ANRS 12249
TasP trial

# From home-based HIV testing to viral suppression: HIV care trajectories in the context of Universal Test-and-Treat in rural South Africa (OC4C)

Delphine Perriat, Mamadou Hassimiou Diallo, François Dabis, Deenan Pillay,
Joanna Orne-Gliemann, Joseph Larmarange for the ANRS 12249 TasP Study Group

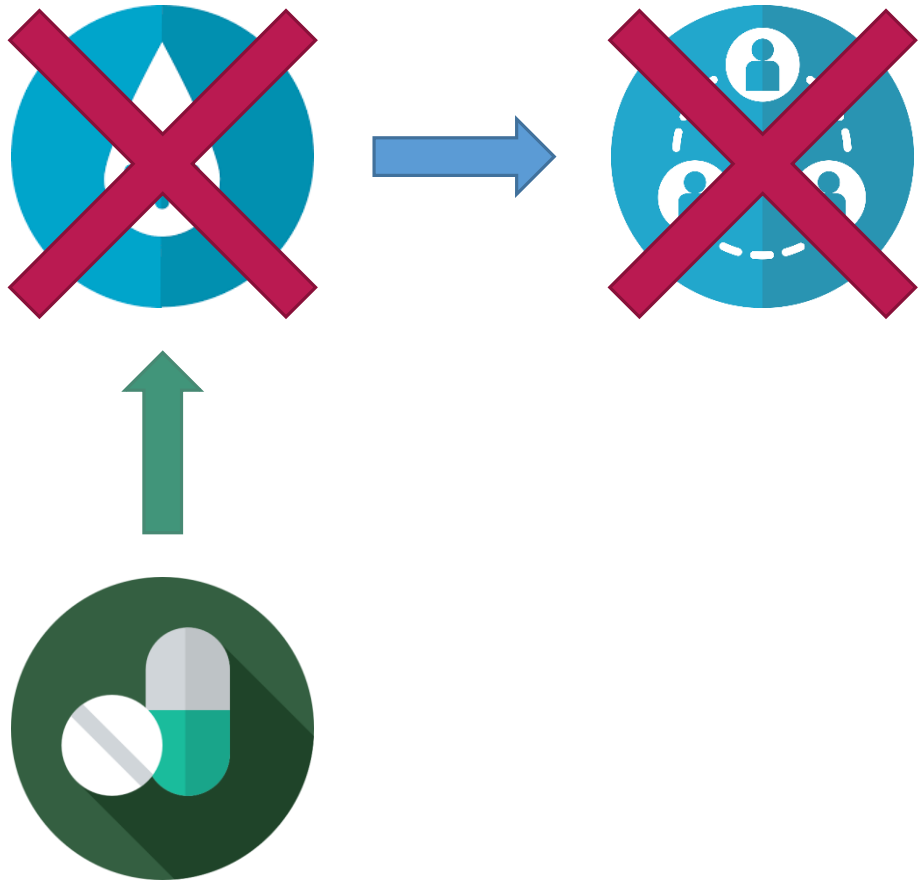
# From individual care trajectories to HIV care cascade at population level in rural KwaZulu-Natal (South Africa): the impact of population dynamics (OC4D)

Joseph Larmarange, Mamadou Hassimiou Diallo, Nuala McGrath, Collins Iwuji, Rodolphe Thiébaut, Frank Tanser,
Till Bärninghausen, Deenan Pillay, François Dabis, Joanna Orne-Gliemann for the ANRS 12249 TasP Study Group

LHRS Conference
Paris • 31 May 2018

# SCIENTIFIC **CONTEXT**

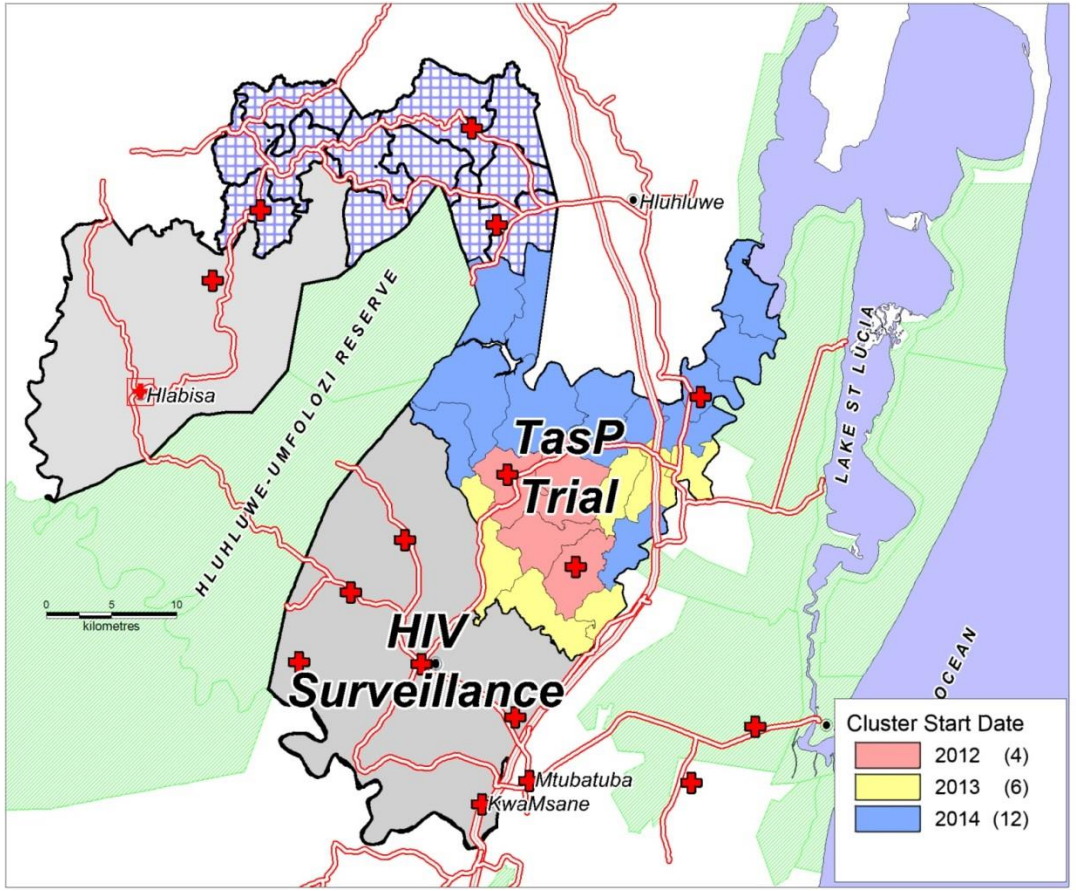
- Viral load (measuring quantity of circulating virus) is the main determinant of HIV transmission
- HIV patients with a suppressed VL (i.e. undetectable) do not transmit HIV
- Antiretroviral treatment (ART) allows to reduce and suppress VL
- **Universal Test and Treat** approach: regular testing of a population and immediate ART for all diagnosed HIV+ ➔ improving the cascade of care
- According to mathematical modelling, UTT would lead to reduction in HIV incidence and potential elimination of the HIV epidemics



**UNAIDS objective:** reaching 90-90-90 by 2020
90% of PLWHIV being diagnosed
90% of those diagnosed being on ART
90% of those on ART being virally suppressed

# THE **ANRS 12249** TASP TRIAL

- One of 5 international trials aiming at evaluating UTT approaches
- *Objective:* Evaluate the impact of immediate antiretroviral treatment on HIV incidence at population level
- *Design:* Cluster-randomised trial
- *Control arm:* universal testing
  *Intervention:* universal testing & treatment
- 22 clusters (2x11)
- ~28 000 individuals aged 16+
- *Timeline:* March 2012-June 2016

