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Multi-level drivers of congenital syphilis, Oregon, 2013–2021

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Abstract

Background: Despite the availability of curative penicillin treatment for syphilis during pregnancy, congenital syphilis (CS) cases have surged in the United States, including in Oregon.

Methods: We conducted a retrospective analysis of individual- and county-level predictors of CS among pregnant people with syphilis in Oregon from 2013–2021. Data were collated from surveillance reports, County Health Rankings, and other sources with upstream county-level data. We used multi-level Poisson regression models to assess associations between CS and individual- and county-level factors.

Results: Among 343 people with syphilis during pregnancy, 95 (27.6%) were associated with a case of CS. At the individual-level, a history of injection drug use and a history of corrections involvement were associated with an increased risk of CS, while a recent gonorrhea diagnosis was associated with a decreased risk of CS. County-level violent crime rate, unemployment, income inequality, and adverse childhood experiences increased the risk of CS. Higher county-level socioenvironmental challenges exacerbated CS risk, particularly among people with corrections involvement.

Conclusions: Injection drug use, corrections involvement, and county-level socioenvironmental challenges increased CS risk among pregnant people with syphilis in Oregon. Urgent interventions are needed, including innovative care models, policy reforms targeting systemic issues, and enhanced collaboration with community services to address the escalating CS crisis.

Short Summary

Pregnant people associated with a case of congenital syphilis in Oregon between 2013–2021 were highly likely to have histories of injection drug use and corrections involvement and reside in counties with greater socioenvironmental challenges.

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Ethical Compliance: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Keywords

congenital syphilis; syphilis; pregnancy; multi-level analysis; Oregon

Introduction

Congenital syphilis marks the failure of health systems in the context of intersecting social and structural determinants of health.[1–3] In the United States (US), there were 3,755 cases of CS in 2022, a 1,121% increase from 335 cases in 2012.[3] Lack of timely testing due to barriers to prenatal care and inadequate treatment among pregnant people with syphilis comprised 88% of the missed opportunities to prevent CS nationally in 2022.[4] In Oregon, there were no cases of CS in 2013 and 37 (65.7 cases per 100,000 live births) in 2022. Concurrently, the rate of primary and secondary syphilis among people assigned female at birth in Oregon increased from 1.6 in 2015 to 16.1 cases per 100,000 population in 2022. There were 18 cases of syphilis during pregnancy per 100,000 live births in 2013 compared to 210 cases per 100,000 live births in 2021.[5] These increases in syphilis among people assigned female at birth and infants are occurring in the context of significant increases methamphetamine and fentanyl overdose morbidity and mortality (in 2022, the crude rates of methamphetamine and fentanyl overdose mortality were 20 and 19 per 100,000, respectively)[6] and increasing rates of houselessness in Oregon.[7]

While inadequate prenatal care, delayed testing, and untreated syphilis during pregnancy consistently emerge as strongest predictors of CS,[4] additional individual-level factors among pregnant people include: early syphilis (comprised of primary, secondary, and asymptomatic nonprimary nonsecondary syphilis occurring in the prior 12 months) compared to late syphilis (*Treponema pallidum* infections of greater than a year's duration),[8] lack of access to prenatal care,[4,9] substance use[9,10] (specifically methamphetamine use),[11] housing instability,[9,11] engaging in anonymous sex,[12] having multiple sex partners,[12] transactional sex,[12] low educational attainment,[13] and mental health challenges.[10] The relationship between incarceration (current or history of) and intimate partner violence with increased risk of CS is less consistent across studies.[9,10]

Understanding the social context and the root causes of CS is crucial to ending the expanding epidemic. Community-level (county, census tract, or ZIP code-level) factors associated with an increased risk of CS in previous studies and predictive models include: female poverty,[14] female educational attainment,[14] income inequality,[15] population proportions of Hispanic, non-Hispanic Black, Native Hawaiian/Pacific Islander above the median,[15] insurance status,[14] urbanicity,[15,16] and violent crime.[16] To guide public health programs and policy to prevent CS, we assessed individual-level and county-level factors associated with CS cases in Oregon from 2013 through 2021.

Methods

We conducted a retrospective analysis of individual- and county-level factors associated with CS cases among pregnant people with syphilis in Oregon from 2013–2021.

Data sources for syphilis and congenital syphilis cases

Syphilis and congenital syphilis data in Oregon originate from clinicians and laboratories who are required to report positive syphilis test results to local public health authorities (LPHAs) in Oregon. LPHA staff investigate cases, gathering information on treatment, sex partners, and social determinants of health. All information is consolidated in the Oregon Public Health Epidemiology User System (ORPHEUS, FileMaker Pro; Claris, Santa Clara, CA), integrating laboratory reports, case investigations, and chart reviews. The Congenital Syphilis Case Investigation and Reporting Form (CDC 73.126, REV. 02–2013) includes demographic characteristics, prenatal care (***only*** collected for pregnant people associated with a case of CS), and clinical data for pregnant people and infants. These case records and surveillance data collected in ORPHEUS were used to create the analytic file for pregnant people diagnosed with syphilis.

