Optimizing ART Adherence to Reach the Third 95

Juliana de Oliveira Costa
Medicines Intelligence Research Program
School of Population Health
UNSW Sydney, Australia

Medicines Intelligence
CRE
real world evidence • smarter medicine use

Adherence 2023 • June 11-13 • Puerto Rico

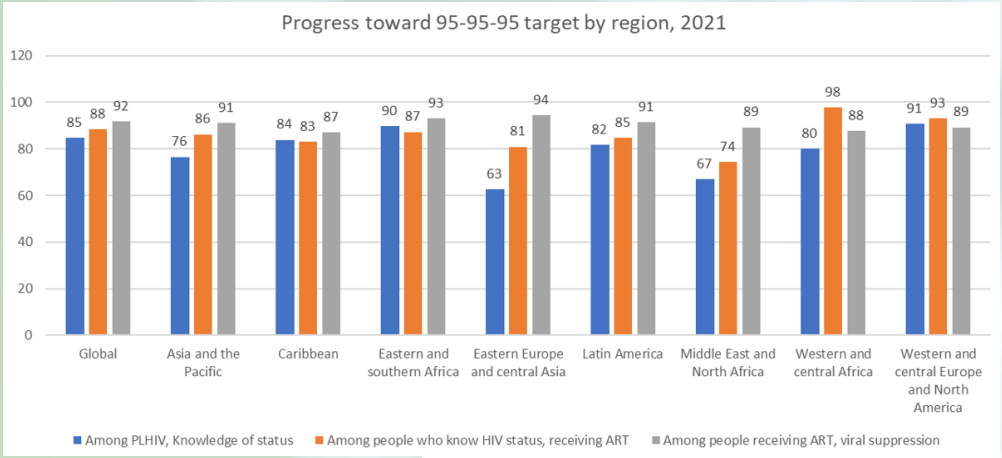
I would like to acknowledge the Bedegal People, the traditional owners of the lands on which I work and live. I pay my respects to their elders past and present and extend that respect to any first nations people joining us today.

With respect to the content of the following presentation I have no actual or potential conflicts of interest or have any financial relationships to disclose

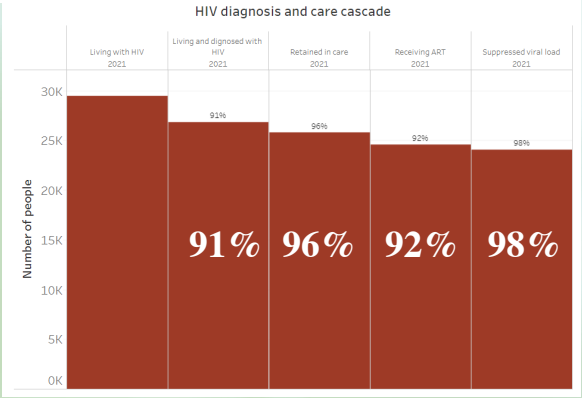
Agenda

1. Monitoring adherence to antiretroviral therapy
2. What are we measuring?
3. How are we measuring adherence to therapy?
4. Identifying vulnerable populations
5. Increasing adherence and retention to care
6. Reflections

1. Monitoring adherence to antiretroviral therapy (ART)



Murphy 2022 AIDS 2022



Australia
data.kirby.unsw.edu.au/hiv

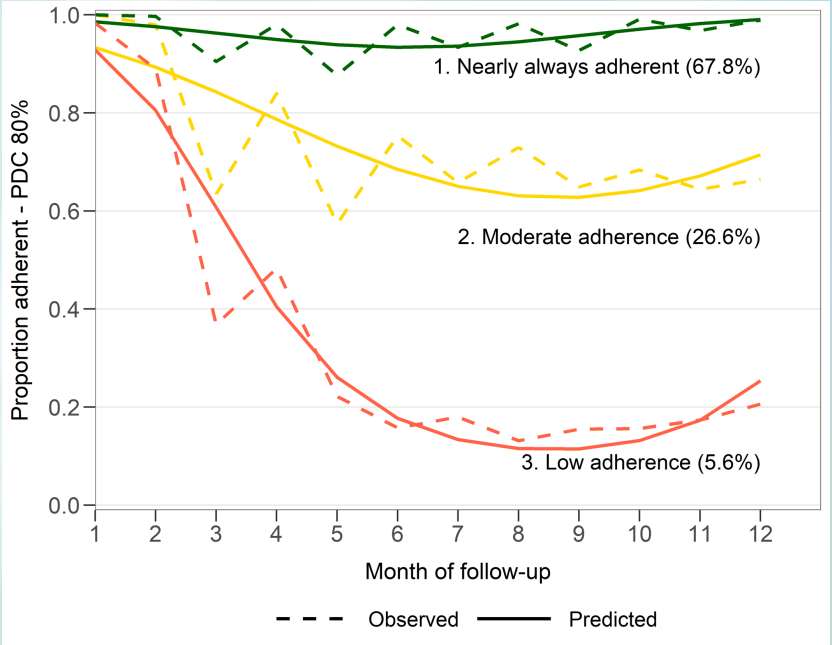
Nachega JB et al. Clin Infect Dis. 2014 Jul;59 Suppl 1(Suppl 1):S21-7
Brown A et al. 2022 AIDS 2022

