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ORCHESTRA Delphi consensus: clinical management of SARS-CoV-2 infection in people with HIV

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ABSTRACT

Objectives: The interaction between HIV and COVID-19 resulted in a syndemic that showed an excess burden of disease for people with HIV (PWH). Four years of the COVID-19 pandemic have raised many unsolved questions about the optimal care of COVID-19 in PWH.
Methods: We performed a study using a three-round Delphi methodology involving a panel of physicians with expertise in HIV and COVID-19 infections. The main aim of the study was to provide recommendations on critical clinical issues of COVID-19 among PWH and to inform physicians and policy-makers for improving care and prevention of COVID-19 in PWH. A total of 27 questions were conceived, focusing on four main areas of interest in the management of COVID-19 in PWH; a panel of 34 experts in HIV and COVID-19 care expressed their level of agreement on each item. Questions that received agreement/disagreement ≥79.4% of panellists were identified and statements were generated accordingly.
Results: Consensus was reached on 19/27 items, resulting in 18 final statements. These statements addressed: (a) risk of COVID-19 progression to severe disease among PWH; (b) COVID-19 diagnostics and laboratory procedures; (c) early treatments with antivirals and/or monoclonal antibodies; (d) use of corticosteroids; (e) COVID-19 preventive strategies.
Discussion: This consensus's study guides infectious diseases physicians in making decisions regarding the care of PWH for COVID-19, where results from the scientific literature are limited or conflicting.
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Introduction

The COVID-19 pandemic is the first overwhelming pandemic that overlaps with another major pandemic and global health challenge of the modern era: HIV/AIDS. Until August 2024, more than 775 million confirmed positive COVID-19 cases and 7 million deaths had been reported worldwide [1]. In 2023, still 39.9 million people were living with HIV, with 1.3 million newly acquired infections and more than 630 000 deaths. HIV remains a leading cause of morbidity and mortality, especially in resource-limited settings [2]. A syndemic has resulted from the interaction of the two conditions, identifying an excess burden of disease for people with HIV (PWH) [3]. This increased risk for PWH is based on several factors: interactions between the two diseases, HIV-driven immune dysfunction even when on effective antiretroviral therapy (ART), presence of additional risk factors for COVID-19 severity such as comorbidities common in PWH; disruption of HIV care due to the involvement of HIV healthcare workers in the COVID-19 response; high rates of socially produced burdens in the form of hesitancy and barriers to vaccination, stigma and discrimination experienced by PWH [4–6].

After more than 4 years since the beginning of the COVID-19 pandemic, with the succession of multiple and different scenarios of variants of concern (VoC), availability of increased number of preventive and treatment drugs, access and efficacy of anti-COVID-19 updated vaccines, a vast amount of scientific literature has been published aimed to unravel the role and peculiarities of the HIV population in COVID-19, but sometimes with seemingly contradictory results or without being able to answer all the constantly emerging questions [7].

To bridge these knowledge gaps, we used the Delphi methodology. This structured and iterative approach is designed to reach a consensus on complex issues among a panel of experts in a given field. The Delphi method is particularly useful when empirical evidence is limited, or expert opinion is essential in decision-making. The Delphi method was selected in this work, to systematically explore and resolve uncertainties surrounding the most pressing clinical management challenges of COVID-19 among PWH and establish a consensus to direct future public health actions [8]. The Delphi methodology has been used previously in the field of HIV [9–12] and COVID-19 management [13–15].

The objective of this study is to address unresolved questions regarding COVID-19 aspects among adult PWH—often focusing on the group of severely immunosuppressed PWH (<200 and/or <350 CD4/mm^3 and/or AIDS)—by leveraging the collective expertise of European and South-American Infectious disease specialists involved in HIV and COVID-19 care. Through the Delphi process, we aim to identify consensus on critical clinical issues of COVID-19 in PWH, define shared statements, and inform physicians and policy-makers to improve the health outcomes of PWH.

Methods

Study design and selection of experts

Using the Delphi method, this cross-sectional research has been conducted within the Working Package 4 (WP4—Fragile population cohorts) of the H2020-funded Orchestra Study [16,17]. We employed a three-round Delphi method to reach a consensus on a list of statements describing recommended management approaches for COVID-19 among adult PWH. Three further Delphi studies on other fragile populations investigated in the Orchestra-WP4 study (rheumatological, solid organ transplant recipients, and haematological patients) were carried out concurrently using the same approach and methodology.

The invitation to participate in the Delphi was sent, by the research team, to a panel of infectious diseases specialists who provide care to PWH and are involved in COVID-19 responses across Europe and America. Panellists were identified based on their clinical experience in HIV care, first of all among the participants in the Orchestra Study and Icona Foundation Scientific Committee [18], relevant peer-reviewed publications on HIV and COVID-19, and participation as members in national and international scientific HIV/AIDS societies (EACS, IAS, BHIVA, and ICAR) taking into account in gender and geographical area. Ninety-three infectious diseases physicians from 15 countries were invited via e-mail to participate; 34 experts (from 10 countries) agreed to participate. Therefore, the final number of participants was sufficiently large to be confident of consensus, given the recommendations for conducting Delphi surveys suggest a panel of 18 experts [19].

This study discusses and presents the statements of the consensus reached and is presented following the ACCORD reporting checklist (Table S1).

Development of questions

Five infectious diseases researchers of the Icona Foundation Steering Committee involved both in HIV and COVID-19 diseases conceived a total of 27 questions, to address clinical, diagnostic, therapeutic and preventive issues related to COVID-19 management in adult PWH for which literature data were still scarce or inconclusive. The following four areas were investigated: (a) risk of COVID-19 progression; (b) COVID-19 diagnostic and laboratory procedures; (c) therapeutic management of COVID-19 (early treatments, drug–drug interactions, and corticosteroids), (d) COVID-19 preventive strategies (pre-exposure prophylaxis [PrEP] and vaccines). A section 'Diagnosis and management of post-COVID-19 condition', including 15 questions, was also investigated in this Delphi. However, the results will be presented with data from the other fragile groups of Orchestra-WP4 in a separate paper.

The research team reviewed the medical and scientific literature and international guidelines on the management of COVID-19, specifically COVID-19 in adult (>18 years old) PWH that was available up to October 2023. The research group determined four topics/areas to be investigated and created the items/questions of the Delphi survey. The final set of questions was intended to stratify PWH based on specific characteristics, such as the presence or absence of known HIV-related risk factors like opportunistic infections and CD4 count strata, rather than treating the various aspects of COVID-19 in the HIV population as a single entity.

Data collection

The three rounds of the Delphi process were conducted anonymously with the first round from May to June 2024, the second round in July 2024, and the third round in August 2024. None of the research teams that conceived the questions participated as experts in the Delphi process; they were aware of the identity of the participants but were blinded to the identity of their responses. The Delphi survey was electronically administered using the REDCap electronic data capture tool of the ORCHESTRA project hosted on the servers of the CINECA Consortium [20]. The Delphi questionnaires were administered via e-mail using the Survey Distribution Tool of RedCap and regular reminder emails were sent every 5 days to ensure survey completion. Participants were asked to answer the 27 questions using a 6-point Likert scale: strongly disagree (1), disagree (2), somewhat disagree (3), somewhat agree (4), agree (5), strongly agree (6). In addition, under each question, panellists were encouraged to make comments using an open-text box.

The consensus was a priori defined in the study protocol by obtaining an agreement in the response of 80% or higher, but for an approximation based on the number of participants recruited, we redefined the consensus as the agreement of at least 27 of the 34 expert respondents (79.4%).

To make it easier to determine a consensus and to assign a strength to the consensus, we divided the six-point scales of the responses into four different categories. The resulting outcomes were as follows:

- Strong disagreement: strongly disagree (1) + disagree (2).
- Moderate disagreement: disagree (2) + somewhat disagree (3).
- Moderate agreement: somewhat agree (4) + agree (5).
- Strong agreement: agree (5) + strongly agree (6).

In the first round, the responses were analysed to determine the level of consensus among all participants. Any item with a consensus of 79.4% or more was excluded from the questionnaire administered in the second round. Some comments reported in the first round by the panellists showed a misinterpretation of the questions on the use of monoclonal antibodies (MoAb); we clarified it in the following rounds using footnotes below the questions. The results of the first round and all the comments received were combined and given to the participants during the second round, using the four-point scale. This approach allowed each expert to re-evaluate their initial response considering the other panellists'—anonymous—responses and comments. Anonymity was essential to avoid biased influence from other panellists and provide an independent response. The same procedures were repeated from the second to the third round.

Final statements for the questions that obtained consensus have been generated, along with the percentage of agreement/disagreement, the round of consensus, and the strength of agreement/disagreement (moderate or strong). During the development of the Delphi rounds, there was a constant review by the team on a monthly basis of new literature evidence on the survey topics, with no significant evidence.

Data analysis

Simple descriptive statistics—absolute and relative frequencies—were used to analyse the results obtained from the three rounds. Calculations were performed using Stata MP v. 18.0.

Ethical

The approval of an Institutional Review Board was not required as this Delphi study does not involve research and data on human subjects or animals. The study was based entirely on the feedback provided by the experts. Participants were asked for their willingness and authorization to participate and to process the data provided for scientific research.

Results

All 34 experts participated in all three rounds without missing. The panels mainly represent the opinion of infectious diseases physicians and researchers from Europe, with the majority ($n = 16$) from Italy, three from Spain, two experts from Germany, France, The Netherlands, Poland, and the United Kingdom, and one from Sweden and Ireland. Four panellists were recruited from Argentina. In total, there were 10 females and 15 males.

The consensus was achieved for 3 of the 27 (11.1%) items after the first round, for 9 of 24 (37.5%) questions of the second round, and for 7 of the 15 (46.6%) remaining in the third round, resulting in 19 final items with a consensus reached (70.4%). A total of 18 final statements were conceived and reported with the strength of the consensus. Questions and related results from the three rounds are all reported in Table 1. Table 2 shows the list of statements resulting from this Delphi study.