Case classification

Cases of syphilis among pregnant people (N=343) and CS (N=95) were classified according to the Council of State and Territorial Epidemiologist (CSTE) case definition.[17] Among the 95 cases of CS, 57 (60%) were defined by maternal criteria only, 7 (7%) were defined by infant criteria only, and 23 (24%) were defined by maternal and infant criteria. CS-related outcomes, irrespective of maternal or infant criteria, included eight (9%) syphilitic stillbirths and 2 (2%) neonatal deaths.

Individual-level factors associated with a case of congenital syphilis among pregnant people with syphilis

We analyzed social and demographic characteristics, including age, race/ethnicity (collected as a single mutually exclusive variable based on Office of Management and Budget [OMB] categories and a crude proxy for current and historical experiences of racism), rurality (based on the Oregon Office of Rural Health Geographic Definitions),[18] and time period (2013–2018, 2019–2021 where the period of 2019–2021 represents a period of rapid growth in the syphilis epidemic among pregnant people and infants).[5] Additionally, we examined syphilis stage, sexual behavior, history of STIs, injection drug use (IDU), and involvement with corrections prior to syphilis diagnosis. Corrections involvement included arrest, incarceration, parole, probation, and outstanding warrants (excluding traffic violations and non-criminal arrests). Data were gathered from multiple sources, including Accurint/LexisNexis, Oregon Judicial Department OJCIN OnLine, and VINElink. These variables were complete for all pregnant people with syphilis.

High levels of missingness were observed for housing status (60.9% missing), transactional sex (36.4% missing), and most commonly used drug in the prior year (65.3% missing), which prevented their inclusion in the analysis as it would severely limit our overall sample size. Additionally, housing status questions varied throughout the study period and large differences in missingness of housing status and most commonly used drug were noted between pregnant people associated with a case of CS (25.3% and 47.4%, respectively) and those not associated with a CS case (74.6% and 71.8%, respectively).

County-level measures associated with being associated with a case of congenital syphilis among pregnant people with syphilis

We used the County Health Rankings model[19] and the scientific literature to select county-level measures that may increase the risk of CS. We chose the average number of poor mental health days,[10] a health outcome measure of quality of life, and factors including health behaviors (food insecurity, methamphetamine overdose deaths);[11,13] social and economic factors (unemployment, violent crime, income inequality, poverty, adverse childhood experiences [ACES]),[9,14–16] and the physical environment (houselessness).[9,11] Supplemental Table 1 presents the specific county-level variables, data sources, and time periods.

The Oregon Health Authority (OHA) Science and Epidemiology Council's Project Review Team deemed this work public health practice and exempt from IRB review.

Statistical analysis

With 343 pregnant people with syphilis nested within 23 of Oregon's 36 counties (1–85 [mean = 15] individuals per county), we used multi-level Poisson regression with county-specific random effects and robust standard error estimation to calculate risk ratios (RRs) and 95% confidence intervals (CIs) to evaluate the associations of individual- and the county-level factors CS.[20] The dataset for the multi-level analysis consisted of a line list including both individual- and county-level data.

Evaluation of individual-level factors

We assessed bivariable models of each of the individual-level predictors followed by a multivariable model that included all the selected individual-level predictors. From this model, we retained the variables of age, race/ethnicity, and time-period and the statistically significant predictors of CS at the $P<0.05$ level to create a parsimonious individual-level model.

Evaluation of county-level measures

We examined bivariable models of each of the county-level measures. Before building multivariable models using the county-level measures, we examined the correlation between each of the county-level measures (Supplemental Table 2). Due to a high level of correlation and because each variable may explain some of the variance in the outcome of CS, we used a principal components analysis (PCA) to create a score that represents a linear combination of the county-level variables and retains the original explanatory variance of each of the variables individually.[21] We performed two PCAs, one that included all the a priori county-level variables (full score) and one that included only those county-level variables associated with CS in bivariable models at the $P<0.05$ level (simple score). We used the first principal component of each PCA because, in both analyses, this component explained the largest proportion of the variance (67.0% and 80.9%, respectively; Supplemental Table 3). Greater scores indicate greater county-level socioenvironmental challenges as defined by higher rates or percentages of each county-level variable.

Evaluation of individual-level factors and county-level scores

We ran bivariable models with unscaled full and simple scores. We then built two multivariable models: the first included the full score and variables from the parsimonious individual-level model, and the second included the simple score and the variables from the parsimonious individual-level model. In the multivariable models, we scaled the scores to the standard deviation of the score such that a value of zero was the mean score, a value of 1 was one standard deviation above the mean, and a value of −1 was one standard deviation below the mean. For all four models, we plotted the natural log of the predicted risk of CS by the scaled full and simple scores (Supplemental Figure 1) and assessed model fit visually (data not shown) and by Hosmer-Lemeshow goodness of fit tests.