In routine care…

20%-45% of PLHIV on therapy

have difficulties remembering to take their medicines every day or stop to take their treatment at some point

Monthly adherence patterns during 360 days in PLHIV on ART in Australia

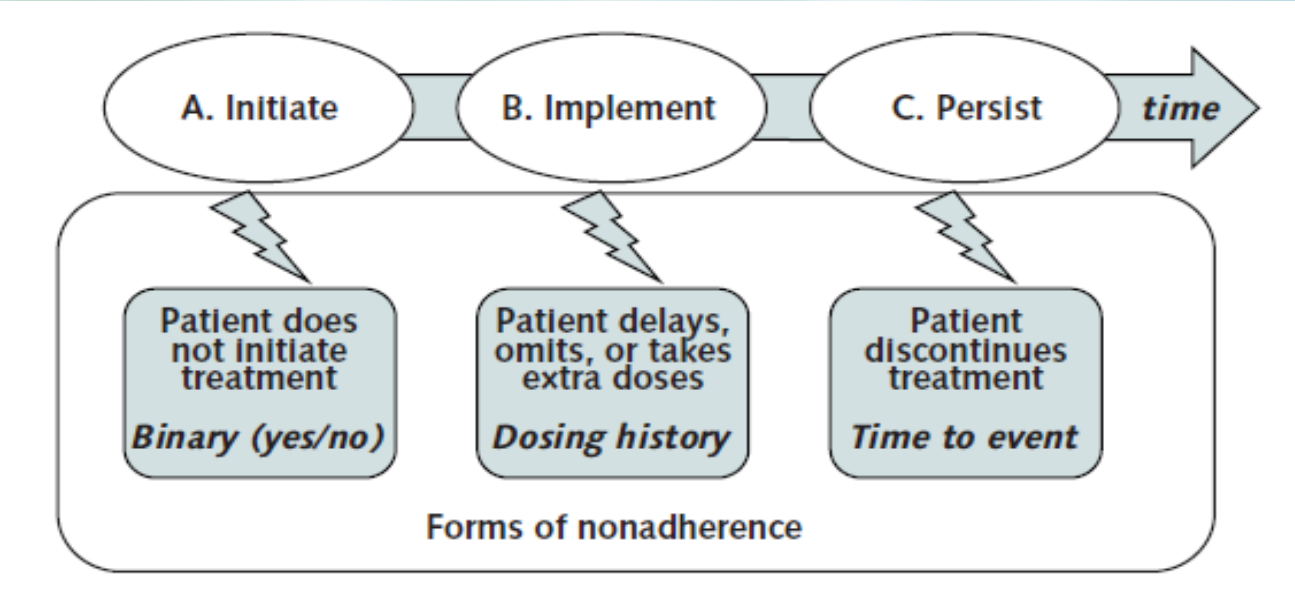


The solid line represents the predicted probability of adherence in each group.
The dashed line represents the observed proportion of people adherent in each group.
de Oliveira Costa J et al. AIDS Patient Care STDS. 2020 Feb;34(2):81-91.