Risk of COVID-19 progression to severe disease

The topic was addressed through four questions (questions #1–4, Table 1).

Question #1 'Excluding known risk factors, do you agree that all PWH diagnosed with COVID-19, independently from HIV-RNA and CD4+ T cells count, present the same risk of progression to severe disease compared with the general population?' reached the consensus of moderate disagreement (85.3%) in the third round, leading to the following statement.

Statement 1: 'PWH have a risk of COVID-19 progression higher than the general population compared for age and other risk factors, independently from CD4 and HIV-RNA' (moderately supported)

Initial data from the first waves of the COVID pandemic did not indicate a different risk of severe COVID-19 among PWH. Still, most of those studies were single centres' small cohorts or case series susceptible to biases [21–23]. Later, some paramount extensive collaborative national studies were published showing the higher risk for COVID-19 in HIV even after adjustments for known confounders [24–28], which were confirmed by research with broader geographical representation [29,30] and meta-analyses [31,32]. These studies, as well as the comments of the Delphi panellist, primarily highlight the central role of viro-immunological status and ART for COVID-19 prognosis in HIV, which are not considered in this first question but discussed in the next ones.

An explanation for this statement considers that COVID-19 pandemic has disproportionately impacted minorities and communities with low socioeconomic status, which have already been deeply affected by the HIV epidemic. HIV and SARS-CoV-2 share common socioeconomic determinants of both their acquisitions and clinical impact and the COVID-19 pandemic exacerbated some public health disparities, resulting in increased morbidity and mortality among some of the socially fragile groups like HIV [33]. There was evidence of a disproportionate risk of severe COVID-19 among Black and Latin/Hispanic PWH in the United States as well as among non-Western migrants with HIV in Europe or PWH living in high-poverty areas [5,27,34,35]. The mechanisms behind this risk of severe outcomes also include social and cultural barriers to COVID-19 testing, a lower possibility of using healthcare services and higher hesitancy and barriers to vaccination, lower treatment adherence [35,36]. Moreover, PWH have an increased rate of comorbidities, like cardiovascular disease, lung disease, kidney disease, cancer, obesity, and diabetes at younger ages compared with the HIV-negative population [37–42]. This earlier onset of such a significant burden of comorbidities can raise the age-related risk of COVID-19 severity, also in younger HIV individuals compared with the general population. All these reasons, and the other well-known HIV infection-related factors (immune status and HIV viral load) not considered in this question, bring the HIV population to a higher risk of COVID-19 progression. However, disentangling the independent role and magnitude of each specific factor remains challenging, as they also interact with each other, leading to a synergistic effect of the various factors.

The question leading to the following statement was question #2 'Excluding known risk factors, do you agree that PWH with CD4+ T cells <200/mm^3 and/or AIDS diagnosed with COVID-19 present the same risk of progression to severe disease compared

Table 1
List of questions and results of the three rounds of the Delphi study.

	Question	Round 1				Round 2				Round 3			
		SD (%)	MD (%)	MA (%)	SA (%)	SD (%)	MD (%)	MA (%)	SA (%)	SD (%)	MD (%)	MA (%)	SA (%)
1	Excluding known risk factors,[a] do you agree that all PLWH diagnosed with COVID-19, independently from HIV-RNA and CD4+ T cells count, present the same risk of progression to severe disease compared with the general population?	44.1	50.0	38.2	26.5	76.5	70.6	8.8	14.7	8.8	85.3	2.9	2.9
2	Excluding known risk factors,[a] do you agree that PLWH with CD4+ T cells <200/mm^3 and/or AIDS diagnosed with COVID-19 present the same risk of progression to severe disease compared with the general population?	64.7	41.2	20.6	17.7	94.1	44.1	5.9	5.9	.	.	.	.
3	Excluding known risk factors,[a] do you agree that PLWH with CD4+ T cells between 200 and 350/mm^3 diagnosed with COVID-19 present the same risk of progression to severe disease compared with the general population?	14.7	38.2	52.9	32.4	11.8	52.9	44.1	20.6	8.8	85.3	2.9	2.9
4	Excluding known risk factors,[a] do you agree that PLWH diagnosed with COVID-19 and concomitantly tuberculosis or other lung opportunistic infections (e.g. PJP) present the same risk of progression to severe disease compared with the general population?	64.7	61.8	20.6	11.8	82.4	67.6	14.7	11.8	.	.	.	.
5	Do you agree that all PLWH with CD4+ T cells <200/mm^3 and/or AIDS diagnosed with symptomatic mild/moderate COVID-19, without evidence of respiratory failure and/or normal oxygen saturation, need anyway a chest CT scan as initial assessment?	41.2	41.2	38.2	29.4	47.1	47.1	41.2	35.3	8.8	58.8	5.9	26.5
6	Regardless of number of COVID-19 doses and timing from the last dose, would you recommend an anti-SARS-CoV-2 titration (anti-S/anti-RBD) for PLWH with CD4+ T cells count <200/mm^3 and/or AIDS, before administration of a monoclonal antibodies therapy	52.9	50.0	29.4	23.5	79.4	61.8	14.7	11.8	.	.	.	.
7	To evaluate SARS-CoV-2 negativization, do you agree that PLWH need to be tested only with RT-PCR test—instead of SARS-CoV-2 antigen testing given the diagnostic performances of these tests?	58.8	67.7	17.7	11.8	85.3	79.4	2.9	2.9	.	.	.	.
8	Do you agree that considering chronic inflammation on HIV, PLWH irrespective of CD4+ T cells count and diagnosed with mild/moderate COVID-19 should receive treatment with nirmatrelvir/ritonavir OR remdesivir according to availability and possible drug −drug interactions?	47.1	29.4	41.2	35.3	64.7	44.1	29.4	29.4	11.8	67.6	5.9	14.7
9	Due to a high probability of persistent SARS-CoV-2 shedding, do you agree that PLWH with CD4+ T cells <200/mm^3 and/or AIDS diagnosed with COVID-19 pneumonia should receive treatment with nirmatrelvir/r PLUS remdesivir	35.3	50.0	41.2	38.2	61.8	58.8	29.4	29.4	6.1	69.7	0.0	24.2
10	Due to a high probability of persistent SARS-CoV-2 shedding, do you agree that PLWH with CD4+ T cells count <200/mm^3 and/or AIDS diagnosed with COVID-19 pneumonia should receive antiviral treatment with nirmatrelvir/r OR remdesivir with longer course of therapy whenever possible?	32.4	47.1	50.0	29.4	55.9	64.7	32.4	23.5	5.9	76.5	5.9	11.8
11	Due to a higher probability of persistent SARS-CoV-2 shedding, do you agree that PLWH with CD4+ T cells count <200/mm^3 and/or AIDS diagnosed with COVID-19 should receive combined treatment with an antiviral (remdesivir OR nirmatrelvir/r) AND a monoclonal antibody?	41.2	61.8	29.4	14.7	70.6	85.3	2.9	0.0	.	.	.	.
12	Do you agree that PLWH with CD4+ T cells 200−350/mm^3 diagnosed with symptomatic mild/moderate COVID-19, independently from other risk factors for clinical progression, have to receive nirmatrelvir/ritonavir OR remdesivir?	23.5	26.5	61.8	35.3	35.3	38.2	52.9	26.5	0.0	52.9	17.6	29.4
13	Due to a high probability of persistent SARS-CoV-2 shedding, do you agree that PLWH with CD4+ T cells count 200−350/mm^3 diagnosed with COVID-19 pneumonia should receive treatment with nirmatrelvir/ritonavir PLUS remdesivir OR longer courses of treatments?	55.9	67.7	23.5	5.9	73.5	76.5	8.8	5.9	8.8	88.2	2.9	0.0
14	Due to a higher probability of persistent SARS-CoV-2 shedding, do you agree that PLWH with CD4+ T cell count 200−350/mm^3 diagnosed with COVID-19 should receive combined treatment with an antiviral (remdesivir or nirmatrelvir/ritonavir) AND a monoclonal antibody?	61.8	67.7	20.6	8.8	85.3	85.3	2.9	0.0	.	.	.	.
15	Do you agree that PLWH with CD4+ T cells count <200/mm^3 and/or AIDS diagnosed with severe COVID-19 should receive high dosage of corticosteroid therapy (6 mg dexamethasone for 10 days)?	14.7	20.6	44.1	67.7	8.8	5.9	52.9	85.3	.	.	.	.
16	Do you agree that all PLWH with AIDS-defining opportunistic infections diagnosed with COVID-19 pneumonia and respiratory failure, requiring to be treated with corticosteroids, have to receive the course of steroid therapy recommended for COVID-19 as in the general population (6 mg dexamethasone for 10 days) independently from other risk factors for clinical progression?	5.9	5.9	64.7	85.3	.	.	.	.	.	.	.	.
17	Do you agree that the use of corticosteroids therapy with higher dosage and/or longer courses as a treatment for post-COVID-19 fibrosis/organizing pneumonia is contraindicated in PLWH with CD4+ T cells count <350 cells/mm^3?	38.2	58.8	32.4	17.7	61.8	70.6	20.6	17.6	0.0	91.2	0.0	8.8
18	Do you agree that, to receive nirmatrelvir/ritonavir, all PLWH diagnosed with mild/moderate COVID-19, on antiretroviral treatment with pharmacokinetic booster ritonavir or cobicistat, have to eventually modify their cART regimens, due to potential toxicities?	23.5	35.3	52.9	41.2	32.4	41.2	58.8	50.0	0.0	55.9	5.9	38.2
19	Regarding COVID-19 pre-exposure prophylaxis with monoclonal antibodies, do you agree with the inclusion of PLWH irrespective of CD4+ T cells count but only if they have known risk factors (e.g. immunosuppressive conditions)?	32.4	23.5	52.9	47.1	23.5	20.6	70.6	50.0	0.0	20.6	5.9	73.5
20	Regarding COVID-19 pre-exposure prophylaxis with monoclonal antibodies, do you agree with the inclusion of PLWH only with CD4+ T cells count <200/mm^3 and/or AIDS and without other known risk factors (e.g. immunosuppressive conditions)?	29.4	29.4	61.8	41.2	23.5	20.6	73.5	52.9	0.0	20.6	8.8	70.6
21	Do you agree with considering the PLWH irrespective of CD4 count a priority in vaccination campaigns along with other immunosuppressed patients?	2.9	11.8	67.7	61.8	5.9	11.8	82.4	64.7	.	.	.	.

