



## Did the COVID-19 pandemic shift the landscape of late HIV diagnosis?



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### ABSTRACT

**Background:** The COVID-19 pandemic profoundly disrupted healthcare services. This study assessed the impact of the pandemic on the incidence, characteristics, and outcomes of late HIV diagnosis (LD) in Italy. **Methods:** All people with HIV (PWH) enrolled in Italian Cohort Naïve Antiretrovirals during 2016–2019 (prepandemic) and 2021–2024 (postpandemic), and diagnosed with HIV within 3 months before enrolment, were included. LD was defined as CD4 < 350 cells/mm<sup>3</sup> or an AIDS-defining event (ADE) within 3 months of HIV diagnosis; AIDS presentation (AIDS-P) was considered an ADE at diagnosis. Annual incidence, socio-demographic determinants, and survival outcomes were compared between periods using Poisson regression, Cox proportional hazards models, and Fine-Gray competing risk models.

**Results:** Among 5724 newly diagnosed PWH, 56% were enrolled in prepandemic and 44% postpandemic. Overall, 58% presented late and 13% as AIDS-P, with proportions stable across periods. Risk factors for LD—female sex, older age, foreign nationality, heterosexual transmission, lower education, and unemployment—remained consistent, with no significant interaction by time ( $P = 0.39$ ). During follow-up, 151 deaths occurred. LD and especially AIDS-P were associated with substantially increased all-cause mortality compared with non-LD, particularly within the first-year postdiagnosis. Adjusted hazard ratios were 2.96 for LD and 6.51 for AIDS-P prepandemic, and 8.64 and 17.99 postpandemic. No excess risk was observed for non-AIDS-related mortality.

**Conclusion:** The prevalence and determinants of LD and AIDS-P in Italy remained stable before and after the COVID-19 pandemic. However, late presentation continues to carry a heavy mortality burden, underscoring the urgent need to strengthen early testing and prompt linkage to care.

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## Introduction

The emergence of the COVID-19 pandemic in early 2020 led governments worldwide to implement unprecedented public health measures aimed at limiting viral transmission and reducing pressure on healthcare systems [1]. Italy, one of the most severely affected countries during the initial stages of the pandemic, was among the first to adopt nationwide restrictions [2]. These interventions significantly disrupted both routine and emergency medical services. A systematic review across multiple countries reported a 37% overall reduction in healthcare system use, with non-COVID-related hospital admissions and outpatient visits reduced by 28% and 42%, respectively, particularly among patients with less severe conditions [3].

This profound reshaping of healthcare services has significantly affected the regular management, assistance, and early diagnosis of many chronic non-COVID-19 pathologies, including HIV infection [4]. Surveillance data from Europe and Italy reported a significant decline in new HIV diagnoses in 2020, followed by an upward trend in subsequent years, likely reflecting a rebound effect due to the gradual restoration of routine testing service [5,6]. Concerningly, recent data showed an increasing number of people with HIV infection (PWH) who presented to care at an advanced stage of infection. In 2023, late HIV diagnoses, defined as CD4 below 350/mm<sup>3</sup> or an AIDS-defining event (ADE) regardless of CD4 count, at presentation to care, accounted for approximately 54% of new HIV cases in Europe and 60% in Italy [5,6].

Beyond the increased rates of late presentation, previous studies have reported a decline in retention in care among PWH following the COVID-19 crisis [7]. Mathematical models further predict a substantial increase in HIV-related morbidity and mortality related to the transitory interruption of HIV prevention and treatment services due to COVID-19 [8]. Despite these concerns, few studies have directly assessed the impact of pandemic-related restrictions on advanced HIV presentation and associated survival outcomes [9,10].

This study aims to evaluate the impact of COVID-19 pandemic on the incidence, clinical profile, and outcomes of late HIV diagnosis and AIDS presentation (AIDS-P) by comparing prepandemic (2016–2019) and postpandemic (2021–2024) periods.

## Materials and methods

### Study design and patients

This is a retrospective analysis of prospectively collected data from the ICONA (Italian Cohort Naïve Antiretrovirals) Foundation cohort, an Italian nationwide observational cohort, set up in 1997, including adult subjects with HIV-1 infection who were ART-naïve at the time of enrolment. Details of the cohort have been described elsewhere [11]. We included all PWH enrolled in ICONA, between January 1, 2016, and December 31, 2024, who received an HIV diagnosis within the 3 months preceding enrolment in the cohort. Individuals diagnosed in 2020 were excluded, given the marked decline in HIV diagnoses during that year, which may have introduced selection bias. Eligible individuals were classified as (1) subjects with CD4 count <350 cells/mm<sup>3</sup> at HIV diagnosis or ADE regardless of CD4 within 3 months from diagnosis (late diagnosis, LD); (2) subjects presenting to care with ADE regardless of CD4 count (AIDS-presenters, AIDS-P); (3) subjects with CD4 count ≥350 cells/mm<sup>3</sup> without a history of ADE (non-LD).

For survival analysis, subjects were stratified in participants without ADE by CD4 cell count (CD ≥ 350 vs <350 cells/mm<sup>3</sup> [LD-CD4 < 350]) or by ADE presence. The CD4 count considered for the classification was the closest to enrolment in the cohort. Par-

ticipants without at least one follow-up after enrolment were excluded.

