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LETTER TO THE EDITOR

Reply to Satapathy et al.'s comment on "Dual cross-sectional and longitudinal perspective on the continuum of HIV care to disentangle natural epidemic evolution from real progress, Belgium 2014–2022"

Dear Editor,

We write in response to the letter by P. Satapathy et al. on our study "*Dual cross-sectional and longitudinal perspective on the continuum of HIV care to disentangle natural epidemic evolution from real progress, Belgium 2014–2022*" [1]. The following points were raised: (i) the use of 1-year cumulative incidence (CI) to describe diagnosis timing; (ii) the inclusion of cause-specific hazards or adjustment for the competing risk of loss to follow-up in our transition models; (iii) the validity of the discussed potential causes of the observed improvements; (iv) the generalisability of the findings to other countries. We appreciate the opportunity to clarify our findings and address the points raised.

Firstly, we chose to present the results of the longitudinal continuum analyses through both cumulative incidence graphs (Fig. 3 in the article) and proportions reaching the endpoint after defined delays—specifically 1 year for diagnosis—the latter chosen for its clarity and ease of interpretation for readers. This approach effectively highlights the stark contrast between the diagnosis stage and subsequent transitions in care: while 31% were diagnosed within a year of HIV infection in 2020–22, for the next transitions in care high proportions of 81% of linkage to care, 91% of ART initiation, and 77% of viral suppression were reached within 3 months. This underscores that the diagnosis stage remains the slowest step in the continuum of care, making the disparity both visually and intuitively clear to readers. Median time to endpoints and IQR, as a supplementary descriptive indicator, are presented in Table 1.

This alternative indicator yields the same conclusions as the published data and, similarly, highlights the sharp differences between the median time from infection to diagnosis, and the median times observed in the other transitions. Moreover, presenting the median time does not capture the tail end any better than the measures already reported in the article. In consequence, this supplementary analysis reaffirms that our indicator is reliable for informing testing policies.

Secondly, Satapathy et al. underline that the cumulative incidence models should account for competing risks such as loss to follow-up. We indeed addressed this in our analysis using Fine–Grey competing risk models. Death was treated as a competing risk for transitions from diagnosis to linkage to HIV care, from linkage to ART initiation and from ART initiation to viral suppression; while for transitions to ART initiation and to viral suppression, loss to follow-up was used as an additional competing risk. While we also assessed cause-specific hazards, the conclusions aligned with those of the Fine–Grey models, so these additional analyses were not included in the published article but they were added here as supplementary material (Supplementary Table S1).

Thirdly, we aimed to highlight in the discussion that the improvements observed in the continuum of HIV care—particularly in the cross-sectional analysis—might partly reflect the natural evolution of the epidemic. This evolution has occurred in the context of widespread antiretroviral therapy (ART) availability since the 1990s, which has led to reduced mortality and a growing proportion of patients with long-term sustained viral suppression. As a result, the observed improvements cannot be automatically attributed solely to active efforts to optimize care. We also highlighted that the longitudinal approach mitigates the strong influence of long-term virally suppressed individuals on the results by focusing on ongoing transitions during the study periods. Overall, our findings suggest that the observed advancements in the continuum of HIV care in Belgium are attributable to both the 'natural evolution' of the epidemic and targeted improvements in care practices.

Regarding the remark on the lack of statistical substantiation for our inference about the primary drivers of the observed improvements: In the discussion section, we contextualise our findings by examining potentially related policy changes in Belgium—an approach that aligns with standard scientific practice. Notably, one of the most significant improvements in the continuum

TABLE 1 Median time to outcome of interest [IQR: Q1; Q3] for all transitions, by subpopulation and period (time in years).

