



# Advances in HIV cohort methodologies



## The past:

20 years of HIV cohort research in Africa

*Mary-Ann Davies*

## The present:

Leveraging cohort data and expertise for emerging infections:  
an example from COVID-19 vaccine effectiveness research

*Reshma Kassanje*

## The future:

Causal artificial intelligence in observational research

*Miguel Hernán*



# The Past: 20 years of HIV cohort research in Africa

Mary-Ann Davies

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Western Cape Government Health and Wellness



# The Past: 20 years of HIV cohort research in Africa

## Cape Town and Cohorts: A story of “C”s



# The first Cohorts - Khayelitsha: ART is feasible and effective in Africa



ART is too costly and not feasible in Africa

## Outcomes after two years of providing antiretroviral treatment in Khayelitsha, South Africa

*AIDS* 2004, 18:887–895

David Coetzee<sup>a</sup>, Katherine Hildebrand<sup>a</sup>, Andrew Boulle<sup>a</sup>, Gary Maartens<sup>b</sup>, Françoise Louis<sup>c</sup>, Veliswa Labatala<sup>c</sup>, Hermann Reuter<sup>c</sup>, Nonthutuzelo Ntwana<sup>c</sup> and Eric Goemaere<sup>c</sup>

**Table 1. Characteristics and starting regimens of patients beginning antiretroviral therapy.**

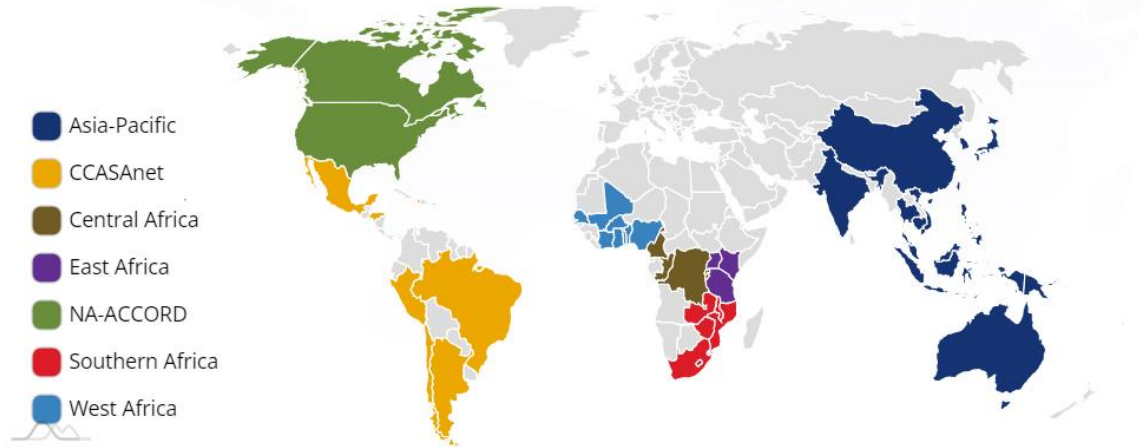
All patients	n = 287 <sup>a</sup>
Median age [years (IQR)]	31 (28–37)
Female [n (%)]	201 (70%)
CD4 lymphocyte count at baseline ( $\times 10^6$ cells/l)	
Median (IQR)	43 (13–94)
Count $< 50 \times 10^6$ cells/l [n (%)]	155 (55)



# Cohort Collaborations and Comparisons

Sharing data with cohort collaborations -  
research questions that need bigger datasets

## IeDEA Regional Cohorts



2.2m people living with or at risk of HIV  
44 countries  
7 regions

## HIV-CAUSAL Participating Studies

Country	Study name
Canada	South Alberta HIV Cohort
	Canadian Co-Infection Cohort
France	ANRSO4 FHDH
	ANRS1220 PRIMO & ANRSO2 SEROCO
	Aquitaine
Greece	AMACS
Italy	ICONA
Netherlands	ATHENA
Spain	CoRIS
	PISCIS
Switzerland	Swiss HIV Cohort Study
United Kingdom	UK CHIC
	UK Register of Seroconverters
United States	VACS
	Partners HIV Cohort
	Boston Medical Center HIV Cohort