### Outcomes and statistical analysis

The main baseline characteristics of the overall population and of participants with LD were described and compared between the two time periods using the chi-square test (Fisher's exact test when appropriate) for categorical variables and the Mann-Whitney or Kruskal–Wallis test, as appropriate, for continuous variables.

Three main outcomes were evaluated: (1) temporal trends in LD and AIDS-P across the two time periods; (2) clinical and socio-demographic characteristics associated with LD in the pre- vs postpandemic periods; (3) survival outcomes of LD-CD4 < 350 and AIDS-P according to the time period of diagnosis.

The first outcome was assessed by calculating the annual incidence risk, defined as the proportion of LD divided by the number of ART initiators, in the pre- and postpandemic periods. For each year, binomial 95% confidence intervals (CI) for proportions were calculated using the Clopper–Pearson exact formula. This approach was selected to guarantee nominal coverage [12].

Secondly, factors associated with LD were explored using univariate Poisson regression models. Separate models were fitted for each covariate of interest, acknowledging that confounding is not a reciprocal property. Effect modification was assessed by including interaction terms between time period (pre- vs postpandemic) and covariates to determine whether associations differed across time periods. For the third outcome, the association of LD-CD4 < 350 and AIDS-P with all-cause mortality was assessed through Kaplan–Meier curves, and unadjusted and adjusted Cox proportional hazards models. Survival analysis was performed separately for participants' diagnoses in the pre- and postpandemic periods, and effect modification by time period was formally tested using the Wald test for interaction. A Fine–Gray competing risk model was performed to evaluate non-AIDS-related mortality, with deaths for other causes treated as competing events. Multivariable models were adjusted for the following baseline covariates—identified a priori as potential confounders on the basis of presumed causal relationships: age, sex at birth, HIV transmission risk group, employment status, alcohol consumption, smoking status, and comorbidities.

All statistical analyses were performed using Stata (18.5, StataCorp LLC, College Station, TX).

## Results

Overall, 5724 newly diagnosed PWH were enrolled during the study period, with 3204 (56%) diagnosed in the prepandemic and 2540 (44%) in the postpandemic period. The main features of the enrolled participants according to the study period are summarized in Table 1.

The population was predominantly male (82.3%), with a median age of 40 years (IQR 31–50), and sexual transmission was the most common route of HIV acquisition (87%). The median nadir CD4 count nadir was 294 cells/mm<sup>3</sup> (IQR 106–492). Several differences were observed between the two time periods. The proportion of HIV acquisition among men who have sex with men (MSM) slightly decreased in post-COVID-19 (49% vs 45%;  $P < 0.001$ ), while the proportion of subjects born abroad increased (26% vs 30%;  $P < 0.001$ ). PWH diagnosed after the pandemic were more likely to be employed (50.1% vs 54.9%;  $P < 0.001$ ) but less likely to have attained higher education (college/university: 14% vs 11%;  $P < 0.001$ ). In the LD subgroup, the median CD4 cell count nadir was stable between the two periods (142 vs 137 cells/mm<sup>3</sup>;  $P = 0.354$ ). Conversely, the distribution of first-line ART regimens

**Table 1**

Participants baseline characteristics according to time period of HIV diagnosis.

