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ORIGINAL ARTICLE

Major revision version 13.0 of the European AIDS Clinical Society guidelines 2025

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Abstract

Background: The European AIDS Clinical Society (EACS) guidelines were revised for the 21st time in 2025, with updates covering all aspects of HIV care.

Key Points of the Guidelines Update: The structure of the guidelines has been reorganized into two parts: Part I focuses on the management and prevention of HIV and related infections, and Part II addresses comorbidities and other relevant topics. In Part I, Version 13.0 recommends the following first-line regimens for adults with HIV-1: tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) with either lamivudine or emtricitabine (XTC), in combination with dolutegravir (DTG), bictegravir (BIC), or doravirine (DOR); or a dual therapy option consisting of XTC plus DTG. Version 13.0 introduces a completely new section on HIV-2. The preferred first-line regimens for HIV-2 include triple therapy with a second-generation integrase inhibitor: either TAF/FTC/BIC or TDF/XTC + DTG. The PrEP section has been updated to include the use of long-acting injectable antiretrovirals. Drug–drug interaction (DDI) tables have been updated to include long-acting antiretrovirals and considerations related to substance use, including drugs used to enhance or prolong sexual activity (chemsex). Tables for preferred and alternative ART regimens in children and adolescents have been updated, with particular attention to neonates. A new section on transition to adult care has also been included. The co-infections section has undergone extensive revision, especially regarding HBV, sexually transmitted infections, opportunistic infections (particularly tuberculosis, leishmaniasis, and cryptococcosis) and mpox, incorporating recent clinical trial data on tecovirimat. In Part II, Version 13.0 introduces major updates to the comorbidities section. In the cancer section, screening recommendations for anal and breast cancer have been updated. Cardiovascular and metabolic health sections have been significantly modified, reflecting recent advances and the use of statins in people with HIV. Topics such as kidney and liver complications, mental health, travel and solid organ transplantation have been thoroughly revised. New sections on sleep health and a unified substance use section have been added.

Conclusions: In 2025, the EACS Guidelines underwent a comprehensive update and restructuring. They now consist of two distinct parts and include several new sections. The recommendations are available as a free mobile app and in an interactive web format.

KEYWORDS

antiretroviral therapy, ART, cardiovascular risk, EACS, European AIDS Clinical Society, guidelines, HIV, long-acting, major updates, mpox, statins, V13.0

INTRODUCTION

The EACS Guidelines have been updated for the 21st time. Since version 12.1, released in November 2024, a significant change in the organization of the content has been implemented. This new structure reflects the evolving and dynamic nature of HIV medicine. Certain topics have seen less new data and changes (e.g., viral hepatitis

co-infections) in recent years, while others have expanded significantly, such as comorbidities, pre-exposure prophylaxis (PrEP) or sexually transmitted infections (STIs). The reorganization also aims to make it easier for readers to locate specific content.

As a result, the guidelines are now divided into two main parts. Part I focuses on the management and prevention of HIV infection itself and related infections. It covers the use of antiretrovirals for treatment and prevention, drug–drug interactions, prescribing considerations and the management of relevant co-infections in HIV medicine, including opportunistic infections, STIs and viral hepatitis co-infections. Immunization for people living with HIV is also included in this section. Part II addresses the prevention and management of non-infectious aspects of HIV medicine. This includes all related comorbidities and specific topics such as travel and organ transplantation in people with HIV. Each section is divided into several sub-sections. The new structure of the guidelines is illustrated in Figure 1.

At the same time, the format of the guidelines has changed: they are now available exclusively as an online web document. PDF versions are no longer produced. This change allows the guidelines to function as a living document, enabling rapid updates in response to emerging concerns or new data (e.g., a new epidemic or pandemic such as COVID-19 or mpox). However, the timeline for major updates remains unchanged, with one formal revision published annually.

Since the previous major update, significant progress has been made in the field of antiretrovirals, particularly with long-acting drugs. Notably, subcutaneous injections of lenacapavir administered twice yearly have demonstrated remarkable efficacy as PrEP [1, 2]. In the area of comorbidities, important new data have emerged, especially in the field of cardiovascular disease prevention. The publication of the REPRIEVE study has highlighted the role of statins not only for individuals at high risk but also for those at intermediate risk of cardiovascular events [3].

The EACS Guidelines aim to provide easily accessible, systematic and comprehensive recommendations across wide geographical settings. The EACS Guidelines promote the participation of experts from all European regions, and also international experts from other parts of the world.

METHODS

All recommendations in the EACS Guidelines are continuously updated to ensure they cover the most relevant questions from everyday clinical practice. The guidelines are developed based on evidence and on expert opinion in any instances where evidence is not available. The different sections of the guidelines are reviewed by HIV experts and governed by a leadership group consisting of a chair, a vice-chair and a young scientist. Guidelines section members are selected following a standard operational procedure and terms of reference, including rotation of section members, gender balance, representation of all European sub-regions and experts from other parts of the world. Community representatives are also included at all stages. Relevant new evidence is identified

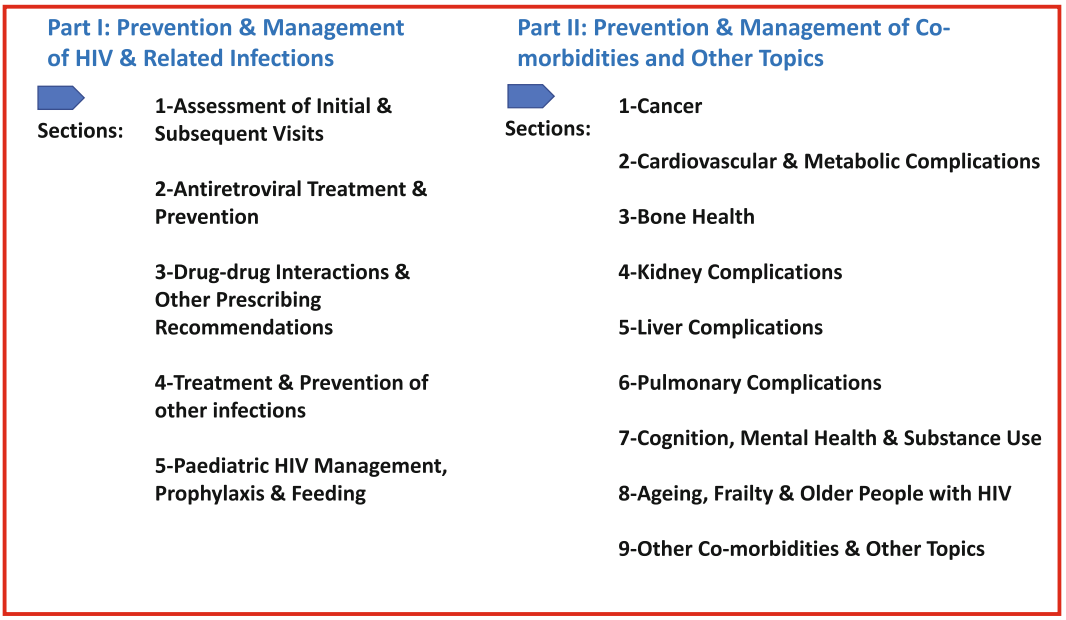


FIGURE 1 Organization of EACS Guidelines V13.0.

