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MAJOR ARTICLE

Impact of Testing Strategies to Combat a Major Syphilis Outbreak Among Australian Aboriginal and Torres Strait Islander Peoples: A Mathematical Modeling Study

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Background. A syphilis outbreak among Australian Aboriginal and Torres Strait Islander people (respectfully referred to as Aboriginal) has resulted in almost 4000 notifications by 2020, with several congenital syphilis cases and infant deaths. Outbreak control efforts became coordinated under a National enhanced test and treat response in 2017. We evaluated the impact of these efforts and of expansion of testing interventions on syphilis prevalence.

Methods. We developed an individual-based mathematical model of infectious syphilis transmission among young heterosexual Aboriginal people aged 15–34 years living in and moving between regional and remote areas, and we assessed the impact of existing and hypothetical outbreak control responses on syphilis prevalence.

Results. The increased testing coverage achieved through the response (from 18% to 39% over 2011–2020) could stabilize the epidemic from 2021. To return to pre-outbreak prevalence (<0.24%) by 2025, testing coverage must reach 60%. The addition of annual community-wide screening, where 30% of youth in communities are tested over 6 weeks, would reduce prevalence to the pre-outbreak level within 4 years. If testing coverage had been scaled-up to 60% at the start of outbreak in mid-2011, the outbreak would have been mitigated.

Conclusions. Our results suggest that to control the syphilis outbreak, the response needs to be delivered to enable the maximum coverage of testing to be reached in the shortest time to reduce the prevalence to pre-outbreak levels. Reduction could be hastened with community-wide screening at similar time periods across all communities together with increases in annual testing coverage.

Keywords. Aboriginal Australians; infectious disease outbreaks; mass screening; mathematical model; *Treponema pallidum*.

An increase in infectious and congenital syphilis among the Indigenous heterosexual populations in several countries has been observed [1–3]. This is of concern because there are significant health disparities and risk factors for syphilis among Indigenous populations, with many Indigenous groups having poor access to healthcare and therefore at risk of delayed treatment and the development of secondary diseases. The 2011 infectious syphilis outbreak among young Aboriginal and Torres Strait Islander people in Australia (hereafter referred to respectfully as Aboriginal) was first detected in the north-west region of the state of Queensland and has spread to other states and territories. By January 2021, more than 3900 notifications had been reported as well as 9 confirmed cases of congenital syphilis and 3 infant deaths (as opposed to 123 notifications in 2009) [4–6].

Given the spread across jurisdictions, an Australian Government Multijurisdictional Syphilis Outbreak (MJSO) Working Group was formed in April 2015 to coordinate outbreak control efforts. The MJSO Working Group focused on improving surveillance and enhancing control strategies to increase testing, timely treatment, and contact management through primary healthcare clinics serving Aboriginal people [7]. Concurrently, a multipronged health promotion campaign was implemented to raise awareness about syphilis and to encourage young people to test. In December 2017, the Australian Health Protection Principal Committee Governance Group developed a National strategic approach that included expanded testing coverage and the rollout of rapid point-of-care testing kits. Between 2014 and 2018, there was a notable increase in syphilis testing by as much as 1.8-fold in affected jurisdictions (Multijurisdictional Syphilis Outbreak [MJSO] Working Group. Unpublished Data. 2019). However, during the same period, a rapid increase in infectious syphilis notifications was reported [8].

We conducted mathematical modeling to assess the potential impact of syphilis testing on the outbreak once it became widespread and endemic across multiple small, interconnected

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but geographically isolated populations. Our analysis assessed the impact of testing-based interventions on infectious syphilis prevalence. In particular, we estimated what effect increases in testing coverage in response to the outbreak have had on infectious syphilis prevalence and the future testing coverage required to return prevalence to the pre-outbreak level. We also investigate impact of community-wide testing, where a large proportion of the community is tested and treated over a short period.

Although community-wide testing in isolation may not be suitable or appropriate for all remote communities and may only have a limited impact [9], it could sufficiently reduce prevalence in the short term to a low enough level for ongoing clinic-based testing and treatment to mitigate the outbreak. Although this type of intervention could be beneficial, it would require extensive community consultation and need to be sensitive to community needs for it to be feasible. Finally, we investigated the impact of an early scale-up of syphilis testing when the outbreak was initially detected to see whether its spread could have been prevented or substantially mitigated.