We examined a post-hoc multivariable multi-level random intercept Poisson regression with an interaction between the full score, history of IDU, and history of corrections involvement. By history of IDU and corrections involvement, we calculated the predicted risk of being associated with a case of CS and the change in that predicted risk with a one-standard deviation increase in the full score using the margins command in STATA.

Finally, we calculated the population attributable fraction (PAF) for statistically significant variables in the final multivariable model, including the full score, where PAF = proportion of pregnant people associated with a case of CS with the exposure of interest*(risk ratio - 1)/ risk ratio. We dichotomized the full score at the mean to calculate the PAF for a score above the mean. The PAF is a measure of the potential impact of an exposure on an outcome.[22]

We used STATA 17.0 (StataCorp, College Station, TX) for all statistical analyses.

Results

From 2013 to 2021, there were 343 pregnant people diagnosed with syphilis. The median age was 27 years (range: 16–43 years; Table 1). Approximately half identified as white (n=181), a quarter lived in rural areas (n=80), and 55% were diagnosed between 2019–2021 (n=189). Over 60% had late or unknown duration syphilis (n=212), 10% reported a partner with early syphilis prior to their diagnosis (n=33), and 14% had a previous syphilis diagnosis (n=48). Nine (n=31) and 18% (n=60) were diagnosed with gonorrhea and chlamydia respectively in the two years before their syphilis diagnosis, while 6% had HCV prior to their syphilis diagnosis (n=20). A quarter reported ever using injection drugs (n=88) or having a partner who used injection drugs (n=85), and over 40% had ever been involved in the correctional system (n=149).

Cases of congenital syphilis, prenatal care, outcomes, and missed opportunities

Ninety-five (27.6%) of the 343 pregnant people with syphilis were associated with a case of CS. Almost 30% of pregnant people associated with a case of CS did not receive prenatal care and were diagnosed with syphilis at delivery (Table 2). The most common missed opportunity for CS prevention was inadequate treatment, defined as not receiving a penicillin-based regimen; not receiving a total of 7.2 million units of benzathine penicillin G for late/unknown duration syphilis or at the appropriate intervals; not completing treatment initiated ≥30 days prior to delivery; and, not receiving treatment during pregnancy. Of those

with inadequate treatment, 17/43 (39%) did not receive a first dose of benzathine penicillin G ≥30 days prior to delivery.

Twenty-one (22%) pregnant people associated with a case of CS had non-reactive syphilis screening at first presentation to prenatal care and reactive testing at a later point in pregnancy (i.e., seroconversion detected during pregnancy). Five of the 21 (24%) had seroconversion detected <45 days prior to delivery while 16 (76%) had seroconversion detected ≥45 days prior to delivery but did not receive a first dose of benzathine penicillin G ≥30 days prior to delivery. Two (2%) pregnant people experienced reinfection defined as a 4-fold increase in RPR titer after treatment during pregnancy in the context of at least one untreated partner; neither received a first dose of benzathine penicillin G ≥30 days prior to delivery.

Evaluation of individual-level factors

In bivariable models, time period (2019–2021 vs 2013–2018), prior HCV diagnosis, history of IDU, having a sexual partner who injects drugs, and corrections involvement were associated with a case of CS (Table 3). In a multivariable model including all the individual-level factors, pregnant people with syphilis who had ever used injection drugs were 1.96 times as likely to be associated with a case of CS compared to pregnant people with syphilis who had never injected drugs. Pregnant people with syphilis with a history of corrections involvement were 1.40 times as likely to be associated with a case of CS compared to pregnant people with syphilis without corrections involvement.

Conversely, pregnant people with syphilis with a diagnosis of gonorrhea in the prior two years were half as likely to be associated with a case of CS compared to pregnant people with syphilis without a diagnosis of gonorrhea in the prior two years. Because ceftriaxone may treat incubating syphilis (though is not a recommended treatment for syphilis in pregnancy and would not alter maternal criteria for CS),[23] we performed a sensitivity analysis by excluding recent gonorrhea diagnoses occurring within a month of the syphilis diagnosis; we observed a similar inverse association (adjusted risk ratio [RR] = 0.62; 95%CI 0.40, 0.95). Six (2.4%) of the pregnant people not associated with a case of CS had a gonorrhea diagnosis within a month of their syphilis diagnosis (one of whom had concurrent diagnoses on the same day). In contrast, one (1.0%) pregnant person associated with a case of CS had a gonorrhea diagnosis concurrent with their syphilis diagnosis.

Both the full and parsimonious models yielded similar conclusions.

Evaluation of county-level measures, full and simple scores

Compared to counties without cases of CS, counties with CS cases had greater rates of methamphetamine overdose death, violent crime, and houselessness; greater percentages of the population experiencing food insecurity and having at least one ACE; and, greater income inequality (Table 4). In bivariable multilevel models, pregnant people residing in counties with a greater violent crime rate, percent of the population experiencing unemployment, income inequality ratio, and percent of the population with at least one ACE were more likely to be associated with a case of CS compared to pregnant people residing in counties with lower values of these measures.