and selected by the section members and discussed internally by each group; crosscheck meetings are later performed to ensure consistency of the content between sections and for approval of the whole content. The guidelines process is managed by the EACS Guidelines chair and coordinator, working closely with the EACS Secretariat. Formal revisions are made annually, with major revisions published every other year (coincident with the EACS Conference) and minor revisions in the years in-between. Interim updates can be carried out in real time if new essential information is released in-between formal revisions. Additionally, members are invited to submit comments during the month following the release of the guidelines, which are reviewed and addressed when appropriate.

The main changes for version 13.0 in each section of the guidelines are summarized below. Access to the complete document is recommended for details.

OVERVIEW OF MAIN CHANGES

Part I

Assessment of initial and subsequent visits

Version 13.0 of the guidelines introduces a simplified and visually enhanced table summarizing key aspects of the initial and follow-up visits for individuals with HIV.

Antiretroviral drugs for treatment and prevention

There are now multiple well-tolerated and highly effective antiretroviral therapy (ART) options available. Assessing a person's readiness to initiate or reinitiate ART remains essential. Considerations for ART readiness have now been included ahead of the initial table of key aspects of initial and subsequent visits. No changes have been made to the recommended initial ART regimens for treatment-naïve adults compared with version 12.1. Preferred options remain: tenofovir (either tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide [TAF]) with either lamivudine or emtricitabine (XTC), in combination with dolutegravir (DTG), bictegravir (BIC) or doravirine (DOR); or a dual therapy option consisting of XTC plus DTG. Doravirine-based combinations remain among recommended regimens pending the results of head-to-head trials versus DTG (see Table 1). DTG/3TC continues to be not recommended for individuals with a baseline HIV viral load >500 000 copies/mL, pending further evidence confirming efficacy above this threshold. In individuals who acquired HIV while using oral PrEP, DTG-XTC dual therapy can be used only if genotype test does not show resistance. In cases involving long-acting cabotegravir (CAB-LA) PrEP failure, a triple therapy regimen including boosted darunavir (DRV) is recommended until a resistance test is available.

Regarding switch strategies in virologically suppressed individuals, data from the CARES study suggest that subtype A1 is unlikely to be associated with an increased risk of virological failure when switching to long-acting CAB-LA plus long-acting rilpivirine (RPV-LA) [4].

This version also introduces an entirely new section on HIV-2. It provides guidance on when to suspect HIV-2, how to diagnose and monitor it and which treatment strategies to use. When treatment is indicated, the preferred first-line regimen includes a triple therapy with a second-generation integrase strand transfer inhibitor (INSTI): either TAF/FTC/BIC or TDF/XTC + DTG. Boosted DRV plus two nucleos(t)ide reverse transcriptase inhibitors (NRTIs) can be used as an alternative (see Table 2). Importantly, HIV-2 is intrinsically resistant to NNRTIs. In the case of virological failure, treatment should be guided by resistance testing, which is available in some European reference laboratories. Therapeutic options are, however, more limited than for HIV-1.

The section on pregnancy and HIV has been extensively revised. Recommended initial regimens for ART-naïve pregnant women now include TAF/FTC/BIC once daily [5, 6], in addition to TDF/XTC or TAF/FTC + DTG and TDF/XTC or TAF/FTC + DRV/r 600 mg/100 mg twice daily, which were already listed as preferred options. The frequency of viral load monitoring has been specified according to the woman's pre-pregnancy viral load:

- Every trimester and at 36 weeks if the woman is durably suppressed with no adherence issues;
- Every two months and at 36 weeks in other cases;
- Every two weeks until HIV RNA <50 cp/mL, then at 36 weeks, if viral suppression has not been achieved by the third trimester.

An elective caesarean section should be scheduled at 38 weeks if HIV RNA is >400 copies/mL at 34–36 weeks of gestation. If the viral load is between 50 and 400 copies/mL, caesarean delivery is no longer systematically recommended but should be discussed case by case on the basis of the risk of viral transmission and the pros and cons of elective caesarean section. In women diagnosed with HIV during labour, a caesarean section should be performed, and immediate initiation of a triple oral regimen including DTG or BIC is advised, along with

TABLE 1 Initial regimens in ART-naïve adults with HIV-1 infection.

Regimen	Main requirements and comments
Recommended regimens	
2 NRTIs + INSTI	
TAF/FTC/BIC	
TAF/FTC or TDF/XTC + DTG	
1 NRTI + INSTI	
XTC + DTG or 3TC/DTG	HBsAg negative HIV-VL < 500 000 copies/mL Not recommended after suspected oral PrEP failure
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + DOR or TDF/3TC/DOR	Not active against HIV-2. Not suitable for rapid ART initiation. Baseline genotype results advisable before initiation to rule out transmitted resistance.
Alternative regimens	
2 NRTIs + INSTI	
ABC/3TC + DTG	HLA-B*57:01 negative
ABC/3TC/DTG	HBsAg negative
TAF/FTC or TDF/XTC + RAL qd or bid	
2 NRTIs + NNRTI	
TAF/FTC or TDF/XTC + EFV or TDF/FTC/EFV	At bedtime or 2 h before dinner
TAF/FTC or TDF/XTC + RPV or TAF/FTC/RPV or TDF/FTC/RPV	CD4 count >200 cells/μL HIV-VL < 100 000 copies/mL Not on gastric pH increasing agents. With food.
2 NRTIs + PI/r or PI/c	
TAF/FTC or TDF/XTC + DRV/c or DRV/r or TAF/FTC/DRV/c	With food. Preferred regimen after CAB LA PrEP failure.

