Prioritizing COVID-19 Vaccines for PWHIV

By Lynda Dee

HIV Exclusion from COVID-19 Vaccine Trials and CDC Vaccination Prioritization for PWHIV

AAB spearheaded a massive community collaboration to ensure that people with HIV (PWHIV) were included in COVID-19 vaccine trials as well as future vaccine trials. We wrote a letter with over 1,500 signatures to Dr. Francis Collins, Director of the National Institutes of Health (NIH), on July 30, 2020, demanding that PWHIV be included in all government funded vaccine trials, and lead other advocacy efforts with the NIH, the Food and Drug Administration (FDA), Industry and media sources. Moderna removed its exclusion on August 5, 2020. Pfizer followed suit on September 12, 2020. See the full story in the December AIDS Action Baltimore (AAB) Bulletin: **PWHIV Excluded from COVID-19 Vaccines Studies and FDA Vaccine Approval Hearings**

AAB has since embarked on advocacy efforts to prioritize COVID-19 vaccines for PWHIV. This has proven to be an even more complicated experience, requiring navigation through the complicated Center for Disease Control and Prevention (CDC) vaccine approval bureaucracy. AAB spearheaded this project with the invaluable assistance of Tim Horn from NASTAD., Wash., DC, Richard Jefferys and Mark Harrington from TAG, NYC, NY, Greg Millett from amfAR, NYC, NY and Jen Kates Kaiser Family Foundation, Wash., DC.

Initially, we prepared a sign-on letter to the CDC, outlining the scientific basis for prioritizing COVID-19 vaccination in PWHIV. Because the CDC's Advisory Committee on Immunization Procedures (ACIP) was conducting a hearing on expanding vaccine prioritization recommendations on December 20, 2020, we decided to officially submit our letter as public comment for the ACIP prioritization hearing. Although our letter did provide scientific references for our position on HIV prioritization, this is a new field with only trending data to date. Thus, we were unsuccessful in including PWHIV in the new 1c CDC vaccination prioritization category unless they are also age 65-74, persons aged 16-64 years with high-risk medical conditions, or essential workers not included in Phase 1b. We will begin this advocacy once again once the data is more mature and persuasive.

A summary of the ACIP hearings on the Pfizer and Moderna vaccines and new prioritization expansion hearing is provided below. While this information is essentially process oriented and may not seem as exciting as purely clinical data per se, it is essential to know and understand CDC procedures and data requirements if we are to ultimately be successful in prioritizing COVID-19 vaccinations for PWHIV.

FDA Hearings/Emergency Use Authorization and CDC Recommendations

The FDA's Center for Biologics Evaluation and Research (CBER) Vaccines and Related Biological Products Advisory Committee (VRBPAC) held open public hearings for the Pfizer vaccine on December 10, 2020, and received FDA Emergency Use Authorization (EUA) on December 18, 2020. The VERBPAC Moderna hearing was held on December 17, 2020. The FDA granted the Moderna vaccine EUA on December 11, 2020. Both vaccines were determined to be safe and extremely effective against COVID-19, with the benefit clearly outweighing the risk of side effects experienced. The benefit/risk ratio question was the only voting question posed to the VRBPAC). EUA is not full FDA approval. Pfizer and Moderna will still be

required to file Biological License Applications (BLAs) in order to obtain full approval once they have more data. See the December AAB Bulletin for more information: **PWHIV Excluded from COVID-19 Vaccines Studies and FDA Vaccine Approval Hearings** The AZ vaccine is still mired in controversy and has not received EUA in the USA, but has received emergency approval in the United Kingdom and India.

Both an open public hearing conducted by the CDC's ACIP and the CDC's ultimate acceptance of ACIP recommendations must occur before these vaccines can be administered to people. The ACIP Pfizer hearings were conducted on December 11 and 13, 2020. The Moderna hearings took place on December 19-20, 2020. Both vaccines were approved by ACIP and the CDC after the laborious analyses described below. While I am well versed in FDA regulatory procedures, these were my first CDC vaccine hearings since there have been no HIV vaccine regulatory hearings. Having learned much about CDC vaccine approval practices, I have come away with a new respect for the CDC's real world considerations displayed at these hearings as well as the highly relevant clinical experience and inquiries of ACIP voting and non-voting members. I thought FDA Advisory Committees hearings were in depth and involved. The CDC's ACIP hearings were even more detailed and regulated. While the ACIP process might seem akin to a byzantine bureaucracy with many voting questions and numerical grading considerations, it was very expeditious and effective at addressing real world issues while the FDA VRBPAC had only one voting question to address.

Initially, ACIP conducted a Grading of Recommendations, Assessment, Development and Evaluation (GRADE) review of the evidence for benefits and harms for both vaccines. GRADE considerations involved specific criteria for different scientific and policy questions, including the type of clinical trial evidence provided, vaccine efficacy, hospitalization utilization, and the certainty of the following estimates, all-cause death, asymptomatic SARS-COV-2 infection, the effect of serious adverse events and reactogenicity. There were specific forms and numerical grading considerations for each GRADE inquiry.

Next an Evidence to Recommendation Framework Analysis was conducted again with specific forms and numerical grading considerations for public health importance, benefits and harms, risks of undesirable anticipated effects, whether the desirable effects outweigh the undesirable effects, the overall certainty of evidence for the critical outcomes, including the opinion of target populations with respect to desirable effects, whether there is important uncertainty about or variability in how much people in specific populations value the main outcomes, whether the vaccine is acceptable to key stakeholders, whether the vaccine represents a reasonable and efficient allocation of resources, the impact of the vaccine on health equity and whether the vaccine is feasible to implement.

