

# Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

## **eMethods: Recommendations Development Process**

### **I. Brief Summary**

The recommendations for antiretroviral therapy in adults with HIV infection recommendations were developed by an international panel of experts in HIV research and patient care. The Panel was established initially in 1995 by the International Antiviral Society–USA (IAS–USA)<sup>1</sup>; members are selected by the IAS–USA Board of Directors and vetted by the organization for suitability for the panel. Panel members serve in a volunteer (uncompensated) capacity and do not participate in industry promotional activities such as speakers' bureaus, paid lectures directly for industry, or other marketing activities during their tenure on the panel. Members of the current panel convened in person and by conference calls from November 2023 to October 2024. The chair (Rajesh T. Gandhi, MD) oversees the discussions of the process and evidence review and manuscript development, and guides the group to consensus. Section leaders (**eBox 3**) and teams were appointed to evaluate evidence and summarize panel discussions for each section. Prior to selection of the section teams and leaders, panel members declared their financial relationships with commercial concerns, discussed potential conflicts of interest (COIs), and recused themselves from serving as section leaders or team members as necessary.

Evidence considered for updating the recommendations was limited to data published in the scientific literature, presented at major peer-reviewed scientific conferences, or released as safety reports by regulatory agencies or data safety and monitoring boards, since the last update in December 2022.<sup>2</sup> Literature searches were conducted by a member (Carlos del Rio) in PubMed and EMBASE for the period June 2022 to July 2024. Publication list is reviewed by a panel member (Michael S. Saag) for relevance. Approximately 249 citations were ultimately identified from a list of more than 2998. After July 2024, the panel closely monitored the literature through October 2024 for new evidence that impacted the recommendations. Abstracts that were presented at scientific conferences between June 2022 and October 2024 were identified by panel members and teams. Manufacturers of antiretroviral drugs were asked to submit lists of relevant publications or abstracts meeting the established criteria. All reference lists, published papers, abstracts, and other relevant reports were organized and stored on a web-based, shared, electronic drive to which all panel members have ongoing access.

These recommendations focus on HIV-1–infected adults in international, developed-world settings where antiretroviral drugs are generally available (approved by regulatory bodies or available by expanded access) or in late-stage development (new drug application filed). Recommendations were made by full-panel consensus and rated according to the strength of the recommendation and the quality of the supporting evidence (**Manuscript Table 1**). For areas in which recommendations have not changed substantially or no or few new data are available, the reader is referred to the previous report.<sup>2</sup>

### **II. Detailed Summary**

#### **a. Background**

The medical management of HIV changes rapidly, owing to the continued rapid advances in pathogenic and clinical knowledge leading to necessary changes in patient care, as well as ongoing availability of new drugs, formulations, and laboratory testing to optimally manage HIV infection. In 1995, on recognizing the rapidly changing knowledge base, the complexity of HIV management and expertise needed to provide quality care, and the lack of current plans to update any existing HIV guidelines, the need to disseminate reliable evidence-based guidance for clinicians involved in HIV management was clear. The IAS–USA International Antiretroviral Recommendations Panel was established in 1995 by the IAS–USA to develop this needed guidance for physicians and other clinicians actively involved in HIV care.

#### **b. The IAS–USA and Its Role in the Recommendations**

The IAS–USA is a 501(c)(3) not-for-profit, mission-based, nonmembership, educational organization that was established in 1992. The mission of the IAS–USA is to improve the prevention, treatment, care, and quality of life for people with or at risk of HIV or other viral infections and their associated health conditions through high-quality, relevant, balanced, and needs-oriented education, and provide information for practitioners and scientists who are actively involved in medical care and research. The IAS–USA delivers annual continuing medical education (CME) programs on HIV and other

viral infections that include live virtual and in-person courses; live webinars; and indexed journal *Topics in Antiviral Medicine*<sup>™</sup>. In addition, the IAS–USA manages and serves as the CME sponsor for the annual HRSA-supported Clinical Conference for Ryan White HIV/AIDS Program Practitioners, and for the annual Conference on Retroviruses and Opportunistic Infections (CROI), a research conference.

The IAS–USA is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide CME for physicians.

IAS–USA has sponsored the development of evidence-based recommendations for viral load monitoring, antiretroviral therapy, HIV drug resistance testing, cytomegalovirus (CMV) infection, and the metabolic complications of antiretroviral therapy, all of which are published in the medical literature.<sup>1,3-21</sup> In addition to the published recommendations, the IAS–USA served as the collaborating partner for the American Association for the Study of Liver Diseases (AASLD)/Infection Diseases Society of America (IDSA)/IAS–USA HCV Guidance ([www.HCVguidelines.org](http://www.HCVguidelines.org)) from its inception until January 2016.

The volunteer members of the IAS–USA Scientific Leadership Board (**eBox 1**) oversee the development of the information and educational programs and are not compensated for their roles in the organization.

IAS–USA funding comes from a variety of sources. The largest single-source of revenue is conference and CME participant registration fees. Other funding sources include grants from the pharmaceutical/diagnostics (commercial) industries, grants and subcontracts from government agencies, private donations, and gifts-in-kind from local community businesses and individuals. The commercial support that IAS–USA accepts is only for selected activities. Our large national CME effort on HIV invite funding in the form of educational grants from industry. Per IAS–USA policy, any effort that uses commercial grants must receive grants from several companies with competing products. Funds are pooled and distributed to activities within the effort at the sole discretion of the IAS–USA. Funders have no input into any activity, including its content, development, or selection of topics or speaker(s). Funders are listed in each activity as applicable.

