

Demographic & Clinical Characteristics of People in OPERA® with HIV & Heavy Treatment Experience

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Background

- Issues of resistance, toxicity, adherence, tolerability, and drug-drug interactions present challenges to the long-term use of antiretroviral therapy (ART) by people with HIV who have heavy treatment experience (PWH-HTE)
- Understanding the characteristics and treatment patterns of PWH-HTE is important for designing clinical outcome studies of persistence and virologic control in the HTE population

Objective

Describe the characteristics and treatment patterns of people with HIV and heavy treatment experience (PWH-HTE)

Methods

Study Population

- OPERA® observational cohort
 - Prospectively captured, routine clinical data from electronic health records in the United States (US)
 - Included 149,657 PWH at the time of analysis (August 2022), which represented ~14% of PWH in the US
- Inclusion criteria
 - HIV-1 infection
 - 18 years of age or older
 - Prescribed ART as of 01DEC2021
 - Heavy Treatment Experience (HTE)
 - Previously discontinued or switched ≥3 antiretroviral core agent classes or current regimen is indicative of HTE (Table 1)
 - Includes PWH-HTE who were virologically suppressed and viremic at start of current regimen
- Current regimen: ART regimen being taken on 01DEC2021

Stratification

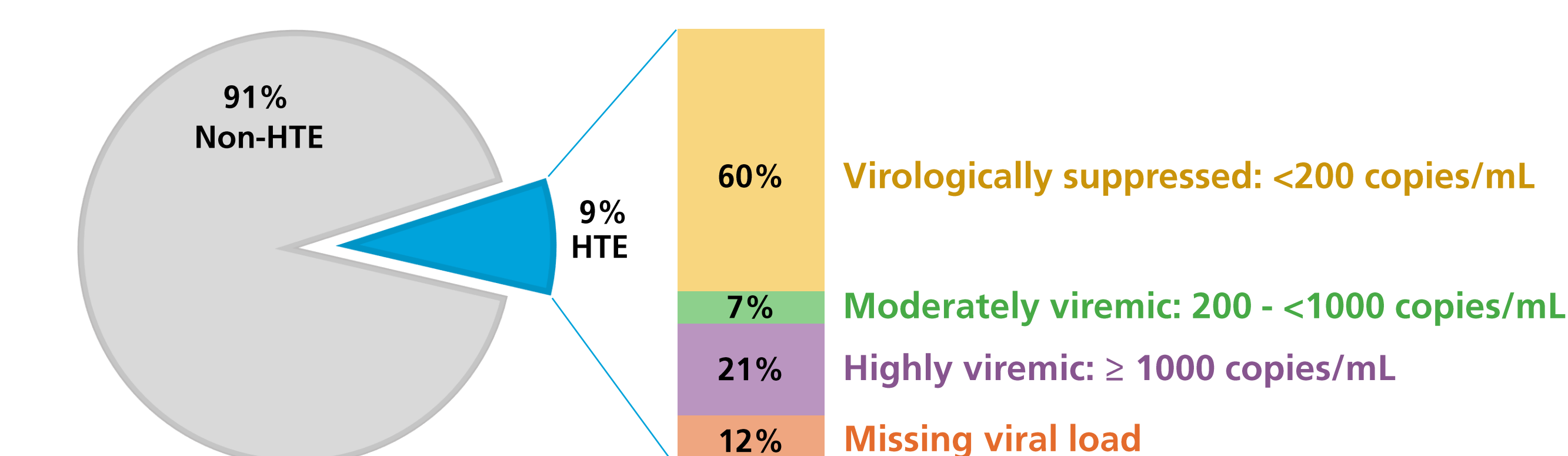
- Virologic status at start of current regimen
 - Virologically suppressed: <200 copies/mL
 - Moderately viremic: 200 - <1,000 copies/mL
 - Highly viremic: ≥1,000 copies/mL
- Determined using the closest viral load (VL) to current regimen start, measured between 18 months before and 7 days after start

Analyses

- Demographics, clinical characteristics, and ART experience described using frequencies (%) for categorical variables and medians (interquartile range) for continuous variables
- PWH-HTE missing a VL at current regimen start were excluded from most descriptions due to substantial missing data