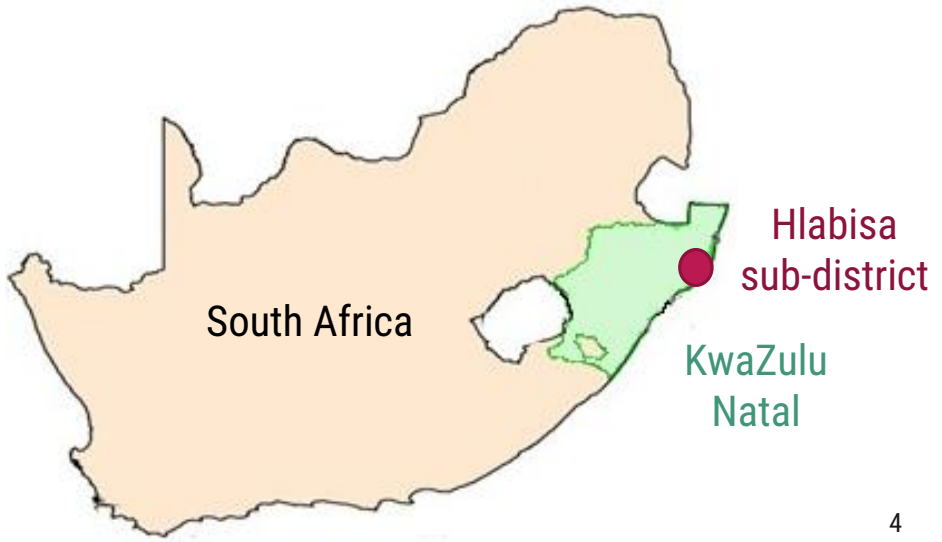



4 clusters (opened in 2012)
+ 6 clusters (opened in 2013)
+ 12 clusters (opened in 2014)

**Total of 22 clusters**

# CONTEXT
## HLABISA SUB-DISTRICT

- isiZulu-speaking inhabitants
- rural
- poor
- only ~10% of adults is employed
- frequent migration
- low marital rates and late marriage
- ~30% of adults are infected by HIV



# TASP TRIAL **PROCEDURES**


**Homestead Identification**
(GPS)

**Homestead visit**

1. Registration of resident adults
2. Household assets questionnaire
3. Update of resident members list
4. Exit forms (death / migration)

**Homestead procedures**

1. Individual questionnaires
2. DBS sample (lab tests)
3. Rapid HIV testing

**repeated every ~six months**

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

**Local governmental clinics**

- *Matching between trial and governmental database at individual level*
- CD4 and viral load results / clinic visits
- Treatment according to national guidelines

**Trial clinics**

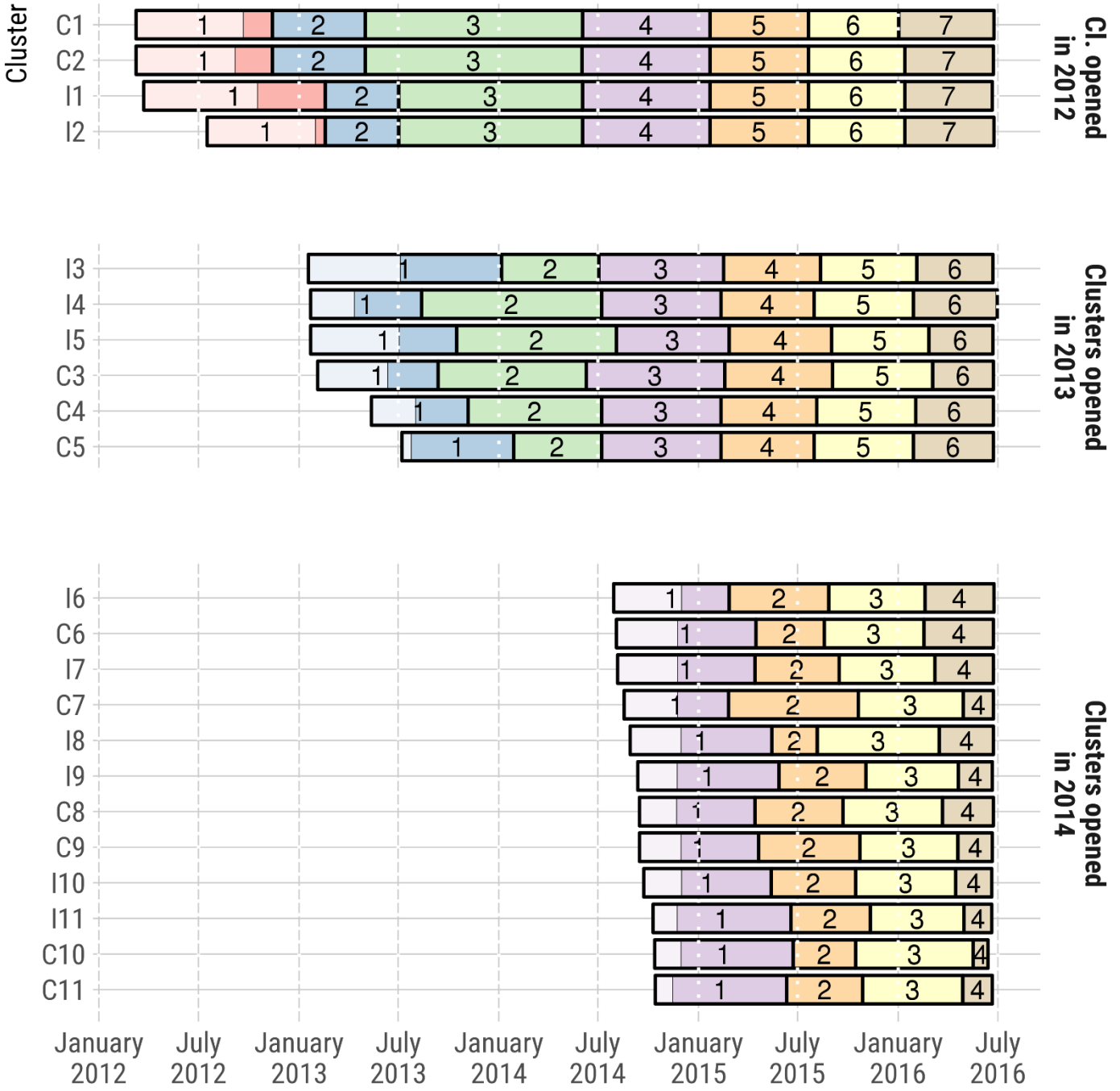
- One per cluster (45 min walk max)
- HIV care and treatment (immediate ART if intervention arm; according to national guidelines if control arm)
- Study questionnaires

**if ascertained HIV+**
(rapid test or self-report)
**referred to trial clinic**

# **TIMING** OF FIELDWORK

- 4 clusters (opened in 2012)
- 6 clusters (opened in 2013)
- 12 clusters (opened in 2014)

*Lights areas indicate the time required to complete the initial census of the population*



# **MAIN RESULT** OF THE TRIAL

- Presented in July 2016
- **Primary outcome:**
  cumulative HIV incidence
  no significant difference between arms
- Low linkage to care in this setting
  ➔ Limited impact on ART coverage
  ➔ no significant difference in ART coverage between arms at the end of the trial
- **Need to better understand the dynamic of the cascade of care in this setting**

# THE **CASCADE** OF HIV CARE

- The “HIV care cascade“ is a cross-sectional concept describing at a given date the position of PLWHIV through the HIV care continuum
- Its evolution over time is determined by **individual longitudinal trajectories** and underlying **population dynamics**
- What is the timing and sequencing of individual trajectories?
- What is the structural effect of the dynamics of the PLWHIV population and its impact on the cross-sectional HIV care cascade?