Abbreviations: /c, boosted by cobicistat; /r, boosted by ritonavir; 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; BIC, bictegravir; bid, twice daily; DOR, doravirine; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; FTC, emtricitabine; HBsAg, hepatitis B surface antigen; HLA human leukocyte antigen; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleos(t)ide reverse transcriptase inhibitors; PI, protease inhibitor; PrEP, pre-exposure prophylaxis; qd, once daily; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; VL, viral load; XTC, lamivudine or emtricitabine.

intravenous zidovudine (ZDV), if available (HIV-RNA above 400 copies/mL).

Principles of shared decision making should be followed when considering choices around infant feeding. Accessible, clear information relating to the very low but non-zero risk of transmission during breastfeeding should be provided to all pregnant women, ideally well before delivery. The option of supported breastfeeding should be provided to persons who are fully adherent to ART, virally suppressed, and have access to regular VL monitoring (also see below, Paediatric section).

Two new sections have been added to the PrEP chapter

- One on long-acting injectable PrEP, covering both cabotegravir and lenacapavir. In case of recent high-risk exposure or before starting CAB-LA or LEN-LA, an HIV RNA test should be performed prior to PrEP initiation to rule out acute HIV infection.
- One on PrEP in persons living with chronic hepatitis B virus (HBV) infection, highlighting that daily PrEP should be used.

New guidance has also been provided in the case of post-exposure prophylaxis (PEP) in individuals using oral PrEP, where it is recommended to take two tablets of the oral PrEP regimen as soon as possible after exposure, followed by one tablet daily until clinical evaluation, to avoid any interruption or delay in coverage [7, 8].

Drug–Drug Interactions (DDI) and Other Prescribing Recommendations

The DDI tables, which provide an at-a-glance view of how individual antiretroviral drugs may interact with

TABLE 2 Initial regimens in ART-naïve adults with HIV-2 infection.

	Main requirement
Recommended first-line regimens	
2 NRTI + INSTI	
TAF/FTC/BIC	
TAF/FTC or TDF/XTC + DTG	
Alternative first-line regimen	
2 NRTIs + INSTI	
ABC/3TC + DTG	HLA-B*57:01 negative
ABC/3TC/DTG	HBsAg negative
TAF/FTC or TDF/XTC + RAL bid	
ABC/3TC + RAL bid	HLA-B*57:01 negative HBsAg negative
2 NRTIs + PI/r or PI/c	
TAF/FTC or TDF/XTC + DRV/c or DRV/r or TAF/FTC/DRV/c	With food
ABC/3TC + DRV/c or DRV/r	With food HLA-B*57:01 negative HBsAg negative

Abbreviations: /c, boosted by cobicistat; /r, boosted by ritonavir; 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; BIC, bictegravir; bid, twice daily; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; FTC, emtricitabine; HBsAg, hepatitis B surface antigen; HLA, human leukocyte antigen; INSTI, integrase strand transfer inhibitor; NNRTI, nonnucleoside reverse transcriptase inhibitor; NRTI, nucleos(t)ide reverse transcriptase inhibitors; PI, protease inhibitor; PrEP, pre-exposure prophylaxis; RAL, raltegravir; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; XTC, lamivudine or emtricitabine.

frequently used comedications within a therapeutic area, have been extended to include DDIs with substance use/chemsex. The gender-affirming hormone therapy table has been updated to include guidance on managing DDIs with oestrogens, medroxyprogesterone, micronized progesterone and the androgen blockers bicalutamide and dutasteride. A note was added to indicate that high-dose testosterone, combined with exercise, may increase muscle growth and muscle blood flow, which could in turn accelerate the release of long-acting intramuscular cabotegravir/rilpivirine from the depot and result in lower concentrations at the end of the dosing interval [9, 10]. Monitoring of viral load and, where available, therapeutic drug monitoring could be considered.

The section on long-acting injectable antiretroviral drugs has been expanded to include guidance on managing missed lenacapavir injections. As for long-acting cabotegravir/rilpivirine, coadministration with strong or moderate inducers can markedly reduce lenacapavir exposure and is therefore not recommended in the European labels for either treatment or prevention. In contrast, the U.S. prescribing information provides dosage modification strategies (supplemental doses) for individuals already receiving lenacapavir who may newly require a moderate or strong inducer [11]. Importantly, no dosing recommendations are provided for initiating lenacapavir in individuals already receiving inducers. Lenacapavir is a moderate CYP3A4 inhibitor; therefore, caution is warranted with sensitive CYP3A4 substrates during coadministration and during the first weeks after lenacapavir is discontinued, as the drug remains in the circulation for a prolonged period.

The resources for the management of older persons with HIV now include principles for prescribing non-HIV medications, namely, start low and go slow; avoid prescribing cascades, simplify regimens; and conduct regular medication reviews.

Detailed information on DDIs can be found in the University of Liverpool website www.hiv-druginteractions.org and real-life experiences on the clinical management of DDIs can be obtained from: https://clinicalcasesddis.com.

Treatment and prevention of other infections

Viral hepatitis co-infection

Various parts of the recommendations for people with HIV and viral hepatitis have been updated. Major updates involve the management of HBV and HDV as well as a new section on HAV. Hepatocellular carcinoma screening recommendations for people with HIV and HBV co-infection without cirrhosis were adapted, mostly based on the recently published EASL HBV guidelines recommendations [12]. Recommendations for HBV vaccination have also been updated (see below, Vaccination section).

The guidance on ART modifications in persons with HBV/HIV co-infection has been updated. The increasing availability of effective ART options, without any anti-HBV active drug or containing only drugs with low genetic barriers (i.e., 3TC/FTC) raised concerns about the use of these regimens in individuals with prior HBV exposure. To balance the risks of HBV reactivation and the benefits associated with simplified ART therapies, pragmatic recommendations were provided to guide clinicians. Discontinuation of TDF/TAF and the use of ART regimens including 3TC or FTC as the only anti-HBV-effective drug, or ART regimens without any anti-HBV activity, are discouraged in persons with HBV/HIV co-infection (HBsAg positive). However, these strategies can be considered in people with HIV and prior exposure to HBV (positive anti-HBc, positive/negative anti-HBsAg Ab, negative HBsAg), as the risk of HBV reactivation is very low. Regular monitoring of transaminases, HBsAg and HBV-DNA should be instituted, especially in those with ART regimens without any HBV-active agents and

in persons with any other immunosuppressive conditions. The table of cut-off values for non-invasive detection of liver fibrosis or cirrhosis in persons with HBV/HIV co-infection has been updated in accordance with recent literature updates [13].

Based on recent trial results [14–16], the recommendations on bulevirtide use for HDV infection were updated, highlighting the need for an extended treatment duration before discontinuation (at least 96 weeks of undetectable HDV-RNA) and the careful post-treatment surveillance of liver function due to the risk of hepatic flares. Combination therapy with bulevirtide and PEG-IFN has been included as a potential treatment option, though clinical data supporting this approach remain limited.

