Impact of adherence on viral suppression and determinants of adherence in people living with HIV

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INTRODUCTION

- Adherence to antiretroviral treatment (ART) is a key factor for sustained virological suppression (VS) in patients with HIV (Paterson 2000, Maggiolo 2005, and Iacob 2017). Poor adherence has been shown to impact treatment effectiveness, drug resistance, onwards disease transmission and health care costs (Nachega 2011, Attia and Hall 2013, & Yu 2018).
- Correlation between adherence and viral load further support the link between optimal adherence and viral suppression maintenance. However, adherence to ART has been poorly studied across the HIV-infected populations and no consensus exists yet on the optimal levels of adherence required to maintain VS. As per World Health Organization, ≥95% level of adherence is required to maintain viral suppression.

OBJECTIVES

- The present study was conducted to report a summary of evidence on the correlation of adherence with VS and to determine the optimal levels of adherence to maintain VS
- Additionally, adherence levels in different geographies, and determinants of adherence in relation to VS were studied

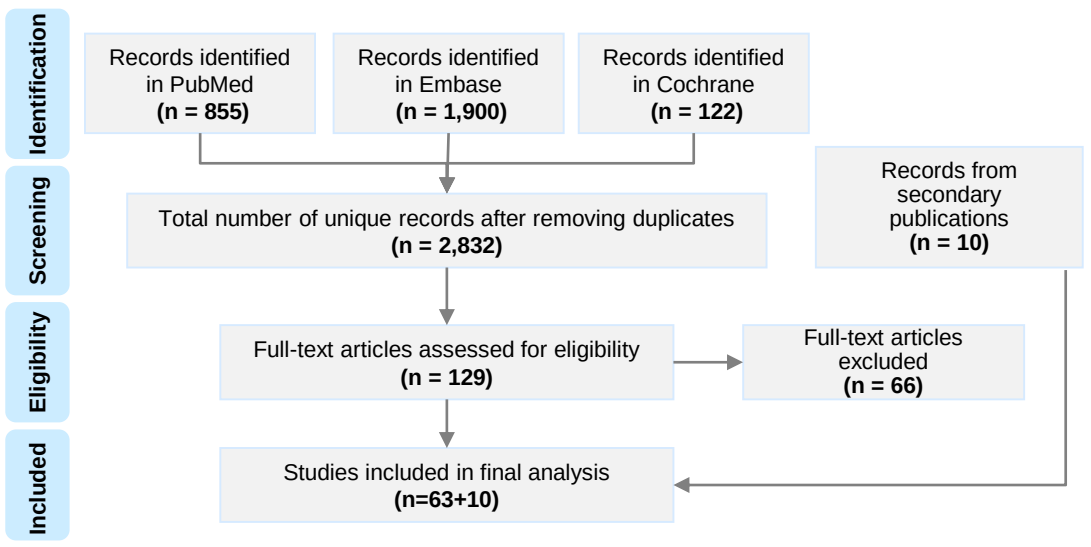
METHODS

- **A systematic literature search was performed in electronic databases:**
  - PubMed/Medline
  - Embase
  - Cochrane Library
- **Studies presented:**
  - Articles from 2014 to 2019 written in English
  - Articles with real world evidence studies on adults with HIV including data on the association between medication adherence and viral load
  - Articles from geographies US, Canada, Australia, Europe, Latin America, selected Asian countries (China and Taiwan) were included.
  - Cross-references of the articles were also searched for any relevant articles from the last 10 years and included.
  - RCTs were excluded

RESULTS

- Of 2,832 screened articles, 42 met the inclusion criteria (Figure 1)

Figure 1: PRISMA flow diagram



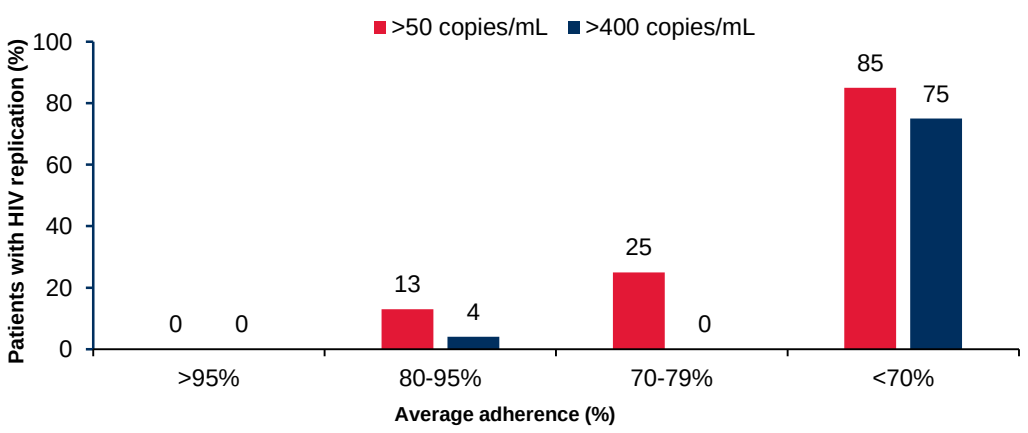
MEASURES OF ADHERENCE

- Medication refill prescription scale was the commonly used measure of adherence followed by a self-reported questionnaire
- Other measures used: MMAS, SMAQ, SHCS-AQ, monthly phone-based unannounced and announced pill counts and Medication Event Monitoring System

