

Significant Impact of Coronavirus Disease 2019 (COVID-19) on Human Immunodeficiency Virus (HIV) Care in Hospitals Affecting the First Pillar of the HIV Care Continuum

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During COVID-19 lockdown, the in-hospital number of HIV indicator conditions decreased disproportionately compared with other non-COVID-19 diseases, which was accompanied by reduced HIV testing rates, number and proportion of positive HIV tests, and new HIV referrals, with more late presentation after lockdown cessation, indicating a significantly impacted HIV care continuum.

Keywords. HIV; indicator conditions; care continuum; COVID-19 impact; HIV testing.

The Netherlands Joint United Nations Program on HIV/AIDS (UNAIDS) 90–90–90 goals are at 93%–93%–96% [1, 2]. The first pillar of the human immunodeficiency virus (HIV) care continuum represents the proportion aware of their HIV infection. To optimize this, HIV testing in risk groups and indicator conditions (ICs) is essential for appropriate patient identification, linkage to care, and treatment as prevention [3].

On 27 February 2020, the first person with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was diagnosed in the Netherlands. In mid-March, the country went into lockdown. Stricter restrictions were stepwise enforced, including closure of schools, restaurants, and sports clubs and banning of all nonessential contact professions [4, 5]. The strictest restrictions were between 16 March and 1 June 2020. To optimize coronavirus disease 2019 (COVID-19) care, regular healthcare

was uniformly downscaled nationwide, with noticeable effects on surgical and oncological non-COVID care in hospitals [6, 7]. These restrictions are also predicted to influence HIV care [8]. The exact impact on the HIV care continuum in hospitals is still unknown.

We aimed to determine the impact of COVID-19 restrictions on the first pillars of the HIV care continuum in clinical settings.

METHODS

For this observational study at Erasmus University Medical Centre, Rotterdam, we used the infrastructure within our #aware.hiv network, an ongoing project supporting HIV testing. The study was conducted according to Declaration of Helsinki principles, Dutch privacy laws, the Medical Treatment Agreement Act (WGBO), and General Data Protection Regulation and was approved by an institutional review board.

Patients aged 18 years and older who visited the hospital and had no objection to the use of routinely collected data were eligible for inclusion. On 1 January 2020, data collection for the #aware.hiv project started. Data were extracted from electronic health records, including newly registered diagnoses and HIV tests performed. The HIV ICs were selected based on European Center for Disease Prevention and Control (ECDC) guidelines [3]. HIV ICs were grouped based on whether HIV testing is recommended per local institutional protocols (hepatitis B/C, lymphoma, and syphilis only). We used monitored electronic databases to retrospectively collect data on the HIV referrals and tests from 2015 to 2020.

A fourth-generation HIV test (Liaison XL HIV Ab/Ag; Diasorin) chemiluminescence immunoassay was used to detect HIV antibodies and/or the p24 antigen. An HIV immunoblot (INNO-LIA HIV I/II Score; Fujirebio), HIV-1 polymerase chain reaction (PCR) (COBAS AmpliPrep/COBAS TaqMan HIV-1 v2 test; Roche Diagnostics) and HIV-2 PCR (in-house assay) confirmed positive fourth-generation HIV test results and defined an HIV infection.

Descriptive data are presented as n (%). No predefined hypothesis on the impact of the COVID-19 pandemic on HIV care was formulated since the project started in 2019. A multivariate Poisson regression model was used to analyze the numbers of HIV tests performed that yielded positive results between 2015 and 2020, including with time interaction terms and using variables associated with $P < .1$ in univariate analysis in the final model.

We evaluated the number of newly registered diagnoses, including HIV ICs and COVID-19, per month from 1 January to 30 June 2020. Within patients with HIV ICs, we calculated the HIV test rate per month. We calculated the absolute number

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of HIV tests and the amount of diagnosed HIV infections, defined as the number of patients with newly diagnosed HIV with confirmed diagnosis over the total number of HIV tests performed from 2015 to 2020. Finally, we evaluated linkage to care by taking the number of days between HIV diagnosis and first visit to the HIV department as well as the number of days between diagnosis and start of antiretroviral therapy. Linkage to care within 30 days was considered adequate [9].

RESULTS

Overall, 41 272 patients presented with newly registered diagnoses in the first half-year of 2020. The average number of newly registered diagnoses per day decreased by approximately 35% from January ($n = 270$) to April ($n = 173$) (Supplementary Figure 1). In April, 154 patients were admitted with COVID-19 out of a total of 328 during the period studied. The number of COVID-19 diagnoses decreased from April ($n = 154$) to June ($n = 26$) while the total number of diagnoses increased, although not yet to prepandemic levels. During lockdown, the number of HIV ICs diagnosed per month decreased, with 69% between January ($n = 111$) and April ($n = 35$) (Figure 1). Absolute numbers of HIV ICs where testing is recommended in local institutional protocols were halved from January ($n = 20$) to April ($n = 9$), while HIV testing rates remained greater than 70%. HIV ICs where testing is not recommended decreased by 72% from January ($n = 93$) to April ($n = 26$) and corresponding testing rates decreased to 27% (Figure 1).