As clusters of acute hepatitis A (HAV) have been described in people with HIV [17], a novel section on HAV has been introduced, suggesting re-testing for HAV infection in persons with symptoms consistent with acute hepatitis, unexplained flares of aminotransferases, and ongoing risk behaviors.

Sexually transmitted infections

The recommendations on sexually transmitted infections (STIs) were updated to include several novel sub-sections. A new section on doxycycline post-exposure prophylaxis (Doxy-PEP) has been added. Based on recent evidence and considering both the benefits of STI prevention and the potential risks of antimicrobial resistance, this section offers clinicians practical guidance on using Doxy-PEP as an additional strategy to help reduce the burden of bacterial STIs. Additionally, the coverage of specific STIs was expanded to include recommendations on diagnosis, management and treatment of diseases caused by *M. genitalium* and *S. scabies*. For the former, several diagnostic and therapeutic approaches, taking into consideration local resources and availability of resistance testing, were proposed to manage the disease manifestations. A comment on viral hepatitis (including hepatitis A transmitted sexually) and the need for annual screening for hepatitis has been included. Minor modifications were also made to the treatment of chlamydial infection, which was simplified and homogenized to other international guidelines, and to the treatment of recurrent HSV, where short-course regimens were added as a possible treatment option. In addition, the recommendations on screening of asymptomatic individuals, use of diagnostic procedures and treatment options have been updated where necessary to emphasize the importance of adapting these approaches to local guidelines and available resources.

Opportunistic infections and other co-infections

The most significant modifications were made to recommendations for the diagnosis and treatment of cryptococcal disease, tuberculosis and mpox.

For cryptococcal disease management, tables on pre-emptive treatment for asymptomatic antigenaemia and treatment of cryptococcal meningitis/disseminated disease were separated.

The tuberculosis (TB) section was extensively reformatted and modified following the release of the novel WHO guidelines [18]. Definitions of latent TB (now referred to as 'TB infection') and of active TB (now referred to as 'TB disease') were updated to homogenize the terminology between different guidelines. Regimens for TB infection treatment were updated, and an additional table for TB infection treatment following exposure to drug-resistant TB was added [19]. For drug-susceptible TB disease treatment, a dosing schedule for dexamethasone adjuvant treatment in case of CNS involvement was added. For drug-resistant TB disease treatment, the need for early involvement of TB specialists to guide therapeutic management was highlighted. A novel, simplified table with treatment options for TB isolates with different drug-resistance profiles was added. Cross-referencing with WHO guidelines was implemented across the entire TB section to provide clinicians a comprehensive view of currently available clinical recommendations.

For mpox, evidence from PALM007 [20], STOMP [21], and UNITY [22] clinical trials on tecovirimat was integrated. Recommendations were reformulated to highlight that individuals who are not immunocompromised and with non-severe disease will most likely not benefit from tecovirimat treatment. The evidence remains inconclusive on the benefit of antiviral therapies in individuals severely immunocompromised and with severe mpox manifestations. In such instances, the use of antivirals alone or in combination could be considered on an individual basis.

Several minor modifications were made to other sections:

- In TB-IRIS treatment, a note was added to highlight the lack of evidence for the use of treatments other than corticosteroids.
- Isavuconazole was added to the treatment options for refractory candida oesophagitis
- A comment on the possibility of using other azoles (voriconazole, posaconazole and isavuconazole) as an alternative consolidation therapy in cases where itraconazole is not available or not clinically appropriate was included in the histoplasmosis section.

- For bacillary angiomatosis with central nervous system, cardiac or other severe clinical manifestations, a comment on the addition of rifampicin 300 mg iv/po bid to doxycycline or clarithromycin was added.
- And finally, the section on leishmaniasis was reformatted to highlight that the efficacy of miltefosine, in association with liposomal amphoterin B, can be lower for some *Leishmania* spp., such as *L. infantum*.

Vaccinations

Vaccination recommendations were expanded to include two new sections on Respiratory Syncytial Virus (RSV) and shingles prevention. For RSV, vaccination was advised for all individuals older than 75 and for younger persons with increased risk of severe RSV, according to local guidelines and resources.

Specific updates were made to the indications for primary HBV immunization and revaccination in HBV non-responders. In those individuals, CpG-adjuvanted vaccine Heplisav B (HepB-CpG) vaccination should be offered, where available, to improve seroconversion rates [23]. As an alternative, when Heplisav is not available, consider AS04C-adjuvanted vaccine (Fendrix) [24] or double-dose Engerix (40 μg) at 3–4 time points (months 0, 1, 2 and 6) which may help to improve response rates to the HBV vaccine.

Recommendations on pneumococcal vaccination were modified to include newly released pneumococcal conjugate vaccines (PCV), and PCV13 was excluded to prioritize the use of vaccines covering a higher number of serotypes, such as PCV21, PCV20 and PCV15.

Finally, following results from a recent clinical trial, a shorter 2-dose schedule for HPV vaccination was included as a possible option for women with well-controlled HIV replication and a CD4 T cell count >500 [25].

Paediatric HIV management, prevention of vertical transmission and feeding

This collaborative section between Penta (an international research network focused on paediatric infectious diseases) and EACS continues to provide updated guidance on preferred and alternative first-line combinations for children living with HIV, taking into account new data and the availability of formulations for use in Europe (Table 3). An important update is the inclusion of dolutegravir as a preferred first-line option in term newborns based on the results of the PETITE-DTG [26] study in line with the programmatic approach of WHO. Additionally, a more detailed guidance on the use of dual therapy with oral or LA injectable agents has been included.

A new section on transition to adult care for young people living with HIV has been introduced. Successful transition from paediatric to adult care relies on a structured, youth-centred approach and collaboration between paediatric and adult services, ideally including joint consultations and continued support post-transfer. Poor outcomes are more likely when transition is unplanned or when young people transfer with detectable viraemia, lower CD4 count and/or AIDS diagnosis in paediatric care [27], while well-managed transitions improve long-term health and engagement in care [28]. Transition is a complex, individualized process that occurs over several years and requires early planning, clear communication and ongoing support. Transition preparations should start once the young person enters adolescence and typically is aware of their HIV diagnosis, and each young person should have a documented comprehensive personalized transition plan in their medical records. Transition should address not only health care needs but also social, emotional, educational, sexual and reproductive health considerations, with a focus on empowering young people to manage their own care.