# Causal questions: when to start ART in children?

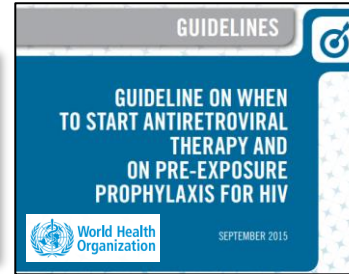


IeDE Africa & Europe  
 IeDE Asia & Latin America  
 IeDE Europe  
 IeDE North America  
 IeDE South America  
 IeDE Western Pacific  
 IeDE Global  
 IeDE Regional  
 IeDE Country  
 IeDE Site  
 IeDE Study  
 IeDE Data  
 IeDE Analysis  
 IeDE Reporting  
 IeDE Governance  
 IeDE Collaboration of Observational HIV Epidemiological Research Europe



Two massive medicine trials will change the way HIV is treated

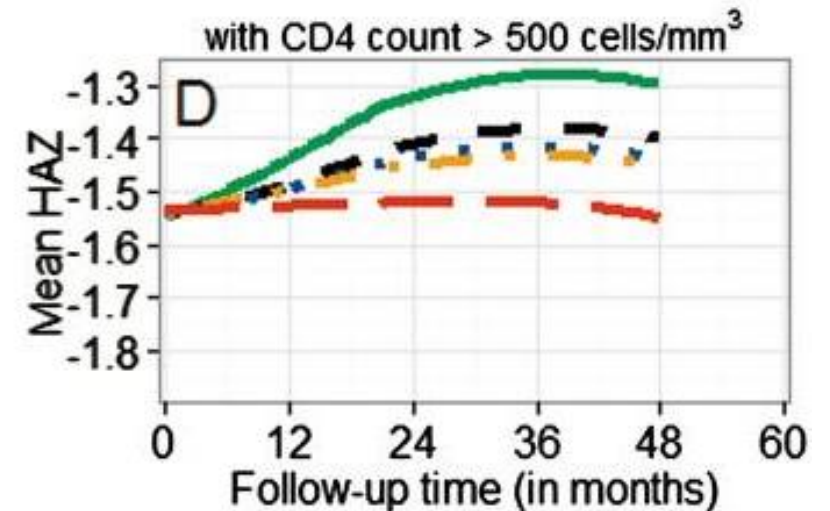
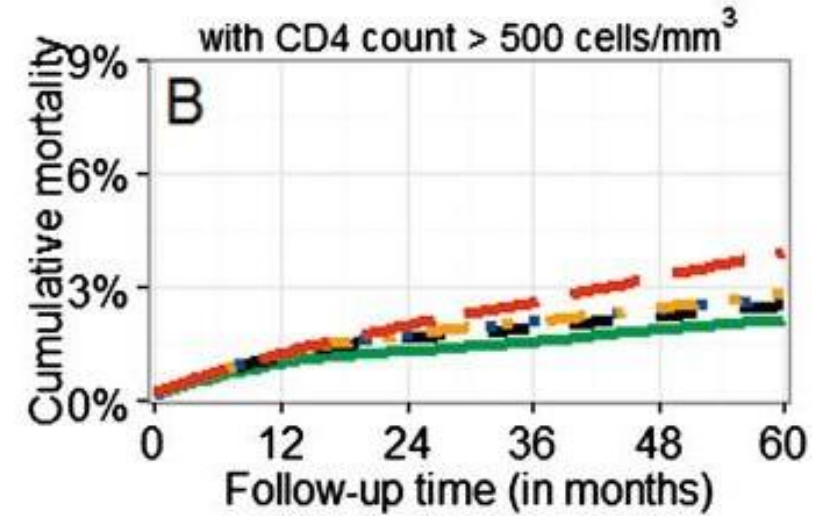
22 July 2015 | Nathan Geffen



- No START/TEMPRANO trial for children age 1-15 yrs
- Applied causal methods using data from cohort collaborations to show:
  - immediate ART vs. deferred ART (CD4 <350/15%):
    - ↓ mortality & ↑ growth
    - (higher mean height-for-age z-score, HAZ)
- Key evidence to inform WHO guideline recommending universal ART for children aged 1-15 years