# **APPROACH**: COMPUTATION OF **DAILY STATUSES**

**for each calendar day**

**RESIDENCY status**
(resident / not resident)

considering initial census of the population (1st survey round)
16th birthday, imputed dates of in-migration events,
documented dates of out-migrations events and deaths

among those residents

**HIV status**
(HIV positive / negative)

using multiple sources: repeat DBS, repeat rapid tests, HIV-positive self-reports and HIV clinic visits in trial and/or local governmental clinics
seroconversion date imputed using a random point approach

among those HIV-positive

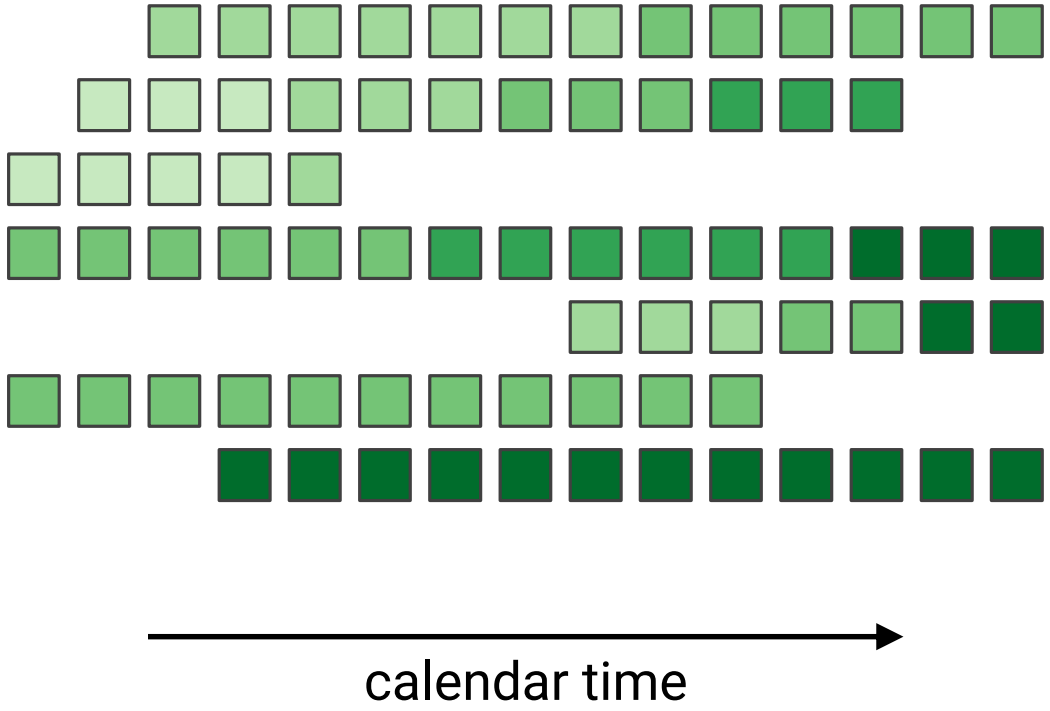
**HIV CARE position**

clinic visits, ART prescription and viral loads of PLWHIV seen in trial clinics
2 additional data sources for local governmental clinics with clinic visits and ART prescriptions for one and CD4 count and viral loads for the other

# **HIV CARE** STATUSES

- infected but not diagnosed
- diagnosed but not in care
- in care but not on ART
- on ART but not virally suppressed
- on ART & virally suppressed

*each row represents a unique individual*
*each column represents a calendar day*



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# OBJECTIVES

to describe the **timing** & **sequencing** of individual HIV care statuses

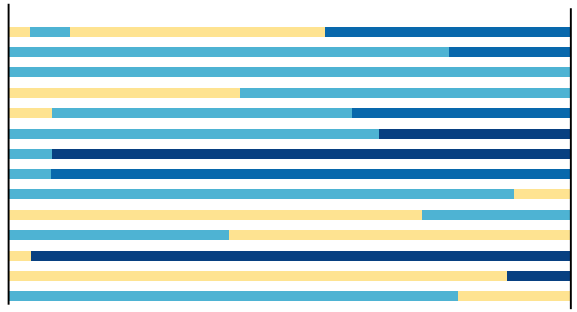
from **clinic referral**
to **viral suppression**

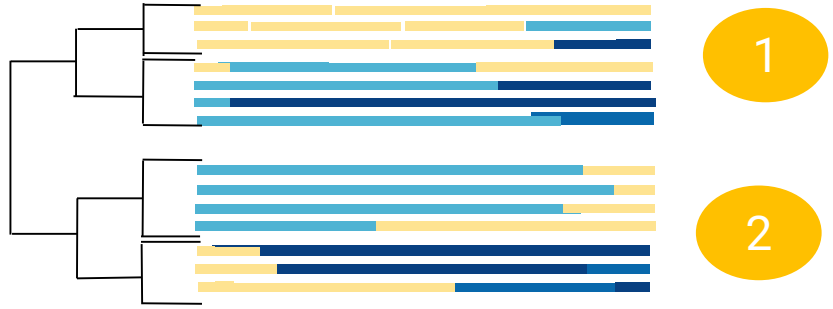
by identifying groups of individuals with similar **HIV care trajectories**

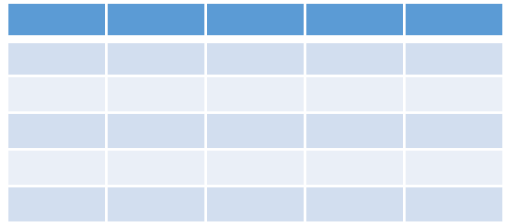
and **factors** associated with each care trajectories group

# METHODS

- Sequence analysis approach
- Distance between sequences of same length using optimal matching (hierarchical costs matrix)
- Hierarchical classification to create homogenous care trajectories groups
- Multinomial logistic regression model (reduced by minimization of AIC)