Following updated review of relevant literature, no significant change has been implemented in the recently added guidance on postnatal prophylaxis and infant feeding. Despite variations in current practice across Europe, general principles are provided regarding transmission risk stratification, the choice and duration of infant postnatal prophylaxis (PNP), decision-making about infant feeding, and supported breastfeeding (see also ART section before), as well as infant HIV testing and monitoring. Standard treatment doses for PNP rather than prophylactic doses should be used to reduce the risk of confusion and to simplify transition to treatment in infants diagnosed with HIV.

As in the previous version, a link to a table with guidance on antiretroviral drug dosing for children and adolescents as well as to refer cases to an international perinatal virtual clinic is provided [29]. The virtual multidisciplinary team is supported by Penta and welcomes referrals relating to HIV treatment in children and adolescents, adults with perinatally acquired HIV as well as management in relation to the prevention of vertical HIV transmission.

Part II

Prevention and management of comorbidities and other topics

The 2025 revision of the EACS Guidelines introduces significant updates to the comorbidities sections, reflecting

TABLE 3 Preferred and alternative first-line antiretroviral options for HIV-1 management in children and adolescents.

	Backbone		Anchor drug (in alphabetical order)	
Age	**Preferred**	**Alternative**	**Preferred**	**Alternative**
0–4 weeks[i]	ZDV[ii] + 3TC ABC[iii] + 3TC	-	DTG [iv]	LPV/r[v, vi] NVP[vi] RAL[vi, vii]
4 weeks–3 years	ABC[iii] + 3TC TAF[viii] + XTC[ix]	ZDV[ii] + 3TC TDF[x] + 3TC	BIC[xi] DTG[xii]	LPV/r[vi] NVP[vi] RAL[vi, vii]
3–6 years	ABC[iii, xiii] + 3TC[xiii] TAF[viii] + XTC[ix]	TDF[x] + XTC[ix] ZDV[ii] + XTC[ix]	BIC[xi] DTG[xii]	DRV/r[xiv] EFV[xiii, xiv] LPV/r[xiv] NVP[xiv] RAL[xiv]
6–12 years	ABC[iii, xiii] + 3TC[xiii] TAF[viii] + XTC[ix]	TDF[x] + XTC[ix]	BIC[xi] DTG[xii]	DRV/r[xiv] EFV[xiii, xiv] EVG/c[xiv] RAL[xiv]
> 12 years	ABC[iii, xiii] + 3TC[xiii] TAF[viii] + XTC[ix]	TDF[x] + XTC[ix]	BIC[xi] DTG[xii]	DRV/b[xiv] DOR[xiv] EFV[xiii, xiv] RAL[xiv] RPV[xiv]

Note: (i) These recommendations apply to term infants weighing ≥2 kg. ZDV, 3TC, NVP are the only antiretrovirals that have been approved for use in preterm (gestational age <37 weeks) infants. No data is available on dosing and safety of DTG, RAL and ABC in preterm infants. LPV/r should be avoided in preterm infants due to increased risk of cardiotoxicity and neurotoxicity. Selecting an appropriate ART regimen for this population should be discussed urgently within an MDT or PVC. (ii) In view of potential long-term toxicity, any child receiving ZDV should be switched to ABC or TAF (preferred for younger children) or TDF (alternative for younger children, with renal/bone toxicity monitoring) once increase in age and/or weight makes EMA approved formulations available. When ABC and TAF are contraindicated or unavailable for young children it is recommended that treatment options are discussed within an MDT or PVC to decide between ZDV or TDF on a case-by-case basis. (iii) Where HLA screening is available, ABC should NOT be prescribed to individuals that are HLA-B*57:01 positive. In areas where HLA-B*57:01 testing is not available ABC can be considered after counselling on HSR risk. ABC is not EMA approved under 3 months of age, but dosing data for younger children are available from the WHO and HHS/NIH. (iv) DTG is EMA approved from 4 weeks and 3 kg. Off-label use of DTG in term infants under 4 weeks is supported by data from the PETITE-DTG and the IMPAACT 2023 study, and recommended by the WHO. DTG can be initiated without delay even in neonates born to mothers receiving DTG. (v) LPV/r should not be administered to neonates before a postmenstrual age of 42 weeks and a postnatal age of at least 14 days although it may be considered if there is a risk of transmitted NVP resistance and appropriate INSTI formulations are unavailable. The neonate should be monitored closely for LPV/r related toxicity (cardiac, metabolic, endocrine). (vi) If starting a non-DTG anchor drug in the neonatal period it is acceptable to continue this option. However, when over 4 weeks and 3 kg, a switch to second-generation INSTI (DTG or BIC) is recommended if and when an appropriate formulation is available. (vii) RAL is an alternative in term neonates under 2 weeks of age if DTG is not available, and there is a risk of transmitted NVP resistance. However, it has a low barrier to resistance. A switch to an agent with a higher barrier to resistance should be made as early as possible to minimize risk of acquired INSTI resistance. If age/weight-appropriate DTG or BIC formulations are not available when over 4 weeks and 3 kg then an interim switch to LPV/r could be considered while awaiting availability of DTG or BIC. (viii) TAF is currently EMA approved for children (from 2 years of age), and adolescents in FDC's including: TAF/FTC (10/200 mg or 25/200 mg when administered with or without a booster (cobicistat or ritonavir) respectively) from 12 years and 35 kg, TAF/FTC/EVG/c (10/200/150/150 mg) from 2 years and 14 kg, TAF/FTC/BIC (15/120/30 mg) from 2 years, and 14 kg to less than 25 kg, TAF/FTC/BIC (25/200/50 mg) from 25 kg, TAF/FTC/DRV/c (10/200/800/150 mg) from 12 years and 40 kg, TAF/FTC/RPV (25/200/25 mg) from 12 years and 35 kg. TAF has been associated with excessive weight gain in adults, especially in combination with INSTI. This has not been demonstrated in paediatric and adolescent randomized clinical trials or observational studies. Families and young people should be counselled about the potential risk of excessive weight gain in general, and weight should be monitored. (ix) XTC indicates circumstances when FTC or 3TC may be used interchangeably. (x) TDF is only EMA approved from 2 years of age. In view of concerns about potential impact on bone development and renal toxicity, TAF is recommended over TDF at all ages, in settings where this is EMA approved and available. (xi) BIC is currently EMA approved in Europe for children and adolescents in the following FDC's: TAF/FTC/BIC (15/120/30 mg) from 2 years, and 14 kg to less than 25 kg. TAF/FTC/BIC (25/200/50 mg) from 25 kg. When BIC is EMA approved in younger ages and weights it should be included as a preferred option. (xii) Dispersible ABC/3TC/DTG tablets (60/30/5 mg) are EMA approved for children from the age of 3 months weighing at least 6 and less than 25 kg. For children weighing ≥25 Kg ABC/3TC/DTG tablets (600/300/50 mg) should be used as dispersible DTG is not bioequivalent to film-coated tablets and therefore appropriate dosing of all 3 component drugs is not achievable. (xiii) At HIV-VL > 100 000 copies/ml ABC + 3TC should not be combined with EFV as anchor drug. (xiv) If preferred anchor drug (BIC or DTG) are not available/appropriate, DRV/b is favoured over the alternative anchor drugs due to a higher barrier to resistance.