|                                                         | Pre-COVID (n = 3204; 56%) | Post-COVID (n = 2520; 44%) | Total (n = 5724) | P-value |
|---------------------------------------------------------|---------------------------|----------------------------|------------------|---------|
| <b>Overall population</b>                               |                           |                            |                  |         |
| Female gender, n (%)                                    | 579 (18%)                 | 434 (17%)                  | 1013 (17.7%)     | 0.40    |
| Age, years, median (IQR)                                | 40 (31–49)                | 41 (32–51)                 | 40 (31–50)       | <0.001  |
| <b>Mode of HIV transmission, n (%)</b>                  |                           |                            |                  | <0.001  |
| – MSM                                                   | 1578 (49%)                | 1135 (45%)                 | 2713 (47%)       |         |
| – Heterosexual                                          | 1274 (40%)                | 1029 (41%)                 | 2303 (40%)       |         |
| – PWID                                                  | 132 (4%)                  | 107 (4%)                   | 239 (4%)         |         |
| Italian nationality, n (%)                              | 2380 (74%)                | 1763 (70%)                 | 4242 (72%)       | <0.001  |
| CD4 cell count nadir, cell/mm <sup>3</sup> (IQR)        | 297 (107–497)             | 291 (104–491)              | 294 (106–492)    | 0.17    |
| Late HIV diagnosis, n (%)                               | 1840 (57%)                | 1568 (58%)                 | 3308 (58%)       | 0.50    |
| AIDS presentation, n (%)                                | 391 (12%)                 | 327 (13%)                  | 718 (13%)        | 0.38    |
| <b>First-line ART</b>                                   |                           |                            |                  |         |
| – Dual regimen                                          | 103 (3%)                  | 242 (10%)                  | 345 (6%)         | <0.001  |
| – INSTI-based                                           | 2196 (69%)                | 1997 (79%)                 | 4193 (73%)       |         |
| – PI/booster-based                                      | 434 (14%)                 | 122 (5%)                   | 556 (10%)        |         |
| – NNRTI-based                                           | 289 (9%)                  | 123 (5%)                   | 412 (7%)         |         |
| <b>Comorbidities</b>                                    |                           |                            |                  |         |
| – Cardiovascular                                        | 33 (1%)                   | 18 (1%)                    | 51 (1%)          | 0.21    |
| – Diabetes                                              | 77 (2%)                   | 40 (2%)                    | 117 (2%)         | 0.03    |
| – HBV and/or HCV co-infection                           | 136 (4%)                  | 85 (3%)                    | 221 (4%)         | <0.001  |
| <b>Education level, n (%)</b>                           |                           |                            |                  |         |
| – Primary/secondary school                              | 1384 (43%)                | 807 (32%)                  | 2191 (38%)       | <0.001  |
| – College/university                                    | 434 (14%)                 | 280 (11%)                  | 714 (13%)        |         |
| <b>Employment status, n (%)</b>                         |                           |                            |                  | <0.001  |
| – Unemployed                                            | 394 (12%)                 | 263 (10%)                  | 657 (12%)        |         |
| – Employed/self-employed                                | 1604 (50%)                | 1383 (59%)                 | 2987 (52%)       |         |
| – Student/occasional                                    | 182 (6%)                  | 100 (4%)                   | 282 (5%)         |         |
| – Retired/housewife                                     | 134 (4%)                  | 128 (5%)                   | 262 (5%)         |         |
| <b>LD population</b>                                    |                           |                            |                  |         |
| CD4 cell count nadir, cell/mm <sup>3</sup> (IQR)        | 142 (46, 249)             | 137 (41, 244)              | 140 (44, 247)    | 0.35    |
| CD4 cell count at diagnosis, cell/mm <sup>3</sup> (IQR) | 144 (47, 253)             | 138 (42, 245)              | 141 (45, 249)    | 0.30    |
| log10 HIV-RNA at ART                                    | 5.22 (5, 6)               | 5.45 (5, 6)                | 5.31 (5, 6)      | <0.001  |
| <b>Total drugs</b>                                      |                           |                            |                  |         |
| 0                                                       | 4 (0.2%)                  | 5 (0.3%)                   | 9 (0.3%)         | <0.001  |
| 1                                                       | 2 (0.1%)                  | 1 (0.1%)                   | 3 (0.1%)         |         |
| 2                                                       | 36 (2%)                   | 67 (4.6%)                  | 103 (3.1%)       |         |
| 3                                                       | 1733 (94.2%)              | 1387 (94.5%)               | 3120 (94.3%)     |         |
| 4                                                       | 65 (3.5%)                 | 8 (0.5%)                   | 73 (2.2%)        |         |
| <b>First-line ART</b>                                   |                           |                            |                  |         |
| – Dual regimen                                          | 36 (2%)                   | 67 (4.6%)                  | 103 (3.1%)       | <0.001  |
| – INSTI-based                                           | 1334 (72.5%)              | 1229 (83.7%)               | 2563 (77.5%)     |         |
| – NNRTI-based                                           | 82 (4.5%)                 | 59 (4%)                    | 141 (4.3%)       |         |
| – Other                                                 | 80 (4.3%)                 | 16 (1.1%)                  | 96 (2.9%)        |         |
| – PI/booster-based                                      | 308 (16.7%)               | 97 (6.6%)                  | 405 (12.2%)      |         |

shifted markedly, with increased use of INSTI-based triple therapy (72.5% vs 83.7%;  $P < 0.001$ ) and dual therapy (2% vs 4.6%;  $P < 0.001$ ), alongside a substantial decline in PI-based regimens (16.7% vs 6.6%;  $P < 0.001$ ).

The overall proportions of LD and AIDS-P remained stable across the two study periods with similar fluctuating trend over time. Particularly, in the prepandemic period, LD and AIDS-P were observed in 57.4% (95% CI: 55.7%–59.1%) and 12.2% (95% CI: 11.1%–13.4%) of cases, respectively. Comparable proportions were seen postpandemic, with LD in 58.2% (95% CI: 56.3%–60.1%) and AIDS-P in 12.9% (95% CI: 11.7%–12.6%) of cases (Supplementary Figure 1).

The determinants of LD showed consistent patterns across the pre- and post-COVID-19 periods (Table 2). Increased risk was associated with female sex, older age, being born abroad, heterosexual transmission, lower educational attainment, and unemployment. A graded association between age and LD risk was observed, with older people experiencing significantly greater risk in both time periods. Heterosexual individuals had a higher risk of LD than MSM, though this difference slightly narrowed post-COVID. The protective effect of higher education was more evident prepandemic, while employment status and nationality showed similar associations across both periods, albeit somewhat attenuated post-

pandemic. No significant interactions with time were observed, indicating that the effect of these factors did not substantially change after the onset of the pandemic (all interaction  $P$ -values  $> 0.39$ ) (Table 2).

A total of 151 deaths occurred during the study period. Among participants enrolled prepandemic, 118 deaths were recorded over a median follow-up of 66 months (IQR 40, 84), of whom 56 were due to ADEs, 44 to serious non-AIDS events (SNAEs), including six related to COVID-19, and 17 to unknown causes. In contrast, among participants enrolled in the postpandemic cohort, 33 deaths occurred over a median follow-up of 17 months (IQR: 7, 28): 31 from ADEs, one from a SNAE, and one of unknown cause. In the non-LD population, only two were attributable to AIDS-related mortality, and they both happened in the prepandemic period.

