SHORT COMMUNICATION

National strategies for vaccination against COVID-19 in people living with HIV in Central and Eastern European region

David Jilich1 | Agata Skrzat-Klapaczyńska2 | Lukas Fleischhans1 | Dominik Bursa2 | Sergii Antoniak3 | Tatevik Balayan4 | Josip Begovac5 | Alma Cicic6 | Gordana Dragovic7 | Deniz Goekengin8 | Arjan Harxhi9 | Kerstin Kase10 | Botond Lakatos11 | Raimonda Matulionyte12 | Velida Mulabdic13 | Cristiana Oprea14 | Antonios Papadopoulos15 | Nino Rukhadze16 | Janez Tomazic17 | Lida Tovba18 | Lubomír Soják19 | Anne Vassilenko20 | Nina Yancheva21 | Oleg Yurin22 | Justyna Kowalska2 | for the ECEE Network Group

1Department of Infectious Diseases, 1st Faculty of Medicine, Charles University in Prague and Faculty Hospital Bulovka, Prague, Czech Republic
2Department of Adults’ Infectious Diseases, Hospital for Infectious Diseases, Medical University of Warsaw, Warsaw, Poland
3Viral Hepatitis and AIDS Department at the Gromashovsky Institute of Epidemiology and Infectious Diseases, Kyiv, Ukraine
4National Center for Disease Control and Prevention, Yerevan, Armenia
5University Hospital for Infectious Diseases, Zagreb, Croatia
6Institute for Public Health of Montenegro, Podgorica, Montenegro
7Department of Pharmacology, Clinical Pharmacology and Toxicology, School of Medicine; University of Belgrade, Belgrade, Serbia
8Ege University, Izmir, Turkey
9University Hospital Center of Tirana, Infectious Disease Service, Tirana, Albania
10West Tallinn Central Hospital, Tallinn, Estonia
11National Institute of Hematology and Infectious Diseases, South-Pest Central Hospital, National Center of HIV, Budapest, Hungary
12Vilnius University, Faculty of Medicine, Vilnius University Hospital Santaros Klinikos, Vilnius, Lithuania
13Clinic for Infectious Diseases, Clinical Center of Sarajevo University, Sarajevo, Bosnia and Herzegovina
14Victor Babes Clinical Hospital for Infectious and Tropical Diseases, Bucharest, Romania
15University General Hospital Attikon - Medical School - National and Kapodistrian University of Athens, Athens, Greece
16Infectious Diseases, AIDS and Clinical Immunology Center, Tbilisi, Georgia
17Department of Infectious Diseases, University Medical Center Ljubljana, Ljubljana, Slovenia
18USMF Nicolae Testemitanu, Chisinau, Moldova
19Department of Infectology and Geographical Medicine, Center for Treatment of HIV/AIDS Patients, Academic L. Déér’s University Hospital, Bratislava, Slovakia
20Republican Scientific and Practical Center for Medical Technologies, Global Fund Grant Management Department, Minsk, Belarus
21Department for AIDS, Specialized Hospital for Active Treatment of Infectious and Parasitic Disease Sofia, Sofia, Bulgaria
22Central Research Institute of Epidemiology, Moskov, Russia

Correspondence
Agata Skrzat-Klapaczyńska, Department of Adults’ Infectious Diseases, Hospital for Infectious Diseases, Medical University of Warsaw, Warsaw, Poland.
Email: agata.skrzatasw@gmail.com

Abstract

Introduction: People living with HIV (PLWH) are at higher risk of poorer COVID-19 outcomes. Vaccination is a safe and effective method of prevention against many infectious diseases, including COVID-19. Here we investigate the
INTRODUCTION

As some studies suggest, people living with HIV (PLWH) are at higher risk of poorer COVID-19 outcomes, including a higher rate of hospitalization and increased mortality as compared with the general population [1–3]. In recent data published by the WHO Global Clinical Platform, there was a significantly higher risk of severe/critical presentation and mortality in individuals with risk factors such as diabetes and hypertension, and those aged > 65 years in a large cohort of hospitalized PLWH [4]. This finding is consistent with well-defined risk factors including severe immunodeficiency in the HIV-negative population [5–7]. Hoffmann et al. [8] found an association between a severe course of COVID-19 and higher mortality even in successfully treated PLWH without severe immunodeficiency and low nadir CD4.