Abbreviations: /c, boosted by cobicistat; /r, boosted by ritonavir; /b, boosted by either cobicistat or ritonavir; 3TC, lamivudine; ABC, abacavir; ART, antiretroviral therapy; BIC, bictegravir; HHS, Health and Human Services; DRV, darunavir; DTG, dolutegravir; EFV, efavirenz; EVG, elvitegravir; FDC, fixed-dose combinations; FTC, emtricitabine; HLA, human leukocyte antigen; HSR, hypersensitivity reaction; INSTI, integrase strand transfer inhibitor; MDT, multidisciplinary team; NIH, National Institute of Health; NRTI, nucleos(t)ide reverse transcriptase inhibitor; NVP, nevirapine; PVC, paediatric virtual clinic; RAL, raltegravir; RPV, rilpivirine; TAF, tenofovir alafenamide; TDF, tenofovir disoproxil fumarate; VL, viral load; WHO, World Health Organization; XTC, lamivudine or emtricitabine; ZDV, zidovudine.

the latest clinical evidence and offering practical, streamlined guidance for the care of people with HIV.

In the **cancer** section, screening recommendations for anal and breast cancer have been clarified. For anal cancer, symptom review, digital rectal examination and cytology with high-risk HPV co-testing are recommended where follow-up is available. Proctoscopy is an acceptable alternative when high-resolution anoscopy is unavailable. For breast cancer, the possibility of initiating screening at age 40 years (particularly in women with HIV and of Black ethnicity) is acknowledged, though no formal recommendation is made. Local healthcare infrastructure and access pathways need to be considered when making screening decisions.

The **cardiovascular disease** section incorporates changes from both the 2024 ESC/ESH hypertension guidelines [30] and the EACS guidance for the primary prevention of cardiovascular disease [31], based on REPRIEVE findings [3]. Blood pressure (BP) targets have shifted, with new targets for systolic BP of 120–129 mmHg, while ≥140/90 mmHg remains the diagnostic threshold. Initial assessments should include serum creatinine, estimated glomerular filtration rate (eGFR), and urine albumin/creatinine ratio, with optional advanced tests (e.g., computerized tomography coronary artery calcium (CAC) scoring). Critically, cardiovascular prevention strategies now emphasize risk-based treatment rather than lipid thresholds alone. In people with HIV at high or very high risk, LDL-C targets are retained. However, in those at low to moderate risk, particularly younger individuals, statin therapy is now recommended even if LDL-C levels are not elevated. This shift, supported by REPRIEVE [3], reflects the higher baseline cardiovascular risk in people with HIV (Table 4) [32, 33]. Routine lipid monitoring is advised 1–3 months after statin initiation, with creatine kinase (CK) testing reserved for symptomatic cases.

The **diabetes** section received minor updates. It reinforces regular monitoring of glucose and HbA1c, particularly given the increasing use of statins and the potential glycaemic impact of some ART regimens. Lifestyle interventions remain central, and the role of GLP-1 receptor agonists is expanding. Metformin is reaffirmed as first-line therapy. While evidence for SGLT2 inhibitors in people with HIV remains limited, their use is considered reasonable. Links to the MASLD section were strengthened to reflect the growing overlap between metabolic comorbidities. The possible association between second-generation INSTI and impaired glycaemic control is acknowledged with caution, pending further data.

The outdated lipodystrophy subsection has been removed, as this condition is now rarely observed in clinical practice. Instead, the guidelines focus on **clinical obesity** as a disease entity defined by excess adiposity with systemic consequences. A weight gain of ≥5% is proposed as a clinically relevant threshold [34]. The definition of obesity has recently changed: it is now understood as an excess of body fat, whereas until now, it has been primarily defined as a body mass index (BMI) above the normal range. These two concepts are closely related, and excess body fat is very likely to be present in individuals with clearly elevated BMI values. Given the long-standing reliance on BMI, we believe it should continue to be used, but it must be supplemented with markers that indicate excess fat. We recommend that BMI continues to be measured routinely in individuals with a BMI above the normal threshold (25 kg/m^2), abdominal (e.g., waist) or total body fat (e.g., DXA) should be assessed to determine whether there is excess fat and, if so, whether associated conditions are present (Figure 2) [35]. Management should be multidisciplinary, prioritizing lifestyle interventions supported by psychological care and pharmacotherapy where appropriate. Bariatric surgery may be considered in severe cases. Switching ART is generally not recommended due to its limited benefits [36] and the toxicity profile of weight-suppressing drugs such as efavirenz (EFV) or TDF.

The **bone health** section has been reformatted for clarity. Definitions of osteoporosis and osteopenia were refined, with updated screening recommendations including low BMI and family history of hip fracture. Vertebral fracture assessment is advised for individuals aged ≥70 years. Given the lack of HIV-specific fracture risk data, FRAX® [37] thresholds as per the general population are used, and clinicians are encouraged to follow national guidelines. Prior fragility fractures are emphasized as treatment triggers, regardless of bone mineral density (BMD). Denosumab has been added as an alternative to bisphosphonates, especially in patients with dental issues or renal impairment. TDF is highlighted as being associated with increased risk of fractures [38].

The **kidney section** has been streamlined for digital use, with clearer staging, urine analysis guidance and a focus on key interventions. SGLT2 inhibitors are now listed as treatment options. Atazanavir remains the ART mostly associated with renal stones, though other boosted PIs may contribute [39]. The section on TDF-related proximal tubulopathy remains, and new warnings were added about glycosuria in patients on SGLT2 inhibitors. Updated data support the use of BIC/TAF/FTC and lamivudine in end-stage renal disease, and TLD (TDF/3TC/DTG) has been added across relevant tables.