METHODS

Governance and Engagement

In 2017, the Australian Government established an MJSO Working Group to provide governance oversight to the outbreak response and introduced an enhanced test and treat strategy. The MJSO Working Group, consisting of representatives from affected jurisdictions, sexual health physicians, experts in Aboriginal health, and the Australian Government Department of Health engaged us to assess the trajectory of the syphilis outbreak and the potential impact of the response. They reviewed and provided oversight of this work, provided relevant data, and informed the development of modeling scenarios. For this study, the MJSO Working Group provided raw testing and notification numbers from 2013 to the first half of 2020, along with the Estimated Resident Population for the calculation of testing coverage and prevalence of infectious syphilis cases.

Model Overview

We extended a previously published individual-based simulation model of sexually transmitted infections (STIs) in heterosexual Aboriginal people to capture the syphilis outbreak across the affected regions [10]. A summary of the model's characteristics and our modeling methodology follows, with the Supplementary Material providing further details. Model code is available as a GitHub repository (https://doi.org/10.5281/zenodo.4057288).

The current model was designed to track the sexual transmission of syphilis among a hypothetical population of 10 550 males and females aged 15–34 years, representing one regional center setting (of 5 550 people) and 10 smaller remote communities (of 500 people each), with connections between communities represented by a complete graph. The sex and age distribution of the modeled populations were based on demographic data for Aboriginal people obtained from the Australian Bureau of Statistics [11].

Population mobility was based on the estimated proportion of individuals away from home at a given time [12]. Individuals in the modeled population can form sexual partnerships when they are located in the same physical location, either their designated home location (the regional center or a remote community) or another location when traveling away from their home). Individuals can establish casual sexual partnerships when traveling even if they have a regular partner at home. The frequency of partner change and the duration of partnerships was determined by a partner acquisition rate estimated from the reported number of partners in the last 12 months for Aboriginal people from a study conducted in 2014 [13].

The modeled natural history of syphilis is illustrated schematically in Figure 1. We used a similar diseases progression structure as previously published models [14–20]. Syphilis can be transmitted, through sexual contact, from an infected individual to a susceptible individual. Infected individuals are infectious if they are in the incubating, primary, secondary, early latent, or recurrent stages. If left untreated, individuals will eventually develop tertiary syphilis. An infected person who receives treatment at or after reaching the latent stage is assumed to be immune from reinfection for 5 years on average, whereas no immunity is acquired if treatment is administered before the latent stage. The duration of infection and the transmission probability per sexual contact varies depending on the stage of infection (see Section 4, Supplementary Material).

Syphilis Testing

Ongoing syphilis testing is carried out in the modeled population. We used the overall number of tests and the estimated resident population size in the outbreak affected regions (Queensland, Northern Territory, South Australia, and Western Australia) between 2013 and 2020 to estimate a crude population testing coverage (Multijurisdictional Syphilis Outbreak

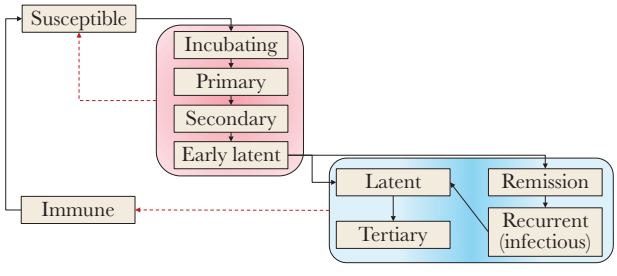

Figure 1. Stages of disease progression for syphilis as captured in the model. Dashed arrows represent the additional pathways for infected individuals who have received treatment.

Table 1. Syphilis Testing Scenarios

Scenario	Description	Testing Coverage at Start of 2013	Testing Coverage at Start of 2020	Increase in Test Coverage From 2021	Community-Wide Testing[a]
0	Counterfactual	18%	18%	None	No
1	Annual testing coverage maintained at 2020 level (baseline)	18%	39%	None	No
2	Increase in annual testing coverage from 2021	18%	39%	Increase to 60% in 2 years	No
3	Increase in annual testing coverage from 2021 at slower rate	18%	39%	Increase to 60% in 5 years	No
4	Community-wide testing at remote locations at 2021	18%	39%	None	Yes
5	Increase in annual testing coverage, with community-wide testing at remote locations from 2021	18%	39%	Increase to 60% in 2 years	Yes

[a]Community-wide testing occurs at the end of 2021 and 2022 in remote locations, whereby 30% of the community is tested over a 6-week period. Community-wide testing starts and finishes in all locations at the same time.

