



OPEN ACCESS

EDITED BY

Marc Jean Struelens,
Université libre de Bruxelles, Belgium

REVIEWED BY

Gengfeng Fu,
Jiangsu Provincial Center for Disease
Control and Prevention, China

*CORRESPONDENCE

Joseph D. Tucker
jdtucker@med.unc.edu

SPECIALTY SECTION

This article was submitted to
Infectious Diseases – Surveillance,
Prevention and Treatment,
a section of the journal
Frontiers in Medicine

RECEIVED 18 March 2022

ACCEPTED 01 August 2022

PUBLISHED 22 August 2022

CITATION

Tucker JD, Marley G, Marks M and
Mabey D (2022) Prioritizing syphilis
control: Now is the time for action.
Front. Med. 9:899200.
doi: 10.3389/fmed.2022.899200

COPYRIGHT

© 2022 Tucker, Marley, Marks and
Mabey. This is an open-access article
distributed under the terms of the
[Creative Commons Attribution License
\(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or
reproduction in other forums is
permitted, provided the original
author(s) and the copyright owner(s)
are credited and that the original
publication in this journal is cited, in
accordance with accepted academic
practice. No use, distribution or
reproduction is permitted which does
not comply with these terms.

Prioritizing syphilis control: Now is the time for action

Joseph D. Tucker^{1,2,3*}, Gifty Marley^{1,3}, Michael Marks^{2,4} and David Mabey^{2,4}

¹Institute for Global Health and Infectious Diseases, University of North Carolina at Chapel Hill, Chapel Hill, NC, United States, ²Clinical Research Department, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, United Kingdom, ³SESH Global, Guangzhou, China, ⁴Hospital for Tropical Diseases, University College London, London, United Kingdom

Syphilis control programs and research received fewer resources and attention compared to HIV and other sexually transmitted infections (STIs) in the pre-pandemic era. The neglect of syphilis within comprehensive STI control efforts may be related to diagnostic (poor diagnostics), historical (legacies of racism in research), public health (limited partner services), and social problems (limited public engagement). At the same time, there are increasingly compelling reasons to prioritize syphilis control programs and research by harnessing lessons learned and advances during COVID-19. The closure of many STI facilities has accelerated new syphilis diagnostic pathways (e.g., syphilis self-testing), providing new ways for people to be screened outside of clinics. COVID-19 has underlined health inequities that fuel syphilis transmission, providing an opportunity to reckon with the historical legacy of racism that is linked to syphilis research. COVID-19 partner tracing efforts have also contributed to additional resources for partner services which may enhance syphilis control efforts. Finally, COVID-19 has demonstrated the importance of public engagement, making the case for greater public involvement in syphilis control and prevention programs. Urgent action is needed to prioritize syphilis control in a wide range of settings.

KEYWORDS

syphilis, advocacy, COVID-19, partner services, crowdsourcing

Introduction

Prior to COVID-19, syphilis was often neglected in global health research and programs. According to an analysis of data on infectious diseases research supported by G20 (a group of twenty countries) countries across 18-years, syphilis received the least amount of research grants per disability-adjusted life year (1). However, syphilis increases the risk of acquiring and transmitting HIV infection (2). Syphilis infection among pregnant women increases the risk of neonatal death, preterm labor, and other adverse birth outcomes (3). In addition, there is substantial stigma associated with syphilis (4). Improving syphilis services could decrease stillbirths, decrease syphilis-related stigma, decrease persistent health disparities related to at-risk groups, and improve the lives of many vulnerable individuals.

Ultimately, repeated calls to action from academic researchers and policy-makers (5) have not resulted in meaningful policy change. Yet the COVID-19 provides a new opportunity to re-think syphilis control because both are infectious diseases that require partner services, have self-testing options, and exacerbate health inequalities. This policy perspective examines the relative neglect of syphilis within comprehensive STI control systems, assessing critical historical, diagnostic, public health, and social issues before COVID-19. We also map out concrete ways that COVID-19 interventions could be used to prioritize syphilis control within health systems.

Malign neglect

The prevailing approach to syphilis control efforts within public health systems may be characterized as one of malign neglect—causing harm by doing nothing. Routine syphilis screening rates are low in many countries (6). The malign neglect of syphilis within comprehensive STI control efforts may be related to historical issues, diagnostics, partner services, and social issues (Figure 1).

