

## Dettaglio abstract

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**Title:** Risk of COVID-19 in-hospital mortality in people living with HIV compared to general population according to age and CD4 strata: data from the Icona network

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### Session/Topic

Emerging issues in HIV-1 infection

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### Abstract

**Background:** Some evidence suggests that people living with HIV (PLWH) are at higher risk of COVID-19 mortality when compared to the general population (GenPop). Our aim was to assess whether PLWH with COVID-19 had an increased risk of in-hospital mortality compared to the GenPop in the Italian setting, according to CD4 cell count (<vs ≥200 cell/mm<sup>3</sup>) and age strata (<vs ≥65 years).

**Methods:** A retrospective observational study was conducted in 19 Italian ICONA centers (February 2020-November 2022). Hospitalized PLWH and GenPop with a confirmed SARS-CoV-2 infection, matched by calendar period of enrolment were included. The main outcome of interest was in-hospital mortality. A competing risk unadjusted and adjusted by Fine-Gray Cox regression model with discharge as the competing event have been used to estimate the association between a 5 levels' exposure (GenPop <65 years vs GenPop ≥65 vs PLWH <65 and CD4 ≥200 vs PLWH <65 and CD4 <200 vs PLWH ≥65 years) and in-hospital mortality. Besides the calendar period, the model was further adjusted for age, sex, ethnicity, lung disease, and region of the enrolling site. A subanalysis including only patients with lung disease or PO<sub>2</sub>/FiO<sub>2</sub><300 at admission was also performed.

**Results:** 7,401 COVID-19 patients have been included in the study, 240 (3.2%) PLWH, and 7,161 (96.8%) GenPop. Characteristics of the study population are reported in Table 1. PLWH were younger [55 (IQR 46-62) vs 68 (55-80) years, p<0.001] and more frequently male (77.7% vs 60.1%, p<0.001) when compared to the GenPop. PLWH showed a median CD4 cell count of 397 (IQR 154-626) cell/mm<sup>3</sup> with 30.2% <200 cells/mm<sup>3</sup> and 23.8% had an HIV-RNA >50cp/mL. The crude in-hospital mortality was higher in the GenPop group when compared to PLWH [1,283/7,161 (17.9%) vs 34/240 (14.2%)]. The unadjusted estimates of in-hospital mortality according to age and CD4 strata are reported in Figure 1. In the final Fine-Gray regression model (Table 2A), after adjusting for potential confounders, when compared to the GenPop <65 years a significantly higher risk of in-hospital death was observed for the GenPop ≥65 years [adjusted Subdistribution Hazard Ratio (aSHR) 1.92 (95% CI 1.48-2.49)], PLWH <65 years with CD4 <200 [aSHR 5.90 (95% CI 3.49-9.98)] and PLWH ≥65 years [aSHR 1.99 (95%CI 1.05-3.77)], whereas

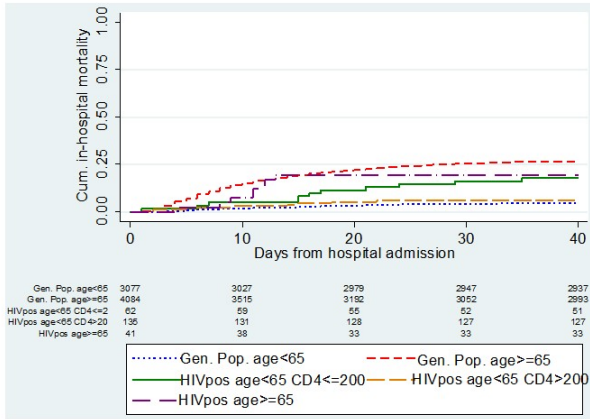
PLWH <65 with CD4  $\geq$ 200 did not [aSHR 1.13 (95%CI 0.53-2.39)]. Data were confirmed in the sub-analysis including only patients with documented pneumonia or PO<sub>2</sub>/FiO<sub>2</sub><300 at admission (Table 2B). **Conclusions:** PLWH with low CD4 count have an increased risk of COVID-19 in-hospital mortality. We found that in PLWH aged <65 with a CD4 cell count <200 cell/mm<sup>3</sup>, COVID-19 in-hospital mortality was 6-fold higher than GenPop, after controlling for the key confounding factors. The effect of low CD4 cell count seems to be mitigated in those aged  $\geq$ 65 where the COVID-19 course is mainly age-drive. This study was funded by a Gilead Srl unrestricted grant (Fellowship Program)

