UNDEGRADUATE STUDENTS, **HEALTH AND BIOMEICAL SCIENCES**

THE RISK OF SEVERE COVID-19 AND MORTALITY FROM COVID-19 IN PEOPLE LIVING WITH HIV COMPARED TO INDIVIDUALS WITHOUT HIV - A SYSTEMATIC REVIEW AND META-ANALYSIS OF 1 268 676 INDIVIDUALS

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INTRODUCTION

HIV epidemic meets COVID-19 pandemic

- As of 2020 at least 38 million people were living with HIV globally, more than two-thirds of PLHIV being in Sub-Saharan Africa¹.
- Since December 2020, the number of confirmed cases of COVID-19 has increased in Sub-Saharan Africa², where health systems are ill equipped to treat surges in the need for hospitalization, mechanical ventilation and intensive care services associated with severe COVID-19.
- Identifying groups of people who are susceptible to severe COVID-19 and death from COVID-19 is a priority, as these groups may need additional protections and prioritization for vaccination against COVID-19^{3,4}.
- There are indications that people living with HIV (PLHIV) may be one such vulnerable group due to persistent immune-suppression⁵.
- There is conflicting evidence about the risk of mortality and severe disease due to COVID-19 in people living with HIV (PLHIV).





AIM

To compare mortality, hospitalization, and the need for intensive care services due to COVID-19 between PLHIV & individuals without HIV based on data from the existing literature

MATERIALS AND METHODS

1st January 2020

A comprehensive search in PubMed, Cochrane Library, Scopus, China Academic Journals Full Text Database, the Database of Abstracts of Reviews of Effectiveness (DARE) and and the medRXIV and bioRxiv databases of preprints was carried out.

