COVID-19 Vaccination Rates in a Global HIV Cohort

Evelynne S. Fulda, BA[1], Kathleen V. Fitch, MSN[1], Edgar T. Overton, MD[2], Markella V. Zanni, MD[1], Judith A. Aberg, MD[3], Judith S. Currier, MD, MSc[4], Michael T. Lu, MD, MPH[5], Carlos Malvestutto, MD, MPH[6], Carl J. Fichtenbaum, MD[7], Esteban Martinez, MD, PhD[8], Triin Umbleja, MSc[9], Pamela S. Douglas, MD[10], Heather J. Ribaudo, PhD[9], Steven K. Grinspoon, MD[1]

[1] Metabolism Unit, Massachusetts General Hospital, Boston, MA 02114, USA
[2] Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham, AL 35294, USA
[3] Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY 10029, USA
[4] Division of Infectious Diseases, University of California at Los Angeles, Los Angeles, CA 90095, USA
[5] Cardiovascular Imaging Research Center, Massachusetts General Hospital, Boston, MA 02114, USA
[6] Division of Infectious Diseases, The Ohio State University Wexner Medical Center, Columbus, OH 43210, USA
[7] Department of Medicine for Translational Research, University of Cincinnati, Cincinnati, OH 45221, USA
[8] Hospital Clinic and University of Barcelona, Barcelona, Spain
[9] Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston MA 02115, USA
[10] Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC 27701, USA

Corresponding Author
Steven K. Grinspoon, M.D.
Mass General Hospital and Harvard Medical School
Boston, MA 02114
sgrispoon@mgh.harvard.edu
P: (617) 724-9109
F: (617) 724-8998

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40-word Summary: Little is known regarding COVID-19 vaccination rates in people with HIV (PWH). Among PWH in REPRIEVE, vaccination rates varied substantially by Global Burden of Disease (GBD) super-region and related to age, race, sex and cardiovascular risk.

ABSTRACT

Little is known regarding COVID-19 vaccination rates in people with HIV (PWH), a vulnerable population with significant morbidity from COVID-19. We assessed COVID-19 vaccination rates among 6952 PWH in the Randomized Trial to Prevent Vascular Events in HIV (REPRIEVE) compared to region- and country-specific vaccination data. The global probability of COVID-19 vaccination through the end of July 2021 was 55% among REPRIEVE participants with rates varying substantially by Global Burden of Disease (GBD) super-region. Among PWH, factors associated with COVID-19 vaccination included residence in high-income regions, age, White race, male sex, BMI, and higher burden of cardiovascular risk.

Key Words: human immunodeficiency virus, COVID-19, vaccination, global-burden of disease region

BACKGROUND

Globally, COVID-19 has taken the lives of more than 4.5 million people[1]. People with HIV (PWH) are immunocompromised and have a higher risk of underlying co-morbidities, placing them at high risk of COVID-related morbidity and mortality[2, 3]. However, little is known regarding global vaccination rates in this high-risk population. The Randomized Trial to Prevent Vascular Events (REPRIEVE) is a global primary cardiovascular prevention trial among PWH[4]. Data collected on COVID-19 vaccination rates in REPRIEVE afford a unique opportunity to assess such rates among PWH across global regions. Here we compare region- and country-specific vaccination rates among PWH enrolled in REPRIEVE to rates among the general population and assess, among PWH, characteristics associated with vaccination.

METHODS

The study was approved by the Mass General Brigham Human Research Committee and by the local institutional review boards of each site. Informed consent was obtained in writing from each participant. Race and ethnicity were self-reported using previously described NIH definitions[5].

Vaccination Data

Vaccination was defined as at least one dose of any COVID-19 vaccine. REPRIEVE vaccination data were collected on the concomitant medication log updated at each study visit scheduled quarterly. The cumulative probability of vaccination was determined from monthly data between January 2021 and the end of July 2021 using Kaplan-Meier estimation. Participants without vaccination were censored at date of last contact. Comparison of targeted baseline characteristics, including age, race, natal sex, BMI, atherosclerotic cardiovascular

disease (ASCVD) risk score by the 2013 ACC/AHA pooled cohort equation[6], CD4 (nadir and baseline), duration of antiretroviral therapy (ART), and history of AIDS defining illness associated with vaccination status was made via visual examination of the Kaplan-Meier-curves and formally compared via log-rank tests. Since REPRIEVE is a large study with high power to detect small differences, conclusions were motivated by clinically meaningful effect sizes.