Results

Figure 1. Prevalence of HTE among adult PWH taking ART on 01DEC2021^a and their virologic status at current regimen start



ART, antiretroviral therapy; HTE, heavy treatment experience; mL, milliliter; PWH, people with HIV
^a Denominator: 64,618 adult PWH taking ART on 01DEC2021 in OPERA®

Table 1. Qualifying HTE criteria^a at current regimen start, N = 5,529

HTE Criterion, n (%)	Virologically Suppressed N = 3,304	Moderately Viremic N = 407	Highly Viremic N = 1,152	Missing Viral Load N = 666
Discontinued ≥3 ARV classes ^b prior to index ART regimen	1,049 (32)	85 (21)	280 (24)	70 (11)
Index ART regimen ^c includes:				
Dolutegravir, twice daily	37 (1)	7 (2)	34 (3)	7 (1)
Darunavir, twice daily	31 (1)	≤ 5 ^d	9 (1)	19 (3)
Etravirine	260 (8)	19 (5)	49 (4)	84 (13)
INSTI ^e + PI	1,956 (59)	312 (77)	852 (74)	501 (75)
Maraviroc	199 (6)	10 (2)	20 (2)	48 (7)
Enfuvirtide	≤ 5 ^d	≤ 5 ^d	≤ 5 ^d	≤ 5 ^d
Doravirine ^f	280 (8)	39 (10)	87 (8)	29 (4)
Ibalizumab	13 (<1)	≤ 5 ^d	13 (1)	≤ 5 ^d
Fostemsavir	47 (1)	10 (2)	21 (2)	6 (1)

ART, antiretroviral therapy; ARV, antiretroviral; HTE, heavy treatment experience; INSTI, integrase strand transfer inhibitor; N, number; PI, protease inhibitor
^a Criteria are not mutually exclusive: PWH-HTE can meet ≥1 criterion at a time; ^b Nucleoside/nucleotide reverse transcriptase inhibitors or boosting agents are excluded; ^c ART regimens may or may not include a backbone of nucleoside/nucleotide reverse transcriptase inhibitor(s); ^d HIPAA privacy requirements preclude the reporting of 5 or fewer observations in any cell; ^e Bictegravir, dolutegravir, or elvitegravir; ^f Single agent add-on to a complete regimen, excluding doravirine/tenofovir disoproxil fumarate/lamivudine or doravirine + tenofovir alafenamide/emtricitabine

Table 2. Demographic characteristics at current regimen start, N = 5,529

Characteristic, n (%)	Virologically Suppressed N = 3,304	Moderately Viremic N = 407	Highly Viremic N = 1,152	Missing Viral Load N = 666
Median age (IQR), years	57 (50, 63)	54 (43, 60)	48 (37, 57)	56 (48, 62)
Female sex	716 (22)	85 (21)	295 (26)	164 (25)
Race				
Black	1,405 (43)	222 (55)	718 (62)	327 (49)
White	1,681 (51)	157 (39)	383 (33)	281 (42)
Other	137 (4)	11 (3)	35 (3)	25 (4)
Hispanic ethnicity	717 (22)	82 (20)	181 (16)	70 (11)
Care received in the Southern US	2,157 (65)	306 (75)	828 (72)	577 (87)
Payer ^a				
Medicaid	1,199 (36)	145 (36)	439 (38)	98 (15)
Commercial insurance	1,414 (43)	150 (37)	366 (32)	141 (21)
ADAP/Ryan White	911 (28)	145 (36)	395 (34)	85 (13)
No payer info	418 (13)	35 (9)	121 (11)	321 (48)

ADAP, AIDS Drug Assistance Program; IQR, interquartile range; n, number; PWH-HTE, people with HIV and heavy treatment experience; US, United States
^a Payer data is not mutually exclusive; PWH-HTE can have ≥1 payer at a time