The development of the Antiretroviral Therapy Recommendations is supported and funded by the IAS–USA. The IAS–USA determined the need for updated recommendations; selected panel members based on expertise in research and care to represent developed-world settings affected by HIV; determined the most appropriate way to disseminate the information (eg, publication in a medical journal rather than publication in the IAS–USA journal, web publication, etc); and provided administrative oversight and financial support.

The Panel itself is responsible for proposing the design and conduct of the work; collection, management, analysis, and interpretation of the data; and preparation, review, and approval of the manuscript. The IAS–USA provided staff support for administrative management, oversight of literature searches, and editorial and production assistance. At least one member of the Scientific Leadership Board serves in each panel to ensure continued alignment with the IAS–USA mission.

### **c. Identifying and Screening Panel Members**

The panel was initially appointed in 1995, and members have rotated periodically since then. In evaluating potential participants for the Panel, the IAS–USA Scientific Leadership Board considered individuals who 1) are recognized as authorities in HIV treatment research and clinical care, 2) have appointments in major medical teaching or research institutions, 3) have a demonstrated ability to review and evaluate evidence in an effort to provide useful recommendations in the field, 4) meet the IAS–USA COI and financial relationship criteria for participation (see below and [www.iasusa.org](http://www.iasusa.org)), and 5) have the ability to work in a collaborative consensus process. In addition, the Scientific Leadership Board emphasize the need for an international, developed world perspective.

Like the IAS–USA Scientific Leadership Board, participants in IAS–USA panels are volunteers and receive no financial compensation for their panel participation. In joining the Panel, members agree to commit substantial time to the effort necessary for evidence review and for participation in the consensus process.

### **d. COI Management**

It is the policy of IAS–USA to ensure balance, independence, objectivity, and scientific rigor in all its activities. All parties with control over the content of IAS–USA activities are required to disclose to the organization and activity audience any financial relationship with ineligible companies (formerly commercial interests) 24 months. Financial relationships can include receipt of grants or research

support, status as employee or consultant, stock or options holder, paid lecturer, writer, or author, or member of speakers bureau. The ACCME defines ineligible companies as “those whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.” Part of the IAS–USA policies to ensure the integrity of its activities is the policy to separate commercial promotion from core IAS–USA educational and informational activities. Individuals who conduct marketing or promotional activities for ineligible companies may not contribute to core IAS–USA programs. A marketing or promotional activity includes any activity in which the ineligible company controls key elements, such as speaker or topic selection, that could be used to serve the entity’s financial interests (eg, speakers bureaus, advertorials, etc). Individuals may not participate in most IAS–USA programs for 12 months after functioning in a promotional or marketing effort for an ineligible company. A notable exception to the separation policy is CROI, which allows research presentations by individuals with some of such relationships (including employment) because of its large focus on the presentations on original research, if their research or work passes rigorous peer review. Panel members who meet general criteria and are appointed, agree not to participate in any promotional activity on behalf of an ineligible company (eg, serve on a speaker bureau, as a paid lecturer, or a similar contribution) while a member of the panel. Any conforming financial relationships with ineligible companies that still represent a real or potential COI(s), will be mitigated so that they do not influence the content or recommendations. Prior to selection of the section teams and leaders, panel members declared their financial relationships with ineligible companies, discussed potential COIs, and recused themselves from serving as section leaders or team members accordingly.

### **III. The IAS–USA Antiretroviral Recommendations Panel**

The members of the IAS–USA Antiretroviral Recommendations Panel are listed in **eBox 2**. The Panel convened in person in November 2023 and October 2024, and regularly by conference call. The chair oversees the discussions of the process and evidence review and manuscript development, and guides the group to consensus. Section leaders and teams were appointed to evaluate evidence and summarize panel discussions for each section.

### **IV. Rating the Recommendations**

The Panel is divided by topic into working sections, each with a section leader. These sections are responsible for reviewing and screening evidence, developing preliminary recommendations, and presenting these to the full Panel for discussion, identification of further evidence, and consensus.

The selected rating system (**Manuscript Table 1**) combines 2 ratings for each recommendation. One rates the strength of the recommendation (strong, moderate, or limited support) and the other rates the quality of the evidence (ranging from Ia, based on evidence from 1 or more randomized controlled clinical trial[s] published in the peer-reviewed literature, to III, based on the Panel’s analysis of the accumulated available evidence).<sup>22</sup>

### **V. Content of the Recommendations**

The Panel agreed on the purpose, audience, and scope of these recommendations and on 9 main content sections (and subsections).

Content Sections:

1. When to Start and What to Start (initiation therapy)
2. When to Switch and What to Use Including New options for Long-Acting ART
3. ART Considerations in the Setting of OIs, Including TB Prevention
4. Laboratory Monitoring
5. Metabolic Complications/Weight Gain
6. HIV and Cancer
7. Substance Use and HIV
8. HIV and STI Prevention
9. Equity
10. Future Directions

Panel members were assigned to content sections based on their expertise and section leaders were appointed (**eBox 3**). The Panel Chair participates in all sections and reviews the entire manuscript, and Michael S. Saag, MD, reviewed literature search results and identified relevant publications, and also reviewed the entire manuscript.

From November 2023 and August 2024, sections met in person and by conference call and e-mail exchange. Initial discussions were used to develop detailed Section outlines, and assign participants to draft subsections. The full Panel reviewed sections and the final manuscript.

