State-space models for engagement, retention, and re-entry in the HIV care cascade

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BACKGROUND
Recently the HIV care cascade which describes essential steps in the whole HIV care continuum has become a central assessment metric to monitor progress and identify gaps in HIV care needs in the US and worldwide.

- **Main use**: Targeting some key questions related to HIV care efforts
  1. When patients are most likely to fall out of care
  2. Where along the phase they are most likely to be lost
  3. Who is most likely to disengage at each phase.

- **Limitations**:
  1. The lack of representing various types of longitudinal patient experiences
  2. Analytical approaches in addressing the questions surrounding the cascade.

- **Objective**: We propose a state space representation of the HIV care cascade and corresponding statistical framework that can describe the longitudinal dynamics along the phases in the cascade.

METHODS
Each phase in the HIV care cascade is viewed as a state.

- State space models (SSM): parameterized by probability of transitioning from one state to another
  \[ S_t = \text{state at time } t \]
  \[ p_{ij} = p(S_t = j | S_{t-1} = i) \]

  - Example: \( S = \{1, 2, 3, 4, 5\} = (\text{HIV diagnosis}, \text{engagement in care, disengagement from care, ART initiation, viral suppression}) \)
  - \( p_{j|i} \): probability of transition from engaged to engaged (retention)
  - \( p_{j|i} \): probability of re-entry into care after disengagement
  - Effect of covariates on \( p_{j|i} \) can be assessed by multinomial logistic regression:
  \[ \logit(p_{j|i}(X)) / p_{i|i}(X_i)) = \beta_j^{x}(S_{t-1}=j) X_i \]

X_i = a collection of covariates
\( J = \text{reference state} \)
\( \beta_j = \text{a log relative ratio} \)

APPLICATION
Application of the framework on existing data requires three main processes:

1. **Operationalization of the care cascade**: best reflect and capture dynamics in a cohort
2. **data preparation**: appropriately incorporates patient monitoring plan
3. **implementation of SSM**: use SSM tailored to step 1.

We illustrate application of the framework using AMPATH (Kenya) data.

**Step 1: Operationalization of the care cascade**
AMPATH data on HIV testing and viral load is limited (cost and resource constraints). Due to the limitations, we represented the current operation by

- State=1: engaged in care
- State=2: disengaged from care
- State=3: transfer-out
- State=4: lost-to-follow-up (LTU)
- State=5: deceased.

Focusing on \textit{retention aspect of care}.

**Step 2: Data preparation**
Patient monitoring plan: Expected return dates by AMPATH protocol is

- Three month if on ART
- + two weeks = at least one visit at every 197 days
- Six month if not on ART
- to be defined as engaged.

Otherwise, disengaged unless transferred-out or died.

- LTU: no clinical visit in a year after disengagement.

**Step 3: Implementation of SSM** Accordingly, 5 state SSMs were considered using engaged in care (state=1) as a reference state.

RESULTS
Participants: 57,596 patients ≥13 years of age (enrolled bw Jan. 2008 - Sep 2012). Sixty seven% female, median age of 35, and median CD4 count at baseline of 239 cells/ml.

1. **Unadjusted SSM**: Temporal trends – \textit{when and where} questions

2. **Adjusted SSM**: Effect of covariates & identify groups at high risk – \textit{when, where, and who} questions

CONCLUSIONS
The proposed approach is the first attempt to capture all possible transition dynamics using longitudinal data and to find determinants of the transitions to seek answers to the \textit{when, where, and who} questions. Findings from SSM-based analysis of the care cascade based on a clinical cohort will inform the development of guidelines that are tailored to patient characteristics in that cohort, customized to sub-populations at highest risk of falling out of care at each stage of the cascade.