The risk of all-cause mortality was significantly higher among LD, particularly AIDS-P, compared with non-LD. This was consistent in both periods and most evident within the first-year postdiagnosis. The 18-month probability of all-cause mortality (95% CI) in the pre-COVID-19 period was 0.46% (95% CI: 0.21, 1.0) for non-LD, 1.4% (95% CI: 0.93, 2.2) for LD-CD4  $< 350$ , and 8.1% (95% CI: 5.8, 11.4) for AIDS-P (log-rank  $P < 0.001$ ). Corresponding probabilities in the postpandemic period were 0.3% (95% CI: 0.07, 1.2), 1.5% (95% CI: 0.9, 2.6), and 5.1% (95% CI: 3.1, 8.4) (log-rank  $P < 0.001$ ) (Figure 1,

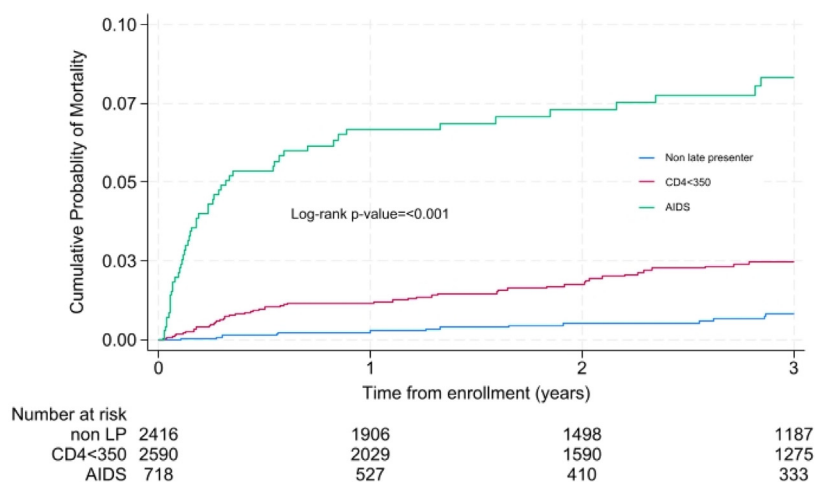
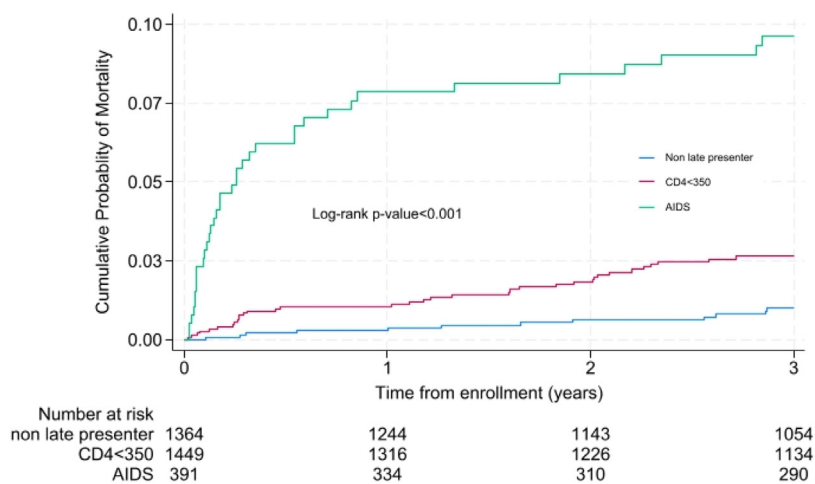
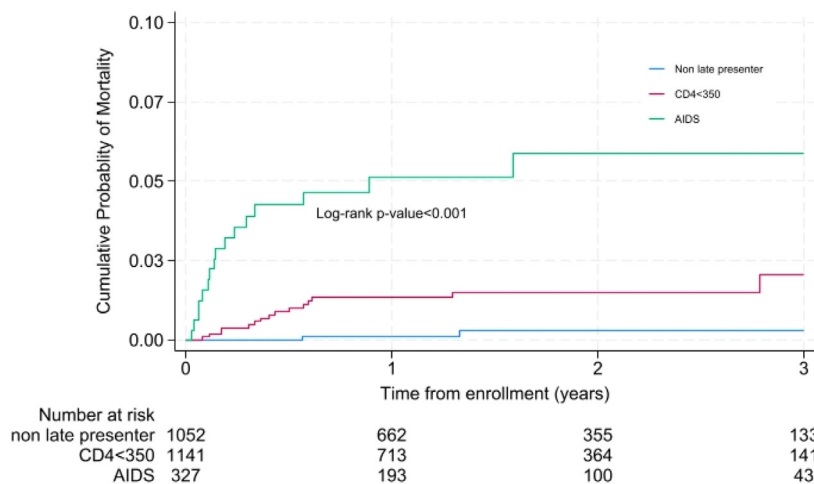
**A. All-cause mortality overall, with stratification****B. All-cause mortality, pre-pandemic with stratification****C. All-cause mortality, post-pandemic with stratification**

**Figure 1.** Estimated probability of all-cause mortality by time period (a. overall; b. prepandemic; c. post pandemic) and stratified by CD4 cell count (non-LD vs LD-CD4 < 350) and AIDS-defining event.