[MJSO] Working Group. Unpublished Data. 2019). We adjusted this estimate to reflect a likely overestimation of the numerator (due to the inclusion of tests conducted in visitors from outside the outbreak affected areas) and multiple tests in individuals (such as from pregnant women) and uncertainty in the population size (denominator). Based on the available data (described in Section 6, Supplementary Material), we multiplied the crude testing coverage by 0.75 to produce a change in testing coverage from 24% in 2013 to 39% in 2020. We assumed a variable testing coverage based on sex, region, and age group. For the period before 2013, we assumed a constant population testing coverage of 18% as reported in a previous study on STI testing [21].

We assumed that syphilis is detected through diagnostic assays with a sensitivity of 98% [22]. After diagnosis, all people are treated within 7 days in regional areas and 85% of people are treated within 4 months in remote areas based on published gonorrhea and chlamydia treatment rates in those areas (because data for syphilis testing are not available), and 15% remain untreated [23]. For simplicity, we assumed there is no treatment failure in the model because we assumed repeated syphilis serology will be carried out posttreatment according to National guidelines such that any treatment failures will be detected and effectively treated [24].

Through consultation with the MJSO Working Group and jurisdictional stakeholders, we developed a range of scenarios that was considered feasible for communities affected by the syphilis outbreak. We used the model to evaluate an increase in annual testing (testing at least once during the year) coverage to 60% and community-wide testing (testing a large proportion of the community in a short period of time, which we specified as 30% of people aged 15–34 in each community to be tested within 6 weeks). A brief description of each scenario is provided in Table 1. Additional scenarios with community-wide testing starting and finishing asynchronously are described in Section 8, Supplementary Material.

We also assessed the potential impact of scaling up testing from mid-2011 (when the outbreak was first detected) to reach 60% by 2013 (as for Scenario 2, but with this high testing coverage reached earlier in the outbreak and starting from a lower level). This analysis was conducted to assess whether earlier scale-up of widespread testing could have prevented the outbreak.

Model Outcomes

For each scenario, results were collated from 100 simulation runs. To establish a baseline, the model was run 5000 times, and the 100 runs with the closest match (smallest square sum) to the reported 6-monthly notification rate for infectious syphilis cases over 2013–2020 were selected [5]. A more comprehensive description of this process is provided in Section 1, Supplementary Material.

We report the estimated prevalence of infectious syphilis in the population up to the year 2030, the date when infectious syphilis prevalence returns to the pre-outbreak level (0.24%), and the date when infectious syphilis prevalence in the modeled population reaches zero (which we refer to as elimination). Results are described by the median of the monthly estimates from the 100 runs with the uncertainty indicated by the interquartile range (IQR).

RESULTS

Figure 2 shows diagnoses per 100 000 population for the counterfactual (Scenario 0, no response) and baseline (Scenario 1, current response) scenarios. These results suggest that if the baseline annual testing coverage achieved by the end of 2019 (39%) can be maintained in outbreak affected areas, the outbreak could stabilize from 2021. For the baseline scenario, the increase in testing results in a higher diagnosis rate initially but this then stabilizes over time as treatment results in lower prevalence. The model predicts that the 6-monthly diagnosis rate will fall slightly from 322 (IQR, 265–370) per 100 000 people at the start of 2020 to 284 (IQR, 170–436) per 100 000 people at the start of 2025. In contrast, if the annual syphilis testing coverage remained at the lower (pre-enhanced response) 2013 level of 24% (Scenario 0), then the estimated diagnosis rate for the

