS) and other population-based observational cohorts identified through this analysis did not meet all criteria for classification as PERs, such as a primary focus on pregnancy or on monitoring the safety of an intervention. Instead, these are systems that cover the population of a particular geographic area, and in which data collection encompasses a broad range of data, including vital statistics and clinical care, but which may not focus on specific drug or vaccine exposures. Participants are longitudinally followed in a prospective fashion and the entire population is monitored. In these cohorts, pregnant women are usually a subset of the monitored population, although particular attention may be paid to this group for specific studies or surveillance efforts.

Observational cohorts identified in this review are located in countries throughout sub-Saharan Africa (particularly in the eastern African region) and South and Southeast Asia, including both INDEPTH members and other sites (Figure 4.2), and all of the systems described in this section are currently active.

Classification as a HDSS indicates that the system periodically collects demographic and health event information from a geographically defined population. A majority of the HDSS resources identified in this review are members of INDEPTH (http://www.indepth-network.org/), a network created in 1998 that currently encompasses 42 independent health research centers and 49 field sites in 19 LMICs. While all INDEPTH member sites collect basic health and epidemiologic data in their populations, systems are included in this review if they have published reports describing the safety of interventions in pregnant women—indicating the presence of targeted activities related to maternal pharmacovigilance.

The Maternal Newborn Health Registry (MNHR) is another large observational cohort, which incorporates sites in 7 LMICs[48]. Begun in 2008 within the US National Institute of Child Health and Human Development (NICHD) Global Network for Women’s and Children’s Health Research, the MNHR is a prospective, population-based research registry that collects data to assess trends in pregnancy outcomes and inform research studies within the network, including interventional trials and other sub-studies.[29] While tailoring the surveillance to the needs of individual studies appears to be possible, the MNHR primarily monitors the outcomes of maternal mortality, neonatal mortality, and stillbirth. Specific example sites for INDEPTH and MNHR have recently been evaluated for their potential use in conducting active safety surveillance following immunization in pregnancy.[49]

The Child Health and Mortality Prevention Surveillance Network (CHAMPS) Pregnancy Surveillance is a cohort surveillance study operating at HDSS sites in several LMICs. Established in 2020 within the infrastructure of the main CHAMPS study, which focuses on determining the etiologies of stillbirth and neonatal death (see Section 4.5 Outcomes-based registries), this study is modeled after the MNHR and enrolls pregnant women prospectively and retrospectively to monitor for major maternal and infant outcomes, including mortality.
Outside of these INDEPTH and MNHR, two additional observational cohorts indicating a focus on maternal pharmacovigilance are included in this report. The Shoklo Malaria Research Unit is a field station based on the Thai-Myanmar border founded in 1986 that conducts research and clinical care provision, with an emphasis on maternal and child health and infectious diseases. Also, the PREPARE project, created in 2020, is an observational study that prospectively enrolls women at a large urban hospital in Uganda during early pregnancy and follows the mother-infant pair through nine months after birth. The intention of this study is to build and optimize a system of monitoring and surveillance in advance of anticipated candidate vaccine clinical trials against Group B *Streptococcus*.

Except for the INDEPTH network, the resources included in this section have a focus on pregnancy and, therefore, pay particular attention to the collection of maternal outcomes—following the mothers through and beyond the time of delivery. All cohorts also capture major infant outcomes through at least the early neonatal period, with some extending one to several months into the first year of life. Studies conducted by INDEPTH sites vary in terms of follow-up duration but, in all cases, evaluate infant outcomes at or near the time of birth. Major obstetric outcomes (including spontaneous abortion, stillbirth, and maternal death) are universally recorded, but some groups (such as the MNHR and PREPARE cohorts) explicitly capture a larger range of conditions like pre-eclampsia/eclampsia, post-partum hemorrhage, and gestational diabetes. The most captured infant outcomes derive from the early neonatal period, including preterm birth, low birth weight, and congenital anomalies; though later outcomes may be identified as follow-up periods allow.

Also included in this category is International Epidemiology Databases to Evaluate AIDS (IeDEA), an international research and data exchange consortium that combines observational cohort datasets representing over 2.2 million people living with and at risk for HIV, with clinical centers and research groups in 44 countries participating. Established in 2005 with US National Institute of Health (NIH) funding, this global collaboration of cohort studies collects and combines data from HIV care and treatment programs to study antiretroviral treatment in populations that include pregnant individuals and follow them for clinical outcomes. IeDEA is organized around seven regional data centers representing major world areas, who work with clinical sites to establish large datasets and conduct analyses. Publications from this network that describe clinical information tracked during pregnancy describe studies in Brazil,[50,51] Malawi,[52] South Africa,[53] and the West African region.[54]

Our search also identified several publications describing research studies conducted as stand-alone analyses of retrospectively collected clinical data to evaluate the occurrence of maternal and/or infant outcomes following exposure to drugs or vaccines during pregnancy. In most cases, these investigations involved reviewing patient medical records at the individual level, often by hand or with minimal automation. While the data analyzed range from a few months to several years, and their population may cover single facilities or larger networks, these analyses were generally time-limited in nature and aimed to answer a specific research question rather than to provide ongoing monitoring or surveillance. Publications from studies that fell into this more limited group are listed in Section 6.4.1. The activities of one research group, however, who conducted a retrospective review of medical records from a set of area hospitals in Kinshasa, DRC, is described here. Two recent publications from this group evaluated the feasibility of using Global Alignment of Immunization Safety Assessment in pregnancy (GAIA) outcome definitions in this low-resource setting, and assessed the ability of their activities to document the impact of the COVID-19 pandemic on maternal and neonatal health outcomes.[55,56] These publications indicated that their work will include a phase of prospective data collection, and therefore this group has been included in this section.
<table>
<thead>
<tr>
<th>Resource Name</th>
<th>Countries</th>
<th>Focus</th>
<th>Time period</th>
<th>Funding source and Implementing organization</th>
<th>Coverage and sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Currently active</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHAMPS (Child Health and Mortality Prevention Surveillance Network) pregnancy surveillance</td>
<td>Global, based in the United States</td>
<td>None specified</td>
<td>2020-present</td>
<td>Funding source: Bill &amp; Melinda Gates Foundation, Emory University and multi-sectoral partners</td>
<td>Not available</td>
</tr>
<tr>
<td>IeDEA (International Epidemiology Databases to Evaluate AIDS)</td>
<td>Multinational</td>
<td>Antiretrovirals</td>
<td>2005-present</td>
<td>Funding source: US NIH, Implementing organization: Indiana University</td>
<td>Various</td>
</tr>
<tr>
<td>INDEPTH</td>
<td>Multinational</td>
<td>None specified</td>
<td>1998-present</td>
<td>Funding source: Multiple donors, Implementing organization: Individual HDSS sites</td>
<td>District 165,820 births during 2009-2014</td>
</tr>
<tr>
<td>Maternal Newborn Health Registry</td>
<td>Multinational</td>
<td>None specified</td>
<td>2008-present</td>
<td>Funding source: US NIH, Implementing organization: Individual sites</td>
<td>Global 60,000 annual enrollment &gt;700,000 cumulative</td>
</tr>
<tr>
<td>PREPARE</td>
<td>Uganda</td>
<td>Antimalarials</td>
<td>2020-present</td>
<td>Funding source: EDCTP, Implementing organization: St. George’s University of London and Makerere University</td>
<td>Hospital 2,000-5,000</td>
</tr>
<tr>
<td>Shoko Malaria Research Unit</td>
<td>Thailand</td>
<td>Antimalarials</td>
<td>1996-present</td>
<td>Funding source: Multiple donors, Implementing organization: Faculty of Tropical Medicine, Mahidol University, Bangkok, Mahidol-Oxford Research Unit (MORU)</td>
<td>District</td>
</tr>
<tr>
<td>UCLA DRC Research Program</td>
<td>Democratic Republic of Congo</td>
<td>None specified</td>
<td>2018-present</td>
<td>Funding source: US FDA, Private charities, Implementing organization: University of California, Los Angeles</td>
<td>District 14,300 (prospective) 7,697 (retrospective)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TOC</th>
<th>SECTION 1: Executive summary</th>
<th>SECTION 2: Introduction</th>
<th>SECTION 3: Methods</th>
<th>SECTION 4: Results</th>
<th>SECTION 5: Discussion</th>
<th>SECTION 6: Appendices</th>
<th>SECTION 7: References</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Table 4.4. Health and Demographic Surveillance Systems and other Observational cohorts.
Table 4.5. Strengths and limitations of selected observational cohorts with available information.

<table>
<thead>
<tr>
<th>Resource</th>
<th>Strengths</th>
<th>Limitations and challenges</th>
</tr>
</thead>
</table>
| **Category-wide attributes** | • Reduced selection and recall bias due to prospective enrollment and data collection  
• Enrollment and monitoring occurs before outcome is known, and often before the exposure occurs  
• Many have been active for years, allowing assessment of trends over time | • Resource intensive  
• Annual enrollment population size may be limited  
• Outcomes of intensively monitored populations may not be generalizable  
• Health information may be self-reported |
| **IeDEA (International Epidemiology Databases to Evaluate AIDS)** | • Large size with substantial LMIC representation  
• Common methods for basic data collection and analysis practiced across sites  
• Shared practices and collaboration across sites  
• Long experience in operation | • Secondary use of data from routine clinical care  
• Potential heterogeneity in site capacities and practices |
| **INDEPTH** | • Large size with substantial LMIC representation  
• Common methods for basic data collection and analysis practiced across sites  
• Shared practices and collaboration across sites  
• Long experience in operation | • PER-specific activities conducted only in a subset of sites  
• Differing capacities and methods among sites for capturing PER-specific data |
| **Maternal Newborn Health Registry** | • Specifically focused on maternal and newborn populations  
• Unified methods and tools for data collection and analysis, resulting in a common dataset  
• Large combined study population  
• Prospective and population-based  
• Wide geographic coverage in LMICs  
• Long experience in operation | • Challenges with participant migration, or travel for delivery |

### 4.5. Outcomes-based registries

Outcomes-based registries may be either open to the general population of pregnant women in a hospital’s catchment area or geographic region, or may target enrollment for groups receiving certain interventions, such as antiretroviral medications. Registries in this category most commonly monitor for congenital malformations (used interchangeably with congenital anomalies and birth defects) in the infant and given their emphasis on the detection and evaluation of these conditions, they often enroll newborns. Information regarding maternal exposures is collected retrospectively, through access to clinical records, electronic medical databases, other data collection systems (e.g., HIV treatment programs), or less commonly, via participant recall. Depending on the registry, outcomes assessment of the infants may be conducted only once, during the neonatal period, or may occur multiple times, allowing for the detection of late-appearing congenital conditions and the observation of infant growth and development. Some registries also assist in locating or providing support to the children identified with anomalies, who may have need for special services.
The geographic distribution of outcomes-based registries identified in this report reflect their main focus (Figure 4.2). Those established to evaluate concerns for malformations related to antiretroviral therapies are mostly located in sub-Saharan Africa, while those more generically conceived birth defects registries that do not emphasize particular treatments and aim to determine incidence rates in the broader population can be found in other regions, including East Asia and South America.

Funding support for registries in this section is most commonly provided by donors and public sources, although a few derive support from manufacturers. A majority are operated by academic or non-profit organizations, at times in collaboration with the local governments.

Given their emphasis on outcomes, most of these registries enroll participants at the time of delivery and birth. Therefore, information regarding drug or vaccine exposures is collected retrospectively (Table 4.6). For the most part, registries aiming to determine the general background rate of birth defects in the population do not focus on specific interventions; however, a limited number (e.g., those listed in Uganda, Eswatini, and Botswana in Table 4.7) were established explicitly to assess the risk of antiretroviral medications such as dolutegravir and cabotegravir. In recent years, several birth defects surveillance programs in Africa have joined together to form the sub-Saharan African Congenital Anomalies Network (sSCAN).[101] sSCAN provides a forum to offer support and build technical capacity at member sites by developing and sharing resources, conducting workshops, and encouraging collaboration.