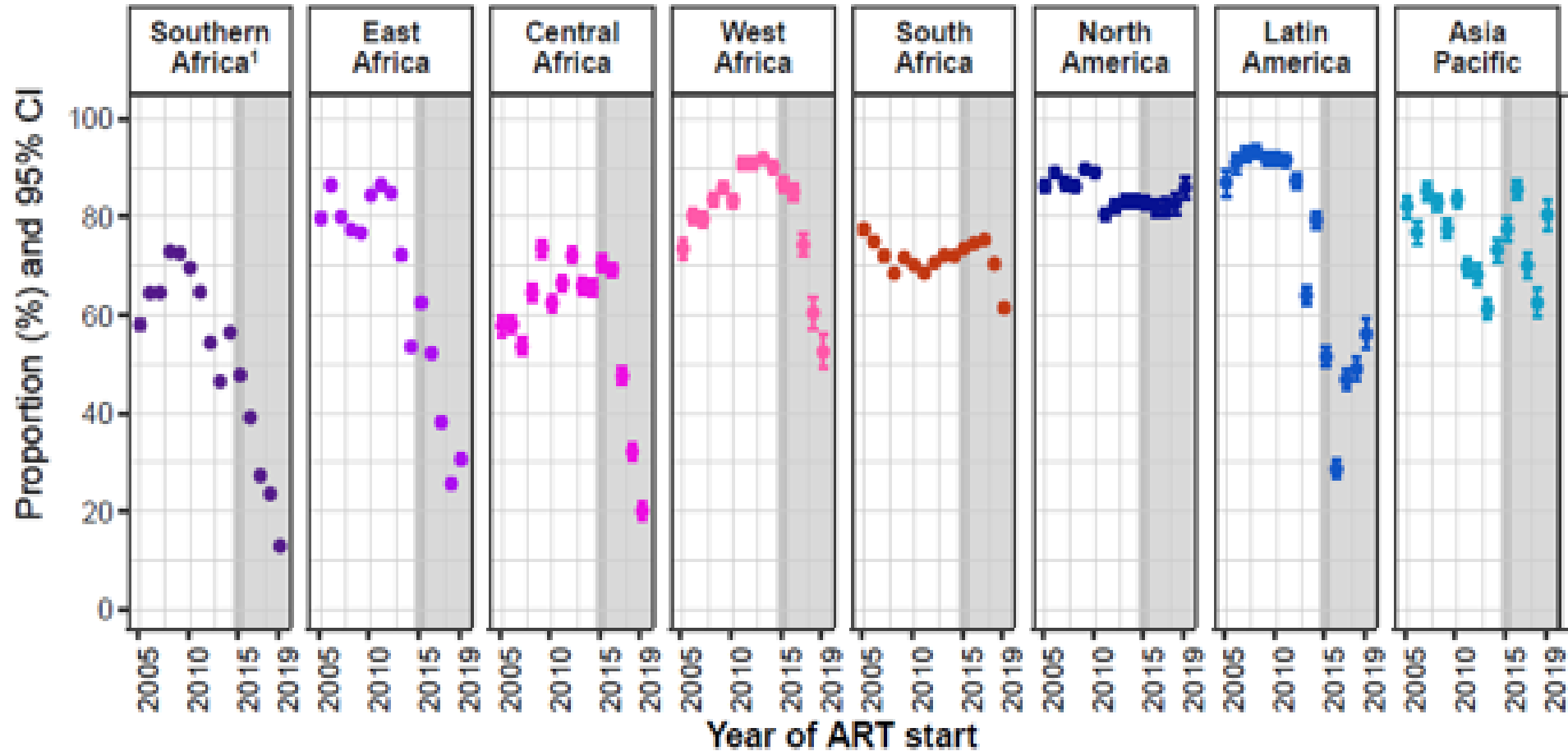
Intervention:
 