The unscaled full and simple scores were greater in counties with at least one CS case compared to counties with no CS cases. In bivariable multilevel models, pregnant people with syphilis residing in a county with a one-unit greater full score were 1.08 times as likely to be associated with a case of congenital syphilis compared to pregnant people with syphilis residing in a county with a lower score. Pregnant people with syphilis residing in a county with a one-unit greater simple score were 1.13 times as likely to be associated with a case of congenital syphilis compared to pregnant people with syphilis residing in a county with a lower score.

Multivariable models of individual-level factors and county-level full and simple scores

In multivariable multilevel models, pregnant people with syphilis residing in counties with a score one standard deviation above the mean were 1.20 (full) and 1.24 (simple) times as likely to be associated with a case of CS, compared to pregnant people residing in a county with a mean score. In both models, history of IDU and corrections involvement were positively and statistically significantly associated with a case of CS while a gonorrhea diagnosis in the prior two years was inversely and statistically significantly associated with a case of CS, mirroring results from multivariable individual-level models.

Post-hoc interaction evaluation

Among pregnant people with syphilis without a history of IDU or corrections involvement and among those with a history of IDU and without a history of corrections involvement, the predicted risk of being associated with a case of CS did not vary significantly with the full score (P=0.613 and P=0.844, respectively; Supplemental Figure 2). Among pregnant people with syphilis with a history of corrections involvement and no history of IDU, the risk of CS increased 0.09 per one standard deviation increase in full score (P=0.013). Finally, among pregnant people with syphilis with both a history of corrections involvement and IDU, the predicted risk of CS increased by 0.14 per one standard deviation increase in full score (P<0.001).

Population attributable fraction

To calculate the PAF, we dichotomized the full score at the mean and ran a multi-level random intercept Poisson regression model with age, race/ethnicity, time-period, history of IDU, history of corrections involvement, and gonorrhea diagnosis in the prior two years. In this model, the adjusted RR for a full score above the mean was 1.47 (95%CI: 1.04, 2.08); 67% of pregnant people with syphilis resided in a county with a score above the mean such that the PAF was 21.4%, (0.67*(1.47–1)/1.47). The PAF for history of IDU was 20.0% (0.43*(1.87–1)/1.87) and the PAF for history of corrections involvement was 15.1% (0.57*(1.36–1)/1.36).

Discussion

Among 343 pregnant people with syphilis in Oregon, the risk of being associated with a case of CS was greater among people with a history of IDU or corrections involvement and among pregnant people residing in counties with higher levels of socioenvironmental inequities. The increase in risk with heightened county-level socioenvironmental challenges

was greatest among those with a history of corrections involvement. We observed a protective effect of a prior diagnosis of gonorrhea even after eliminating diagnoses within one month of the syphilis diagnosis. Gonorrhea may be a salient marker of risk such that pregnant people with a history of gonorrhea are more likely to be screened for syphilis during pregnancy[24] leading to diagnosis and treatment. We did not see the same effect for a prior chlamydia diagnosis. In Oregon, chlamydia diagnoses are not routinely investigated by LPHAs while gonorrhea diagnoses are, particularly among people who can become pregnant, which may explain this observed difference.

Since 2015, OHA has recommended routine, universal syphilis screening in pregnancy at the first presentation to prenatal care, in the early third trimester, and at delivery.[25] As of April 2024, the American College of Obstetricians and Gynecologists also recommends routine, universal syphilis screening at three time points during pregnancy.[26] Based on our data, 23/95 (24.2%) pregnant people associated with a case of CS experienced seroconversion or reinfection during pregnancy and did not receive timely diagnosis or treatment. Routine third trimester screening may have detected these seroconversions or reinfections earlier leading to timely diagnosis and treatment and aversion of almost one-quarter of CS cases. Screening three times during pregnancy has been shown to be cost-effective even before the large increase in CS in the US[27] and cost-avoidant during an outbreak of CS.[28]

Furthermore, universal screening in pregnancy acknowledges that the risk of syphilis acquisition may result from a partner or a sexual network rather than the behaviors of pregnant people themselves.[29,30] In fact, in the current analysis, we found that pregnant people who reported partners who used injection drugs were 1.5 times as likely to be associated with a case of CS compared to those who did not. This association was not statistically significant in multivariable analysis, however. Oregon LPHAs endeavor to provide partner services to all pregnant people and pregnancy-capable with syphilis. Partner testing and treatment is critical to avoiding reinfection and client and partner interviews provide important contextual information for CS prevention.