Given their design, most outcomes-based registries emphasize the detection of congenital malformations identifiable at the time of birth, typically through surface examination. Maternal outcomes (including miscarriages or other obstetric complications) might not be captured, particularly if they do not result in a live birth. While most registries focus on assessments at a single visit, some systems may follow infants for longer periods (e.g., six weeks) to capture conditions that appear later, but typically do not capture abnormalities in growth or development that may be detected in late infancy.

Outcomes-based registries generally enroll a large sample size numbering in the thousands, which may reflect the efficiencies allowed by study designs centered on a single visit at birth, allowing resources to be directed toward capturing an expanded number of infants. In many of these registries, considerable attention is given to detailed examination and classification of the detected malformations and expert adjudication on their classification. In addition, follow-up care and support of the children found to have malformations may be an important component of the registry. In most cases, no explicit comparator population is used; however, unaffected mother-infant pairs can be selected from the screened population to make comparisons with affected pairs to calculate the risk associated with exposures of interest.

The Child Health and Mortality Prevention Surveillance study is unique in focusing on identifying the causes of stillbirths and neonatal deaths. Identified through demographic and mortality surveillance at sites in multiple countries, fatal cases are evaluated through verbal autopsy, clinical records, and tissue sampling within 24 hours to determine causes of death.
Table 4.6. Outcomes-based registries.

<table>
<thead>
<tr>
<th>Resource Name</th>
<th>Countries</th>
<th>Focus</th>
<th>Time period</th>
<th>Funding source and Implementing organization</th>
<th>Coverage and sample size</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBDSFP (Bogota Birth Defects Surveillance and Follow-up Program)</td>
<td>Colombia</td>
<td>None specified</td>
<td>2011-present</td>
<td>Funding source: Public</td>
<td>City 9,724 during 2006-2015</td>
</tr>
<tr>
<td>CHAMPS (Child Health and Mortality Prevention Surveillance)</td>
<td>Multinational</td>
<td>None specified</td>
<td>2016-present</td>
<td>Funding source: Bill &amp; Melinda Gates Foundation</td>
<td>Multinational Community surveillance 10,731 as of 2023</td>
</tr>
<tr>
<td>CTBC (China Teratology Birth Cohort)</td>
<td>China</td>
<td>Antiretrovirals; Antimalarials; Medicines related to autoimmune, cancer, diabetes, and epilepsy</td>
<td>2019-present</td>
<td>Funding source: Public</td>
<td>Multi-provincial Sample size N/A</td>
</tr>
<tr>
<td>Eswatini Birth Defects Study</td>
<td>Eswatini</td>
<td>Antiretrovirals</td>
<td>2021-present</td>
<td>Funding source: Viv HealthCare</td>
<td>Multi-district 18,877 during 2021-2022</td>
</tr>
<tr>
<td>Makerere Birth Defects Surveillance Project</td>
<td>Uganda</td>
<td>Antiretrovirals; Tetanus toxoid vaccine</td>
<td>2015-present</td>
<td>Funding source: US CDC</td>
<td>Hospital Sub-district 48,000 per year 200,000 total</td>
</tr>
<tr>
<td>Malawi Birth Defects Surveillance</td>
<td>Malawi</td>
<td>None specified</td>
<td>2016-present</td>
<td>Funding source: US CDC</td>
<td>Multi-hospital Multi-district 146,163 during 2016-2022</td>
</tr>
<tr>
<td>Tsepamo Study</td>
<td>Botswana</td>
<td>Antiretrovirals</td>
<td>2014-present</td>
<td>Funding source: US NIH</td>
<td>Multi-hospital 200,000 target</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Design and Eligibility and duration of follow-up</th>
<th>Maternal Outcomes</th>
<th>Neonatal and Infant/child outcomes</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Retrospective All deliveries</td>
<td>Maternal illnesses by ICD code</td>
<td>Congenital anomalies</td>
<td>[102–104]</td>
</tr>
<tr>
<td>Retrospective Stillbirths and neonatal deaths</td>
<td>stillbirth, spontaneous abortion</td>
<td>Neonatal death</td>
<td>[77,105]</td>
</tr>
<tr>
<td>Prospective Comparison group All deliveries</td>
<td>stillbirth, spontaneous abortion</td>
<td>Congenital anomalies, preterm birth, post-term birth, low birth weight, macrosomia, small for gestational age, large for gestational age, low Apgar score</td>
<td>[106]</td>
</tr>
<tr>
<td>Retrospective Comparison group</td>
<td>N/A</td>
<td>Major and minor surface birth defects</td>
<td>[107,108]</td>
</tr>
<tr>
<td>Retrospective Comparison group</td>
<td>Spontaneous abortion, stillbirth</td>
<td>Congenital anomalies; congenital infections</td>
<td>[109–111]</td>
</tr>
<tr>
<td>Retrospective All deliveries</td>
<td>Major external birth defects</td>
<td></td>
<td>[112,113]</td>
</tr>
<tr>
<td>Retrospective Comparison group</td>
<td>Preterm delivery, stillbirth</td>
<td>Congenital anomalies, preterm birth, small for gestational age, or neonatal death</td>
<td>[114–120]</td>
</tr>
</tbody>
</table>
### Table 4.7: Strengths and limitations of selected outcomes-based registries with available information.

<table>
<thead>
<tr>
<th>Resource</th>
<th>Strengths</th>
<th>Limitations and challenges</th>
</tr>
</thead>
</table>
| **Category-wide attributes** | • Can provide detailed data regarding the incidence and characterization of uncommon infant outcomes, such as congenital anomalies  
• Emphasis on training HCW on newborn surface examination, expert adjudication and classification  
• Usually a single neonatal visit (with follow-up if needed), thus fewer resources needed per participant, and sample size can be large | • Single visit may limit amount of information collected, e.g., maternal outcomes, later infant outcomes  
• Information on exposures is mostly retrospective, thus subject to recall bias, misclassification, or incomplete records |
| BBDSFP (Bogota Birth Defects Surveillance and Follow-up Program) | • In operation since 2001  
• Able to enroll control groups with no abnormalities for additional analysis | • Data on exposures are self-reported at time of delivery |
| CHAMPS (Child Health and Mortality Prevention Surveillance) | • Wide geographic distribution of sites  
• Standardized methods  
• Use of minimally invasive tissue sampling and placental examination to determine cause of death | • Focus on fatal infant outcomes  
• Focus on proximate causes of stillbirth/neonatal death, e.g., hypoxia, infections, rather than more remote drug or vaccine exposures |
| CTBC (China Teratology Birth Cohort) | • Prospective cohort study  
• Detailed information on drug exposures is collected  
• High rate of facility-based deliveries in the population | • Pregnant women attending hospitals specific for infectious diseases or psychiatric conditions are not yet included  
• Early abortions are under-represented  
• Data are not publicly accessible |
| Makerere Birth Defects Surveillance Project | • Large sample size  
• High rate of hospital deliveries in the population  
• Active case ascertainment, including stillbirths and spontaneous abortions  
• Antenatal care records are all on site at delivery hospitals  
• Antiretroviral records maintained through national program  
• Able to compare women with/without HIV and with/without ARV exposure | • May miss early pregnancy losses managed at home  
• Does not include diagnoses after newborn discharge or data on infant follow-up and survival  
• Referral patterns and urban population may limit generalizability |
| Tsepmo Study | • Large sample size  
• Nationally representative  
• Comprehensive information on HIV infection status and ARV regimen | • Identifies only abnormalities detected by surface examination |
### 4.6. Maternal conditions-based registries

Registries included in this section are those developed to monitor the safety of treatments given to pregnant women with specific underlying health conditions such as epilepsy, HIV, or cardiac disease (Table 4.8). Pregnancy registries centered around the presence of a selected health condition typically enroll women who receive medicines in an associated product class, such as anti-epileptic drugs, antiretrovirals, anti-coagulants, or cardiac medicines. Vaccination is rarely a focus in these efforts. These registries are often established due to a known or suspected safety signal associated with these medicines such as a particular congenital malformation or neonatal complication. These registries, therefore, emphasize detection of infant outcomes. Some of them, however, will also monitor maternal outcomes associated with the underlying health condition such as seizure frequency or worsening heart failure.

Other than those focused on HIV, the registries identified in this category are more commonly located in middle-income countries such as India, Brazil, and Argentina. This pattern may reflect that physicians specializing in fields such as neurology or cardiology may have a greater capacity to gather together larger patient cohorts in countries with higher economic levels.

As with outcomes-based registries, funding support for registries based on maternal conditions is mostly provided by donors and public sources, and these registries are operated by academic groups, clinical departments, or non-profit organizations, at times registries are managed in collaboration with the local governments.

Registries based on maternal underlying conditions are more likely to be prospective in design because the participants are often already identified and followed by the clinics providing the relevant specialty care (Table 4.9). Registries operated by individual clinics or academic centers involve a smaller study population. Even those with national or multi-national coverage generally do not reach the sample sizes achieved by the outcomes-based registries. Since exposures are often documented prospectively, comparator groups of unexposed pregnant women may be enrolled. In other cases, comparisons of non-pregnancy-related maternal health outcomes may be made with non-pregnant women that receive the intervention of interest.
**Table 4.8.** Maternal conditions-based registries.

<table>
<thead>
<tr>
<th>Resource Name</th>
<th>Countries</th>
<th>Focus</th>
<th>Time period</th>
<th>Funding source and Implementing organization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kerala registry of Epilepsy and Pregnancy (KREP)</td>
<td>India</td>
<td>Anti-epileptics</td>
<td>1998-present</td>
<td>Funding source: Public Implementing organization: KREP Study Group, Sri Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST)</td>
</tr>
<tr>
<td>REBECGA Brazilian Registry of Pregnancy and Heart Disease</td>
<td>Brazil</td>
<td>Cardiac medications</td>
<td>Retrospective analysis 2017–2020 Prospective analysis 2023–26</td>
<td>Funding source: Donor Implementing organization: Women’s Cardiology Department of University of Sao Paulo and the Brazilian Society of Cardiology</td>
</tr>
<tr>
<td>Tamil Nadu Pregnancy and Heart Disease Registry (TNPHDR)</td>
<td>India</td>
<td>Heart disease</td>
<td>2020–2023</td>
<td>Funding source: Public Implementing organization: Madras Medical College and Research Institute</td>
</tr>
<tr>
<td>Epilepsy Pregnancy Registry in Argentina</td>
<td>Argentina</td>
<td>Anti-epileptics</td>
<td>1995–2002</td>
<td>Funding source: Funding N/A Implementing organization: Instituto de Investigaciones Neurologicas Raul Carrea-FLENI, Buenos Aires</td>
</tr>
<tr>
<td>European Collaborative Study (ECS) in Ukraine</td>
<td>Ukraine</td>
<td>Antiretrovirals</td>
<td>2000–2012</td>
<td>Funding source: European Union Implementing organization: University College of London</td>
</tr>
<tr>
<td>Shifa International Hospital Registry of Antiepileptic Drugs in Pregnancy</td>
<td>Pakistan</td>
<td>Anti-epileptics</td>
<td>2018–2020</td>
<td>Funding source: Funding N/A Implementing organization: Shifa International Hospital, Islamabad</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Coverage and sample size</th>
<th>Design and Eligibility and duration of follow-up</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital 1998–2017</td>
<td>Prospective, enrolled in the preconception period or first trimester</td>
<td></td>
</tr>
<tr>
<td>1,962 exposed</td>
<td>Exposed and unexposed (comparator)</td>
<td>[121–128]</td>
</tr>
<tr>
<td>340 unexposed</td>
<td>Pregnant women with epilepsy</td>
<td></td>
</tr>
<tr>
<td>Multi-hospital</td>
<td>Prospective (longitudinal) and retrospective (cross-sectional) stages</td>
<td></td>
</tr>
<tr>
<td>Prospective phase: 300-350/year</td>
<td>Pregnant women with heart disease</td>
<td>[129]</td>
</tr>
<tr>
<td>State/provincial</td>
<td>Prospective</td>
<td>[130]</td>
</tr>
<tr>
<td>2,461</td>
<td>Pregnant women with heart disease</td>
<td></td>
</tr>
<tr>
<td>Multi-hospital 114</td>
<td>Prospective</td>
<td></td>
</tr>
<tr>
<td>HIV-positive pregnant women</td>
<td>Pregnant women with epilepsy taking anti-epileptic drugs</td>
<td>[131]</td>
</tr>
<tr>
<td>Multi-hospital 8,863</td>
<td>Prospective</td>
<td>[132–134]</td>
</tr>
<tr>
<td>Hospital 65</td>
<td>Prospective</td>
<td></td>
</tr>
<tr>
<td>Pregnant women with epilepsy at the time of conception</td>
<td>[135]</td>
<td></td>
</tr>
</tbody>
</table>
### Table 4.9. Strengths and limitations of maternal conditions-based registries.