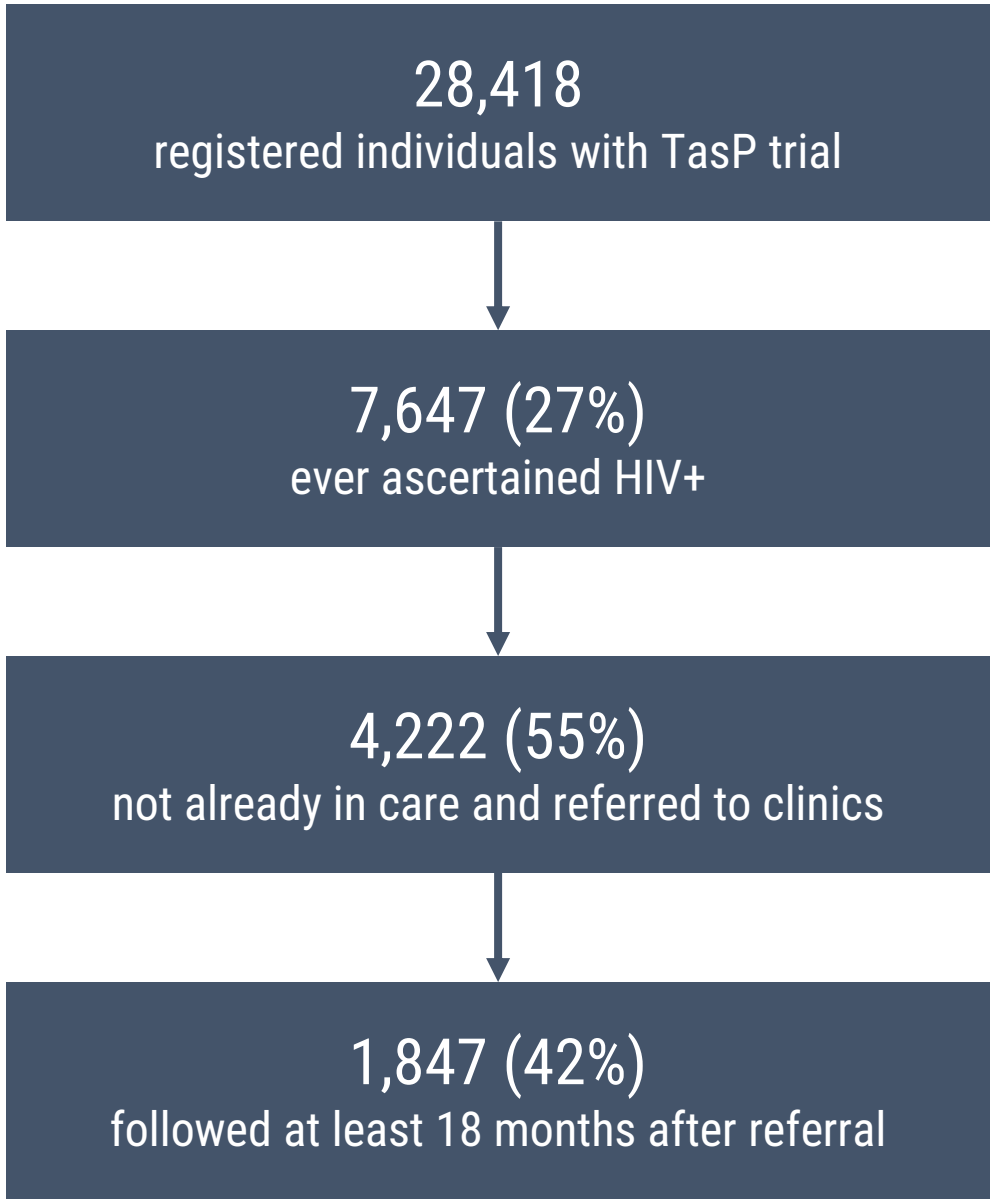





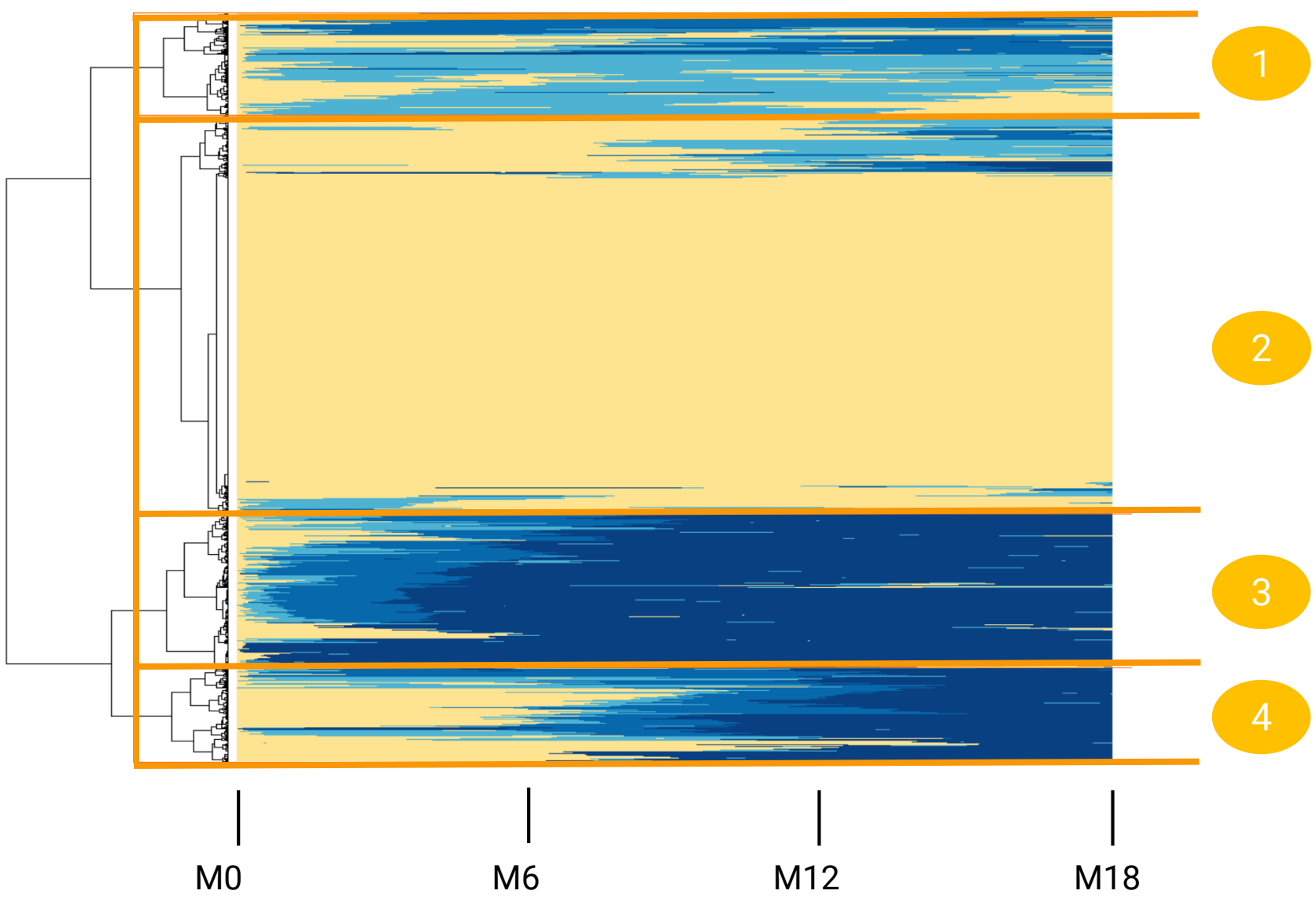



# STUDY **POPULATION**

- 74% of women
- Median age: 34 years old [27-45]
- 77% unemployed
- HIV care status at referral
  - 30% lost to follow-up
  - 57% already diagnosed, never entered care
  - 13% newly diagnosed
- 84% think that ART make people less infectious

