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Population-Based Linked Longitudinal Surveillance of Pregnant People and Their Infants: A Critical Resource for Emerging, Re-Emerging, and Persistent Threats

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Abstract

Public health emergencies, from Zika to COVID-19, have underscored the importance of addressing the needs of pregnant people and their infants. Recent events have underlined the critical role of mother–infant-linked longitudinal surveillance to characterize and assess the impacts of emerging, re-emerging, and persistent threats, including infectious diseases, on these populations. In partnership with state, local, and territorial health departments, CDC's National Center on Birth Defects and Developmental Disabilities activated the Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET) to capture information about pregnant people with laboratory-confirmed infection with SARS-CoV-2 (the virus that causes COVID-19) and their infants. SET-NET data were critical in recognizing the severe risks of COVID-19 during

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Authors' Contributions

V.T.T. contributed to conceptualization, writing—original draft, review and editing, and supervision; K.R.W. was involved in writing—review and editing; E.B. carried out evaluation; N.S. contributed to writing—original draft, review, and editing; A.A. was in charge of writing—original draft, review, and editing; S.M.G. was in charge of writing—review and editing; and D.M.-D. was in charge of writing—original draft, review, and editing.

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The authors declare that they have no conflict of interest. SET-NET does not collect data on sex or gender of birthing people. We use the term "mother" or "maternal" throughout this publication to describe characteristics of birthing people, though they may be of any gender. We continue to work through the challenge of finding the most inclusive language that is clear and scientifically accurate.

Author Disclosure Statement

No competing financial interests exist.

Supplementary Material

Supplementary Material

Supplementary Table S1

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pregnancy, which ultimately informed clinical decisions and public health policy, specifically vaccine prioritization at the local, state, and national levels. This commentary describes the activation of SET-NET to monitor COVID-19 in pregnancy and highlights the experiences of health departments. We provide examples of how SET-NET findings informed COVID-19 prevention efforts and public health policy. Lastly, we identify opportunities to improve and advance surveillance efforts to protect the health of pregnant people and their infants in the United States from current and future threats.

Keywords

pregnancy; infant; surveillance; COVID-19; emergency response

Background

Public health emergencies, from Zika to COVID-19, have underscored the importance of addressing the needs of pregnant people and their infants. Recent events have underlined the critical role of mother–infant-linked longitudinal surveillance, meaning the identification of people experiencing a health threat during pregnancy and following them longitudinally to understand health effects for both pregnant people and their infants. These data are essential to characterize and assess the impacts of emerging threats, including infectious diseases, on pregnant people and infants. More broadly, these data help inform timely clinical decisions and guide public health policy at the local, state, and national level.

On January 20, 2020, the U.S. Centers for Disease Control and Prevention (CDC) activated a public health emergency response to support public health partners in responding to the COVID-19 outbreak caused by a novel coronavirus—severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] As part of the public health response, state, local, and territorial health departments voluntarily send data to CDC using the National Notifiable Diseases Surveillance System (NNDSS)[2] to monitor cases of confirmed and probable SARS-CoV-2 infection, including cases among pregnant people; however, NNDSS is an event-based reporting system that captures limited information specific to the infectious disease.

To understand the impact of COVID-19 among pregnant people and their infants, a national population-based surveillance approach was needed to capture detailed clinical information about COVID-19 during pregnancy, including the timing of infections; maternal comorbidities; other risk factors for adverse outcomes; and pregnancy, fetal, and infant outcomes.

To address this need, the CDC COVID-19 response activated the Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET) to conduct mother–infant linked longitudinal surveillance of COVID-19 during pregnancy and follow-up of infants through 6 months of age. Findings from SET-NET informed clinical guidance and public health policies, including infection prevention and control practices and COVID-19 prevention (*i.e.*, vaccine) and management strategies.

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This commentary describes the activation of SET-NET to monitor pregnant people with COVID-19 and their infants and highlights the experiences of health departments participating in SET-NET. We provide examples of SET-NET data informing COVID-19 prevention efforts and public health policy. Lastly, we identify opportunities to improve and advance surveillance efforts to protect the health of pregnant people and their infants.