Mao L. Health Soc Care Community. Jul 2018;26(4):486-494.
Siefried KJ et al. PLoS One. 2017 Apr 3;12(4):e0174613
Grierson J. HIV Futures Seven. 2013

2. What are we measuring?

Conceptualization of adherence to therapy



De Geest et al. Ann Intern Med. 2018 Jul 3;169(1):30-35

3. How are we measuring adherence to therapy?

Methods of assessment	*Advantages*	*Disadvantages*
Direct		
Measurement of drug/ metabolite levels	Accurate Objective, proving the ingestion of the drug	Costly Invasive Inter individual differences
Indirect		
Pill counts	Simple Mostly used in clinical trials	No evidence of ingested medication
Electronic databases	Easy to use Inexpensive Non-invasive, patients not aware that they are being monitored Especially specific to identify non-adherent patients	Evidence of the drug being dispensed but not ingested
Self-reported (questionnaires, visual analogue scales)	Easy to use Inexpensive	Overestimate adherence Subjective, influenced by recall or reporting bias
Electronic monitoring systems	Objective Additional information on degree of adherence One of the most accurate methods	The patient is aware of the evaluation No actual evidence that the medication is being ingested

Anghel LA, Farcas AM, Oprean RN. Med Pharm Rep. 2019 Apr;92(2):117-122.

Performs as well as self-report, pill count and electronic monitoring in predicting HIV viral suppression

Almeida-Brasil CC et al. AIDS Care 2019;31(6):647-59

Berg KM, Arnsten JH. J Acquir Immune Defic Syndr. 2006 Dec 1;43 Suppl 1:S79-87

3. How are we measuring adherence to therapy?

Considerations for using electronic databases

Coverage	Are all dispensings/prescriptions recorded?
Time period	Cumulatively over the year? Monthly basis?
Best measure	Adherence: Medication possession ratio, proportion of days covered? Persistence: Time to first discontinuation or proportion of patients covered (considering re-initiation)?
Adherence to multiple medicines	Which active ingredients or medicines to consider?

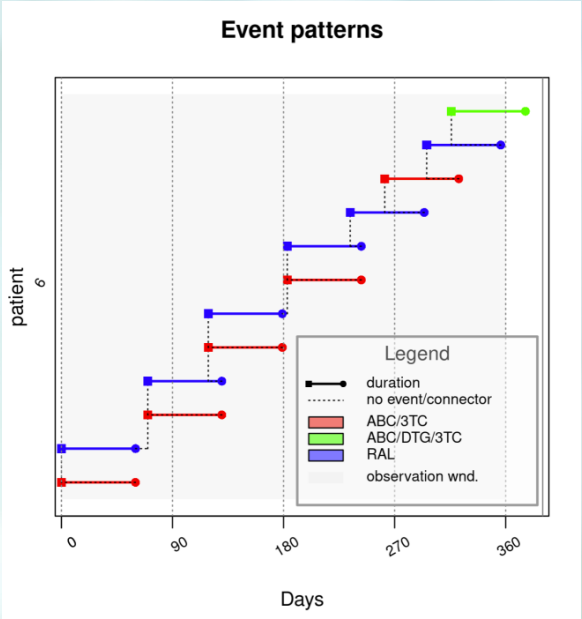
Berg KM, Arnsten JH. J Acquir Immune Defic Syndr. 2006 Dec 1;43 Suppl 1(Suppl 1):S79-8
de Oliveira Costa J et al. AIDS Care. 2023 Jul;35(7):970-975
Rasmussen L et al. Pharmacoepidemiol Drug Saf. 2018 Aug;27(8):867-871

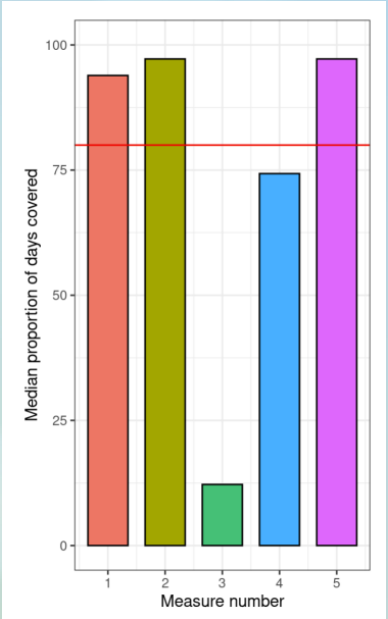
Adherence to multiple medicines: covered day?