During lockdown, the most commonly diagnosed HIV ICs were hepatitis B/C, cervical dysplasia/cancer, and lymphoma (Supplementary Table 1). Overall, the numbers of diagnosed HIV ICs decreased during lockdown, although lymphomas became a dominant diagnosed HIV IC in May/June, exceeding pre-lockdown numbers. This indicates that diseases with more alarming clinical presentations were seen despite COVID-19 restrictions. Numbers of other frequently observed HIV ICs showed recovery after the lockdown was lifted in June.

Pre-lockdown (1 January–15 March), the total numbers of HIV tests and test positivity rate were comparable to previous years (Supplementary Table 2). During lockdown (16 March–31 May), a significant decrease in the weekly number of HIV tests was observed, accompanied by a 56% reduction in the test positivity rate compared with pre-lockdown and dissimilar to the pattern in previous years (Supplementary Figure 2). Poisson modeling confirmed this reduction ($P = .002$), after adjusting for the effects of age on testing practices and also suggested ongoing decreased positivity rates post-lockdown ($P = .016$) despite a recovered number of HIV tests conducted (Supplementary Table 3).

In 2020, linkage to care was not negatively affected by COVID-19 restrictions (Supplementary Tables 4–6). Compared with 2015–2019, referrals for new HIV diagnoses decreased by 37%, with comparable proportions adequately linked to care within 30 days. The difference in median CD4+ T-cell count of those entering care in the second half ($0.29 \times 10^9/L$) compared

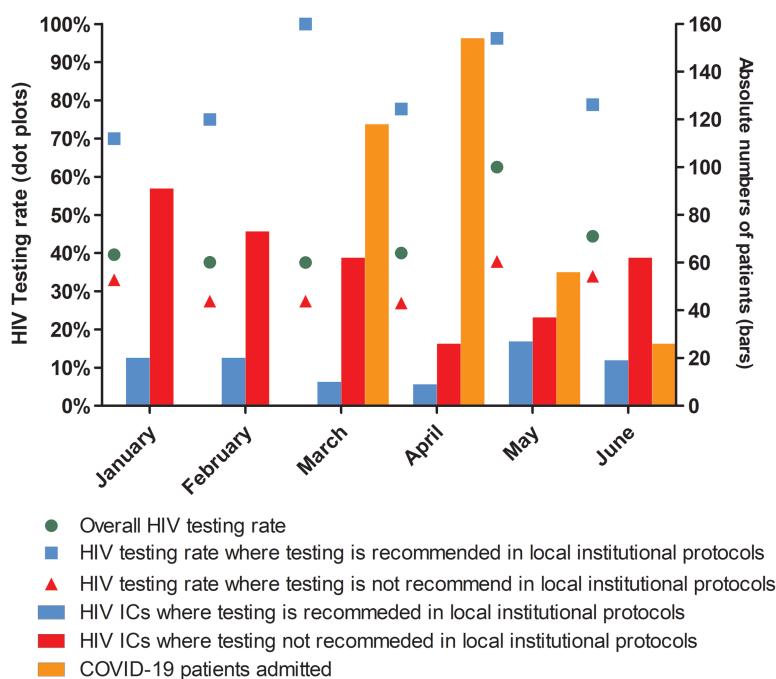


Figure 1. Absolute numbers of patients presenting with HIV ICs and COVID-19 and corresponding HIV testing rates per month during the first 6 months of 2020 before (January/February), during (March–May), and after (June) the nationwide lockdown for COVID-19 in the Erasmus University Medical Centre, the Netherlands. HIV testing is divided into 2 groups based on whether testing is recommended as per institutional guidelines for HIV ICs. Abbreviations: COVID-19, coronavirus disease 2019; HIV, human immunodeficiency virus; IC, indicator condition.

with the first half of 2020 ($0.42 \times 10^9/L$) was $0.13 \times 10^9/L$ lower, which was unexpected in light of the pattern observed in 2015–2019.

DISCUSSION

We demonstrate the significant impact of COVID-19 restrictions on the HIV care continuum in hospital settings. Fewer patients at risk for undiagnosed HIV presented, HIV testing rate dropped, test positivity rate was lower, and fewer patients were referred for new HIV diagnoses. Notably, we also found indications of significant effects post-lockdown with lower-than-expected HIV positivity rates and more advanced disease at entry in clinical care. These signals should prompt healthcare professionals to put effort into maintaining the UNAIDS goals during subsequent COVID-19 waves.

Strikingly, the number of patients with HIV ICs who entered care suffered from a disproportional decrease, which was almost 2-fold the average decrease. The observed effects on the HIV care continuum are likely related to multiple factors, including temporary closure of public health centers for HIV testing. Patient delay due to fear of contracting COVID-19 is also realistic [10]. General practitioners (GPs) and hospitals focused on COVID-19 with increased barriers to personal consultation. Combined, they probably explain part of the observations, but we are uncertain why this also led to the disproportionate drop in HIV ICs since many factors equally affected other non-COVID-19 care. HIV ICs might be more prone to doctor or patient delays related to a lower level of HIV awareness during healthcare crises, stigma, or fear of testing. Of those who entered care with an HIV IC, our data clearly support including standardized HIV testing to identify patients unaware of their HIV infection.