(*continued on next page*)

Table 1 (*continued*)

	Question	Round 1				Round 2				Round 3			
		SD (%)	MD (%)	MA (%)	SA (%)	SD (%)	MD (%)	MA (%)	SA (%)	SD (%)	MD (%)	MA (%)	SA (%)
22	Do you agree that PLWH with CD4+ T cells count <200/mm^3 and/or AIDS should be vaccinated annually for COVID-19 as in the case of other vaccines such as influenza?	5.9	2.9	55.9	82.4	.	.	.	.	.	.	.	.
23	Do you agree that PLWH with CD4+ T cells count 200–350/mm^3 should be vaccinated annually for COVID-19 as in the case of other vaccines such as influenza?	0.0	8.8	61.8	79.4	.	.	.	.	.	.	.	.
24	Do you agree that PLWH with CD4+ T cells count >350/mm^3 should be vaccinated annually for COVID-19 as in the case of other vaccines such as influenza?	5.9	14.7	64.7	52.9	8.8	17.6	73.5	64.7	0.0	9.4	3.1	87.5
25	Do you agree that PLWH should be vaccinated annually for COVID-19 with a variant-adapted mRNA vaccine due to higher immunogenicity compared with others types of vaccines platforms (viral-vectors, recombinant protein-based, inactivated virus)?	5.9	11.8	58.8	73.5	2.9	8.8	76.5	79.4	.	.	.	.
26	Do you agree that to improve the immune response of COVID-19 vaccination in new diagnosis of HIV, one should wait for the virological suppression and CD4+ T cells recovery before vaccination?	32.4	47.1	38.2	20.6	50.0	58.8	35.3	29.4	0.0	88.2	0.0	11.8
27	Do you agree that to improve the immune response of COVID-19 vaccination in new diagnosis with CD4+ T cells <200/mm^3 and/or AIDS, one should undergo first to pre-exposure prophylaxis and once achieved CD4 count recovery (>200 cells/mm^3), receive COVID-19 vaccination?	32.4	50.0	38.2	23.5	44.1	67.6	32.4	23.5	0.0	85.3	5.9	8.8

cART, combined antiretroviral therapy; CT, computed tomography; MA, moderate agreement; MD, moderate disagreement; PJP, *Pneumocystis jirovecii* pneumonia; PLWH, people living with HIV; SA, strong agreement; SD, strong disagreement.

[a] General risk factors: older age, male sex, smoking, obesity, multimorbidity, especially pre-existing lung disease, renal insufficiency, diabetes mellitus, hypertension, and coronary heart disease.

with the general population?' The panel strongly disagreed by the second round, with a percentage of 94.1%.

Statement 2: 'PWH with CD4 cell count <200 cells/mm^3 and or AIDS, or lung opportunistic infections have a risk of COVID-19 progression higher than the general population compared for age and other risk factors' (strongly supported)

This consensus is in line with the growing evidence that PWH with CD4<200 cells/mm^3 or AIDS are at higher risk of progression while infected with SARS-CoV-2. Despite mixed previous results, more recent studies with larger sample sizes, complete viro-immunological data and adequate study design, led to this panel opinion [26,34,43,44]. PWH with CD4<200 cells/mm^3 had an impaired immune response leading to an increased vulnerability to viral infections, like COVID-19 and to other concomitant infectious complications [45]. Moreover, humoral and cellular response to COVID-19 vaccination is lower in this group [46].

Statement 3 is related to question #3 'Excluding known risk factors*, do you agree that PWH with CD4+ T cells between 200 and 350/mm^3 diagnosed with COVID-19 present the same risk of progression to severe disease compared with the general population?' that obtained 85.3% of moderate disagreement at the third round.

Statement 3: 'PWH with CD4 cell count 200–350 cells/mm^3 diagnosed with COVID-19 have a risk of COVID-19 progression higher than general population compared for age and other risk factors' (moderately supported)

Although recent literature supports more clearly the threshold of <200 CD4/mm^3, which has historically been associated with increased clinical risk of disease progression in HIV [47], few works have investigated the 350 CD4/mm^3 threshold with robust sample size and appropriate methodology, and for the panellist remain in the first rounds a 'grey zone', that depends on HIV viral load and the co-occurrence of other risk factors. Some studies identified a higher risk in PWH with CD4<350 cells/mm^3 without comparison with the HIV-negative group [48,49]. Still, Giacomelli et al. [43] instead identified a four-times higher risk of COVID-19 in-hospital death in PWH with CD4 between 200 and 350 cells/mm^3 compared with the general population of the same age strata. This is a large Italian study, well-known by some panellists and the iterative procedure of the Delphi study enabled also the consensus for CD4 between 200 and 350 cells/mm^3 strata. The strength of the statement compared with the previous one reflects the evidence currently available, which is more limited compared with the other threshold of CD4 count.

For question #4 'Excluding known risk factors, do you agree that PWH diagnosed with COVID-19 and concomitantly tuberculosis (TB) or other lung opportunistic infections (e.g. *Pneumocystis jirovecii* pneumonia [PJP]) present the same risk of progression to severe disease compared with general population?' the panellists strongly disagree with a percentage of 82.4% at the second round.

Statement 4: 'Excluding known risk factors, PWH diagnosed with COVID-19 and concomitantly TB or other lung opportunistic infections (e.g. PJP) present a higher risk of progression to severe disease compared with the general population' (strongly supported)

TB/COVID-19 coinfection has been extensively studied during the pandemic; both diseases have significant pulmonary involvement: COVID-19 pneumonia enhances TB progression and concomitantly TB—with HIV—exacerbate COVID-19 course, with impaired immune responses and increased angiotensinconverting enzyme 2 (ACE-2) expression in respiratory epithelial cells. In particular, the highest expression of ACE2 was identified in patients with TB/HIV co-infected COVID-19 [50,51]. Co-infections with HIV-related lung opportunistic infections are rare but reported particularly for PJP, essentially among severely immunosuppressed HIV. The current evidence is limited to different case reports but PJP infection appears to have several sequels among immunocompromised patients [52]. Furthermore, identifying COVID-19 and PJP coinfection is complicated because the two have clinical and radiological similarities, resulting in delays in diagnosis and treatments [53].

COVID-19 diagnostics and laboratory procedures

The panel addressed the diagnostic area through three questions (#5, #6, and #7, Table 1), resulting in two statements.

Question #6 'Regardless of number of COVID-19 doses and timing from the last dose, would you recommend an anti-SARS-CoV-2 titration (anti-S/anti-RBD) for PWH with CD4+ T cells count <200/mm^3 and/or AIDS, before administration of a MoAb therapy' obtained strongly disagreement by 79.4% of experts in the second round.

Statement 5: 'Anti-SARS-CoV-2 titration (anti-S/anti-RBD) for PWH with CD4+ T cells count <200/mm^3 and/or AIDS, is not recommended, regardless of the number of COVID-19 vaccine

Table 2
Statements on the management of COVID-19 among persons with HIV.

Statement no.	Statement	Agreement %	Round	Strength
Statement 1	PWH have a risk of COVID-19 progression higher than the general population compared for age and other risk factors, independently from CD4 and HIV-RNA	85.3	3rd	Moderate
Statement 2	PWH with CD4 cell count <200 cells/mm^3 and or AIDS, or lung opportunistic infections have a risk of COVID-19 progression higher than the general population compared for age and other risk factors	94.1	2nd	Strong
Statement 3	PWH with CD4 cell count 200–350 cells/mm^3 diagnosed with COVID-19 have a risk of COVID-19 progression higher than general population compared for age and other risk factors	85.3	3rd	Moderate
Statement 4	Excluding known risk factors, PWH diagnosed with COVID-19 and concomitantly tuberculosis or other lung opportunistic infections (e.g. PJP) present a higher risk of progression to severe disease compared with the general population	82.4	2nd	Strong
Statement 5	Anti-SARS-CoV-2 titration (anti-S/anti-RBD) for PWH with CD4+ T cells count <200/mm^3 and/or AIDS is not recommended, regardless of the number of COVID-19 doses and timing from the last dose, before administration of a monoclonal antibodies therapy	79.4	2nd	Strong
Statement 6	There is no need to test with RT-PCR—instead of SARS-CoV-2 antigen, to evaluate SARS-CoV-2 negativization in PWH	85.3	2nd	Strong
Statement 7	Combination treatment with two antiviral (remdesivir AND nirmatrelvir/ritonavir) OR longer course of treatment is not recommended for PWH with CD4+ T cells count 200–350/mm^3 and/or AIDS affected by COVID-19 pneumonia	88.2	3rd	Moderate
Statement 8	There is no need to treat PWH with CD4+ T cells count <200/mm^3 and/or AIDS affected by COVID-19, with a combined treatment with an antiviral (remdesivir OR nirmatrelvir/ritonavir) AND a monoclonal antibody, considering the circulating variant of concerns of Omicron sublineages and the currently available monoclonal antibody	85.3	2nd	Moderate
Statement 9	There is no need to treat PWH with CD4+ T cells count 200–350/mm^3 and/or AIDS affected by COVID-19, with a combined treatment with an antiviral (remdesivir OR nirmatrelvir/ritonavir) AND a monoclonal antibody, considering the circulating variant of concerns of Omicron sublineages and the currently available monoclonal antibody	85.3	2nd	Strong
Statement 10	PWH with CD4+ T cells count <200/mm^3 and/or AIDS diagnosed with severe COVID-19 should receive a high dosage of corticosteroid therapy (6 mg dexamethasone for 10 days)	85.3	2nd	Strong
Statement 11	PWH with AIDS-defining opportunistic infections diagnosed with COVID-19 pneumonia and respiratory failure, requiring to be treated with corticosteroids, have to receive the course of steroid therapy recommended for COVID-19 as in the general population (6 mg dexamethasone for 10 days) independently from other risk factors for clinical progression	85.3	1st	Strong
Statement 12	The use of higher dosage and/or longer courses of corticosteroids as treatment for post-COVID-19 fibrosis/organizing pneumonia is not contraindicated in PWH with CD4+ T cells count <350 cells/mm^3	91.2	3rd	Moderate
Statement 13	PWH should be prioritized in vaccination campaigns irrespective of CD4 count	82.4	2nd	Moderate
Statement 14	PWH with CD4+ T cell counts between <350/mm^3 and/or AIDS should receive annual COVID-19 vaccinations similar to influenza	82.4 79.4	1st 1st	Strong Strong
Statement 15	PWH with CD4+ T cell counts>350/mm^3 should receive annual COVID-19 vaccinations similar to influenza	87.5	3rd	Strong
Statement 16	PWH should receive annual COVID-19 vaccinations with a variant-adapted mRNA vaccine due to its higher immunogenicity compared with other platforms (viral vectors, recombinant protein-based, inactivated virus)	79.4	2nd	Strong
Statement 17	In newly diagnosed PWH, there is no need to wait until virological suppression and CD4+ T cell recovery to improve the immune response to COVID-19 vaccination	88.2	3rd	Moderate
Statement 18	Newly diagnosed PWH with CD4+ T cells <200/mm^3 and/or AIDS can receive COVID-19 vaccination without waiting for immunological recovery (CD4 >200 cells/mm^3) and without undergoing a previous pre-exposure prophylaxis	85.3	3rd	Moderate