Example of antiretroviral dispensing in the Pharmaceutical Benefits Scheme dataset by patient ID

Note: This is for illustration only

ID	Dispensing number	Supply date	Antiretroviral	Duration (days)
6	1	03/03/2016	ABC/3TC	60
6	1	03/03/2016	RAL	60
6	2	12/05/2016	ABC/3TC	60
6	2	12/05/2016	RAL	60
6	3	30/06/2016	ABC/3TC	60
6	3	30/06/2016	RAL	60
6	4	02/09/2016	ABC/3TC	60
6	4	02/09/2016	RAL	60
6	5	23/10/2016	RAL	60
6	6	20/11/2016	ABC/3TC	60
6	7	24/12/2016	RAL	60
6	8	13/01/2017	ABC/DTG/3TC	60





1) exposure to ≥3 antiretrovirals at the same time
2) exposure to any antiretroviral
3) lowest number of days covered per antiretroviral
4) average of days covered over all antiretrovirals
5) highest number of days covered per antiretroviral

de Oliveira Costa J et al. AIDS Care. 2023 Jul;35(7):970-975

4. Identifying vulnerable populations

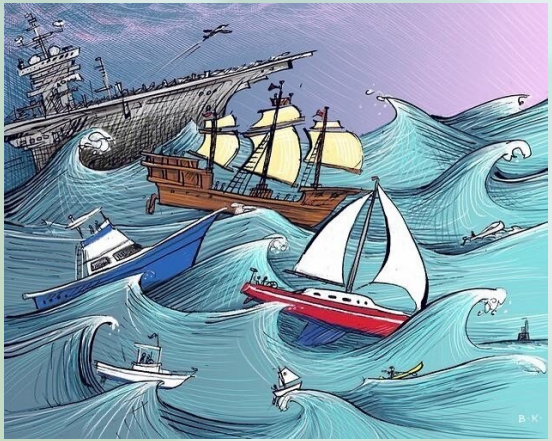


Illustration by Barbara Kelley
www.damianbarr.com/

Population groups: Transgender people, people who inject drugs, migrants, postpartum women, incarcerated people

Age: Young people

Race and ethnicity: Black people, Indigenous peoples

Clinical characteristics: People on multiple medicines, with mental health conditions, with specific co-morbidities, early HIV infection

Socioeconomic: Lower socioeconomic status, living in disadvantaged areas/ remote areas

IN DANGER: UNAIDS Global AIDS Update 2022
Cloete A et al. Lancet HIV. 2023 Jun;10(6):e375-e384
Cuadros DF. medRxiv [Preprint]. 2023 Apr 26:2023.04.24.23289044.
Wang L et al. HIV Research Network. Lancet HIV. 2019 Aug;6(8):e531-e539
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4. Identifying vulnerable populations (and measuring outcomes)

International Journal of *Environmental Research and Public Health*

MDPI

Review

Generating Real-World Evidence on the Quality Use, Benefits and Safety of Medicines in Australia: History, Challenges and a Roadmap for the Future

Sallie-Anne Pearson [1,*], Nicole Pratt [2], Juliana de Oliveira Costa [1], Helga Zoega [1,3], Tracey-Lea Laba [4], Christopher Etherton-Beer [5], Frank M. Sanfilippo [5], Alice Morgan [6], Lisa Kalisch Ellett [2], Claudia Bruno [1], Erin Kelty [5], Maarten IJzerman [7], David B. Preen [5], Claire M. Vajdic [1] and David Henry [8]

1 Centre for Big Data Research in Health, Faculty of Medicine and Health, UNSW Sydney, Sydney 2052, Australia; j.costa@unsw.edu.au (J.d.O.C.); h.zoega@unsw.edu.au (H.Z.); c.bruno@unsw.edu.au (C.B.); claire.vajdic@unsw.edu.au (C.M.V.)
2 Quality Use of Medicines and Pharmacy Research Centre, Clinical and Health Sciences, University of South Australia, Adelaide 5000, Australia; nicole.pratt@unisa.edu.au (N.P.); lisa.kalisch@unisa.edu.au (L.K.E.)
3 Centre of Public Health Sciences, Faculty of Medicine, University of Iceland, 102 Reykjavik, Iceland
4 Centre for Health Economics Research and Evaluation, Faculty of Health, University of Technology Sydney, Sydney 2006, Australia; Tracey.Laba@chere.uts.edu.au
5 WA Centre for Health and Ageing, Medical School, University of Western Australia, Perth 6009, Australia; Christopher.Etherton-Beer@uwa.edu.au (C.E.-B.); frank.sanfilippo@uwa.edu.au (F.M.S.); erin.kelty@uwa.edu.au (E.K.); david.preen@uwa.edu.au (D.B.P.)
6 Research School of Population Health, College of Health and Medicine, Australian National University, Canberra 2601, Australia; alice.morgan@anu.edu.au
7 Centre for Cancer Research and Centre for Health Policy, Melbourne School of Population and Global Health, University of Melbourne, Melbourne 3000, Australia; maarten.ijzerman@unimelb.edu.au
8 Institute for Evidence Based Healthcare, Bond University, Gold Coast 4229, Australia; dhenry@bond.edu.au
* Correspondence: sallie.pearson@unsw.edu.au