<table>
<thead>
<tr>
<th>Resource</th>
<th>Strengths</th>
<th>Limitations and challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td>Category-wide attributes</td>
<td>• Typically study a specific product class of drugs, thus can be focused on specific safety signals or issues, e.g., certain birth defects</td>
<td>• Typically smaller, focused on a specific subset of the maternal population</td>
</tr>
<tr>
<td></td>
<td>• Most are conducted prospectively, often with enrollment prior to conception</td>
<td>• Limited ability to include comparator participants, depending on how commonly the drug is used</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• May be less able to incorporate new drugs or vaccines, unless there is particular interest in their safety in the population</td>
</tr>
</tbody>
</table>
Registries in this group are distinguished from others by being funded, and usually operated, by the manufacturer of a specific product (Table 4.10). The registry can focus on an individual drug or vaccine, or can monitor all products (e.g., all vaccines) in the same class made by the manufacturer. These systems are often established due to a regulatory commitment for post-licensure safety monitoring, which can be based on prior detection of a safety signal or due to a more general concern about the use of the product in pregnancy. Regardless, these systems are intended to add to the product’s post-licensure safety database, with the potential inclusion of resulting data in the product’s label. Most manufacturer registries are run by multinational corporations based in HICs that have well-resourced pharmacovigilance departments, and a large proportion of their data come from these markets. The registries may accept reports from other areas of the world, however, and can therefore be considered global in coverage, although these participants may only represent a small fraction of the populations analyzed. Some registries created to comply with a post-licensure commitment are designed to answer a specific scientific question and, therefore, may have a pre-defined timeframe or sample size limit. In other cases, the registries may be continued indefinitely in order to continue monitoring the use of the products during pregnancy.

Manufacturer-based registries typically use a passive surveillance design in which the operators sporadically receive voluntary reports of exposures originating from patients or providers (Table 4.11). At times, outreach to potential physicians, individual patients, or patient groups can occur, particularly if the product is to be used in specific patient populations such as those with autoimmune disorders. In most cases, however, contact information and instructions on how to enroll are simply provided in the product’s package insert, product literature, or the company website. Given the global reach of coverage of these registries and their operation by a dedicated pharmacovigilance unit with substantial expertise, manufacturers are often able to conduct epidemiological analyses that can potentially detect risks.

Not included in this report are other types of observational clinical studies conducted by manufacturers that employ active surveillance or other more resource-intensive methods to recruit and monitor recipients to answer specific scientific questions, since they are usually classified as Phase 4 studies rather than registries.

In general, outcomes monitoring within these registries will encompass maternal as well as infant outcomes. The completeness of these registries can be limited by the voluntary nature of reporting by participants. In many cases, however, once a person has been enrolled, registry staff will contact them subsequently to solicit information on outcomes.
### Table 4.10. Manufacturer registries

<table>
<thead>
<tr>
<th>Resource Name</th>
<th>Countries</th>
<th>Focus</th>
<th>Time period</th>
<th>Funding source and implementing organization</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Currently active</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>API (Antiretroviral Pregnancy Registry)</strong></td>
<td>Multinational (70-80% US)</td>
<td>Antiretrovirals (HIV and HBV)</td>
<td>1989-present</td>
<td>Funding source: Manufacturer implementing organization: Contract research organization</td>
</tr>
<tr>
<td><strong>Bayer pharmacovigilance (PV) database</strong></td>
<td>International, with select middle-income countries (Russia, South Africa)</td>
<td>Interferon-beta-2b (Betaferon(R), Betaseron(R), Extavia(R))</td>
<td>1995-present</td>
<td>Funding source: Manufacturer</td>
</tr>
<tr>
<td><strong>EURAP: International Registry of Antiepileptic Drugs and Pregnancy</strong></td>
<td>Mainly high-income countries, but also India, Philippines</td>
<td>Anti-epileptics</td>
<td>1999-present</td>
<td>Funding source: Manufacturer implementing organization: The EURAP Study Group</td>
</tr>
<tr>
<td><strong>Novartis Multi-National Gilenya Pregnancy Exposure Registry in Multiple Sclerosis</strong></td>
<td>Global, including select middle-income countries (Brazil, Russia, Argentina)</td>
<td>Medicines for multiple sclerosis (fingolimod)</td>
<td>2011-2021</td>
<td>Funding source: Manufacturer implementing organization: Contract research organization (Quintiles, IQVIA)</td>
</tr>
<tr>
<td><strong>Sanofi Pasteur Pregnancy Surveillance Program</strong></td>
<td>Global</td>
<td>Vaccines (Menactra, Adacel, Fluzone, MenQuadfi (US only), Dengvaxia, Flublok (US only))</td>
<td>2005- (Menactra) 2005- (Adacel) 2015-19 (Fluzone intradermal) 2013-2019 (quadvalent influenza vaccine) 2021-2028 (MenQuadfi) 2022-2024 (Dengvaxia)</td>
<td>Funding source: Manufacturer</td>
</tr>
<tr>
<td><strong>No longer active</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GARFIELD-VTE registry</strong></td>
<td>Multi-national</td>
<td>Anticoagulants</td>
<td>2014-2020</td>
<td>Funding source: Manufacturer (unrestricted grant from Bayer AG) implementing organization: Thrombos Research Institute</td>
</tr>
<tr>
<td><strong>Tysabri® (natalizumab) pregnancy exposure registry</strong></td>
<td>Focus on United States and Canada, with a “rest of the world” component</td>
<td>Natalizumab (Tysabri)</td>
<td>2007-2012</td>
<td>Funding source: Manufacturer implementing organization: Biogen</td>
</tr>
</tbody>
</table>

### Coverage and sample size

<table>
<thead>
<tr>
<th>Catologue</th>
<th>Design and Eligibility and duration of follow-up</th>
<th>Maternal Outcomes</th>
<th>Neonatal and Infant/child outcomes</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multinational</td>
<td>1,300–1,700 per year, &gt;25,000 total</td>
<td>Prospective</td>
<td>Spontaneous abortion, miscarriage, pregnancy loss</td>
<td>Congenital anomalies / birth defects, death, live birth, preterm birth, small size for gestational age / restricted fetal growth, stillbirth</td>
</tr>
<tr>
<td>Multinational</td>
<td>Through 2018: 2581 prospective and 1,935 retrospective</td>
<td>Prospective Retrospective (for comparison)</td>
<td>Spontaneous abortions, stillbirth / fetal death, ectopic pregnancies</td>
<td>Congenital anomalies</td>
</tr>
<tr>
<td>Multinational</td>
<td>29,953 worldwide</td>
<td>Prospective (cases that are enrolled after 16 wks, after prenatal dx, or after birth are reported descriptively)</td>
<td>Exome frequency</td>
<td>Stillbirths, elective terminations due to fetal abnormalities</td>
</tr>
<tr>
<td>Multinational</td>
<td>&gt;20,000</td>
<td>Prospective Retrospective Comparison group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multinational</td>
<td>500 (target)</td>
<td>Prospective Retrospective</td>
<td>Pregnant women</td>
<td>Varies by product; includes spontaneous abortion</td>
</tr>
<tr>
<td>Multinational</td>
<td>199 pregnant patients (of 16,870 enrolled)</td>
<td>Prospective</td>
<td>Patients with venous thromboembolic event, pregnant women as a subset</td>
<td>Not available</td>
</tr>
<tr>
<td>Multinational</td>
<td>376</td>
<td>Prospective</td>
<td>Women with multiple sclerosis or Crohn’s disease exposed to Tysabri within 90 days of last menstrual period or during pregnancy Followed through four weeks after delivery</td>
<td>Spontaneous abortions, elective or therapeutic abortions, fetal losses including stillbirths, and ectopic pregnancies</td>
</tr>
</tbody>
</table>
Electronic medical record (EHR) systems are computerized databases that collect and record clinical information prospectively on all patients within a healthcare system. EHR platforms may be implemented nationally, within certain health systems or sectors, or by individual facilities. Pregnant women and their infants may make up only a subset of an EHR’s patient population but, by collecting and storing the clinical data electronically, the resulting databases can be searched for specific information and analyzed using structured, reproducible methods.

This report includes initiatives that have published studies or reports (either in the scientific literature or in the gray literature) that tracked drug or vaccine exposures during pregnancy and subsequent outcomes using an EHR database. In these cases, investigators may have developed programming and/or algorithms to identify pregnancies in their database, extract the data needed, and classify outcomes appropriately. Identified EHR databases include SmartCare in Zambia, the Baobab Health Antiretroviral Therapy (BART) system in Malawi, and the Provincial Health Data Centre (PHDC) system in the Western Cape province of South Africa.

### Table 4.11. Strengths and limitations of manufacturer registries.

<table>
<thead>
<tr>
<th>Resource</th>
<th>Strengths</th>
<th>Limitations and challenges</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• Global coverage and centralized, therefore can enroll larger numbers</td>
<td>• Passive surveillance, voluntary and sporadic enrollment</td>
</tr>
<tr>
<td></td>
<td>• Manufacturer is knowledgeable about the product</td>
<td>• Timing of enrollment cannot always be controlled; participants may enroll after outcomes are known</td>
</tr>
<tr>
<td></td>
<td>• Prospective enrollment is usually encouraged</td>
<td>• Data are not verified, particularly if self-reported; medical records for verification might be requested, but consent may be required, which is resource-intensive</td>
</tr>
<tr>
<td></td>
<td>• Data may be used for regulatory purposes, and thus may have a more direct impact on use</td>
<td>• Data and analyses are not always made publicly available</td>
</tr>
<tr>
<td></td>
<td>• Safety monitoring can be better resourced by the manufacturer if considered a priority (e.g., due to a regulatory commitment or a known safety signal)</td>
<td>• Often not operated by independent researchers; manufacturer staff may be considered to have a conflict of interest</td>
</tr>
<tr>
<td></td>
<td>• Monitoring of multiple products from the same manufacturer can be harmonized, or even combined</td>
<td>• Less likely to incorporate additional interventions that are not from the same manufacturer</td>
</tr>
<tr>
<td></td>
<td>• The APR in particular has a long experience in operation, monitors a large number of antiretrovirals, and has multinational representation</td>
<td>• Developing country vaccine manufacturers (DCVMs) typically do not have mature pharmacovigilance departments with the expertise needed to manage registries and analyze results</td>
</tr>
</tbody>
</table>

## 4.8. Electronic health records and other clinical software platforms

Electronic medical record (EHR) systems are computerized databases that collect and record clinical information prospectively on all patients within a healthcare system. EHR platforms may be implemented nationally, within certain health systems or sectors, or by individual facilities. Pregnant women and their infants may make up only a subset of an EHR’s patient population but, by collecting and storing the clinical data electronically, the resulting databases can be searched for specific information and analyzed using structured, reproducible methods.

This report includes initiatives that have published studies or reports (either in the scientific literature or in the gray literature) that tracked drug or vaccine exposures during pregnancy and subsequent outcomes using an EHR database. In these cases, investigators may have developed programming and/or algorithms to identify pregnancies in their database, extract the data needed, and classify outcomes appropriately. Identified EHR databases include SmartCare in Zambia, the Baobab Health Antiretroviral Therapy (BART) system in Malawi, and the Provincial Health Data Centre (PHDC) system in the Western Cape province of South Africa.
Another set of systems within this category are software platforms such as DHIS2. DHIS2 is an open-source web-based software platform designed for collecting and analyzing data at the population and individual patient levels, and can be designed for facilities, health systems, or national programs. Data are entered into the system as part of medical care, rather than collected by study staff during dedicated visits, as would be done in surveillance system such as a HDSS. By the end of 2022, DHIS2 is being used in more than 75 LMICs, with 69 countries using DHIS2 at a national scale.[167,168] DHIS2 has the ability to provide for individual patient clinical care and to conduct epidemiological analyses for surveillance and research.[169] DHIS2 is comprehensive and encompassing data capture for multiple aspects of healthcare provision, including analytics and data management, individual case management, surveillance, and even logistics and supplies. Health care providers and researchers can address data collection and analysis for specific health topics such as HIV, tuberculosis, or immunizations through pre-configured installable metadata packages. These modules include a Reproductive, Maternal, Newborn, Child and Adolescent Health (RMNCAH) package, which provides a structure to track exposures and outcomes during pregnancy.