PJP, *Pneumocystis jirovecii* pneumonia; PWH, people with HIV.

doses and timing from last dose, before administration of a MoAb therapy' (strongly supported)

The primary criticism—in the comments—focused on the lack of efficacy of current available MoAb. However, the challenge of obtaining fast results to start the treatment rapidly and the potential lack of correlation between the titration of anti-S/anti-RBD and the neutralization activity on the infecting VoCs should be also taken into account for not considering the SARS-CoV-2 Ab titration before administration of a MoAb therapy [54].

Eighty-five per cent of the experts strongly disagreed with the need for a more sensitive method to evaluate the negativization of SARS-CoV-2 (question #7, Table 1).

Statement 6: 'There is no need to test with RT-PCR—instead of SARS-CoV-2 Antigen, to evaluate SARS-CoV-2 negativization in PWH' (strongly supported)

Indeed, according to the WHO recommendations, SARS-CoV-2 antigen rapid detection tests (Ag-RDTs) are recommended for various uses, including primary case detection, contact tracing and testing negativization and enable additional individual and social benefits [55]. With the emergence of the COVID-19 pandemic, Ag-RDTs for SARS-CoV-2 became widely available. Although less accurate than the reference standard nucleic acid amplification tests, Ag-RDTs enabled easy-to-use and rapid point-of-care [56] and a sensitivity target of ≥80% has been recommended. Moreover, Ag-RDTs are effective in overcoming a limitation of rRT-PCR that can lead to persistent positive results after the period of transmission and recovery [55]. Several experts' comments stated that the test of cure should not be used in general for PWH, regardless of the method, referring to the period of contagiousness and release from isolation. In contrast, other experts suggested using the reference standard with RT-PCR, which minimizes the false negative, could be a valid option in PWH with CD4<200 cells/mm^3. Still, this remark did not go through the consensus of the panellists with a specific question. SARS-CoV-2 can cause persistent infections in subsets of severely immunocompromised individuals, contributing to post-COVID-19 condition pathology. Moreover, SARS-CoV-2 replication in subjects with suboptimal immune responses allows SARS-CoV-2 to evolve to other phenotypes/variants [57–60]. According to CDC guidelines [61], immunocompromised persons should be isolated for at least 10 days and their health status should be checked before isolation is suspended. In any case, it is impossible to generalize and an evaluation should be done case by case and in the epidemiological context is needed.

No consensus was obtained in all the rounds on question #5 regarding the usefulness of a chest CT scan as initial assessment in all PWH with CD4+ T cells <200/mm^3 and/or AIDS diagnosed with

symptomatic mild/moderate COVID-19, without evidence of respiratory failure and/or normal oxygen saturation.

Therapeutic management of COVID-19

Early treatment

This topic was addressed to the panel through six questions (#8–#14, Table 1).

Treatment with antivirals. Questions #8, #9, #10, #12, and #13 concerned the opportunity of using the two available antivirals as early treatment for COVID-19 (nirmatrelvir/ritonavir and remdesivir) among PWH with COVID-19 according to CD4 cell count strata and severity of disease.

The following statement related to question #13 (Table 1) obtained 88.2% of moderate disagreement in the third round.

Statement 7: 'Combination treatment with two antiviral (remdesivir and nirmatrelvir/ritonavir) OR longer course of treatment is not recommended for PWH with CD4+ T cells count 200–350/mm^3 and/or AIDS affected by COVID-19 pneumonia' (moderately supported)

In this case, the moderate disagreement seems to be mostly related to the absence of consistent data on the combined use of antivirals or the extension of treatment with antivirals to reduce viral shedding, not only in the PWH, but also in individuals with other immunodeficiencies [62]. Different authors have reported a high risk of the selection of mutant SARS-CoV-2 strains in immunocompromised hosts, including those with advanced HIV disease, increasing the risk of immune escape of vaccines and SARS-CoV-2 variants, with implications for vaccine breakthroughs and reinfections [59,63]. Nevertheless, published data on viral decay and nasopharyngeal swab negativization of combination therapy with double antivirals or prolonged single antiviral time in immunocompromised patients with different diseases are scarce and it is challenging to extrapolate consistent results. In particular, such data in PWH are anecdotal [64].

No consensus was obtained on using nirmatrelvir/ritonavir or remdesivir as early treatment for moderate/mild COVID-19, in PWH irrespective of CD4 cell count (question #8).

As refers to the group of PWH with CD4<200 cells/mm^3 and/or AIDS affected by COVID-19 pneumonia, it has not been reached any consensus on the usage of the combination of two antivirals together (question #9) nor a longer course of treatment (question #10).

Although the literature data on progression to severe COVID-19 indicate an increased risk in persons with CD4<350/mm^3 [43], the lack of consensus seems to be because CD4 alone does not reflect the individual risk of progression that may also correlate with other known risk factors.

Drug–drug interaction. The panel did not agree on question #18 on the need to modify boosted-based ART regimens to receive nirmatrelvir/ritonavir. The absence of consensus could be interpreted, according to the comments of the panel, with some opinions of marginal benefits of nirmatrelvir/ritonavir in PWH at low CD4 cell count (as suggested by the absence of consensus in questions #8 and #12). Furthermore, several panellists considered that the drug–drug interaction could be easily managed, without changing ART and just handling the potential toxicities to the higher dose of booster for only 5 days.

Combined treatment with MoAb and antivirals. The following statement refers to question #11, which obtained 85.3% of disagreement in the second round.

Statement 8: 'There is no need to treat PWH with CD4+ T cells count <200/mm^3 and/or AIDS affected by COVID-19, with a combined treatment with an antiviral (remdesivir OR nirmatrelvir/ritonavir) AND a monoclonal antibody, considering the circulating variant of concerns of Omicron sublineages and the currently available monoclonal antibody.' (moderately supported)

Statement 9 refers to question #14, which obtained 85.3% of consensus in the second round.

Statement 9: 'There is no need to treat PWH with CD4+ T cells count 200–350/mm^3 and/or AIDS affected by COVID-19, with a combined treatment with an antiviral (remdesivir OR nirmatrelvir/ritonavir) AND a monoclonal antibody, considering the circulating variant of concerns of Omicron sublineages and the currently available monoclonal antibody.' (strongly supported)

As referred in the two statements previously, on the use of combined treatment of antiviral treatment and MoAb in PWH according to CD4 cell count, the disagreement expressed by the panel seems to be due to the lack of therapeutic utility of the current MoAb against circulating VoC of SARS-CoV-2 [54]. The difference in the strengths between statements 8 and 9 is due to the concerns of some panellists to treat with only one drug severely immunosuppressed patients, even if current available MoAbs might not be effective. Although data on MoAbs efficacy against more recent VoC such as Omicron variants from *in vitro* studies are known, the effects on hospitalization and mortality are still controversial. Meta-analyses [65,66] showed that using MoAbs reduces the risk of hospitalization and death in patients with COVID-19 but did not include Omicron-positive patients. Other studies showed beneficial effects concerning clinical outcomes when MoAbs were administered either as prophylaxis or during the first 7 days from the onset of symptoms among SARS-CoV-2 Omicron-positive patients, with a reduction of probability for hospitalization by 44% in favour of SARS-CoV-2 Omicron-positive patients treated with MoAbs [67]. Specific concerns may be suggested for immunocompromised individuals, because the use of sotrovimab has been associated with SARS-CoV-2 evolution, leading to the development of mutations within the spike protein at positions 337 or 340 associated with resistance [68]. It is reasonable that the conflicting results on this aspect, particularly in PWH with CD4 cell count <350 cells/mm^3, could have led to the negative agreement on these two statements.

Corticosteroids

The questions regarding this topic (#15–#17) obtained high percentages of concordance, resulting in the following statements:

Statement 10: 'PWH with CD4+ T cells count <200/mm^3 and/or AIDS diagnosed with severe COVID-19 should receive a high dosage of corticosteroid therapy (6 mg dexamethasone for 10 days)' (strongly supported)

This statement, related to question #15, obtained 85.3% of agreement in the second round.

Statement 11: 'PWH with AIDS-defining opportunistic infections diagnosed with COVID-19 pneumonia and respiratory failure, requiring to be treated with corticosteroids, have to receive the course of steroid therapy recommended for COVID-19 as in the general population (6 mg dexamethasone for 10 days) independently from other risk factors for clinical progression' (strongly supported).

This statement obtained 85.3% agreement in the first round (question #16).