Table 3. Clinical characteristics at current regimen start, N=4,863

Characteristic, n (%)	Virologically Suppressed N = 3,304	Moderately Viremic N = 407	Highly Viremic N = 1,152
Median viral load (IQR), copies/mL	19 (19, 40)	370 (261, 607)	37,175 (8055, 129000)
Median VACS score (IQR)	22 (12, 33)	23 (13, 34)	36 (23, 56)
AIDS-defining event	1,616 (49)	194 (48)	650 (56)
Syphilis ever	920 (28)	133 (33)	412 (36)
Comorbid conditions	2,971 (90)	351 (86)	930 (81)

AIDS, acquired immunodeficiency syndrome; IQR, interquartile range; mL, milliliter; n, number; PWH-HTE, people with HIV and heavy treatment experience; VACS, Veterans Aging Cohort Study

Table 4. Current ART regimen characteristics, N = 4,863

Characteristic, n (%)	Virologically Suppressed N = 3,304	Moderately Viremic N = 407	Highly Viremic N = 1,152
Median mos since initiation (IQR)	27 (11, 43)	27 (11, 46)	26 (10, 44)
Core agent classes			
> 1 core agent	2,585 (78)	365 (90)	976 (85)
INSTI	625 (19)	35 (9)	158 (14)
Core agents			
Dolutegravir	1,940 (59)	270 (66)	783 (68)
Darunavir	1,984 (60)	322 (79)	876 (76)
No NRTI(s) backbone	1,129 (34)	109 (27)	351 (30)

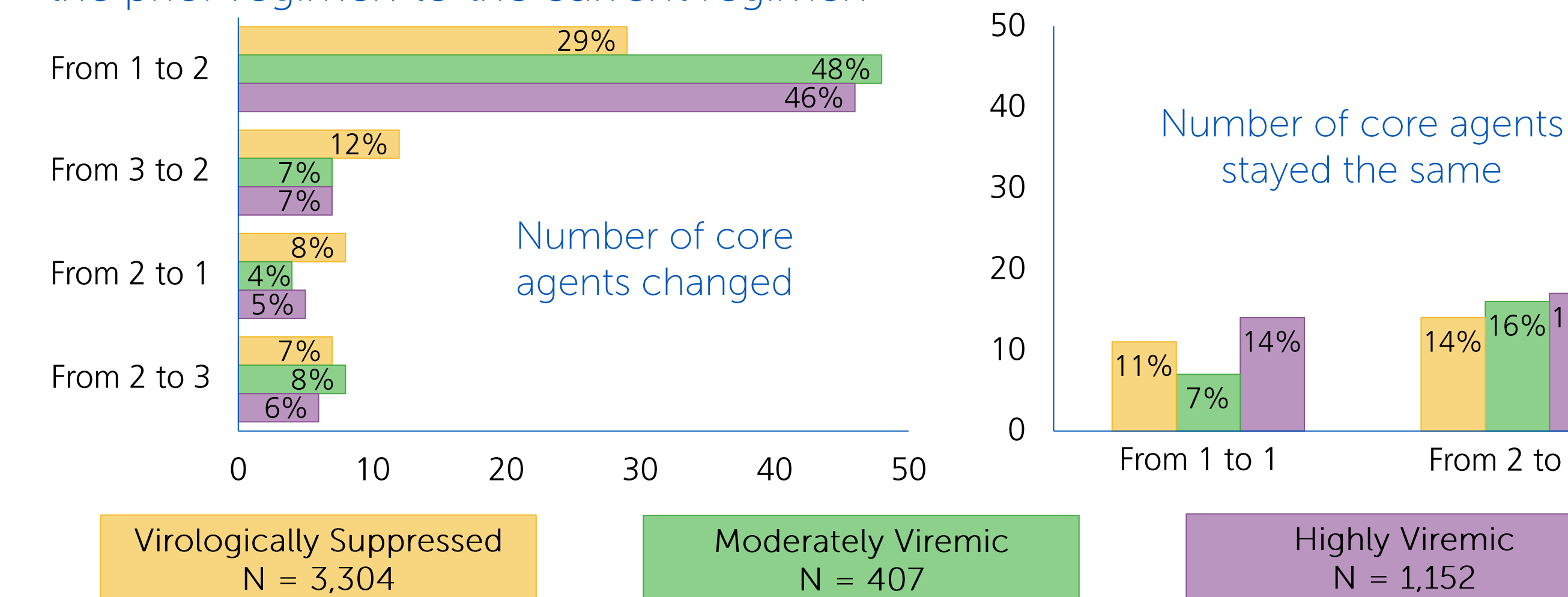
ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; mos, months; n, number; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PWH-HTE, people with HIV & heavy treatment experience