Vaccination is an effective and safe method to prevent many infectious diseases (ID), including COVID-19. There is a consensus of national and international professional associations about the need for vaccinating PLWH against COVID-19 despite the fact that accurate data about efficacy and safety in this subpopulation are currently very limited [9–11]. Nor is there a clear recommendation for the preferred type of vaccines. In registration trials of mRNA-based vaccines, PLWH were included, but they were not analysed separately [12,13]. Some small sample studies with vector COVID-19 vaccines show high immunogenicity among PLWH [9,10]. On the other hand, there is a safety concern about Ad5-based vaccines in Ad5-seropositive individuals [14]. Other vaccines for which PLWH were included in the study cohort are under development [15]. There is still a need for a clear consensus about the preferred vaccine,
vaccination scheme and timing of booster dose. A significant proportion of HIV centres in Europe have faced various problems and barriers during the COVID-19 era, e.g. shorter working hours, reduced staff, limitations of normal activities (blood tests, visits) and providing care for PLWH from other centres (or even foreign countries) who were not able to return to their place of residence [16]. In our survey-based study, we present the status of national programmes as of March 2021 for vaccination against COVID-19 in PLWH in the heterogenous region of central and eastern Europe.

METHODS

The Euroguidelines in Central and Eastern Europe (ECEE) Network Group consists of professionals from 24 countries actively involved in HIV care. On 16 March 2021 we decided to review the readiness of member countries to start the process of vaccination against COVID-19 in PLWH. For this purpose, we proceeded with an online survey which consisted of 20 questions (see Appendix S1). Respondents were recruited from the ECEE members, based on their involvement in HIV care, and they were contacted via e-mail. Database closure was established on 19 March 2021.

RESULTS

In total, 22 out of 24 country representatives (91.6% response rate) participated the survey, namely Albania, Armenia, Belarus, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Estonia, Georgia, Greece, Hungary, Lithuania, Moldova, Montenegro, Poland, Romania, Russia, Serbia, Slovakia, Slovenia, Turkey and Ukraine. All 22 respondents (100%) responded to all 20 questions. The majority of respondents (19/22; 86%) were ID specialists or HIV specialists directly involved in HIV care and working in HIV centres of different size (the number of patients in follow-up care was in the range 220–4777). Most centres (13/20; 65%) were in-patient clinics at ID departments and seven (25%) operated as outpatient HIV clinics.

Vaccine availability

At the time of the survey, vaccination against COVID-19 had already started in all but two countries (Armenia, Bosnia and Herzegovina). The earliest start of vaccination was recorded in Russia, in November 2020. Twelve countries had started vaccinations in December 2020, three in January 2021, two in February and three in March 2021 (Table 1).

Availability and use of different vaccines vary among countries (Table 1). Vaxzevria vaccine (Oxford/Astra-Zeneca) was available in 15 countries (75%), Comirnaty (Pfizer/BioNTech) in 13 countries (65%), Anti-COVID-19 Moderna (Moderna/NIAID) in 11 countries (55%), Sputnik V (Gamaleya Research Institute of Epidemiology and Microbiology) in five countries (25%), Vero Cell (Sinofarm Life Sciences) in three countries (15%), EpiVacCorona (Vector State Research Center) in one country (5%) and Covishield (Serum Institute of India) in one country (5%). In all participating countries there was no specific recommendation/preference for use of particular vaccine(s) in PLWH. Vaccination practice was based on availability of vaccines in particular countries Table 2.

HIV status prioritization and vaccination coverage

Upon database closure, 21 countries (Albania, Belarus, Bosnia and Herzegovina, Bulgaria, Croatia, Czech Republic, Estonia, Georgia, Greece, Hungary, Lithuania, Moldova, Montenegro, Poland, Romania, Russia, Serbia, Slovakia, Slovenia, Turkey and Ukraine) were planning or had already started COVID-19 vaccination, following a national strategy, which was promoted in the local media or on official websites. In 17/21 countries (81%) vaccinated persons were centralized within the national registry. All countries (21/21) identified different subgroups to be prioritized for vaccination but only in 8/21 countries (38%) were PLWH prioritized (Czech Republic, Greece, Hungary, Lithuania, Montenegro, Romania, Slovakia, Slovenia), and only three (14.2%) countries (Czech Republic, Greece, Serbia) had national guidelines for vaccination of PLWH. Some of those countries have prioritized all HIV-infected persons (e.g. Czech Republic, Poland), others have prioritized those with advanced HIV disease only (e.g. Slovakia). During the study period the official local recommendation for vaccination of PLWH did not change significantly across our region, but the process of implementation was ongoing and vaccination availability has mostly improved. In 13/21 (62%) countries vaccination of PLWH started before 19 March 2021 as part of their national programmes, including groups prioritized due to other risk factors. In these countries PLWH vaccination coverage (on 19 March 2021) varies widely, ranging from 1.1% to 23% for partial coverage (one dose) and from <1% to 4.1% for full coverage (two doses).

Mode of vaccination delivery/distribution

In 11/16 (68.7%) countries, vaccination of PLWH against COVID-19 is concentrated within specialized centres. In
one out of 16 countries (6.2%), the preferred scenario is a specialized centre or a department of infectious diseases, and in another one (6.2%) it is a specialized centre together with general medical services. A department of infectious diseases together with general medical services is the preferred model in three out of 16 (18.7%) countries, and in one country, vaccination is provided by general medical services only (6.2%).

