Prior exposure to antiretroviral therapy among adult patients presenting for HIV treatment initiation or re-initiation in sub-Saharan Africa: A systematic review

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Background and objectives

- Same-day/rapid ART initiation + high rates of disengagement from care have created a large and growing pool of individuals who present for initiation of treatment with prior ART experience (“non-naïve re-initiators”)
- By definition, non-naïve re-initiators previously were unable to overcome barriers to care and may face those same barriers again, without tailored interventions
- There are many estimates but few empirical data on the proportion of non-naïve re-initiators in various populations
- We conducted a rapid review of published reports with data on proportions of adult patients initiating ART who were treatment non-naïve in sub-Saharan Africa.

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Methods

Parameter	Summary	Inclusion criteria	Exclusion criteria
Population	Adults initiating ART	Ages ≥18; confirmed HIV positive; presenting for initiation of any regimen of lifelong ART	Ages <18; currently only receiving ART for HIV prevention (PrEP)
Geographic region	Africa	Sub-Saharan Africa	None
Study design	Any with primary data	Reports primary, patient-level data from retrospective or prospective cohorts; any study design (trial, observational) with or without comparison group; systematic reviews, meta-analyses	Case series or reports, purely qualitative studies, treatment guidelines, mathematical models, editorials, commentaries, protocols
Required descriptive data	Basic description of population and services	Describes all of patients, location, timing of ART initiation, facility type, service delivery models and services provided through public health facilities or NGO/private programs that serve the uninsured sector	Insufficient description of the characteristics needed to describe the study population and outcome
Outcomes	**% non-naïve at initiation**	Reports proportion of patients initiating ART who are ART naïve and proportions of patients previously experienced on ART for any duration after initiation.	Insufficient detail provided to estimate of outcome
Timing	Since 2016	A majority of data collected for ART initiation on or after January 1, 2016	A majority of data accrued before January 1, 2016

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Methods

- Searched PubMed, EMBASE, Web of Science, IAS, CROI
- Primary outcome
  - Proportion of adults presenting for ART initiation in public sector HIV programs in sSA who are not ART-naïve
- Evidence of prior ART use
  - Self-reported
  - Viral load suppression at ART initiation
  - Medical record evidence
  - Biological measurements of ART metabolites

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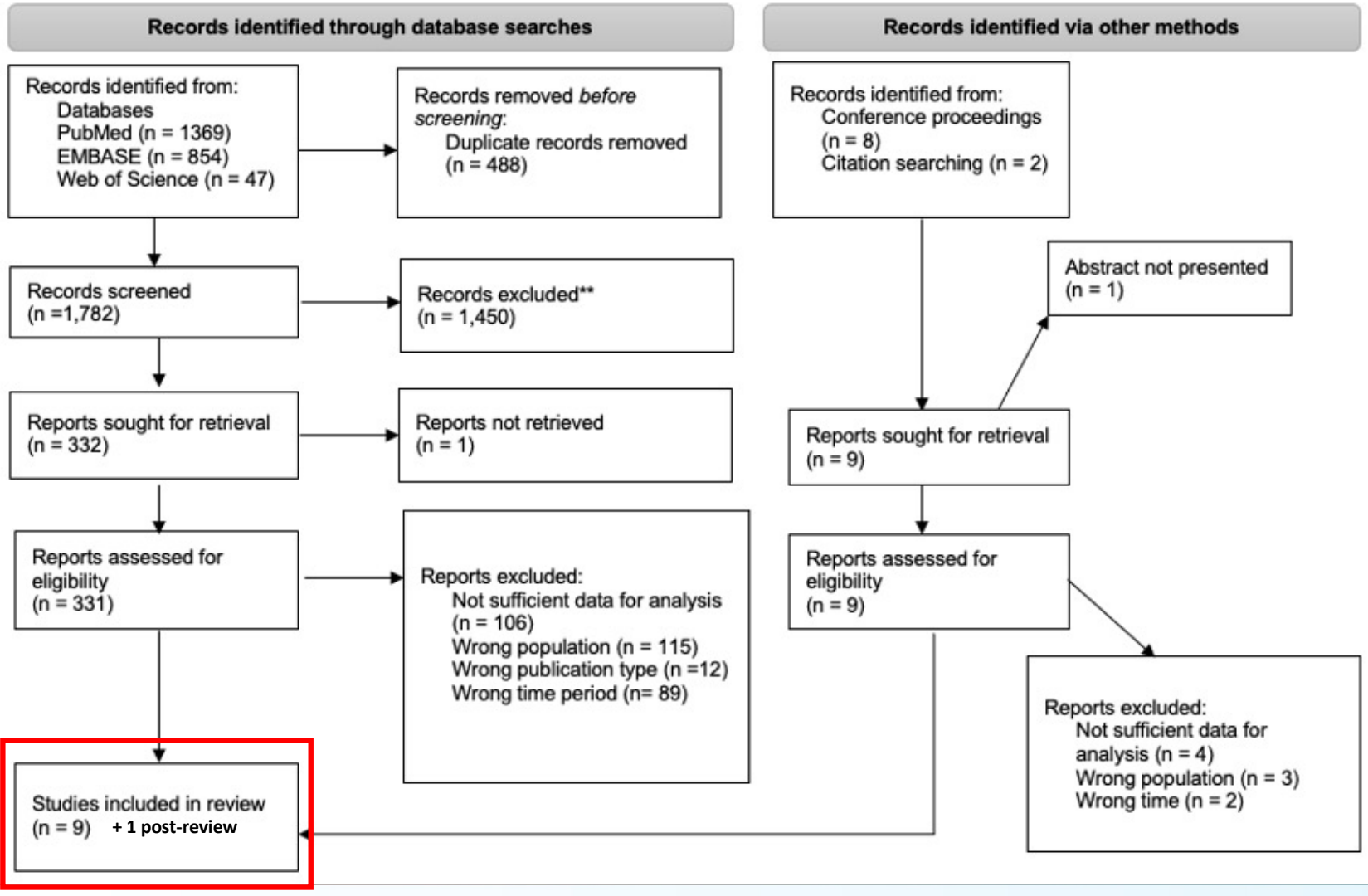
Records identified through database searches
Records identified via other methods
Records identified from:
Databases
PubMed (n = 1369)
EMBASE (n = 854)
Web of Science (n = 47)
Records removed *before screening*:
Duplicate records removed (n = 488)
Records identified from:
Conference proceedings (n = 8)
Citation searching (n = 2)
Abstract not presented (n = 1)
Records screened (n =1,782)
Records excluded** (n = 1,450)
Reports sought for retrieval (n = 332)
Reports not retrieved (n = 1)
Reports sought for retrieval (n = 9)
Reports assessed for eligibility (n = 331)
Reports excluded:
Not sufficient data for analysis (n = 106)
Wrong population (n = 115)
Wrong publication type (n =12)
Wrong time period (n= 89)
Reports assessed for eligibility (n = 9)
Reports excluded:
Not sufficient data for analysis (n = 4)
Wrong population (n = 3)
Wrong time (n = 2)
Studies included in review (n = 9) + 1 post-review