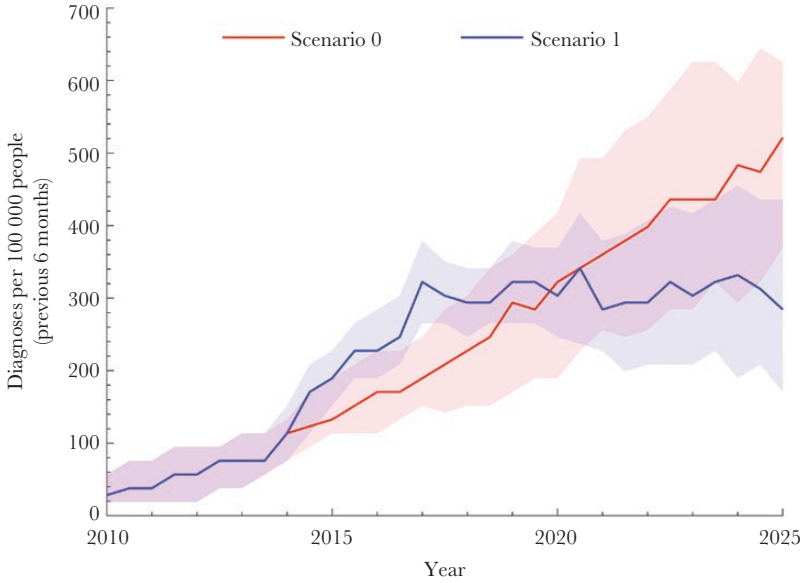

Figure 2. Diagnoses per 100 000 people from 2010 to 2025 for the counterfactual scenario (Scenario 0 in red; where testing rates remain at 2013 levels) and the baseline scenario (Scenario 1 in blue). The solid lines and shading are the median and interquartile range from the 100 selected model runs, respectively.

previous 6 months will initially be lower than for the baseline scenario (as the lower testing rate finds fewer infections) at 284 (IQR, 190–389) per 100 000 people at the end of 2019, but it will then increase rapidly to 521 (IQR, 370–626) per 100 000 people by 2025. Under Scenario 0, infectious syphilis prevalence is predicted to increase from 0.38% (IQR, 0.27%–0.50%) at the end of 2011 to 1.59% (IQR, 1.09%–2.06%) by the end of 2019, and to 2.96% (IQR, 2.08%–3.67%) by the end of 2025. In contrast, under Scenario 1, prevalence is only predicted to increase to 0.66% (IQR, 0.57%–0.77%) by the end of 2019 and to 0.75% (IQR, 0.38%–1.10%) by the end of 2025.

Increases in annual syphilis testing coverage are predicted to substantially reduce infectious syphilis prevalence (Figure 3). Increasing testing coverage from 39% to 60% by 2023 (Scenario 2) is predicted to result in infectious syphilis prevalence declining from 0.69% (IQR, 0.51%–0.83%) in 2021 to 0.15% (IQR, 0.07%–0.29%) by 2026. If this increase is not achieved until 2026 (Scenario 3), prevalence would only decline to 0.31% (IQR, 0.17%–0.45%) by 2026. We estimate that increasing annual testing coverage to 60% would increase the probability of eliminating syphilis by 2044 from 19% (Scenario 1; baseline) to above 90% under Scenarios 2 and 3. Under these scenarios, the time required for elimination is reduced from 15 years to 9 years or 11 years, respectively (Table 2).

Figure 3 shows that community-wide syphilis testing has only a small impact on syphilis prevalence when implemented in isolation (Scenario 4). However, if community-wide testing is combined with increased ongoing annual testing (Scenario 5), the time required for infectious syphilis prevalence to return to the pre-outbreak level (0.24%) is reduced by 0.5 years with prevalence declining to 0.15% by 2026 (Figure 3). As shown in Section 8, Supplementary Material, in general, spreading out community-wide screening across locations over time (instead of at all locations simultaneously) would increase the time required for syphilis prevalence to return to the pre-outbreak level by as much as 30% (see Scenario 5b-XI, Section 8, Supplementary Material)

If annual testing coverage had been increased to 60% within 2 years from mid-2013, syphilis prevalence would have returned to the pre-outbreak level (0.24%) by 2017, and by 2014 if the increase to 60% was achieved by mid-2013 (2 years after first detection) (see Section 7, Supplementary Material).

DISCUSSION

Our study focuses on remote Aboriginal communities in Australia but also has implications for other Indigenous or First Nations populations across the world who often live in remote regions with limited access to healthcare and are disproportionately affected by STIs. The findings from our modeling analysis suggest that the increase in testing achieved since the beginning of the outbreak helped stabilize the epidemic and averted a substantially worse one. It is unlikely that infectious syphilis will be eliminated in the affected regions within 5 years unless annual testing coverage is substantially increased. We estimate that the addition of annual episodes of community-wide testing in remote locations would further reduce the time required for infectious syphilis prevalence to return to the pre-outbreak levels. However, community-wide testing on its own does not reduce the time required for syphilis elimination, and it has no incremental benefit in terms of reducing infectious syphilis prevalence beyond 2026, because spread from the regional center to remote locations is not affected by community-wide testing.