- immediate ART
- <500 or -2
- <350 or -2
- <200 or -2
- no ART



# Unintended Consequences

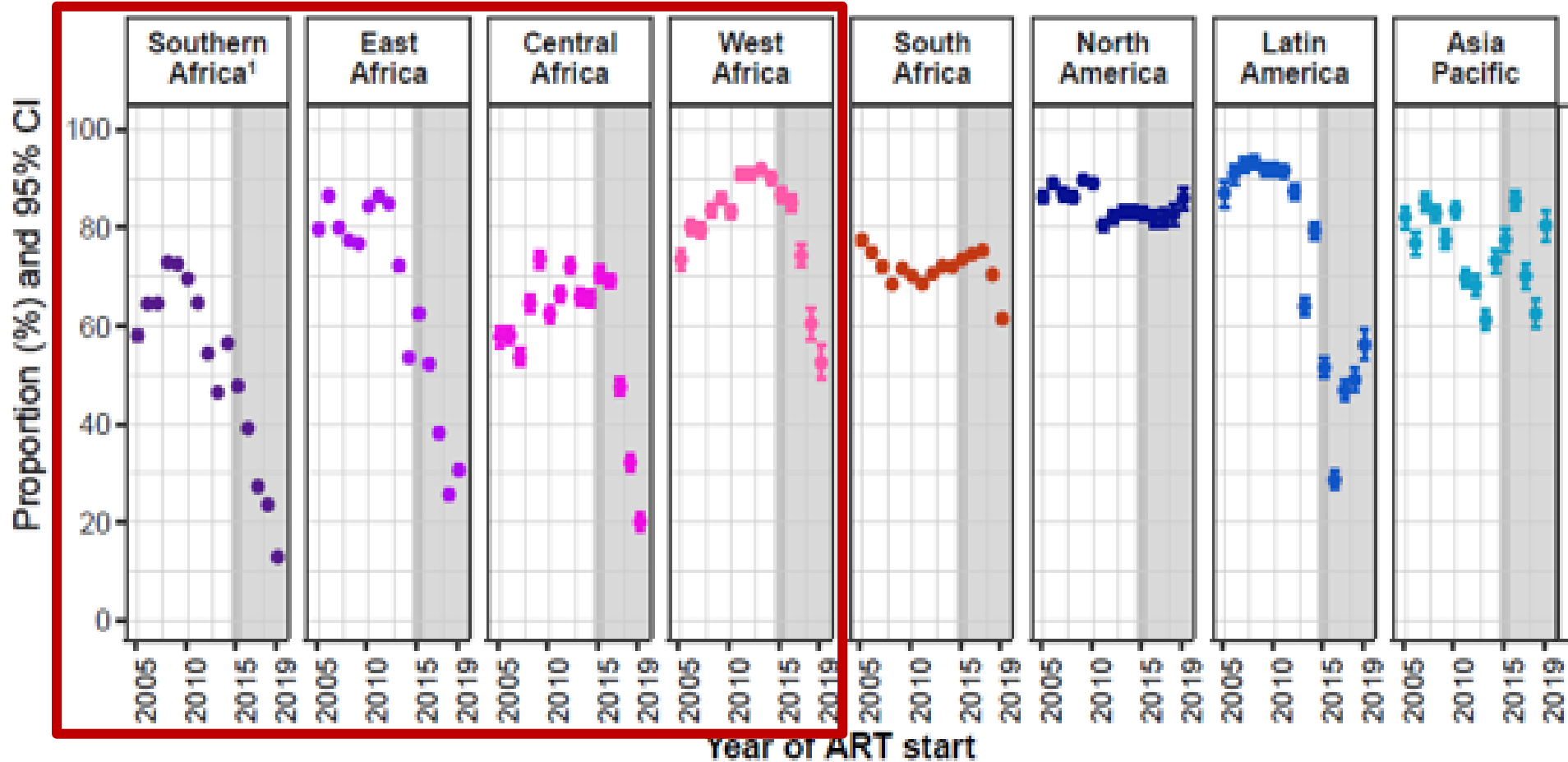
Proportion with CD4 count measured at ART start in 1,349,290 PWH in IeDEA



Shift to universal ART in 2015 → dramatic reduction in proportion with CD4 measured at ART start in sub-Saharan Africa (13-53%)