Activating the SET-NET for COVID-19

In August 2019, CDC's National Center on Birth Defects and Developmental Disabilities launched SET-NET to understand the effects of emerging, re-emerging, and persistent threats on pregnant people and their infants, building on the surveillance approach established during the Zika epidemic.[3,4] Uniquely, SET-NET is the only population-based surveillance platform that collects linked longitudinal surveillance from event-based reporting and other existing data sources, and the data collected are used to inform clinical decision making and public health action, particularly during public health emergencies.

During Zika and COVID-19, this surveillance approach, which leverages the foundation of public health reporting of NNDSS, has provided some of the first data to understand the effects of infectious disease threats in pregnant people and infants.

During the first year of SET-NET (only 8 months before it being activated for COVID-19), CDC supported 13 health departments to monitor exposures of concern, hepatitis C, syphilis, and Zika, during pregnancy and collect follow-up data on affected infants over time. SET-NET established a standard set of variables for data collection to allow for aggregation and analysis across all reporting jurisdictions (Fig. 1).

Data collection is structured to include a standard set of information, called "general" variables, that pertain to all pregnant people or infants (*e.g.*, sociodemographic, prepregnancy conditions, pregnancy complications, and pregnancy outcomes), regardless of the infection of interest, and "modular" variables, which comprise information relevant to the unique infectious disease of interest (*e.g.*, detailed risk factors, laboratory testing, and known outcomes).[5]

The first SET-NET data dictionary with general and modular variables for hepatitis C and syphilis was disseminated to funded health departments in January 2020. By design, SET-NET was created to be easily adaptable for any new or re-emerging infection by adding a new infection-specific module to the existing framework. This approach allowed SET-NET to serve as a nimble, "ready to-go" preparedness network that could activate for public health emergencies involving emerging, re-emerging, or persistent threats.

In April 2020, CDC notified health departments that SET-NET would be activated to begin COVID-19 surveillance during pregnancy. At this time, very little was known about COVID-19 during pregnancy, including whether the virus was associated with adverse maternal, pregnancy, or infant outcomes. With supplemental COVID-19 funding through the Coronavirus Aid, Relief, and Economic Security Act, CDC was able to support 30 health departments who activated SET-NET for COVID-19. With this expansion, SET-NET jurisdictions expanded potential coverage from 1.4 to 2.2 million births in the United States

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(Fig. 2). In addition, some jurisdictions participated in SET-NET COVID-19 surveillance without funding support.

The activation of SET-NET for COVID-19 focused on (1) improving case ascertainment of laboratory-confirmed SARS-CoV-2 infection during pregnancy through matching of cases to other existing sources (*e.g.*, vital records and administrative data), (2) monitoring pregnancy, birth, and infant outcomes among people with laboratory-confirmed SARS-CoV-2 infection during pregnancy, and (3) following up infants born to these individuals up to 6 months of age. The SET-NET COVID-19 cohort included pregnancies with positive maternal testing by reverse transcriptase polymerase chain reaction between January 20, 2020, and December 31, 2021.

Selected topics posed for the surveillance of COVID-19 during pregnancy included describing risk factors for severe disease, clinical course, complications, and treatment among pregnant people with COVID-19; defining the frequency and range of pregnancy and birth outcomes (*e.g.*, preterm birth and birth defects); describing the frequency, timing, and characteristics of neonatal testing and infection; and assessing maternal vaccination status on pregnancy outcomes during the surveillance period. A full list of key surveillance questions that SET-NET sought to answer is provided in Table 1.

Jurisdictional Adaptation of Existing Surveillance Infrastructure for COVID-19 Surveillance

An evaluation of 18 jurisdictions' adaptations of SET-NET for use with COVID-19 was conducted in 2021. Additional details of the evaluation are provided in the Supplementary Materials, and important themes are provided here. As part of this evaluation, several factors were identified that facilitated rapid case ascertainment, data collection, and reporting of COVID-19 infections during pregnancy to CDC. Jurisdictions cited the importance of existing data sharing agreements allowing programs from infectious disease and/or maternal child health to share data, including pregnancy status, a key piece of information required for the rapid activation of COVID-19 case ascertainment.

Approximately 40% (7/18) of jurisdictions reported having an existing data sharing agreement applicable for COVID-19 data, and two-thirds (12/18) of jurisdictions reported having existing access to vital statistics or birth records data. However, despite the ability to access these data sources, linkage to maternal or infant records was challenging. Respondents reported that many data sets did not have unique identifiers that were common across a multitude of data sets (*e.g.*, electronic laboratory reports and vital records).