The **liver disease** section adopts metabolic dysfunction-associated steatotic liver disease (MASLD) terminology (replacing non-alcoholic fatty liver disease/non-alcoholic steatohepatitis) and shifts focus from

TABLE 4 EACS Recommendations on the use of statin therapy for the primary prevention of ASCVD in people with HIV, stratified according to the level of ASCVD risk.

	Individuals at very high risk of ASCVD	Individuals at high risk of ASCVD	Individuals at low-to-moderate risk of ASCVD
Level of ASCVD risk	Individuals with established ASCVD or DM with target organ damage or severe CKD or SCORE2 ≥ 10% or >7.5% if younger than 50 years	Individuals with SCORE2 ≥ 5% to <10% or ≥2.5% if younger than 50 years	Individuals with SCORE2 <5%
Age ≥ 40 years	Recommend high-intensity statin therapy[c]: Atorvastatin 40 mg or 80 mg od Rosuvastatin 20 mg or 40 mg od	Recommend moderate or high-intensity statin therapy depending on ASCVD risk category High-intensity statin[a,c]: Atorvastatin 40 mg or 80 mg od Rosuvastatin 20 mg or 40 mg od Moderate-intensity statin[b,c]: Pitavastatin 4 mg od Atorvastatin 20 mg od Rosuvastatin 10 mg od	Moderate-intensity statin therapy may be considered[a]: Pitavastatin 4 mg od Atorvastatin 20 mg od Rosuvastatin 10 mg od
Additional notes	With LDL-cholesterol target goal <55 mg/dL (1.4 mmol/L) and 50% decrease from baseline LDL-cholesterol	With LDLc target goal <70 mg/dL (1.8 mmol/L) and 50% decrease from baseline LDL-cholesterol	Shared medical decision between health care professional and patient

Abbreviations: ACR, albumin-to-creatinine ratio; ASCVD, atherosclerotic cardiovascular disease; CKD, chronic kidney disease; DM, diabetes mellitus; EACS, European AIDS Clinical Society; LDLc, low-density lipoprotein cholesterol; od, once daily; Severe CKD, eGFR < 30 mL/min/1.73 m^2 or eGFR 30–44 mL/min/1.73 m^2 and ACR > 30.

[a]High-intensity statin is recommended in individuals with at least one markedly elevated risk factor, in particular: (i) Total cholesterol >8 mmol/L (>310 mg/dL), LDL cholesterol >4.9 mmol/L (>190 mg/dL), or blood pressure ≥ 180/110 mmHg. (ii) Individuals with familial hypercholesterolaemia without other major risk factors. (iii) People who have had diabetes for at least 10 years or another additional risk factor without target organ damage. (iv) Moderate CKD (eGFR 30–44 mL/min/1.73 m^2 and ACR < 30 or eGFR 45–59 mL/min/1.73 m^2 and ACR 30–300 or eGFR ≥ 60 mL/min/1.73 m^2 and ACR > 300) SCORE2 ≥ 7.5% in people aged <50 years, ≥10% in people aged 50–69 years and ≥15% in people aged >70 years.

[b]For individuals not considered as per the listed criteria above, moderate-intensity statin is recommended.

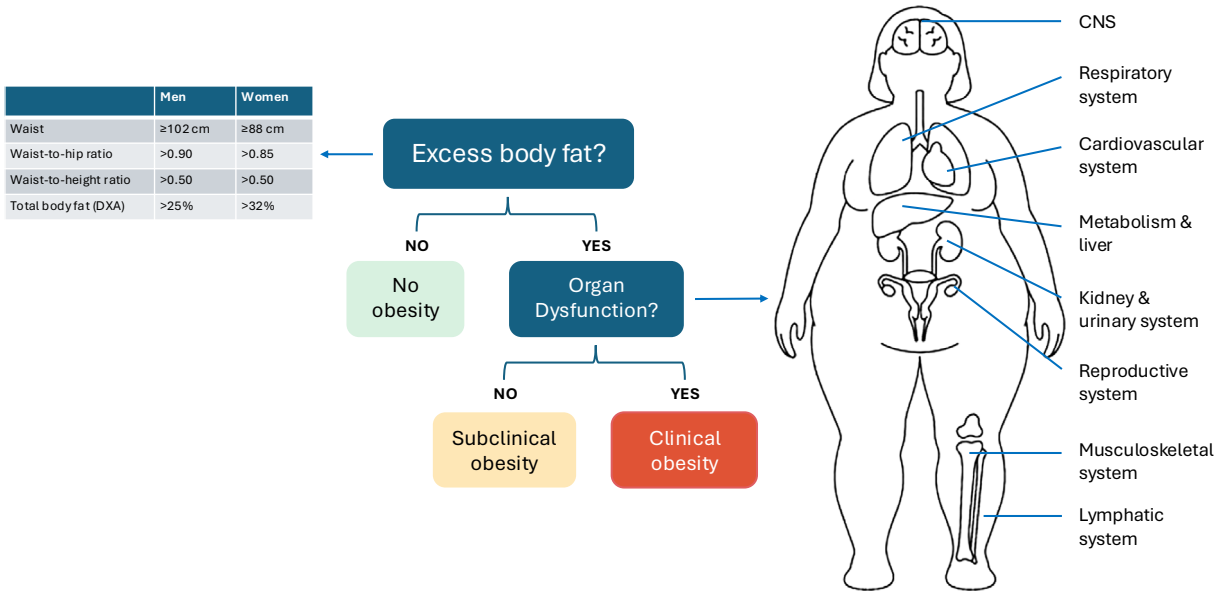
[c]Statin dose to be adjusted considering the risk of drug–drug interactions with the concurrent antiretroviral treatment.

prevalence to identifying advanced fibrosis. The guidelines endorse various non-invasive screening methods, including Fibroscan, elastography and FIB-4, with practical thresholds for referral. The impact of ART on liver steatosis, particularly weight gain on INSTI and insulin resistance from protease inhibitors, is acknowledged. Cirrhosis management remains largely unchanged, but a new visual tool supports decision-making. HCC screening has been reorganized to distinguish between viral and non-viral causes.

The **chronic lung disease** section has been updated to align with the 2025 GOLD guidelines [40]. It focuses exclusively on COPD, reflecting both its prevalence and clinical relevance in people with HIV.

The **mental health** subsection introduces a key update in terminology, replacing 'psychotherapy' with 'psychological treatment' to better reflect multidisciplinary approaches. Mental health remains a central factor influencing sleep quality, substance use and treatment adherence. While the depression and anxiety management algorithms are unchanged, the section emphasizes the need for proactive screening and support in routine care. There is now stronger integration with patient-reported outcomes (PROs), sleep disorders, and substance use pathways. Consistent with this, the guidelines recommend that clinicians consider psychological comorbidities when assessing fatigue, insomnia or persistent somatic symptoms. Cross-links to menopause, sexual dysfunction and ageing are included, reflecting the broad psychosocial impact of mental health in people with HIV.