**Table 2**  
Prevalence risk ratio of LD by socio-demographic characteristics.

|                           | Risk ratio of LD (95% CI) |                  | Interaction<br><i>P</i> -value <sup>a</sup> |
|---------------------------|---------------------------|------------------|---------------------------------------------|
|                           | Pre-COVID                 | Post-COVID       |                                             |
| <b>Sex at birth</b>       |                           |                  | 0.759                                       |
| Male                      | 1                         | 1                |                                             |
| Female                    | 1.13 (1.01-1.27)          | 1.10 (0.97-1.26) |                                             |
| <b>Age</b>                |                           |                  | 0.957                                       |
| <30 years old             | 1                         | 1                |                                             |
| 30-39 years old           | 1.35 (1.16-0.57)          | 1.25 (1.04-1.50) |                                             |
| 40-49 years old           | 1.59 (1.37-1.84)          | 1.51 (1.27-1.81) |                                             |
| 50-59 years old           | 1.74 (1.49-2.03)          | 1.76 (1.47-2.11) |                                             |
| 60-69 years old           | 1.85 (1.51-2.28)          | 1.78 (1.42-2.23) |                                             |
| ≥70 years old             | 2.32 (1.70-3.18)          | 2.10 (1.52-2.90) |                                             |
| <b>Nationality</b>        |                           |                  | 0.391                                       |
| Non-Italian               | 1                         | 1                |                                             |
| Italian                   | 0.86 (0.78-0.96)          | 0.92 (0.83-1.03) |                                             |
| <b>Transmission route</b> |                           |                  | 0.610                                       |
| MSM                       | 1                         | 1                |                                             |
| Heterosexual              | 1.43 (1.30-1.58)          | 1.38 (1.24-1.55) |                                             |
| PWID                      | 1.12 (0.87-1.43)          | 1.26 (0.97-1.62) |                                             |
| <b>Education</b>          |                           |                  | 0.601                                       |
| Primary school            | 1                         | 1                |                                             |
| Secondary school          | 0.76 (0.61-0.95)          | 0.86 (0.59-1.25) |                                             |
| College university        | 0.59 (0.45-0.75)          | 0.75 (0.50-1.12) |                                             |
| <b>Employment</b>         |                           |                  | 0.982                                       |
| Unemployed                | 1                         | 1                |                                             |
| Employed/self-employed    | 0.95 (0.82-1.09)          | 0.90 (0.76-1.06) |                                             |
| Student/occasional        | 0.71 (0.55-0.91)          | 0.70 (0.50-0.97) |                                             |
| Retired/housewife         | 1.30 (1.04-1.64)          | 1.19 (0.93-1.53) |                                             |

<sup>a</sup> Interaction test socio-demographic characteristics and time-period.

Supplementary Figure 2). After adjusting for potential confounders, the higher risk of all-cause mortality among LD-CD4 < 350 and particularly AIDS-P compared to non-LD remained significant in both study periods. In the prepandemic period, adjusted hazard ratios (aHRs) were 2.96 (95% CI: 1.75, 5.03;  $P < 0.001$ ) for LD-CD4 < 350, and 6.51 (95% CI: 3.55-11.95;  $P < 0.001$ ) for AIDS-P, both compared to non-LD. In the postpandemic period, the corresponding aHRs were even higher: 8.64 (95% CI: 2.03-36.78;  $P < 0.001$ ) for LD-CD4 < 350, and 17.99 (95% CI: 3.85-84.17;  $P < 0.001$ ) for AIDS-P. The interaction by time period was not statistically significant ( $P > 0.10$ ) (Figure 2).

Conversely, LD was not associated to an increased risk of non-AIDS-related mortality compared to non-LD in both periods (subdistribution hazard ratio [SHR] 1.23 [95% CI: 0.66-2.30;  $P$  0.51]) and following the COVID-19 pandemic onset (SHR 1.17, 95% CI: 0.18-7.20,  $P$  0.869) (Figure 3).

## Discussion

In this large observational study including newly enrolled PWH in the ICONA cohort before (2016-2019) and after (2021-2024) the onset of the COVID-19 pandemic, the prevalence of late HIV diagnosis and AIDS-P in Italy remained stable over time, affecting approximately 57%-58% and 12-13% of new cases, respectively. The socio-demographic profile of those at risk also remained essentially unchanged, with no evidence of shifts in the strength or direction of key associations across the two periods.

These findings are in line with national surveillance data, which reported similar proportion of LD (58% of new HIV diagnoses in 2019 and 60% in 2023) and AIDS-P (23.8% in 2019 and 25.5% in 2023) in pre- and postpandemic periods [5]. When considering new HIV diagnoses in the context of national HIV testing data in Italy, national data from 2018 to 2023 indicate largely stable temporal trends, with almost a million tests performed, not including hospitalized patients and blood/organ donors. However, as expected, a marked decrease was observed in 2020. Overall,

the reported temporal trends in HIV testing rates and HIV diagnoses were similar during this period [13]. Additionally, in line with our results, Italian surveillance data do not indicate a marked shift in the socio-demographic characteristics of individuals with LD between the pre- and postpandemic periods. Although gradual changes have been observed—such as a higher proportion of AIDS-Ps among older individuals, people born abroad (33.1%), and MSM (31%), and a decline among women—these appear to be indicative of ongoing epidemiological trends rather than a clear transition due to the COVID-19 pandemic. This data is consistent with findings from other settings, including a study from Poland showing no pandemic-related changes in the prevalence or characteristics of late HIV diagnosis [14].