Two other common barriers to reporting data to SET-NET were timeliness of the data (*i.e.*, provisional vital records data were received at different intervals) and the large number of case-level data to process, link, and store, which often required increased computing power and larger data storage. Most jurisdictions (13/18, 72%) reported modifying their current data systems to add COVID-19 rather than developing a new system, with some citing that the SET-NET data structure readily enabled the addition of a new threat. For example, the SET-NET data structure allowed for data collection for outcomes for multiple gestations and

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detailed laboratory testing. These features were leveraged in the activation of data collection for COVID-19.

In general, robust quality data collection for SET-NET requires medical record abstraction of birth hospitalizations and infant follow-up visits. Thus, direct access to medical records facilitated data abstraction. A third of SET-NET jurisdictions surveyed (6/18) had direct access to any electronic medical records (EMRs), and another third (6/18) received electronic versions of medical records. However, most of the jurisdictions initially only had direct electronic medical record access to less than half of the hospitals in their jurisdiction. Half of the jurisdictions (9/18) reported that their access to medical records improved because of COVID-19 social mitigation efforts and clinics scaling up remote access to meet the needs of public health.

Although access to medical records may have improved because of the pandemic, the load of cases that met CDC's inclusion criteria overwhelmed the capacity of health departments to conduct quality medical record abstraction. As a result, jurisdictions requested assistance from CDC to sample a representative number of pregnancies for medical record abstraction as opposed to abstracting the entire cohort.

Given the need to quickly report data for clinical decision making and public health action and to minimize the burden on already strained health departments, CDC developed a sampling approach to support jurisdictions in the collection of population-based data.[6] The sampling approach produced estimates representative of the full population and reduced missingness, particularly for measures of the clinical course and disease severity, which are often incomplete in the COVID-19 case surveillance data.

Lastly, logistical barriers, including limited staffing, time, and resource constraints due to the competing priorities and demands of the COVID-19 emergency response, had to be considered when communicating priorities for data submissions to CDC. However, most respondents (15/18, 83%) reported being ready in case of a new emerging threat (Fig. 3). The high proportion of respondents who felt more ready in case of a new emergency suggests the potential success of the SET-NET program to be able to pivot and collect data for new and re-emerging threats, as exemplified through the COVID-19 response.

Accelerating Data to Action at the National, State, Local, and Territorial Levels

SET-NET data provided valuable information during the COVID-19 pandemic, characterizing the risk of infection among pregnant people and the impact of severe illness from COVID-19 on pregnancy, birth, and infant outcomes. The rapid collection, analysis, and reporting of data directly informed policy for vaccine prioritization and clinical care and management of pregnant people with COVID-19.[7]

From November 2020 to November 2022, CDC reported SET-NET data publicly through an interactive data dashboard, including the number of infections by trimester, pregnancy, and birth outcomes and infant COVID-19 testing.[8] As of November 2022, 34 jurisdictions have

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submitted data on pregnancies with confirmed SARS-CoV-2 infection to CDC providing a large population-based surveillance cohort of COVID-19–infected pregnant people and their infants (Fig. 4).

Key findings on COVID-19 collected through SET-NET, thus far among infections occurring in 2020, include the following:

- SET-NET data identified an increased frequency of preterm birth among people with laboratory-confirmed SARS-CoV-2 infection during pregnancy, compared with the national baseline rate.[3] Those with infection in the third trimester had a higher frequency of preterm birth than those with infections combined from the first or second trimesters.[9] No signals have been seen for increased frequency of birth defects or small-for-gestational-age in relation to national baseline estimates.
- SET-NET data helped identify factors that increased the risk of developing more severe COVID-19 illness among pregnant people: age older than 25 years, employment as health care workers, and presence of underlying medical conditions (*e.g.*, prepregnancy obesity, chronic lung disease, chronic hypertension, and pregestational diabetes mellitus).[10] Risk for severe COVID-19 illness increased along with the number of underlying conditions a pregnant person had.
- SET-NET data provided information on risks for adverse outcomes based on timing of infection during pregnancy: people who became critically ill with COVID-19 during their second or third trimester of pregnancy were four times more likely to have a preterm delivery (before 37 weeks of pregnancy) compared with people who had mild illness at these same trimesters of their pregnancy.[11]
- SET-NET data were also used to show that pregnant persons diagnosed with symptomatic SARS-CoV-2 infections might be recurrently positive by RNA tests for up to 416 days after symptom onset.[12]
- SET-NET data identified that neonatal SARS-CoV-2 infection was rare among neonates born to people with SARS-CoV-2 infection during pregnancy.[13] Most neonatal infection occurred in those born to pregnant people who had an infection around the time of delivery.
- People who had COVID-19 14 days or less before delivery and who did not room-in with their newborn after delivery were less likely to feed their infants breast milk during their delivery hospitalization and may benefit from additional lactation support.[14]