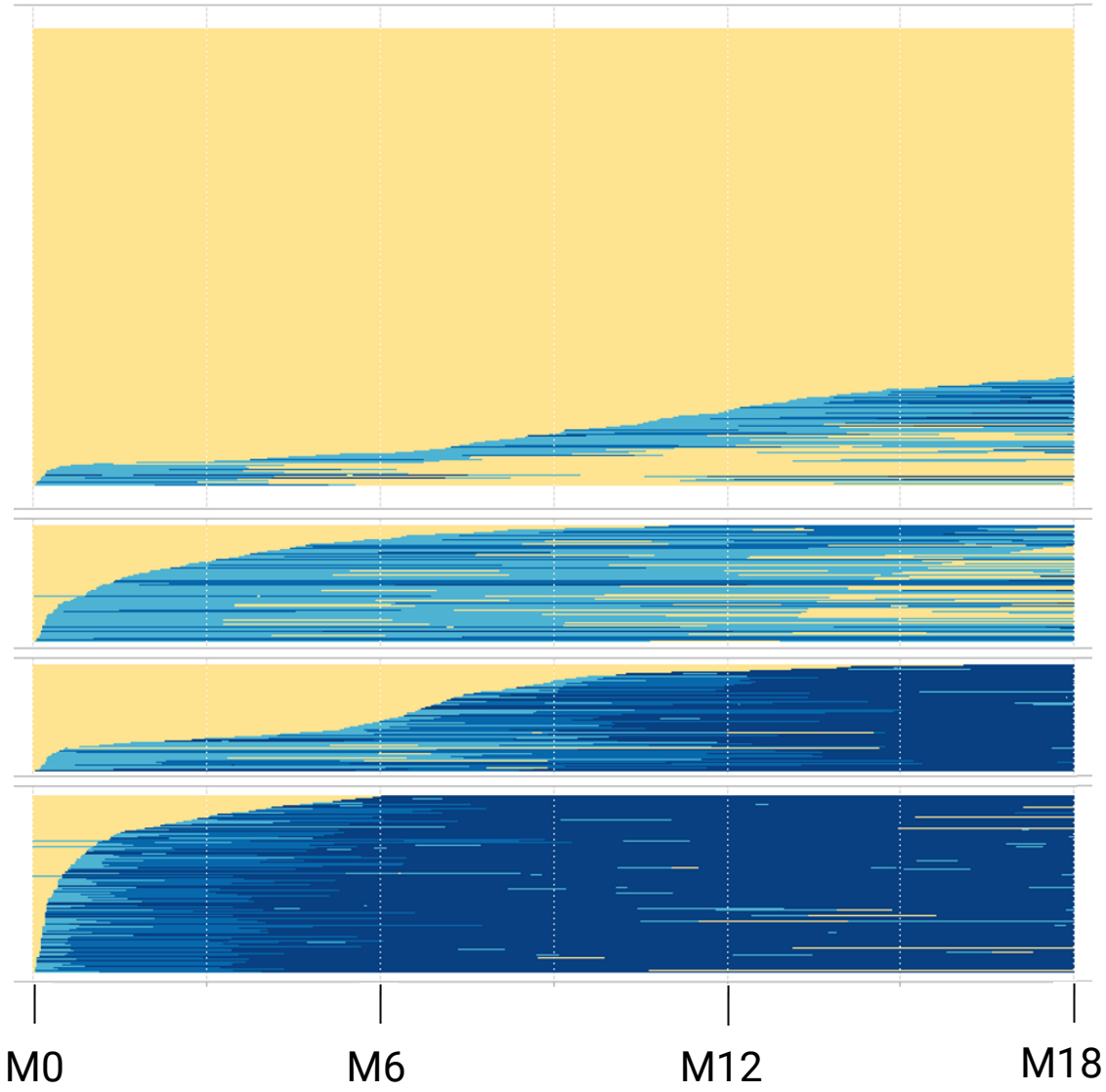


# IDENTIFICATION OF **TRAJECTORIES GROUPS**




Not in care
In care, not on ART
On ART, not virally suppressed
On ART and virally suppressed

# DESCRIPTION OF **TRAJECTORIES GROUPS**




Not in care
In care, not on ART
On ART, not virally suppressed
On ART and virally suppressed

**Absence of care** (n=978, 53%)

**Inconstant care** (n=250, 14%)
- 50% initiated ART
- 63% exited care

**Slow and continuous care** (n=230, 12%)
- 6 months to enter care
- 8 months to initiate ART

**Rapid and continuous care** (n=379, 21%)
- 15 days to enter care
- 1 month to initiate ART

Reference group for multinomial model

# **FACTORS** ASSOCIATED WITH TRAJECTORIES GROUPS

| Factor | Absence vs. rapid | Inconstant vs. rapid | Slow vs. rapid |
|---|---|---|---|
| Being newly diagnosed at referral | ++ | ++ | |

Multivariate multinomial logistic regression model. n=1835. Model also adjusted on household wealth (assets).

# **FACTORS** ASSOCIATED WITH TRAJECTORIES GROUPS

| Factor | Absence vs. rapid | Inconstant vs. rapid | Slow vs. rapid |
|---|---|---|---|
| Being newly diagnosed at referral | ++ | ++ | |
| ≥ 50 years old vs. < 50 | - - | - - | - |

Multivariate multinomial logistic regression model. n=1835. Model also adjusted on household wealth (assets).

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| Being newly diagnosed at referral | ++ | ++ | |
| ≥ 50 years old vs. < 50 | - - | - - | - |
| Local HIV prevalence > 35% (➔ clinics being more busy) | | | - |

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| Being newly diagnosed at referral | ++ | ++ | |
| ≥ 50 years old vs. < 50 | - - | - - | - |
| Local HIV prevalence > 35% (➔ clinics being more busy) | | | - |
| Distance to a trial clinic | + | | |

Multivariate multinomial logistic regression model. n=1835. Model also adjusted on household wealth (assets).

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| Distance to a governmental clinic | - - | | |

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|---|---|---|---|
| Being newly diagnosed at referral | ++ | ++ | |
| ≥ 50 years old vs. < 50 | - - | - - | - |
| Local HIV prevalence > 35% (➔ clinics being more busy) | | | - |
| Distance to a trial clinic | + | | |
| Distance to a governmental clinic | - - | | |
| Intervention arm vs. control (➔ immediate ART in trial clinics) | - - | - - | |

Multivariate multinomial logistic regression model. n=1835. Model also adjusted on household wealth (assets).

# DISCUSSION

- Diversity and complexity of care trajectories patterns
- Only 21% performed well (rapid care), and even less (7%) among those newly diagnosed at referral
- Linkage to care constitutes the main bottleneck of HIV programs in this setting, associated in qualitative work with perceived stigma
- The perspective of immediate treatment seems to have a positive effect, even on the first steps of the care cascade

**To maximize the impact of UTT strategies, new interventions are required, especially between diagnosis and ART initiation and for those recently diagnosed**

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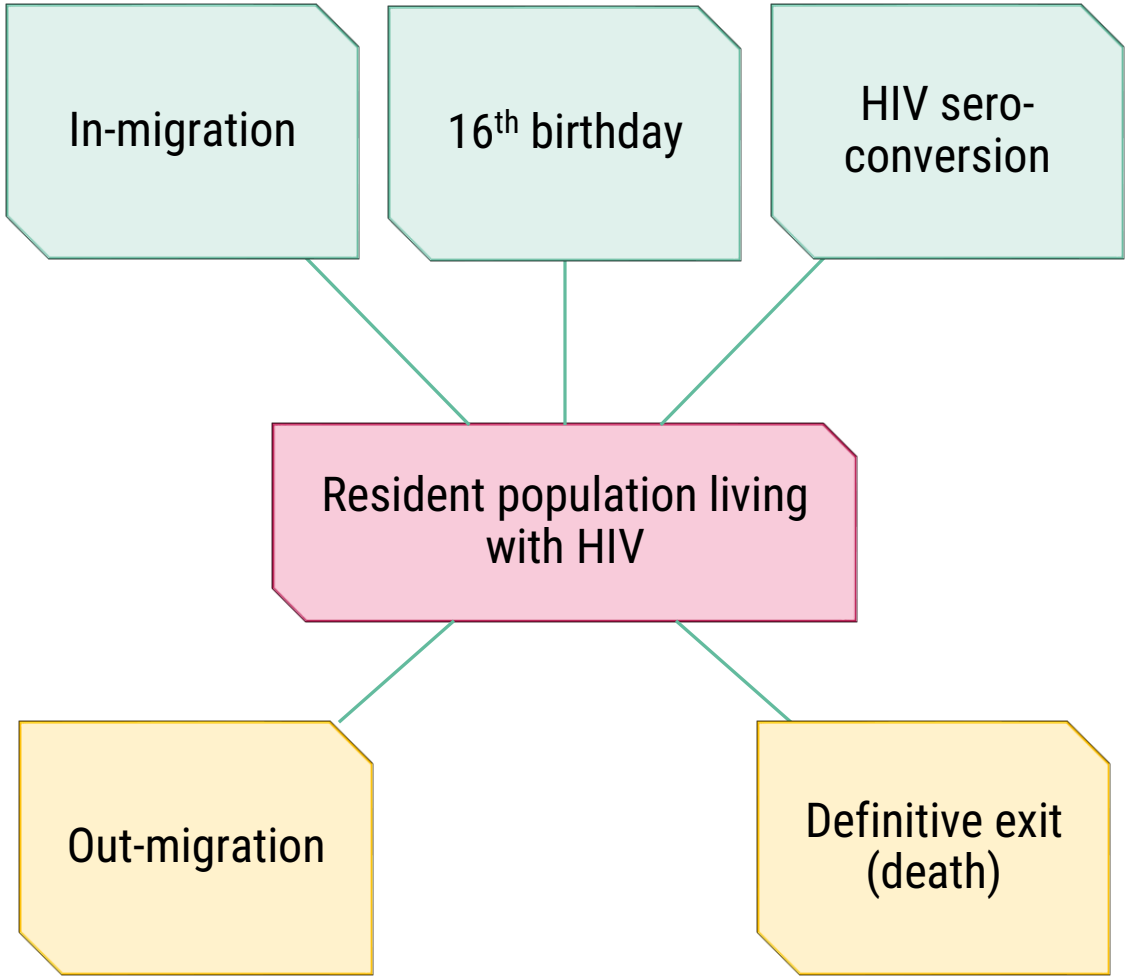
# OBJECTIVES