While use of the RMNCAH package is likely active in multiple settings, this review only identified one clear example in which DHIS2 was used to track maternal exposures and outcomes in Palestine. In this instance, deployment of the DHIS2 platform was initiated specifically in MNCH clinics, with the expansion of the system to other sectors afterwards. Though this one example occurred in Palestine, the potential for such data collection within the DHIS2 system could be considered for other countries.[49]

Other open-source clinical software platforms, such as OpenMRS and OpenEMR, have been promoted in LMICs worldwide and could theoretically provide similar functionality to conduct pharmacovigilance in pregnant women.[11] However, no publications or online sources describing their use for monitoring drug safety during pregnancy were found in our search.

The Perinatal Information System (Sistema Informatico Perinatal [SIP]) is a free standardized perinatal clinical record developed by the Pan American Health Organization (PAHO) and run by PAHO’s Latin American Center for Perinatology/Women’s Health and Reproductive Health (CLAP/WR) in Montevideo, Uruguay.[170,171] First publicized in 1983, facilities have used this database throughout Latin America and the Caribbean. Using this program, facilities can produce reports and combine their data with other facilities’ using the same platform, allowing studies to be conducted at the regional or national level.[171–173] While no publications related specifically to pregnancy exposure pharmacovigilance using SIP were identified as part of this review, the capability appears to be possible, at least at the facility level.

Finally, our review found one study in which researchers in China analyzed data from a national insurance claims database to assess the safety of medication use in pregnancy. The use of administrative insurance databases to perform epidemiological studies, including those associated with drug or vaccine safety, is common in HICs where methods are well developed and coverage is relatively high. While national health insurance is generally expanding in LMICs[174] (particularly in MICs),[175] the expansion has been particularly slow in the lower-resource areas of Africa and Southeast Asia. Research involving claims databases have been even fewer,[176–179] but may increase if health insurance becomes more common. This review, however, found no studies in additional LMICs relating to the use of insurance databases to conduct maternal pharmacovigilance.
Table 4.12. Electronic health records and other clinical software platforms.

<table>
<thead>
<tr>
<th>Resource Name</th>
<th>Countries</th>
<th>Focus</th>
<th>Time period</th>
<th>Funding source and Implementing organization</th>
<th>Coverage and sample size</th>
<th>Design and Eligibility and duration of follow-up</th>
<th>Maternal Outcomes</th>
<th>Neonatal and Infant/child outcomes</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Currently active</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baobab Health Trust</td>
<td>Malawi</td>
<td>None specified</td>
<td>2001-present</td>
<td>Funding source: Donor Implementing organization: Baobab Health Trust</td>
<td>Multi-district</td>
<td>Maternal Outcomes: Thrombosis, gestational diabetes, gestational hypertension, PIH, preterm labor, pre-eclampsia/eclampsia, post-partum hemorrhage, maternal death, placenta previa</td>
<td></td>
<td>Neural death, congenital anomalies, neonatal infections, preterm birth, stillbirth, low birthweight, small for gestational age, respiratory distress, later infancy infections, respiratory illness</td>
<td>[180,181]</td>
</tr>
<tr>
<td>CHIRA (China Health Insurance Association database)</td>
<td>China</td>
<td>None specified</td>
<td>2007-present</td>
<td>Funding source: Public Implementing organization: Chinese government via basic medical insurance (BMI)</td>
<td>National</td>
<td>Maternal Outcomes: Thrombosis, gestational diabetes, gestational hypertension, PIH, preterm labor, pre-eclampsia/eclampsia, post-partum hemorrhage, maternal death, placenta previa</td>
<td></td>
<td>Neonatal death, congenital anomalies, neonatal infections, preterm birth, stillbirth, low birthweight, small for gestational age, respiratory distress, later infancy infections, respiratory illness</td>
<td>[182]</td>
</tr>
<tr>
<td>Sip (Perinatal Informatic System)</td>
<td>Latin America (multiple countries)</td>
<td>None specified</td>
<td>1983-present</td>
<td>Funding source: Donor (PAHO) Implementing organization: PAHO</td>
<td>Hospital</td>
<td>Maternal Outcomes: Thrombosis, gestational diabetes, gestational hypertension, PIH, preterm labor, pre-eclampsia/eclampsia, post-partum hemorrhage, maternal death, placenta previa</td>
<td></td>
<td>Preterm birth, stillbirth, small for gestational age, congenital anomalies</td>
<td>[170–173,189]</td>
</tr>
<tr>
<td>Western Cape Provincial Health Data Centre (PhDC)</td>
<td>South Africa</td>
<td>None specified</td>
<td>2015-present</td>
<td>Funding source: Public Implementing organization: Western Cape Provincial Department of Health</td>
<td>Multi-district (single province)</td>
<td>Maternal Outcomes: Thrombosis, gestational diabetes, gestational hypertension, PIH, preterm labor, pre-eclampsia/eclampsia, post-partum hemorrhage, maternal death, placenta previa</td>
<td></td>
<td>Neonatal death, congenital anomalies, neonatal infections, preterm birth, stillbirth, low birthweight, small for gestational age, respiratory distress, later infancy infections, respiratory illness</td>
<td>[40,53,169, 193,194]</td>
</tr>
</tbody>
</table>
**Table 4.13.** Strengths and limitations of electronic medical record and clinical software platforms.

<table>
<thead>
<tr>
<th>Resource</th>
<th>Strengths</th>
<th>Limitations and challenges</th>
</tr>
</thead>
</table>
| Category-wide attributes | • Costs of adding maternal pharmacovigilance capabilities to a system are incremental, without requiring large new investments in infrastructure or human resources  
• Able to link records between mother and child, over time, and across different health and administrative databases (e.g., pharmacy)  
• Able to capture larger numbers of pregnant women and relevant exposures across a healthcare system  
• Uses automated methods for searching and extracting data | • Requires investment to create specific algorithms, work procedures, and programming  
• Medical terminology and clinical coding may not be used widely or accurately in low-resource settings  
• Gestational dates may not be captured in the database. Algorithmic methods to calculate gestational timing may be imprecise  
• Will only capture facility-based pregnancies |
Section 5
Discussion
This landscape analysis, consisting of a scoping review that screened over 200 records, publications, and additional sources, yielded 45 PERs and related systems pertinent to maternal pharmacovigilance in LMICs. Of these, 36 were presently in operation as of the date of this review. The identified resources cover a wide range of methodologic approaches and areas of focus ranging from standalone pregnancy exposure registries and other forms of active surveillance to analyses based on electronic health care records systems. Table 5.1 lists key features of each resource type, highlighting the relative advantages and disadvantages of specific designs.

Among the resource types described in this report, classically designed PERs remain an essential tool for monitoring the safety of vaccines and drugs used during pregnancy. PERs employ rigorous methods, including prospective design whereby women are enrolled before outcomes are known, thereby avoiding recall and reporting biases of both patients and providers. Moreover, PERs can use standardized methods to assess multiple pregnancy outcomes, gestational dating, and may also include a comparison group. However, these features make these studies more expensive and resource intensive. Therefore, they can be time-limited, require significant staffing, and involve smaller populations and/or limited geographic coverage. Few PERs are designed specifically for monitoring immunization safety that are operating to a significant extent in LMICs. The majority of PERs identified in this review focus on ARV pharmacovigilance, reflecting the high HIV disease burden relevance to many LMIC populations. This work is valuable for the sustained monitoring of ARVs, which continue to expand in use and new potential safety issues arise, particularly among pregnant women, (e.g., the concerns over the safety of dolutegravir, necessitating the need for continuous operation and support of PERs for ARVs). Ongoing PERs can also be adapted to include new drug or vaccine exposures of interest. For example, while the focus of the MiMBa registry is antimalarial drugs, the project has also been systematically recording exposures to COVID-19 vaccines during pregnancy.

Observational cohorts that don’t meet the formal definition of a PER but are embedded within larger surveillance research studies or networks such as MNHR, IeDEA, or an HDSS, or embedded within a set of clinical trials, such as the Microbicides Trial Network, represent another important approach to maternal safety surveillance. Additional resources may be required to adapt observational cohort studies to include monitoring the safety of medicines used by pregnant women to ensure appropriate details of the exposures and relevant outcomes are recorded. Nevertheless, HIV-focused cohorts in particular are generally comprehensive in terms of clinical data collection, and designed to follow participants longitudinally, and can include comparison groups.
Observational cohorts conducted within the context of HDSS are widespread throughout LMICs and have a long history of operation by researchers, expert in epidemiologic approaches. HDSS sites are well suited to address questions around the safety of medicines used during pregnancy. While most HDSS's include some reporting of baseline indicators, including monitoring of births, maternal deaths, etc., maternal pharmacovigilance requires some adaptation and investment of resources, including methods for identifying women early in their pregnancies, perform gestational dating, ensure accurate reporting of exposures (date, dosing, lot number, etc.), and ensure complete capture of a comprehensive list of adverse events in both the mother and infant over time. Depending on their design, some HDSS's have significant community surveillance components, thus allowing monitoring and capture of pregnancies and deliveries that occur outside health facilities. By embedding their analyses within a larger set of surveillance activities, HDSS's can sometimes establish comparator populations, determine background rates (e.g., in non-pregnant populations, or in unexposed pregnant populations) and calculate relative risk estimates. Ultimately, these are operated as research studies of significant intensity, and require substantial investment in terms of funding, human resources, and community engagement. HDSS and other sentinel population cohorts provide a platform for adding information relevant for monitoring MNCH health and disease and standard reporting for AEFIs. HDSS sites have been used for pharmacovigilance projects in pregnancy, coordinated by the INDEPTH MNCH Working Group.

Electronic medical record systems and associated clinical software platforms, such as DHIS2 or Smartcare, represent another potential avenue for maternal safety surveillance that involves embedding a circumscribed set of activities within a broader data collection structure. Much of the data collection is performed as part of clinical care, and thus additional training of staff is not needed. However, data quality is subject to the level of training and quality of the data input by health care workers. Data analysis requires standardized terminologies or algorithms to detect diagnoses, treatments, and conditions. Once designed, relevant data extractions and analyses can be reproduced at periodic intervals. If such a system is available in a country, or being adopted or expanded, maternal PV would be a relatively small incremental investment to incorporate the added capabilities.

Birth defects surveillance and other outcomes-based registries can be adapted to assess the safety of medicines used during pregnancy if the interest is in specific birth defects that may be uncommon in the general population and if information on pregnancy exposures can be collected in a valid and reliable manner. These registries usually involve few interactions with the vast majority of participants to identify and document outcomes, with follow-up needed only when potential outcomes of interest are detected. The trade-off is that the focus is on specific outcomes, often limited to those that can be detected in the neonatal period, and information regarding exposures is collected retrospectively. Thus, these studies are potentially subject to bias or incomplete verification, or the information collected may be imprecise (in terms of dose, timing, etc.). All obstetric events would be similarly collected via subject recall, and overall, there is generally less emphasis on the mother’s health. In addition, these systems are designed to identify adverse events that do not result in a live birth, such as spontaneous abortion or stillbirth.
### Table 5.1. Key features of pregnancy exposure registries and related data collection systems, by resource type.