RELATIONSHIP BETWEEN ADHERENCE AND VIRAL LOAD

- Overall 29 studies reported outcome data related to relationship of adherence with viral load: Europe (n= 10), US (n= 15), Latin America (n= 2), Asia (n= 2).
- The population size in these studies ranged from 72- 22,740. Most of the studies, were conducted in treatment-experienced patients. Some studies were also conducted in special populations like IDUs and populations with alcohol/ substance abuse.
- Most of the studies suggested a strong correlation between higher adherence levels and virological suppression (n=25), especially in treatment experienced virologically suppressed patients. This was true as per all geographies studied, irrespective of adherence-thresholds, benchmarks used to measure viral-suppression, and types of intervention.
- ART adherence was significantly associated with residual viremia (HR 2.08, p=0.02, Li 2012), while lack of treatment adherence had a marked impact on virological outcome, especially in patients with baseline VL ≥50 copies/mL (Arathoon 2017). Another study with treatment-experienced patients with a follow-up period of 2 years reported virological suppression rates by average percentage of adherence to boosted PI. (Figure 2, adapted from Pareinti 2010)
- The use of multistate models in Blitz 2017 showed that in participants who had initiated ARTs and were virologically suppressed, poor adherence was associated with transitions from suppressed to unsuppressed VL (HR: 1.88, 95% CI: 1.19, 2.98) compared to those who were adherent.

Figure 2*: Virologic suppression rates, based on the average percent adherence



Adapted from Parienti 2010

- Few studies failed to identify a positive trend between virological suppression and adherence levels (n=4). In a study with random-effect logistic regression model, the odds of virological suppression with adherence levels between 80% and 84% were not significantly different compared to those with adherence levels ≥95% (Viswanathan 2015 b). In a study with longitudinal pharmacy refill data collected prospectively for 10 years, there was no difference between the virologically suppressed patients achieving 90-94% or ≥95% of adherence [OR (95% CI): 1.10 (0.89, 1.36) (Viswanathan a 2015).

OPTIMAL ADHERENCE

- Adherence levels of 90-95% were found to maximize the possibility of achieving viral suppression irrespective of treatment regimen and patient treatment status (naïve, experienced or suppressed), Table 1.
- Few studies have also reported optimal adherence in the range 80-90% (Gordon 2015).

Table 1: Publications presenting optimal level of adherence across various geographies

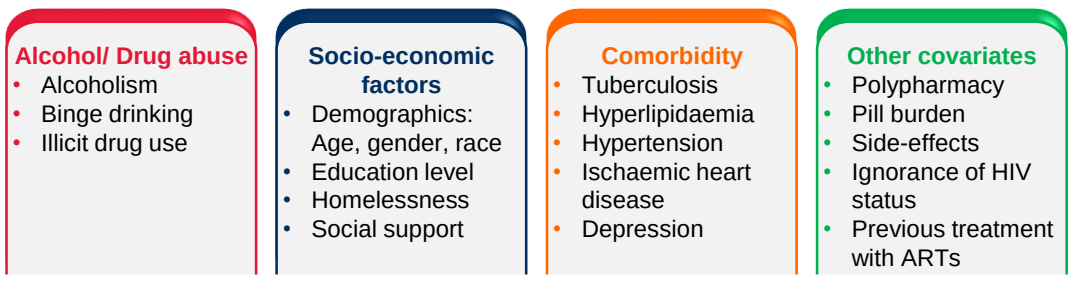
Optimal Adherence	Author	Geography	Study design, sample size(n)	VL threshold [adherence measure]	Patient population	Findings
95%	Li 2012	US	Pooled analysis; n=236	>200c/mL [clinic-based pill count, 4-day, and 7-day recall]	Treatment-naïve	• Risk of VF at different adherence levels [HR (95% CI), p compared to ≥95% adherence] ▪ *80–94%*: 2.0 [1.3–3.2], p=0.004 ▪ *60–79%*: 3.1 [1.9–5.0], p<0.001 ▪ *<60%*: 12.6 [9.4– 17.0], p<0.001
	Jiamsakul 2014	Asia (Multi-countries)	Prospective study; n=105	<400c/mL [self-reported VAS]	First-line failure	• In patients with adherence ≥95% in the 1st year of 2nd line regimen, odds of achieving VS was at least 9 times higher than those who ever reported <95% during the year (OR=9.33, 95% CI (2.43-35.81), p=0.001).
90-95%	Glass 2015	Switzerland	Prospective study; n=1,986	>50c/mL, >500c/mL [self-reported adherence]	Treatment-naïve	• Percentage adherence [HR (95% CI) vs. ≥95% adherence level] ▪ VF*(>50 copies/ml) 90–95%: 1.56 (0.93–2.63) <90%: 7.79 (4.65–13.04)* ▪ *VF(>500 copies/ml) 90–95%: 1.93 (1.03–3.64) <90%: 6.47 (3.94–10.63*)
90-94%	Viswanathan 2015	US	Prospective study; n=21,865	<400c/mL [pharmacy refill]	Unclear	• VS for persons with 90-94% adherence did not differ from those with ≥95% adherence [(OR) 95% CI: 1.05 (0.91, 1.21)].
>90%	Martin 2008	Spain	Prospective study; n=1,142	>200c/mL [pharmacy records]	Mixed	• Relative risk of VF at different adherence levels compared with ≥90%, OR (95% CI): • Adherence at 80-89.9%: 9.0 (4.0–20.1) • Adherence at 70-79.9%: 45.6 (19.9–104.5) • Adherence at <70%: 77.3 (34.2–174.9)
80-89%	Gordon 2015	US	Retrospective study; n=1,915	>200c/mL [Medication Possession Ratio]	Treatment naïve and suppressed	• Gold-standard adherence threshold for older ARV regimens was 95%, but an 80–90% MPR appears sufficient to maintain VS. ▪ VF rate [% (95% CI)] ▪ ≥90% MPR: 0.51 (0.21–1.05) ▪ 80-90% MPR: 0.98 (0.12–3.50)
80- 84%	Viswanathan 2015	US	Prospective study; n=1,215	<50c/mL [self reported adherence]	Unclear (MSM/IDUs)	• For adherence between 80% and 84%, the odds of VL suppression were not significantly different than with levels ≥95%, OR (95% CI): 1.43 (0.61, 3.33)
75-<95%	Cheng 2018	US	Retrospective study; n=10,274	<400c/mL [pharmacy refill]	Treatment-naïve	• Regardless of regimens, the viral suppression rate among patients at initial adherence of 75 to <95% was not statistically different from patients at adherence of ≥95%; however, the differences might be clinically significant