## VI. Evidence Collection and Literature Searches

Panel members were selected based on their active work in the field of HIV research and care, and detailed knowledge of available evidence (published and presented at major scientific conferences).

Literature searches in PubMed and Embase were conducted and designed by an expert in systematic reviews, Kimberly R Powell and one of the panel members, Carlos del Rio (**eTable 1**). The initial literature search provided data available since the 2022 publication of the recommendations through July 2024; approximately 249 references were ultimately identified. Relevant abstracts publicly presented at recent scientific conferences were identified by panel members. All manufacturers of FDA-approved antiretroviral drugs were asked to submit lists of publications or abstracts meeting the established criteria (**eTable 2**). Drug manufacturers were instructed to provide references and electronic copies of the published or presented papers or abstracts only and not to comment on the design, methods, results or implications of any of the work. All reference lists, published papers, abstracts, and other relevant reports were organized and stored on a web-based, shared, electronic drive to which all panel members have ongoing access.

## REFERENCES

1. Carpenter CCJ, Fischl MA, Hammer SM, et al. Antiretroviral therapy for HIV infection in 1996: recommendations of an international panel. *JAMA*. 1996;276(2):146-154.  
Ref ID: 795
2. Saag MS, Gandhi RT, Hoy JF, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2020 recommendations of the International Antiviral Society-USA Panel. *JAMA*. 2020;324(16):1651-1669. 2771873 [pii];10.1001/jama.2020.17025 [doi].  
Ref ID: 16689
3. Carpenter CCJ, Fischl MA, Hammer SM, et al. Antiretroviral therapy for HIV infection in 1997: updated recommendations of the International AIDS Society–USA panel. *JAMA*. 1997;277:1962-1969.  
Ref ID: 989
4. Carpenter CCJ, Fischl MA, Hammer SM, et al. Antiretroviral therapy for HIV infection in 1998: updated recommendations of the International AIDS Society–USA panel. *JAMA*. 1998;280:78-86.  
Ref ID: 1382
5. Carpenter CCJ, Cooper DA, Fischl MA, et al. Antiretroviral therapy for HIV infection in adults: updated recommendations of the International AIDS Society–USA panel. *JAMA*. 2000;283(3):381-390.  
Ref ID: 1978
6. Hammer SM, Eron JJ, Jr., Reiss P, et al. Antiretroviral treatment of adult HIV infection: 2008 recommendations of the International AIDS Society-USA panel. *JAMA*. 2008;300(5):555-570.  
Ref ID: 7755
7. Hammer SM, Saag MS, Schechter M, et al. Treatment for adult HIV infection: 2006 recommendations of the International AIDS Society-USA panel. *JAMA*. 2006;296:827-843.  
Ref ID: 6062

8. Thompson MA, Aberg JA, Cahn P, et al. Antiretroviral treatment of adult HIV infection: 2010 recommendations of the International AIDS Society-USA panel. *JAMA*. 2010;304(3):321-333.  
Ref ID: 9521
9. Thompson MA, Aberg JA, Hoy JF, et al. Antiretroviral treatment of adult HIV infection: 2012 recommendations of the International Antiviral Society-USA panel. *JAMA*. 2012;308(4):387-402.  
Ref ID: 11418
10. Yeni PG, Hammer SM, Carpenter CCJ, et al. Antiretroviral treatment for adult HIV-1 infection in 2002: updated recommendations of the International AIDS Society-USA panel. *JAMA*. 2002;288:222-235.  
Ref ID: 4066
11. Yeni PG, Hammer SM, Hirsch MS, et al. Treatment for adult HIV infection: 2004 recommendations of the International AIDS Society-USA panel. *JAMA*. 2004;292:251-265.  
Ref ID: 5128
12. Hirsch MS, Conway B, D'Aquila RT, et al. Antiretroviral drug resistance testing in adults with HIV infection: implications for clinical management. International AIDS Society–USA Panel. *JAMA*. 1998;279(24):1984-1991.  
Ref ID: 1304
13. Hirsch MS, Brun-Vézinet F, D'Aquila RT, et al. Antiretroviral drug resistance testing in adult HIV-1 infection: recommendations of an International AIDS Society-USA Panel. *JAMA*. 2000;283(18):2417-2426.  
Ref ID: 2244
14. Hirsch MS, Brun-Vézinet F, Clotet B, et al. Antiretroviral drug resistance testing in adults infected with human immunodeficiency virus type 1: 2003 recommendations of an International AIDS Society-USA panel. *Clin Infect Dis*. 2003;37:113-128.  
Ref ID: 4617
15. Hirsch MS, Günthard HF, Schapiro JM, et al. Antiretroviral drug resistance testing in adult HIV-1 infection: 2008 recommendations of an International AIDS Society-USA panel. *Clin Infect Dis*. 2008;47(2):266-285.  
Ref ID: 7276
16. Schambelan M, Benson CA, Carr A, et al. Management of metabolic complications associated with antiretroviral therapy for HIV-1 infection: recommendations of an International AIDS Society-USA panel. *JAIDS*. 2002;31(3):257-275.  
Ref ID: 3494
17. Whitley RJ, Jacobson MA, Friedberg DN, et al. Guidelines for the treatment of cytomegalovirus diseases in patients with AIDS in the era of potent antiretroviral therapy. *Arch Intern Med*. 1998;158:957-969.  
Ref ID: 1393
18. Saag MS, Holodniy M, Kuritzkes DR, et al. HIV viral load markers in clinical practice. *Nat Med*. 1996;2(6):625-629.  
Ref ID: 836
19. Martin DF, Dunn JP, Davis JL, et al. Use of the ganciclovir implant for the treatment of cytomegalovirus retinitis in the era of potent antiretroviral therapy: recommendations of the International AIDS Society–USA panel. *Am J Ophthalmol*. 1999;127(3):329-339.  
Ref ID: 2330