The strong agreement between these two statements is related to the robust evidence of clinical efficacy for the use of corticosteroids in COVID-19 pneumonia, which has demonstrated efficacy even in the presence of immunosuppression and whose positive effect does not appear to be affected by the degree of

immunodepression, either in terms of efficacy or safety [69]. Nevertheless, it should be pointed out that in RECOVERY trial PWH represented a very small proportion of immunosuppressed patients, so conclusions on PWH should be more cautious.

In contrast, the panel reached a consensus for moderate disagreement (91.2%) only in the third round to question #17 'Do you agree that the use of corticosteroids therapy with higher dosage and/or longer courses as a treatment for post-COVID-19 fibrosis/organizing pneumonia is contraindicated in people living with HIV with CD4+ T cells count <350 cells/mm^3?' resulting in the following statement:

Statement 12: 'The use of higher dosage and/or longer courses of corticosteroids as treatment for post-COVID-19 fibrosis/organizing pneumonia is not contraindicated in PWH with CD4+ T cells count <350 cells/mm^3' (moderately supported)

In the case of persistent lung interstitial involvement after COVID-19 pneumonia, systemic glucocorticoids are frequently used. The corticosteroid treatment downregulates a broad spectrum of proinflammatory and pro-fibrotic molecules (interleukin [IL]-1, IL-2, IL-4, IL-5, IL-8, IL-13, ICAM, VCAM, etc.). It can thus help to resolve inflammatory and fibrogenic changes through multiple pathways [70]. However, the appropriate timing of the treatment is likely essential and it has not been defined. The existing literature suggests possible benefits of glucocorticoids for selected individuals with a respiratory form of post-COVID-19 syndrome, especially in cases of persistent organizing pneumonia, but their general use is currently not recommended [71–73], in particular, no studies are available in PWH where the contraindication and side effects of corticosteroids may counterbalance the efficacy on lung function.

Preventive strategies

Pre-exposure prophylaxis

No statement has been established on PrEP strategies for PWH, as both questions #19 and #20 did not obtain consensus by the panel.

In detail, question #19 'Regarding COVID-19 PrEP with MoAb, do you agree with the inclusion of PWH irrespective of CD4+ T cell count but only if they have known risk factors (e.g. immunosuppressive conditions)?' and question #20 'Regarding COVID-19 PrEP with MoAb, do you agree with the inclusion of PWH only with CD4+ T cell count <200/mm^3 and/or AIDS, and without other known risk factors (e.g. immunosuppressive conditions)?' reached agreement rates in the final round of 73.5% and 70.6%, respectively.

The lack of consensus is attributed to concerns about the current ineffectiveness of MoAb tixagevimab/cilgavimab against the most recent circulating variants [74]. These views are based on existing data on the general effectiveness of PrEP in immunocompromised individuals using tixagevimab/cilgavimab. It is worth noting that there have been contentious issues on the appropriate dosage of this compound during the Omicron era, as a consequence, the food and drug administration (FDA) in February 2022 supported a double dose (300/300 mg instead of 150/150 mg), and then pausing and withdrawing authorization in the United States [75]. In contrast, the European Medicines Agency, continued to support using this compound as a PrEP strategy, though not for treatment, with a 150/150 mg dosage. Thus, it has remained a preventive strategy in Europe for immunocompromised patients, with varying efficacy rates depending on the immunocompromising condition and circulating Omicron variants [76].

A noteworthy recent meta-analysis [76] suggests that tixagevimab/cilgavimab used for PrEP effectively prevented COVID-19, with no significant differences between low and high dosages (300 mg vs. 600 mg). However, it should be highlighted that tixagevimab/cilgavimab was not tested at all in PWH.

COVID-19 vaccination

Seven questions have addressed the COVID-19 vaccination section (#21 to #28, Table 1).

In round 2, the panel reached moderate agreement (82.4%, question #21) on prioritizing vaccination for PWH regardless of CD4 count at the time of vaccination.

Statement 13: 'PWH should be prioritized in vaccination campaigns irrespective of CD4 count' (moderately supported)

Several considerations lead to this statement. It is agreed that PWHs have a higher risk of severe outcomes from COVID-19 infection [6,28,29,32]. Vaccines have played a crucial role in controlling the pandemic, although immunosuppressed patients with AIDS were not included in all phase 2/3 trials. Observational studies involving PWH showed that HIV infection is linked to altered cellular and humoral immune responses, particularly in untreated or chronic infections. Even PWH with suppressed viral loads can have chronic immune impairments, such as partially recovered CD4 counts and persistent immune activation and dysfunction related to HIV [77]. These conditions may lead to suboptimal antibody production and reduced vaccine efficacy; indeed, reduced antibody responses have been observed in PWH with AIDS after vaccinations for agents like *Streptococcus pneumoniae*, tetanus toxoid, influenza, and hepatitis B [78,79].

In response to questions #22 and #23, the panel reached a strong consensus in the first round, with 82.4% and 79.4% agreement, respectively.

Statement 14. 'PWH with CD4+ T cell counts between <350/mm^3 and/or AIDS should receive annual COVID-19 vaccinations similar to influenza' (strongly supported)

Some comments noted the lack of concrete evidence and the need for more data. However, it is widely recognized that SARS-CoV-2, like influenza, poses a serious threat to PWH not on ART, those with low CD4 counts, alongside other immunocompromised individuals. Observational studies have demonstrated that PWH with low CD4 counts respond less effectively to vaccination [80]. Two studies specifically examined the humoral and cellular immune response in PWH with CD4 counts <200 cells/mm^3 and with or without AIDS, finding that, after adjusting for confounding factors, these individuals had significantly lower IgG titres, neutralizing antibodies, and T cell responses compared to PWH with CD4 counts above 500 cells/mm^3 and HIV-negative controls [46,81].

The panel reached a strong agreement only after three rounds (87.5%) for question #24, leading to the following statement.

Statement 15: 'PWH with CD4+ T cell counts>350/mm^3 should receive annual COVID-19 vaccinations similar to influenza' (strongly supported)

Data on the vaccine response in PWH with CD4 counts between 200 and 500 cells/mm^3 are less consistent. Several studies and meta-analyses found that CD4 count ≥350 cells/mm^3 and receiving mRNA-based COVID-19 vaccines were independently associated with a higher likelihood of vaccine response than <200/mm^3 and comparable to those found in the general population without HIV infection [82,83]. Nevertheless, a booster dose could help restore higher antibody levels, which are retained for around 5 months when considering the original virus strain, but for a shorter time against Omicron sublineages.

The panel strongly agreed (79.4% in the second round) with the statement from question #25 (Table 1), resulting in the following statement.

Statement 16: 'PWH should receive annual COVID-19 vaccinations with a variant-adapted mRNA vaccine due to its higher immunogenicity compared with other platforms (viral vectors,

recombinant protein-based, inactivated virus)' (strongly supported)

SARS-CoV-2, like other RNA viruses, mutates rapidly, leading to new variants. As a result, vaccines targeting current Omicron subvariants were introduced during recent campaigns for vulnerable groups, including PWH. Efficacy data on new vaccines, in terms of humoral responses (neutralizing antibodies, anti-S/RBD IgG) and T cell responses in PWH, show varying effectiveness based on circulating variants, with better responses to vaccines that target specific variants [84,85]. Some studies and meta-analysis suggest that mRNA vaccines are most strongly associated with a robust humoral response in PWH compared with other platforms [86,87]. However, unpublished studies indicate promising results for targeted protein vaccines as well.

For questions #26 and #27 (see Table 1) the panel moderately disagreed, with 88.2% and 85.3% disagreement in the third round.

Statement 17: 'In newly diagnosed PWH, there is no need to wait until virological suppression and CD4+ T cell recovery to improve the immune response to COVID-19 vaccination' (moderately supported)

Statement 18: 'Newly diagnosed PWH with CD4+ T cells <200/mm^3 and/or AIDS can receive COVID-19 vaccination without waiting for immunological recovery (CD4>200 cells/mm^3) and without undergoing a previous PrEP' (moderately supported)

The comments highlighted a lack of evidence to support delaying vaccination and the potential detrimental effect of not vaccinating in time, which could increase the risk of severe COVID-19. One alpha/delta era study showed that 86% of PWH with CD4 counts below 200 cells/mm^3 developed a serological response and 70% developed a neutralizing response after receiving mRNA vaccines, and a satisfactory T cell response [46].

Limitations

Although Delphi is a reliable method for assessing degrees of consensus in different areas where scientific evidence is weak, it has several limitations unique to the methodology added to the specific limits of our study. First, it must be recognized that the evidence derived from a process of expert opinions is at the lower level in the hierarchy of evidence and cannot, and is not intended to, substitute more robust evidence from the literature.

Second, the domains investigated and the final set of questions were conceived by a research team composed of members of the steering committee of Icona Foundation in the same country (Italy), potentially introducing bias in selecting the issues to be addressed. In every Delphi survey, identifying areas of concern is one of the main challenges along with constructing the panel of experts. Despite the efforts to build a heterogenous panel, our study over-represented judgements of European experts, mainly Italian, and it included only four experts from Argentina as representatives of middle-income countries. Need to be noted panellists from sub-Saharan African nations are lacking. The research team a priori decided to not include them because the impact and the management of HIV and COVID are very different from the experience of European and South African physicians. Furthermore, the HIV/AIDS field has been historically a successful example of how the active involvement of PWH together with clinicians and policy-makers led to positive results in terms of health interventions [88,89]. A truly people-centred healthcare approach must undergo patients' opinions in every process that could lead to a health decision. However, due to the technical topics and details covered in this Delphi, it was decided to limit the panel to infectious diseases specialists.

Moreover, all the procedures were conducted using anonymous surveys, and there was no live meeting at the end of the three rounds, where the panellists could discuss individual opinions and final results together. However, the experts could express the reasons underlying their opinions in an open-text box, leading to a more comprehensive view of those issues. Nevertheless, the statements of this Delphi study were circulated among the panellists to obtain their approval.

Finally, some critical areas did not obtain a consensus (*pre-exposure prophylaxis* section) or did not have a clear expert opinion indication, like how to handle early treatment strategies among PWH, reflecting the status of knowledge by literature evidence on these fields.