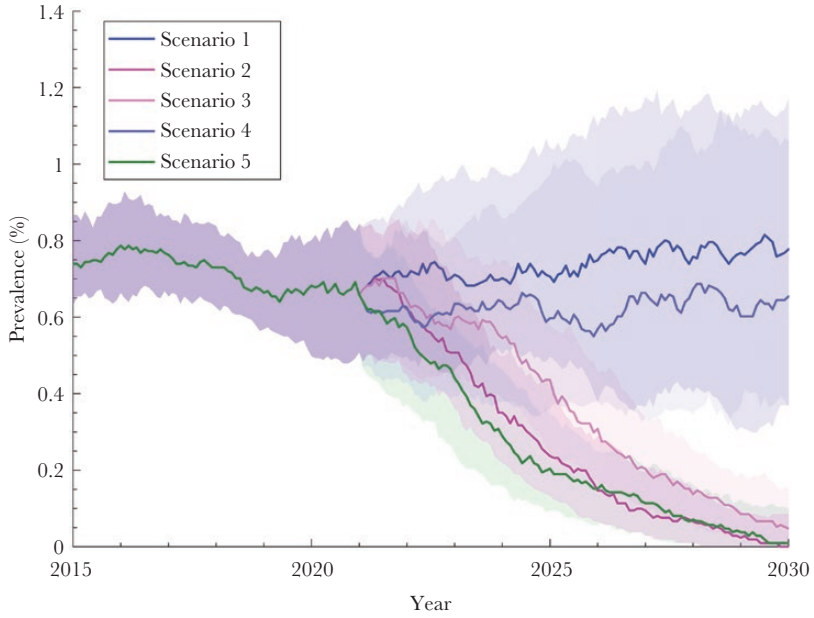

Figure 3. Infectious syphilis prevalence trajectories for Scenarios 1–5 over the period 2015–2030. The solid lines and shading are the median and interquartile range, respectively, from 100 model runs that provide the closest match (in terms of smallest summed square differences) with the notification rate from 2013 to the start of 2020.

If community-wide testing is only feasible for smaller remote locations, our findings suggest that this should ideally be carried out at all locations at the same time. Similar to the findings in Pourbohloul et al [9], however, we also find that without a concomitant increase in annual testing coverage, infectious syphilis prevalence rebounds quickly after episodes of community-wide testing and treatment, with the time required for prevalence to return to pre-outbreak levels essentially the same as the time required if no community-wide testing is implemented. Results in the Supplementary Material also suggest that if a delay between the initiation of community-wide testing across communities is inevitable, then the delay should be as short as possible.

Not surprisingly, our modeling predicts that if the scaling up of syphilis testing coverage across the population had happened at an earlier stage of the outbreak, a much smaller outbreak would have occurred (see Section 7, Supplementary Material). It should be noted, however, that our model and scenarios were designed to assess the impact on a syphilis outbreak once it became established and had spread. It is likely the outbreak started within a small undetected cluster and then spread to and expanded within multiple regions. If this cluster was detected earlier with a faster initial response together with a robust implementation of other public health interventions (eg, contact tracing) not investigated here, then the outbreak may not have become endemic across wide parts of Australia even if overall testing coverage remained low. This highlights the importance of a rapid and committed response to emerging outbreaks of syphilis globally.

When interpreting our findings, the limitations of the analysis need to be considered. The model was calibrated in terms of notification and testing data from syphilis affected regions,

Table 2. Percentage of Simulations and Time Required for the Infectious Syphilis Prevalence to Reach and Remain Below 0.24% (columns 1 and 2, Respectively), and Infectious Syphilis to be Eliminated (Columns 3 and 4, Respectively), Under Each of the Scenarios Evaluated[a]

Scenario	Percentage of Simulations for Which Infectious Syphilis Prevalence Reaches and Remains Below 0.24% (N = 100)	Median Number of Years Required For Infectious Syphilis Prevalence to Reach and Remain Below 0.24% (IQR)	Percentage of Simulations for Which Infectious Syphilis Is Eliminated by 2044 (N = 100)	Median Number of Years Required for Infectious Syphilis to Be Eliminated (IQR)
0	2	0.1 (0.1–0.1)	2	4.8 (4.3–5.2)
1	28	12.8 (4.6–18.8)	19	15.8 (9.1–17.8)
2	99	4.6 (3.2–6.0)	99	8.8 (7.2–11.4)
3	100	6.1 (4.6–8.6)	98	11.1 (9.1–13.5)
4	33	13.8 (5.2–19.2)	20	12.7 (7.4–19.6)
5	100	4.1 (2.6–6.5)	99	9.2 (7.1–12.9)

Abbreviations: IQR, interquartile range.