Previous reports on the impact of COVID-19 pandemic on HIV epidemiology have yielded conflicting findings. Indeed, while evidence consistently indicates a marked reduction in HIV-testing during the early phase of pandemic, as a result of lockdown and restriction measures, across different settings [15], data on the impact of pandemic on HIV diagnosis and, particularly, on late HIV diagnosis, appear more heterogeneous. Several reports from different healthcare settings documented a decrease in HIV diagnosis during the early phase of the pandemic [4,9,16-18], while others found no substantial change, especially among high-risk subpopulations [19] or even an increase of HIV diagnosis [20]. Notably, a Dutch study reported that undiagnosed individuals with HIV indicator conditions, especially those with subtler clinical manifestations, were less likely to access care during lockdown [4]. Consistently, a large retrospective cohort study including data from 44 countries reported an increased proportion of positive tests in the very early phase of the pandemic, likely reflecting a more selective testing strategy focused on symptomatic individuals or those perceived to be at higher risk [20]. Taken together, these findings, alongside reduced routine testing, may partially explain the delays in HIV diagnosis observed during and after the pandemic [2], as well as the increase in late HIV diagnoses over the same period reported in several studies [4,10,16,21], although this data has not been consistently confirmed.

In our cohort, we did not observe an apparent increase in late diagnoses during the postpandemic period; notably, median CD4 counts among individuals with LD were similar across both timeframes. However, this finding should be interpreted with caution, as the data originate from ICONA centers, which include most of the referral national HIV centers and may not fully reflect national-level trends. In addition, most of the available studies focused on the early phase of the pandemic (2020-2021), when the most stringent restriction measures were in place, whereas our analysis spans a longer period (2021-2024), potentially diluting short-term effects on LD. Of note, the absolute number of new HIV diagnoses declined during the pandemic and early postpandemic period in the ICONA cohort, mirroring the surveillance in Italy.

Although the long-term impact of the pandemic-related healthcare disruption on survival remains uncertain, modelling studies from sub-Saharan Africa predicted that interruptions of HIV testing and ART distribution due to COVID-19 could significantly increase mortality within 1 year [22]. Real-world data further suggest a significant increase in AIDS deaths due to late HIV diagnosis (6.9% in 2020 vs 13.9% in 2021), despite an overall decrease in HIV/AIDS diagnoses and HIV-related death, highlighting the negative impact of COVID-19 control measures on HIV programs [16].

Notably, our study is among the few that have focused on the long-term outcomes of the COVID-19 outbreak and the subsequent disruption of healthcare programs, particularly in late HIV diagnosis, as it relates to survival [16,23]. In line with previous evidence [24], late presentation to care and, in particular, AIDS-P, were strongly associated with an increased all-cause mortality risk