MORTALITY

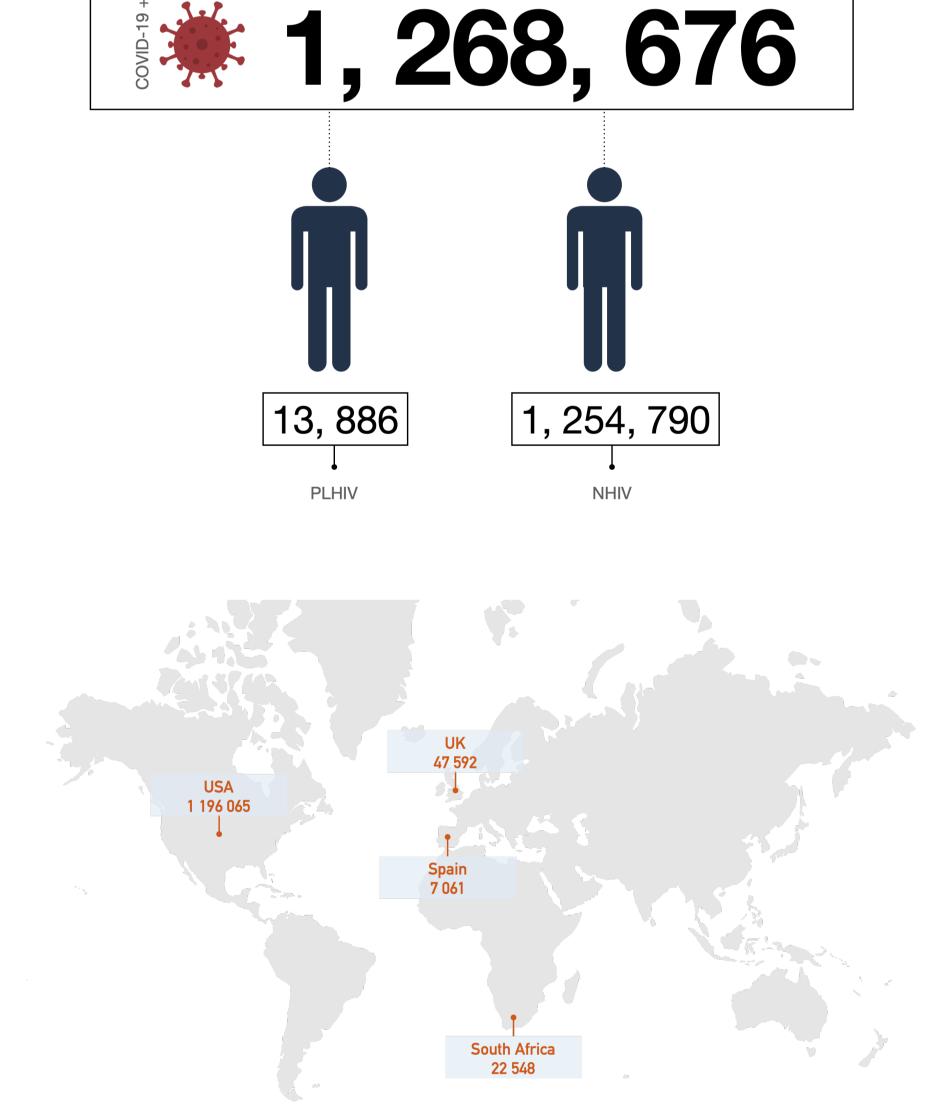
20th February 2020

- Eligible studies were case control, cross-sectional and cohort studies where participants had confirmed COVID-19.
- From each study, data on numbers of PLHIV and individuals without HIV for each outcome were extracted.



Study quality was assessed using the MethodologicAl STandard for Epidemiological Research (MASTER) scale. Data synthesis used a bias adjusted model and predefined age and geographical subgroups were analysed.

RESULTS



In pooled analyses, there were a total of 428 deaths out of 7 836 PLHIV, compared to 33 440 deaths out of 502 778 individuals without HIV (NHIV)

- The pooled unadjusted OR for overall mortality in PLHIV, compared to individuals without HIV, was 1.3 $(95\%CI\ 0.9-2.0, p = 0.198)$ with high heterogeneity ($I^2 = 78.6\%$, p<0.001)
- In people aged <60 years, the pooled odds of mortality in PLHIV were almost three-fold the odds for mortality in NHIV (OR 2.7, 95%CI 1.1-6.5, $I^2 = 95.7\%$, p < 0.001). In people aged ≥ 60 years, the odds for mortality in PLHIV were similar to the odds in the overall model (OR 1.3, 95%CI 0.8 - 2.0, $I^2 = 58.2\%$, p =0.092)

				Odds	s Ratio	%
Studyid	Country	PLHIV	No HIV	(95%	CI)	Weight
Tesoriero 2021	USA	2988	375260	• 1.85	(1.60, 2.13)	47.74
Miyashita 2020	USA	161	8751	1.01	(0.65, 1.58)	2.46
Boulle 2020	South Africa	3978	18330	1.04	(0.85, 1.28)	23.64
Cabello 2021	Spain	31	7030	0.23	(0.03, 1.66)	1.55
Geretti 2020	UK	111	43015	0.72	(0.48, 1.10)	7.65
Hadi 2020	USA	404	49763	1.58	(1.01, 2.49)	6.40
Sigel 2020	USA	88	405	1.06	(0.60, 1.86)	4.62
Stoeckle 2020	USA	30	90	0.39	(0.08, 1.82)	1.70
Karmen-Tuohy 2020	USA	21	42	1.28	(0.39, 4.18)	1.95
Parker 2020	South Africa	24	92	0.89	(0.32, 2.51)	2.30
Overall, QE $(l^2 = 78.6\%)$	p_{p} , $p = 0.000$			1.31	(0.87, 1.99)	100.00
Figure 1: Odds ratios for ov	verall mortality in PL	HIV compared to	o NHIV	.25 1 4		
NOTE: Weights are from Doi's	Quality Effects model					

Age categories	Country				Odds Ratio	%
and Authors	of Study	PLHIV	No HIV		(95% CI)	Weight
<60 years						
Boulle 2020	South Africa	3826	15827		1.91 (1.47, 2.48)	20.62
Tesoriero 2021	USA	1892	254966	>	4.47 (3.51, 5.68)	23.64
Miyashita 2020	USA	243	11201	+	1.09 (0.76, 1.57)	4.51
Subgroup, QE (I ²	= 95.7%, p = 0.0	000)		\Leftrightarrow	2.73 (1.14, 6.54)	48.77
≥60 years						
Boulle 2020	South Africa	152	2503	-	1.65 (1.09, 2.51)	8.90
Tesoriero 2021	USA	1096	119291	•	1.23 (1.03, 1.47)	40.88
Miyashita 2020	USA	41	3320	→	0.63 (0.29, 1.37)	1.45
Subgroup, QE (I ²	= 58.2%, p = 0.0	092)		\Diamond	1.27 (0.83, 1.95)	51.23
Heterogeneity bet	ween groups: p	= 0.124				
Overall, QE ($I^2 = 9$	4.2%, p = 0.000	0)		\Diamond	1.85 (0.98, 3.48)	100.00
Figure 2: Odds ratio fo	r mortality in PLHIV	compared to NH	IIV, by age	.25 1 4		
NOTE: Weights and bety	ween-subgroup heter	ogeneity test are f	from Doi's Quality Effect	s model		