<table>
<thead>
<tr>
<th>Type of Resource</th>
<th>Prospective enrollment of pregnant women</th>
<th>Exposure ascertainment</th>
<th>Maternal characteristics ascertainment</th>
<th>Maternal and infant outcomes ascertainment</th>
<th>Ability to include a comparison group</th>
<th>Ability to calculate rates and relative risk</th>
<th>Ability to assess new drugs or vaccines of interest</th>
<th>Complexity and resources requirements</th>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Sometimes</td>
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<tr>
<td>Maternal conditions-based registries</td>
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<td>Yes</td>
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<td>Yes</td>
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<tr>
<td>Manufacturer registries</td>
<td>Sometimes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Sometimes</td>
<td>Sometimes</td>
<td>Sometimes</td>
<td>Sometimes</td>
</tr>
<tr>
<td>EMR databases and clinical software platform with pregnancy exposure module</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

1. Enrollment of the pregnant woman before the outcome of pregnancy is known. Can be before or after the exposure has occurred.
2. Vaccine and drug type, dose, frequency, duration, timing in relation to gestation.
3. Can include relevant demographic information, concomitant illnesses and medications, and reproductive history.
4. Comparison group may be unexposed pregnant participants, exposed non-pregnant participants, or unexposed non-pregnant participants.
5. May be mitigated if routine clinical data can be accessed and are detailed and prospectively entered into medical records and if standardized terminology is used.
6. Yes, if surveillance captures all deliveries or other relevant denominator in a population. Typically does not include spontaneous abortions.
7. Can calculate an incidence rate among a population of exposed; cannot calculate a relative risk unless a comparison group is enrolled.
8. Yes, if routine clinical data are detailed and prospectively entered into medical records and if standardized terminology is used.
9. Can be done through record linkage.
10. If health system covers an entire population.
This landscape analysis has identified that a substantial level of resources has been dedicated to maternal PV in LMICs, but it is clear that more safety surveillance is needed. It is important to note that not all countries will need their own systems, but the selection of resource type must be matched to the context, such as the questions to be answered, funding available, and infrastructure that exists, to make it suitable for purpose. Strengths of this analysis include a structured and standardized scoping review approach that included a comprehensive literature search strategy supplemented by grey literature and expert consultation. The online survey and interviews helped to fill in gaps, particularly for resources that do not have any publications. With the exception of those studies that are tightly focused on specific populations, most registries and other resources identified can likely be modified to incorporate capture of vaccinations, including new maternal vaccines that are projected to be launched in the coming years, if adequate resources are provided. Relevant factors that are more desirable, such as early enrollment and prospective data collection, focus on maternal/obstetric experiences, enumerated populations for denominator-based rates, etc. should be included when considering which systems to support.

This review does have some limitations. A number of PER’s and other relevant resources, particularly in LMICs, have not yet published their data, and may have minimal online presence, such as a website. Some of these resources were identified by reference lists, expert consultations, grey literature, and other web searching, but this process may have left several uncaptured. Many publications and online resources contained minimal or incomplete information on the methods used, including the specific outcomes monitored and their definitions. In some cases, we were able to contact informants, including through the survey, to supplement our information, but some could not be reached.

This analysis identifies a number of registries that are currently active and may be similar or flexible enough to combine data or analyses. Such information could enable studies to prepare LMICs for new drugs or vaccines intended for use in pregnancy, particularly among those funded through public or charitable sources. However, true assessment of compatibility among these resources will require more granular information regarding the structure, data variables, and methodologic approaches of the registries of interest. It is also possible that registries may expand beyond their current areas and operate regionally. An improved understanding of the current status of maternal PV in LMICs will allow programmatic staff and policymakers to identify major gaps in our understanding of maternal safety and opportunities for strengthening these efforts.
Section 6

Appendices
6.1. Search strategies by database

6.1.1. PubMed

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55 #21 AND #54 39,859
54 #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 850,027
53 “Product Surveillance, Postmarketing/statistics and numerical data”[MeSH Terms] 2,361
52 “Maternal Health Services/statistics and numerical data”[MeSH Terms] 7,290
51 “Maternal Exposure/statistics and numerical data”[MeSH Terms] 1,123
49 “Product Surveillance, Postmarketing”[mesh:noexp] 7,553
### 6.1.2. Embase

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data accuracy/ (1596)
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health survey/ (213987)
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population surveillance/ (117)
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factual database/ (27912)
clinical decision support system/ (4716)
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15 and 40 [PREGNANCY - DATA COLLECTION, REGISTRIES] (71373)
1 or 41 [PERs, PREGNANCY - DATA COLLECTION, REGISTRIES] (71381)
(afghanistan or albania or algeria or american samoa or angola or "antigua and barbuda" or antigua or barbuda or argentina or armenia or armenian or aruba or azerbaijan or bahRAIN or bangladesh or barbados or republic of belarus or belarus or byelarus or belorussia or byelorussian or belize or british honduras or benin or dahomey or bhutan or bolivia or "bosnia and herzegovina" or bosnia or herzegovina or botswana or bechuanaland or brazil or brasil or bulgaria or burkina faso or burkina faso or upper volta or burundi or urundi or cabo verde or cape verde or cambodia or cambodian or cameroon or central african republic or ubangi shari or Chad or chile or china or colombia or comoros or comoro islands or ile comores or mayotte or democratic republic of the congo or democratic republic congo or congo or congo or zaire or costa rica or "cote d'ivoire" or "cote d'ivoire" or cote divoire or cote d ivoire or ivory coast or croatia or czech republic or czechoslovakia or djibouti or french somaliland or dominica or dominican republic or ecuador or egypt or united arab republic or el salvador or equatorial guinea or spanish guinea or eritrea or estonia or eswatini or swaziland or ethiopia or fiji or gabon or gabonese republic or gambia or "georgia (republic)" or georgian or ghana or gold coast or gibraltar or greece or grenada or guam or guatemala or guiana or guinea or guinea bissau or guyana or british guiana or haiti or honduras or hungary or india or indonesian republic or iran or iraq or ireland or irish republic or israel or italy or japan or jordan or kazakhstan or kazakh or kenya or "democratic people's republic of korea" or korea or north korea or south korea or republic of korea or korean or kosovo or kyrgyzstan or kirghizia or kirghizstan or kirghizia or kirghizia or kirghizia or "kyrgyz republic" or kyrgyz or kyrgyzstan or latvia or Lebanon or lebanese republic or lesotho or basutoland or liberia or libya or libyan arab jamahiriya or lithuania or macau or macao or republic of north macedonia or macedonia or madagascar or malagasy republic or malawi or myanmar or burma or namibia or nepal or netherlands antilles or nicaragua or niger or nigeria oroman or muscat or pakistan or palau or papua new guinea or new guinea or new guinea or paraguay or peru or philippines or philippine islands or poland or russian federation or puerto rico or romania or russia or turkmenistan or turkey or turkey (republic) or turkmen or uganda or united arab emirates or venezuela or vietnam or viet nam or viet nam or west bank or gaza or palestine or yemen or yugoslavia or zambia or zimbabwe or zimbabwe or zimbabwe)
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44 43 or 44 [LMICs] (2518149)

45 42 and 45 [PERS, PREGNANCY - DATA COLLECTION, REGISTRIES - LMICs] (18846)

46 global health/ (16219)

47 (global or international* or world*) and health*.ti,kw,kf. (45947)

48 exp adverse drug reaction/ (586248)

49 ((drug or drugs or medicine or medicines or medication* or pharmaceutical* or pharma-ceutical*) and expos*).ti,kw,kf. (9329)

50 (ae or co).fs. (2915988)

51 (safe or safety or side effect or side effects or undesirable effect or undesirable effects or treatment emergent or tolerability or toxicity or adrs).ti,kw,kf. (514988)

52 (adverse effect or adverse effects or adverse reaction or adverse reactions or adverse event or adverse events or adverse outcome or adverse outcomes).ti,kw,kf. (70731)

53 (AEFI and adverse).ti,kw,kf. (157)

54 “Global Alignment of Immunisation Safety Assessment in Pregnancy”.tw,kw,kf. (20)

55 (GAIA and (alignment or immunisation or safety or pregnan*)).tw,kw,kf. (71)

56 exp vaccination/ (205483)

57 vaccine/ (67719)
exp bacterial vaccine/ or exp cell-based vaccine/ or conjugate vaccine/ or edible vaccine/ or exp fungus vaccine/ or exp inactivated vaccine/ or live vaccine/ or exp meningitis vaccine/ or exp nucleic acid vaccine/ or exp parasite vaccine/ or exp peptide vaccine/ or protein vaccine/ or exp subunit vaccine/ or exp toxoid vaccine/ or exp vector vaccine/ or virosome vaccine/ or exp virus vaccine/ (304544)

vaccin*.ti,kw,kf. (251220)

immunization/ (104541)

passive immunization/ (12623)

(immunit* and transfer*).ti,kw,kf. (1262)

(immunit* and (maternally-acqui* or passive*)).ti,kw,kf. (766)

((antibod* or anti-bod*) and transfer*).ti,kw,kf. (2375)

((maternal or pregnan*) and immuni#ation*).ti,kw,kf. (1766)

exp malaria/pc [Prevention] (14654)

exp antimalarial agent/ (161880)

(antimalarial* or anti-malarial*).ti,kw,kf. (11586)

exp cytomegalovirus infection/pc [Prevention] (5146)

respiratory syncytial virus infection/pc [Prevention] (1057)

exp Streptococcus infection/pc [Prevention] (10568)

exp Zika fever/pc [Prevention] (780)

exp antiretrovirus agent/ (216196)

(antiretroviral* or anti-retroviral* or “anti-HIV” or “anti-AIDS” or “AIDS drug” or “AIDS drugs”).ti,kw,kf. (46286)

exp fetus development/ (29871)

((fetal or foetal or fetus* or foetus*) and develop*).ti,kw,kf. (14926)

exp prenatal exposure/ (37294)

((fetal or foetal or fetus* or foetus* or prenatal* or pre-natal*) and expos*).ti,kw,kf. (16619)

pregnancy outcome/ (72177)

((birth or births or matern* or neonat* or neo-nat* or perinatal* or peri-natal* or peripartum or “peri-partum” or postnatal* or post-natal* or postpartum or “post-partum” or post-birth* or pregnant*) and outcome*).ti,kw,kf. (55800)

((birth or births) and defect*).ti,kw,kf. (4849)

child health/ (32206)

maternal welfare/ (15842)

(MNCH and (maternal* or newborn* or child*)).ti,kw,kf. (49)

or/47-85 [DRUGS, VACCINES, SAFETY, OUTCOMES] (4592324)

46 and 86 [PERs, PREGNANCY - DATA COLLECTION, REGISTRIES - LMICs - DRUGS, VACCINES, SAFETY, OUTCOMES] (5663)

exp animal/ or exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (30677570)

exp human/ or exp human experimentation/ or exp human experiment/ (23737031)

88 not 89 (6941713)

87 not 90 [ANIMAL-ONLY REMOVED] (5643)

teditorial.pt. (729310)

91 not 92 [EDITORIALS REMOVED] (5614)

limit 93 to yr=“2000-current” (5299)
6.1.3. CINAHL

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<td>(MH &quot;Child Health&quot;)</td>
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<td>TI (birth OR births) and defect*</td>
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<td>TI ((antibod* or (anti W0 bod*)) and transfer*)</td>
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<td>TI immunit* AND (passive* or &quot;maternally-acquired&quot;)</td>
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<td>(MH &quot;Viral Vaccines+&quot;)</td>
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<td>TI AEFI and adverse</td>
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<td>TI &quot;adverse effect&quot; or &quot;adverse effects&quot; or &quot;adverse reaction&quot; or &quot;adverse reactions&quot; or &quot;adverse event&quot; or &quot;adverse events&quot; or &quot;adverse outcome&quot; or &quot;adverse outcomes&quot;</td>
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<td>TI safe or safety or &quot;side effect&quot; or &quot;side effects&quot; or &quot;undesirable effect&quot; or &quot;undesirable effects&quot; or &quot;treatment emergent&quot; or tolerability or toxicity or adrs</td>
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<td>TI (drug or drugs or medicine or medicines or medication* or pharmaceutical* or pharma-ceutical*) AND expos*</td>
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<td>S39 AND S44</td>
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<td>TI (&quot;high burden country&quot; or &quot;high burden countries&quot; or &quot;high-burden country&quot; or &quot;high-burden countries&quot; or &quot;countdown country&quot; or &quot;countdown countries&quot;) OR AB (&quot;high burden country&quot; or &quot;high burden countries&quot; or &quot;high-burden country&quot; or &quot;high-burden countries&quot; or &quot;countdown country&quot; or &quot;countdown countries&quot;)</td>
<td>188</td>
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TOC