Other forthcoming reports will be focused on characterizing 6-month outcomes of infants born to pregnant people with COVID-19 and the impact of COVID-19 vaccination and periods of Delta variant predominance on pregnancy, birth, and infant outcomes.

In addition to these findings, jurisdictions used SET-NET data to support communication efforts, make public health recommendations, issue guidance, and publish reports. One state health department described using SET-NET infrastructure to identify groups

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disproportionately affected by COVID-19 during pregnancy, which helped prioritize resources to address racial and ethnic inequities, including prevention and vaccination, for these impacted, yet under-served, groups.[15] Several jurisdictions also created public facing dashboards and health communication announcements using SET-NET data.

Furthermore, several state and local jurisdictions described new methods of collaboration; partnerships improved within their health department and with external organizations. One jurisdiction specifically noted that working with their maternal and child health programs has been helpful to ensure information from SET-NET is communicated to health care providers and pregnant people. Another jurisdiction described how they were collaboratively using SET-NET data to develop and implement programs to assist those who have been diagnosed with COVID-19 during pregnancy. CDC continues to facilitate cross-jurisdictional exchange of best practices and strategies for quality surveillance, from data to action, through data use working group calls and office hours.

Lessons Learned and Opportunities for Future Surveillance Efforts

SET-NET's rapid activation for COVID-19 surveillance in pregnant people demonstrated that it is a flexible and ready-to-launch surveillance approach for public health emergencies. The investment and sustainment of SET-NET filled a critical gap in our nation's preparedness and response infrastructure, and ensured needs of a population disproportionally impacted by emerging threats were prioritized within the COVID-19 emergency response efforts. Without SET-NET, months and perhaps years may have gone by without a clear understanding of the effects of COVID-19 on pregnant people and their infants. Data systems and processes were successfully leveraged and expanded to collect critical data on COVID-19, which resulted in these findings that informed national, state, and local action.

Similar to past public health emergencies, such as H1N1 and Zika, the COVID-19 pandemic highlights the importance of collecting pregnancy status in a timely, accurate, and standardized manner for public health surveillance. The SET-NET approach to improve case ascertainment of pregnancy status through linkages to existing data sets (*e.g.*, vital statistics, newborn screening, and birth defects registry) was used by jurisdictions to improve their local data COVID-19 case surveillance.

However, reporting lags and under-reporting still exist, a challenge that should be considered within current data modernization efforts. Innovation and system-based approaches may improve the timeliness, accuracy, and consistency of capturing pregnancy status, including utilizing more timely data sources (*e.g.*, electronic laboratory reporting and electronic case reporting) for case reporting and standardization of pregnancy status data elements for interoperable health exchange in electronic health records within both jurisdictional and federal surveillance systems.[16]

Many jurisdictions had existing data use agreements, allowing them to conduct surveillance for a new infectious disease quickly, but others reported delays in reporting to establish new agreements. A flexible data use agreement, irrespective of disease threat, can be

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leveraged during a public health emergency. Ready access to data sets to confirm case status and pregnancy status can decrease the time to initiate surveillance efforts, and data sets with demographic information, risk factors, and health outcomes can help to gain a comprehensive understanding of how emerging threats impact pregnant people and their infants.

Also, increased access to EMRs allowed for more timely collection of data elements that only exist in medical records. As most jurisdictions reported having coverage for only half of hospitals in their jurisdiction, increasing access to a higher percentage of hospital EMRs is important. In addition, manual abstraction of medical records requires substantial staff and time.

SET-NET is exploring technologies that can rapidly facilitate data exchange and analytic methods that can sift through structured and unstructured free text information from EMR data that can improve timeliness of reporting and analyses.[17] Finally, flexible data collection systems help to efficiently collect and report data during public health emergencies. Thus, continued modernization of SET-NET and jurisdictional data systems to create integrated and real-time public health data may help sustain this maternal and infant health network.

