Supplemental Online Content

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

eBox 1. IAS–USA Antiretroviral Therapy Recommendations Panel

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eBox 2. Working Sections of the IAS–USA Antiretroviral Therapy Recommendations Panel

- **When to Start**
  Section Team: Melanie A. Thompson, MD (Co-Leader), Gerd Fätkenheuer, MD (Co-Leader), Constance A. Benson, MD, Carlos del Rio, MD, and Paul A. Volberding, MD

- **Recommended Initial Regimes**
  Section Team: Rajesh T. Gandhi, MD (Co-Leader), Paul E. Sax, MD (Co-Leader), Constance A. Benson, MD, Joseph J. Eron, Jr, MD, Gerd Fätkenheuer, MD, Huldrych F. Günthard, MD, and Jennifer H. Hoy, MBBS

- **When and How to Switch**
  Section Team: Jennifer F. Hoy, MBBS (Leader), Carlos del Rio, MD, Joseph J. Eron, Jr, MD, Gerd Fätkenheuer, MD, and Rajesh T. Gandhi, MD, and Paul E. Sax, MD

- **Laboratory Monitoring**
  Section Team: Davey M. Smith, MD (Leader), Huldrych F. Günthard, MD, and Melanie A. Thompson, MD

- **Prevention**
  Section Team: Raphael J. Landovitz, MD (Leader), Susan P. Buchbinder, MD, Jean-Michel Molina, MD, PhD, and Michael S. Saag, MD

- **Aging and HIV**
  Section Team: Melanie A. Thompson, MD (Leader), Carlos del Rio, MD, Rajesh T. Gandhi, MD, Huldrych F. Günthard, MD, and Jennifer H. Hoy, MBBS

- **Cost**
  Section Team: Paul E. Sax, MD (Leader), Huldrych F. Günthard, MD, and Davey M. Smith, MD

- **Ending the Epidemic**
  Section Team: Carlos del Rio, MD (Leader), Raphael J. Landovitz, MD, and Melanie A. Thompson, MD

- **New Directions/Emerging Trends**

Section Team: Joseph J. Eron, Jr, MD (Leader), Rajesh T. Gandhi, MD, Raphael J. Landovitz, MD, and Michael S. Saag, MD

eBox 3. Volunteer IAS–USA Board of Directors, June 2020

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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) [1]; 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 October 2019 to June 2020. The chair (Michael S. Saag, MD) oversees the discussions of the process and evidence review and manuscript development, and guides the group to consensus. Section leaders (**eBox 2**) 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 January 2018 through August 2020. [2] Literature searches are conducted by a systematic review methodologist at the University of California San Francisco and Emory University. Publication list is reviewed by panel members (Carlos del Rio, MD, and Paul A. Volberding, MD) for relevance. Approximately 549 citations were ultimately identified from a list of more than 4980. Relevant abstracts publically presented at recent scientific conferences were identified by panel members. 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 individuals with or at risk for HIV infection in international, developed-world settings where antiretroviral drugs are generally available (approved by regulatory bodies or available by expanded access). 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.[3]

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 treatment, care, and quality of life for people with HIV, hepatitis C virus (HCV), or other viral infections through high-quality, relevant, balanced, and needs-oriented education and information for practitioners who are actively involved in medical care. The IAS–USA delivers annual continuing medical education (CME) programs on HIV and HCV that include live courses; live intensive, interactive workshops; live webinars;\);

and the peer-reviewed, indexed journal *Topics in Antiviral Medicine.*™ In addition, 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.[1,4-22] 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) from its inception until January 2016.

The volunteer members of the IAS–USA Board of Directors (**eBox 3**) oversee the development of the information and educational programs and are not compensated for their roles in oversight and governance of the organization.

IAS–USA funding comes from a variety of sources. 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. One large national CME effort invites 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 disease; determined the most appropriate way in which to dissemble 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. IAS–USA provided staff support for administrative management, oversight of literature searches and editorial and production assistance. At least one member of the Board serves in each panel to ensure continuing 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 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), and 5) have the ability to work in a collaborative consensus process. In addition, the Board emphasized the need for an international, developed world perspective.

