TABLE. Summary of HIV guideline development, Estonia. Supplementary material to article Reinap M, et al. Strengthening guideline contextualization in the WHO European Region. Bull World Health Organ; 2024 (ID: BLT.24.291779)

No	WHO guideline(s)				Contextualisation of the Estonian national guideline "Pre- and post-exposure prophylaxis of HIV infection and treatment of people living with HIV" (2019)				
	Question (original)	Evidence source(s)	Recommendation(s)	Strength of recommendation, certainty of evidence	Question	Evidence source(s)	Local considerations	Recommendation	Strength of recommendation, certainty of evidence
1	Should oral PrEP (containing tenofovir) be used for preventing HIV infection among people at substantial risk of HIV infection?	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition, WHO; 2016	Oral pre-exposure prophylaxis (PrEP) containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches	Strong recommendation, high-quality evidence	Should oral pre-exposure prophylaxis be offered in addition to standard prevention methods (ie, condom) for people at substantial risk of HIV infection? ***In Estonian:*** *Kas inimestel, kellel on oluline HIV nakatumise risk, peaks HIV nakatumise vähendamiseks kasutama lisaks tavapärastele ennetusmeetmetele PrEP või mitte?*	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition, WHO; 2016 Additional evidence from updated systematic literature search using WHO 2016 original search strategy	Because of high cost, PrEP has not been accessible in Estonia. Due to generics entering the market, the availability is expected to increase considerably	Oral pre-exposure prophylaxis should be offered in addition to standard prevention methods (ie, condom) for people at substantial risk of HIV infection ***In Estonian:*** *Inimestele, kel on oluline HIV-i nakatumise risk, soovitage nakatumise vältimiseks lisaks tavapärastele ennetusmeetmetele (kondoomi kasutamine) ka PrEP-i*	Strong recommendation, high-quality evidence
2	(P) Individuals with exposure that has the potential for HIV transmission. (I) [DTG] [RAL] [ATV/r] [DRV/r] [EFV] in combination with an age appropriate NRTI backbone (TDF+XTC in adults and adolescents or AZT+3TC in children), (C) Current WHO recommendations: TDF+XTC+LPV/r for adults and adolescents, AZT+3TC+LPV/r for children	[1]WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition, WHO; 2016 [2]WHO. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV. WHO; 2018	**Overall** An HIV post-exposure prophylaxis regimen with two ARV drugs is effective, but three drugs are preferred[1] **Adults and adolescents** TDF + 3TC (or FTC) is recommended as the preferred backbone regimen for HIV post-exposure prophylaxis[1] DTG is recommended as the preferred third drug for HIV post-exposure prophylaxis[2] When available, ATV/r, DRV/r, LPV/r and RAL may be considered as alternative third drug options for post-exposure prophylaxis[2]	Conditional recommendation, low-certainty evidence Strong recommendation, low-certainty evidence Strong recommendation, low-certainty evidence Conditional recommendation, low-certainty evidence	Should PEP be recommended for people at risk of HIV infection after exposure? ***In Estonian:*** *Kas inimestel, kellel on kokkupuute järgselt oluline HIV nakatumise risk, peaks HIV nakatumise vältimiseks kasutama PEPi või mitte?*	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition, WHO; 2016 (main components) WHO. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV. WHO; 2018 (preferred active substances) Additional evidence from updated systematic literature search using WHO 2018 guideline original search strategy Additional evidence from systematic literature search related to PEP effectiveness	At the time of guideline development, there was no national programme for PEP in Estonia. The GDG took into consideration that the use of PEP is common practice in other countries. As PEP did not demonstrate significant adverse affects compared to placebo, and the duration of treatment is short, the positive effect outweights the potential limitations	TDF/FTC + RAL, TDF/FTC + DRV/r(c) or TDF/FTC + DTG is recommended for HIV post-exposure prophylaxis (PEP) for people at risk of HIV infection. HIV PEP should be started as soon as possible after the exposure, preferably in the first 72h. Treatment lasts for 28 days ***In Estonian:*** *Inimestel, kel on HIV-i nakatumise risk, kasutage kokkupuutejärgse profülaktikana kombinatsiooni TDF/FTC + RAL, TDF/FTC + DRV/r(c) või TDF/FTC + DTG. Alustage profülaktikat võimalikult kiiresti, eelistatult 72 tunni jooksul pärast kokkupuudet. Profülaktika kestab 28 päeva*	Strong recommendation, low-certainty evidence