Vaccination rates among REPRIEVE participants were compared between Global Burden of Disease (GBD; groupings: High-income (US, Canada, USA); Latin America and Caribbean (Brazil, Haiti, Peru, Puerto Rico), Southeast/East Asia (Thailand), South Asia (India), Sub-Saharan Africa (Botswana, South Africa, Uganda, Zimbabwe)) super-regions and with country-specific vaccination rates among the general population, derived from public databases, including Our World in Data[1], World Bank[7], and CDC[8]. As a note, the countries represented for analysis represent only a subset of the GBD super-regions. The Our World in Data (OWD) dataset is open access and aggregates country-specific data from governmental databases, including the WHO and the CDC, and is updated daily by employees of OWD. Data establishing background vaccination rates from the Our World in Data database was compared to publicly available country-specific data from the WHO, showing significant concordance (See Supplemental Table 1 for sources of OWD Data and comparison of country specific data to WHO). For the US, country-specific vaccination rates among individuals age 40-74 were obtained from public data sets from the CDC[8], for comparison against rates among REPRIEVE participants of comparable age. For other countries, public data were more limited, but we were able to determine rates among the population of individuals 15 or older, to infer an eligible population for comparison. Overall population size for each country, as well as adult population 15 years of age and older was collected from the World Bank database. We utilized data on at least one vaccination given

the multiplicity of regimens across regions and countries (See Supplemental Table 2), to best harmonize the data and most accurately reflect vaccine rates over a given time period. Comparisons with public data sets used this same metric.

RESULTS

Study Population

7770 male and female PWH, aged 40 – 75, on stable ART and without known CVD and low-to-moderate ASCVD risk, were recruited into REPRIEVE[4]. Enrollment occurred between March 2015 and July 2019 in 12 countries. COVID-19 vaccination rates were determined in 6952 participants active in REPRIEVE as of January 1, 2021 (**Supplemental Table3**) including participants in Brazil (N=1,042), Botswana (N=273), Canada (N=123), Haiti (N=136), India (N=469), Peru (N=142), South Africa (N=527), Spain (N=198), Thailand (N=582), Uganda (N=175), the United States (N=3162), and Zimbabwe (N=123).

Cumulative Vaccination Rates among REPRIEVE Participants

The cumulative vaccination rate among REPRIEVE participants through the end of July 2021 was 55% (**Figure 1A**), though rates varied substantially by GBD super-region and by country (**Figure 1B, Supplemental Figure 1**). Cumulative vaccination rates were highest in the High-Income super-region (71%), followed by Latin America and the Caribbean (59%), South Asia (49%), Southeast/East Asia (41%), and Sub-Saharan Africa (18%). Country-specific rates varied dramatically, with vaccination rates highest in the United States, Peru, and Brazil, 72%, 69%, and 63% and lowest in South Africa, Uganda, and Haiti with 18%, 3%, and 0%, respectively.

Comparison to Vaccination Rates among the General Population

Vaccination rates were generally comparable among PWH in REPRIEVE compared to the general population (**Figure 1C**), in most GBD super-regions, though key differences were observed in comparison to the general population in specific countries (**Supplemental Figure 1**).

Characteristics Associated with Vaccination among REPRIEVE Participants

Among the overall REPRIEVE population, vaccinated participants were more likely to come from high-income GBD super-region countries and to be White, male, older, have a higher BMI, higher ASCVD risk score, and longer duration of ART, but did not differ by either nadir or baseline CD4 count (**Supplemental Figures 2-8**). Vaccination rates were overall higher among men in the high income and the S. East/East Asia regions with similar trends in Latin America and the Caribbean and South Asia. In the high-income GBD super-region, differences in vaccination rates by race were seen (**Figure 2**).

