Impact of coronavirus disease 2019 epidemics on prevention and care for HIV and other sexually transmitted infections

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Objective: To assess the impact of coronavirus disease 2019 (COVID-19) epidemics on the prevention and care for HIV and other sexually transmitted infections at a major reference centre providing preventive and clinical services in Catalonia, Spain.

Design: We retrospectively compared anonymized clinical and laboratory data from March to December 2020 vs. 2019.

Methods: Monthly clinical data on HIV preexposure and postexposure prophylaxis users and on adults with HIV infection were retrieved from the administrative hospital database. Monthly tests for HIV, hepatitis B and C, *Treponema pallidum*, *Neisseria gonorrhoeae*, and *Chlamydia trachomatis*, and plasma lipids and glucose were recovered from the laboratory database.

Results: There were less ($\downarrow 28\%$, P = 0.003) but more advanced (mean CD4⁺ cells/µl 305 vs. 370, P < 0.001) HIV infections and more gonorrhoea ($\uparrow 39\%$, P < 0.001) and chlamydia ($\uparrow 37\%$, P < 0.001) infections in 2020 vs. 2019. In people with HIV, rates of HIV RNA at least 50 copies/ml remained stable (11 vs. 11%, P = 0.147) despite less scheduled visits ($\downarrow 25\%$, P < 0.001). However, they had less antiretroviral prescription changes ($\downarrow 10\%$, P = 0.018), worse plasma lipids [mean total cholesterol 190 vs. 185 mg/ dl, P < 0.001; mean low-density lipoprotein (LDL) cholesterol 114 vs. 110 mg/dl, P < 0.001; mean triglycerides 136 vs. 125 mg/dl, P < 0.001; mean high-density lipoprotein (HDL) cholesterol 47 vs. 48 mg/dl, P = 0.06], and an excess of mortality ($\uparrow 264\%$, P = 0.006) due in great part not only to COVID-19 but also to other causes.

Conclusion: In our setting, COVID-19 epidemics was associated with an increase in some prevalent sexually transmitted infections, with less but more advanced HIV infections, and with worse nonvirologic healthcare outcomes and higher mortality in people living with HIV.

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Introduction

As of 12 October 2021, coronavirus disease 2019 (COVID-19) pandemic has caused more than 237 million confirmed cases and more than 4.8 million deaths worldwide [1]. Governments across the globe dictated severe physical and social contact restrictions aimed to drastically reduce viral transmission. Spain was one of the hardest hit countries at the beginning of the pandemic. Due to the exceptional nature of the situation, the Spanish government approved a first state of alarm on 14 March 2020 and imposed a strict home lockdown for all citizens with the exception of essential workers. With the slow but steady reduction in the number of cases, measures became more flexible from 11 May 2020 until 21 June 2020 when the first state of alarm officially ended. Unfortunately, during the summer, the number of cases progressively increased and the Spanish government declared a second state of alarm from 25 October 2020 until 9 May 2021. Mass vaccination against COVID-19 in Spain started on 27 December 2020 [2]. Figure 1 shows the epidemic curve of laboratory-confirmed COVID-19 cases in Spain along with key milestones dates through 2020.

Beyond the direct toll on morbidity and mortality, SARS-CoV-2 pandemic have severely affected healthcare access and quality throughout the world. Healthcare resources were urgently and widely prioritized for SARS-CoV-2 diagnosis and clinical care of COVID-19 patients. As a result, the screening and the diagnosis for common chronic diseases was dramatically reduced and the availability of specific therapies was significantly delayed [3,4]. These factors ultimately led to increasing morbidity and mortality because of illnesses other than COVID-19 [5,6].

The emergence of SARS-CoV-2 epidemics may have also affected established measures for the prevention and diagnosis of HIV infection and other sexually transmitted diseases and the clinical care of HIV-infected patients, although data are limited [7,8]. The WHO warned that the access to HIV medicines could be severely impacted by COVID-19 [9]. Mathematical models predicted an increase of HIV-related mortality if antiretroviral therapy supply was temporarily interrupted [10,11]. In Spain, telephone calls or electronic messaging kept minimum standards for HIV clinical care during lockdown, and antiretroviral therapy dispensation was facilitated with the



Fig. 1. Epidemic curve of laboratory-confirmed coronavirus disease 2019 cases in Spain along with key milestones dates. Adapted from: https://cnecovid.isciii.es/covid19/#provincias. Accessed on 13 September 2021.

development of home delivery programmes through the national public postal service, the national civil protection system, or private couriers [12].