Collaboration between infectious disease and maternal and child health programs within health departments, including clinical networks, has proven to be important to ensure that data collection is targeted on those key questions that would inform clinical management and prevention efforts, assist with data collection, and support outreach efforts. Jurisdictions emphasized the value of SET-NET for their constituents and policymakers, and SET-NET has expanded collaboration within and outside of their health departments. Best practices for data collection and collaboration, particularly from past emergency responses, have been applied to this surveillance effort, and SET-NET can continue to acquire and adapt to lessons learned through robust evaluation processes.

Conclusions

The SET-NET surveillance approach was created to be flexible, with the potential to collect mother–infant linked longitudinal data on emerging, re-emerging, and persistent threats. This was proven by its rapid and impactful activation for COVID-19, contributing to the discovery of the severe risks of COVID-19 during pregnancy and birth outcomes. Data collected through SET-NET directly influenced clinical decisions and public health policy amid the COVID-19 pandemic, including vaccine prioritization.

Activating SET-NET for threats at the local, state, or national level should be considered when the impacts of known or unknown threats (*e.g.*, congenital cytomegalovirus and monkeypox) on pregnant people and their infants are of public health importance and need further characterization and description to inform clinical decisions and policies.[18,19] SET-NET has demonstrated the benefits of institutionalizing and standardizing monitoring of pregnant people, in the setting of public health emergencies, to protect the health of pregnant people and their infants in the United States for current and future threats.

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Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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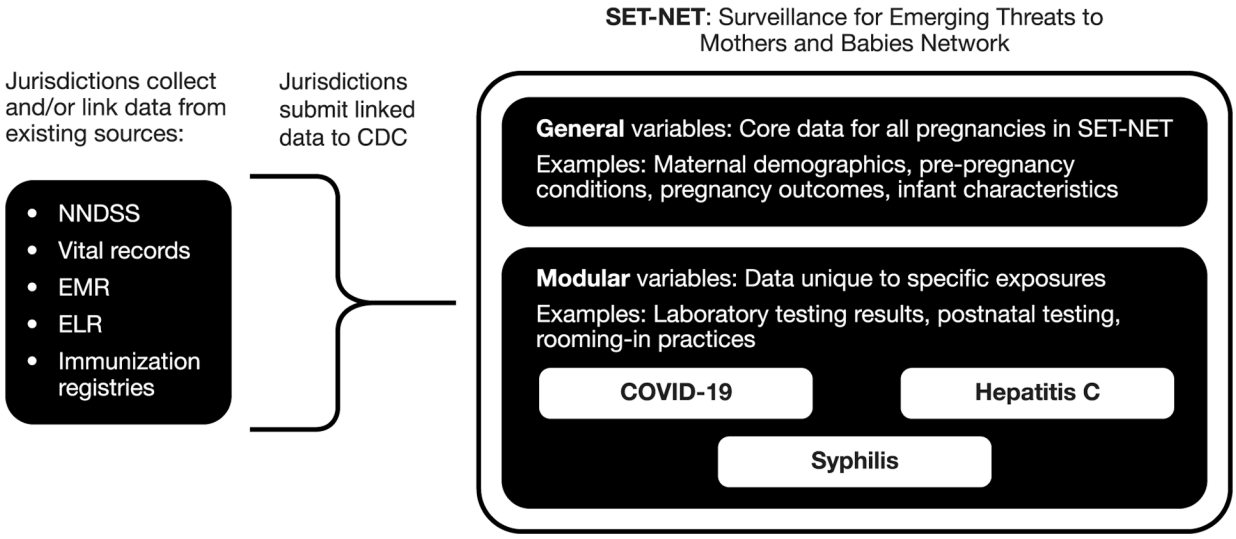

FIG. 1.

Health departments and CDC: SET-NET data sources and collection. ELR, electronic laboratory reporting; EMR, electronic medical records; NNDSS, National Notifiable Diseases Surveillance System; SET-NET, Surveillance for Emerging Threats to Mothers and Babies Network.