DISCUSSION

To our knowledge, this analysis presents the first and largest investigation of vaccination rates among PWH. Among REPRIEVE participants, vaccination rates were greatest in high-income countries compared to low-income countries. For example, overall vaccine rates for PWH in REPRIEVE ranged from 71% in the high-income super-region to 18% in Sub-Saharan Africa, and by country from 72% in the US to 0% in Haiti. Overall, vaccination rates mirrored rates for the general population in most GBD super-regions, with specific differences seen in individual countries. These data allow a specific examination of rates among PWH, in the context of global rollout policies that differed by region and country (**see**

Supplemental Table 2 for summary of country specific roll-out timelines). Moreover, these data permitted an examination of factors associated with COVID-19 vaccination for the first time among PWH.

Our data highlight major differences in COVID-19 across GBD super-regions. Further, our data demonstrate that COVID-19 vaccination rates among PWH are consistent with the general population in many regions and countries. This disparity in COVID-19 vaccination rates among PWH across income regions may increase morbidity from COVID-19 in the most vulnerable HIV populations. For example, the two countries with the largest share of deaths from HIV/AIDS (Botswana and South Africa)[9] demonstrated very low vaccination rates in general compared to high-income countries.

In our cohort, vaccinated PWH were more likely to be older, have more co-morbidities, including higher BMI, and higher overall ASCVD risk, across most regions. Increased co-morbidities among those receiving the vaccine may suggest that such participants were motivated out of concerns about COVID-related morbidity/mortality, and/or that physicians recommended the vaccination more often in this context, consistent with many public health recommendations[10]. Overall, women were less likely to receive the vaccination in high-income regions and S. East/East Asia, with similar trends in most regions except Sub-Saharan Africa.

In the high-income super-region, with a significant representation of participants from the US, vaccination rates were higher among Whites than Blacks. These data confirm lower vaccination rates for people of color living with HIV globally, for example in sub-Saharan Africa and Haiti, and also compared to Whites within higher GBD super-regions such as the

US[11]. Given data for higher morbidity from COVID-19 among people of color with HIV[2], this disparity is likely to have significant public health implications.

Our analysis was characterized by strengths and limitations. We established region and country-specific rates in a diverse, global population of PWH, with 66% people of color and 32% women. Given the design and data collected in REPRIEVE, we were able to assess vaccination rates in association with key demographics and well-established cardiovascular risk metrics. Vaccination rates for the general population were calculated for most countries and in most regions in a broadly defined eligible population (≥ 15 years of age), given data availability. For the large REPRIEVE population in the US, we were able to compare to the general population age 40-74. REPRIEVE participants were recruited as part of a large, multinational, primary ASCVD prevention trial and are representative of the global population of PWH on antiretroviral therapy[12]. Decisions on vaccination were made by the individual participants in REPRIEVE, without a central recommendation or requirement from the study. Though participants were enrolled in a research cohort, the study population is reflective of a highly relevant global population of PWH, for whom vaccination data are critical. Moreover, the uniform study conditions and assessments in the cohort permitted determination of global rates and key comparisons across GBD regions. In this context, we observed tremendous differences in rates and key factors associated with vaccination across GBD regions, providing the first such data on PWH. Collection of COVID-19 vaccination data is ongoing in REPRIEVE. Future data collection will allow for further refinement of cumulative rates and examination of evolving COVID-19 vaccination patterns.

These data from REPRIEVE inform the field on the critical question of COVID-19 vaccination rates among PWH and highlight inequities in vaccination rates across GBD

super-regions. Furthermore, the data highlight subgroups among the larger global population of PWH who have low vaccine rates and should be targeted for vaccination.

FOOTNOTES

Corresponding Author:
Steven K. Grinspoon, M.D.
Mass General Hospital and Harvard Medical School
Boston, MA 02114
sgrispoon@mgh.harvard.edu
P: (617) 724-9109
F: (617) 724-8998

The authors consent to personal communication.

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Disclosures/Conflicts of Interest:

The views expressed in this article are those of the authors and do not necessarily represent the views of the National Heart Lung and Blood Institute (NHLBI) or the National Institute of Allergy and Infectious Diseases; the National Institutes of Health, or the Department of Health and Human Services.

The manuscript represents valid work, and neither this manuscript nor one with substantially similar content has been published or is being considered for publication elsewhere.