After balancing the competing interests, ACIP decided that the desirable consequences clearly outweigh undesirable consequences in most settings, and that there was sufficient information to move forward with the CDC's recommendations. The following links provide more information on the detailed ACIP analyses process for the Pfizer and Moderna vaccines:

https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html
https://www.cdc.gov/mmwr/volumes/69/wr/mm6950e2.htm?s_cid=mm6950e2_w;
https://www.cdc.gov/mmwr/volumes/69/wr/mm695152e1.htm?s_cid=mm695152e1_w

The ACIP COVID-19 vaccination prioritization hearing occurred on December 20, 2020, after the Moderna vaccine approval hearing. Relevant ACIP medical condition prioritization criteria is also very detailed and regulated. The following medical conditions were officially amended on December 23, 2020, with the following qualification: "The below list of underlying medical conditions is not exhaustive and only includes conditions with sufficient evidence to draw conclusions", and can be found at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html

"Adults of any age with certain underlying medical conditions are at increased risk for severe illness from the virus that causes COVID-19. Severe illness from COVID-19 is defined as hospitalization, admission to the ICU, intubation or mechanical ventilation, or death.

Adults of any age with the following conditions **are at increased risk of severe illness** from the virus that causes COVID-19:

Cancer

Chronic kidney disease

COPD (chronic obstructive pulmonary disease)

Down Syndrome

Heart conditions, such as heart failure, coronary artery disease, or cardiomyopathies

Immunocompromised state (weakened immune system) from solid organ transplant

Obesity (body mass index [BMI] of 30 kg/m2 or higher but < 40 kg/m2)

Severe Obesity (BMI ≥ 40 kg/m2)

Pregnancy

Sickle cell disease

Smoking

Type 2 diabetes mellitus

COVID-19 is a new disease. Currently there are limited data and information about the impact of many underlying medical conditions on the risk for severe illness from COVID-19. Based on what we know at this time, adults of any age with the following conditions **might be at an increased risk for severe illness** from the virus that causes COVID-19:

Asthma (moderate-to-severe)

Cerebrovascular disease (affects blood vessels and blood supply to the brain)

Cystic fibrosis

Hypertension or high blood pressure

Immunocompromised state (weakened immune system) from blood or bone marrow transplant, immune deficiencies, **HIV**, use of corticosteroids, or use of other immune weakening medicines

Neurologic conditions, such as dementia

Liver disease

Overweight (BMI > 25 kg/m2, but < 30 kg/m2)

Pulmonary fibrosis (having damaged or scarred lung tissues)

Thalassemia (a type of blood disorder)

Type 1 diabetes mellitus"

"The level of evidence for each condition was determined by CDC reviewers based on available information about COVID-19. Conditions were added to the list (if not already on the previous underlying medical conditions list [originally released in March 2020]) if evidence for an association with severe illness from COVID-19 met any of the following criteria", and can be found at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/evidence-table.html

"Strongest and most consistent evidence: Defined as consistent evidence from multiple small studies or a strong association from a large study,

Mixed evidence: Defined as multiple studies that reached different conclusions about risk associated with a condition, or

Limited evidence: Defined as consistent evidence from a small number of studies."

A summary of the December 20, 2020 ACIP prioritization recommendations is provided below. These recommendations and the definition of non-health care frontline essential workers can be found at: https://www.cdc.gov/mmwr/volumes/69/wr/mm695152e2.htm?s_cid=mm695152e2_w

"On December 1, the Advisory Committee on Immunization Practices (ACIP) recommended that health care personnel and long-term care facility residents be offered COVID-19 vaccination first (Phase 1a).

On December 20, ACIP updated interim vaccine allocation recommendations. In Phase 1b, COVID-19 vaccine should be offered to persons aged ≥75 years and non-health care frontline essential workers, and in Phase 1c, to persons aged 65-74 years, persons aged 16–64 years with high-risk medical conditions, and essential workers not included in Phase 1b.

Federal, state, and local jurisdictions should use this guidance for COVID-19 vaccination program planning and implementation."

Implementation strategies for the recommendations can be found at: https://www.cdc.gov/vaccines/covid-19/implementation-strategies.html

Further information for HIV and other medical conditions can be found at: https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/underlying-conditions.html

The HIV information is provided below.

"People with HIV and those with weakened immune systems due to other illnesses or medication might be at increased risk for severe COVID-19. They may receive a COVID-19 vaccine. However, they should be aware of the limited safety data:

Information about the safety of mRNA COVID-19 vaccines for people who have weakened immune systems in this group is not yet available.

People living with HIV were included in clinical trials, though safety data specific to this group are not yet available at this time.

People with weakened immune systems should also be aware of the potential for reduced immune responses to the vaccine, as well as the need to continue following all current guidance to protect themselves against COVID-19."

Unfortunately, given the very specific CDC recommendation categories, it is currently not possible to include PWHIV in the new CDC 1c category unless they are age 65-74, 16-64 years old with previously listed high-risk medical conditions, or essential workers not included in Phase 1b. At best, the evidence for PWHIV being at increased risk of severe illness from COVID-19 arguably falls into the CDC mixed evidence category: "Defined as multiple studies that reached different conclusions about risk associated with a condition." Once we have more data, we will resume our PWHIV prioritization advocacy. More mature, persuasive data is definitely needed to successfully change the current COVID-19 vaccine prioritization for PWHIV. [1]

[1]When Epidemics Collide: Why People with HIV May Have Worse COVID-19 Outcomes and Implications for Vaccination, Virginia A Triant, Rajesh T Gandhi; Clinical Infectious Diseases, ciaa1946, 04Jan2021; https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1946/6062462.