Clinician education and comfort around diagnosing and treating syphilis are also crucial in preventing CS.[31] Pregnant people diagnosed with syphilis in hospital or emergency department settings were more likely to be associated with a case of CS compared to other healthcare settings.[12] OHA promotes the policy that for pregnant people, all visits are prenatal visits, so that when pregnant people attend the emergency room or an urgent care clinic, access drug use health programs (e.g., substance use disorder treatment programs, syringe service programs), or are admitted to a carceral setting, they should have prenatal labs drawn, including for syphilis, when their prenatal care status is uncertain or unknown. Conversely, all people pregnancy-capable with syphilis should be tested for pregnancy and where possible pregnancy status should be reported to local and state public health departments concurrently with laboratory and clinician syphilis case reports.

From 2020 to 2021, Oregon experienced a 50% increase in diagnoses of primary and secondary syphilis cases and an 80% increase in diagnoses of primary and secondary syphilis among people assigned female at birth. Like others, we found that risk-based screening would miss almost 50% of cases of syphilis among people assigned female at

birth.[29] Therefore, OHA recommends universal screening[25] for all sexually active adults 45 years of age and younger who have not been screened for syphilis since January 1, 2021. OHA provides guidance for who should be screened more frequently, based on individual-level (e.g, housing status, substance use, corrections involvement, prior HIV/STI or HCV diagnosis), partner-level (e.g., housing status, substance use, corrections involvement, gender of partners' sex partners), and contextual-level (e.g., location of care including sexual health and family planning clinics, carceral settings, emergency rooms, substance use disorder treatment programs) indications.

While injection drug use, corrections involvement, and county-level socioenvironmental inequities do not explain all the variation in the outcome of CS and may operate through multiple causal pathways, the multilevel analyses and PAFs ranging from 15–21% provide evidence for addressing substance use, incarceration, and the role that poverty, mental health, trauma, and community violence play in the syphilis epidemic. Substance use and corrections involvement at the individual- and county-level affect whether people might access or persist in prenatal care. In the US, there is a legacy of curtailing reproductive autonomy through the medical system, particularly for pregnant people who are Black, Indigenous, Latinx, and Pacific Islander, are immigrants, are experiencing poverty, use substances, have mental health challenges or other disabilities, or are or have been involved in the criminal justice system.[31s,32s] Many pregnant people face punitive consequences should they seek healthcare while pregnant, which could range from poor care to mistreatment to being reported to law enforcement or child welfare services.[9,34s] Thus, the (real or perceived) risks of accessing prenatal care may be too high for some pregnant people.

Improving access to prenatal care requires new partnerships, programs, care models and policies.[35s] First, while pregnant people with syphilis may not access prenatal care, they may access other community and social services. In case interviews with pregnant people with syphilis, Oregon LPHA staff have started collecting information on utilization of services like special supplemental nutrition program for women, infants and children (WIC), food banks, shelters, peer support services, substance use disorder treatment, mental health care, visiting nurse programs (universally offered in Oregon), street medicine programs, intimate partner violence resources, and anti-poverty programs (e.g., supplemental nutritional assistance program [SNAP], temporary assistance for needy families [TANF], and housing vouchers). Partnerships with these programs and resources could be leveraged not only for CS prevention but also for prenatal care engagement and persistence to improve outcomes among infants and pregnant people. OHA has additionally developed 340B partnerships with local jails and the Oregon Department of Corrections to increase STI screening in correctional settings. We recently issued recommendations to healthcare providers on best practices for preventing CS with the Oregon Perinatal Collaborative,[36s] part of the National Network of Perinatal Quality Collaboratives.[37s] To further support providers in screening for syphilis during pregnancy and to implement Oregon's universal syphilis screening recommendation, we are also working with a non-profit organization that tailors electronic medical record systems for federally qualified health centers and public health clinics to create best practice alerts. In partnership with the Oregon Public Health Accountability Board, we developed public health metrics to track the work of state and local public health

in reducing CS with a goal of encouraging Oregon Medicaid to adopt metrics and incentives for syphilis screening in pregnancy.

Second, innovative programs like the Abundant Birth Project,[38s] which provides Black and Pacific Islander pregnant people in five California counties with an unconditional monthly income supplement to address racial and economic disparities in outcomes of pregnant people and infants, may also prevent CS. Third, we must restructure care provision for pregnant people. Low-barrier, trauma-informed, anti-racist prenatal care models that are mobile or drop-in, and co-located with trusted, community-based supportive services may improve access to care and prevent morbidity among pregnant people and infants, including syphilis and CS.[39s]

Finally, all policy is health policy.[40s] Policies addressing systemic racism, housing instability, poverty, violence, mass incarceration, substance use, mental health, and childhood trauma will impact rates of CS.

Limitations

This work is subject to several limitations. First, there was significant missingness for potentially important predictors among pregnant people with syphilis in our surveillance data, and that missingness varied by whether the pregnant person was associated with a case of CS due more complete public health follow-up. In addition, prenatal care variables were only available for those who were associated with a case of CS. Second, surveillance data are not medical records data so we cannot assess why a pregnant person may have not received prenatal care, was not screened in the early third trimester, or did not receive adequate treatment. In addition, we cannot always know the care context of syphilis diagnosis and some pregnant people with syphilis may receive testing and treatment outside of prenatal care. Third, the county-level variables reflected different time frames during the study period based on the availability of data at the time of analysis and the associations of the county-level variables with CS risk may not be constant over time. While a smaller geographic area (e.g., census tract, zip code) may be more appropriate with respect to exposure to area-level disadvantage and its impact on health outcomes, there would be very few observations per area limiting the potential for robust statistical analysis. In addition, creating a score from a PCA does not allow for the evaluation of interactions between the county-level variables. Finally, these data represent a single state experience and may not generalize to other jurisdictions.

