Supplementary Table 1 Sensitivity multivariable analysis using the Prentice method

Factor (at ART initiation)	Prentice method for case-cohort design Multivariable hazard ratio (95% CI)	p	Logistic regression including same factors (unmatched case-control) Multivariable odds ratio (95% CI)	p
Factors selected by Prentice method with p<0.1 in primary logistic regression				
In immunology substudy (vs no)	0.12 [0.07,0.22]	<0.0001	0.08 [0.04,0.16]	<0.0001
CD4 for-age (per 2-fold higher)	0.63 [0.56,0.71]	<0.0001	0.56 [0.48,0.65]	<0.0001
IL-6 (per 2-fold higher)	1.53 [1.24,1.88]	0.0002	1.52 [1.15,2.02]	0.003
BMI-for-age (per unit Z-score higher)	0.78 [0.65,0.93]	0.006	0.87 [0.71,1.07]	0.19
Additional factors identified using the Prentice method				
Country/Centre Zimbabwe/Harare (urban) Uganda/Entebbe (non-urban) Uganda/JCRC (urban) Uganda/PIDC (urban)	 1.00 2.80 [1.36,5.75] 1.04 [0.56,1.93] 1.59 [0.90,2.79]	0.03 0.005 0.89 0.11	 1.00 2.24 [.02,4.93] 0.98 [0.50,1.93] 1.24 [0.63,2.43]	0.21 0.045 0.96 0.53
Primary carer (mother vs other)	0.43 [0.27,0.67]	0.0002	0.72 [0.43,1.21]	0.21

Note: no other factor in Table 1 provided additional (p≤0.05) prognostic information to the Prentice model. Although cases independently had lower pre-ART CD4-for-age, the magnitude (but not direction) of this effect varied by primary carer (weaker with mother; interaction p=0.0008) and centre (interaction p=0.007). In the logistic regression, case risk decreased with increased CD4-for-age regardless of BMI-for-age but, at the very lowest CD4-for-age (median ratio ≤ ~0.05), risk increased rather than decreased with increased BMI-for-age (interaction p=0.001). Other model coefficients similar. There were no additional (p≤0.01) interactions.

Supplementary Table 2 Factor loadings from the principal component analysis

	Principal component 1	Principal component 2	Principal component 3	Principal component 4
% variation explained	26%	22%	14%	11%
CD4 for-age	-.25	+.57	-.27	*+.08*
CD8-for-age	*-.09*	+.57	*+.01*	+.15
IL-7 (pg/mL)	+.26	*-.08*	+.61	+.66
CRP (mg/L)	+.51	*+.07*	-.41	+.26
IL-6 (pg/mL)	+.54	*+.09*	-.27	+.10
sCD14 (mg/L)	+.40	-.13	-.19	-.27
TNFa (pg/mL)	+.22	+.52	+.26	*-.06*
VL (log10 c/ml)	+.33	+.19	+.46	-.62

Note: loadings <0.1 shown in italics and not described below

- Principal component 1 essentially represents a contrast between all the inflammatory biomarkers, IL-7 and VL (high levels imply poor status) vs CD4-for-age (high levels imply good status).
- Principal component 2 essentially represents a contrast between VL, TNF-α, CD4- and CD8- for age (response of the total CD4/CD8 compartment to virus and virus-associated cytokines) vs sCD14
- Principal component 3 essentially represents a contrast between CRP, IL-6, sCD14 (total inflammation) and CD4-for-age (CD4 response to inflammation) vs IL-7 (CD4 homeostasis), TNF-α (virus associated cytokines) and VL
- Principal component 4 essentially represents a contrast between CRP, IL-6, IL-7 and CD8-for-age vs sCD14 and viral load

Supplementary Table 3 Current WHO 3/4 illness at baseline

	Group-1 N=135 n (%)	Group-2 N=48 n (%)	Group-3 N=264 n (%)	Group-4 N=131 n (%)
Current WHO 3/4 illness at baseline	42 (31.1%)	21 (43.8%)	111 (42.0%)	19 (14.5%)
Moderate unexplained malnutrition not adequately responding to standard therapy	16 (11.9%)	7 (14.6%)	48 (18.2%)	9 (6.9%)
Unexplained persistent diarrhoea	2 (1.5%)	1 (2.1%)	6 (2.3%)	0
Unexplained persistent fever	1 (0.7%)	0	0	1 (0.8%)
Persistent oral candidiasis	9 (6.7%)	7 (14.6%)	6 (2.3%)	1 (0.8%)
Oral hairy leukoplakia	1 (0.7%)	0	1 (0.4%)	0
Pulmonary tuberculosis	8 (5.9%)	2 (4.2%)	20 (7.6%)	3 (2.3%)
Severe recurrent presumed bacterial pneumonia	1 (0.7%)	0	1 (0.4%)	1 (0.8%)
Unexplained anaemia, neutropenia or thrombocytopenia for > 1 month	0	0	1 (0.4%)	0
Chronic HIV-associated lung disease including bronchiectasis	1 (0.7%)	0	8 (3.0%)	1 (0.8%)
Symptomatic Lymphoid interstitial pneumonia	0	0	5 (1.9%)	0
TB lymphadenitis	2 (1.5%)	0	2 (0.8%)	0
Unexplained severe wasting or severe malnutrition not adequately responding to therapy	4 (3.0%)	10 (20.8%)	15 (5.7%)	3 (2.3%)
Pneumocystis pneumonia	1 (0.7%)	0	3 (1.1%)	0
Extrapulmonary TB	1 (0.7%)	1 (2.1%)	3 (1.1%)	1 (0.8%)
Oesophageal candidiasis	3 (2.2%)	0	1 (0.4%)	0
HIV encephalopathy	3 (2.2%)	1 (2.1%)	16 (6.1%)	2 (1.5%)
Details not known	0	0	1 (0.4%)	0

Events are not mutually exclusive therefore total to more than the total number of patients with WHO 3/4 illness at baseline