3	In treatment naive adults and adolescents with HIV is using a regimen of 2 NRTIs with an INSTI compared to 2 NRTIs with efavirenz as first line ART more effective?	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016	First-line ART for adults a should consist of two nucleoside reverse-transcriptase inhibitors (NRTIs) plus a non-nucleoside reverse-transcriptase inhibitor (NNRTI) or an integrase inhibitor (INSTI) TDF + 3TC (or FTC) + EFV as a fixed-dose combination is recommended as the preferred option to initiate ART If TDF + 3TC (or FTC) + EFV is contraindicated or not available, one of the following alternative options is recommended: - AZT + 3TC + EFV - AZT + 3TC + NVP - TDF + 3TC (or FTC) + NVP TDF + 3TC (or FTC) + DTG or TDF + 3TC (or FTC) + EFV 400 mg/day may be used as alternative options to initiate ART	Strong recommendation, moderate-quality evidence Strong recommendation, moderate-quality evidence Conditional recommendation, moderate-quality evidence	In treatment naive adults with HIV is using a regimen of 2 NRTIs+INSTI compared to 2 NRTI with efavirenz as first line ART more effective? ***In Estonian:*** *Kas ravinaivsetel HIV-positiivsetel isikutel on esimese rea ravis efektiivsem 2 NRTI+INSTIga või 2 NRTI+efavirenz?*	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016 Additional evidence from updated systematic literature search using WHO 2016 guideline original search strategy WHO. Systematic literature review and network meta-analysis to assess first-line ART treatments to inform the WHO consolidated ARV guidelines. Technical Report. WHO; 2019	Due to the size of the market, active substance specific recommendations are not possible in Estonia. ART is covered by the Estonian goverement, procured by Estonian Health Insurance Fund and is free of charge for people living with HIV. The GDG also considered the results of the cost-effectiveness of ART in the health technology assessment (HTA) report	First line ART should consist of two NRTIs + INSTI ***In Estonian:*** *HIV-positiivsete isikute ARV-ravi esmakordsel alustamisel kasutage kombinatsiooni 2 NRTI + INSTI.*	Strong recommendation, moderate-quality evidence
4	In individuals with HIV on ART does an integrase inhibitor-containing regimen compared to a non-integrase inhibitor-containing regimen result in lower incidence of toxicities?	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016	Countries should discontinue d4T use in first-line regimens because of its well-recognized metabolic toxicities	Strong recommendation, moderate-quality evidence	In individuals with HIV on ART does an INSTI-containing regimen compared to a non-INSTI-containing regimen result in lower incidence of adverse effects? ***In Estonian:*** *Kas HIV-positiivsetel isikutel, kes saavad INSTI-t sisaldavat ARV ravi, on lühi- ja pikaajalisi kõrvaltoimeid vähem võrreldes INSTI-t mitte sisaldavate ravikeemidega?*	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016 Additional evidence from updated systematic literature search using WHO 2016 guideline original search strategy WHO. Systematic literature review and network meta-analysis to assess first-line ART treatments to inform the WHO consolidated ARV guidelines. Technical Report. WHO; 2019	-	No recommendation against any active substance was given	NA