Citation: Pearson, S.-A.; Pratt, N.; de Oliveira Costa, J.; Zoega, H.; Laba, T.-L.; Etherton-Beer, C.; Sanfilippo, F.M.; Morgan, A.; Kalisch Ellett, L.; Bruno, C.; et al. Generating Real-World Evidence on the Quality Use, Benefits and Safety of Medicines in Australia: History, Challenges and a Roadmap for the Future. *Int. J. Environ. Res. Public Health* **2021**, *18*, 13345. https://doi.org/10.3390/ijerph182413345

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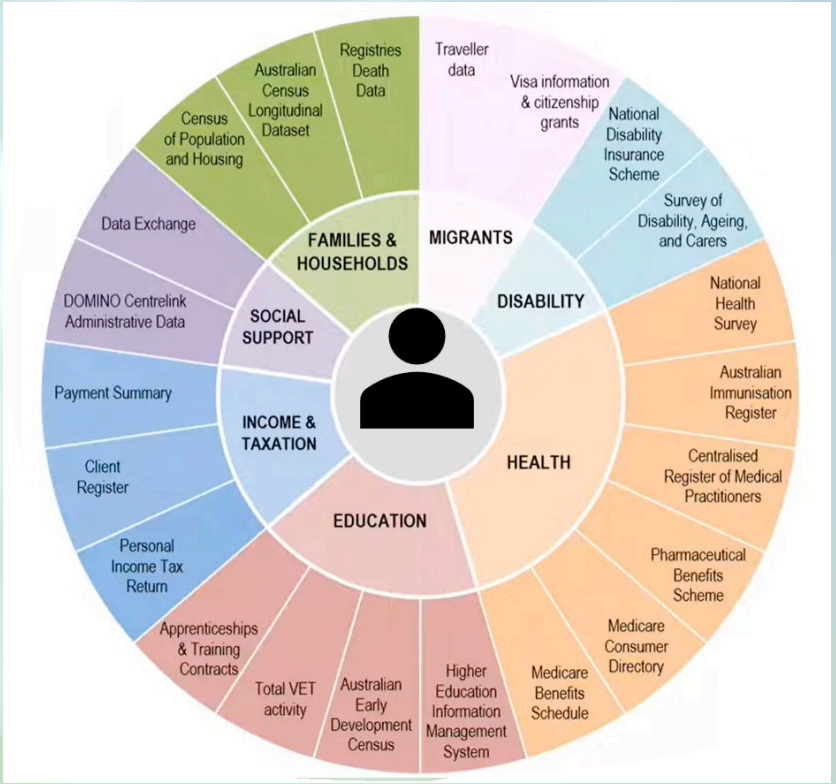
Abstract: Australia spends more than $20 billion annually on medicines, delivering significant health benefits for the population. However, inappropriate prescribing and medicine use also result in harm to individuals and populations, and waste of precious health resources. Medication data linked with other routine collections enable evidence generation in pharmacoepidemiology; the science of quantifying the use, effectiveness and safety of medicines in real-world clinical practice. This review details the history of medicines policy and data access in Australia, the strengths of existing data sources, and the infrastructure and governance enabling and impeding evidence generation in the field. Currently, substantial gaps persist with respect to cohesive, contemporary linked data sources supporting quality use of medicines, effectiveness and safety research; exemplified by Australia's limited capacity to contribute to the global effort in real-world studies of vaccine and disease-modifying treatments for COVID-19. We propose a roadmap to bolster the discipline, and population health more broadly, underpinned by a distinct capability governing and streamlining access to linked data assets for accredited researchers. Robust real-world evidence generation requires current data roadblocks to be remedied as a matter of urgency to deliver efficient and equitable health care and improve the health and well-being of all Australians.