20. Saag MS, Benson CA, Gandhi RT, et al. Antiretroviral drugs for treatment and prevention of HIV infection in adults: 2018 recommendations of the International Antiviral Society-USA panel. *JAMA*. 2018;320(4):379-396. 10.1001/jama.2018.8431.  
Ref ID: 15875
21. Gunthard HF, Calvez V, Paredes R, et al. HIV drug resistance: 2018 recommendations of the International Antiviral Society-USA panel. *Clin Infect Dis*. 2018;[Epub ahead of print] 10.1093/cid/ciy463.  
Ref ID: 15813
22. Canadian Task Force on the Periodic Health Examination. The periodic health examination. *Can Med Assoc J*. 1979;121(9):1193-1254.  
Ref ID: 11289
23. National Institute on Drug Abuse (NIDA). Smoking and substance involvement screening (NIDA-Modified ASSIST). <https://nida.nih.gov/sites/default/files/pdf/nmassist.pdf>. Accessed October 15, 2024.  
Ref ID: 18125
24. Skinner HA. The drug abuse screening test. *Addict Behav*. 1982;7(4):363-371. 0306-4603(82)90005-3 [pii];10.1016/0306-4603(82)90005-3 [doi].  
Ref ID: 17354
25. Yudko E, Lozhkina O, Fouts A. A comprehensive review of the psychometric properties of the Drug Abuse Screening Test. *J Subst Abuse Treat*. 2007;32(2):189-198. S0740-5472(06)00259-5 [pii];10.1016/j.jsat.2006.08.002 [doi].  
Ref ID: 14652
26. McNeely J, Strauss SM, Saitz R, et al. A brief patient self-administered substance use screening tool for primary care: two-site validation study of the substance use brief screen (SUBS). *Am J Med*. 2015;128(7):784-19. S0002-9343(15)00178-3 [pii];10.1016/j.amjmed.2015.02.007 [doi].  
Ref ID: 17355
27. Wickersham JA, Azar MM, Cannon CM, Altice FL, Springer SA. Validation of a brief measure of opioid dependence: the rapid opioid dependence screen (RODS). *J Correct Health Care*. 2015;21(1):12-26. 21/1/12 [pii];10.1177/1078345814557513 [doi].  
Ref ID: 17356
28. Hedlund JL, Vieweg BW. The Michigan alcoholism screening test (MAST): a comprehensive review. *Journal of Operational Psychiatry*. 1984;15:55-65.  
Ref ID: 18126
29. Di Paola A, Farabee D, Springer SA. Validation of two diagnostic assessments for opioid and stimulant use disorder for use by non-clinicians. *Psychiatr Res Clin Pract*. 2023;5(3):78-83. RCP21074 [pii];10.1176/appi.prcp.20230022 [doi].  
Ref ID: 18115
30. Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption--II. *Addiction*. 1993;88(6):791-804.  
Ref ID: 9459
31. McNeely J, Wu LT, Subramaniam G, et al. Performance of the tobacco, alcohol, prescription medication, and other substance Use (TAPS) tool for substance use screening in primary care patients. *Ann Intern Med*. 2016;165(10):690-699. 2546703 [pii];10.7326/M16-0317 [doi].

Ref ID: 18127



## **eBox 1. Volunteer IAS–USA Scientific Leadership Board, October 2024**

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Professor of Medicine  
Co-Director, Center for AIDS Research  
Director, AIDS Research Institute  
University of California San Francisco  
San Francisco, California

Douglas D. Richman, MD, Co-Chair  
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Veterans Affairs San Diego Healthcare  
System  
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Director, Antiviral Research Center (AVRC)  
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## eBox 2. IAS–USA Antiretroviral Therapy Recommendations Panel

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### **eBox 3. Working Sections of the IAS–USA Antiretroviral Therapy Recommendations Panel**

- **When to Start/What to Start**  
Section Team: Huldrych F. Günthard, MD (Leader), Constance A. Benson, MD, Joseph J. Eron, Jr, MD, Paul E. Sax, MD, and Melanie A. Thompson, MD
- **When to Switch and What to Use**  
Section Team: Paul A. Sax, MD (Leader), Roger Bedimo, MD, Jennifer H. Hoy, MBBS, and Huldrych F. Günthard, MD
- **ART Considerations in the Setting of OIs, Including TB Prevention**  
Section Team: Constance A. Benson, MD (Leader), Brenda Crabtree-Ramirez, and Huldrych F. Günthard, MD
- **Laboratory Monitoring**  
Section Team: Davey M. Smith, MD (Leader), Huldrych F. Günthard, MD, and Clara Lehmann, MD
- **Metabolic Complications/Weight Gain**  
Section Team: Melanie A. Thompson, MD (Leader), Roger Bedimo, MD, Huldrych F. Günthard, MD, and Jennifer H. Hoy, MBBS
- **HIV and Cancer**  
Section Team: Clara Lehmann, MD
- **Substance Use and HIV**  
Section Team: Sandra Springer, MD (Leader), Ellen Eaton, MD, and Carlos del Rio, MD
- **HIV and STI Prevention**  
Section Team: Raphael J. Landovitz, MD (Leader), Susan P. Buchbinder, MD, Carlos del Rio, MD, Jean-Michel Molina, MD, PhD, and Sandra Springer, MD
- **Equity**  
Section Team: Brenda Crabtree-Ramirez (Leader), Carlos del Rio, MD, Ellen Eaton, MD, and Sandra Springer, MD
- **Future Directions**  
Section Team: Joseph J. Eron, Jr, MD (Leader), Raphael J. Landovitz, MD, Clara Lehmann, MD, and Paul E. Sax, MD