	Period	Total	BMSM	EMSM	OMSM	BH	SSAH	OH	PWID
Infection to diagnosis	2014–2016	1.98 [0.40; 5.10]	0.88 [0.19; 3.27]	1.27 [0.31; 4.08]	1.40 [0.35; 4.54]	2.42 [0.52; 5.48]	3.56 [1.17; 7.15]	3.58 [1.12; 7.21]	2.58 [0.73; 5.92]
	2017–2019	2.50 [0.58; 6.02]	1.10 [0.21; 3.79]	1.81 [0.46; 4.88]	1.90 [0.48; 5.40]	3.10 [0.79; 6.81]	3.90 [1.29; 7.71]	3.69 [1.19; 7.63]	3.06 [0.85; 6.58]
	2020–2022	2.62 [0.65; 6.12]	1.06 [0.23; 3.42]	1.83 [0.42; 5.15]	1.92 [0.48; 5.06]	3.06 [0.96; 6.21]	4.29 [1.69; 8.31]	4.12 [1.42; 8.23]	3.13 [1.02; 6.71]
Diagnosis to linkage to care	2014–2016	0.03 [0.00; 0.10]	0.02 [0.00; 0.06]	0.00 [0.00; 0.06]	0.01 [0.00; 0.09]	0.03 [0.00; 0.11]	0.04 [0.00; 0.18]	0.03 [0.00; 0.19]	0.06 [0.00; 4.72]
	2017–2019	0.03 [0.00; 0.11]	0.02 [0.00; 0.05]	0.00 [0.00; 0.07]	0.02 [0.00; 0.09]	0.03 [0.01; 0.10]	0.04 [0.00; 0.18]	0.04 [0.00; 0.80]	0.04 [0.00; 0.21]
	2020–2022	0.03 [0.00; 0.13]	0.02 [0.00; 0.06]	0.01 [0.00; 0.24]	0.02 [0.00; 0.14]	0.03 [0.01; 0.11]	0.05 [0.00; 0.20]	0.02 [0.00; 0.15]	0.04 [0.00; 0.61]
Linkage to care to ART initiation	2014–2016	0.10 [0.04; 0.41]	0.09 [0.03; 0.27]	0.10 [0.04; 0.46]	0.12 [0.04; 0.54]	0.09 [0.03; 0.52]	0.09 [0.04; 0.47]	0.10 [0.03; 0.48]	0.44 [0.07; 1.33]
	2017–2019	0.04 [0.01; 0.10]	0.02 [0.00; 0.07]	0.03 [0.00; 0.09]	0.04 [0.01; 0.13]	0.03 [0.01; 0.06]	0.06 [0.02; 0.19]	0.05 [0.02; 0.13]	0.06 [0.03; 0.19]
	2020–2022	0.02 [0.00; 0.05]	0.01 [0.00; 0.04]	0.02 [0.00; 0.06]	0.02 [0.00; 0.06]	0.02 [0.00; 0.04]	0.04 [0.00; 0.07]	0.02 [0.00; 0.08]	0.03 [0.00; 0.06]
ART initiation to VL < 200	2014–2016	0.15 [0.09; 0.28]	0.14 [0.08; 0.26]	0.15 [0.09; 0.30]	0.15 [0.08; 0.30]	0.17 [0.09; 0.31]	0.15 [0.09; 0.30]	0.22 [0.10; 0.35]	0.21 [0.13; 0.28]
	2017–2019	0.14 [0.09; 0.27]	0.14 [0.09; 0.25]	0.15 [0.10; 0.33]	0.13 [0.10; 0.30]	0.13 [0.08; 0.25]	0.16 [0.09; 0.35]	0.13 [0.08; 0.31]	0.21 [0.11; 0.85]
	2020–2022	0.13 [0.08; 0.24]	0.11 [0.08; 0.23]	0.12 [0.08; 0.21]	0.13 [0.08; 0.27]	0.11 [0.08; 0.22]	0.14 [0.08; 0.26]	0.13 [0.09; 0.25]	0.13 [0.07; 0.26]
Infection to diagnosis, with correction for immigration	2014–2016	0.88 [0.25; 3.08]		0.51 [0.19; 1.86]	0.56 [0.23; 1.89]		0.71 [0.29; 2.25]	0.97 [0.28; 3.07]	1.25 [0.35; 3.15]
	2017–2019	1.02 [0.30; 3.37]		0.70 [0.27; 2.00]	0.60 [0.25; 1.79]		0.79 [0.29; 2.35]	1.15 [0.38; 3.37]	1.36 [0.31; 4.13]
	2020–2022	1.02 [0.31; 3.08]		0.63 [0.23; 1.88]	0.62 [0.27; 1.80]		0.75 [0.33; 2.25]	1.00 [0.31; 3.02]	1.25 [0.24; 3.73]

of care was the reduced time to ART initiation in the more recent periods. We, therefore, explored which policy changes occurred within the corresponding timeframe that could plausibly explain this trend. This aligns with the expansion of ART reimbursement criteria in December 2016, which extended reimbursement to all people living with HIV without restrictive eligibility conditions. In the Fine-Grey model for the time between linkage to care and ART initiation (with LTFU and death as two competing risks) we included CD4 at the time of linkage to care as a covariate, which means our subdistribution hazard ratios are adjusted for CD4 which was the main eligibility condition for ART reimbursement until December 2016. This means that our main effect for calendar period was significant despite adjustment for CD4 count from which it can be inferred that other factors must have contributed to the observed decrease in time to ART initiation. A formal statistical analysis of the impact of this and all other HIV-related policy changes implemented in Belgium during the study period was beyond the scope of our work. However, our interpretation offers a plausible contextual explanation consistent with the observed data and relevant policy developments.

The authors of the letter suggest performing an analysis excluding long-term virally suppressed patients from the denominator. However, this is not relevant to our analysis. In the estimation of cumulative incidence of ART initiation following linkage to care, individuals who are already long-term virally suppressed are, by definition, excluded from the risk set, since they have already initiated ART and achieved viral suppression.

Finally, all statistical and interpretative concerns raised in the letter were addressed, demonstrating that none of them undermine the reliability or validity of our study's findings. The results were interpreted and contextualised within the specific Belgian healthcare and policy environment. We did not claim generalisability beyond this context. However, the methodological approach illustrated in our work—combining cross-sectional and longitudinal perspectives to provide a more nuanced understanding of care dynamics—is broadly applicable [2]. Its implementation, nonetheless, should be tailored to the data structures and health information systems available in each country.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author upon approval of a project proposal to the HIV surveillance Steering Committee and clearance by the Belgian Information Security Committee.

ETHICS STATEMENT

The data were collected and analysed as part of the infectious disease surveillance and control by Sciensano, the Belgian Institute of Health, which is legally entitled to conduct the surveillance of infectious diseases as part of its public health surveillance mandate. The HIV surveillance has been approved by an independent administrative authority protecting privacy and personal data (https://www.ehealth.fgov.be/ehealthplatform/file/cc73d96153bbd5448a56f19d925d05b1379c7f21/1cb59e77715c6cbc5910c153fe009af6be0bdd78/14-017-f102-surveillance-epidemiologique-du-vih-et-du-sida-en-belgique-modifiee-le-5-mars-2024.pdf). A strict attention to confidentiality is present at every stage of data collection, analysis and storage.

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