Strengths included that we could benefit from a sensitive, automated, monitored tracking network for HIV ICs, established before COVID-19, and similar COVID-19 restrictions were enforced nationwide. Although causality cannot be demonstrated, the observed effects are therefore likely a consequence of exposure to these restrictions and generalizable.

Limitations were a lack of a control group with another hospital or with another GP since our tracking network was not operational at these sites. We cannot fully exclude the possibility that HIV care shifted to peripheral hospitals, but this is unlikely since HIV care in the Netherlands is concentrated in specific hospitals, which all sustained uniform downscaling of non-COVID-19 care. Furthermore, an even nationwide distribution of hospitalized patients with COVID-19 was centrally coordinated and ensured. The intensively monitored diagnosis registration system, essential to patient quality and financial reimbursement, significantly decreases chances of human registration errors. Last, the estimated undiagnosed HIV infection numbers in the Netherlands have had a downward trend, which

we accounted for by Poisson modeling [2]. Most measured outcomes of HIV care recovered towards pre-lockdown levels, suggesting that the observed effects are unlikely confounded by concurrent phenomena—for instance, organizational alterations in HIV testing and care.

In conclusion, these data indicate that the HIV care continuum in hospitals concerning adequate testing and diagnosing was significantly affected in a lockdown during the COVID-19 pandemic. The impact observed in a highly structured HIV care setting of the Netherlands is a worrisome signal and should prompt clinicians to put effort into maintaining the UNAIDS goals during subsequent COVID-19 waves. COVID-19, and possible future pandemics, should not take the focus away from identification and testing of patients with undiagnosed HIV if we are to end the HIV/AIDS epidemic.

Supplementary Data

Supplementary materials are available at *Clinical 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.

Notes

Author Contributions. K. S. H. and C. C. E. J.: data collection, data analysis, writing, verified underlying data. J. J. A. v. K. helped with data collection. D. A. M. C. v. d. V. designed the model and the computational framework. K. S. H., C. C. E. J., and C. R. conceptualized the study and wrote the manuscript. All authors contributed to data interpretation and writing as well as reviewing the manuscript and approving the final version. C. R. supervised the project and is responsible for the #aware.hiv network.

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All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Joint United Nations Program on HIV/AIDS (UNAIDS). 90-90-90: An ambitious treatment target to help end the AIDS epidemic. Available at: https://www.unaids.org/sites/default/files/media_asset/90-90-90_en.pdf. Accessed 23 February 2021.

2. van Sighem AI, Wit FWNM, Boyd A, Smit C, Matser A, Reiss P. Monitoring report 2019. Human immunodeficiency virus (HIV) Infection in the Netherlands. Amsterdam, Netherlands: Stichting HIV Monitoring, 2020.
3. HIV in Europe Initiative. HIV indicator conditions: guidance for implementing HIV testing in adults in health care settings. Available at: <http://www.eurotest.org/Portals/0/Guidance.pdf.pdf>. Accessed 23 February 2021.
4. Government of the Netherlands. COVID-19: additional measures in schools, the hospitality sector and sport. Available at: <https://www.government.nl/topics/coronavirus-covid-19/news/2020/03/15/additional-measures-in-schools-the-hospitality-sector-and-sport>. Accessed 23 February 2021.
5. Government of the Netherlands. Coronavirus: additional measures introduced on 23 March. Available at: <https://www.government.nl/topics/coronavirus-covid-19/news/2020/03/24/additional-measures-introduced-on-23-march>. Accessed 23 February 2021.
6. Schuivens PME, Buijs M, Boonman-de Winter L, et al. Impact of the COVID-19 lockdown strategy on vascular surgery practice: more major amputations than usual. *Ann Vasc Surg* 2020; 69:74–9.
7. Dinmohamed AG, Visser O, Verhoeven RHA, et al. Fewer cancer diagnoses during the COVID-19 epidemic in the Netherlands. *Lancet Oncol* 2020; 21:750–1.
8. Hogan AB, Jewell BL, Sherrard-Smith E, et al. Potential impact of the COVID-19 pandemic on HIV, tuberculosis, and malaria in low-income and middle-income countries: a modelling study. *Lancet Glob Health* 2020; 8:e1132–41.
9. Dombrowski J, Spach DH. Linkage to HIV care. Available at: <https://www.hiv.uw.edu/go/screening-diagnosis/linkage-care/core-concept/all>. Accessed 23 February 2021.
10. Patiëntenfederatie Nederland. Weer zorg na de coronacrisis. Available at: <https://www.patiëntenfederatie.nl/downloads/peiling/324-onderzoek-weer-huisartsenzorg-na-coronacrisis/file>. Accessed 23 February 2021.