**eTable 1. Summary of Evidence Collection**

| Evidence Identification  | Number of References From the Initial Search | Number of References Considered Possibly Relevant (Ultimately) |
|--|--|--|
| <b>August 2024 Submission</b>  |  |  |
| Relevant published reports and meeting abstracts <ul style="list-style-type: none"> <li>• PubMed and Embase searches (June 2022 to August 2024)</li> </ul> | <b>&lt; 2998</b>                             | <b>249</b>   |
| <ul style="list-style-type: none"> <li>• Panel members' identification*</li> </ul>   | ongoing                                      |  |
| Number of relevant references reported in manuscript (submitted <b>110</b> )   |  | <b>110</b>   |

\*Of note, individual panel members collected relevant evidence throughout the process and reviewed materials submitted by manufacturers (particularly for safety issues) and this process cannot be quantified.

**eTable 2. Search Terms Used and Results of Embase and PubMed Literature Searches\***

**SEARCH STRATEGY**

| Search | EMBASE QUERY   | Results |
|--------|--|---------|
| #1     | ('human immunodeficiency virus infection'/mj OR 'human immunodeficiency virus'/mj OR 'human immunodeficiency virus infected patient'/mj) AND ('antiretrovirus agent'/exp OR 'highly active antiretroviral therapy'/exp) AND [14-10-2022]/sd AND [english]/lim NOT (([child]/lim OR pediatr*:ti OR paediatr*:ti OR adolescen*:ti OR child*:ti OR infan*:ti OR neonat*:ti OR newborn*:ti) NOT ([adult]/lim OR [aged]/lim OR adult*:ti)) AND ('clinical article'/de OR 'clinical trial'/de OR 'clinical trial (topic)'/de OR 'cohort analysis'/de OR 'controlled study'/de OR 'longitudinal study'/de OR 'major clinical study'/de OR 'multicenter study'/de OR 'observational study'/de OR 'practice guideline'/de OR 'prospective study'/de OR 'randomized controlled trial'/de OR 'randomized controlled trial (topic)'/de OR 'retrospective study'/de OR 'systematic review'/de) NOT ([animals]/lim NOT [humans]/lim) NOT ('conference abstract'/it OR 'conference paper'/it OR 'conference review'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) | 3082    |

| Search | PUBMED QUERY   | Results |
|--------|--|---------|
| #2     | ("Aged"[Mesh] OR senior[tw] OR "older adult"[tw] OR elderly[tw] OR geriatric[tw] OR ageing[tw] OR "older person"[tw]) AND ("HIV Infections"[Mesh] OR "HIV positive"[tw] OR "HIV Seropositivity/diagnosis"[Mesh] OR "Anti-Retroviral Agents"[Mesh] OR "antiretrovirals"[tw]) AND ("Aging"[Mesh] OR "Frailty"[Mesh] OR frailty[tw] OR "Polypharmacy"[Mesh] OR polypharmacy[tw] OR "Social Isolation"[Mesh] OR "social isolation"[tw] OR "Depression"[Mesh] OR depression[tw] OR "Cognition"[Mesh] OR "neurocognitive function"[tw] OR "Mass Screening"[Mesh] OR "Adverse effects"[tw] OR "Drug-Related Side Effects and Adverse Reactions"[Mesh] OR "adverse events"[tw] OR "Pharmacokinetics"[Mesh] OR "pharmacokinetics"[tw] OR "Quality of Life"[Mesh] OR "quality of life"[tw] OR "Cognitive Dysfunction"[Mesh] OR "neurocognitive impairment"[tw] OR "integrated geriatric care"[tw] OR "CPE score"[tw] OR "ARV Stewardship"[tw]) AND ("2022/10/14"[PDat] : "3000/12/31"[PDat]) AND English[lang] | 215     |
| #3     | ((((("HIV Infections"[Majr]) AND "Anti-Retroviral Agents"[Mesh] AND ((Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb]) AND hasabstract[text] AND ("2022/10/14"[PDat] : "3000/12/31"[PDat]) AND English[lang] AND adult[MeSH]))) OR (((HIV AND antiretroviral*) NOT medline[sb] AND ((clinical[Title/Abstract] AND trial[Title/Abstract]) OR  | 738     |