Like the IAS–USA Board of Directors, 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 interest or other relationship with the manufacturer(s) of any commercial product(s) or provider(s) of commercial services with interests discussed in the activity

(eg, presentation, article, etc) within at least the past 12 months. Financial interests or other relationships can include receipt of grants or research support, status as employee or consultant, stock or options holder, paid lecturer, paid lecturer, writer, or author, or member of speakers bureau, of the party or of his or her spouse or partner. The ACCME defines a financial interest as an interest of any dollar amount. 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 commercial firms may not contribute to core IAS–USA programs. A marketing or promotional activity includes any activity in which the commercial entity controls key elements, such as speaker or topic selection, that could be used to serve the entity's commercial 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 a commercial firm. A notable exception to the separation policy is the annual Conference on Retroviruses and Opportunistic Infections (CROI) which allows research and symposia 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 a pharmaceutical or medical device 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 commercial entities that still may represent a real or potential COIs, will be resolved so that they do not influence the content of the recommendations. Prior to selection of the section teams and leaders, panel members declared their financial relationships with commercial concerns, 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 1**. The Panel convened in person in December 2019 to June 2020, 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).[23]

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
2. Recommended Initial Regimes
3. When and How to Switch
4. Laboratory Monitoring
5. Prevention
6. Aging and HIV
7. Cost
8. Ending the Epidemic
9. New Directions/Emerging Trends

Panel members were assigned to content sections based on their expertise and section leaders were appointed (**eBox 2**). The Panel Chair participates in all sections and reviews the entire manuscript, and Carlos del Rio, MD, and Paul A. Volberding, MD, oversaw the literature searches, reviewed search results, and identified relevant publications, and also reviewed the entire manuscript.

From October 2019 to August 2020, the panel 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 (see **eTable 2 and eTable 3** for search strategies and keywords). The initial literature search provided data available since the 2018 publication of the recommendations through May 2020; approximately 549 references were ultimately considered possibly relevant. For aging and HIV, a separate search was conducted which produced 336 more non-duplicated citations.

And additional (bridge) literature search was conducted in August 2020, approximately 915 references were identified. Relevant abstracts publically 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 1**). 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.

eReferences

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Ref ID: 6062

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Ref ID: 16523

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Ref ID: 16527

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Ref ID: 16028

eTable 1. Information Requested From Antiretroviral Drug Manufacturers

Manufacturer	Information Requested	Date Requested	Date Received
AbbVie	● Presented at national or international conferences or has been published in the peer-reviewed literature ● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies) ● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.	11/07/19	**N/A**
Boehringer Ingelheim Pharmaceuticals, Inc	● Presented at national or international conferences or has been published in the peer-reviewed literature ● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies) ● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful. ●	11/07/19	**N/A**
Bristol-Myers Squibb	● Presented at national or international conferences or has been published in the peer-reviewed literature ● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies) ● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.	11/07/19	**N/A**
Gilead Sciences, Inc	● Presented at national or international conferences or has been published in the peer-reviewed literature ● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies) ● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.	11/07/19	12/17/19
Janssen Therapeutics	● Presented at national or international conferences or has been published in the peer-reviewed literature ● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies) ● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.	11/07/19	01/13/20
Merck & Co, Inc	● Presented at national or international conferences or has been published in the peer-reviewed literature	11/07/19	01/10/20

Manufacturer	Information Requested	Date Requested	Date Received
	● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies) ● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.		
Roche-Genentech	● Presented at national or international conferences or has been published in the peer-reviewed literature ● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies) ● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful. ●	11/07/19	**N/A**
Theratechnologies	● Presented at national or international conferences or has been published in the peer-reviewed literature ● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies) ● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.	11/07/19	12/17/19
ViiV Healthcare	● Presented at national or international conferences or has been published in the peer-reviewed literature ● Data should be from prospective clinical trials (ie, properly randomized controlled trials), cohort studies, and ancillary trials (pharmacologic and drug interaction studies) ● Any information about newly recognized toxicities and complications associated with your product(s) would be helpful.	11/07/19	12/17/19

eTable 2. Summary of Evidence Collection

Evidence Identification	**Number of References From the Initial Search**	**Number of References Considered Possibly Relevant (Ultimately)**	
August 2020 Submission			
Relevant published reports and meeting abstracts ● PubMed and EMBASE searches (January 2018 to August 2020)	**< 4980**	**549**	
● Panel members' identification*	ongoing		
Number of relevant references reported in manuscript (submitted **August 2020)**			**105**

*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 3. Search Terms Used and Results of Embase and PubMed Literature Searches*

SEARCH STRATEGY (January 2018 to May 2020)

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 [1-1-2018]/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)	2848

Search	PUBMED QUERY	Results
#3	("Aged"[Mesh] OR senior[tw] OR “older adult”[tw] OR elderly[tw] OR geriatric[tw]) **AND** ("HIV Infections"[Mesh] OR “HIV positive”[tw] OR "HIV Seropositivity/diagnosis"[Mesh]) **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]) **AND** ("2018/01/01"[Date - Publication] : "2020/05/31"[Date - Publication]) AND English[lang]	336
#2	(((((("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 ("2012/07/01"[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 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 ("2012/07/01"[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 ("2012/07/01"[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 ("2012/07/01"[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	83