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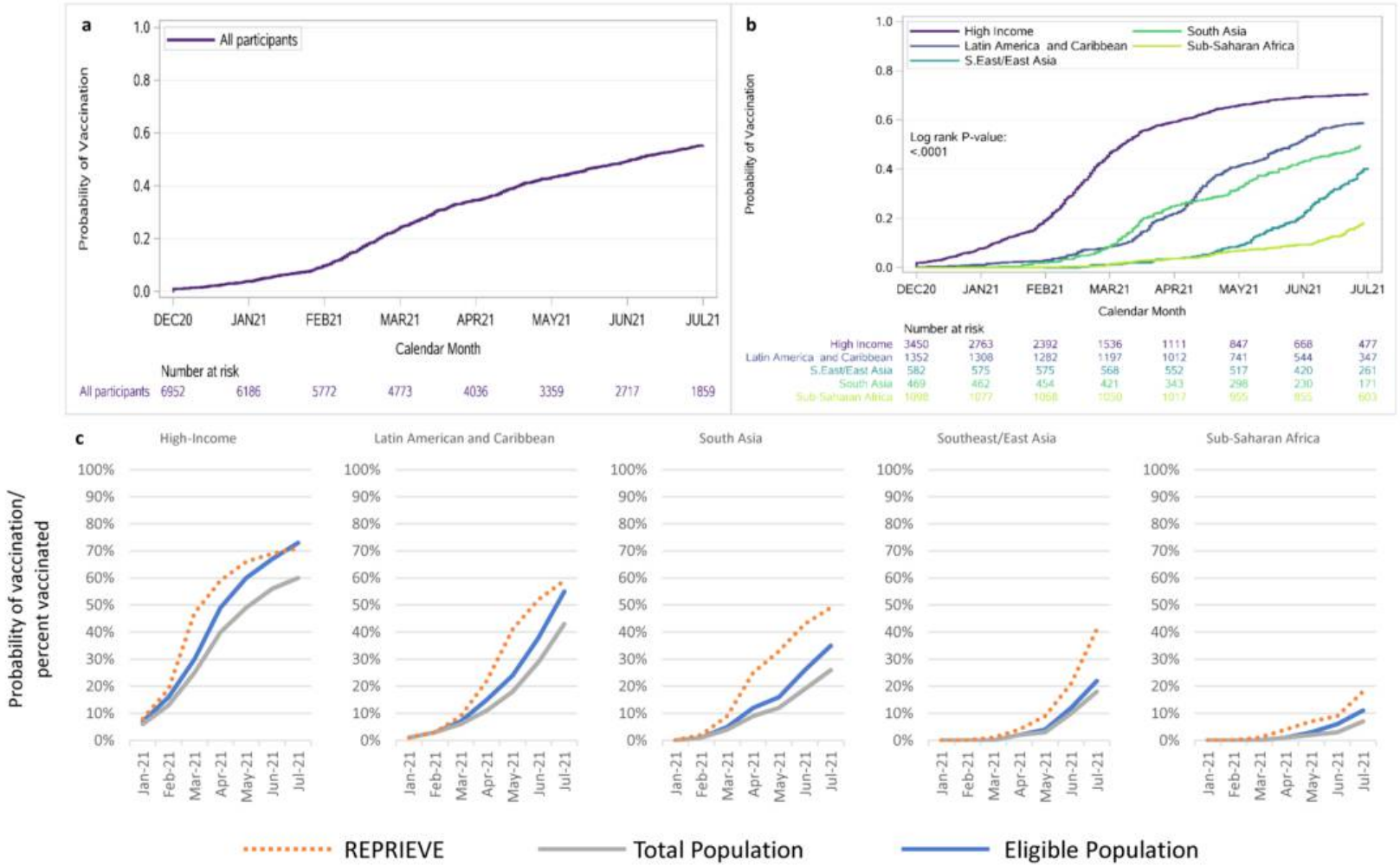
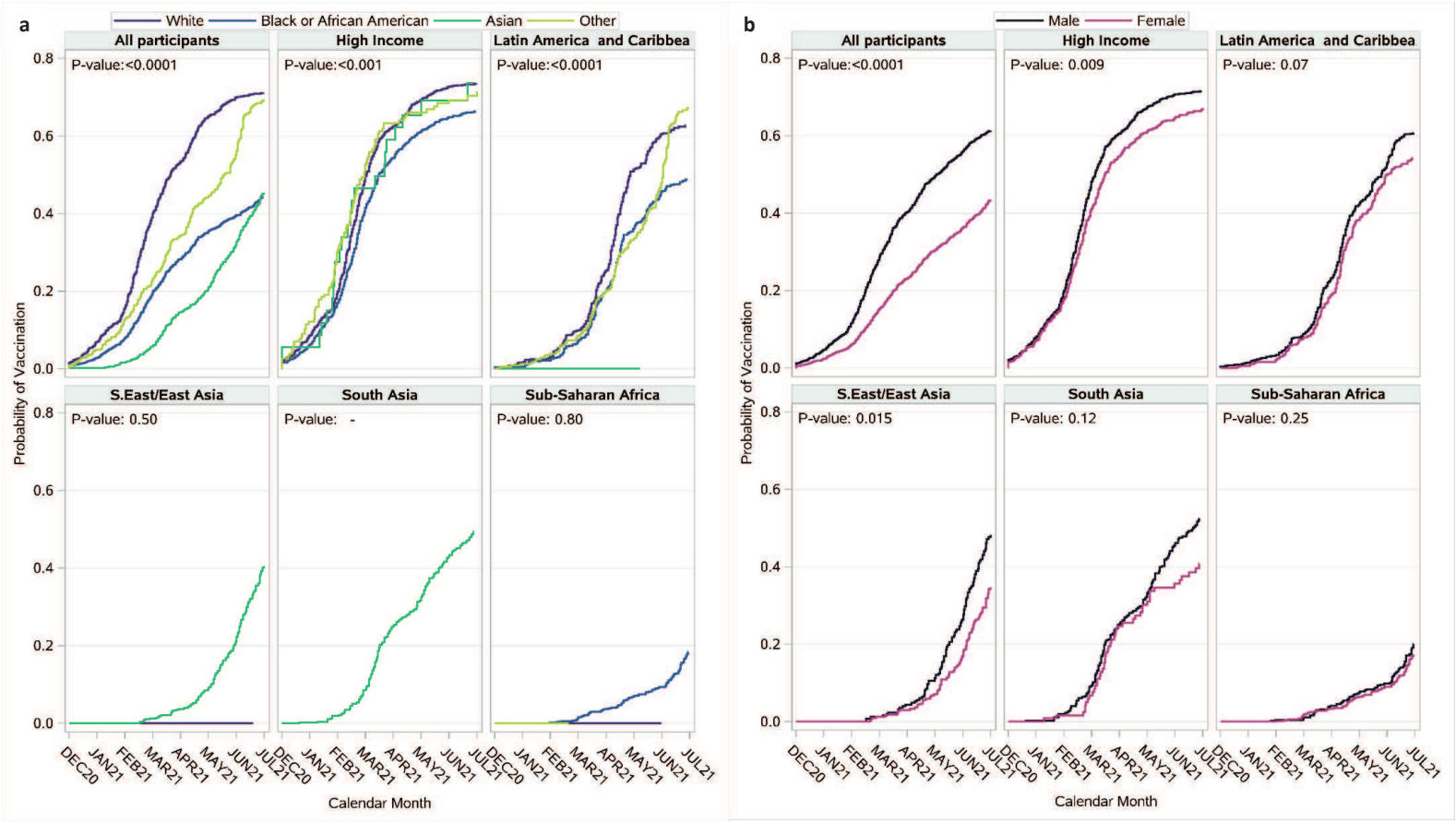
Figure Legends

Figure 1. Vaccination Rates Among REPRIEVE Participants and the General Population. Panel A, Kaplan-Meier curve depicting probability of vaccination among REPRIEVE participants through July 2021. Panel B, Kaplan-Meier curve depicting probability of vaccination among REPRIEVE participants by GBD super-region. Panel C, Comparisons of vaccination rates between PWH in REPRIEVE and the general and eligible populations among GBD super-regions.

Figure 2. Cumulative Probability of Vaccination over Time among REPRIEVE Participants by Race and Sex. Panel A, Vaccination rates among GBD super-regions by Race. Panel B, Vaccination rates among each GBD super-region by Sex.





Participants with no follow-up in 2021 are censored at January 1, 2021. X-axis tick marks are given at the end of a given month.