# Unintended Consequences

Proportion with CD4 cell count measured at ART start in 1,349,290 PWH in IeDEA



Shift to universal ART in 2015 → dramatic reduction in proportion with CD4 measured at ART start in sub-Saharan Africa (13-53%)



# Beyond disease-specific cohorts: Comorbidities, Co-infections and COVID-19

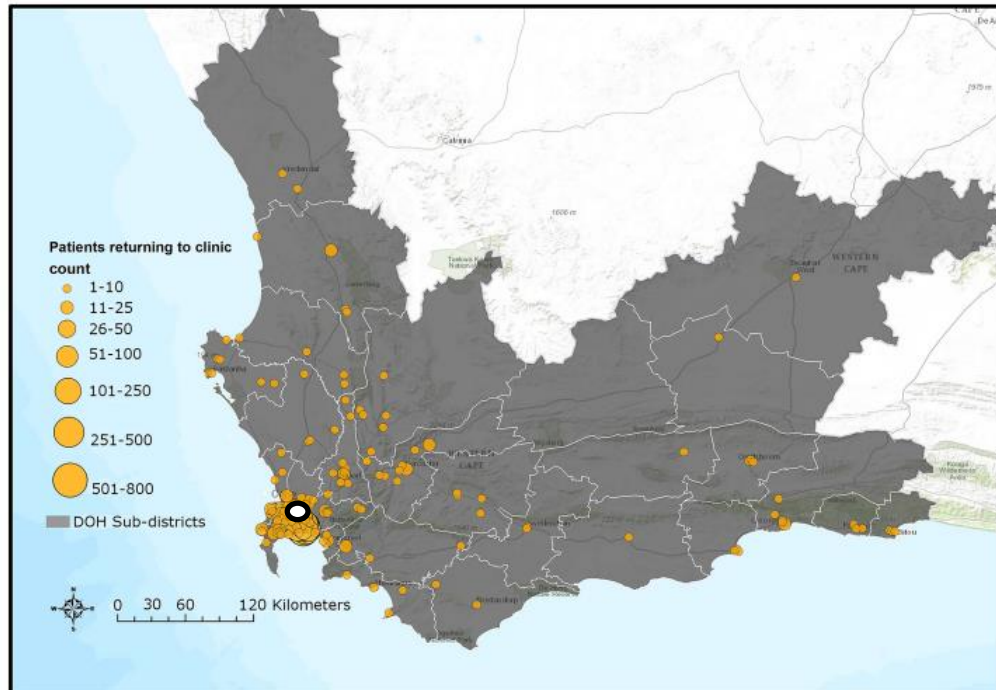
Contemporary disengagement from antiretroviral therapy in Khayelitsha, South Africa: A cohort study PLOS MEDICINE

PLoS Med 14(11): e1002407

Samantha R. Kaplan<sup>1\*</sup>, Christa Oosthuizen<sup>2</sup>, Kathryn Stinson<sup>2,3</sup>, Francesca Little<sup>4</sup>, Jonathan Euvrard<sup>2</sup>, Michael Schomaker<sup>2</sup>, Meg Osler<sup>2</sup>, Katherine Hilderbrand<sup>2,3</sup>, Andrew Boule<sup>2,5,6‡</sup>, Graeme Meintjes<sup>7‡</sup>

- 39,884 PLHIV on ART in Khayelitsha in 2013/2014
- 23% “disengaged from care” (no visit for 180 days)
  - 33% returned to care after 180 days
  - 25% alive but not in care