|    |  |      |
|----|--|------|
|    | <p>clinical trials[MeSH Terms] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[MeSH Terms] OR therapeutic use[MeSH Subheading])) AND hasabstract[text] AND ("2022/10/14"[PDat] : "3000/12/31"[PDat])) OR (HIV Infections[majr] AND Anti-Retroviral Agents[mh] AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb]) AND ("2022/10/14"[PDat] : "3000/12/31"[PDat]) AND English[lang] NOT (child[mh] OR pediatr*[ti] OR paediatr*[ti] OR adolescen*[ti] OR child*[ti] OR infan*[ti] OR neonat*[ti] OR newborn*[ti] NOT (adult[mh] OR adult*[ti]))) OR (HIV Infections/dt[majr] AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb]) AND ("2022/10/14"[PDat] : "3000/12/31"[PDat]) AND English[lang] NOT (child[mh] OR pediatr*[ti] OR paediatr*[ti] OR adolescen*[ti] OR child*[ti] OR infan*[ti] OR neonat*[ti] OR newborn*[ti] NOT (adult[mh] OR adult*[ti]))) OR (HIV Infections[majr] AND Antiretroviral Therapy, Highly Active[mh] AND (Clinical Trial[ptyp] OR Comparative Study[ptyp] OR Controlled Clinical Trial[ptyp] OR Meta-Analysis[ptyp] OR Multicenter Study[ptyp] OR Randomized Controlled Trial[ptyp] OR systematic[sb]) AND ("2022/10/14"[PDat] : "3000/12/31"[PDat]) AND English[lang] NOT (child[mh] OR pediatr*[ti] OR paediatr*[ti] OR adolescen*[ti] OR child*[ti] OR infan*[ti] OR neonat*[ti] OR newborn*[ti] NOT (adult[mh] OR adult*[ti]))) NOT letter[pt]</p> |      |
| #4 | <p>HIV OR "HIV Infections"[Mesh]) AND (antiretroviral* OR anti-retroviral* OR "Anti-Retroviral Agents"[Mesh] OR "HIV Infections/drug therapy"[Mesh]) AND ((clinical[tiab] AND trial[tiab]) OR "clinical trials as topic"[MeSH Terms] OR random*[tiab] OR "Random Allocation"[Mesh] OR "Clinical Trial"[Publication Type] OR "Comparative Study" [Publication Type] OR "Controlled Clinical Trial" [Publication Type] OR "Meta-Analysis" [Publication Type] OR "Multicenter Study" [Publication Type] OR "Randomized Controlled Trial" [Publication Type] OR systematic[sb]) NOT ("Child"[Mesh] OR "Adolescent"[Mesh] OR "Infant"[Mesh] OR pediatr*[tiab] OR paediatr*[tiab] OR adolescen*[tiab] OR child*[tiab] OR infan*[tiab] OR neonat*[tiab] OR newborn*[tiab] NOT ("Adult"[Mesh] OR adult*[tiab])) AND English[lang] AND ("2022/10/14"[PDat] : "3000/12/31"[PDat])</p>  | 1068 |

**Pooling and Deduplicating Embase and PubMed results for October 14, 2022 through March 28, 2024 (including “ahead of print” records): 3998**

**eTable 3. Information Requested From Antiretroviral Drug Manufacturers**

| Manufacturer         | Information Requested   | Date Requested | Date Received |
|----------------------|---|----------------|---------------|
| AbbVie               | <ul style="list-style-type: none"> <li>● Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul> | 01/23/24       | 02/16/24      |
| Gilead Sciences, Inc | <ul style="list-style-type: none"> <li>● Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul> | 01/23/24       | 03/21/24      |
| Janssen Therapeutics | <ul style="list-style-type: none"> <li>● Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul> | 01/23/24       | 04/01/24      |
| Merck & Co, Inc      | <ul style="list-style-type: none"> <li>● Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> </ul>  | 01/23/24       | 03/13/24      |

|                   |   |          |          |
|-------------------|---|----------|----------|
|                   | <ul style="list-style-type: none"> <li>Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul>   |          |          |
| Monogram-Labcorp  | <ul style="list-style-type: none"> <li>Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul> | 04/02/24 | 04/18/24 |
| Theratechnologies | <ul style="list-style-type: none"> <li>Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul> | 01/23/24 | N/A      |
| ViiV Healthcare   | <ul style="list-style-type: none"> <li>Presented at national or international conferences or has been published in the peer-reviewed literature</li> <li>Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies)</li> <li>Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.</li> </ul> | 01/23/24 | 03/22/24 |



**eTable 4. Common Drug Abbreviations by Drug Class; Drugs in Alphabetical Order in Each Class**

| <b>Drug class</b>  | <b>Abbreviation</b> |
|--|---------------------|
| Nucleoside/nucleotide reverse transcriptase inhibitors (NRTIs) |                     |
| Abacavir   | ABC                 |
| Emtricitabine  | FTC                 |
| Lamivudine   | 3TC                 |
| Emtricitabine (or lamivudine)                                  | XTC                 |
| Tenofovir alafenamide  | TAF                 |
| Tenofovir disoproxil fumarate                                  | TDF                 |
| Tenofovir alafenamide or tenofovir disoproxil fumarate         | TXF                 |
| Nonnucleoside reverse transcriptase inhibitors (NNRTIs)        |                     |
| Dapivirine   | DPV                 |
| Doravirine   | DOR                 |
| Efavirenz  | EFV                 |
| Rilpivirine  | RPV                 |
| Long-acting rilpivirine  | RPV-LA              |
| Protease Inhibitors (PIs)                                      |                     |
| Atazanavir   | ATV                 |
| Darunavir  | DRV                 |
| Ritonavir  | RTV                 |
| Integrase strand transfer inhibitors (InSTIs)                  |                     |
| Bictegravir  | BIC                 |
| Cabotegravir   | CAB                 |
| Dolutegravir   | DTG                 |
| Elvitegravir   | EVG                 |
| Long-acting cabotegravir                                       | CAB-LA              |
| Raltegravir  | RAL                 |
| Capsid inhibitors  |                     |
| Lenacapavir  | LEN                 |
| Entry inhibitors   |                     |
| Fostemsavir  | FTR                 |
| Ibalizumab   | IBA                 |
| Maraviroc  | MVC                 |
| Pharmacokinetic enhancers                                      |                     |
| Cobicistat   | COBI                |
| Ritonavir  | RTV                 |