- Studies that used pharmacy-based measures of adherence also indicated a wide interval in the optimum adherence levels. The mentioned optimum level were 90-94% (Viswanathan 2015 a) 80-89% (Gordon 2015) and 75-<95% (Cheng 2018).
- The optimum adherence levels also varied as per the treatment class. For PI-based regimens, shift from high- to medium-level adherence was found to have significant effect on viral suppression. However for NNRTI- or INSTI-based regimens, adherence did not have significant influence on viral suppression rate, until reduced to the lowest level (Cheng 2018).

DETERMINANTS OF ADHERENCE

- Alcohol abuse and illicit drug use were the strongest determinants for lower adherence. In one of the study alcohol use was significantly associated with virological failure [HR (95% CI): 1.83 (1.0–3.35)] (Li 2013), Figure 3.
- Other factors independently associated with non-adherence (spearman correlation, p value) were gender (0.04, <0.05), race/ethnicity (-0.17, <0.001), substance use (-0.15, <0.001), at risk-alcohol-use (-0.04, 0.07), and depressive symptoms (-0.19, <0.001) (Feldman 2013).

Figure 3: Major determinants of adherence and viral load suppression



Conclusions

- Viral suppression in HIV patients is driven by treatment adherence. Adherence level of 90-95% was the most commonly reported threshold needed to achieve sustained virological response.
- Both the self-reported and pharmacy measures (MPR, pill count, pharmacy refill) for adherence indicated a similar direction in relationship between adherence and viral suppression.
- Alcohol/ substance abuse, socio-economic factors and comorbidity were important determinants for lower/non-adherence.
- Patients living with HIV with treatment adherence levels, typically below 95%, could potentially benefit from new long-acting directly-observed HIV treatments.

Abbreviations: IDU: Injecting drug users: MMAS: Morisky medication adherence scale; MSM: Men having sex with men; SMAQ: Simplified medication adherence questionnaire; SHCS-AQ: Swiss HIV cohort sky study adherence questionnaire

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References:

Attia 2009 AIDS. 2009;23:1397-404. Beer 2012. Open AIDS J; 6: 213-23. Blitz 2017. J Acquir Immune Defic Syndr.76;303-310. Cheng 2018. Medicine (Baltimore). 97:e9430. Eber 2017. Ther Adv Infect Dis. 4;135-142. Feldman 2013. AIDS Behav.17;307-18. Glass 2015. AIDS. 29; 2195-200. Gordon 2015. AIDS Patient Care STDS. 29:384-8. Hall 2013. AIDS Behav. 17;1632-6. Iacob 2017. Front Pharmacol. 23;831-831.

Jiamsakul 2014. J Int AIDS Soc.17:19053. Kalichman 2014. Int J Behav Med. 21;811-20. Li 2012. AIDS. 26;185-92. Maggiolo 2005.40;158-63.

Martin 2008. AIDS Res Hum Retroviruses. 24;1263-8. Parienti 2010. Clin Infect Dis. 50;1192-7. Paterson 2000;133;21-30. Viswanathan a 2015. J Acquir Immune Defic Syndr. 69;493-8. Viswanathan b. 2015. AIDS Behav.19; 601-11.