The unique history of syphilis research has cast a long shadow on subsequent syphilis research. For example, in the United States, the Tuskegee trial enrolled poor, black men who were intentionally misled about the research study and denied treatment (7). An analysis of US Centers for Disease Control mortality data found that disclosure of the Tuskegee mistreatment in 1972 was correlated with greater mortality, medical mistrust, and delayed care health care seeking among black men in the United States (8). The Tuskegee mistreatment of black men and related inequalities may partly explain the higher burden of syphilis among black men at the time (9). Similar unethical syphilis research was organized by US government scientists in Guatemala (10) and these unethical trials have helped to inform human subjects training. The history of unethical syphilis research may discourage investigators from focusing on syphilis and research participants from joining syphilis studies.

Until recently, poor syphilis diagnostics have been another major barrier to expanded syphilis research in many settings. Syphilis diagnostics remained largely unchanged over the course of the 20th century (11). The most commonly used non-treponemal test (rapid plasma regain, RPR) required equipment, reagents, and training that many resource-constrained clinics lacked (12). Centralized syphilis testing at clinics made it difficult for many key populations to receive regular syphilis testing. In recent years, affordable, sensitive and specific point of care serological tests (13) have become available using the lateral flow format. This requires no equipment and has been widely used by the general public for SARS-CoV2 self-testing, opening

new opportunities for syphilis screening in resource-limited settings (14).

Partner notification and testing services are essential components of a comprehensive syphilis response, but have historically been constrained by limited financial resources. Partner services include identification, testing, and treatment of sexual partners of confirmed syphilis cases. Syphilis transmission rates are extremely high (51–64% per sexual partnership) (15), underlining the importance of timely partner services. Incomplete partner services before COVID-19 have thwarted syphilis control programs. Syphilis partner services are chronically under-funded within many public health departments (16), contributing to incomplete partner service programs for early syphilis cases (17).

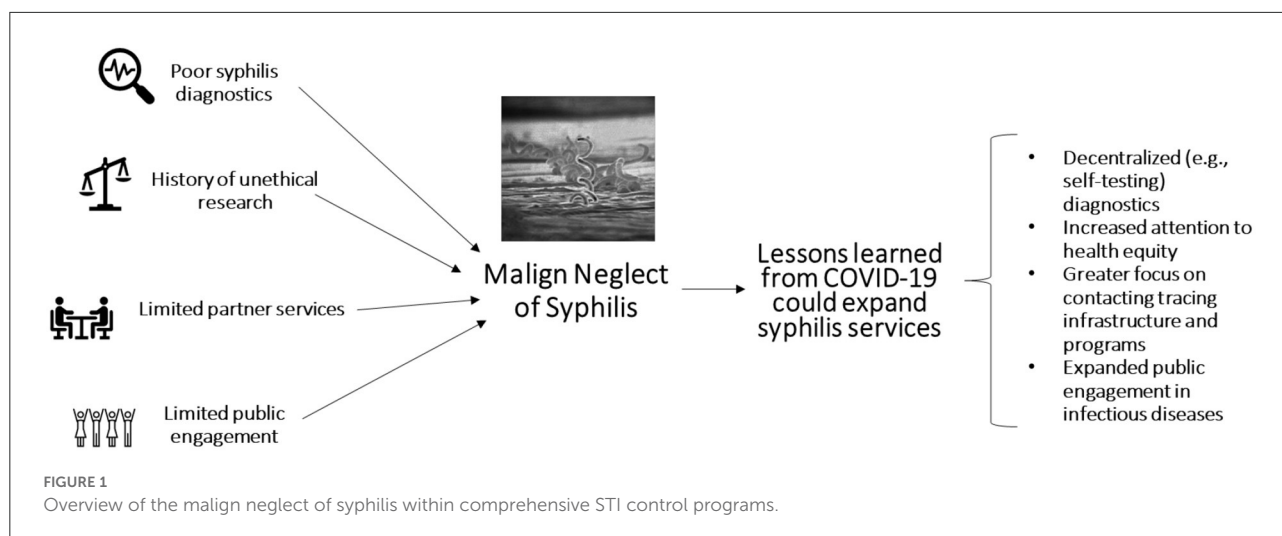
Finally, public engagement in syphilis research has been under-developed. Public engagement refers to a mutually beneficial interaction between specialists and non-specialists to develop solutions. Whereas, HIV control benefitted from strong public engagement in research dating back to the 1980s (18, 19), syphilis has not inspired widespread public engagement programs. There have been fewer public engagement programs to engage local communities about syphilis infection compared to HIV. Public health HIV screening programs have generally not been integrated with syphilis screening programs in many health systems (5), despite strong public engagement focused on other STIs.