Table 5. ART history among PWH-HTE with prior ART records, N = 4,323

Characteristic, n (%)	Virologically Suppressed N = 2,957	Moderately Viremic N = 370	Highly Viremic N = 996
Median mos since ART initiation (IQR)	84 (39, 145)	62 (22, 111)	66 (29, 110)
Median # core agent classes ever used (IQR)	3 (2, 3)	2 (1, 3)	2 (1, 3)
Any prior use of:			
INSTI	2,617 (89)	302 (82)	838 (84)
PI	2,595 (88)	284 (77)	781 (78)
NNRTI	1,927 (65)	182 (49)	550 (55)
ART regimen prior to current regimen			
Median mos of use (IQR)	12 (3, 35)	11 (3, 32)	13 (4, 30)
> 1 core agent	1,533 (52)	146 (39)	353 (35)
No NRTI(s) backbone	773 (26)	63 (17)	158 (16)

ART, antiretroviral therapy; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; mos, months; n, number; NNRTI, non-nucleoside reverse transcriptase inhibitors; NRTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; PWH-HTE, people with HIV & heavy treatment experience

Figure 2. Most common changes in number of core agents prescribed from the prior regimen to the current regimen



Discussion

Identification of PWH-HTE

- Of 64,618 PWH taking ART on 01DEC2021 in the OPERA® cohort:
 - 9% (n = 5,529) met HTE criteria (Fig 1; Table 1)
 - 65% were taking both an INSTI and PI
 - 27% previously discontinued or switched ≥3 core agent classes
 - 2% (n = 1,559) were HTE and viremic at current regimen start (Fig 1)
 - 5% (n = 3,304) were HTE and suppressed at current regimen start (Fig 1)
- Of the 5,529 PWH-HTE, 12% were missing a VL measurement at current regimen start (Fig 1)
 - Missing data may have been the result of:
 - Recent transfer to OPERA® clinic
 - Limited healthcare interactions during the COVID-19 pandemic
 - Decreased engagement in regular HIV care
 - Most (87%) were cared for in the Southern US (Table 2)
- There is no standard definition for classifying PWH as HTE in the absence of resistance data
 - A combination of prior and current ART exposures is often used in observational research
 - This study's definition of HTE captured both PWH with complete ART histories and PWH with poorly documented ART history who were prescribed an ART regimen that is typically only prescribed to PWH-HTE

Demographics, clinical characteristics, and ART experience of PWH-HTE

- Virologically suppressed and viremic PWH-HTE differed across many characteristics (Tables 2-5)
 - Suppressed PWH-HTE were older than viremic PWH-HTE at current regimen start and initiated ART longer ago (median 84 months vs. median 62 and 66 months among moderately and highly viremic PWH, respectively)
 - Syphilis was more common among viremic (35%) than suppressed (28%) PWH; in OPERA®, syphilis was previously associated with worse outcomes
- Changes in ART experience from the prior (Table 5) to the current regimen (Table 4) are common in a PWH-HTE population on complex ART regimens
 - The proportion of PWH-HTE on > 1 core agent increased (Suppressed: 52% to 78%; Viremic: 37% to 86%)
 - The proportion of PWH-HTE on an ART regimen without a NRTI backbone increased (Suppressed: 26% to 34%; Viremic: 16% to 30%)
 - The most common regimen change was an increase from 1 to 2 core agents, regardless of virologic status at current regimen start (Fig 2)

Key Findings

This cross-sectional glimpse into the most recent ART experiences of a heterogeneous group of PWH-HTE may aid in future studies of virologic control among PWH who require more highly tailored ART regimens

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