The Hospital Clínic is a community hospital for an area of influence with a population of 540 000 inhabitants in the city of Barcelona (Spain), and at the same time, operates as a reference care facility for specific diseases, such as HIV infection for the whole region of Catalonia (https:// www.clinicbarcelona.org/en). The hospital currently provides ambulatory care, supply of antiretroviral therapy, and hospital admission if necessary for more than 6000 adults with HIV infection being the largest HIV care centre in Spain. It has been also providing HIV postexposure prophylaxis since 2003 and HIV preexposure prophylaxis as it was approved by the Spanish National Health System in November 2019. We aimed to assess the impact of COVID-19 epidemics on the prevention and clinical care of HIV infection and on the screening and diagnosis of HIV infection and other sexually transmitted diseases in the setting of Hospital Clínic of Barcelona.

Methods

Study design

We retrospectively compared anonymized clinical and laboratory data from the first 10 months of the COVID-19 epidemics in Spain (March 2020 to December 2020) with those from the same time period 1 year earlier (March 2019 to December 2019) considered as the reference for the purpose of this study. The only exception was HIV preexposure prophylaxis as it became available in Spain from November 2019. For the sake of simplicity, we will refer as 2020 or 2019 for the corresponding study periods.

The study was approved by the local Institutional Review Board. According to current Spanish regulations [13], informed consent was waived because of the retrospective nature of the study and the use of anonymous data for the analysis.

Procedures

Monthly clinical data on HIV preexposure and postexposure prophylaxis users and on persons with HIV infection were retrieved from the hospital administrative database. By protocol, preexposure and postexposure visits include screening tests for HIV and the other sexually transmitted infections evaluated in this study. Monthly laboratory data including tests for HIV (fourth generation ELISA tests for people unknown to be HIVpositive, and plasma HIV RNA for people known to be HIV), hepatitis B (HBsAg) and C (anti-HCV, RNA VHC), *Treponema pallidum* (IgM, VDRL, PCR), *Neisseria gonorrhoeae* (PCR), and *Chlamydia trachomatis* (PCR) were obtained from the microbiology laboratory database whereas plasma lipids and glucose were recovered from the chemistry laboratory database. PCR tests for sexually transmitted infections were obtained from urinary, anal, pharyngeal sites. As fasting is explicitly requested for routine blood tests in our hospital, we assumed that plasma lipids and glucose values of chemistry tests were fasting. De novo HIV, hepatitis B, or hepatitis C-positive tests were considered when a person had a first known positive laboratory diagnosis (i.e. a positive laboratory diagnosis with previous respective tests negative or not done). Data were entered into an electronic case report form specifically designed for the purpose of this study using the Research Electronic Data Capture (REDCap) system hosted at the Hospital Clínic of Barcelona.

The following data per month were collected: number of HIV preexposure prophylaxis visits; number of HIV postexposure prophylaxis visits; number of HIV diagnostic tests performed and number of de novo positive ones; number of outpatient visits in persons with HIV; number of plasma HIV RNA tests done and number of plasma HIV RNA tests with viral load above the level of detection (50 copies/ml); mean values of total, LDL, and HDL cholesterol, triglycerides, and glucose in routine blood chemistries of persons with HIV; number of changes in antiretroviral regimens; number of hospital admissions; number and causes of deaths; number of hepatitis B tests and number of de novo hepatitis B diagnosis (defined by a positive HBsAg); number of hepatitis C tests and number of de novo hepatitis C diagnosis (defined by positive antibodies plus measurable RNA confirmation); number of T. pallidum tests and number of active syphilis diagnoses (defined by at least a positive IgM, a VDRL titer >1/8, or a positive PCR); number of N. gonorrhoeae tests and number of active gonorrhoea diagnoses (defined by a positive PCR); number of C. trachomatis tests and number of active chlamydia infection diagnoses (defined by a positive PCR). In people with de novo HIV diagnosis, CD4⁺ cell counts and the presence of AIDS-defining conditions at HIV diagnosis was also collected.