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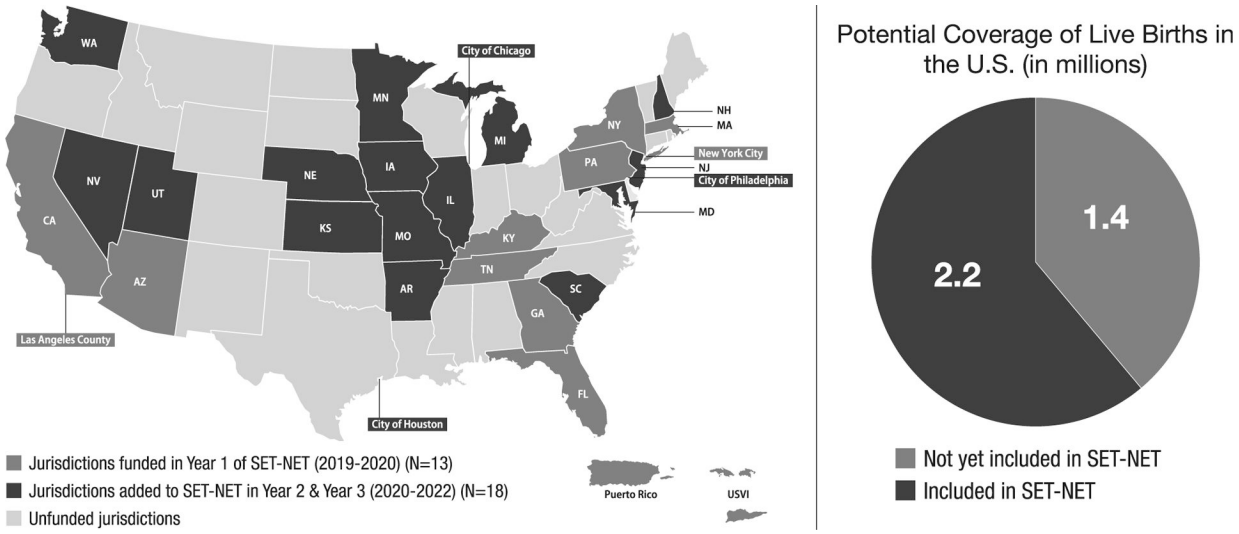

FIG. 2.

Map of 31 state, local, and territorial sites, and potential coverage of live births in the United States, SET-NET, 2019–2022.

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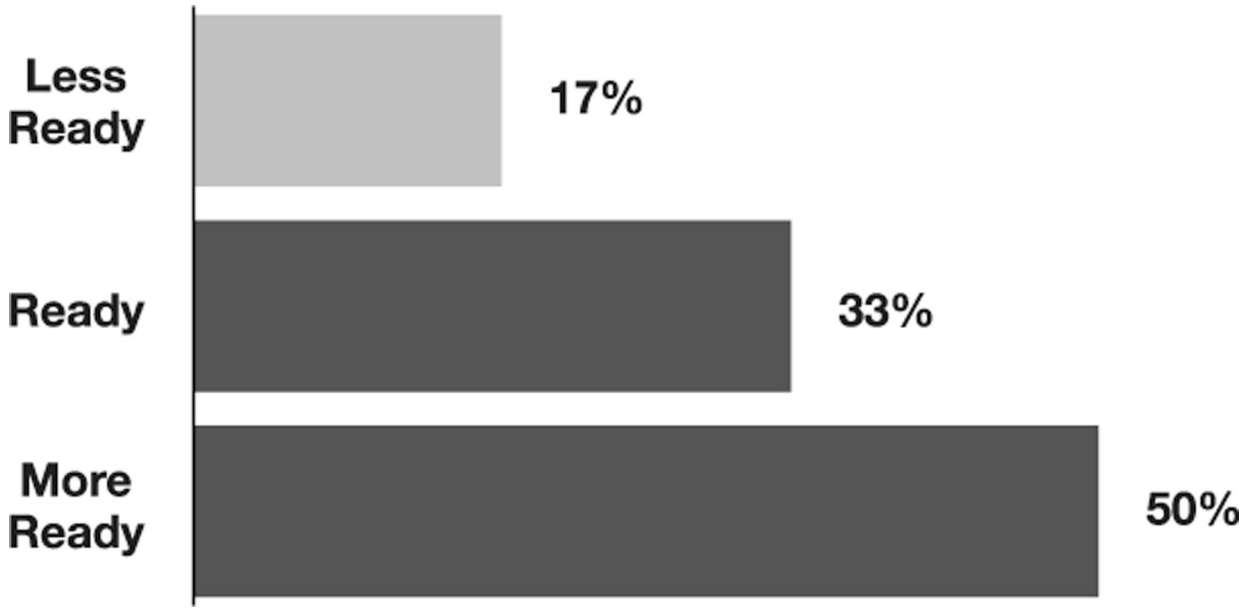

FIG. 3.