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Results

Country	N	Study design, source of data	Study population (all enrolled adults only)	Years of ART initiation	Indicator of prior exposure	% non-naïve at initiation
Botswana[a]	800	Baseline data for intervention arm of cluster randomized trial of HIV prevention	HIV-positive during community HIV prevention campaign and linked to HIV care	2016-2018	Not stated	**7%**
DR Congo[b]	177	Observational prospective cohort of patients receiving dolutegravir	Presenting for ART initiation or ongoing ART treatment at all ART clinics in Busia	2019-2021	Viral load suppressed at ART initiation	**52%**
Ethiopia[c]	430	Observational, cross-sectional study of first line treatment failure	Received at least 6 months of ART	2017	Self-report	**21%**
Kenya[d]	63	Observational prospective cohort	Men who have sex with men (MSM)	2015-2016	Viral load suppressed at ART initiation	**30%**
Kenya[e]	477	Baseline data for intervention arm of clinical trial of same-day ART initiation	Presenting for ART initiation at 3 public sector hospitals	2017-2018	Self-report	**8%**
Zambia[f]	248	Baseline data for study of recent HIV infection	Presenting for ART initiation at 2 public sector clinics	2021-2022	Viral load suppressed at ART initiation	**27%**
South Africa[e] (Gauteng)	600	Baseline data for intervention arm of clinical trial of same-day ART initiation	Presenting for ART initiation at 3 public sector clinics	2017-2018	Self-report	**2%**
South Africa[g] (KZN)	390	Baseline data for randomized controlled trial of POC HIV viral load testing	Clinically stable on ART and due for 6-month viral load testing	2016-2017	Self-report	**5%**
South Africa[h] (Gauteng)	296	Baseline data for intervention arm in clinical trial of same-day ART initiation	Presenting for ART initiation at 3 public sector clinics	2018	Self-report	**11%**
South Africa[i] (KZN)	193	Subset of baseline data from clinical trial of home-based ART initiation	Non-pregnant, self-reported naïve, presenting for ART initiation at 2 public sector clinics, with CD4 >100 and no active TB	2018	Viral load undetectable at ART initiation	**32%**
South Africa[j] (Limpopo)	77	Baseline samples from clinical trial of drug resistance	Self-reported naïve, presenting for ART initiation at 3 public sector clinics	2017-2019	Presence of TDF, EFV, and/or FTC metabolites in blood and/or hair	**53%**

Strengths and limitations

- Strengths
  - Comprehensive review using multiple databases and conference abstract archives.
  - Focused on recent data in the years since UTT adopted, increasing ART access (and thus disengagement and re-initiation)
  - Recognized a wide range of reporting indicators for prior exposure to ARVs.

- Limitations
  - Only used published reports (and in English)
  - Most recent data not published yet (or not at all)
  - Very constrained by the lack of standardized reporting of prior ARV exposure.

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Summary of findings

- Proportion non-naïve differs widely, between studies and by method of defining
  - Self-report **2-21%** (5 studies)
  - Viral suppression at ART initiation **27-52%** (4 studies)
  - Laboratory analysis of ARV metabolites **53%** (1 study)
- There is a lack of published evidence on this question
  - **Only identified 10 studies in total**, half of them in South Africa
  - All small sample sizes; some excluded relevant sub-groups (e.g. self-reported non-naïve clients)
  - Most report naïve vs non-naïve status incidentally as a cohort descriptor
  - 80% of data earlier than 2020—probability of prior exposure must be increasing year on year
- Available indicators of prior exposure are problematic
  - Self-report is unreliable
  - Most clients don't receive viral load tests at initiation; viral suppression fades with time off ART
  - Lack of unique identifiers limits use of medical record data (e.g. previous lab tests)
  - Metabolite tests are expensive and only reflect immediately preceding period

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How should we address this gap?

- Create standard definitions for re-initiation, prior exposure, etc.
- Start reporting the data we have (and asking about prior use if not already doing so)
- Link NHLS laboratory and Tier.Net clinic records to identify prior CD4 counts and viral load tests
- Conduct targeted studies of ARV metabolites for specific populations of interest
- **Make self-report credible—Improve our approach to service delivery among re-engagers so that clients are more willing to admit to prior exposure (Welcome Back…)**

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Thank you!

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