Statistical analysis

The monthly and the total number of events in the 2019 and 2020 together with the 95% confidence interval estimated using the delta method was compared between the 2 years by means of the Incidence Rate Ratio (IRR) (excepting for HIV preexposure prophylaxis, as previously mentioned). The events were considered following a Poisson distribution. The trend over time in lipid profile was estimated using a mixed-effects linear regression. For triglycerides and glucose, a log-transformation was applied to improve the normality of the residuals and the predicted mean was presented as geometric mean. $CD4^+$ cell counts and the presence of AIDS-defining conditions at HIV diagnosis were compared with chisquared and *t* tests, respectively. The statistical analysis was



Fig. 2. Monthly data on HIV preexposure (a) and postexposure (b) prophylaxis visits, number of HIV diagnostic tests performed (c), and proportion of de novo HIV diagnoses (d).

performed using Stata (StataCorp. 2019. Stata: Release 16.1. Statistical Software; StataCorp LLC, College Station, Texas, USA).

Results

The program of preexposure prophylaxis at the hospital started on November 2019. The steady increase in the number of participants visited per month was severely impacted during the first wave (April and May 2020) and at the beginning of the second wave (August 2020), although the increasing trend in the number of visits peaked by the end of 2020. There were 753 postexposure prophylaxis visits in 2020 vs. 1380 in 2019, showing a 45% reduction (IRR 0.55, 95% CI 0.50-0.60, P < 0.001). There were 14349 HIV diagnostic tests performed in 2020 vs. 14625 in 2019, showing no significant difference (IRR 0.98, 95% CI 0.96-1.00, P = 0.105). There were 143 persons with a de novo diagnosis of HIV in 2020 vs. 199 in 2019, showing a 28% reduction (IRR 0.72, 95% CI 0.58–0.89, P = 0.003). Mean (SD) CD4⁺ cell counts/ μ l at HIV diagnosis were 305 (167) in 2020 and 370 (170) in 2019 (P < 0.001). Twenty-six (18%) persons had AIDS-defining conditions at HIV diagnosis in 2020 as compared with 20 (10%) in 2019 (P=0.03). Figure 2 shows monthly data on HIV preexposure (Fig. 2a) and postexposure (Fig. 2b) prophylaxis visits, number of HIV diagnostic tests performed (Fig. 2c), and proportion of de novo HIV diagnoses (Fig. 2d).

There were 9830 outpatient visits in persons with HIV in 2020 vs. 13 024 in 2019, showing a 25% reduction (IRR 0.75, 95% CI 0.74–0.77, P < 0.001). Although prior to the pandemic, all outpatient visits were done face-to-face, during the 2020 pandemic period 3851 (39%) outpatient visits were done virtually. There were 9612 plasma HIV RNA tests done in 2020 vs. 9814 in 2019, showing no significant difference (IRR 0.98, 95% CI 0.95–1.01, P=0.147). There were 1068 (11%) plasma HIV RNA tests with viral load above the level of detection in 2020 vs. 1031 (11%) in 2019, showing no significant difference (IRR 0.98, 95% CI 0.95–1.01, P=0.147). There were 1017 changes in antiretroviral regimens in 2020 vs. 1127 in 2020, showing a 10% reduction (IRR 0.90, 95% CI 0.83–0.98, P=0.018). Figure 3 shows monthly data on



Fig. 3. Monthly data on outpatient visits in persons with HIV (a), number of plasma HIV RNA tests done (b), proportion of plasma HIV RNA tests with viral load above the level of detection per 100 HIV RNA tests performed per month (c), and changes in antiretroviral regimens (d).

outpatient visits in persons with HIV (Fig. 3a), number of plasma HIV RNA tests done (Fig. 3b), proportion of plasma HIV RNA tests with viral load above the level of detection per 100 HIV RNA tests performed per month (Fig. 3c), and changes in antiretroviral regimens (Fig. 3d).

There were 10147 blood chemistry tests with plasma lipids and glucose determinations in persons with HIV in 2020 vs. 11271 in 2019, showing a 10% reduction (IRR 0.90, 95% CI 0.88–0.92, P < 0.001). Relative to 2019, in 2020 mean total cholesterol (190 vs. 185 mg/dl, P < 0.001), LDL cholesterol (114 vs. 110 mg/dl, P < 0.001), and triglycerides increased (136 vs. 125 mg/dl, P = 0.006) decreased, and glucose (93 vs. 93 mg/dl, P = 0.961) remained unchanged. Figure 4 shows the mean monthly values of total cholesterol (Fig. 4a), LDL cholesterol (Fig. 4b), HDL cholesterol (Fig. 4c), triglycerides (Fig. 4d), and glucose (Fig. 4e) in routine blood chemistries of persons with HIV.