Eighteen respondents (18/21; 85.7%) claimed they were planning to follow up the outcomes of vaccination, mostly by measuring antibody levels and checking COVID-19 incidence (11/21; 52.3%); in two countries this was to be done by measuring of antibodies only (2/21; 9.5%) and two other countries by checking COVID-19 incidence in vaccinated PLWH only (2/21; 9.5%).

**TABLE 1 National COVID-19 vaccination programmes details**

| Country                 | Starting date | Comirnay and Moderna | Sputnik-V | Vaxzevria | Other | Centralized registration programmes | Dedicated centres as other persons |
|-------------------------|--------------|----------------------|-----------|-----------|-------|-------------------------------------|----------------------------------|
| Albania                 | 11 January 2021 | Yes                  |           |           |       | Yes                                 | Yes                              |
| Belarus                 | 18 January 2021 | Yes                  |           |           |       | No                                  | Yes                              |
| Bosnia and Herzegovina  | 11 March 2021  | Yes                  |           |           |       | No                                  |                                  |
| Bulgaria                | 27 December 2020 | Yes                  | Yes       |           |       | Yes                                 | Yes                              |
| Croatia                 | 27 December 2020 | Yes                  |           |           |       | Yes                                 |                                  |
| Czech Republic          | 27 December 2020 | Yes                  | Yes       |           |       | Yes                                 | Yes                              |
| Estonia                 | 27 December 2020 | Yes                  | Yes       |           |       | Yes                                 | Yes                              |
| Georgia                 | 14 March 2021   | Yes                  |           |           |       | Yes                                 |                                  |
| Greece                  | 27 December 2020 | Yes                  | Yes       |           |       | Yes                                 | Yes                              |
| Hungary                 | 26 December 2020 | Yes                  | Yes       | Yes       | Sinofarm Vero-Cell                  | Yes                              | Yes                              |
| Lithuania               | 27 December 2020 | Yes                  | Yes       |           |       | Yes                                 |                                  |
| Moldova                 | 2 March 2021    | Yes                  |           |           |       | Yes                                 |                                  |
| Montenegro              | 20 February 2021 | Yes                  |           |           |       | No                                  |                                  |
| Poland                  | 27 December 2020 | Yes                  | Yes       |           |       | Yes                                 | Yes                              |
| Romania                 | 27 December 2020 | Yes                  | Yes       |           |       | Yes                                 | Yes                              |
| Russian Federation      | 1 November 2020  | Yes                  |           |           | EpiVacKorona by ‘Vector’ Institute, Novosibirsk | Yes | Yes |
| Serbia                  | 24 December 2020 | Yes                  | Yes       |           | Sinofarm Vero-Cell                  | Yes                              | Yes                              |
| Slovakia                | 26 December 2020 | Yes                  |           | Yes       |       | Yes                                 |                                  |
| Slovenia                | 27 December 2020 | Yes                  |           | Yes       |       | Yes                                 |                                  |
| Turkey                  | 14 January 2021  | Coronavac by Sinovac China | Yes |           |      | Yes                                 | Yes                              |
| Ukraine                 | 24 February 2021 |                      |           |           | Covishield, Serum Institute of India | Yes | Yes |

**DISCUSSION**

We found that only a few countries from central and eastern Europe specified PLWH as a prioritized group in a COVID-19 national vaccination programme. This reflects ambiguous data evaluating evidence for higher susceptibility and risk of severe course of COVID-19 in PLWH available at the time of data collection [11,17–20].

A recently published European Centre for Disease Prevention and Control (ECDC) report of COVID-19 vaccination strategies mainly discusses the prioritization of certain subgroups (people aged > 80, health and social care workers) and the types of vaccines used [21]. In contrast to the ECDC report, besides the mRNA and vector-based...
vaccines we have recorded other vaccines which are not registered in the EU but are being used in a number of ECEE member countries.

During the COVID-19 era, only 30% of European countries continued operating their HIV centres in a normal way and the continuation of HIV care was limited or at least endangered, so the intention to prevent COVID-19 in risk groups of patients including PLWH should be emphasized [16,22]. As most of the ECEE member countries administer vaccination in designated medical centres, it is unlikely that HIV-positive patients will be identified and effective surveillance for such a specific group of patients will be provided, taking into account the high burden of stigmatization and social disclosure in the region. The responsibility of the post-vaccination follow-up in PLWH should be systematized, and the position of HIV centres during this process should be clearly defined. As provided by our respondents, such a plan is already in place, with the majority of clinics claiming to be prepared to play an active role in follow-up care focused on immune response and post-vaccination incidence of COVID-19.