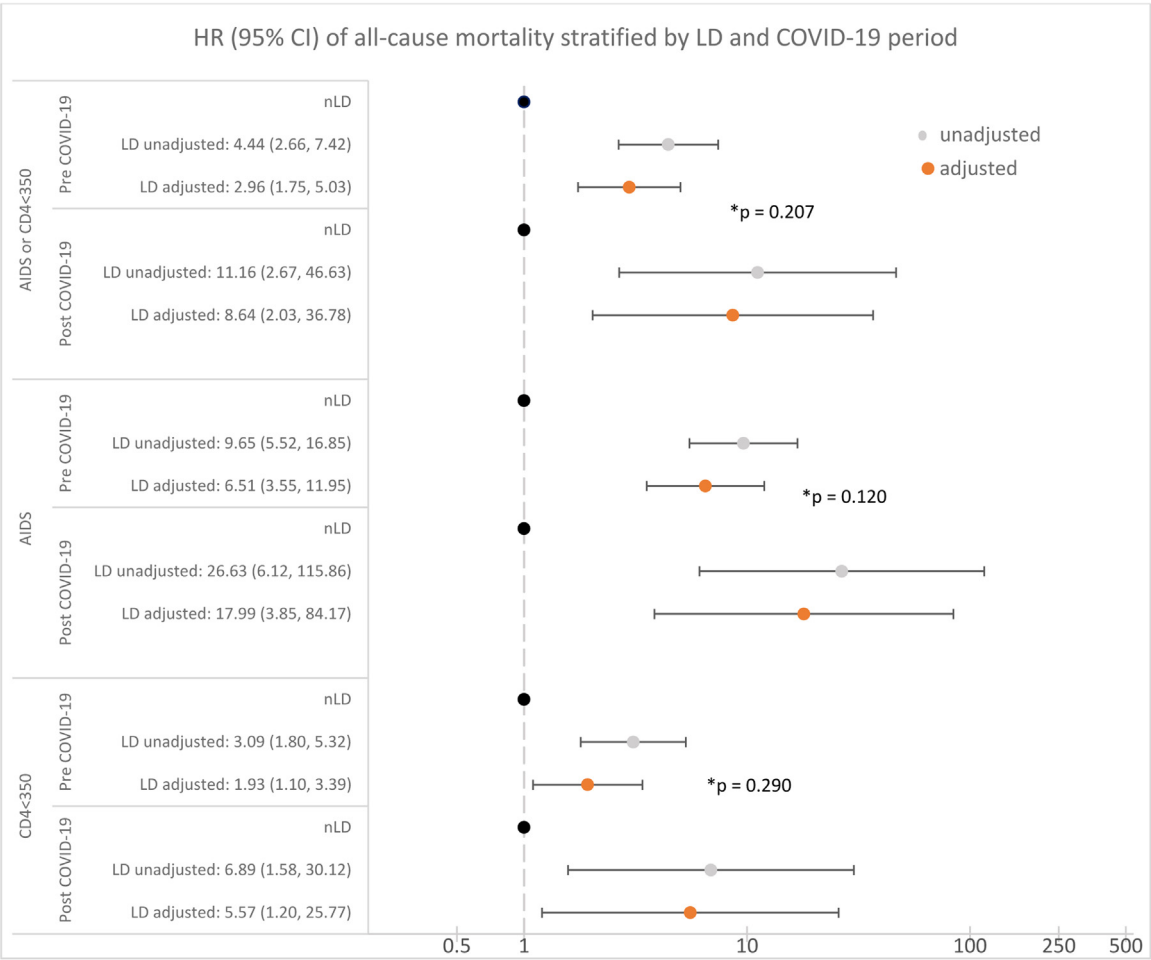


Figure 2. Hazard ratio of all-cause mortality stratified by late diagnosis and time period.

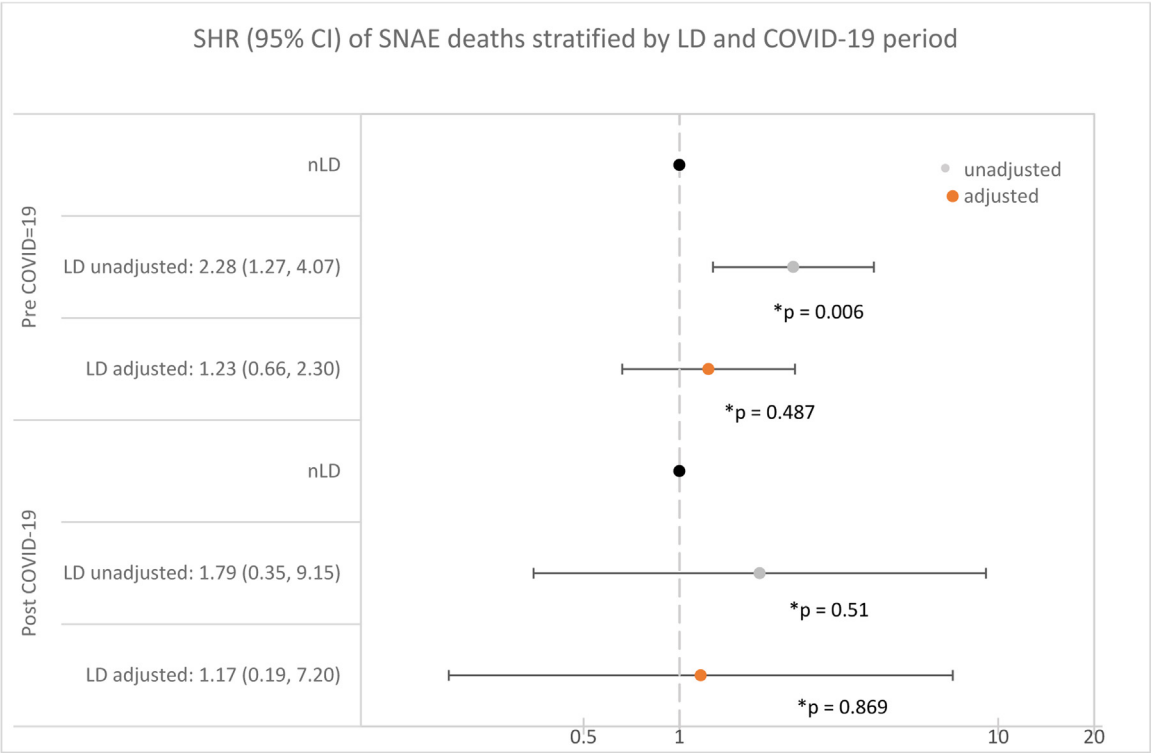


Figure 3. Sub-distribution hazard ratio of non-AIDS-related mortality by late diagnosis and time period.

in both observation periods in our study, with some evidence suggesting this risk may have been more pronounced in the postpandemic period. In fact, although the interaction by time period was not statistically significant, the relatively higher hazard ratios observed postpandemic suggest a possible trend toward worse outcomes in the more recent years.