HOSPITALIZATION

- 5 studies⁶⁻⁸ with a total sample size of 1 215 846 of which 13 451 were PLHIV and 1 202 395 had no HIV, reported data on hospitalization due to COVID-19. In pooled analyses, a total of 3 583 individuals out of 13 451 PLHIV were hospitalized for COVID-19, compared to 233 051 individuals out of 1 202 395 NHIV.
- The pooled OR for hospitalization in PLHIV, compared to NHIV was 1.7 (95% CI 1.3-2.1,) with high heterogeneity ($I^2 = 96.0\%$, p<0.001).

Studyid	Country	PLHIV	No HIV		(95% CI)	Weight
Tesoriero 2021	USA	2988	375260		2.19 (2.02, 2.37)	31.48
Boulle 2020	South Africa	3978	18330	•	1.19 (1.08, 1.32)	23.33
Cabello 2021	Spain	31	7030	→	0.69 (0.34, 1.39)	7.26
Hadi 2020	USA	404	49763	+	2.03 (1.58, 2.60)	10.55
Kohler 2020	USA &Spain	6050	752012	•	1.82 (1.72, 1.92)	27.39
Overall, QE ($I^2 = 96.0\%$,	p = 0.000			\Q	1.65 (1.27, 2.13)	100.00
Figure 3: Odds ratio for hospi		n PLHIV compare	d to NHIV	.25 1	1 4	

ICU SERVICES

- 8 studies⁹⁻¹⁰ with a total of 6 239 PLHIV and 693 066 NHIV, reported data comparing the need for intensive care services. In pooled analysis, 401 individuals out of 6 239 PLHIV needed intensive care services, compared to 29 006 individuals out of 693 066 NHIV.
- The pooled OR for the need of intensive care services for PLHIV, compared to NHIV, was 1.4 (95% CI 0.9-2.0) with substantial heterogeneity ($I^2 = 74\%$, p <0.001).

Studyid	Country	PLHIV	No HIV		(95% CI)	We
Miyashita 2020	USA	161	8751	+;	1.01 (0.69, 1.46)	5.7
Cabello 2021	Spain	31	7030	 ->	1.44 (0.34, 6.07)	7.4
Geretti 2020	UK	122	46497	→	2.79 (1.90, 4.08)	16
Kohler 2020	USA &Spain	5762	630159	•	1.63 (1.45, 1.84)	35
Sigel 2020	USA	88	405	 ;	0.86 (0.49, 1.52)	11
Stoeckle 2020	USA	30	90		0.63 (0.22, 1.85)	7.8
Karmen-Tuohy 2020	USA	21	42	 •>	2.00 (0.57, 6.96)	7.6
Parker 2020	South Africa	24	92		0.45 (0.15, 1.31)	8.3
Overall, QE (I2 = 74.0%	p = 0.000			\Diamond	1.35 (0.91, 2.01)	10

CONCLUSION

- In this meta-analysis of 11 studies with 1 268 676 individuals with confirmed COVID-19, we found a stronger difference in mortality by HIV status for those individuals below the age of 60 years, and over this age, HIV had an attenuated effect on mortality, suggesting that age-related mortality overshadows PLHIV related mortality.
- Further, PLHIV had increased odds of being hospitalized and needing intensive cares services, probably related to increased COVID-19 severity in PLHIV.
- A secondary analysis of the included studies suggested no difference in the prevalence of pre-existing conditions.

IMPLICATIONS



Our findings suggest that PLHIV are at higher risk than the general population and should be prioritized for vaccine coverage and monitoring if diagnosed with COVID-19. This is especially important for countries in Sub-Saharan Africa that have a high burden of HIV in the younger populations who are more vulnerable

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