A unified **substance use** section consolidates prior content on alcohol, opioids and chemsex. A simple screening approach is proposed: one initial question, followed by more detailed tools only if clinically indicated. Diagnostic criteria align with ICD-10, and guidance is offered on when to refer. For alcohol, the AUDIT-C is the preferred screening tool, followed by a brief intervention or motivational interviewing based on patient readiness. In the chemsex and other sexualized substance chapter, a new DDI table categorizes substances by pharmacologic class, with clear clinical notes. Substances are categorized



Adapted from: Macek P et at. Diabetes Metab Syndr Obes 2020; Rubino F et al. Lancet Diabetes Endocrinol 2025.

FIGURE 2 New definition of obesity: Excess of fat plus organ dysfunction.

by pharmacological class. Opioid guidance has been updated and incorporated, including new terminology consistent with international standards.

A new section on **sleep health** addresses the high prevalence of sleep disorders in people with HIV [41]. Routine assessment is encouraged, starting with a simple screening question and, if indicated, validated tools such as the Insomnia Severity Index [42] and Epworth Sleepiness Scale questionnaires [43] can be used. The section outlines common disorders including insomnia, excessive daytime sleepiness and obstructive sleep apnea. It emphasizes non-pharmacological management, such as behavioral strategies and sleep hygiene, and highlights modifiable risk factors like mental health disorders, alcohol excess and recreational drug use, ART effects, and weight review. ART-related sleep disturbances are addressed, particularly those associated with EFV and second-generation INSTI.

The chapter on **older adults with HIV** brings together content on frailty, prescribing, and falls. Structured assessment of geriatric domains (including cognition, nutrition, vision, hearing and psychological well-being) is encouraged. Frailty screening from age 50 years is supported. A comprehensive geriatric assessment may be conducted by trained HIV clinicians. The ICOPE framework is mentioned as a reference, though not formally adopted due to feasibility concerns. Vitamin D supplementation is only recommended in people with confirmed deficiency.

The section on **solid organ transplantation** reflects current clinical practice, highlighting the growing use of donor organs from people with HIV. Recommended ART regimens pre- and post-transplant are selected to minimize DDI and improve graft outcomes. Hepatitis C infection is no longer considered a contraindication to transplantation, and long-acting injectable ART drugs have shown promising safety profiles in transplant recipients [44]. The guidelines reinforce pre-transplant vaccination and therapeutic drug monitoring to optimize outcomes.

The **travel section** has been updated for clarity. Physician's assessment of air travel safety should be considered for people with recent hospitalization for a respiratory illness, such as pneumocystis pneumonia or pneumothorax [45]. Guidance is included for managing long-acting injectable ART during extended trips, with bridging strategies in case of missed injections.

The **PROs** chapter has been reorganized to highlight their role in person-centred care. Domains include mental and physical health, stigma, sexual wellbeing, adherence, substance use and social determinants. Tools should be brief, validated and locally adapted. The emphasis is on using PROs to guide decisions, identify unmet needs and enhance communication between patients and clinicians. A future objective is to endorse specific PROs measures (PROMS) using consensus-based methods.

The section on **sexual dysfunction** retains its domain-based structure and includes new content. Lubricants are recommended as first-line for symptom relief, with hormonal treatments used as appropriate. Delayed ejaculation and pain in women are addressed more explicitly, and interdisciplinary input is encouraged. ART–drug interactions (e.g., with PDE5 inhibitors) are referenced.

These updates respond to the evolving needs of people with HIV and support clinicians in delivering holistic, evidence-based care that effectively addresses common comorbidities in this population.

CONCLUSIONS

Version 13.0 of the EACS Guidelines offers a more appropriate organization of its content. All sections and chapters have been reviewed and updated to reflect the evolving needs of people with HIV. Version 13.0 strengthens the participation of experts from across Europe and other parts of the world, providing recommendations applicable to various settings.

AUTHOR CONTRIBUTIONS

Juan Ambrosioni, Laura Levi, Jasmini Alagaratnam, Andrea Mastrangelo, Abiu Sempere, Paolo Paioni, Catia Marzolini, Alexandra Calmy, Charles Béguelin, Cristiana Oprea, Esteban Martínez and Jürgen K. Rockstroh prepared the first draft of different manuscript sections. All authors have seen, corrected and approved the final version. The EACS Governing Board consists of: Karoline Aebi-Popp, Juan Ambrosioni, Sanjay Bhagani, Christoph Boesecke, Deniz Gökengin, Ole Kirk, Justyna Kowalska, Agnès Libois, Paddy Mallon, Esteban Martínez, Tetiana Melnyk, Silvia Nozza, Miłosz Parczewski, Ann Sullivan and Annemarie Wensing.

CONFLICT OF INTEREST STATEMENT

Declarations of interest of all panel members are available upon request. Please contact info@eacsociety.org. Juan Ambrosioni has received personal fees from and participated in advisory boards for ViiV, Gilead, Janssen and MSD; has received funding for research from ViiV, Gilead and MSD; and has been a member of data safety monitoring boards for HIPRA and Grifols, all outside the current work. Jasmini Alagaratnam has received speaker's fees and/or advisory board honoraria and/or conference travel support from Gilead Sciences Ltd., MSD, and ViiV Healthcare, unrelated to this work. Giovanni Guaraldi has received research grants and personal fees for consulting or speaking at educational events from Gilead, MSD, Janssen and ViiV. Alasdair Bamford has received personal fees for consulting from Gilead. Alexandra Calmy has received institutional educational grants from MSD, ViiV Healthcare and Gilead paid to the Geneva University Hospitals. Catia Marzolini has received research grants from Gilead. Susanne Dam Nielsen has received research grants and personal fees for consulting or speaking at educational events from Gilead, ViiV/GSK and Takeda. Esteban Martínez has received grants from ViiV and consultation fees from ViiV, Gilead, MSD and Janssen. Cristiana Oprea has received consultation fees from ViiV, MSD and Gilead. Steven Welch has received support for PENTA training from ViiV, Janssen and Gilead. Jürgen K. Rockstroh has received personal fees for consulting or speaking at educational events from AbbVie, Boehringer, Gilead, MSD, Janssen and ViiV. Laura Levi, Abiu Sempere, Andrea Mastrangelo, Paolo Paioni, Anna Koval and Luis Mendao have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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