Search	PUBMED QUERY	Results
	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 ("2012/07/01"[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]	
#1	(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 ("2012/07/01"[PDat] : "3000/12/31"[PDat])	1676

- Pooling and Deduplicating Embase and PubMed results for 09/17/19 through January 2020 (including “ahead of print” records): 4065
- Aging PubMed results: 336

SEARCH STRATEGY (August 2020)

Search	PUBMED QUERY	Results
#1	("Aged"[Mesh] OR senior[tw] OR “older adult”[tw] OR elderly[tw] OR geriatric[tw]) AND ("HIV Infections"[Mesh] OR “HIV positive”[tw] OR “HIV-positive”[tw] OR "HIV Seropositivity/diagnosis"[Mesh]) 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]) AND ("2020/01/01"[Date - Publication] : "2020/08/21"[Date - Publication]) AND English[lang] ("HIV Infections"[Majr] OR “HIV positive”[tw] OR “HIV-positive”[tw] OR "HIV Seropositivity/diagnosis"[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	915

Search	PUBMED QUERY	Results
	infan*[tiab] OR neonat*[tiab] OR newborn*[tiab] NOT ("Adult"[Mesh] OR adult*[tiab])) AND English[lang] AND ("2019/12/01"[Date - Publication] : "2020/08/21"[Date - Publication])	

Search	PUBMED QUERY	Results
#1	("Aged"[Mesh] OR senior[tw] OR “older adult”[tw] OR elderly[tw] OR geriatric[tw]) AND ("HIV Infections"[Mesh] OR “HIV positive”[tw] OR “HIV-positive”[tw] OR "HIV Seropositivity/diagnosis"[Mesh]) 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]) AND ("2020/01/01"[Date - Publication] : "2020/08/21"[Date - Publication]) AND English[lang] ("HIV Infections"[Majr] OR “HIV positive”[tw] OR “HIV-positive”[tw] OR "HIV Seropositivity/diagnosis"[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 ("2019/12/01"[Date - Publication] : "2020/08/21"[Date - Publication])	915

- Pooling and Deduplicating Embase and PubMed results for August 2020 (including “ahead of print” records): 915 of which 79 were considered possibly relevant and shared with panel.

eTable 4. Frailty Assessment Tools

Tool	Variables	Interpretation
Fried's Frailty Phenotype[24] Consists of 5 measures of physical performance	1. Unintentional weight loss of >10 lbs (>4.5 kg) or >5% of body mass in the last year	1. Obtained from patient, caregiver, or medical records
	2. Weakness (assessment based on the handgrip strength measurement)	2. Interpretation of results takes into account sex and body mass index
	3. Exhaustion scale	3. Self-report based on 2 questions from Center for Epidemiological Studies Depression (CES-D)
	4. Slow gait (walking time over a distance of 15 feet [4.5 meters]))	4. Takes into account sex and height; slow if ≥15.3 seconds if height ≤173 cm (≤159 cm in women), and ≥13.1 seconds if height >173 cm in men (>159 cm in women)
	5. Low physical activity	5. Energy expenditure <383 kcal/week for men and <270 kcal/week for women, based on the modified Minnesota Leisure Time Activity Questionnaire.
Short Physical Performance Battery (SPPB)[25] Consists of 3 assessments of time to complete a task or ability to complete a task	1. Repeated chair stands (from sitting position, stand then sit 5 times) 2. Balance tests (stand with feet side-by-side for 10 seconds, if able to do side-by-side move to stand with feet semi-tandem (one foot in front of the other foot, with big toe touching heel of the other foot) and then tandem (1 foot directly behind other foot with all toes touching heel of the other foot) for 10 seconds 3. A 4-meter (10-foot) walk test Available at: https://geriatrictoolkit.missouri.edu/SPPB-Score-Tool.pdf	A final summary performance score out of 12 is calculated. In order to classify people as frail, prefrail and nonfrail, the following cutoffs are used: SPPB 0-6 (frail), SPPB 7-9 (prefrail), SPPB 10 to 12 (nonfrail).