The 83% of surveyed jurisdictions perceive themselves as ready or more ready to conduct an emergency response using SET-NET for a new emerging threat after implementation of COVID-19 surveillance.

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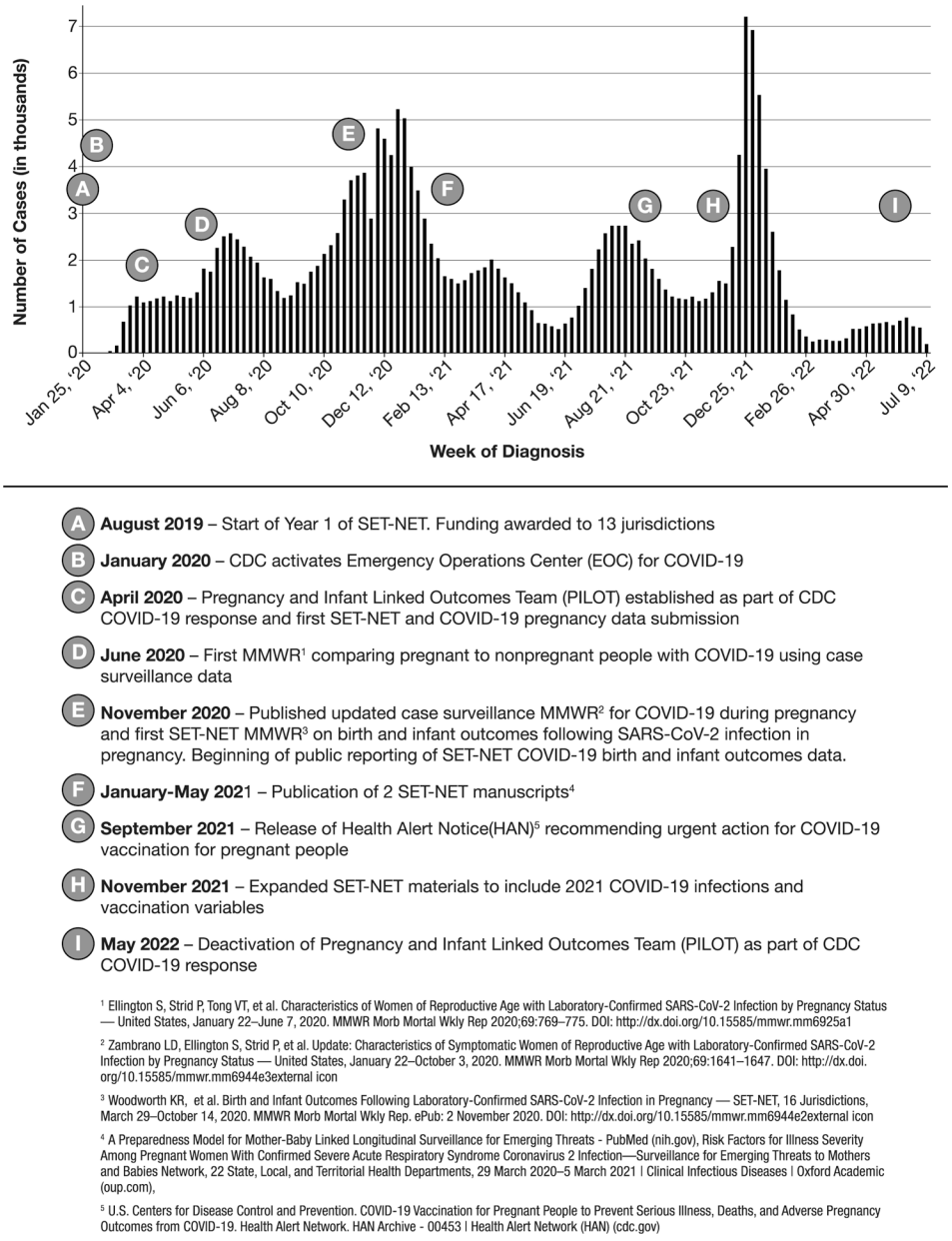

FIG. 4.