Although previous evidence documented excess mortality among PWH during the initial phase of the COVID-19 pandemic, largely driven by COVID-19-related deaths [25], we did not observe significant differences in non-AIDS-related mortality between the two periods. This finding suggests that, in our study, the mortality burden among late presenters was primarily driven by AIDS-related causes rather than by comorbid conditions. These observations, although consistent with previous reports [16], should be interpreted with caution. Longer-term follow-up will be essential to confirm these trends and to determine the full impact of pandemic-related disruptions on HIV care outcomes.

This study has several limitations. First, its observational design makes it susceptible to residual confounding from unmeasured variables, such as behavioral or social factors not fully captured in the dataset. Secondly, the relatively limited follow-up period in the postpandemic phase may have constrained our ability to fully assess long-term survival trends or the delayed effects of late HIV diagnosis. Additionally, the study may be underpowered to detect interaction effects, particularly regarding time as a potential effect modifier for mortality. Future studies with larger sample sizes and extended follow-up are needed to explore these associations more robustly. Furthermore, our analysis of the pandemic's impact on survival in LD and AIDS-p was restricted to all-cause and non-AIDS-related mortality, due to the relatively small sample and the lack of AIDS-related death in non-LD population in the postpandemic period, limiting further conclusions on mortality associations. Finally, incomplete or misclassified data on causes of death—particularly in distinguishing HIV-related from COVID-19-related mortality—may limit the interpretation of specific mortality trends.

## Conclusions

In conclusion, our findings indicate that the frequency and socio-demographic pattern of late HIV diagnoses remained stable before and after the COVID-19 pandemic. Late presentation and especially AIDS-P were consistently associated with increased mortality, with some indication that this risk may have been more pronounced in the postpandemic period. Although no significant differences emerged in non-AIDS-related events, the potential long-term impact of pandemic-related disruptions warrants continued monitoring. These results highlight the urgent need to enhance early HIV testing [26] and linkage to care.

## Ethical approval

The ICONA Foundation study was approved by the local ethics committees of participating clinical sites. All patients signed a consent form for study participation and processing of data in accordance with the ethical standards of the Committee on Human Experimentation and the Helsinki Declaration (last amended in October 2013).

## Author contributions

Conception: GMi, AM, and AA. Study design: AM, AR, ACL, and AA. Accessing, verifying of data, and statistical analysis: AR and ACL. Draft of the manuscript: GMi and AM. Review of the article and critical revision for important intellectual content: all the au-

thors. Reading and final approval of the submitted version: all the authors. Supervision: ACL and AA.

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## Data availability

The data sets generated during the current study are not publicly available because they contain sensitive data to be treated under data protection laws and regulations. Appropriate agreement of data sharing can be arranged after a reasonable request to the corresponding author.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships, which may be considered as potential competing interests: GMi, AR, IL, ADM: None. AM: Received speaker honoraria from Gilead Sciences and ViiV Healthcare; travel fees; and participated in advisory boards sponsored by ViiV Healthcare, independent of the submitted work. LT: Attended advisory boards, served as consultant, or received grants for conference participation from Gilead Sciences and ViiV Healthcare; research grants for her institution from Gilead Sciences, independent of the submitted work. VM: Received institutional research grant from Gilead Sciences; speaking honoraria for congress from ViiV Healthcare; consultation fees from Viatrix and Gilead Science, independent of the submitted work. GMA: Participated in the advisory boards of Gilead Sciences, ViiV Healthcare, Angelini, and Janssen-Cilag and received travel grants from ViiV Healthcare, MSD, and Janssen-Cilag, independent of the submitted work. LS: Received travel grants from Gilead, Merck, Pfizer, fees for lectures and expertise from Merck, Gilead, AbbVie, Angelini, AstraZeneca, GSK, independent of the submitted work. AG: Received grants or contracts from ViiV, Bristol-Myers Squibb, and Gilead; consulting fees from ViiV Healthcare, Gilead, Janssen-Cilag, Merck Sharp and Dohme, Bristol-Myers Squibb, Pfizer, and Novartis; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from ViiV Healthcare, Gilead, Janssen-Cilag, Merck Sharp and Dohme, Bristol-Myers Squibb, Pfizer, and Novartis; support for attending meetings and/or travel from ViiV Healthcare, Gilead, Janssen-Cilag, Merck Sharp and Dohme, Bristol-Myers Squibb, Pfizer, and Novartis; Scientific consulting and research funding Janssen, ViiV, MSD, Bristol-Myers Squibb, AbbVie, Gilead, Novartis, Pfizer, Astellas, AstraZeneca, Angelini, Moderna, Novavax, Shionogi, independent of the submitted work. GL: Received speaking grants or consultancy fees from ViiV Healthcare, Pfizer Srl, In-smed, and Gilead Srl over the past 5 years, independent of the submitted work. CM: Received research grants from Gilead; speaker honoraria from Gilead, ViiV Healthcare, MSD, and Johnson & Johnson; travel grants from Gilead, independent of the submitted work. EG: Received speaker's fee from ViiV and Gilead; research grant from Gilead, independent of the submitted work. ACL: Received research grants/contracts from Icona Foundation Study (money paid to UCL) and the European Union ("EuCARE" project, Grant Agreement No 101046016, money paid to UCL; "VIROMARKERS Consortium Agreement," Grant Agreement No 101194735, money paid to UCL), independent of the submitted work. AA: Served as a paid

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2026.108437.

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