5	For individuals with HIV on antiretroviral treatment, do regimens with fixed-dose combination ARVs compared to non-fixed-dose ARVs result in better adherence?	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016	Fixed-dose combinations and once-daily regimens are preferred for antiretroviral therapy	Strong recommendation, moderate-quality evidence	For individuals with HIV on ART, do regimens with fixed-dose 1 tablet a day compared to non-fixed-dose 2-3 tablets a day result in better adherence? ***In Estonian:*** *Kas HIV-positiivsetel ARV ravi saavatel isikutel tagab parema ravikuulekuse fikseeritud doosiga üks-tablett-päevas raviskeem või 2-3 tabletti päevas raviskeem?*	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016 Additional evidence from updated systematic literature search using WHO 2016 guideline original search strategy	TThe GDC considered that the evidence is unclear. According to the patient representative, adherence is negatively impacted more in case tablets are taken more than once a day than how many tablets are taken.	Once-daily regimens are preferred for antiretroviral therapy ***In Estonian:*** *ARV-ravi määramisel eelistage kord päevas manustatavaid ravimeid mitu korda päevas manustatavatele ravimitele.*	Strong recommendation, low-certainty evidence
6	In individuals with HIV who have been on ART for 12 months and have achieved viral suppression is measuring viral load every 6 months compared to every 12 months more effective?	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016	Routine viral load monitoring can be carried out at 6 months, at 12 months and then every 12 months thereafter if the patient is stable on ART to synchronize with routine monitoring and evaluation reporting	Conditional recommendation, very low-quality evidence	In individuals with HIV who have achieved viral suppression is measuring viral load every 6 months compared to every 12 months more effective? ***In Estonian:*** *Kas HIV-positiivsetel isikutel, kellel on ARV raviga saavutatud viiruse supressioon, on tulemuslikum HIV-1 VL määramine 6 kuu või 12 kuu järel?*	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016 Updated systematic literature search using WHO 2016 guideline original search strategy was performed, however, no additional evidence was identified	The GDG considered that regular monitoring may decrease risk of treatment resistance, increase early detection of drug adverse effects and interactions with other medications, and improve adherence and disease awareness	Routine viral load monitoring can be carried out every 6-12 months in people who have achieved viral suppression ***In Estonian:*** *HIV-positiivsetel isikutel, kel on ARV-raviga saavutatud viiruse supressioon, määrake HIV VL iga 6–12 kuu järel*	Conditional recommendation, very low-quality evidence
7	Not asked in WHO HIV guidelines	NA	NA	NA	What are the generally accepted criteria to define viral failure and switch treatment? ***In Estonian:*** *Kas on kindlad kriteeriumid ARV ravi ebaõnnestumise hindamiseks ja ravi vahetamiseks HIV-positiivsetel ARV ravi saavatel isikutel või mitte?*	Evidence from a systematic literature search related to viral failure	Repeated HIV RNA levels above detection may indicate treatment resistance and increase risk of HIV transmission	Generally accepted criteria to define viral failure have not been agreed. Treatment adherence, adverse effects, interactions (drug-drug, drug-food) and psychosocial status should be assessed if HIV RNA is above detection but below 200 copies/ml. In most cases, treatment switch is not necessary. Perform resistance testing and consider treatment switch if HIV RNA is ≥ 200 copies/ml at multiple assessments. In Estonian: Ravi viroloogilise ebaõnnestumise defineerimiseks puuduvad kindlad kriteeriumid. Kui HIV RNA on üle labori määramispiiri, kuid vähem kui 200 koopiat / ml, hinnake ravisoostumust, kõrval- ja koostoimete (ravim-ravim, ravim-toit) esinemist ning psühhosotsiaalseid probleeme. Ütlduhul ei ole ravi vahetamine vajalik. Kui HIV RNA on korduvalt võrdne või suurem kui 200 koopiat / ml, suureneb ravimiresistentsuse tekkerisk, seega määrake lisaks eelnevale resistentsus ja kaaluge ravi vahetamist.	Strong recommendation, very low-quality evidence