Clinics in WC where patients silently transferred / re-engaged



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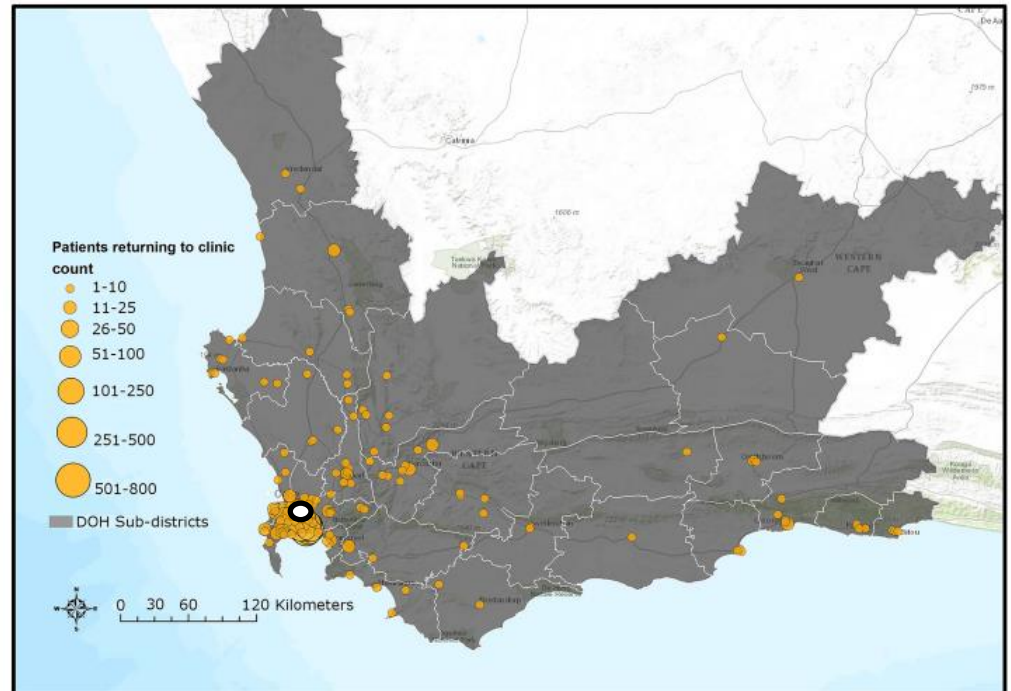
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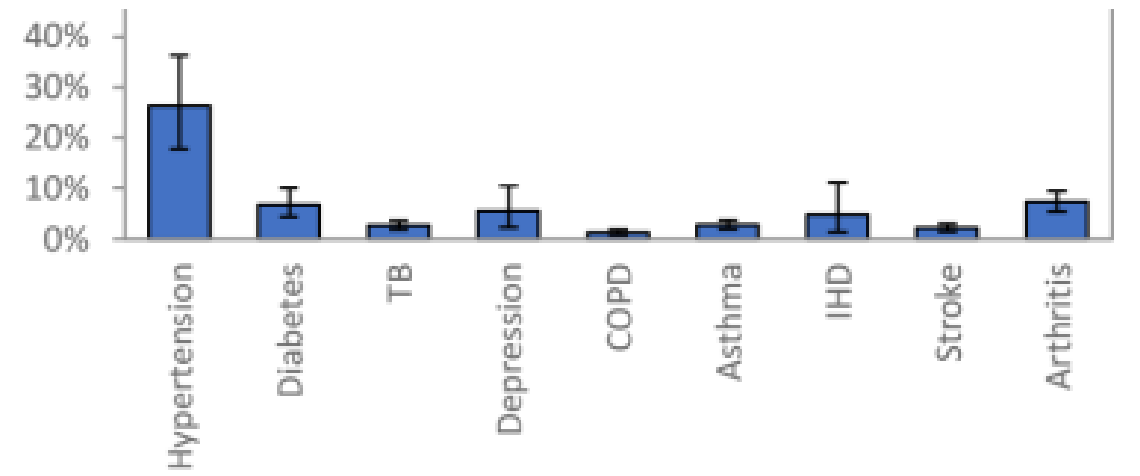
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A model-based approach to estimating the prevalence of disease combinations in South Africa  
BMJ Global Health 2024;9:e013376

Leigh F Johnson<sup>1</sup>, Reshma Kassanjee<sup>1</sup>, Naomi Folb<sup>2</sup>, Sarah Bennett<sup>2</sup>, Andrew Boule<sup>1,3</sup>, Naomi S Levitt<sup>4</sup>, Robyn Curran<sup>5</sup>, Kirsty Bobrow<sup>4</sup>, Rifqah A Roomaney<sup>6</sup>, Max O Bachmann<sup>7</sup>, Lara R Fairall<sup>5,8</sup>