There were 429 hospital admissions in people with HIV during 2020 vs. 486 during 2019, showing a 12%

reduction (IRR 0.88, 95% CI 0.78–1.01, P=0.060). There were 29 deaths in people with HIV during the study period of 2020 vs. 11 during 2019, showing a 264% increase (IRR 2.64, 95% CI 1.32–5.28, P=0.006). Causes of death included: COVID-19 (n=11) (all in 2020), neoplasia (n=10) (4 in 2020, and 6 in 2019), cardiovascular (n=8) (7 in 2020, and 1 in 2019), non-COVID-19 infections (n=6) (3 in 2020, and 3 in 2019), cirrhosis (n=3) (2 in 2020, and 1 in 2019), drug overdose (n=1, in 2020), and polytrauma (n=1, in 2020); all the persons who died from non-COVID causes in 2020 had been SARS-CoV-2-negative confirmed. Figure 5 shows number of hospital admissions in people with HIV per month (Fig. 5a), and proportion of deaths per 100 people with HIV in the cohort per month (Fig. 5b).

There were 3202 HBsAg tests done in 2020 vs. 3208 in 2019, showing no statistical difference (IRR 1.00, 95% CI 0.95–1.05, P=0.940). There were four de novo hepatitis B diagnosed in 2020 vs. 4 in 2019, showing no statistical difference (IRR 1.00, 95% CI 0.25–4.00, P=1). There were 4475 hepatitis C antibodies done in 2020 vs. 5288 in 2019, showing a 15% reduction (IRR

6 AIDS 2022, Vol 36 No 00



Fig. 4. Mean monthly values of total cholesterol (a), low-density lipoprotein cholesterol (b), high-density lipoprotein cholesterol (c), triglycerides (d), and glucose (e) in routine blood chemistries of persons with HIV.

0.85, 95% CI 0.81–0.88, P < 0.001). There were 839 hepatitis C RNA tests done in 2020 vs. 923 in 2019, showing a 9% reduction (IRR 0.91, 95% CI 0.83–1.00, P=0.045). There were 86 de novo hepatitis C diagnosed in 2020 vs. 112 in 2019, showing no statistical difference (IRR 0.77, 95% CI 0.58–1.02, P=0.065). Supplementary Figure 1, http://links.lww.com/QAD/C436 shows number of hepatitis B surface antigen tests done per month (Supplementary Fig. 1a, http://links.lww.com/QAD/C436), proportion of de novo hepatitis B

diagnoses per 100 hepatitis B tests performed per month (Supplementary Fig. 1b, http://links.lww.com/QAD/ C436), number of hepatitis C antibody tests done per month (Supplementary Fig. 1c, http://links.lww.com/ QAD/C436), number of hepatitis C RNA tests done per month (Supplementary Fig. 1d, http://links.lww.com/ QAD/C436), and proportion of de novo hepatitis C diagnoses per 100 hepatitis C tests performed per month (Supplementary Fig. 1e, http://links.lww.com/QAD/ C436). 20

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Fig. 5. Number of hospital admissions in people with HIV per month (a), and proportion of deaths per 100 people with HIV in the cohort per month (b).

Dec

Sep

2020

Jul Aug month

2019

Oct

Nov

There were 10978 VDRL tests done in 2020 vs. 12237 in 2019, showing a 10% reduction (IRR 0.90, 95% CI 0.87-0.92, P < 0.001). There were 1452 IgM tests done in 2020 vs. 1493 in 2019, showing no significant difference (IRR 0.97, 95% CI 0.90–1.05, P = 0.450). There were 310 T. pallidum PCR tests done in 2020 vs. 242 in 2019, showing a 28% increase (IRR 1.28, 95% CI 1.08–1.52, P = 0.004). There were 952 active syphilis C diagnosed in 2020 vs. 944 in 2019, showing no statistical difference (IRR 1.01, 95% CI 0.92–1.10, P = 0.854), although the number of syphilis diagnosis made through PCR almost doubled in 2020 (n=281) vs. 2019 (n = 143). There were 1667 N. gonorrhoeae PCR tests done in 2020 vs. 1501 in 2019, showing a 11% increase (IRR 1.11, 95% CI 1.04–1.19, P = 0.003). There were 341 (20%) active gonorrhoea episodes diagnosed in 2020 vs. 246 (16%) in 2019, showing a 39% increase (IRR 1.39, 95% CI 1.18–1.63, P < 0.001). There were 1667 C. trachomatis PCR tests done in 2020 vs. 1501 in 2019, showing a 11% increase (IRR 1.11, 95% CI 1.04-1.19, P = 0.003). There were 249 (15%) active C. trachomatis infections diagnosed in 2020 vs. 182 (12%) in 2019, showing a 37% increase (IRR 1.37, 95% CI 1.13-1.66, P < 0.001). Supplementary Figure 2, http://links.lww.com/QAD/C436 shows the number of VDRL (Supplementary Fig. 2a, http://links.lww.com/QAD/C436), *T. pallidum* IgM (Supplementary Fig. 2b, http://links.lww.com/QAD/C436), and *T. pallidum* PCR (Supplementary Fig. 2c, http://links.lww.com/QAD/ C436) tests done per month, and the proportion of active syphilis diagnoses per 100 syphilis tests performed per month (Fig. 2d); the number of N. gonorrhoeae PCR tests done per month (Supplementary Fig. 2e, http:// links.lww.com/QAD/C436) and the proportion of active gonorrhoea diagnoses per 100 gonorrhoea tests performed per month (Supplementary Fig. 2f, http:// links.lww.com/QAD/C436); the number of C. trachomatis PCR tests done per month (Supplementary Fig. 2g,