Conclusions

Injection drug use, corrections involvement, and greater county-level socioenvironmental challenges increased the risk of being associated with a case of CS among pregnant people with syphilis in Oregon. New partnerships, programs, care models, and policies are urgently needed to address the crisis of CS at local, state, and national levels.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Individual-level socio-demographic and clinical factors and social determinants of health among pregnant people with syphilis, Oregon, 2013–2021.

	Pregnant people with syphilis		
	Total (n = 343)	**Not associated with a case of CS (n = 248)**	**Associated with a case of CS (n = 95)**
Socio-demographic			
Age, years; median (range)	27 (16–43)	27 (18–43)	26 (16–43)
Race/ethnicity			
NH American Indian/Alaska Native	10 (2.9)	6 (2.4)	4 (4.2)
NH Asian	8 (2.3)	8 (3.2)	0
NH Black/African American	25 (7.3)	20 (8.1)	5 (5.3)
Hispanic/Latinx	65 (19.0)	46 (18.6)	19 (20.0)
NH Native Hawaiian/Pacific Islander	15 (4.4)	10 (4.0)	5 (5.3)
NH White	181 (52.8)	125 (50.4)	56 (59.0)
Another or multiple race/ethnicity[a]	39 (11.4)	33 (13.3)	6 (6.3)
Rural or frontier zip code	80 (23.3)	59 (23.8)	21 (22.1)
Time period			
2013–2018	154 (44.9)	118 (47.6)	36 (37.9)
2019–2021	189 (55.1)	130 (52.4)	59 (62.1)
Clinical			
Syphilis stage			
Early	131 (38.2)	99 (40.0)	32 (33.7)
Late/unknown duration	212 (61.8)	149 (60.1)	63 (66.3)
One or more contacts with early syphilis	33 (9.6)	22 (8.9)	11 (11.6)
History of syphilis	48 (14.0)	35 (14.1)	13 (13.7)
Gonorrhea in the 2 years prior to current syphilis diagnosis	31 (9.0)	25 (10.1)	6 (6.3)
Chlamydia in the 2 years prior to current syphilis diagnosis	60 (17.5)	41 (16.5)	19 (20.0)
HCV diagnosis prior to current syphilis diagnosis	20 (5.8)	12 (4.8)	8 (8.4)
Social determinants of health			
Injection drug use, ever	88 (25.7)	47 (19.0)	41 (43.2)

	Pregnant people with syphilis		
	Total (n = 343)	**Not associated with a case of CS (n = 248)**	**Associated with a case of CS (n = 95)**
Corrections involvement, ever	149 (43.4)	95 (38.3)	54 (56.8)
Partner uses injection drugs	85 (24.8)	53 (21.4)	32 (33.7)

[a]Includes people who reported “Other” for their race/ethnicity, reported more than one race/ethnicity, or had a missing race/ethnicity. Race/ethnicity categories are mutually exclusive.

CS, congenital syphilis; HCV, hepatitis C virus; IQR, interquartile range; NH, non-Hispanic

Table 2.

Timing of prenatal care, syphilis diagnosis, maternal treatment, outcomes, and missed opportunities for congenital syphilis prevention among pregnant people associated with a case of congenital syphilis, Oregon, 2013–2021.

	N = 95
Trimester of first prenatal care visit	
First	26 (27.4)
Second	22 (23.2)
Third	19 (20.0)
No prenatal care	28 (29.5)
Trimester of syphilis diagnosis	
First	12 (12.6)
Second	26 (27.4)
Third	29 (30.5)
At/after delivery	28 (29.5)
Trimester of first benzathine penicillin G dose	
Before pregnancy	1 (1)
First	6 (6.3)
Second	15 (15.8)
Third	36 (37.9)
At/after delivery	14 (14.7)
No treatment	23 (24.2)
Seroconversion detected during pregnancy	21 (22.1)
Reinfection during pregnancy	2 (2)
Neonatal outcome	
Stillborn	8 (9)
Neonatal demise	2 (2)
Missed opportunity for congenital syphilis prevention (mutually exclusive hierarchy)	
No prenatal care	28 (29.5)
Prenatal care less than 45 days prior delivery	13 (13.7)
Syphilis testing less than 45 days prior to delivery	11 (11.6)

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	N = 95
Inadequate treatment	43 (45.3)
Did not receive a penicillin-based regimen	3
Did not receive three doses of long-acting benzathine penicillin G for late/unknown duration syphilis (< 7.2M units total)	6
Did not receive treatment in 6-9-day intervals	13
Did not receive a first dose more than 30 days prior to delivery	17
Did not receive treatment during pregnancy	4

Table 3.