SECTION 1. Executive summary
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SECTION 5. Discussion
SECTION 6. Appendices
SECTION 7. References

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Query

S42  TI ("developing country" or "developing countries" or "developing nation" or "developing nations" or "developing population" or "developing populations" or "developing world" or "less developed country" or "less developed countries" or "less developed nation" or "less developed nations" or "less developed population" or "less developed populations" or "less developed world" or "lesser developed country" or "lesser developed countries" or "lesser developed nation" or "lesser developed nations" or "lesser developed population" or "lesser developed populations" or "lesser developed world" or "under developed country" or "under developed countries" or "under developed nation" or "under developed nations" or "under developed population" or "under developed populations" or "under developed world" or "underdeveloped country" or "underdeveloped countries" or "underdeveloped nation" or "underdeveloped nations" or "underdeveloped population" or "underdeveloped populations" or "underdeveloped world" or "middle income country" or "middle income countries" or "middle income nation" or "middle income nations" or "middle income population" or "middle income populations" or "low income country" or "low income countries" or "low income nation" or "low income nations" or "low income population" or "low income populations" or "lower income country" or "lower income countries" or "lower income nation" or "lower income nations" or "lower income population" or "lower income populations" or "underserved country" or "underserved countries" or "underserved nation" or "underserved nations" or "underserved population" or "underserved populations" or "underserved world" or "under served country" or "under served countries" or "under served nation" or "under served nations" or "under served population" or "under served populations" or "under served world" or "poor country" or "poor countries" or "poor nation" or "poor nations" or "poor population" or "poor populations" or "poor world" or "poorer country" or "poorer countries" or "poorer nation" or "poorer nations" or "poorer population" or "poorer populations" or "poorer world" or "developing economy" or "developing economies" or "less developed economy" or "less developed economics" or "lesser developed economy" or "lesser developed economics" or "underdeveloped economy" or "underdeveloped economies" or "middle income economy" or "middle income economies" or "low income economy" or "low income economies" or "lower income economy" or "lower income economies" or "low gdp" or "low gnp" or "low gross domestic" or "low gross national" or "lower gdp" or "lower gnp" or "lower gross domestic" or "lower gross national" or "lmic" or "lmics" or "third world" or "lami country" or "lami countries" or "transitional country" or "transitional economies" or "emerging economy" or "emerging economies" or "emerging nation" or "emerging nations") OR AB ("developing country" or "developing countries" or "developing nation" or "developing nations" or "developing population" or "developing populations" or "developing world" or "less developed country" or "less developed countries" or "less developed nation" or "less developed nations" or "less developed population" or "less developed populations" or "less developed world")

Results

39,219
or "lesser developed country" or "lesser developed countries" or "lesser developed nation" or "lesser developed nations" or "lesser developed population" or "lesser developed populations" or "lesser developed world" or "under developed country" or "under developed countries" or "under developed nation" or "under developed nations" or "under developed population" or "under developed populations" or "underdeveloped country" or "underdeveloped countries" or "underdeveloped nation" or "underdeveloped nations" or "underdeveloped population" or "underdeveloped populations" or "middle income country" or "middle income countries" or "middle income nation" or "middle income nations" or "middle income population" or "middle income populations" or "low income country" or "low income countries" or "low income nation" or "low income nations" or "low income population" or "low income populations" or "lower income country" or "lower income countries" or "lower income nation" or "lower income nations" or "lower income population" or "lower income populations" or "underserved country" or "underserved countries" or "underserved nation" or "underserved nations" or "underserved population" or "underserved populations" or "underserved world" or "under served country" or "under served countries" or "under served nation" or "under served nations" or "under served population" or "under served populations" or "under served world" or "deprived country" or "deprived countries" or "deprived nation" or "deprived nations" or "deprived population" or "deprived populations" or "deprived world" or "poor country" or "poor countries" or "poor nation" or "poor nations" or "poor population" or "poor populations" or "poor world" or "poorer country" or "poorer countries" or "poorer nation" or "poorer nations" or "poorer population" or "poorer populations" or "poorer world" or "developing economy" or "developing economies" or "less developed economy" or "less developed economies" or "lesser developed economy" or "lesser developed economies" or "under developed economy" or "under developed economies" or "underdeveloped economy" or "underdeveloped economies" or "middle income economy" or "middle income economies" or "low income economy" or "low income economies" or "lower income economy" or "lower income economies" or "low gdp" or "low gdp" or "low gross domestic" or "low gross national" or "lower gdp" or "lower gnp" or "lower gross domestic" or "lower gross national" or "lmic or lmics" or "third world" or "lami country" or "lami countries" or "transitional country" or "transitional economies" or "emerging economy" or "emerging economies" or "emerging nation" or "emerging nations")
Query

TI (mali or malta or micronesia or "federated states of micronesia" or kiribati or "marshall islands" or nauru or "northern mariana islands" or palau or tuvalu or mauritania or mauritius or mexico or moldova or moldovian or mongolia or montenegro or morocco or ifni or mozambique or "portuguese east africa" or myanmar or burma or namibia or nepal or "netherlands antilles" or nicaragua or niger or nigeria or oman or muscat or pakistan or panama or "papua new guinea" or "new guinea" or paraguay or peru or philippines or philippines or philippines or poland or "polish people's republic" or portugal or "portuguese republic" or "puerto rico" or romania or russia or "russian federation" or ussr or "soviet union" or "union of soviet socialist republics" or rwanda or ruanda or samoa or "pacific islands" or polynesia or "samoan islands" or "navigator island" or "navigator islands" or "sao tome and principe" or "saudi arabia" or senegal or serbia or seychelles or "sierra leone" or slovakia or "slovak republic" or slovenia or melanesia or "solomon island" or "solomon islands" or "norfolk island" or "norfolk islands" or somalia or "south africa" or "south sudan" or "sri lanka" or ceylon or "saint kitts and nevis" or "st. kitts and nevis" or "saint lucia" or "saint lucia" or "saint Vincent and the grenadines" or "saint vincent" or "st. vincent" or grenadines or sudan or suriname or surinam or "dutch guiana" or "netherlands guiana" or syria or "syrian arab republic" or tajikistan or tadzhikistan or tadzhikistan or tadzhikistan or tanzania or tanganyika or thailand or siam or "timor leste" or "east timor" or togo or "togoese republic" or tonga or "Trinidad and tobago" or trinidad or tobago or tunisia or turkey or turkmenistan or turkmen or ukraine or uruguay or uzbekistan or uzbek or vanuatu or "new hebrides" or venezuela or vietnam or "viet nam" or "middle east" or "west bank" or gaza or palestine or yemen or yugoslavia or zambia or zimbabwe or "northern rhodesia" or "global south" or "africa south of the sahara" or "sub-saharan africa" or "sub-saharan africa" or "africa, central" or "central africa" or "africa, northern" or "north africa" or "northern africa" or magreb or maghrib or sahara or "africa, southern" or "african republic" or "africa, eastern" or "east africa" or "eastern africa" or "africa, western" or "west africa" or "western african" or "western african" or "west indies" or caribbean or "central america" or "latind" or "latam" or "south and central america" or "south america" or "asia, central" or "central asia" or "asia, northern" or "north asia" or "northern asia" or "northern asia, central" or "northern asia" or "asia, southeastern" or "southeastern asia" or "southeast asia" or "southeast asia" or "southeast asia" or "southeast asia" or "southeast asia" or "eastern asia" or "east asia" or "eastern asia" or "east asia" or "east asia" or "europe, eastern" or "east europe" or "european" or "europe, eastern" or "east europe" or "eastern europe") OR AB (mali or malta or micronesia or "federated states of micronesia" or kiribati or "marshall islands" or nauru or "northern mariana islands" or palau or tuvalu or mauritania or mauritius or mexico or moldova or moldovian or mongolia or montenegro or morocco or ifni or mozambique or "portuguese east africa")

Results

148,518
or “syrian arab republic” or tajikistan or tadzhikistan or tadzhikistan or tadzhik or tanzania or tanganyika or thailand or siam or “timor leste” or “east timor” or togo or “togolese republic” or tonga or “Trinidad and Tobago” or trinidad or tobago or tunisia or turkey or turkmenistan or turkm or uganda or ukraine or uruguay or uzbekistan or uzbek or vanuatu or “new hebrides” or venezuela or vietnam or “viet nam” or “middle east” or “west bank” or gaza or palestine or yemen or yugoslavia or zambia or zimbabwe or “northern rhodesia” or “global south” or “africa south of the sahara” or “sub-saharan africa” or “subsaaharan africa” or “africa, central” or “central africa” or “africa, northern” or “north africa” or “northern africa” or magreb or maghrib or sahara or “africa, southern” or “southern africa” or “africa, eastern” or “east africa” or “eastern africa” or “africa, western” or “west africa” or “western africa” or “west indies” or caribbean or “central america” or “latin america” or “south and central america” or “south america” or “asia, central” or “central asia” or “asia, northern” or “north asia” or “northern asia” or “asia, southeastern” or “southeastern asia” or “south eastern asia” or “southeast asia” or “south east asia” or “asia, western” or “western asia” or “europe, eastern” or “europe, central” or “central europe” or “western europe” or “europe, western” or “europe, north” or “north europe” or “northern europe” or “northern europe”).
or cameroun or "central african republic" or "ubangi shari" or chad or chile or china or colombia or comoros or "comoro islands" or "iles comores" or mayotte or "democratic republic of the congo" or "democratic republic congo" or congo or zaire or "costa rica" or "cote d'ivoire" or "cote d'ivoire" or "cote divoire" or "cote d'ivoire" or "ivory coast" or croatia or cuba or cyprus or "czech republic" or czechoslovakia or djibouti or "french somalliland" or dominica or "dominican republic" or ecuador or egyp or "united arab republic" or "el salvador" or "equatorial guinea" or "spanish guinea" or eritrea or estonia or eswatini or swaziland or ethiopia or fiji or gabon or "gabonese republic" or gambia or "georgia (republic)" or georgian or ghana or "gold coast" or gibraltar or greece or grenada or guam or guatemala or guinea or "guinea bissau" or guyana or "british guiana" or haiti or hispaniola or honduras or hungary or india or indonesia or iraq or iran or iraq or "isle of man" or jamaica or jordan or kazakhstan or kazakh or keny or "democratic people's republic of korea" or "republic of korea" or "north korea" or "south korea" or korea or kosovo or kyrgyzstan or kirghizia or kirgizstan or "kyrgyz republic" or kirghiz or laos or "lao pdr" or "lao people's democratic republic" or latvia or lebanon or lebanese republic or lesotho or basutoland or liberia or libya or "libyan arab jamahiriya" or lithuania or macau or macao or republic of "north macedonia" or macedonia or madagascar or "malagasy republic" or malawi or nyasaland or malaysia or "malay federation" or "malaya federation" or maldives or "indian ocean islands" or "indian ocean")