Tool	Variables	Interpretation
Frailty Index[26] Consists of 37 health variables falling into 3 domains	1. Physical (18 variables) 2. Psychological (5 variables) 3. Social/Functional (14 variables) [See e**Table 5** below for listing of variables]	The Frailty Index score (between 0-1) is derived from the number of deficits divided by the number of health variables assessed. <.08 = robust .08 to .24 = prefrail ≥ .25 = frail

eTable 5. Frailty Index Variables

Domain	Deficit Cut-off
Physical Domain	
Lost more than 5 kg in the last year	Yes = 1; No = 0
Stayed in bed at least half the day due to health (in the last month)	Yes = 1; No = 0
Cut down in usual activity (in the last month)	Yes = 1; No = 0
Walk outside	<3 days = 1; ≥3 days = 0
High blood pressure	Yes = 1; Suspected = 0.5; No = 0
Congestive heart failure	Yes = 1; No = 0
Stroke	Yes = 1; No = 0
Cancer	Yes = 1; No = 0
Diabetes	Yes = 1; Suspected = 0.5; No = 0
Osteoarthritis	Yes = 1; Suspected = 0.5; No = 0
Chronic lung disease	Yes = 1; No = 0
MMSE	<10 = 1; 11-17 = 0.75; 18-20 = 0.5; 20-24 = 0.25; >24 = 0
Urinary incontinence	Yes = 1; No = 0
BMI	18.5 – <25 =0; 25 – <30 = 0.5; ≥30 = 1; <18.5 = 1
Grip Strength (GS)	If BMI ≤24, GS ≤29 = 1; If BMI >24 – 28, GS ≤30 = 1; If BMI >28, GS ≤32 = 1
Timed gait (TG) of 10 m, usual pace	If height ≤173 cm, TG ≥15.3 s =1; If height >173 cm, TG ≥13.1s =1
Self rating of health	Poor = 1; Fair = 0.75; Good = 0.5; Very Good = 0.25; Excellent = 0
How health has changed in the last year	Worse = 1; Better/Same = 0
Psychologic Domain	
Feel everything is an effort	Most of the time = 1; Sometimes = 0.5; Rarely = 0
Feel depressed	Most of the time = 1; Sometimes = 0.5; Rarely = 0
Feel happy	Most of the time = 0; Sometimes = 0.5; Rarely = 1
Feel lonely	Most of the time = 1; Sometimes = 0.5; Rarely = 0
Have trouble getting going	Most of the time = 1; Sometimes = 0.5; Rarely = 0
Social/Functional Domain (Activities of Daily Living)	
Help bathing	Yes = 1; No = 0
Help dressing	Yes = 1; No = 0
Help getting in/out of a chair	Yes = 1; No = 0
Help walking around the house	Yes = 1; No = 0
Help eating	Yes = 1; No = 0
Help grooming	Yes = 1; No = 0
Help using the toilet	Yes = 1; No = 0
Help up/down stairs	Yes = 1; No = 0
Help lifting 5 kg	Yes = 1; No = 0
Help shopping	Yes = 1; No = 0
Help with housework	Yes = 1; No = 0
Help with meal preparation	Yes = 1; No = 0
Help taking medications	Yes = 1; No = 0
Help with finances	Yes = 1; No = 0

Abbreviations: BMI, body mass index; MMSE, mini-mental state examination. Adapted from: Searle SD, et al. *BMC geriatrics*. 2008.[26]

eTable 6. Selected Novel Antiretroviral Agents in Clinical Development

Agent	Mechanism of Action	Stage of Development	Mode of administration	Patient populations under study; trial number at clinicaltrials.gov
Islatravir[27-29]	NRTTI	Phase III	Oral once daily, once weekly, once monthly (PrEP)	Treatment naive, switch and HTE patients, PrEP; NCT04233879 NCT04223778 NCT04233216 NCT04003103
GS 6207[30]	Capsid inhibitor	Phase IIb	Oral and subcutaneous every 6 months	Treatment-naive and HTE patients; NCT04143594 NCT04150068
Leronlimab[31]	CCR5- binding mAb blocking HIV entry	Phase IIb/III	Weekly subcutaneous injection	HTE patients and as single-agent maintenance therapy; NCT03902522 NCT02859961
UB-421[32]	CD4-binding mAb blocking HIV entry	Phase II	Weekly IV infusion	HTE patients and as single agent maintenance therapy; NCT04406727 NCT03149211
Broadly HIV neutralizing antibodies[33,34]	Bind HIV envelope trimer at different epitopes	Phase I/II	IV and subcutaneous infusion	Maintenance of suppression, clearance of HIV reservoir, HIV prevention; NCT03739996 NCT04340596 NCT02568215 NCT02716675

NRTTI = nucleoside reverse transcriptase translocation inhibitor

HTE= heavily treatment experienced

mAb = monoclonal antibody