

THE LANCET HIV

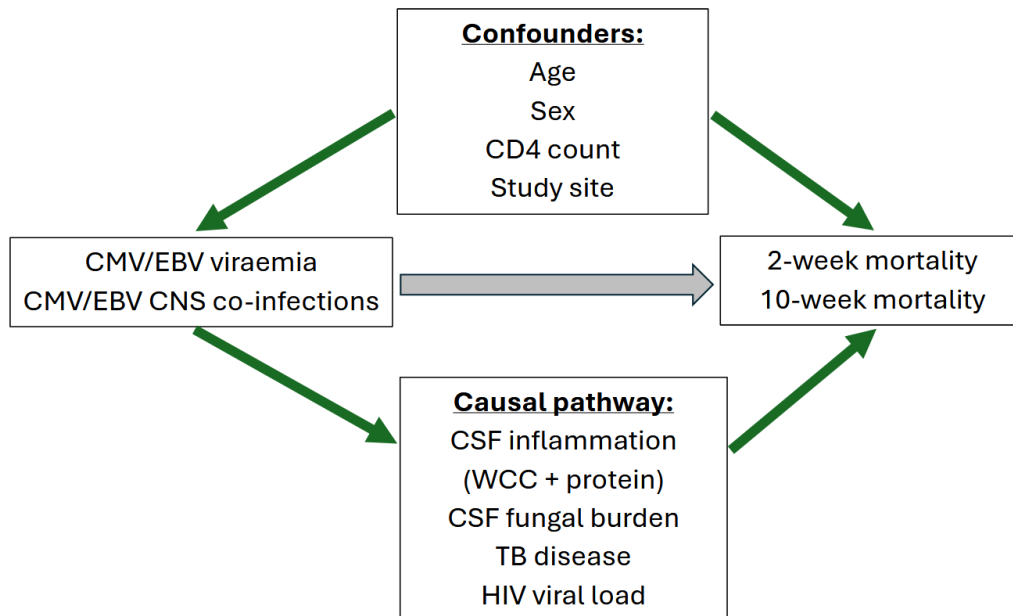
Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed.
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Supplement to: Ellis J, Gropelli E, Doyle R, et al. Epstein–Barr virus and cytomegalovirus co-infections and mortality risk in patients with HIV-associated cryptococcal meningitis: a post-hoc analysis of a prospective nested cohort in the AMBITION-cm randomised controlled trial. *Lancet HIV* 2025; published online Sept 4. [https://doi.org/10.1016/S2352-3018\(25\)00163-8](https://doi.org/10.1016/S2352-3018(25)00163-8).

Appendix

Supplementary figure 1: Directed Acyclic Graph (DAG)



Supplementary tables:

Supplementary table 1a: Multivariate analysis of the association between EBV viraemia and 2-week and 10-week mortality using logistic regression modelling, stratified by EBV plasma viral load:					
Cryptococcal Meningitis Cohort Group	2-week mortality N/N (%)	cOR for 2-week mortality (95% CI)	P-value	aOR for 2-week mortality¹ (95% CI)	P-value
Total cohort	104/811 (12.8)				
No EBV viraemia	30/219 (13.7)	1		1	
EBV viraemia <1,000 IU/ml	41/302 (13.6)	0.90 (0.60-1.64)	0.97	0.90 (0.52-1.53)	0.69
EBV viraemia ≥1,000 IU/ml	32/283 (11.3)	0.80 (0.47-1.37)	0.42	0.87 (0.49-1.57)	0.65
Cryptococcal Meningitis Cohort Group	10-week mortality N/N (%)	cOR for 10-week mortality (95% CI)	P-value	aOR for 10-week mortality¹ (95% CI)	P-value
Total cohort	218/811 (26.9)				
No EBV viraemia	55/219 (25.1)	1		1	
EBV viraemia <1,000 IU/ml	88/302 (29.1)	1.22 (0.83-1.82)	0.31	1.09 (0.71-1.65)	0.70
EBV viraemia ≥1,000 IU/ml	74/283 (26.1)	1.06 (0.70-1.58)	0.79	0.99 (0.63-1.54)	0.95
Supplementary table 1b: Multivariate analysis of the association between EBV CNS co-infection and 2-week and 10-week mortality using logistic regression modelling, stratified by EBV CSF viral load:					
Cryptococcal Meningitis Cohort Group	2-week mortality N/N (%)	cOR for 2-week mortality (95% CI)	P-value	aOR for 2-week mortality¹ (95% CI)	P-value
Total cohort	104/811 (12.8)				
No EBV CNS co-infection	72/517 (13.9)	1		1	
EBV CNS co-infection <1,000 IU/ml	13/129 (10.1)	0.69 (0.37-1.29)	0.25	0.79 (0.42-1.52)	0.49
EBV CNS co-infection ≥1,000 IU/ml	9/62 (14.5)	1.05 (0.50-2.22)	0.90	1.07 (0.47-2.40)	0.88
Cryptococcal Meningitis Cohort Group	10-week mortality N/N (%)	cOR for 10-week mortality (95% CI)	P-value	aOR for 10-week mortality¹ (95% CI)	P-value
Total cohort	218/811 (26.9)				
No EBV CNS co-infection	145/517 (28.0)	1		1	
EBV CNS co-infection <1,000 IU/ml	36/129 (28.0)	0.99 (0.65-1.53)	0.98	0.98 (0.62-1.55)	0.95
EBV CNS co-infection ≥1,000 IU/ml	16/62 (25.8)	0.89 (0.49-1.63)	0.71	0.98 (0.52-1.86)	0.96

CMV = Cytomegalovirus, EBV = Epstein–Barr virus, CNS = central nervous system, cOR = crude unadjusted odds ratio, aOR = adjusted odds ratio.
1= Adjusted for age (continuous variable), baseline CD4 count (continuous variable), sex and study site.

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