Conclusions

Management of adult COVID-19 remains a challenge, particularly for a group of socially- and health-fragile individuals like PWH, with pending questions and new issues constantly being formulated by the evolving pandemic. A total of 18 statements have been proposed as the results of this work, representing the expert opinion based on available evidence and the personal view on four significant areas of COVID-19/HIV coinfection. These statements represent a guide on improving clinical management and therefore health of PWH. Briefly, the panel expressed a consensus on the higher risk of COVID-19 progression among PWH, particularly those with lower CD4 cell strata and opportunistic infections; confirmed the role of SARS-CoV-2 antigen assay in monitoring viral negativization of SARS; renewed the perplexity on the use of MoAb in the current Omicron scenario, as well as the combination of two antivirals together or with longer courses; recommended the use of high-dosage corticosteroids also for severely immunosuppressed PWH with COVID-19 pneumonia and also did not express contraindication on its usage for post-COVID-19 lung fibrosis. Above all, the panel highlighted the key role of prevention in this fragile group, with the need to prioritize PWH for COVID-19 annual vaccination campaigns, regardless of CD4 cell count and using mRNA-based vaccine. Moreover, the panel suggested vaccinating PWH with <200 CD4/mm^3 without waiting for viral suppression, immunological recovery and PrEP for COVID-19. The results of this consensus highlight that, among the most relevant clinical aspects in the management of PWH and COVID-19, therapeutic strategies aimed at preventing progression to a severe form of COVID-19 through the use of unconventional therapies such as the combination of two antiviral drugs, or an antiviral and a monoclonal antibody, or even using the same therapies for longer periods, did not reach consensus among experts. Although this outcome might have been expected due to the lack of guidelines in this area, it also emphasizes the need for ad hoc studies in this specific population, with adequate sample sizes, to define the proper use of such therapeutic strategies.

New evidence will emerge in the next years and the understanding of COVID-19 and the epidemiological scenario will evolve. Therefore, our statements are to be considered for the historical period in which the study was conceived and conducted (2023–2024) and ideally should be periodically updated.

Beyond its immediate clinical implications, this Delphi process underscores the value of establishing networks of experts who can rapidly generate consensus-driven recommendations in the face of emerging infectious diseases. The iterative and inclusive nature of the Delphi method facilitates the synthesis of different perspectives and the incorporation of evolving evidence, providing a dynamic framework for adapting clinical practice in real time during a pandemic. Furthermore, as we move towards an era of increasingly sophisticated data analysis and evidence synthesis tools, the Delphi process can be streamlined and enhanced through automation. The lessons learned from this study can inform the development of future platforms for real-time evidence assessment and guideline

generation, enabling a more agile and effective response in vulnerable populations to future public health crises.

Author contributions

A.T., A.V., A.C., F.B., A.d.M., M.G.C., Z.R.P.-B., and E.T. were responsible for conception and design of study. A.M.A., A.A., and G.L.H. were responsible for acquisition of data. A.T., A.V., A.C., and A.d.M. were responsible for the interpretation of the data. A.T. was responsible for formal analysis. A.T., A.V., A.C., and A.d.M. were responsible for writing—original draft preparation. All the authors were responsible for review and editing, and they have read and agreed to the published version of the manuscript. A.T. and A.V. contributed equally to this work.

Transparency declaration

Potential conflict of interest

The authors declare that they have no conflicts of interest.

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Data availability

Data will be available from the corresponding author on reasonable request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cmi.2025.03.006.

References

[1] World Health Organization. COVID-19 cases | WHO COVID-19 dashboard n.d. https://data.who.int/dashboards/covid19/cases. Accessed September 17, 2024.
[2] World Health Organization. HIV data and statistics n.d. https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/hiv/strategic-information/hiv-data-and-statistics. [Accessed 17 September 2024].
[3] Shiau S, Krause KD, Valera P, Swaminathan S, Halkitis PN. The burden of COVID-19 in people living with HIV: a syndemic perspective. AIDS Behav 2020;24:2244–9. https://doi.org/10.1007/s10461-020-02871-9.
[4] Augello M, Bono V, Rovito R, Tincati C, Marchetti G. Immunologic interplay between HIV/AIDS and COVID-19: adding fuel to the flames? Curr HIV/AIDS Rep 2023;20:51–75. https://doi.org/10.1007/s11904-023-00647-z.
[5] Braunstein SL, Lazar R, Wahnich A, Daskalakis DC, Blackstock OJ. Coronavirus disease 2019 (COVID-19) infection among people with human immunodeficiency virus in New York City: a population-level analysis of linked surveillance data. Clin Infect Dis 2021;72:e1021–9. https://doi.org/10.1093/cid/ciaa1793.
[6] Ambrosioni J, Blanco JL, Reyes-Urueña JM, Davies M-A, Sued O, Marcos MA, et al. Overview of SARS-CoV-2 infection in adults living with HIV. Lancet HIV 2021;8:e294–305. https://doi.org/10.1016/S2352-3018(21)00070-9.
[7] Clinical Info HIV.gov. Guidance COVID-19 and people HIV n.d. https://clinicalinfo.hiv.gov/en/page-404. [Accessed 17 September 2024].
[8] Nasa P, Jain R, Juneja D. Delphi methodology in healthcare research: how to decide its appropriateness. World J Methodol 2021;11:116–29. https://doi.org/10.5662/wjm.v11.i4.116.
[9] Tsui S, Denison JA, Kennedy CE, Chang LW, Koole O, Torpey K, et al. Identifying models of HIV care and treatment service delivery in Tanzania, Uganda, and Zambia using cluster analysis and Delphi survey. BMC Health Serv Res 2017;17:811. https://doi.org/10.1186/s12913-017-2772-4.
[10] Batterham RL, Bedimo RJ, Diaz RS, Guaraldi G, Lo J, Martínez E, et al. Cardiometabolic health in people with HIV: expert consensus review. J Antimicrob Chemother 2024;79:1218–33. https://doi.org/10.1093/jac/dkae116.
[11] Boffito M, Ryom L, Spinner C, Martinez E, Behrens G, Rockstroh J, et al. Clinical management of ageing people living with HIV in Europe: the view of the care providers. Infection 2020;48:497–506. https://doi.org/10.1007/s15010-020-01406-7.
[12] Maggiolo F, Lo Caputo S, Bonora S, Borderi M, Cingolani A, D'Ettorre G, et al. Optimizing the antiretroviral treatment focusing on long-term effectiveness and a person-centered approach. Consensus guidance using a Delphi process. New Microbiol 2024;46:367–80. PMID: 38252048.
[13] Soriano JB, Murthy S, Marshall JC, Relan P, Diaz JV. WHO clinical case definition working group on post-COVID-19 condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis 2022;22:e102–7. https://doi.org/10.1016/S1473-3099(21)00703-9.
[14] Escobar C, Bover Freire R, García-Moll Marimón X, González-Juanatey C, Morillas M, Valle Muñoz A, et al. A Delphi consensus on the management of anticoagulation in the COVID-19 pandemic: the Monaco study. Cardiovasc Diagn Ther 2023;13:777–91. https://doi.org/10.21037/cdt-23-76.
[15] Rabie AA, Elhazmi A, Azzam MH, Abdelbary A, Labib A, Combes A, et al. Expert consensus statement on venovenous extracorporeal membrane oxygenation ECMO for COVID-19 severe ARDS: an international Delphi study. Ann Intensive Care 2023;13:36. https://doi.org/10.1186/s13613-023-01126-9.
[16] ORCHESTRA - EU Horizon 2020 cohort to tackle COVID-19 internationally. Orch Cohort n.d. https://orchestra-cohort.eu/. [Accessed 17 September 2024].
[17] Azzini AM, Canziani LM, Davis RJ, Mirandola M, Hoelscher M, Meyer L, et al. How European research projects can support vaccination strategies: the case of the ORCHESTRA project for SARS-CoV-2. Vaccines 2023;11:1361. https://doi.org/10.3390/vaccines11081361.
[18] Fondazione ICONA - Italian cohort Naive antiretrovirals. n.d. https://www.fondazioneicona.org/index.php. [Accessed 17 September 2024].
[19] Okoli C, Pawlowski SD. The Delphi method as a research tool: an example, design considerations and applications. Inf Manag 2004;42:15–29. https://doi.org/10.1016/j.im.2003.11.002.
[20] Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research Electronic Data Capture (REDCap) - a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009;42:377–81. https://doi.org/10.1016/j.jbi.2008.08.010.
[21] Blanco JL, Ambrosioni J, Garcia F, Martínez E, Soriano A, Mallolas J, et al. COVID-19 in patients with HIV: clinical case series. Lancet HIV 2020;7:e314–6. https://doi.org/10.1016/S2352-3018(20)30111-9.
[22] Vizcarra P, Pérez-Elías MJ, Quereda C, Moreno A, Vivancos MJ, Dronda F, et al. Description of COVID-19 in HIV-infected individuals: a single-centre, prospective cohort. Lancet HIV 2020;7:e554–64. https://doi.org/10.1016/S2352-3018(20)30164-8.
[23] Gervasoni C, Meraviglia P, Riva A, Giacomelli A, Oreni L, Minisci D, et al. Clinical features and outcomes of patients with human immunodeficiency virus with COVID-19. Clin Infect Dis 2020;71:2276–8. https://doi.org/10.1093/cid/ciaa579.
[24] Western Cape Department of Health in collaboration with the National Institute for Communicable Diseases, South Africa. Risk factors for coronavirus disease 2019 (COVID-19) death in a population cohort study from the Western Cape Province, South Africa. Clin Infect Dis 2021;73:e2005–15. https://doi.org/10.1093/cid/ciaa1198.
[25] Tesoriero JM, Swain CE, Pierce JL, Zamboni L, Wu M, Holtgrave DR, et al. COVID-19 outcomes among persons living with or without diagnosed HIV infection in New York State. JAMA Netw Open 2021;4:e2037069. https://doi.org/10.1001/jamanetworkopen.2020.37069.
[26] Yang X, Sun J, Patel RC, Zhang J, Guo S, Zheng Q, et al. Associations between HIV infection and clinical spectrum of COVID-19: a population level analysis based on US National COVID cohort collaborative (N3C) data. Lancet HIV 2021;8:e690–700. https://doi.org/10.1016/S2352-3018(21)00239-3.
[27] Bhaskaran K, Rentsch CT, MacKenna B, Schultze A, Mehrkar A, Bates CJ, et al. HIV infection and COVID-19 death: a population-based cohort analysis of UK primary care data and linked national death registrations within the OpenSAFELY platform. Lancet HIV 2021;8:e24–32. https://doi.org/10.1016/S2352-3018(20)30305-2.
[28] Geretti AM, Stockdale AJ, Kelly SH, Cevik M, Collins S, Waters L, et al. Outcomes of coronavirus disease 2019 (COVID-19) related hospitalization among people with human immunodeficiency virus (HIV) in the ISARIC World Health Organization (WHO) clinical characterization protocol (UK): a prospective