Estimated prevalence of different comorbidities in PLHIV

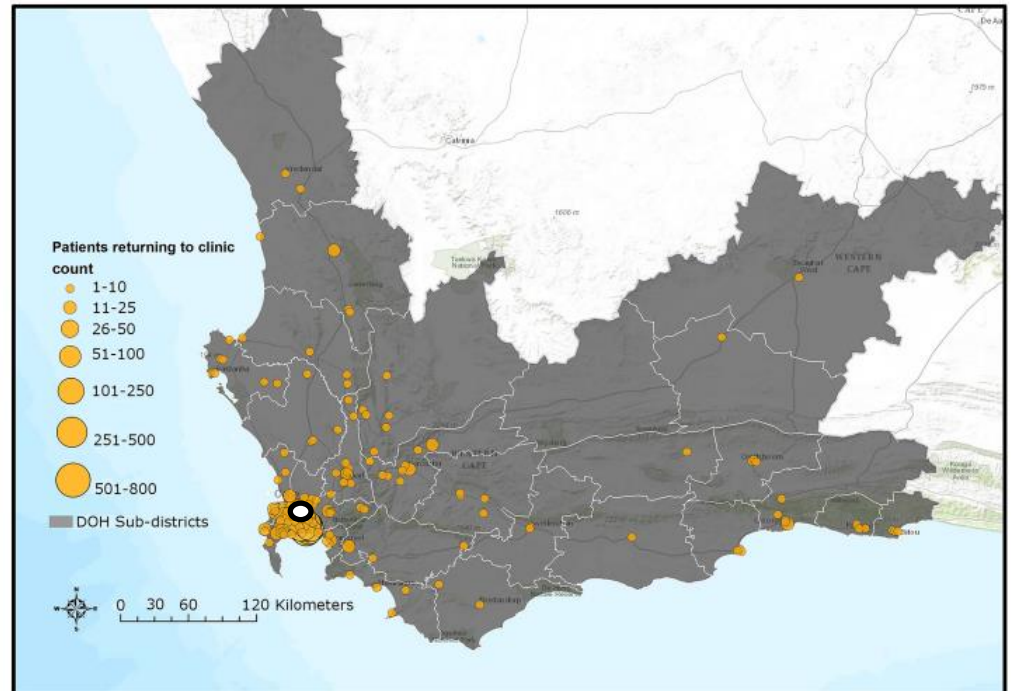


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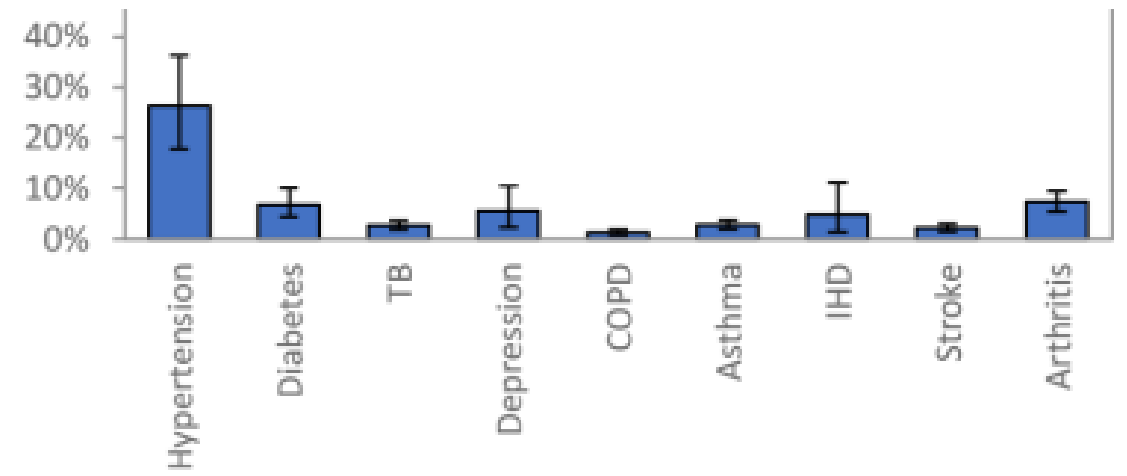
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Mpox in people with advanced HIV infection: a global case series  
Mitja et al. Lancet 2023; 401: 939-49