1. to document the dynamics of the PLWHIV population, distinguishing the different components of population change
2. to identify the position within the HIV care continuum of individuals joining/leaving the PLWHIV population
3. to compare their care position with the rest of the local PLWHIV population
4. to quantify the contribution of each component of population change on the cross-sectional HIV care cascade

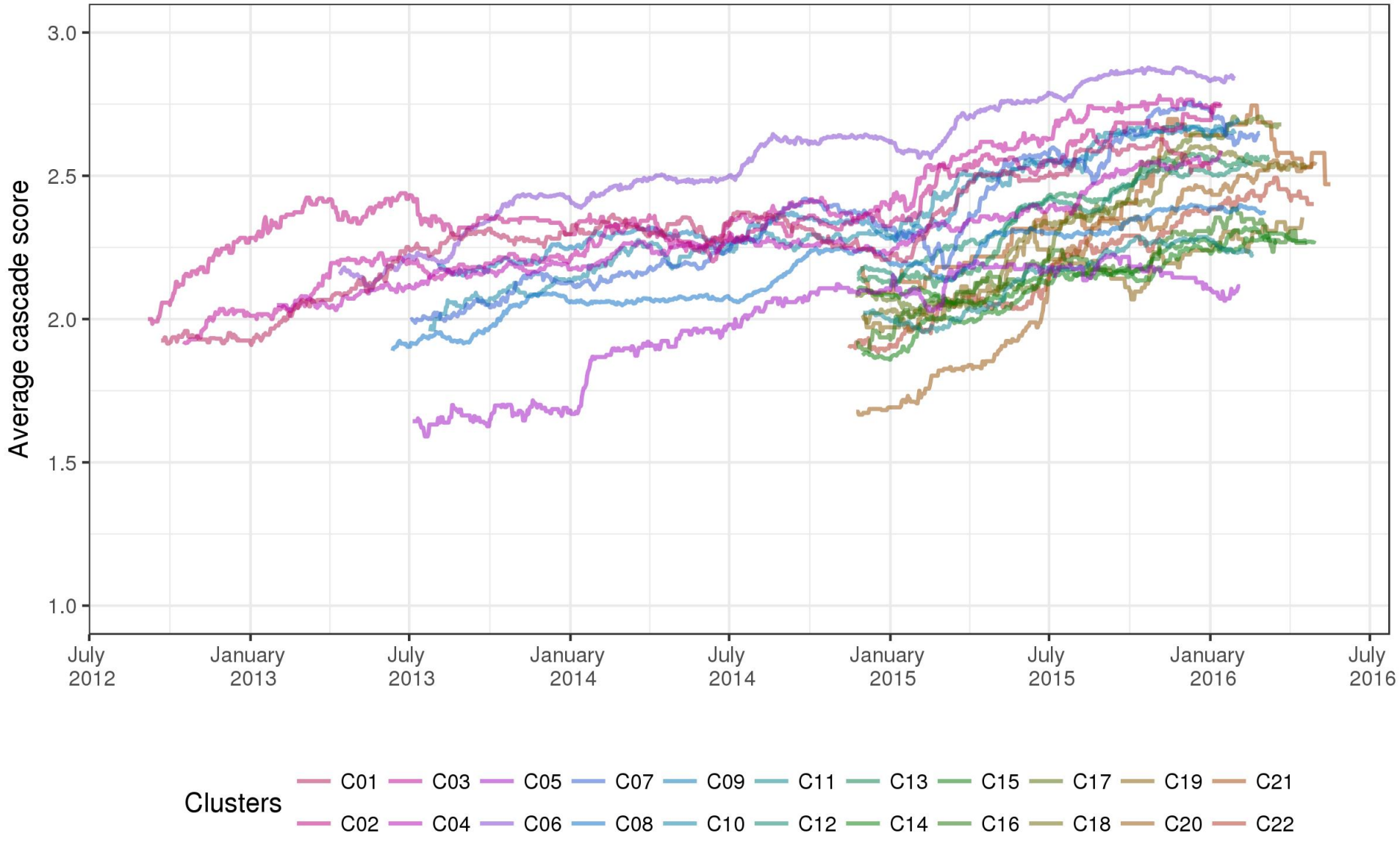
## COMPONENTS OF PLWHIV **POPULATION CHANGE**



# METHODS

- Position within HIV care continuum summarized as a **score** ranging from 0 (undiagnosed) to 4 (virally suppressed)
- Analysis performed at cluster-level
- For each cluster, an **average score** could be computed for each calendar day

# **AVERAGE CASCADE SCORE** OVER TIME BY CLUSTER



# METHODS

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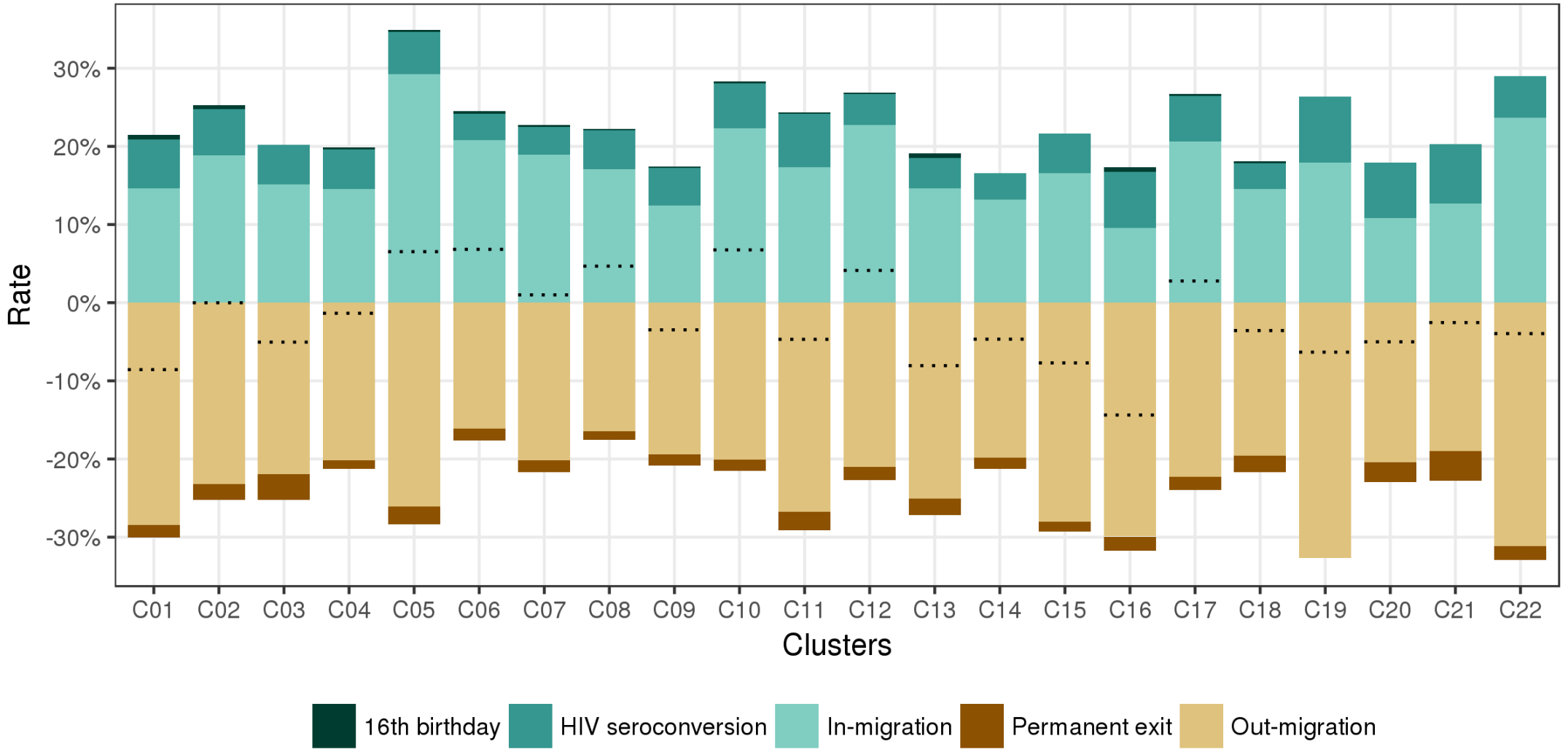
- Rates of each population change component computed per cluster