8	In adults and adolescents with HIV who are failing an NNRTI-based regimen is switching to DRV/r containing regimen equivalent compared to an ATV/r or LPV/r containing regimen?	WHO. Systematic Review to inform the World Health Organization Consolidated Antiretroviral Therapy Guidelines: Which ART regimen to switch to when failing first-line treatment. WHO; 2019	NA	NA	In adults with HIV who are failing an NNRTI-based regimen is switching to DRV/r containing regimen compared to an ATV/r or LPV/r containing regimen or 2NRTI + DTG more effective? ***In Estonian:*** *Kas NNRTI põhise ravi ebaõnnestumisel on efektiivsem teise rea ravina DRV/r või ATV/r või LPV/r või üleminek kahe toimeainega ravile PI + INSTI või üleminek 2NRTI + DTG?*	WHO. Systematic Review to inform the World Health Organization Consolidated Antiretroviral Therapy Guidelines: Which ART regimen to switch to when failing first-line treatment. WHO; 2019 Additional evidence from clinical trials assessing active substances not included in the WHO systematic review	Resistance testing is available for all HIV patients in Estonia. Due to the size of the market, active substance specific recommendations are not reasonable in Estonia	If NNRTI based treatment fails, switch treatment using at least two, preferably three active substances based on results from resistance testing ***In Estonian:*** *NNRTI-põhise ravi ebaõnnestumisel muutke raviskeemi, kasutage vähemalt kahte, eelistatult kolme aktiivset toimeainet vastavalt resistentsustesti tulemusele*	Strong recommendation, moderate-quality evidence
9	Do less frequent clinic visits compared to monthly visits have comparable programme and patient outcomes? Does less frequent pickup of ARV, CTX, or IPT compared to monthly pickup have comparable programme and patient outcomes?	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016	Less frequent clinical visits (3–6 months) are recommended for people stable on ART Less frequent medication pickup (3–6 months) is recommended for people stable on ART	Strong recommendation, moderate-quality evidence Strong recommendation, low-quality evidence	Do less than once per month clinic visits and medication pickup compared to once per month have comparable treatment outcomes in people with HIV on ART? ***In Estonian:*** *Kas HIV positiivsete ARV ravi saavate isikute arstikülastused ja ravimite väljastus harvem kui üks kord kuus annab sama hea ravitulemuse kui üks kord kuus?*	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016 Updated systematic literature search using WHO 2016 guideline original search strategy was performed, however, no additional evidence was identified	Waiting time for HIV specialists' appointments are relatively short in Estonia. If a patient misses an appointment, they are contacted by the HIV clinic.	Clinical visits every 6–12 months and medication pickup every 3–6 months are recommended for people stable on ART who have achieved viral suppression ***In Estonian:*** *Püsivalt supresseeritud viiruskoormusega ARV-ravil olevatele HIV-positiivsetele isikutele soovitage arsti visiiti iga 6–12 kuu järel ja ravimite väljastust 3–6 kuu järel.*	Conditional recommendation, very low-quality evidence
10	Which interventions improve retention in HIV care? Which interventions improve adherence in HIV care?	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016	Programmes should provide community support for people living with HIV to improve retention in HIV care The following community-level interventions have demonstrated benefit in improving retention in care: - package of community-based interventions - adherence clubs - extra care for high-risk people	Strong recommendation, low-quality evidence very low-quality evidence moderate-quality evidence very low-quality evidence	Which interventions improve adherence and retention in HIV care? ***In Estonian:*** *Millised meetmed parandavad ravi kuulekust ja ravil püsimist HIV positiivsetel isikutel?*	WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach - second edition. WHO; 2016 Additional evidence from two updated systematic literature searches using WHO 2016 guideline original search strategies	There is relevant clinical experience with directly observed ART in Estonia.	The following interventions are recommended for improving adherence and retention in care: - psychosocial and behavioural interventions - directly observed ART combined with psychosocial interventions ***In Estonian:*** *Ravisoostumuse ja ravil püsimise parandamiseks kasutage järgmisi meetmeid:* *- psühhosotsiaalsed ja käitumuslikud sekkumised (sh juhtumi-korraldus, tugilisikuteenus, motiveeriv intervjueerimine, kogemus-nõustamine);* *- otseselt kontrolliitav farmakoloogiline ravi (ARV-, TBC- ja sõltuvusravi, viirushepatiitide ravi) kombineerituna psühho-sotsiaalsete sekkumistega.*	Strong recommendation, low-quality evidence