Bivariable and multivariable multilevel Poisson regression models of individual-level socio-demographic and clinical factors and social determinants of health among pregnant people with syphilis, Oregon, 2013–2021.

	Bivariable RR (95% CI)	*P* value	Full multivariable RR (95% CI)	*P* value	Parsimonious multivariable RR (95%CI)	*P* value
Socio-demographic						
Age, years	1.00 (0.97, 1.03)	0.989	0.99 (0.96, 1.03)	0.746	0.99 (0.97, 1.02)	0.683
Race/ethnicity						
NH American Indian/Alaska Native	1.29 (0.64, 2.63)	0.478	1.53 (0.66, 3.54)	0.320	1.43 (0.62, 3.32)	0.399
NH Asian	Not estimable		Not estimable		Not estimable	
NH Black/African American	0.65 (0.39, 1.06)	0.084	0.72 (0.37, 1.42)	0.343	0.70 (0.34, 1.42)	0.321
Hispanic/Latinx	0.94 (0.57, 1.57)	0.827	1.17 (0.75, 1.82)	0.493	1.19 (0.78, 1.80)	0.416
NH Native Hawaiian/Pacific Islander	1.08 (0.52, 2.22)	0.840	1.55 (0.73, 3.25)	0.250	1.54 (0.74, 3.17)	0.246
NH White	REF		REF		REF	
Another or multiple race/ethnicity	0.50 (0.21, 1.15)	0.103	0.60 (0.30, 1.23)	0.164	0.57 (0.28, 1.15)	0.116
Rural or frontier zip code	0.93 (0.58, 1.50)	0.775	0.86 (0.54, 1.39)	0.550		
Time period						
2013–2018	REF		REF		REF	
2019–2021	1.34 (1.04, 1.72)	0.024	1.09 (0.83, 1.43)	0.521	1.11 (0.85, 1.44)	0.449
Clinical						
Early syphilis	0.82 (0.51, 1.33)	0.423	0.80 (0.51, 1.25)	0.328		
One or more contacts with early syphilis	1.23 (0.81, 1.87)	0.332	1.15 (0.66, 2.02)	0.617		
History of syphilis	0.97 (0.60, 1.57)	0.915	1.14 (0.70, 1.88)	0.594		
Gonorrhea in the 2 years prior to current syphilis diagnosis	0.68 (0.43, 1.08)	0.102	0.49 (0.30, 0.80)	0.005	0.51 (0.35, 0.75)	0.001
Chlamydia in the 2 years prior to current syphilis diagnosis	1.18 (0.81, 1.72)	0.389	1.15 (0.72, 1.84)	0.546		
HCV diagnosis prior to current syphilis diagnosis	1.48 (1.09, 2.02)	0.012	0.96 (0.77, 1.20)	0.698		
Social determinants of health						
Injection drug use, ever	2.20 (1.68, 2.88)	<0.001	1.96 (1.26, 3.05)	0.003	1.92 (1.38, 2.66)	<0.001
Corrections involvement, ever	1.71 (1.42, 2.07)	<0.001	1.40 (1.09, 1.79)	0.009	1.36 (1.09, 1.71)	<0.001
Partner uses injection drugs	1.54 (1.05, 2.26)	0.026	0.96 (0.56, 1.63)	0.878		

	Bivariable RR (95% CI)	*P* value	Full multivariable RR (95% CI)	*P* value	Parsimonious multivariable RR (95%CI)	*P* value
Fixed intercept (95% CI)			0.23 (0.10, 0.53)		0.22 (0.09, 0.50)	
Variance of the random effect			0.0159		0.0236	
Bayesian Information Criterion (BIC)			523.4269		484.1037	

CI, confidence interval; HCV, hepatitis C virus; NH, non-Hispanic; REF, reference; RR, risk ratio

Table 4.

Descriptive statistics (mean [standard deviation] and median [interquartile range]) and bivariable multilevel Poisson regression models of county-level measures among pregnant people with syphilis, Oregon, 2013–2021.