observational study. Clin Infect Dis 2021;73:e2095–106. https://doi.org/10.1093/cid/ciaa1605.
[29] Bertagnolio S, Thwin SS, Silva R, Nagarajan S, Jassat W, Fowler R, et al. Clinical features of, and risk factors for, severe or fatal COVID-19 among people living with HIV admitted to hospital: analysis of data from the WHO global clinical platform of COVID-19. Lancet HIV 2022;9:e486–95. https://doi.org/10.1016/S2352-3018(22)00097-2.
[30] World Health Organization. Clinical features and prognostic factors of COVID-19 in people living with HIV hospitalized with suspected or confirmed SARS-CoV-2 infection n.d. https://iris.who.int/bitstream/handle/10665/342697/WHO-2019-nCoV-Clinical-HIV-2021.1-eng.pdf. [Accessed 17 September 2024].
[31] Mellor MM, Bast AC, Jones NR, Roberts NW, Ordóñez-Mena JM, Reith AJM, et al. Risk of adverse coronavirus disease 2019 outcomes for people living with HIV. AIDS Lond Engl 2021;35:F1–10. https://doi.org/10.1097/QAD.0000000000002836.
[32] Danwang C, Noubiap JJ, Robert A, Yombi JC. Outcomes of patients with HIV and COVID-19 co-infection: a systematic review and meta-analysis. AIDS Res Ther 2022;19:3. https://doi.org/10.1186/s12981-021-00427-y.
[33] McGowan VJ, Bambra C. COVID-19 mortality and deprivation: pandemic, syndemic, and endemic health inequalities. Lancet Public Health 2022;7:e966–75. https://doi.org/10.1016/S2468-2667(22)00223-7.
[34] Wit FWNM, Reiss P, Rijnders B, Rokx C, Roukens A, Brinkman K, et al. COVID-19 in people with HIV in The Netherlands. AIDS 2023;37:1671–81. https://doi.org/10.1097/QAD.0000000000003597.
[35] Nomah DK, Díaz Y, Bruguera A, Moreno-Fornés S, Aceiton J, Reyes-Urueña J, et al. Disparities in coronavirus disease 2019 clinical outcomes and vaccination coverage among migrants with human immunodeficiency virus in the PISCIS cohort: a population-based propensity score-matched analysis. Open Forum Infect Dis 2024;11:ofad693. https://doi.org/10.1093/ofid/ofad693.
[36] Tavelli A, Cicalini S, Barbanotti D, Antinori S, Segala D, Guaraldi G, et al. Proportion of PLWH not vaccinated for COVID-19 in Italy and predictors, #865; CROI 2022: Conference on Retroviruses and opportunistic infection Virtual. 12-16 February 2022. https://www.croiconference.org/abstract/proportion-of-plwh-not-vaccinated-for-covid-19-in-italy-and-predictors/. [Accessed 18 September 2024].
[37] Triant VA. Cardiovascular disease and HIV infection. Curr HIV/AIDS Rep 2013;10:199–206. https://doi.org/10.1007/s11904-013-0168-6.
[38] Fitzpatrick ME, Kunisaki KM, Morris A. Pulmonary disease in HIV-infected adults in the era of antiretroviral therapy. AIDS Lond Engl 2018;32:277–92. https://doi.org/10.1097/QAD.0000000000001712.
[39] Winston JA. HIV and CKD epidemiology. Adv Chronic Kidney Dis 2010;17:19–25. https://doi.org/10.1053/j.ackd.2009.08.006.
[40] Silverberg MJ, Leyden W, Hernández-Ramírez RU, Qin L, Lin H, Justice AC, et al. Timing of antiretroviral therapy initiation and risk of cancer among persons living with human immunodeficiency virus. Clin Infect Dis 2021;72:1900–9. https://doi.org/10.1093/cid/ciaa1046.
[41] Guaraldi G, Bonfanti P, Di Biagio A, Gori A, Milić J, Saltini P, et al. Evidence gaps on weight gain in people living with HIV: a scoping review to define a research agenda. BMC Infect Dis 2023;23:230. https://doi.org/10.1186/s12879-023-08174-3.
[42] De Wit S, Sabin CA, Weber R, Worm SW, Reiss P, Cazanave C, et al. Incidence and risk factors for new-onset diabetes in HIV-infected patients: the data collection on adverse events of anti-HIV drugs (D:A:D) study. Diabetes Care 2008;31:1224–9. https://doi.org/10.2337/dc07-2013.
[43] Giacomelli A, Gagliardini R, Tavelli A, De Benedittis S, Mazzotta V, Rizzardini G, et al. Risk of COVID-19 in-hospital mortality in people living with HIV compared to general population according to age and CD4 strata: data from the ICONA network. Int J Infect Dis 2023;136:127–35. https://doi.org/10.1016/j.ijid.2023.09.015.
[44] Dandachi D, Geiger G, Montgomery MW, Karmen-Tuohy S, Golzy M, Antar AAR, et al. Characteristics, comorbidities, and outcomes in a multicenter registry of patients with human immunodeficiency virus and coronavirus disease 2019. Clin Infect Dis 2021;73:e1964–72. https://doi.org/10.1093/cid/ciaa1339.
[45] Höft MA, Burgers WA, Riou C. The immune response to SARS-CoV-2 in people with HIV. Cell Mol Immunol 2024;21:184–96. https://doi.org/10.1038/s41423-023-01087-w.
[46] Antinori A, Cicalini S, Meschi S, Bordoni V, Lorenzini P, Vergori A, et al. Humoral and cellular immune response elicited by mRNA vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in people living with human immunodeficiency virus receiving antiretroviral therapy based on current CD4 T-lymphocyte count. Clin Infect Dis 2022;75:e552–63. https://doi.org/10.1093/cid/ciac238.
[47] Baker JV, Peng G, Rapkin J, Abrams DI, Silverberg MJ, MacArthur RD, et al. CD4+ count and risk of non-AIDS diseases following initial treatment for HIV infection. AIDS Lond Engl 2008;22:841–8. https://doi.org/10.1097/QAD.0b013e3282f7cb76.
[48] Sun J, Patel RC, Zheng Q, Madhira V, Olex AL, Islam JY, et al. COVID-19 disease severity among people with HIV infection or solid organ transplant in the United States: A nationally-representative, multicenter, observational cohort study. medRxiv [Preprint]. 2021:2021.07.26.21261028. DOI:https://doi.org/10.1101/2021.07.26.21261028.
[49] Oprea C, Quirke S, Ianache I, Bursa D, Antoniak S, Bogdanic N, et al. HIV disease metrics and COVID-19 infection severity and outcomes in people living with HIV in central and eastern Europe. HIV Med 2024;25:343–52. https://doi.org/10.1111/hiv.13578.
[50] Cioboata R, Biciusca V, Olteanu M, Vasile CM. COVID-19 and tuberculosis: unveiling the dual threat and shared solutions perspective. J Clin Med 2023;12:4784. https://doi.org/10.3390/jcm12144784.
[51] Ziegler CGK, Allon SJ, Nyquist SK, Mbano IM, Miao VN, Tzouanas CN, et al. SARS-CoV-2 receptor ACE2 is an interferon-stimulated gene in human airway epithelial cells and is detected in specific cell subsets across tissues. Cell 2020;181. https://doi.org/10.1016/j.cell.2020.04.035. 1016–35.e19.
[52] Chong WH, Saha BK, Chopra A. Narrative review of the relationship between COVID-19 and PJP: does it represent coinfection or colonization? Infection 2021;49:1079–90. https://doi.org/10.1007/s15010-021-01630-9.
[53] Jeican II, Inișca P, Gheban D, Tăbăran F, Aluaș M, Trombitas V, et al. COVID-19 and *Pneumocystis jirovecii* pulmonary coinfection-The first case confirmed through autopsy. Medicina (Kaunas) 2021;57:302. https://doi.org/10.3390/medicina57040302.
[54] Planas D, Bruel T, Staropoli I, Guivel-Benhassine F, Porrot F, Maes P, et al. Resistance of Omicron subvariants BA.2.75.2, BA.4.6, and BQ.1.1 to neutralizing antibodies. Nat Commun 2023;14:824. https://doi.org/10.1038/s41467-023-36561-6.
[55] World Health Organization. Antigen-detection in the diagnosis of SARS-CoV-2 infection: Interim guidance, 6 October 2021 n.d. https://www.who.int/publications/i/item/WHO2019-nCoVAntigen_Detection2021.1. [Accessed 17 September 2024].
[56] Brümmer LE, Katzenschlager S, McGrath S, Schmitz S, Gaeddert M, Erdmann C, et al. Accuracy of rapid point-of-care antigen-based diagnostics for SARS-CoV-2: an updated systematic review and meta-analysis with meta-regression analyzing influencing factors. PLoS Med 2022;19:e1004011. https://doi.org/10.1371/journal.pmed.1004011.
[57] Machkovech HM, Hahn AM, Garonzik Wang J, Grubaugh ND, Halfmann PJ, Johnson MC, et al. Persistent SARS-CoV-2 infection: significance and implications. Lancet Infect Dis 2024;24:e453–62. https://doi.org/10.1016/S1473-3099(23)00815-0.
[58] Dioverti V, Salto-Alejandre S, Haidar G. Immunocompromised patients with protracted COVID-19: a review of "Long Persisters". Curr Transplant Rep 2022;9:209–18. https://doi.org/10.1007/s40472-022-00385-y.
[59] Cele S, Karim F, Lustig G, San JE, Hermanus T, Tegally H, et al. SARS-CoV-2 prolonged infection during advanced HIV disease evolves extensive immune escape. Cell Host Microbe 2022;30. https://doi.org/10.1016/j.chom.2022.01.005. 154–62.e5.
[60] Proal AD, VanElzakker MB, Aleman S, Bach K, Boribong BP, Buggert M, et al. SARS-CoV-2 reservoir in post-acute sequelae of COVID-19 (PASC). Nat Immunol 2023;24:1616–27. https://doi.org/10.1038/s41590-023-01601-2.
[61] Patel P, Twentyman E, Koumans E, Rosenblum H, Griffin-Blake S, Jackson B, et al. Information for persons who are immunocompromised regarding prevention and treatment of SARS-CoV-2 infection in the context of currently circulating Omicron sublineages - United States, January 2023. MMWR Morb Mortal Wkly Rep 2023;72:128–31. https://doi.org/10.15585/mmwr.mm7205e3.
[62] Kinsella PM, Moso MA, Morrissey CO, Dendle C, Guy S, Bond K, et al. Antiviral therapies for the management of persistent coronavirus disease 2019 in immunocompromised hosts: a narrative review. Transpl Infect Dis 2024;26:e14301. https://doi.org/10.1111/tid.14301.
[63] Maponga TG, Jeffries M, Tegally H, Sutherland A, Wilkinson E, Lessells RJ, et al. Persistent severe acute respiratory syndrome coronavirus 2 infection with accumulation of mutations in a patient with poorly controlled human immunodeficiency virus infection. Clin Infect Dis 2023;76:e522–5. https://doi.org/10.1093/cid/ciac548.
[64] Longo BM, Venuti F, Gaviraghi A, Lupia T, Ranzani FA, Pepe A, et al. Sequential or combination treatments as rescue therapies in immunocompromised patients with persistent SARS-CoV-2 infection in the Omicron era: a case series. Antibiotics (Basel) 2023;12:1460. https://doi.org/10.3390/antibiotics12091460.
[65] Hernandez AV, Piscoya A, Pasupuleti V, Phan MT, Julakanti S, Khen P, et al. Beneficial and harmful effects of monoclonal antibodies for the treatment and prophylaxis of COVID-19: systematic review and meta-analysis. Am J Med 2022;135:1349–1361.e18. https://doi.org/10.1016/j.amjmed.2022.06.019.
[66] Kow CS, Ramachandram DS, Hasan SS. The use of neutralizing monoclonal antibodies and risk of hospital admission and mortality in patients with COVID-19: a systematic review and meta-analysis of randomized trials. Immunopharmacol Immunotoxicol 2022;44:28–34. https://doi.org/10.1080/08923973.2021.1993894.
[67] Miljanovic D, Cirkovic A, Lazarevic I, Knezevic A, Cupic M, Banko A. Clinical efficacy of anti-SARS-CoV-2 monoclonal antibodies in preventing hospitalisation and mortality among patients infected with Omicron variants: a systematic review and meta-analysis. Rev Med Virol 2023;33:e2439. https://doi.org/10.1002/rmv.2439.
[68] Rockett R, Basile K, Maddocks S, Fong W, Agius JE, Johnson-Mackinnon J, et al. Resistance mutations in SARS-CoV-2 delta variant after sotrovimab use. N Engl J Med 2022;386:1477–9. https://doi.org/10.1056/NEJMc2120219.
[69] RECOVERY Collaborative Group, Horby P, Lim WS, Emberson JR, Mafham M, Bell JL, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med 2021;384:693–704. https://doi.org/10.1056/NEJMoa2021436.
[70] Stary G, Klein I, Bauer W, Koszik F, Reininger B, Kohlhofer S, et al. Glucocorticosteroids modify Langerhans cells to produce TGF-β and expand