http://links.lww.com/QAD/C436) and the proportion of active chlamydia diagnoses per 100 chlamydia tests performed per month (Supplementary Fig. 2h, http://links.lww.com/QAD/C436).

Discussion

As expected [3,4], prescheduled in-person activities such as HIV preexposure or postexposure prophylaxis visits or outpatient visits in persons with HIV decreased. Of note, a substantial proportion (39%) of outpatient visits during the COVID-19 epidemic were done virtually, which prevented a much higher negative impact on HIV care. Despite the decrease in prescheduled activities, the number of HIV diagnostic tests performed in persons not known to be HIV-infected and the number of plasma HIV RNA-monitoring tests in persons with HIV on routine care remained stable in 2020 relative to 2019 suggesting specific efforts to maintain a minimum of HIV testing and care. Although the number of de novo HIV diagnosis in 2020 decreased, persons newly diagnosed showed significantly less CD4⁺ cell counts and more advanced disease suggesting a delay and a probable underestimation in the diagnosis. Furthermore, people with HIV showed worse nonvirologic healthcare outcomes and higher mortality in 2020 than in 2019.

We detected a significant decrease in the changes of antiretroviral regimens. As the rates of persons with unsuppressed HIV viremia between both periods remained stable, we presume that this decrease might have preferentially affected persons with suppressed HIV viremia suggesting that therapy optimization was likely moved into the background.

Total cholesterol, LDL cholesterol, and tryglycerides increased whereas HDL cholesterol decreased suggesting

12

10

9

2020

8 month

2019

11

8 AIDS 2022, Vol 36 No 00

a worse metabolic status. Although weight was not available in the cohort, the profile of lipid changes may be consistent with weight gain [14,15]. COVID-19 lockdown promoted unhealthy dietary changes and increases in body weight at the population level [16,17]. Dyslipidaemia promotes low-level inflammation and chronic immune activation [18]. As a consequence, the lipid changes observed if they persist over time could further contribute to increase the risk of cardiovascular disease in the cohort of people with HIV.

The number of deaths in the cohort of people with HIV was almost three times higher in 2020 relative to 2019. Paradoxically, the number of hospital admissions tended to decrease. The lower number of hospital admissions in the HIV cohort could be due at least in part to the competing skyrocketing number of admissions because of COVID-19 in the general population. Of note, nearly 40% of deaths in the HIV cohort in 2020 had laboratory-confirmed COVID-19 at the time of death. COVID-19 explains in part the excess of deaths in the HIV cohort in 2020 relative to 2019, although the number of non-COVID-19 deaths (particularly, cardiovascular complications) in 2020 was still higher than that in 2019. COVID-19 may be associated with a higher mortality in people with HIV than in the general population [19]. The increase in mortality because of non-COVID-19 causes may have been promoted at least in part by disruptions in society that diminished or delayed access to healthcare and the social determinants of health (e.g. jobs, income, food security) [20-22]. Our findings further support that general and non-COVID-19 mortality in people with HIV may have increased during COVID-19 pandemics as well.

The number of hepatitis B tests and number of de novo hepatitis B diagnosis remained stable. The incidence of hepatitis B in Spain is very low [23]. In contrast, the number of hepatitis C tests decreased but the number of de novo hepatitis C diagnoses among those tested also decreased. These results are in contrast with those from models predicting increased nondiagnosed cases of hepatitis C in Spain during the COVID-19 epidemics [24] but they are in accordance with recent real data from the USA [25]. De novo hepatitis C diagnosis in our setting has been more commonly linked to high-risk sexual practices and sexualized substance use [26]. It is possible that these practices may have been more affected by the epidemic than other sexual encounters.