There is a large discrepancy in terms of prioritization of population subgroups including PLWH. According to our data, only eight out of 21 countries prioritize PLWH in COVID-19 vaccination and just three out of 21 have their own guidelines for vaccination of PLWH, while Armenia has not even begun any preparations whatsoever, due to economic and political reasons. Therefore partial/one-dose vaccination coverage at the end of our data collection (19 March 2021) varies extremely, ranging from 1.1% (in the Czech Republic) to 23% (in Hungary). In comparison with the general population, vaccination coverage data are heterogeneous. In the same period, partial vaccination coverage in the HIV-negative population ranges from 4.7% (in Poland) to 15.6% (in Hungary) and full coverage/two doses from 3.6% (in the Czech Republic) to 4.8% (in Hungary) [23–26]. It is questionable whether PLWH should be vaccinated at HIV centres instead of designated vaccination centres in order to ensure better access to vaccines and secure confidentiality. It is therefore very important to re-evaluate national vaccination strategies to establish a consensus across European countries to ensure equity of access to COVID-19 prevention.

Based on lack of relevant data on efficacy and safety, real-life data become essential in making progress towards better vaccination practice for COVID-19. Therefore

| HIV-positive priority | National guidelines for HIV-positive COVID vaccination | Vaccinated HIV-positive patients in your practice | Plan to vaccinate at HIV centre | Do you plan to follow-up HIV-positive vaccinated? |
|-----------------------|-------------------------------------------------------|-----------------------------------------------|-------------------------------|-----------------------------------------------|
| Albania               | No                                                   | Yes                                           | No                            | Yes                                           |
| Belarus               | No                                                   | No                                            | No                            | No                                            |
| Bosnia and Herzegovina| No                                                   | Yes                                           | Yes                           | Yes                                           |
| Bulgaria              | No                                                   | Yes                                           | No                            | Yes                                           |
| Croatia               | No                                                   | No                                            | Yes                           | Yes                                           |
| Czech Republic        | Yes                                                  | Yes                                           | Yes                           | Yes                                           |
| Estonia               | No                                                   | Yes                                           | Yes                           | No                                            |
| Georgia               | No                                                   | No                                            | Yes                           | Yes                                           |
| Greece                | Yes                                                  | Yes                                           | No                            | Yes                                           |
| Hungary               | Yes                                                  | Yes                                           | Yes                           | Yes                                           |
| Lithuania             | Yes                                                  | Yes                                           | Yes                           | Yes                                           |
| Moldova               | No                                                   | No                                            | No                            | Yes                                           |
| Montenegro            | Yes                                                  | No                                            | Yes                           | Yes                                           |
| Poland                | No                                                   | Yes                                           | Yes                           | Yes                                           |
| Romania               | Yes                                                  | Yes                                           | No                            | Yes                                           |
| Russian Federation    | No                                                   | Yes                                           | Yes                           | Yes                                           |
| Serbia                | No                                                   | Yes                                           | No                            | Yes                                           |
| Slovakia              | Yes                                                  | Yes                                           | No                            | Yes                                           |
| Slovenia              | Yes                                                  | No                                            | No                            | Yes                                           |
| Turkey                | No                                                   | No                                            | Yes                           | No                                            |
| Ukraine               | No                                                   | No                                            | Yes                           | Yes                                           |
regional systematic collaboration, e.g. registry, clinical trials, guidelines and long-term follow-up of vaccinated persons, is the way forward to collecting enough data (and not just data on safety and efficacy of vaccines) within a relatively short period of time.

There is a need for more extensive data on efficacy and safety of COVID vaccines in PLWH, originating from large cohorts including people of different age, current immunostatus, nadir CD4 and comorbidities. Based on accurate data on post-vaccination protection, appropriate timing of a booster dose should be identified and included in updated guidelines. Nevertheless, clinicians should use all existing tools to highlight the importance of vaccination in PLWH and aim for the highest vaccination coverage to prevent COVID-19-related morbidity, mortality and sequelae.

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AUTHOR CONTRIBUTIONS
DJ, ASK, LF, and JK has contributed study design, statistics, preparing the text. DB, SA, TB, JB, AC, GD, DG, AH, KK, BL, RM, VM, CO, AP, NR, JT, LT, LS, AV, NY, and OY has contributed collection of data, approving the text.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID
Agata Skrzat-Klapaczynska @ https://orcid.org/0000-0002-6367-5633
Dominik Bursa @ https://orcid.org/0000-0001-5289-1974
Tatevik Balayan @ https://orcid.org/0000-0003-4478-4129
Justyna Kowalska @ https://orcid.org/0000-0003-1166-4462

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SUPPORTING INFORMATION
Additional supporting information may be found in the online version of the article at the publisher’s website.

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