regulatory T cells. J Immunol 1950 2011;186:103–12. https://doi.org/10.4049/jimmunol.1002485.
[71] Bieksiene K, Zaveckiene J, Malakauskas K, Vaguliene N, Zemaitis M, Miliauskas S. Post COVID-19 organizing pneumonia: the right time to interfere. Medicina (Kaunas) 2021;57:283. https://doi.org/10.3390/medicina57030283.
[72] Mongardon N, Piagnerelli M, Grimaldi D, Perrot B, Lascarrou J-B, COVADIS study group investigators. Impact of late administration of corticosteroids in COVID-19 ARDS. Intensive Care Med 2021;47:110–2. https://doi.org/10.1007/s00134-020-06311-z.
[73] Tlayjeh H, Mhish OH, Enani MA, Alruwaili A, Tleyjeh R, Thalib L, et al. Association of corticosteroids use and outcomes in COVID-19 patients: a systematic review and meta-analysis. J Infect Public Health 2020;13:1652–63. https://doi.org/10.1016/j.jiph.2020.09.008.
[74] Solera JT, Arbol BG, Ferreira VH, Kurtesi A, Hu Q, Ierullo M, et al. Differential serum neutralisation of omicron sublineages in patients receiving prophylaxis with tixagevimab-cilgavimab. Lancet Infect Dis 2023;23:528–30. https://doi.org/10.1016/S1473-3099(23)00208-6.
[75] Research C for DE and. FDA announces Evusheld is not currently authorized for emergency use in the U.S. FDA; 2024.
[76] Glhoom S, Fergany A, El-Araby D, Abdelkhalek AA, Gomaa A, Zayed EO, et al. The efficacy of tixagevimab/cilgavimab (Evusheld) in prophylaxis and treatment of COVID-19 in immunocompromised patients: a systematic review and meta-analysis. Eur J Med Res 2024;29:27. https://doi.org/10.1186/s40001-023-01549-x.
[77] Deeks SG. HIV infection, inflammation, immunosenescence, and aging. Annu Rev Med 2011;62:141–55. https://doi.org/10.1146/annurev-med-042909-093756.
[78] Kernéis S, Launay O, Turbelin C, Batteux F, Hanslik T, Boëlle P-Y. Long-term immune responses to vaccination in HIV-infected patients: a systematic review and meta-analysis. Clin Infect Dis 2014;58:1130–9. https://doi.org/10.1093/cid/cit937.
[79] Parmigiani A, Alcaide ML, Freguja R, Pallikkuth S, Frasca D, Fischl MA, et al. Impaired antibody response to influenza vaccine in HIV-infected and uninfected aging women is associated with immune activation and inflammation. PLoS One 2013;8:e79816. https://doi.org/10.1371/journal.pone.0079816.
[80] Vergori A, Tavelli A, Matusali G, Azzini AM, Augello M, Mazzotta V, et al. SARS-CoV-2 mRNA vaccine response in people living with HIV according to CD4 count and CD4/CD8 ratio. Vaccines 2023;11:1664. https://doi.org/10.3390/vaccines11111664.
[81] Benet S, Blanch-Lombarte O, Ainsua-Enrich E, Pedreño-Lopez N, Muñoz-Basagoiti J, Raïch-Regué D, et al. Limited humoral and specific T-cell responses after SARS-CoV-2 vaccination in PWH with poor immune reconstitution. J Infect Dis 2022;226:1913–23. https://doi.org/10.1093/infdis/jiac406.
[82] Corma-Gómez A, Fernández-Fuertes M, García E, Fuentes-López A, Gómez-Ayerbe C, Rivero-Juárez A, et al. Severe immunosuppression is related to poorer immunogenicity to SARS-CoV-2 vaccines among people living with HIV. Clin Microbiol Infect 2022;28:1492–8. https://doi.org/10.1016/j.cmi.2022.05.018.
[83] Vergori A, Cozzi-Lepri A, Matusali G, Cicalini S, Bordoni V, Meschi S, et al. Long term assessment of anti-SARS-CoV-2 immunogenicity after mRNA vaccine in persons living with HIV. Vaccines 2023;11:1739. https://doi.org/10.3390/vaccines11121739.
[84] Vergori A, Cozzi-Lepri A, Matusali G, Colavita F, Cicalini S, Gallì P, et al. SARS-CoV-2 omicron variant neutralization after third dose vaccination in PLWH. Viruses 2022;14:1710. https://doi.org/10.3390/v14081710.
[85] Vergori A, Matusali G, Lepri AC, Cimini E, Fusto M, Colavita F, et al. Neutralizing activity and T-cell response after bivalent fifth dose of messenger RNA vaccine in person living with HIV. Int J Infect Dis 2023;134:195–9. https://doi.org/10.1016/j.ijid.2023.06.010.
[86] Stuart ASV, Shaw RH, Liu X, Greenland M, Aley PK, Andrews NJ, et al. Immunogenicity, safety, and reactogenicity of heterologous COVID-19 primary vaccination incorporating mRNA, viral-vector, and protein-adjuvant vaccines in the UK (Com-COV2): a single-blind, randomised, phase 2, non-inferiority trial. Lancet 2022;399:36–49. https://doi.org/10.1016/S0140-6736(21)02718-5.
[87] Zhou Q, Liu Y, Zeng F, Meng Y, Liu H, Deng G. Correlation between CD4 T-cell counts and seroconversion among COVID-19 vaccinated patients with HIV: a meta-analysis. Vaccines 2023;11:789. https://doi.org/10.3390/vaccines11040789.
[88] Geffen N. The role of activists in access to HIV and tuberculosis treatment and prevention. Curr Opin HIV AIDS 2017;12:398–402. https://doi.org/10.1097/COH.0000000000000381.
[89] World Health Organization. Consolidated guidelines on person-centred HIV patient monitoring and case surveillance n.d. https://www.who.int/publications/i/item/978-92-4-151263-3. [Accessed 17 September 2024].