COVID-19 and syphilis

Lessons learned from COVID-19 have the potential to transform sexual health service delivery systems, including syphilis-specific strategies globally. Despite the lack of direct links between COVID-19 interventions and syphilis, there are several COVID-19 developments that could indirectly help to prioritize syphilis in broader STI control research and programs. Programs and research focused on COVID-19 inequities, diagnostics, partner services, and public engagement may enhance syphilis projects during and beyond the COVID-19 pandemic.

First, COVID-19 has accelerated public health systems for decentralized diagnostic testing, including self-testing, self-sampling, and community-based testing. Self-testing involves a person conducting and interpreting their own test result. Clinic closures and travel restrictions during COVID-19 have accelerated syphilis self-testing uptake (20, 21) and expanded self-sampling pilots (22). Expanding these opportunities for syphilis testing in diverse settings could help to catalyze more syphilis control programs, policies, and research.

Second, COVID-19 has highlighted the impact of inequities in delivering health services. Many COVID-19 programs have explicitly focused on better serving the needs of ethnic and racial minorities. Racial disparities in COVID-19 vaccine uptake have



increased urgency to rebuild trust in care providers (23). While these are necessarily long-term efforts, the renewed attention on health equity could help galvanize trust in medicine among people at greater risk for syphilis.

Third, COVID-19 pandemic has increased attention to the science and logistics of contact tracing which could help syphilis contact tracing. Responses to the COVID-19 pandemic have bolstered local public health infrastructure, especially providing resources for contact tracing, rapid testing, and related components of partner services. In some settings, the pandemic response has also altered in-person partner services toward digital adaptations. For example, a syphilis outbreak investigation during COVID-19 organized by a local health department was conducted entirely online (24).

Finally, COVID-19 provides an opportunity to strengthen public engagement in infectious diseases service delivery. Community-based coalitions that include diverse groups have formed in response to COVID-19 and could be adapted for syphilis responses (25, 26). In addition, innovative methods for public engagement such as crowdsourcing have helped to inform COVID-19 programs (27) and demonstrated to be effective in randomized controlled trials (28). Crowdsourcing has a group of people solve all or part of a problem and then implement selected solutions (29). Crowdsourcing methods have been used to increase syphilis test uptake (30, 31).

Discussion

As COVID-19 restrictions are lifted and there is additional scope for sexual health programs, syphilis deserves greater attention. This greater focus has implications for research, implementation, and policy. From a research perspective, increased public health research on decentralized testing pathways that could be implemented in diverse settings is

needed. Many people at greatest risk of syphilis do not attend centralized clinics where serological syphilis testing is available. From an implementation perspective, more intensive programs to support the dual elimination of HIV and syphilis among pregnant women through service integration is warranted. This aligns with the WHO call for the elimination of mother-to-child transmission of HIV and syphilis. From a policy perspective, partner services need to be more completely transitioned into the digital age. While COVID-19 has supported pilots, research and policies are needed.

This perspective also underlines the need for *action* at several levels of the public health system. Within local public health programs, syphilis self-testing could provide a new service delivery mechanism that does not require laboratory equipment or trained staff. Syphilis self-testing could be used in many remote settings and spur follow-up testing. At national ministries of health, more financial resources for syphilis control programs will be essential for strengthening control responses. Finally, at the global level, innovative programs to encourage syphilis testing and linkage to clinical care are necessary. Now is the time for action on syphilis.

Ethics statement

Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin, for the publication of any potentially identifiable images or data included in this article.

Author contributions

JT wrote the first draft. All authors contributed to the manuscript and read and agreed with the final manuscript.

Funding

This research was supported by the NIH (NICHD UH3HD096929, NIAID K24AI143471, and NIAID R01AI158826).