S39 S1 OR S38 15,244
S38 S16 AND S37 15,243
S37 S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 354,620
S36 (MH "Product Surveillance+/SN") 1
S35 (MH "Maternal Health Services+/SN") 1,245
S34 Ti pharmacovigilan* or (pharmaco W0 vigilan*) 846
S33 (MH "Product Surveillance+") 2,417
S32 Ti "data system" or "data systems" or "information system" or "information systems" 4,466
S31 (MH "Health Information Systems") 3,566
S30 Ti (decision* AND support* AND clinical*) 1,865
S29 (MH "Decision Support Systems, Clinical") 6,139
S28 Ti surveillance*
S27 (MH "Population Surveillance+") 15,975
S26 Ti survey*
S25 (MH "Surveys") 71,609
S24 Ti registry or registries or eregistr* or "e-registry" or "e-registries" 157,567
S23 Ti (preliminary or "pilot project" or "pilot projects") AND data 16,019
S22 Ti "focus group" or "focus groups" 13,946
S21 (MH "Focus Groups") 682
S20 Ti databas* or "data base" or "data bases" or databank* or "data bank" or "data banks" or dataset* or "data set" or "data sets" 2,957
S19 Ti data AND (accumulat* or accura* or assembl* or captur* or collect* or compil* or coordinat* or co-ordinat* or gather* or hub or hubs) 48,414
S18 (MH "Data Curation") 4,425
S17 (MH "Data Collection") 184
6.1.4. Global Index Medicus

tw:((tw:(pregnan* exposure* database*)) OR (tw:(pregnan* exposure* “data base”)) OR (tw:(pregnan* exposure* “data bases”)) OR (tw:(pregnan* exposure* databank*)) OR (tw:(pregnan* exposure* “data bank”)) OR (tw:(pregnan* exposure* “data banks”)) OR (tw:(pregnan* exposure* register)) OR (tw:(pregnan* exposure* registries)) OR (tw:(pregnan* exposure* registry)) OR (tw:(pregnan* exposure* registries))) – 108 records

tw:((ti:((pregnan* OR prenatal* OR antenatal* OR “ante-natal” OR “ante-natally” OR antepartum OR “ante-partum” OR perinatal* OR “peri-natal” OR “peri-natally” OR peripartum OR “peri-partum” OR maternal*) AND (data OR database* OR databank* OR register OR registers OR registry OR registries OR survey* OR surveillance OR pharmacovigilan* OR “pharmaco-vigilance”) AND (safe OR safety OR “side effect” OR “side effects” OR “undesirable effect” OR “undesirable effects” OR “treatment emergent” OR tolerability OR toxicity OR adrs OR aefi))) – 361 records
tw:(ti:((pregnan* OR prenatal* OR antenatal* OR “ante-natal” OR “ante-natally” OR antepartum OR “ante-partum” OR perinatal* OR “peri-natal” OR “peri-natally” OR peripartum OR “peri-partum” OR maternal*) AND (data OR database* OR databank* OR register OR registers OR registry OR registries OR survey* OR surveillance OR pharmacovigilan* OR “pharmaco-vigilance”) AND (MNCH or “maternal health” or “child health” or “infant health” or “birth defect” or “birth defects” or “birth outcome” or “birth outcomes” or “pregnancy outcome” or “pregnancy outcomes” or “neonatal outcome” or “neonatal outcomes”)) – 50 records

tw:(ti:((pregnan* OR prenatal* OR antenatal* OR “ante-natal” OR “ante-natally” OR antepartum OR “ante-partum” OR perinatal* OR “peri-natal” OR “peri-natally” OR peripartum OR “peri-partum” OR maternal*) AND (data OR database* OR databank* OR register OR registers OR registry OR registries OR survey* OR surveillance OR pharmacovigilan* OR “pharmaco-vigilance”) AND (vaccine or vaccines or vaccination* or immunization* or immunization* OR “maternally-acquired”)) – 0 records

tw:((ti:((pregnan* OR prenatal* OR antenatal* OR “ante-natal” OR “ante-natally” OR antepartum OR “ante-partum” OR perinatal* OR “peri-natal” OR “peri-natally” OR peripartum OR “peri-partum” OR maternal*) AND (data OR database* OR databank* OR register OR registers OR registry OR registries OR survey* OR surveillance OR pharmacovigilan* OR “pharmaco-vigilance”) AND (drug OR drugs OR medicine OR medicines OR medication* OR pharmaceutical* OR “pharma-ceutical” OR “pharma-ceuticals” OR vaccin* OR immun* OR antimalarial* OR “anti-malarial” OR “anti-malarials” OR antiviral* OR “anti-viral” OR “anti-virals” OR antiretroviral* OR “anti-retroviral” OR “anti-retrovirals” OR “Anti-HIV” OR “Anti-AIDS”))) – 10 records

tw:(ti:((pregnan* OR prenatal* OR antenatal* OR “ante-natal” OR “ante-natally” OR antepartum OR “ante-partum” OR perinatal* OR “peri-natal” OR “peri-natally” OR peripartum OR “peri-partum” OR maternal*) AND (data OR database* OR databank* OR register OR registers OR registry OR registries OR survey* OR surveillance OR pharmacovigilan* OR “pharmaco-vigilance”) AND (fetal* OR foetal* OR fetus* OR foetus* OR neonat* OR newborn* OR infant OR infants OR infanc* OR child*)) – 125 records

tw:(ti:((pregnan* OR prenatal* OR antenatal* OR “ante-natal” OR “ante-natally” OR antepartum OR “ante-partum” OR perinatal* OR “peri-natal” OR “peri-natally” OR peripartum OR “peri-partum” OR maternal*) AND (data OR database* OR databank* OR register OR registers OR registry OR registries OR survey* OR surveillance OR pharmacovigilan* OR “pharmaco-vigilance”) AND (drug OR drugs OR medicine OR medicines OR medication* OR pharmaceutical* OR “pharma-ceutical” OR “pharma-ceuticals” OR vaccin* OR immun* OR antimalarial* OR “anti-malarial” OR “anti-malarials” OR antiviral* OR “anti-viral” OR “anti-virals” OR antiretroviral* OR “anti-retroviral” OR “anti-retrovirals” OR “Anti-HIV” OR “Anti-AIDS”))) – 71 records

**TOTAL:** 725 records

**6.1.5. Google Scholar**

“pregnant|pregnancy|prenatal”+“registry|registries|surveillance|pharmacovigilance” + “expose|exposed|exposes|exposure|exposures”+[names of LMICs]
6.2. Data extraction form

PART 1: STUDY IDENTIFICATION / INCLUSION STATUS

Resource title:

Author(s):

Year of publication:

Resource type:
1. 1 - Peer reviewed journal
2. 2 - Grey literature
3. 3 - Registry
4. 4 - Website
5. 5 - Key informant survey / interview
6. 6 - Other

Database resource pulled from:

Final status:
1. 1 - included
2. 2 - excluded
3. 3 - incomplete/unclear

If excluded, explain reasoning:

PART 2: REGISTRY INFORMATION OR OTHER RESOURCE

Name of registry or other resource:

Primary goals/aims:

Funding source:

Years of operation:

Current status
1. Active
2. Inactive
3. On hold
Country(ies) where located:

Country representativeness:
1. Multi-national
2. National
3. State/Provincial
4. District
5. Sub-district
6. Community
7. Health clinic
8. Hospital
9. Other

Drug/vaccine exposure name and type:

Duration of follow up:

Current sample size:
1. <500 participants
2. 500 - 1,999 participants
3. 2,000 - 5,000 participants
4. 5,001 - 10,000 participants
5. 10,001 - 20,000 participants
6. >20,000 participants

Data collection:
1. Administrative databases
2. Medical databases
3. Registries
4. Research study
5. Program implementation
6. Other

Methodology:

Terminology and data system used:

**PART 3: CHARACTERISTICS OF INCLUDED POPULATION**

Age ranges included:

Target population:
1. Pregnant women
2. Non-pregnant women / women of reproductive age
3. Children
4. Infants (<28 days old)
5. General population
6. Other
Gestational age
1. First trimester
2. Second trimester
3. Third trimester

Underlying medical condition(s):

Maternal outcome(s) recorded:
1. Thrombosis and/or thrombocytopenia syndrome
2. Antenatal hospitalization (not including delivery)
3. Disability
4. Gestational diabetes
5. Gestational hypertension
6. Premature rupture of membranes
7. Preterm labor
8. Preeclampsia / Eclampsia
9. Post-partum hemorrhage
10. Antenatal hemorrhage
11. Corporeal infection
12. Spontaneous abortion / miscarriage / pregnancy loss (example: prior to 20 weeks gestation)
13. Maternal death (example: within 42 days of termination of pregnancy)
14. Late maternal death (example: >42 days of termination of pregnancy)
15. Other

Maternal death cause:
1. Direct cause
2. Indirect cause

Neonatal outcome(s) recorded:
1. Preterm birth
2. Small size for gestational age / restricted fetal growth
3. Still birth (death after 28 weeks of pregnancy but before birth)
4. Live birth
5. Congenital anomaly / birth defect
6. Death
7. Other

Neonatal death timeframe
1. Early neonatal (0-7 days)
2. Late neonatal (8-28 days)
3. Post neonatal (29 days - 1 year)
Which congenital anomaly does this monitor (if any)?

Infant/child outcome(s) recorded:
1. Infections
2. Respiratory illness
3. Developmental outcomes
4. Other

What is the duration of follow up?

**PART 4: KEY FINDINGS**

Populate as best you can if information is provided; answer N/A if it is not relevant or N/P if it is not provided.

Strengths of the registry or other resource:

Weaknesses / gaps of registry or other resource:

Challenges of registry or other resource in its specific context:

Does this resource have the possibility to add new interventions?
1. Yes
2. No
3. Maybe
4. Unknown Why?

Can this resource be combined with other systems?
1. Yes
2. No
3. Maybe
4. Unknown Why?

Any upcoming changes to the resource:

Additional comments
PART 1: STUDY IDENTIFICATION / INCLUSION STATUS

Resource title:

Author(s):

Year of publication:

Resource type:
1. 1 - Peer reviewed journal
2. 2 - Grey literature
3. 3 - Registry
4. 4 - Website
5. 5 - Key informant survey / interview
6. 6 - Other

Database resource pulled from:

Final status:
1. 1 - included
2. 2 - excluded
3. 3 - incomplete/unclear

If excluded, explain reasoning:

PART 2: REGISTRY INFORMATION OR OTHER RESOURCE

Name of registry or other resource:

Primary goals/aims:

Funding source:

Years of operation:

Current status
1. Active
2. Inactive
3. On hold
Country(ies) where located:

Country representativeness:
1. Multi-national
2. National
3. State/Provincial
4. District
5. Sub-district
6. Community
7. Health clinic
8. Hospital
9. Other

Drug/vaccine exposure name and type:

Duration of follow up:

Current sample size:
1. <500 participants
2. 500 - 1,999 participants
3. 2,000 - 5,000 participants
4. 5,001 - 10,000 participants
5. 10,001 - 20,000 participants
6. >20,000 participants

Data collection:
1. Administrative databases
2. Medical databases
3. Registries
4. Research study
5. Program implementation
6. Other

Methodology:

Terminology and data system used:
PART 3: CHARACTERISTICS OF INCLUDED POPULATION

Age ranges included:

Target population:
1. Pregnant women
2. Non-pregnant women / women of reproductive age
3. Children
4. Infants (<28 days old)
5. General population
6. Other

Gestational age
1. First trimester
2. Second trimester
3. Third trimester

Underlying medical condition(s):

Maternal outcome(s) recorded:
1. Thrombosis and/or thrombocytopenia syndrome
2. Antenatal hospitalization (not including delivery)
3. Disability
4. Gestational diabetes
5. Gestational hypertension
6. Premature rupture of membranes
7. Preterm labor
8. Preeclampsia / Eclampsia
9. Post-partum hemorrhage
10. Antenatal hemorrhage
11. Corporeal infection
12. Spontaneous abortion / miscarriage / pregnancy loss (example: prior to 20 weeks gestation)
13. Maternal death (example: within 42 days of termination of pregnancy)
14. Late maternal death (example: >42 days of termination of pregnancy)
15. Other

Maternal death cause:
1. Direct cause
2. Indirect cause

Neonatal outcome(s) recorded:
1. Preterm birth
2. Small size for gestational age / restricted fetal growth
3. Still birth (death after 28 weeks of pregnancy but before birth)
4. Live birth
5. Congenital anomaly / birth defect
6. Death
7. Other
Neonatal death timeframe
1. Early neonatal (0-7 days)
2. Late neonatal (8-28 days)
3. Post neonatal (29 days - 1 year)

Which congenital anomaly does this monitor (if any)?

Infant/child outcome(s) recorded:
1. Infections
2. Respiratory illness
3. Developmental outcomes
4. Other

What is the duration of follow up?

PART 4: KEY FINDINGS

Populate as best you can if information is provided; answer N/A if it is not relevant or N/P if it is not provided.

Strengths of the registry or other resource:

Weaknesses / gaps of registry or other resource:

Challenges of registry or other resource in its specific context:

Does this resource have the possibility to add new interventions?
1. Yes
2. No
3. Maybe
4. Unknown Why?

Can this resource be combined with other systems?
1. Yes
2. No
3. Maybe
4. Unknown Why?