	All Counties (n = 23)	Counties with no CS cases (n = 6)	Counties with at least one CS case (n = 17)	Bivariable RR (95% CI)	*P*-value
Average poor mental health days	4.9 (0.2) 4.9 (4.3, 5.4)	4.9 (0.1) 4.9 (4.7, 5.0)	4.9 (0.3) 4.9 (4.3, 5.4)	1.42 (0.77, 2.60)	0.259
% of the population that is food insecure	12 (2) 12 (8, 15)	11 (1) 10.5 (10, 12)	12 (2) 12 (8, 15)	1.08 (0.99, 1.17)	0.070
Methamphetamine overdose death rate per 100K population	4.3 (4.2) 3.6 (0, 18)	1.9 (2.1) 1.8 (0, 4.1)	5.2 (4.5) 3.6 (0.9, 18)	1.02 (0.98, 1.06)	0.250
Violent crime rate per 100K population	217 (88) 219 (108, 474)	176 (58) 164 (108, 264)	231 (94) 222 (112, 474)	1.02 (1.01, 1.03)[a]	<0.001
% unemployment	7.7 (1.1) 7.8 (5.2, 10.9)	7.8 (0.6) 7.9 (7.1, 8.7)	7.6 (1.2) 7.8 (5.2, 10.9)	1.22 (1.04, 1.43)[b]	0.013
% population in poverty	13.5 (3.2) 13.4 (7.5, 21.1)	14.1 (3.4) 13.7 (7.5, 21.1)	12.0 (2.0) 11.9 (9.8, 14.3)	1.02 (0.97, 1.07)	0.350
Income inequality ratio	4.4 (0.4) 4.3 (3.7, 5.1)	4.3 (0.4) 4.3 (3.7, 4.8)	4.4 (0.4) 4.3 (3.9, 5.1)	1.73 (1.23, 2.43)	0.001
% of population with at least one adverse childhood experience	67 (4) 67 (56, 72)	66 (7) 68 (56, 72)	67 (3) 66 (62, 72)	1.08 (1.02, 1.13)	0.004
Houseless rate per 100K population	36 (27) 30 (6, 110)	34 (19) 33 (8, 61)	37 (29) 28 (6, 110)	1.00 (0.99, 1.01)	0.418
Full score (unscaled)	−0.54 (2.04) −0.94 (−4.04, 3.12)	−1.19 (0.96) −1.19 (−2.62, 0.17)	−0.31 (2.28) −0.93 (−4.04, 3.12)	1.08 (1.01, 1.15)[c]	0.018
Simple score (unscaled)	−0.69 (1.50) −1.10 (−2.60, 2.45)	−1.01 (0.98) −1.19 (−2.40, 0.58)	−0.57 (1.65) −0.67 (−2.60, 2.45)	1.13 (1.08, 1.19)[c]	<0.001

Interpretation:

[a]Pregnant people with syphilis residing in a county with a 10-unit greater violent crime rate 1.02 times as likely to be associated with a case of congenital syphilis compared to pregnant people with syphilis residing in a county with a lower violent crime rate. Per 10-unit change in violent crime rate

[b]Pregnant people with syphilis residing in a county with a one percentage greater unemployment rate were 1.22 times as likely to be associated with a case of congenital syphilis compared to pregnant people with syphilis residing in a county with a lower unemployment rate.

[c]Pregnant people with syphilis residing in a county with a one-unit greater score were 1.08 times as likely to be associated with a case of congenital syphilis compared to pregnant people with syphilis residing in a county with a lower score.

CI, confidence interval; CS, congenital syphilis; RR, risk ratio

Table 5.

Bivariable and multivariable multilevel Poisson regression models of the scaled full and simple scores among pregnant people with syphilis, Oregon, 2013–2021.

	Bivariable RR (95% CI)	***P*–value**	**Bivariable RR (95% CI)**	***P*–value**	**Multivariable RR[a] (95% CI)**	***P*–value**	**Multivariable RR (95% CI)**	***P*–value**
Scaled full score	1.17 (1.03, 1.33)[b]	0.018			1.20 (1.05, 1.47)	0.011		
Scaled simple score			1.20 (1.12, 1.30)	<0.001			1.24 (1.12, 1.36)	<0.001
Injection drug use, ever					1.90 (1.38, 2.62)	<0.001	1.85 (1.34, 2.58)	<0.001
Corrections involvement, ever					1.42 (1.10, 1.83)	0.007	1.36 (1.06, 1.76)	0.016
Gonorrhea diagnosis, prior 2 years					0.50 (0.34, 0.76)	0.001	0.49 90.33, 0.74)	0.001
Fixed intercept (95% CI)	0.26 (0.23, 0.30)		0.25 (0.22, 0.28)		0.21 (0.08, 0.52)		0.22 (0.09, 0.52)	
Variance of the random effect	$7.41x10^{-33}$		$1.26x10^{-33}$		$2.36x10^{-34}$		$5.63x10^{-35}$	
Bayesian Information Criterion (BIC)	442.4303		440.8499		474.7596		473.2694	
Hosmer-Lemeshow goodness of fit test (df, chi^2, *P*–value)	6, 4.36294 *P*=0.628		8, 4.217833 *P*=0.837		9, 5.808911 *P*=0.759		9, 1.806891 *P*=0.994	

[a]Multivariable models are adjusted for age, race, and time-period. Because there were no CS cases among Asian pregnant people with syphilis, they were excluded from the model to allow for model convergence.

[b]Example interpretation: pregnant people with syphilis residing in a county with a full score one standard deviation above the mean were 1.17 times as likely to be associated with a case of congenital syphilis compared to pregnant people with syphilis living in a county with a mean full score.

CI, confidence interval; RR, risk ratio