Treponema pallidum tests most commonly performed were VDRL tests, followed by IgM, and finally PCR. The number of tests done decreased for VDRL, kept stable for IgM, and increased for PCR. Although the total number of active syphilis diagnoses remained unchanged, positivity of PCR diagnosis almost doubled from 2019 to 2020. *N. gonorrhoeae* and *C. trachomatis* testing were exclusively performed with PCR. Similar to *T. pallidum* PCR testing, *N. gonorrhoeae* and *C. trachomatis* PCR testing increased in 2020 relative to 2019. The cases of active gonorrhoea and active chlamydia infection diagnoses increased in 2020, as well as the cases of active syphilis as diagnosed by PCR. PCR tests have been increasingly used for testing of sexually transmitted infections [27]. They are more rapid and may have been better available than standard tests during the pandemic period. The increased PCR diagnosis of sexually transmitted infections in 2020 relative to 2019 is worrisome and suggests that overall transmission was not reduced despite pandemic restrictions. This fact further suggests that the real risk of HIV transmission could have been also higher and a proportion of de novo HIV diagnosis may remain undetected evolving to a more advanced stage. During the early months of the COVID-19 pandemic testing for sexually transmitted infections decreased likely because of disruptions to healthcare and sexually transmitted infections testing services [28,29]. Reduced access to testing and diagnoses in the first months of the pandemics may have led some people to unwittingly spread infection as shown by the higher rates of sexually transmitted infections in the last months of 2020[30-32].

This study has limitations. We used 2019 as a convenient recent reference for comparisons with 2020 but incidence of HIV and other sexually transmitted infections in the city of Barcelona has been changing over time [33]. It is possible that the reduction in new HIV diagnosis may have not been only impacted by the epidemics but also by the initiation of the HIV preexposure prophylaxis program. By using an anonymized administrative database, some patients may have contributed multiple datapoints because of possibly repeated high-risk exposures or easier access to a clinical setting, biasing findings. We were unable to provide data on other sexually transmitted infections that are mainly diagnosed clinically, such as genital warts or herpes. An unknown proportion of HIV and hepatitis B and C tests were routinely performed in hospitalized COVID-19 patients with pneumonia as part of the management protocol of the Spanish Ministry of Health [34]; although this might have contributed to the diagnosis of some de novo infections, it increased artificially the number of screening tests performed. We have not included information on antimicrobial resistance and therapeutic management of HIV and other sexually transmitted infections.

In summary, we detected less HIV and hepatitis C infections and more gonorrhoea and chlamydia infections during the SARS-CoV-2 epidemics than in the previous year despite overall similar or even higher testing. However, de novo HIV infections showed more advanced disease. It is possible that the number of de novo HIV infections may be larger than detected. There were less scheduled visits for HIV care but this did not result in worse virological control. However, people with HIV had less antiretroviral prescription changes, worse plasma lipids, and more importantly an excess of mortality due in great part not only to COVID-19 but also to other non-COVID-19

Impact of COVID-19 on prevention and care for HIV and other STIs de Lazzari et al.

causes. Our findings suggest that, in the years to come, healthcare services must be prepared to respond to the impact of COVID-19 on HIV and sexually transmitted infections testing and care. Providers and facilities should build on the lessons learned so far to further improve mitigation strategies and establish care priorities for both the pandemic and the postpandemic periods.

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Authors' contribution: M.A.M. and E.M. designed the study. E.d.L. undertook the statistical analyses. All authors were involved in the interpretation of data. E.d.L., A.M.-M., M.A.M., and E.M. drafted the manuscript. All authors critically reviewed and subsequently approved the final version.

Conflicts of interest

A.G.-C., M.L., J.L.B., A.I., B.T., M.M.-R., J.A., J.M., and E.M. have received honoraria for lectures or advisory boards and their institution has received research grants from Gilead, Janssen, MSD, and ViiV. J.M.M. has received honoraria for lectures or advisory boards and their institution has received research grants from Angelini, Contrafect, Cubist, Genentech, Gilead Sciences, Jansen, Lysovant, Medtronic, MSD, Novartis, Pfizer, and ViiV. E.d.L., A.M.-M., I. C., M.M.M., J.C., J.B., M.A.-M., A.U., L.d.l.M., E.F., J.C.H., and M.A.M.: none to declare.

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9

10 AIDS 2022, Vol 36 No 00

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