Any upcoming changes to the resource:

Additional comments
6.3. Key informant survey and interview

6.3.1. Pregnancy Exposure Data and Resources Stakeholder Survey

We are conducting a landscape analysis in collaboration with WHO to identify current and recent resources, including pregnancy exposure and surveillance registries, databases, cohort surveys, and routinely collected data, that record exposure to medicines and vaccines during pregnancy and maternal and perinatal outcomes in low- and middle-income countries (LMICs). We are asking for your help in identifying examples of these resources. We may follow up with you to discuss the appropriateness or fit for purpose of the resource you identify. Our goal is to understand what is currently available in LMICs and make connections for future evaluation of maternal use of medicines and vaccines in the product pipeline.

You have been identified as someone who is knowledgeable about or involved with these resources in LMICs. Please complete the following form for each resource you know of. We will ask for your name and contact information so that we may follow up with you for further information, if necessary. All of the personal information you provide will be kept confidential. When we report our findings, if we need to mention something you have said or information you have provided, we will refer to you by a unique study ID to keep your identity confidential. By submitting the form, you are agreeing to participate and allow us to use the information you have provided.

Please fill out the following questions to the best of your knowledge. If there are any specific points that are not included as options in the dropdown menus that are relevant to the resource, please type in the answer and hit “enter”.

6.3. Key informant survey and interview

6.3.1. Pregnancy Exposure Data and Resources Stakeholder Survey

We are conducting a landscape analysis in collaboration with WHO to identify current and recent resources, including pregnancy exposure and surveillance registries, databases, cohort surveys, and routinely collected data, that record exposure to medicines and vaccines during pregnancy and maternal and perinatal outcomes in low- and middle-income countries (LMICs). We are asking for your help in identifying examples of these resources. We may follow up with you to discuss the appropriateness or fit for purpose of the resource you identify. Our goal is to understand what is currently available in LMICs and make connections for future evaluation of maternal use of medicines and vaccines in the product pipeline.

You have been identified as someone who is knowledgeable about or involved with these resources in LMICs. Please complete the following form for each resource you know of. We will ask for your name and contact information so that we may follow up with you for further information, if necessary. All of the personal information you provide will be kept confidential. When we report our findings, if we need to mention something you have said or information you have provided, we will refer to you by a unique study ID to keep your identity confidential. By submitting the form, you are agreeing to participate and allow us to use the information you have provided.

Please fill out the following questions to the best of your knowledge. If there are any specific points that are not included as options in the dropdown menus that are relevant to the resource, please type in the answer and hit “enter”.
Participant details

Please note we may contact you to follow up about the resource you describe if we have any questions.

Name*: ____________________________________________________________

Email*: ____________________________________________________________

Organization*: ______________________________________________________

Job Title: _____________________________________________________________

Resource details

Below we will be asking you to fill in information about any resources you are familiar with as outlined above. If you know of multiple resources that should be brought to our attention, please fill out a separate survey for each resource. As a reminder, resources can include pregnancy exposure and surveillance registries, databases, cohort surveys, and routinely collected data, that record exposure to medicines and vaccines during pregnancy and maternal and perinatal outcomes in low- and middle-income countries (LMICs)

Resource or Project Name: ______________________________________________

Please provide a link to the resource if available: ____________________________

What location(s) does the resource cover (country/countries or region(s))? _________________

Who oversees or maintains the resource? Please provide the name of the organization/s or specific person(s) and their contact information if available.

Name of organization: _________________________________________________

Primary contact name: _________________________________________________

Primary contact email: _________________________________________________

How is data collected? Select all that apply.

- Administrative databases
- Medical databases
- Registries
- Research study
- Program implementation
- Other

If you selected “other”, please specify: _______________________________________

Any additional details you would like to provide?: ________________________________
The data in this resource are captured at a:

- Multi-national
- National
- State / Provincial
- District
- Sub-district
- Community
- Health clinic
- Hospital
- Other

If you selected “other”, please specify: __________________________________________________________

How are these data collected?

- Retrospectively
- Prospectively

How many individuals are enrolled in this resource (total)?

- <500 participants
- 500 – 2,000 participants
- 2,000 – 5,000 participants
- 5,001 – 10,000 participants
- 10,001 – 20,000 participants
- >20,000 participants

What population(s) are the target for this resource. Select all that apply.

- Pregnant women
- Non-pregnant women / women of reproductive age
- Breastfeeding women
- Children
- Infants (<28 days old)
- General population

What intervention(s) does this resource include? Select all that apply.

- Vaccine/Immunization
  - COVID-19
  - Influenza
  - Meningococcus
  - Tetanus toxoid
  - Pertussis
  - Other
If you selected “other”, please specify: ________________________________

- Medicines/Drugs/Biologics
  - Antimalarials
  - Antiretrovirals/HIV/AIDS
  - Medicines related to mental health
  - Medicines related to autoimmune diseases
  - Medicines related to cancer
  - Medicines related to diabetes
  - Medicines related to epilepsy
  - Other

If you selected “other”, please specify: ________________________________

What outcome(s) is/are recorded while under observation in this resource? Please select all that apply.

- Maternal outcomes
  - Thrombosis and/or thrombocytopenia syndrome
  - Antenatal hospitalization not including delivery
  - Disability
  - Gestational diabetes
  - Gestational hypertension
  - Premature rupture of membranes
  - Preterm labor
  - Preeclampsia / eclampsia
  - Post-partum hemorrhage
  - Antenatal hemorrhage
  - Corporeal infection
  - Spontaneous abortion / miscarriage / pregnancy loss (example: prior to 20 weeks gestation)
  - Maternal death (example: within 42 days of termination of pregnancy)
  - Late maternal death (example: >42 days – 1 year after termination of pregnancy)
  - Other

If you selected “maternal death” or “late maternal death”, please specify the cause of death:

- Direct
- Indirect

If you selected “other”, please specify: ________________________________

- Neonatal outcomes
  - Preterm birth
  - Small size for gestational age / restricted fetal growth
  - Stillbirth (death after 28 weeks of pregnancy but before birth)
  - Live birth
  - Congenital anomalies / birth defects
  - Death
  - Other
If “congenital anomalies / birth defects” is selected, please specify: ________________________________

If neonatal “death” was selected, please specify the timeframe:

○ Early neonatal (0-7 days)
○ Late neonatal (8-28 days)
○ Post neonatal (29 days – 1 year)

If you selected “other”, please specify: _____________________________________________________

● Infant/child outcomes
  ○ Neonatal infections
  ○ Respiratory illness
  ○ Developmental outcomes
    ■ Specify (motor, cognitive, neurologic, autism, etc.): ______________________________
  ○ Other

If you selected “other”, please specify: _____________________________________________________

What is the duration of follow up? ______________________________

Resource start date: _____________________________________________

Resource end date (if applicable): __________________________________

What is the current status of the resource?

○ Open
○ Closed

Who has access to this resource and its data? ____________________________

Do you participate in the running of this resource?

○ Yes
○ No

Do you contribute data to this resource?

○ Yes
○ No
○ Not applicable
6.3.2. PERLA Key Informant Interview

**Consent script**

Hello, my name is _____________ and I work at PATH, an international NGO working in health. We are conducting a landscape analysis in collaboration with WHO to identify available resources, including pregnancy exposure and surveillance registries, databases, surveys, and routinely collected data, that record exposure to medical products during pregnancy and maternal and perinatal outcomes in low- and middle-income countries (LMICs). You either filled out a survey about one or more resources that fit this description, or have been identified as someone who may have more information on these types of resources and may be interested in telling us more. This interview will take between 15-30 minutes and we will ask for your feedback and impressions on the resource(s) you’ve identified. Please keep in mind there are no right or wrong answers, and we are interested in your understanding of the resource as someone who maintains or interacts with these types of resources. We may record this session to help us later with our report. No video footage will be recorded, only audio. Participation is voluntary and if you would like to stop or not answer a question, you may do so at any time. Your name or identity will not be associated with the feedback you provide. Results may be compiled into a report, peer reviewed manuscript, or other communications materials that will be made publicly available. If we make reference to something you have said in our report, you would be referred to as “Participant #1, or #2, etc.” Please confirm your interest in participating in this session?

○ Yes
○ No

Thank you for agreeing to participate in this interview. Let’s get started. (I will start the recording now.)

This is an interview with participant __________.
Interviewee information

For interviewer only: Please fill this section out before the interview and do not speak any identifying information over the recording. If any sections of their survey have been left blank, please include those as follow up questions.

Unique ID. Please reference the sheet if they have already filled out a survey and use their unique ID here. If they did not fill out a survey, assign them a new unique ID. ______________________________________________________

Name: ________________________________________________________________

Email: _________________________________________________________________

Organization: __________________________________________________________

Title: _________________________________________________________________

Did they complete a survey form?

○ Yes

○ No

Resource information

For interviewers only: If “No” is selected under the previous question, all the questions from the survey will show up. If “Yes” is selected, the survey questions that have been answered will be skipped and go straight into the following questions.

We are interested in understanding whether this resource is well equipped or well suited for its designed role or purpose. This could include the possibility of the resource to be combined with others for broader safety surveillance purposes and to understand its impact on supporting maternal health generally.

1. Can you tell me about the overall goals of the resource you have described to us?

________________________________________________________________________________________

________________________________________________________________________________________

________________________________________________________________________________________

Probe: target population, intervention monitored, outcomes monitored, enrollment size, etc.
2. How have findings from this resource been used? In particular, have they been useful decision-making?

________________________________________________________________________________________

________________________________________________________________________________________

________________________________________________________________________________________

Probe: in public health? In regulation? For clinicians? For other healthcare bodies?

3. What are the advantages of this resource?

________________________________________________________________________________________

________________________________________________________________________________________

________________________________________________________________________________________

Probe: Comprehensiveness (outcomes or breadth of resources), coverage, timeliness, usefulness, accuracy, completeness.

4. What are the most important gaps or needs of this resource?

________________________________________________________________________________________

________________________________________________________________________________________

________________________________________________________________________________________

Probe on gaps: Comprehensiveness (outcomes or breadth of resources), coverage, timeliness, usefulness, accuracy, completeness.

5. What are the challenges this resource faces in the current context?

________________________________________________________________________________________

________________________________________________________________________________________

________________________________________________________________________________________

Probe on challenges: Cost, time requirements to maintain the resource, software limitations, etc.
6. Could data from this resource be able to be combined with other health surveillance resources that are used in this region?

Probe: Why/why not? Are there any challenges you foresee?

Probe: How could these systems link?

7. Are you aware of any changes that will be made to this resource in the foreseeable future?

8. Is there anyone else you know who might have useful information about resources like the ones we discussed today?

That was my last question. Before we finish, do you have any questions or additional comments regarding the topics discussed during this interview?

Thank you for your time today. Your input is greatly appreciated.
6.4. Other listings

6.4.1 Retrospective Stand-alone studies


[203] Oliveira MS de. Farmacovigilância de medicamentos anti-retrovirais em gestantes portadoras de HIV e em crianças expostas ao HIV durante a gestação em uso de profilaxia da transmissão vertical: estudo piloto de incidência 2007;x,123-x,123.
6.4.2 Resources identified through the online survey of informants

<table>
<thead>
<tr>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perinatal Information System</td>
</tr>
<tr>
<td>Jos Antimalarials in Pregnancy Cohort</td>
</tr>
<tr>
<td>USAID MTAPS (Mali specifically)</td>
</tr>
<tr>
<td>National PV Centers (Egypt, Yemen)</td>
</tr>
<tr>
<td>National PV Centers with possible data collection activities focused on pregnancy (Tunisia, Mali, Algeria, Azerbaijan)</td>
</tr>
<tr>
<td>National PV perinatal database launching (Burundi)</td>
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<td>MTN (Microbicide Trial Network)-032 in Uganda</td>
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Birth Defects Surveillance in Malawi - Project brief n.d.


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Kaumba PC. Factors affecting the implementation of the SmartCare EHR system in Zambia. Social Sciences & Humanities Open 2023;7:100399. https://doi.org/10.1016/j.ssaho.2023.100399


Oliveira MS de. Farmacovigilância de medicamentos anti-retrovirais em gestantes portadoras de HIV e em crianças expostas ao HIV durante a gestação em uso de profilaxia da transmissão vertical: estudo piloto de incidência 2007-x,123-x,123.