[a]Note that the median number of years required for prevalence to remain below 0.24% or elimination (columns 3 and 5, respectively) are calculated from the subset of simulations that achieved those targets by 2044 (see columns 2 and 4, respectively). For scenarios 0, 1 and 4 most simulations did not result in elimination with less than 20% of simulations being used in the median time calculation as shown in column 5.

with the affected regions included changing dynamically as the outbreak progressed. This means that the assumed testing coverage might not accurately reflect the actual testing coverage within a specific region. We assumed the number of syphilis tests reported overestimated the actual testing coverage due to several contributing factors (see Section 6, Supplementary Material), and the testing coverage was adjusted during the model calibration and for the baseline scenario. The sensitivity of this adjustment was assessed, with additional simulation results conducted without the adjustment provided in Section 6, Supplementary Material. We also assumed individuals are treated for syphilis within the same time frame as reported for a positive diagnosis of gonorrhea or chlamydia due to a lack of data on the acceptability and efficacy of syphilis treatment in this population. It is possible that treatment has generally been initiated and completed sooner in the outbreak-affected areas due to the enhanced response to the syphilis epidemic. For this study, we focused on the impact of increased testing coverage on the infectious syphilis outbreak and did not consider the other strategies such increased timeliness of treatment, contact tracing, and antenatal care, as outlined in the Enhanced Response Action Plan [25]. We did this to provide a conservative estimate of the impact of feasible increases in testing coverage on overall prevalence and incidence, which the other strategies could build on. A larger reduction in prevalence and disease outcomes would be expected if these additional strategies were implemented, although their implementation could be challenging for some of the affected regions [26, 27]. Likewise, other effects of the enhanced response, such as changes in testing and/or treatment seeking and sexual behavior that reduce the risk of acquisition due to the parallel rollout of communication and education materials across the outbreak affected regions were not modeled due to the lack of data, although recent data suggest an increase in the partner exchange rate among the high activity group [28].

The population size and distribution used in the model are based on data from the 2016 census for syphilis affected states, as well as representative regions such as Alice Springs in the Northern Territory of Australia as a regional center [29, 30]. We aimed to capture the broad characteristics of the Aboriginal population, and the population assumptions used were informed through consultation with jurisdictional stakeholders and the MJSO Working Group. However, they might not be a true representation of specific regions affected by the syphilis outbreak; for example, the population of regional centers in Western Australia is generally considered to be smaller than the population of regional centers in the eastern states of Australia [31].

The model was not designed to investigate or identify the cause of the outbreak, and the possible spread of syphilis within Indigenous men who have sex with men was not investigated because the spread of the syphilis outbreak thus far has been concentrated in the heterosexual population. Instead, simulations were only included in this analysis if an outbreak occurred and became established. This selection process means the syphilis persistence shown in our baseline scenario (Scenario 1) does not fully show the stochasticity in the output generated by the model with syphilis outbreaks not persisting in the majority of simulations.

The key parameters related to the natural history of syphilis, including the transmissibility and response to treatment during different stages of syphilis infection, remained uncertain for this study. This is particularly relevant in the context of remote Aboriginal populations in Australia, where access to health services is often limited, and detailed diagnoses and assessment of treatment outcomes are unavailable due to resources constraint. In this study, syphilis was modeled using a simplified interpretation from a previous model [14], where syphilis transmission was maximized to produce a conservative measure of outbreak control.

The coronavirus disease 2019 (COVID-19) pandemic that commenced in early 2020 has led to rapidly implemented control measures aimed to reduce severe acute respiratory syndrome coronavirus 2 transmission within remote communities of Australia [32, 33]. Components of these measures, such as social distancing and closure or communities, likely had an effect on both syphilis transmission and control. Although the full impact of COVID-19 on syphilis transmission cannot be addressed directly in this study, we have outlined some possible effects in Supplementary Material, Section 10.

CONCLUSIONS

Our analysis suggests that the overall response to the syphilis epidemic in remote Indigenous communities of Australia to date has contributed to the stabilization of the epidemic. However, this response needs to be maintained for many years to come, and additional interventions that lead to increased annual testing coverage are needed to reduce syphilis prevalence to the pre-outbreak level within 5 years. Introducing community-wide testing in addition to increases in annual testing coverage could hasten this reduction.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Potential conflicts of interest. All authors: No reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

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- Aboriginal Medical Services Alliance Northern Territory
- Northern Territory Department of Health
- Queensland Aboriginal and Islander Health Council
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- Aboriginal Health Council of Western Australia
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