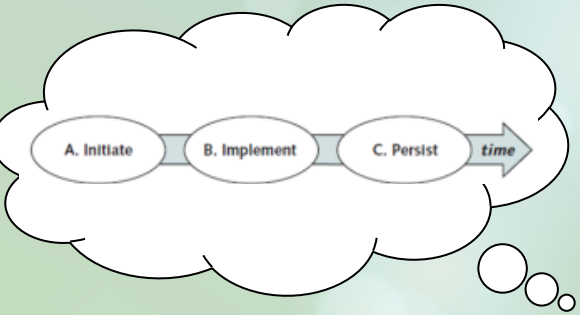
Multi-Agency Data Integration Project (MADIP)



Pearson SA et al. Int J Environ Res Public Health. 2021 Dec 18;18(24):13345

Liu B et al. Lancet preprint. http://dx.doi.org/10.2139/ssrn.4445191

5. Increasing adherence and retention to care



Adherence toolbox

Nonjudgmental multidisciplinary health care team

Strengthen early linkage to care and retention in care

Patient's knowledge about HIV

Behavioural and psychosocial challenges

Language and literacy

Beliefs, perceptions, and expectations

Assess structural issues

Medication-taking skills

Involve the patient in ARV regimen selection

Use positive reinforcement to foster adherence success

Identify the type of and reasons for poor adherence and target ways to improve adherence

Select from among available effective adherence and retention interventions

Place patients with apparent cART adherence problems on regimens with high genetic barriers to resistance

IAPAC Guidelines for Optimizing the HIV Care Continuum, 2021

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV. 2023

5. Increasing adherence and retention to care

Public health measures

- Make **free HIV care and treatment** available to **all people residing** in Australia
- Enable all people newly diagnosed with HIV to commence treatment within 14 days of their diagnosis
- Double the **number of cART prescribers** in by 2025 and **increase reimbursements** for HIV-related services
- **Clinic audits** to identify patients with poor HIV treatment outcomes
- Implement a **tailored person-centred** support programs

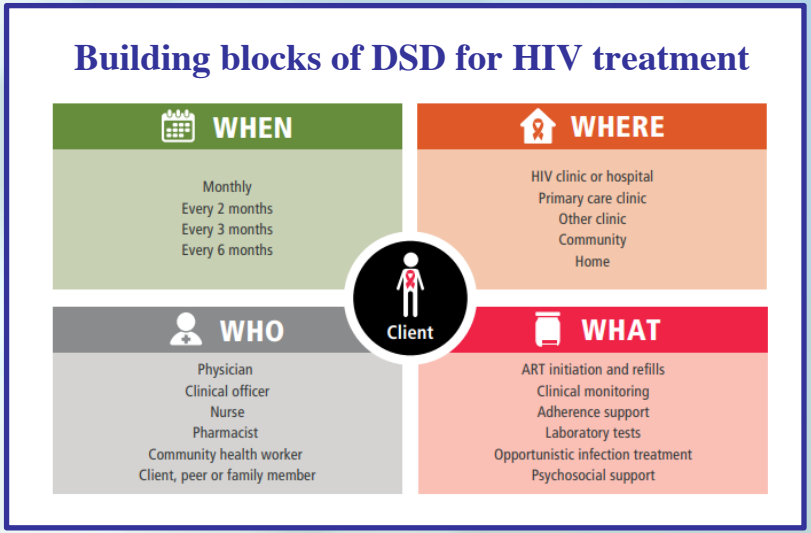
Changing models of care for increasing adherence and retention

Cash transfer programmes

- Increase retention in care for specific populations (eg. pregnant women), cART coverage, potentially increases adherence to cART [1,2]

Community-based interventions

- Differentiated service delivery (DSD), peer-led DSD and adherence clubs improve retention, adherence and/ or viral suppression [3-7]



AIDS2022 Knowledge Toolkits

1 Richterman A et al. Nat Hum Behav. 2022 Oct;6(10):1362-1371
2 Guimarães NS et al. Lancet HIV. 2023 Jun;10(6):e394-403
3 Munyayi FK et al. Int J Environ Res Public Health. 2022 Mar 25;19(7):3940
4 Penn AW et al. PLoS One. 2018 Dec 14;13(12):e0208814
5 Jo Y et PLoS One. 2023 Mar 14;18(3):e0280748
6 Atuhaire L et al. Syst Rev. 2021 May 6;10(1):137
7 Muhula S et al. 2022. PLoS ONE 17(2): e0263663

6. Reflections

- Monitoring adherence to therapy is key for optimising ART, both at the individual and the population-level
- Different measures tackle different aspects of adherence
- Reaching vulnerable populations is necessary to close gaps in the HIV care cascade and reach the third 95 target
- Tools used to improve adherence and retention should align with identified barries and target population, including customised models of care
- These strategies should be supported by public health measures addressing structural barriers for health care access

Acknowledgements

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real world evidence ▪ smarter medicine use

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IAPAC INTERNATIONAL ASSOCIATION OF PROVIDERS OF AIDS CARE

Thank you!

Muchas gracias

j.costa@unsw.edu.au