SET-NET major events with COVID-19 among pregnant people by week of diagnosis. Data were collected from 224,587 women and date of diagnosis was available for 224,587 (100%) women. Data: CDC COVID Data Tracker: Pregnant People: COVID-19 Illness and Outcomes.

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Table 1.

Surveillance for Emerging Threats to Mothers and Babies Network COVID-19 Surveillance Key Questions

COVID-19 in pregnancy
What are the demographics and risk factors for disease in pregnant people with COVID-19, including occupational exposure (*e.g.*, health care workers)?
What is the timing for illness onset and presence of symptoms (*e.g.*, trimester at infection, asymptomatic vs. symptomatic)?
What is the clinical course of COVID-19 in pregnant people? • Complications (*e.g.*, pneumonia, respiratory distress, abnormal chest X-ray) • Severity (*e.g.*, hospitalizations, intensive care unit admission, intubation, ECMO) • Treatments (*e.g.*, antivirals, supportive treatments) • Outcomes (*e.g.*, mortality)
Does illness severity vary by time period when genetic variants (*e.g.*, Delta) were predominant compared with prior time periods?
What is the frequency of reinfection among pregnant people?
What is the frequency of infection by maternal vaccination status? What is the clinical course of COVID-19 by maternal vaccination status?
Birth and neonatal outcomes of COVID-19 during pregnancy
What is the frequency of different pregnancy outcomes (*e.g.*, live birth, stillbirth, miscarriage) among pregnant people with COVID-19? Does this differ by time period when genetic variants were predominant? Does this differ by maternal vaccination status?
What is frequency of induction and type of delivery (*e.g.*, vaginal, nonemergent c-section, emergency c-section) among pregnant people with COVID-19?
What is the frequency and range of adverse birth outcomes (*e.g.*, birth defects, preterm birth, low birth weight, small for gestational age, ICU admission, neonatal mortality) among neonates born to pregnant people with COVID-19 infections? • Do these outcomes differ by timing and severity of maternal COVID-19 infection, or time period when genetic variants were predominant?
What is the frequency of neonates diagnosed with COVID-19? • Describe timing of neonates testing positive for SARS-CoV-2 (*e.g.*, at birth, 24–48 hours, >48 hours) • Describe the frequency based on maternal disease characteristics (*e.g.*, gestational age at onset, severity of maternal illness, timing of infection to delivery) or delivery characteristics (*e.g.*, vaginal vs. c-section) • Describe treatment administered (*e.g.*, antivirals, supportive treatments)
Did the neonate room-in with mom and what is the frequency of breast milk feeding among people with COVID-19? Do these feeding practices differ by infant testing results and maternal characteristics, such as timing of infection or severity of maternal infection?
Infant outcomes
What is the frequency of postnatal SARS-CoV-2 infection among infants born to people with COVID-19 during pregnancy? Does this frequency differ by maternal characteristics that may influence passive immunity (*e.g.*, trimester of infection, disease severity)? Does this differ by time period when genetic variants (*e.g.*, Delta) were predominant compared with prior time periods? Does this differ by maternal vaccination status?
Among infants with SARS-CoV-2 infection, what is the severity of postnatal infection, including need for hospitalization and mortality?

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COVID-19 in pregnancy
What are the growth patterns seen among infants born to people with COVID-19 during pregnancy? Do growth patterns differ by infant characteristics (*e.g.*, preterm, low birthweight, breastfeeding), infant testing results, and maternal characteristics, such as timing of infection, severity of maternal infection, or hospital infection and control practices?
What is the range and frequency of other adverse infant outcomes (*e.g.*, failure to thrive, dehydration, jaundice, hospitalization) among infants born to people with COVID-19 during pregnancy? Do these outcomes differ by infant testing results and maternal characteristics, such as timing of infection, severity of maternal infection, and/or hospital infection and control practices (*e.g.*, maternal-infant separation)?
Are infants born to people with COVID-19 during pregnancy receiving recommended in-person outpatient follow-up and does this differ by maternal characteristics (*e.g.*, demographics, socioeconomic indicators, and/or timing of maternal infection)?