**eTable 5. Screening Tools for Substance Use Disorders**

|  |   |
|--|---|
| NIDA Quick Screen and then reflex to NIDA Alcohol, Smoking and Substance Involvement Screening Test (ASSIST) <sup>23</sup> | Up to 6 dozen items, depending on “skip outs”   |
| Drug Abuse Screening Test (DAST) <sup>24,25</sup>  | 10 items, no information about drug of concern  |
| Substance Use Brief Screen (SUBS) <sup>26</sup>  | 4 items, preliminary testing in primary care  |
| Rapid Opioid Dependence Screen (RODS) <sup>27</sup>  | 8 items, DSM-IV Opioid Dependency Validated, PWH, Justice-involved, good sensitivity & specificity                                |
| Michigan Alcohol Screening Test (MAST) <sup>28</sup>   | 10 items, severity measure  |
| Rapid Opioid Use Disorder Assessment (ROUDA) <sup>29</sup>   | 8-items, DSM-5 Validated Moderate to severe OUD, non-clinicians can administer, good sensitivity & specificity                    |
| Rapid Substance Use Disorder Assessment (RSUDA) <sup>29</sup>  | 8-items, DSM-5 Validated Moderate to Severe Stimulant use Disorder, Non-clinicians can administer, good sensitivity & specificity |
| Alcohol Use Disorders Identification Test (AUDIT) <sup>30</sup>  | 10 items, well-validated  |
| Tobacco, Alcohol, Prescription medication, and other Substance Use Tool (TAPS) <sup>31</sup>                               | Two part free screening tool for all substance use . Taps 1 is 4 items and Taps 2 is 9 items.                                     |

**eTable 6. Example of Use of NIDA Quick Screen for OUD then reflex NIDA ASSIST Prior to More In Depth SUD Screening/  
Diagnosis**

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|   |
|---|
| NIDA Quick Screen (OUD)   |
| In the past year, how often have you used the following?  |
| Prescription drugs for non-medical reasons: <ul style="list-style-type: none"><li>• Once or twice • monthly • weekly • daily or almost daily</li></ul>  |
| Illegal drugs: <ul style="list-style-type: none"><li>• Once or twice • monthly • weekly • daily or almost daily</li></ul>   |
| <i>Reflex positive to NM ASSIST</i>   |
| Adapted from: The National Institute on Drug Abuse. NIDA Drug Screening Tool, NIDA-Modified ASSIST (NM ASSIST). <a href="https://www.drugabuse.gov/nmassist/">https://www.drugabuse.gov/nmassist/</a> . Accessed November 18, 2019. |

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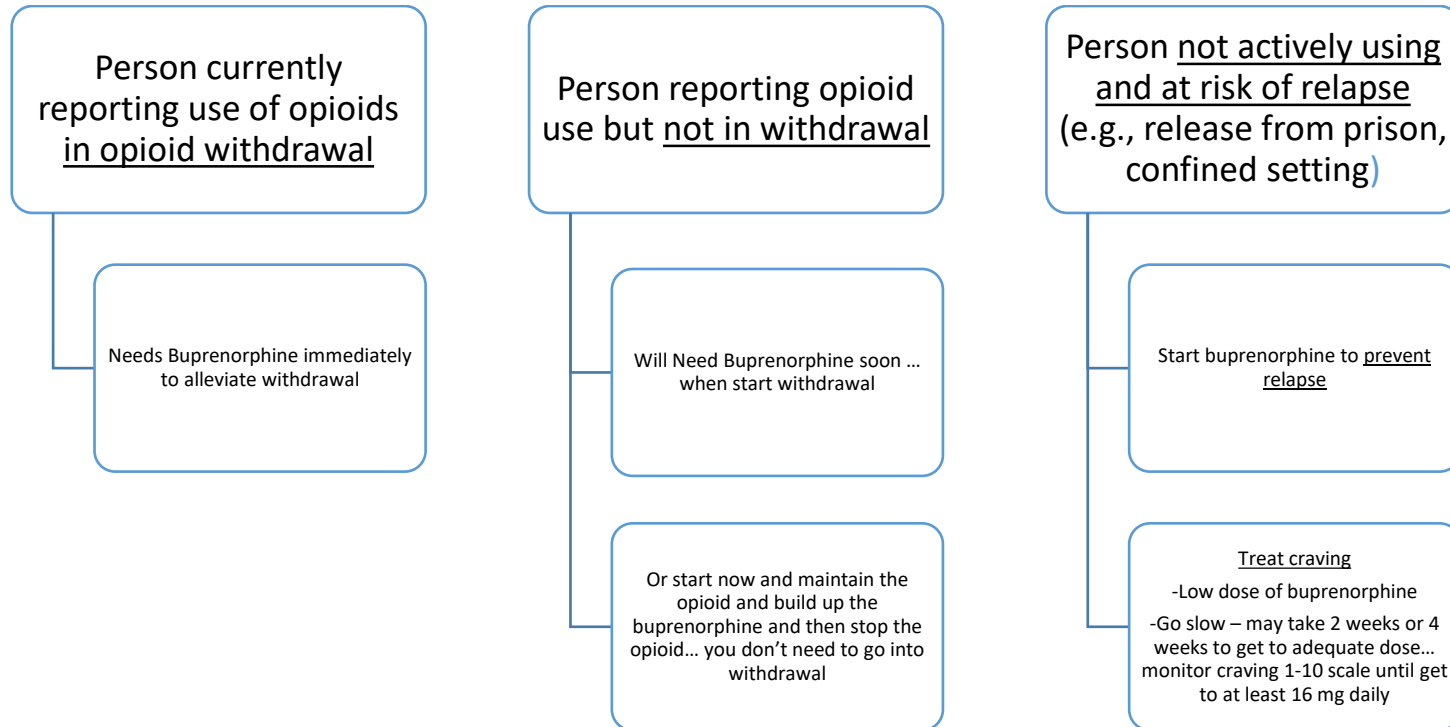
**eTable 7. FDA-approved Medication Treatments of Opioid Use Disorder (MOUD)**