# ANNUAL **GROWTH RATES** OF THE PLWHIV POPULATION




All clusters combined: **+0.2%** **+4.8%** **+17.3%** **-1.6%** **-21.0%**

# METHODS

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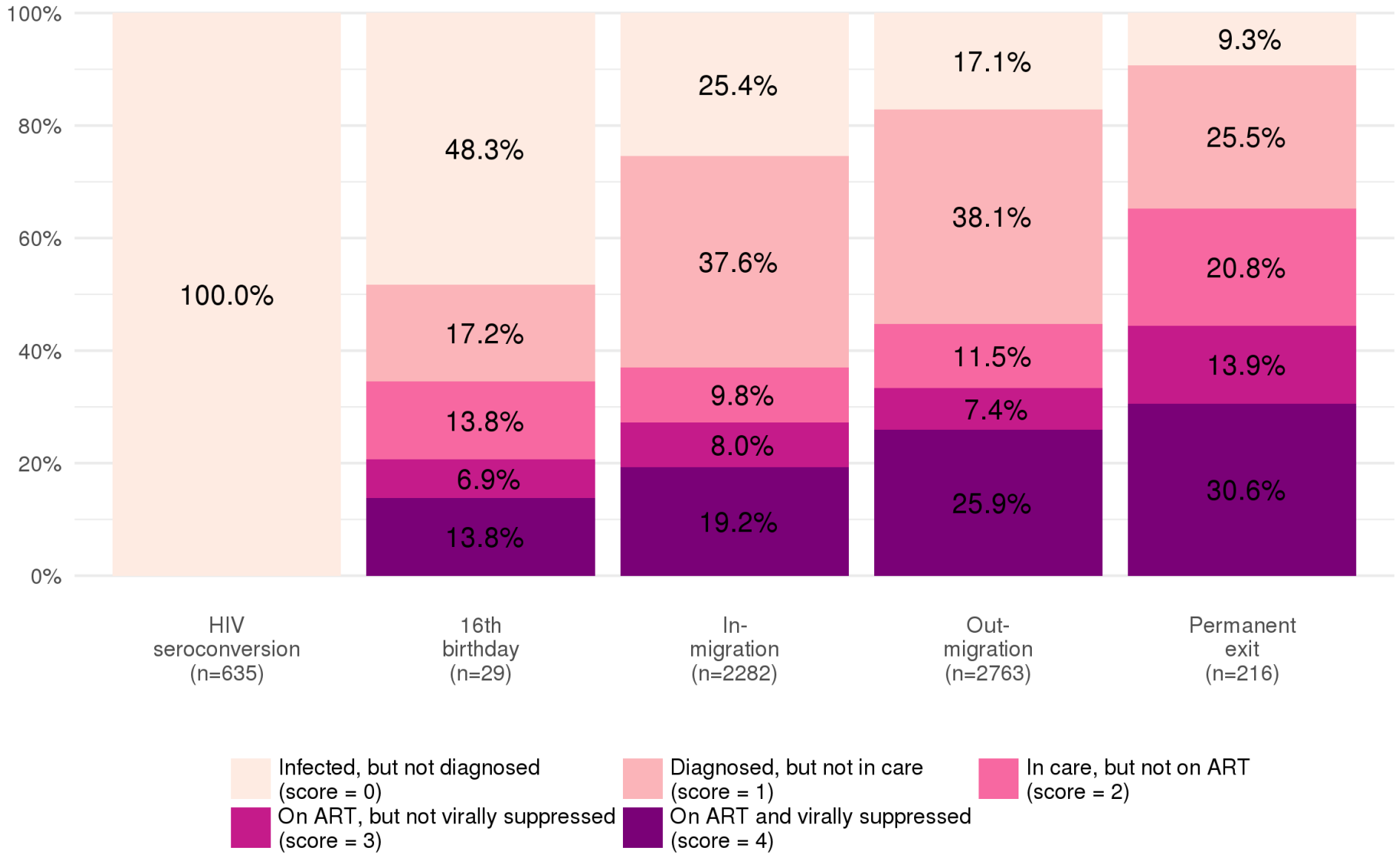
- Rates of each population change component computed per cluster
- Position within the HIV care continuum at the date of entry/exit was identified for each event, by population change component

# **HIV CARE STATUS** AT THE DATE OF ENTRY/EXIT



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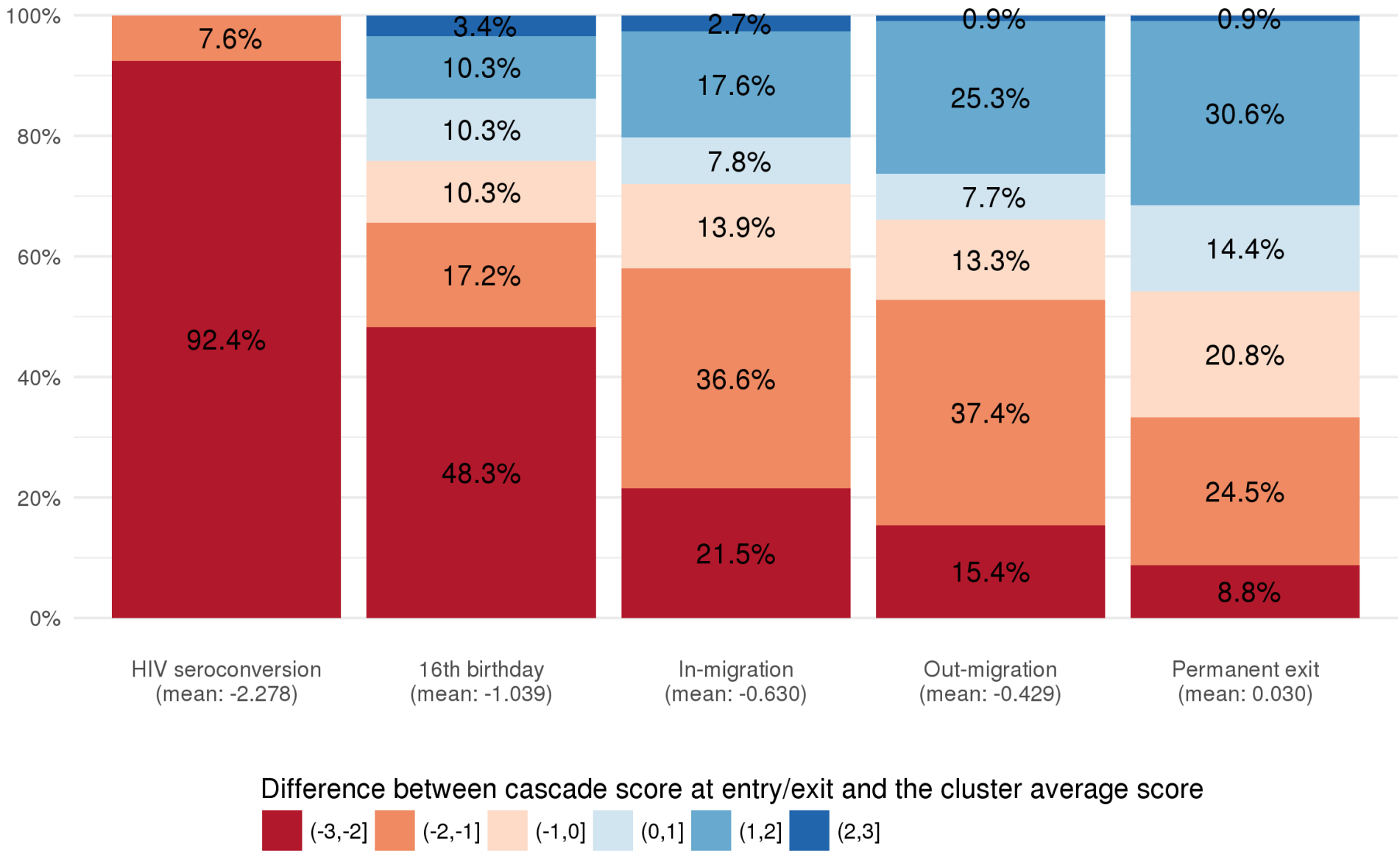
- Position within the HIV care continuum at the date of entry/exit was identified for each event, by population change component

- The corresponding score was compared with the cluster average score by difference

# **DIFFERENCES** CASCADE SCORE AND CLUSTER AVERAGE SCORE




**In-migrants and out-migrants had lower cascade score than the average population**

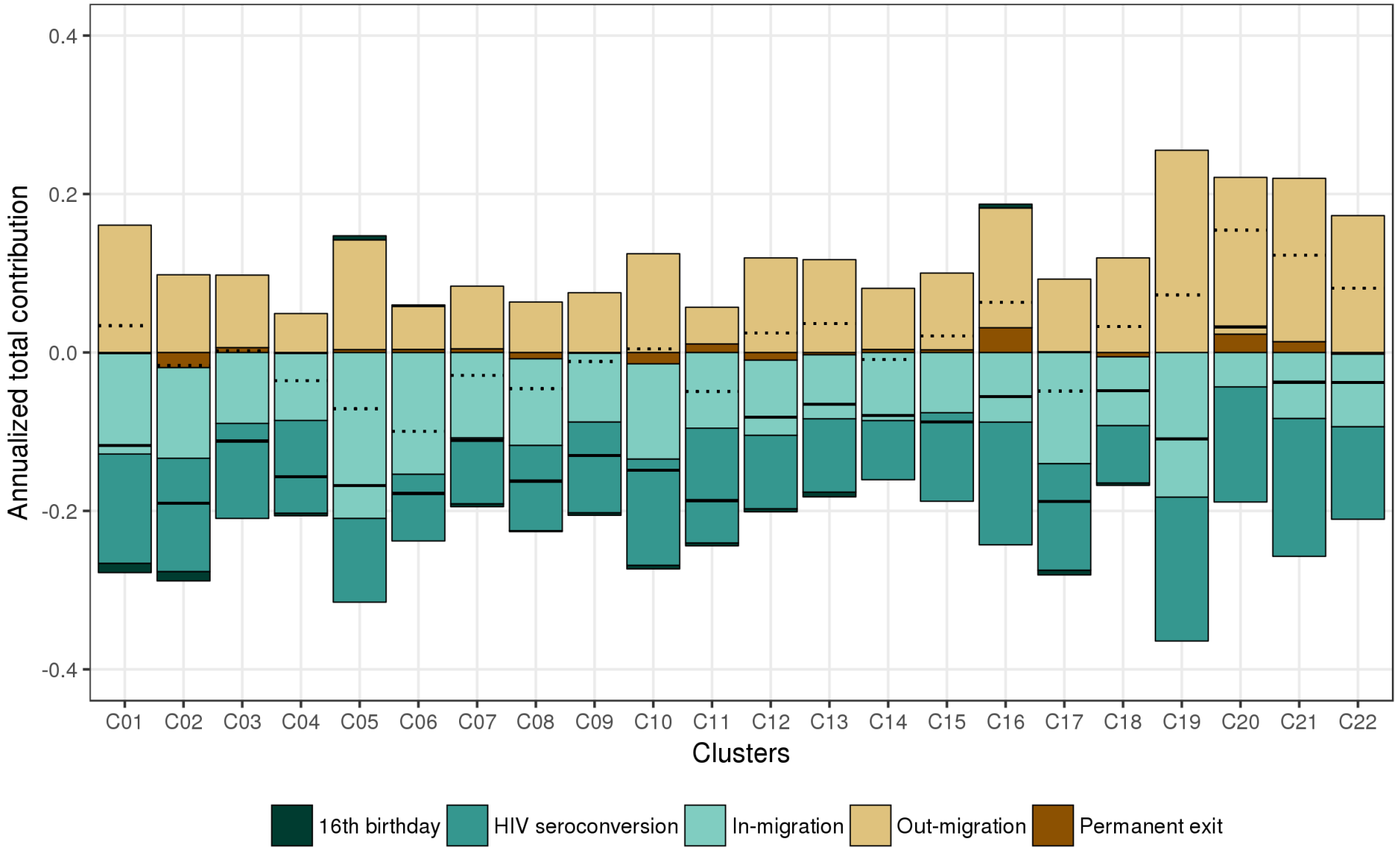
**By definition, newly infected individuals are at the first step of the cascade (i.e. undiagnosed) at the time of infection**

# METHODS

- Position within HIV care continuum summarized as a **score** ranging from 0 (undiagnosed) to 4 (virally suppressed)
- Analysis performed at cluster-level
- For each cluster, an **average score** could be computed for each calendar day
- Rates of each population change component computed per cluster
- Position within the HIV care continuum at the date of entry/exit was identified for each event, by population change component

- The corresponding score was compared with the cluster average score by difference
- The contribution of a specific event on the cluster average cascade score depends on the PLWHIV population size at that date
- For a given cluster, the sum of all event contributions provides the total contribution of population change on the average cascade score over time
- As all clusters were not observed for the same amount of time, we annualized these total contributions for comparing clusters

# ANNUALIZED **TOTAL CONTRIBUTION** OF POPULATION CHANGE




*Dotted lines indicate the sum of the total contribution of in- and out-migration.*

*Black lines indicate the sum of total contribution of all events.*

**In-migration and Out-migration compensate each other**

**Total contribution negative in all clusters, due to the flow of new HIV infections**

# SUMMARY

- While the average cascade score increased over time in all clusters, that increase was constrained by population dynamics
- Permanent exits and aging into the PLWHIV cohort had a marginal effect
- Both in-migrants and out-migrants were less likely to be retained at each step of the HIV care continuum
- However, their overall impact on the cross-sectional cascade was limited as the effect of in- and out-migration balanced each other
- The contribution of HIV seroconversions was negative in all clusters

# CONCLUSION

- Migrants face specific vulnerabilities that limit their retention at each step of the HIV care continuum
- Coordination to facilitate continued access to care when people move should be developed
- In a context of high HIV incidence, the continuous flow of newly infected slows down efforts to increase overall ART coverage and population viral suppression, ultimately attenuating any population-level impact on HIV incidence.
- Identifying specific interventions to reach newly infected people as early as possible is a crucial step on the way towards the end of the epidemic

# **LIMITATIONS** (BOTH ANALYSIS)

- Proxy indicators used to measure HIV care status in governmental clinics
- Care received in governmental clinics probably underestimated due to participants not matched with governmental datasets
- Care received in private sector not captured
- 9.5% of trial population with no observed HIV status and excluded from the analysis

# GENERAL **DISCUSSION**

- Care cascade improved in both arms, but similarly
- Main challenges are outside the clinics
- Mobility dilutes the impact of interventions at population level

- Quite unique context allowing to observe trajectories on a daily basis
- Added value of longitudinal perspective to measure care trajectories

# ACKNOWLEDGMENTS

ANRS 12249
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- Trial participants
- Africa Centre staff
- Traditional Authorities
- Department of Health, South Africa
- Merck/Gilead

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