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships

References

1. Head MG, Brown RJ, Newell M-L, Scott JAG, Batchelor J, Atun R. The allocation of US\$105 billion in global funding from G20 countries for infectious disease research between 2000 and 2017: a content analysis of investments. *Lancet Global Health*. (2020) 8:e1295–304. doi: 10.1016/S2214-109X(20)30357-0
2. Wu MY, Gong HZ, Hu KR, Zheng HY, Wan X, Li J. Effect of syphilis infection on HIV acquisition: a systematic review and meta-analysis. *Sex Transm Infect*. (2021) 97:525–33. doi: 10.1136/sextrans-2020-054706
3. Gomez GB, Kamb ML, Newman LM, Mark J, Broutet N, Hawkes SJ. Untreated maternal syphilis and adverse outcomes of pregnancy: a systematic review and meta-analysis. *Bull World Health Organ*. (2013) 91:217–26. doi: 10.2471/BLT.12.107623
4. Zhang X, Wang X, Wang H, He X, Wang X. Stigmatization and social support of pregnant women with HIV or syphilis in Eastern China: a mixed-method study. *Front Public Health*. (2022) 10:764203. doi: 10.3389/fpubh.2022.764203
5. Peeling RW, Mabey D, Fitzgerald DW, Watson-Jones D. Avoiding HIV and dying of syphilis. *Lancet*. (2004) 364:1561–3. doi: 10.1016/S0140-6736(04)17327-3
6. Tucker JD, Hawkes SJ, Yin YP, Peeling RW, Cohen MS, Chen XS. Scaling up syphilis testing in China: implementation beyond the clinic. *Bull World Health Organ*. (2010) 88:452–7. doi: 10.2471/BLT.09.070326
7. Brandt AM. Racism and research: the case of the Tuskegee Syphilis Study. *Hastings Cent Rep*. (1978) 8:21–9. doi: 10.2307/3561468
8. Alsan M, Wanamaker M. Tuskegee and the Health of Black Men*. *Q J Econ*. (2017) 133:407–55. doi: 10.1093/qje/qjx029
9. Hahn RA, Magder LS, Aral SO, Johnson RE, Larsen SA. Race and the prevalence of syphilis seroreactivity in the United States population: a national sero-epidemiologic study. *Am J Public Health*. (1989) 79:467–70. doi: 10.2105/AJPH.79.4.467
10. Reverby SM. “Normal Exposure” and Inoculation Syphilis: A PHS “Tuskegee” Doctor in Guatemala, 1946–1948. *J Policy Hist*. (2011) 23:6–28. doi: 10.1017/S0898030610000291
11. Peeling RW, Mabey D, Kamb ML, Chen X-S, Radolf JD, Benzaken AS. Syphilis. *Nat Rev Dis Prim*. (2017) 3:17073. doi: 10.1038/nrdp.2017.73
12. Satyaputra F, Hendry S, Braddick M, Sivabalan P, Norton R. The laboratory diagnosis of syphilis. *J Clin Microbiol*. (2021) 59:e0010021. doi: 10.1128/JCM.00100-21
13. Tucker JD, Bu J, Brown LB, Yin YP, Chen XS, Cohen MS. Accelerating worldwide syphilis screening through rapid testing: a systematic review. *Lancet Infect Dis*. (2010) 10:381–6. doi: 10.1016/S1473-3099(10)70092-X
14. Mabey DC, Sollis KA, Kelly HA, Benzaken AS, Bitarakwate E, Chungalucha J, et al. Point-of-care tests to strengthen health systems and save newborn lives: the case of syphilis. *PLoS Med*. (2012) 9:e1001233. doi: 10.1371/journal.pmed.1001233
15. Stoltey JE, Cohen SE. Syphilis transmission: a review of the current evidence. *Sex Health*. (2015) 12:103–9. doi: 10.1071/SH14174
16. Rietmeijer CA, Kissinger PJ, Guilamo-Ramos V, Gaydos CA, Hook EW 3rd, Mead A, et al. Report From the National Academies of Sciences, engineering and medicine-STI: adopting a sexual health paradigm-A synopsis for sexually transmitted infection practitioners,

that could be construed as a potential conflict of interest.

Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

17. Cuffe KM, Gift TL, Kelley K, Leichter JS. Assessing partner services provided by state and local health departments, 2018. *Sex Transm Dis*. (2021) 48:429–35. doi: 10.1097/OLQ.0000000000001328
18. Taggart T, Ritchwood TD, Nyhan K, Ransome Y. Messaging matters: achieving equity in the HIV response through public health communication. *Lancet HIV*. (2021) 8:e376–86. doi: 10.1016/S2352-3018(21)00078-3
19. Caswell G, Dubula V, Baptiste S, Etya'ale H, Syarif O, Barr D. The continuing role of communities affected by HIV in sustained engagement in health and rights. *J Int AIDS Soc 24 Suppl*. (2021) 3:e25724. doi: 10.1002/jia2.25724
20. Cheng W, Wang C, Tang W, Ong JJ, Fu H, Marks M, et al. Promoting routine syphilis screening among men who have sex with men in China: study protocol for a randomised controlled trial of syphilis self-testing and lottery incentive. *BMC Infect Dis*. (2020) 20:455. doi: 10.1186/s12879-020-05188-z
21. Sri-Pathmanathan C, Nhamo D, Mamvuto T, Chapwanya G, Terris-Prestholt F, Mahaka I, et al. Syphilis self-testing to expand test uptake among men who have sex with men: a theoretically informed mixed methods study in Zimbabwe. *Sex Transm Infect*. (2021). doi: 10.1101/2020.11.30.20240788
22. Leenen J, Hoebe C, Ackens RP, Posthouwer D, van Loo IHM, Wolffs PFG, et al. Pilot implementation of a home-care programme with chlamydia, gonorrhoea, hepatitis B, and syphilis self-sampling in HIV-positive men who have sex with men. *BMC Infect Dis*. (2020) 20:925. doi: 10.1186/s12879-020-05658-4
23. Lin C, Tu P, Terry TC. Moving the needle on racial disparity: COVID-19 vaccine trust and hesitancy. *Vaccine*. (2022) 40:5–8. doi: 10.1016/j.vaccine.2021.11.010
24. Davis C, Wright SS, Babcock M, Kingdon E, Broussard D, Oyervides O, et al. Lessons learned from a centers for disease control and prevention virtual partner services technical assistance pilot project to respond to a local syphilis outbreak. *Sex Transm Dis*. (2022) 49:166–8. doi: 10.1097/OLQ.0000000000001547
25. AuYoung M, Rodriguez Espinosa P, Chen WT, Juturu P, Young MT, Casillas A, et al. Addressing racial/ethnic inequities in vaccine hesitancy and uptake: lessons learned from the California alliance against COVID-19. *J Behav Med*. (2022) 22:1–14. doi: 10.1007/s10865-022-00284-8
26. van Staden Q, Laurenzi CA, Toska E. Two years after lockdown: reviewing the effects of COVID-19 on health services and support for adolescents living with HIV in South Africa. *J Int AIDS Soc*. (2022) 25:e25904. doi: 10.1002/jia2.25904
27. Day S, Li C, Hlatshwako TG, Abu-Hijleh F, Han L, Deitelzweig C, et al. Assessment of a crowdsourcing open call for approaches to University community engagement and strategic planning during COVID-19. *JAMA Netw Open*. (2021) 4:e2110090. doi: 10.1001/jamanetworkopen.2021.10090

28. Wang C, Han L, Stein G, Day S, Bien-Gund C, Mathews A, et al. Crowdsourcing in health and medical research: a systematic review. *Infect Dis Poverty*. (2020) 9:8. doi: 10.1186/s40249-020-0622-9
29. Tucker JD, Day S, Tang W, Bayus B. Crowdsourcing in medical research: concepts and applications. *PeerJ*. (2019) 6:e6762. doi: 10.7717/peerj.6762
30. Tang W, Ritchwood TD, Wu D, Ong JJ, Wei C, Iwelunmor J, et al. Crowdsourcing to improve HIV and sexual health outcomes: a scoping review. *Curr HIV AIDS Rep*. (2019) 16:270–8. doi: 10.1007/s11904-019-00448-3
31. Iwelunmor J, Ezechi O, Obiezu-Umeh C, Gbaja-Biamila T, Musa AZ, Nwaozuru U, et al. Enhancing HIV self-testing among Nigerian youth: feasibility and preliminary efficacy of the 4 youth by youth study using crowdsourced youth-led strategies. *AIDS Patient Care STDS*. (2022) 36:64–72. doi: 10.1089/apc.2021.0202