**Table 1. Characteristics of the study population.**

	Total	GenPop	PLWH	p
<b>Age, median (IQR)</b>	7401 (100%)	7161 (96.8%)	240 (3.2%)	
Age, median (IQR)	68 (54-80)	68 (55-80)	55 (46-62)	<0.001
≥65 years, n (%)	4127 (55.8)	4084 (57.0)	43 (17.8)	<0.001
<b>Male sex at birth, n (%)</b>	4492 (60.7)	4307 (60.1)	185 (77.7)	<0.001
<b>Ethnicity, n (%)</b>				<0.001
Caucasian	6362 (85.9)	6191 (86.5)	171 (71.2)	
Latinix	357 (4.8)	322 (4.5)	35 (14.6)	
Asian	294 (4.0)	290 (4.0)	4 (1.7)	
Black	82 (1.1)	55 (0.8)	27 (11.2)	
Maghreb/Arab	277 (3.7)	274 (3.8)	3 (1.2)	
Missing	27 (0.4)	27 (0.4)	0 (0.0)	
<b>Comorbidities, n (%)</b>				
Cerebro/cardiovascular disease	1103 (14.9)	1086 (15.2)	17 (7.0)	0.001
CKD	528 (7.1)	510 (7.1)	18 (7.5)	0.823
Asthma	144 (1.9)	132 (1.8)	12 (5.0)	0.001
Immune disorders/Autoimmune disorders	170 (2.3)	161 (2.2)	9 (3.8)	0.127
Cancer	637 (8.6)	605 (8.4)	32 (13.3)	0.008
Diabetes	999 (13.5)	970 (13.5)	29 (12.0)	0.514
Liver Diseases (non ESLD)	165 (2.2)	147 (2.0)	18 (7.5)	<0.001
ESLD	48 (0.6)	41 (0.6)	7 (2.9)	<0.001
Hypertension	1774 (27.1)	1731 (27.4)	43 (18.6)	0.004
COPD	393 (5.3)	386 (5.4)	7 (2.9)	0.093
Lung Diseases (Asthma+COPD+Other Lung disease)	877 (11.8)	844 (11.8)	33 (13.7)	0.354
Neurological Diseases	109 (2.8)	94 (2.5)	15 (7.0)	<0.001
<b>Obesity, n (%)</b>				<0.001
No	3708 (50.1)	3528 (49.3)	180 (74.7)	
Yes	1296 (17.5)	1263 (17.6)	33 (13.7)	
unknown	2397 (32.4)	2370 (33.1)	27 (11.2)	
<b>VOC period of admission, n (%)</b>				0.123
WT/Alpha/Gamma (<15Jun21)	4966 (67.1)	4803 (67.1)	161 (67.1)	
Delta (15Jun21-19Dec21)	913 (12.3)	892 (12.5)	21 (8.7)	
Omicron (≥20Dec21)	1523 (20.6)	1464 (20.4)	58 (24.2)	
<b>P/F at admission, median (IQR)</b>	310 (239-379)	309 (238-376)	348 (267-448)	<0.001
missing	726	691	35	
<b>CRP (mg/L), median (IQR)</b>	50.7 (19.9-97.8)	51.2 (20.2-97.8)	34.2 (8.0-86.7)	<0.001
missing	636	633	3	
<b>COVID-19 primary cycle vaccine complete, n (%)</b>	1207 (17.4)	1165 (17.3)	42 (21.2)	0.140
missing	459	416	43	
<b>Region, n (%)</b>				<0.001
Lombardy	6145 (83.0)	6055 (84.6)	90 (37.3)	
Lazio	995 (13.4)	907 (12.7)	88 (36.5)	
Emilia_Romagna	121 (1.6)	105 (1.5)	16 (6.6)	
Sardinia	100 (1.3)	93 (1.3)	7 (2.9)	
Liguria	20 (0.3)	0 (0.0)	20 (8.3)	
Campania	10 (0.1)	0 (0.0)	10 (4.1)	
Marche	5 (0.1)	0 (0.0)	5 (2.1)	
Apulia	3 (0.0)	0 (0.0)	3 (1.2)	
Sicily	2 (0.0)	0 (0.0)	2 (0.8)	

List of abbreviations: GenPop, general population; PLWH, people living with HIV; n, number; IQR, Inter Quartile Range; VOC, variants of concern; WT, wild type; P/F, PaO2/FiO2; CRP, C reactive protein; CKD, chronic kidney disease; ESLD, end stage liver disease.

**Figure 1. Kaplan-Meier curves of in-hospital death according to HIV status, CD4 and age using levels' exposure**



**Table 2. Fine-Gray Cox regression model with discharge as the competing event to estimate the association between a 5 levels' exposure (A) all participants, (B) subgroup of patients with PO2/FiO2 <300 or pneumonia at admission**

	aSHR	95%CI
<b>(A) all participants</b>		
GenPop <65 years	1	-
GenPop ≥65 years	1.92	1.48-2.49
PLWH <65 years and CD4 ≥200 cells/mmc	1.13	0.53-2.40
PLWH <65 years and CD4 <200 cells/mmc	5.90	3.48-9.98
PLWH ≥65 years	1.99	1.05-3.77
<b>(B) PO2/FiO2&lt;300 or pneumonia at admission</b>		
GenPop <65 years	1	-
GenPop ≥65 years	1.85	1.42-2.41
PLWH <65 years and CD4 ≥200 cells/mmc	1.35	0.56-3.27
PLWH <65 years and CD4 <200 cells/mmc	7.46	4.10-13.57
PLWH ≥65 years	2.65	1.34-5.23