| <b>Medication</b>   | <b>Methadone</b>  | <b>Buprenorphine</b>  | <b>Extended-Release Naltrexone</b>   |
|---|---|---|--|
| Mechanism   | Full $\mu$ agonist  | Partial $\mu$ agonist, partial $\kappa$ antagonist  | Full $\mu$ antagonist  |
| Delivery  | Oral, daily   | Sublingual, film, implant, injection (daily, monthly, 6-mo)   | Injection, monthly   |
| Setting   | Licensed facility   | No special licensing or certification required  | No special licensing or certification required   |
| Notes   | <ul style="list-style-type: none"> <li>• Highly structured (safety concerns)</li> <li>• OD potential</li> <li>• Interacts with some ARVs</li> </ul> | <ul style="list-style-type: none"> <li>• Safer than methadone, without major OD potential</li> <li>• Less interactions with ARVs</li> <li>• Improves VS in HIV treatment</li> </ul> | <ul style="list-style-type: none"> <li>• Also treats AUD</li> <li>• Adherence advantage</li> <li>• No overdose or diversion concerns</li> <li>• Improves VS</li> </ul> |
| <b>ALL MOUD OPTIONS REDUCE HIV RISK BEHAVIORS and REDUCE OPIOID OVERDOSE RISK</b> |   |   |  |

**eTable8. Medication Treatments for Alcohol Use Disorder**

|                     | <b>Naltrexone</b>   | <b>XR- Naltrexone (Vivitrol®)</b>  | <b>Acamprosate</b>  | <b>Disulfiram</b>  |
|---------------------|---|--|---|--|
| Mechanism of Action | Full $\mu$ antagonist   | Full $\mu$ antagonist  | Blocks N-methyl D-aspartate receptors   | Inhibits acetaldehyde dehydrogenase  |
| Delivery            | Oral  | IM   | Oral  | Oral   |
| Frequency           | 50mg Daily  | Monthly  | 2 tablets 3 times day   | Daily  |
| Other               | <ol style="list-style-type: none"> <li>1. Also treats OUD;</li> <li>2. Poor adherence</li> <li>3. Good efficacy;</li> </ol> | <ol style="list-style-type: none"> <li>4. Also treats OUD;</li> <li>5. no diversion;</li> <li>6. no dependence or respiratory depression</li> <li>7. increased adherence over oral naltrexone</li> </ol> | <ol style="list-style-type: none"> <li>8. Not proven to be better than NTX;</li> <li>9. compliance issues;</li> <li>10. can be used with buprenorphine/methadone</li> </ol> | <ol style="list-style-type: none"> <li>11. Poor compliance</li> <li>12. poor efficacy</li> </ol> |

**eFigure 1. Considerations of How to Initiate Buprenorphine in a Person with Opioid Use Disorder**



**eFigure 2. Patient Handout- Sublingual Buprenorphine Induction While Using Opioids or Not Protocol**

Sample of a patient hand-out using 2mg-0.5mg SL Tablets















**Micro-dosing schedule**

Instructions:

Begin taking Suboxone as soon as you pick it up from the pharmacy. It’s better to start this process while opioids are still in your system.

Follow the instructions listed below for each day. Continue the instructions **EVEN IF YOU USE** opioids. Keep increasing the dose as described.

Record when you took your dose and bring this paper back to clinic. Record when and if you took any opioids. We need to know this information to provide the best care for you.

|       |                      | Take each time | Morning dose  | Evening dose  | Please check:            |                          | <u>Any other</u>         |
|-------|----------------------|----------------|---|---|--------------------------|--------------------------|--------------------------|
|       |                      |                |   |   | Morning                  | Evening                  | <u>opioid use?</u>       |
|       |                      |                |   |   |                          |                          | <u>Y or N</u>            |
| Day 1 | 0.5 mg once per day  | 1/4 tablet     |   |   | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Day 2 | 0.5 mg twice per day | 1/4 tablet     |  |  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Day 3 | 1 mg twice per day   | 1/2 tablet     |  |  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Day 4 | 2 mg twice per day   | 1 tablet       |  |  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Day 5 | 3 mg twice per day   | 1 & 1/2 tablet |  |  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Day 6 | 4 mg twice per day   | 2 tablets      |  |  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Day 7 | 4 mg twice per day   | 2 tablets      |  |  | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |