Supplementary Table 1. Number of patients included in the analysis for each participating cohort.

			Age group				
Cohort	Region	Country	$1-5$	$5-10$	$10-16$	all	%
ATHENA Network	Europe	Netherlands	61	42	27	130	0.63
Centre de Prise en Charge Enfant	West Africa	Cote d'Ivoire	314	324	145	783	3.81
Collaborative HIV Paediatric Study	Europe	UK& Ireland	298	283	193	774	3.76
Centre Hospitalier Universitaire de Cocody	West Africa	Cote d'Ivoire	186	151	88	425	2.07
Hopital Charles De Gaulle, Ouagadougou	West Africa	Burkina Faso	91	85	50	226	1.10
Centre Hospitalier Universitaire de Yopougon	West Africa	Cote d'Ivoire	278	215	124	617	3.00
CoRISpes Catalonia	Europe	Spain	9	4	4	17	0.08
CoRISpes Madrid	Europe	Spain	15	10	7	32	0.16
French perinatal cohort (EPF/ANRS)	Europe	France	17	17	4	38	0.18
Harriet Shezi Children's Clinic	Southern Africa	South Africa	2,073	1,519	666	4,258	20.69
Hlabisa HIV Treatment and Care Programme	Southern Africa	South Africa	1,112	1,039	855	3,006	14.61
Korle Bu Teaching Hospital	West Africa	Ghana	396	291	98	785	3.82
Khayelitsha ART Programme	Southern Africa	South Africa	584	305	138	1,027	4.99
Lighthouse Trust Clinic	Southern Africa	Malawi	733	817	663	2,213	10.76
McCord Hospital	Southern Africa	South Africa	766	832	534	2,132	10.36
Centre MTCT-Plus	West Africa	Cote d'Ivoire	46	46	12	104	0.51
Newlands Clinic	Southern Africa	Zimbabwe	448	572	655	1,675	8.14
Rahima Moosa Mother and Child Hospital	Southern Africa	South Africa	1,032	669	218	1,919	9.33
Hopital Albert Royer, Dakar	West Africa	Senegal	206	137	72	415	2.02
Total			8,665	7,358	4,553	20,576	100.00

Supplementary Table 2. Number of deaths stratified by follow-up month and age group.

age/month	1	3	6	9	12	15	18	21	24	27	30	33	36	39	42	45	48	51	54	57	Total
1 to 5	90	87	50	34	28	22	10	13	14	6	6	4	4	8	4	2	4	2	4	1	393
5 to 10	57	54	26	29	20	18	14	9	5	6	7	3	1	5	5	6	3	4	2	2	276
10 to 16	47	67	32	17	15	7	11	13	8	8	13	5	5	5	4	6	4	6	1	7	281
Overall	194	208	108	80	63	47	35	35	27	20	26	12	10	18	13	14	11	12	7	10	950

Supplementary Table 3. Evolution of CD4 count, CD4%, WAZ, HAZ, BMIAZ over time; (a) overall and (b) for different regions[1]

(a) overall	first visit	12 months	24 months	36 months	48 months
CD4 count	14563 (70.8%)	5479 (34.8%)	4482 (39.4%)	3476 (37.4%)	2708 (37.8%)
Median (1^{st}; 3^{rd} quartile)	440 (205; 757)	634 (404; 990)	713 (470; 1070)	720 (474; 1045)	717 (480; 1025)
CD4%	12479 (60.7%)	4550 (28.9%)	3649 (32.1%)	2810 (30.2%)	2233 (31.2%)
Median (1^{st}; 3^{rd} quartile)	16 (9; 23)	23 (17; 29)	26 (20; 32)	27 (21; 33)	28 (22; 34)
WAZ	10806 (52.5%)	4562 (29.0%)	3703 (32.5%)	2828 (30.4%)	2093 (29.2%)
Median (1^{st}; 3^{rd} quartile)	-1.5 (-2.6; -0.6)	-1.0 (-1.8; -0.3)	-0.8 (-1.6; -0.2)	-0.8 (-1.5; -0.1)	-0.8 (-1.0; -0.1)
HAZ	11437 (55.6%)	5143 (32.6%)	4611 (40.5%)	3839 (41.3%)	3202 (44.7%)
Median (1^{st}; 3^{rd} quartile)	-2.1 (-3.1; -1.1)	-1.9 (-2.7; -1.0)	-1.7 (-2.5; -0.8)	-1.5 (-2.3; -0.7)	-1.4 (-2.2; -0.6)
BMIAZ	6504 (31.6%)	3002 (19.1%)	2597 (22.8%)	2106 (22.7%)	1700 (23.7%)
Median (1^{st}; 3^{rd} quartile)	-0.6 (-1.6; 0.2)	-0.3 (-1.0; 0.4)	-0.3 (-1.0; 0.4)	-0.3 (-1.0; 0.4)	-0.3 (-1.1; 0.4)

[1]Available follow-up data refers to measurements at the respective time point ±1.5 months. For example, available data at 12 months is defined to be a measurement that was taken between 10.5 and 13.5 months. The choice for the width of the intervals was determined by the width of the intervals used by the g-computation algorithm.

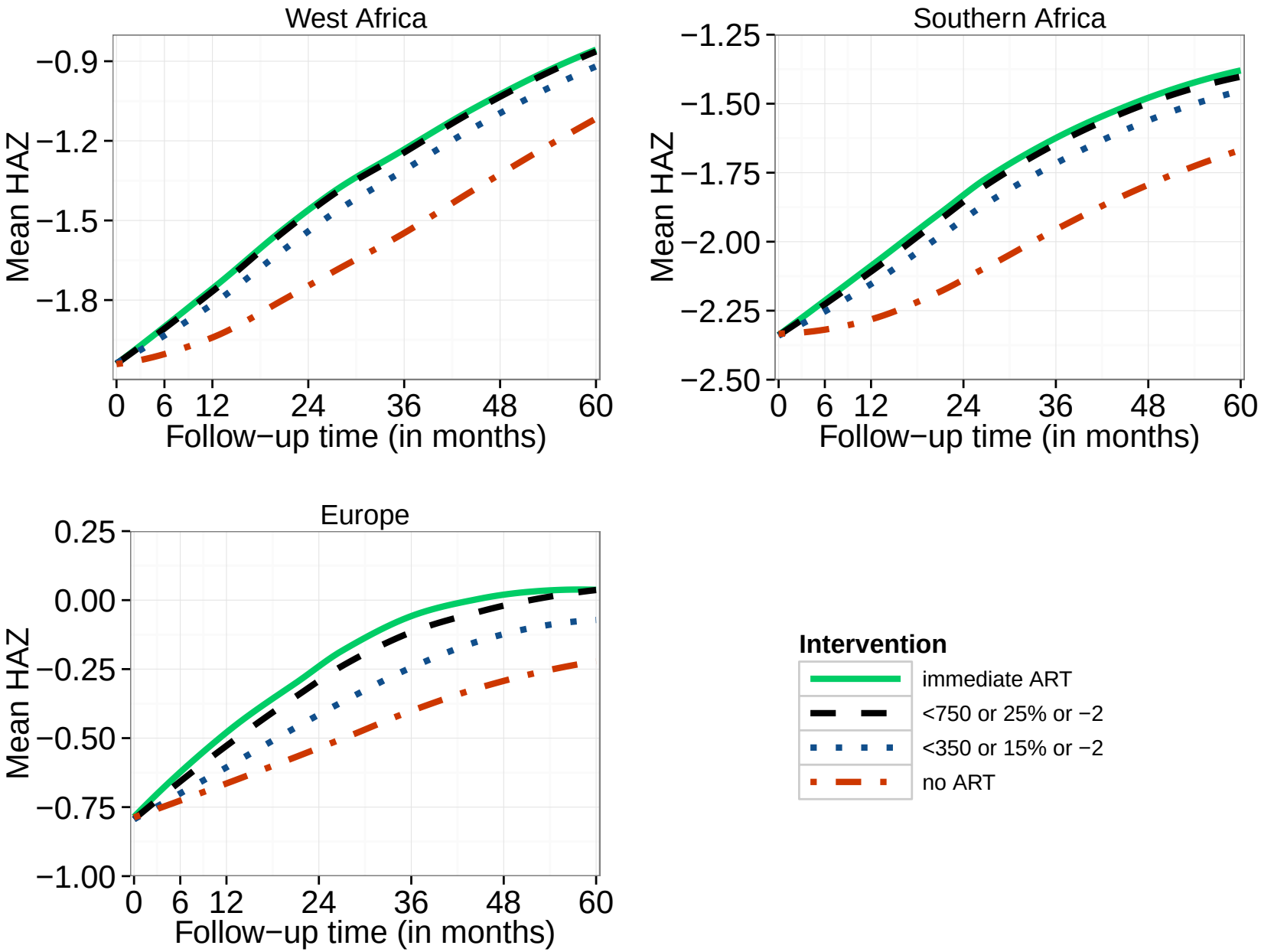
(b) by region

South Africa	first visit	12 months	24months	36 months	48 months
CD4 count	11077 (68.3%)	4031 (33.7%)	3237 (37.4%)	2462 (35.1%)	1783 (33.5%)
Median (1^{st}; 3^{rd} quartile)	421 (200; 725)	629 (393; 988)	723 (470; 1072)	731(494; 1055)	724 (485; 1047)
CD4%	9668 (59.6%)	3318 (27.7%)	2551 (29.5%)	1920 (27.3%)	1425 (26.8%)
Median (1^{st}; 3^{rd} quartile)	15 (9; 23)	23 (17; 29)	26 (20; 32)	28 (21; 33)	28 (22; 34)
WAZ	8189 (50.5%)	3366 (28.1%)	2730 (31.6%)	2099 (29.9%)	1532 (28.8%)
Median (1^{st}; 3^{rd} quartile)	-1.5 (-2.5; -0.6)	-1.0 (-1.8; -0.3)	-0.9 (-1.6; -0.2)	-0.9 (-1.5; -0.2)	-0.9 (-1.5; -0.2)
HAZ	8545 (52.7%)	3772 (31.5%)	3359 (38.8%)	2840 (40.4%)	2335 (43.9%)
Median (1^{st}; 3^{rd} quartile)	-2.2 (-3.2; -1.3)	-2.0 (-2.8; -1.2)	-1.8 (-2.6; -1.1)	-1.7 (-2.4; -1.0)	-1.6 (-2.4; -0.9)
BMIAZ	4905 (30.2%)	2206 (18.4%)	1893 (21.9%)	1573 (22.4%)	1255 (23.6%)
Median (1^{st}; 3^{rd} quartile)	-0.6 (-1.5; 0.2)	-0.2 (-0.9; 0.4)	-0.3 (-0.9; 0.3)	-0.3 (-1.0; 0.3)	-0.3 (-1.1; 0.4)

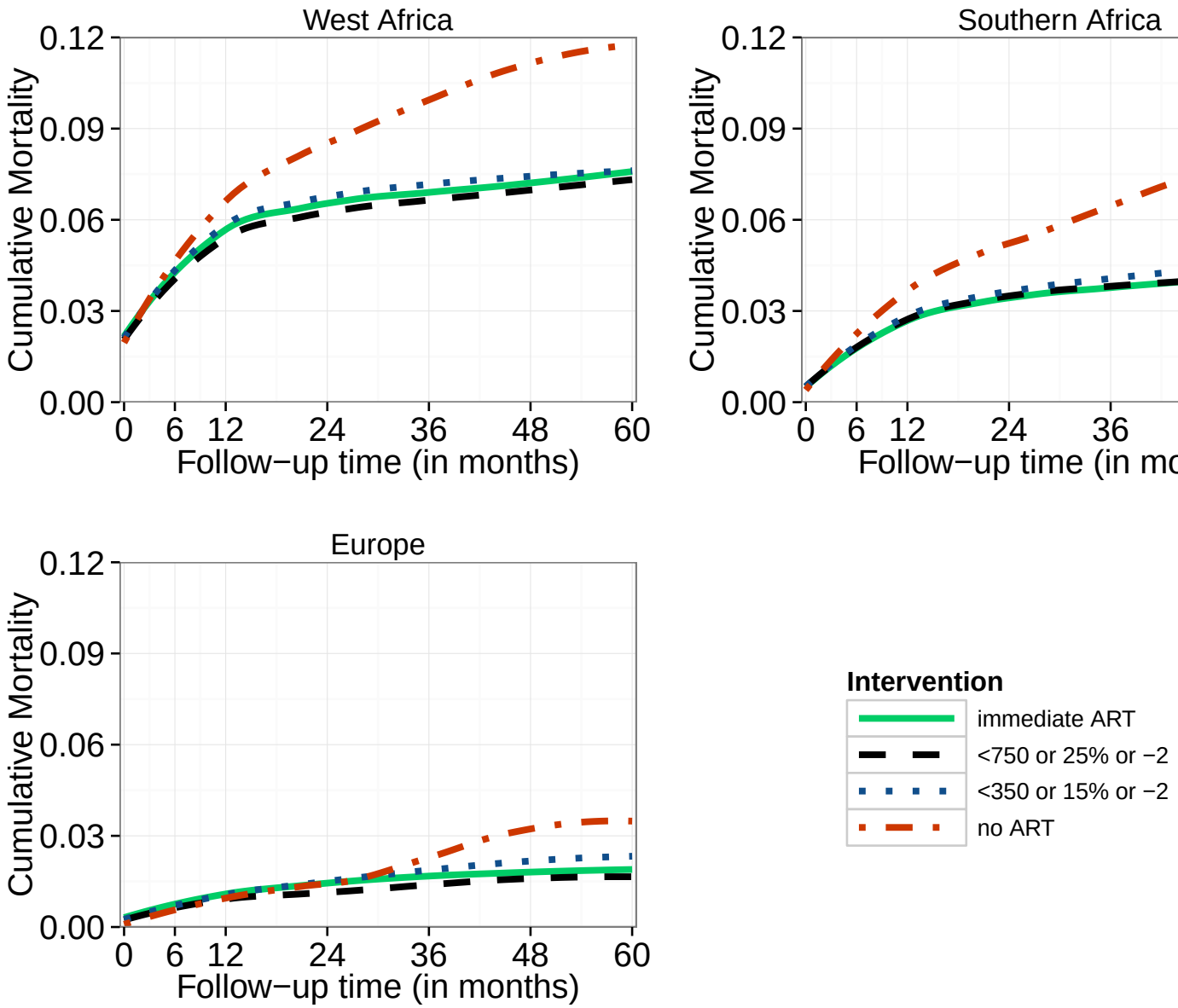
West Africa	first visit	12 months	24months	36 months	48 months
CD4 count	2651 (79.0%)	836 (29.4%)	650 (35.3%)	474 (32.8%)	403 (36.9%)
Median (1^{st}; 3^{rd} quartile)	489 (198; 841)	672 (434; 1033)	711 (488; 1116)	720 (460; 1031)	712 (464; 1002)
CD4%	2012 (60.0%)	656 (23.1%)	540 (29.3%)	389 (26.9%)	326 (29.9%)
Median (1^{st}; 3^{rd} quartile)	15 (8; 22)	22 (16; 28)	24 (19; 32)	26 (19; 31)	26 (20; 33)
WAZ	2002 (59.7%)	835 (29.4%)	628 (34.1%)	455 (31.5%)	320 (29.3%)
Median (1^{st}; 3^{rd} quartile)	-1.9 (-3.3; -1.0)	-1.4 (-2.2; -0.6)	-1.2 (-2.0; -0.5)	-1.1 (-2.0; -0.4)	-1.1 (-1.8; -0.5)
HAZ	2125 (63.3%)	885 (31.1%)	758 (41.1%)	565 (39.1%)	460 (42.1%)
Median (1^{st}; 3^{rd} quartile)	-2.0 (-2.9; -1.0)	-1.8 (-2.6; -0.9)	-1.5 (-2.4; -0.7)	-1.4 (-2.1; -0.6)	-1.3 (-2.0; -0.5)
BMIAZ	1125 (33.5%)	489 (17.2%)	415 (22.5%)	281 (19.5%)	227 (20.8%)
Median (1^{st}; 3^{rd} quartile)	-1.4 (-2.7; -0.4)	-0.9 (-1.6; -0.2)	-1.0 (-1.8; -0.2)	-1.0 (-1.9; -0.3)	-1.1 (-1.7; -0.3)

Europe	first visit	12 months	24months	36 months	48 months
CD4 count	835 (84.3%)	612 (64.9%)	595 (66.9%)	540 (65.2%)	522 (69.5%)
Median (1^{st}; 3^{rd} quartile)	555 (299; 879)	631 (423; 957)	664 (460; 990)	674 (440; 1004)	693 (480; 968)
CD4%	799 (80.6%)	576 (61.1%)	558 (62.8%)	501 (60.5%)	482 (64.2%)
Median (1^{st}; 3^{rd} quartile)	20 (13; 27)	23 (19; 29)	26 (21; 32)	27 (21; 32)	28 (22; 34)
WAZ	615 (62.1%)	361 (38.3%)	345 (38.8%)	274 (33.1%)	241 (32.1%)
Median (1^{st}; 3^{rd} quartile)	-0.1 (-0.9; 0.7)	0.1 (-0.7; 0.9)	0.1 (-0.5; 0.8)	0.2 (-0.4; 0.9)	0.2 (-0.5; 0.9)
HAZ	767 (77.4%)	486 (51.5%)	494 (55.6%)	434 (52.4%)	407 (54.2%)
Median (1^{st}; 3^{rd} quartile)	-0.7 (-1.4; 0.2)	-0.6 (-1.2; 0.2)	-0.4 (-1.0; 0.4)	-0.3 (-1.1; 0.4)	-0.2 (-0.9; 0.4)
BMIAZ	474 (47.8%)	307 (32.6%)	289 (32.5%)	252 (30.4%)	218 (29.0%)
Median (1^{st}; 3^{rd} quartile)	0.2 (-0.5; 0.9)	0.4 (-0.3; 1.1)	0.4 (-0.2; 1.1)	0.4 (-0.3; 1.2)	0.3 (-0.4; 1.1)

Supp. Figure 1. Growth trajectories for different regions. Results are reported for the children aged 1-5 and the main scenario (regular follow-up, as in a trial).

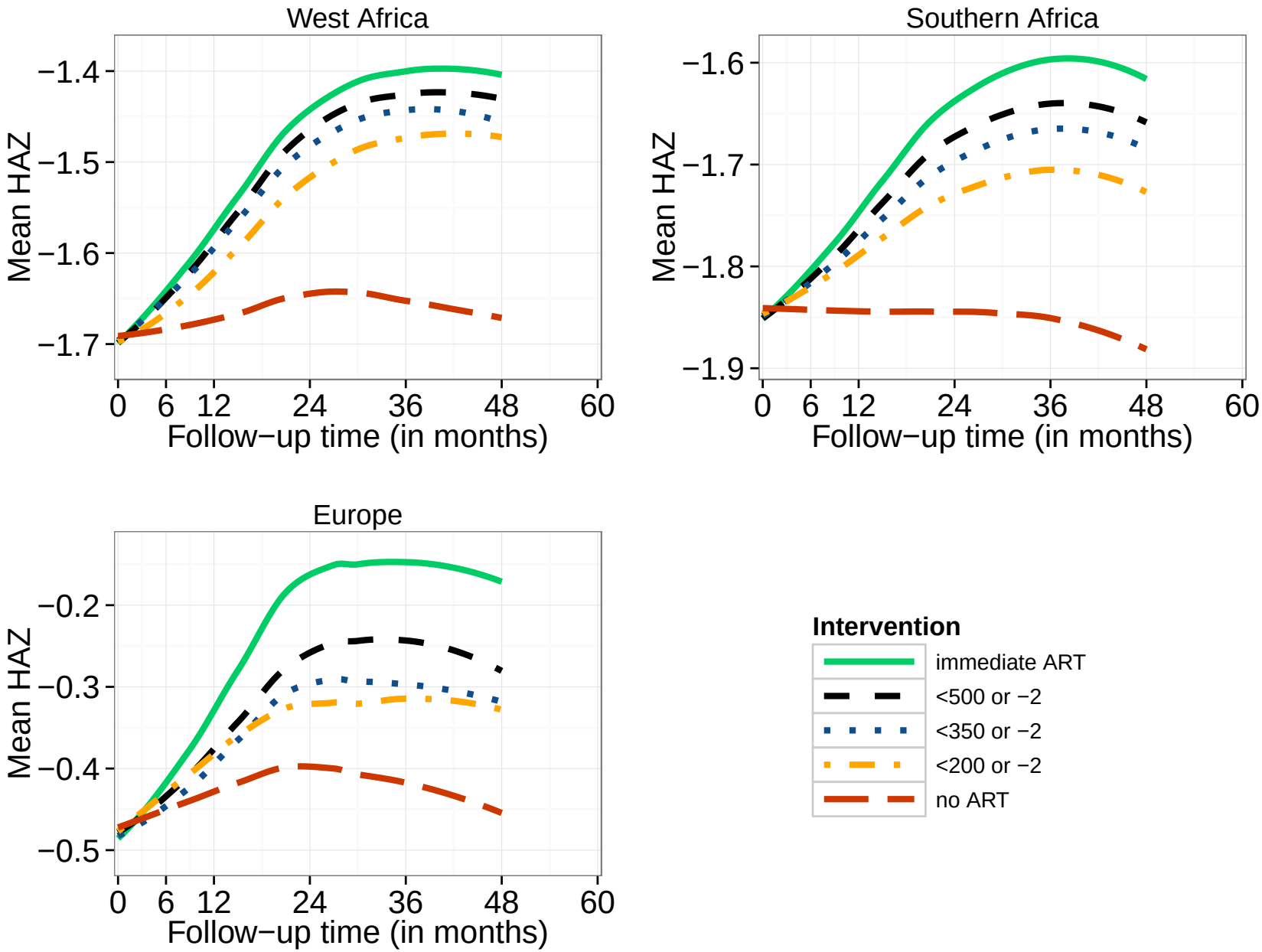


Supp. Figure 2. Cumulative mortality for different regions. Results are reported for the children aged 1-5 and the main scenario (regular follow-up, as in a trial)[2].

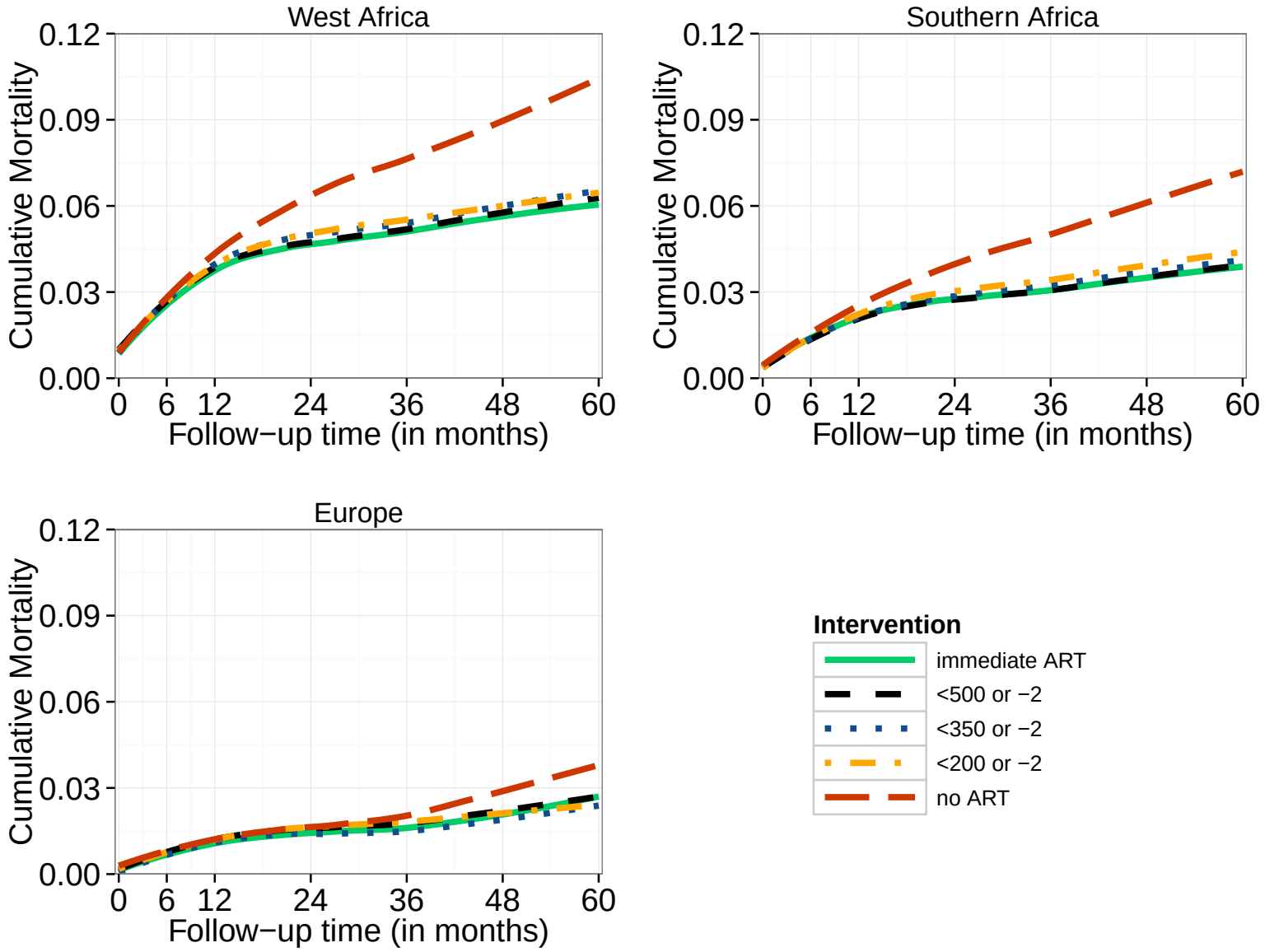


[2]The trajectories are smoothed. The mortality estimates at the first visit may therefore not exactly correspond to 0.

Supp. Figure 3. Growth trajectories for different regions. Results are reported for the children aged 5-10 and the main scenario (regular follow-up, as in a trial).

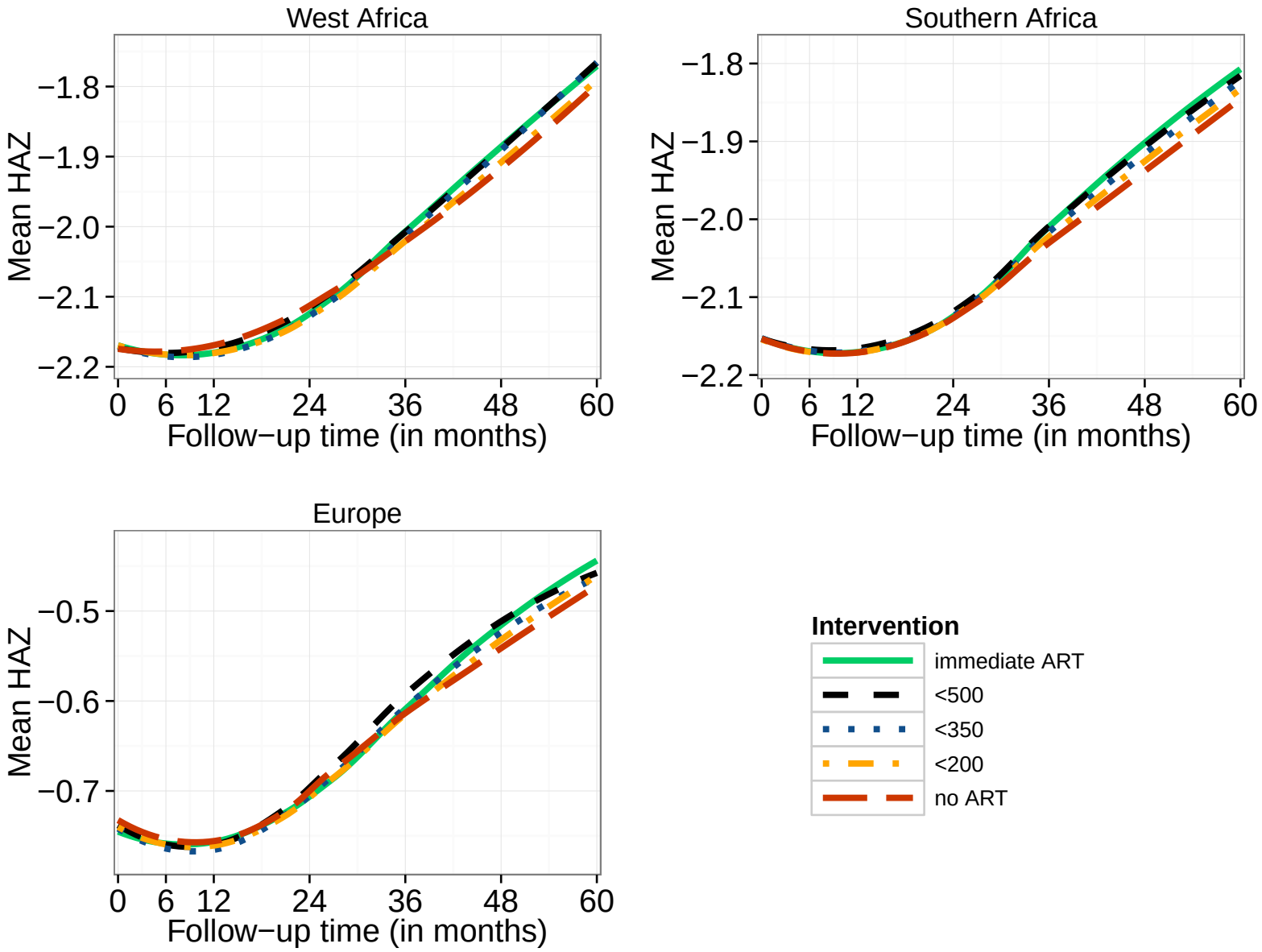


Supp. Figure 4. Cumulative mortality for different regions. Results are reported for the children aged 5-10 and the main scenario (regular follow-up, as in a trial)[3].



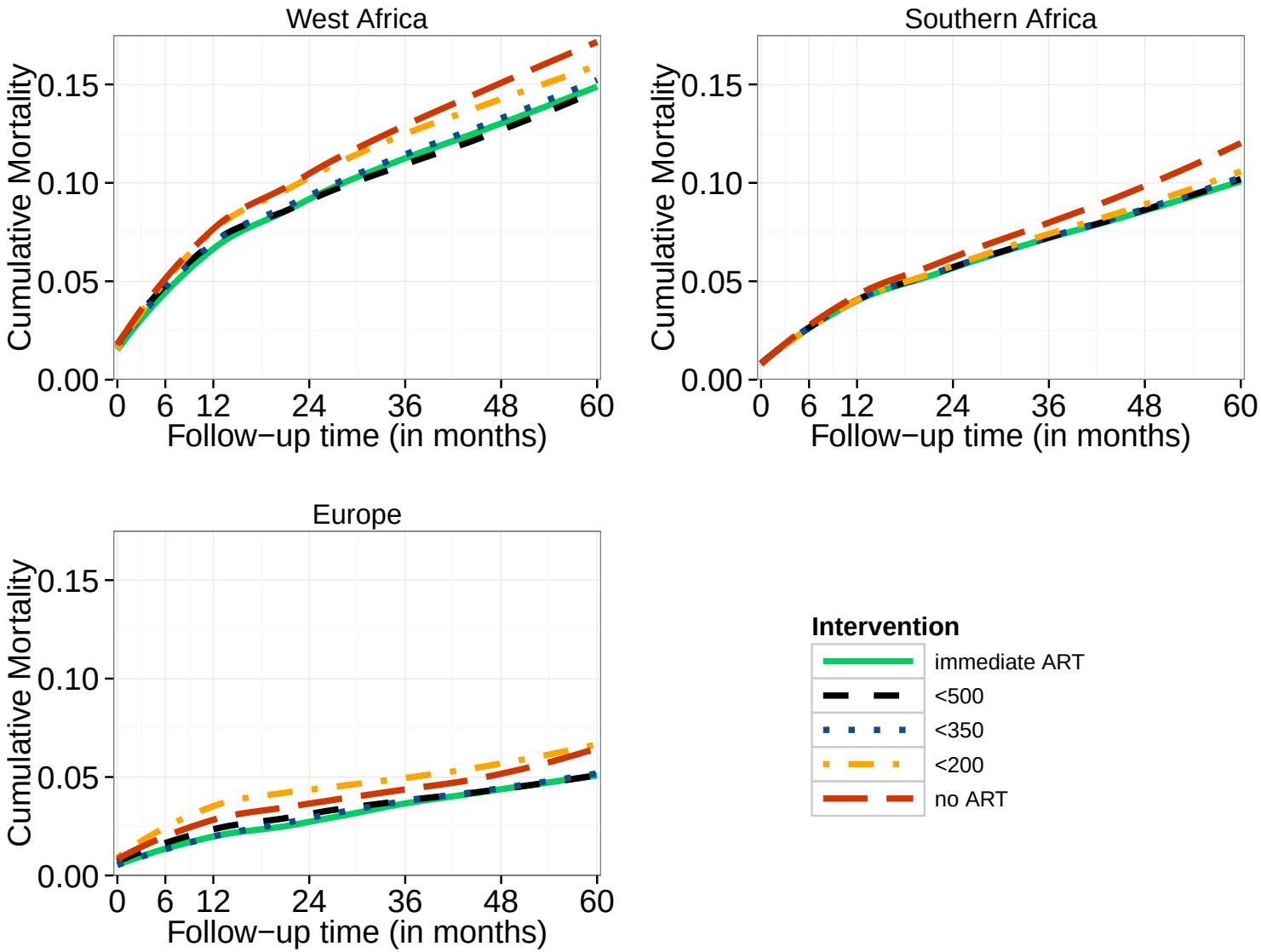
[3]The trajectories are smoothed. The mortality estimates at the first visit may therefore not exactly correspond to 0.

Supp. Figure 5. Growth trajectories for different regions. Results are reported for the children aged 10-16 and the alternative scenario [4].



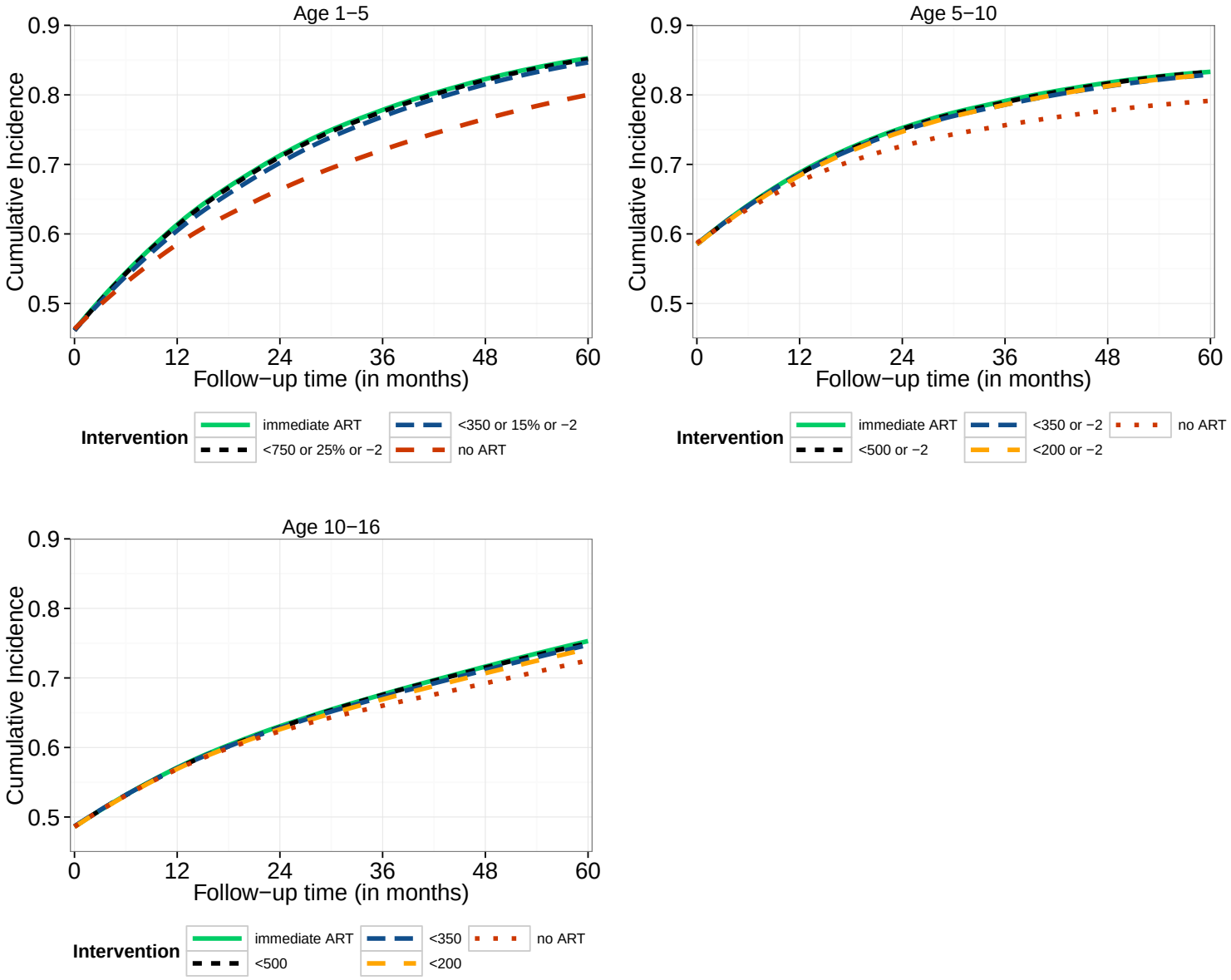
[4]The alternative scenario is chosen due its somewhat better performance in the natural course scenario, see eTables 8-9

Supp. Figure 6. Cumulative mortality for different regions. Results are reported for the children aged 10-16 and the alternative scenario[5].



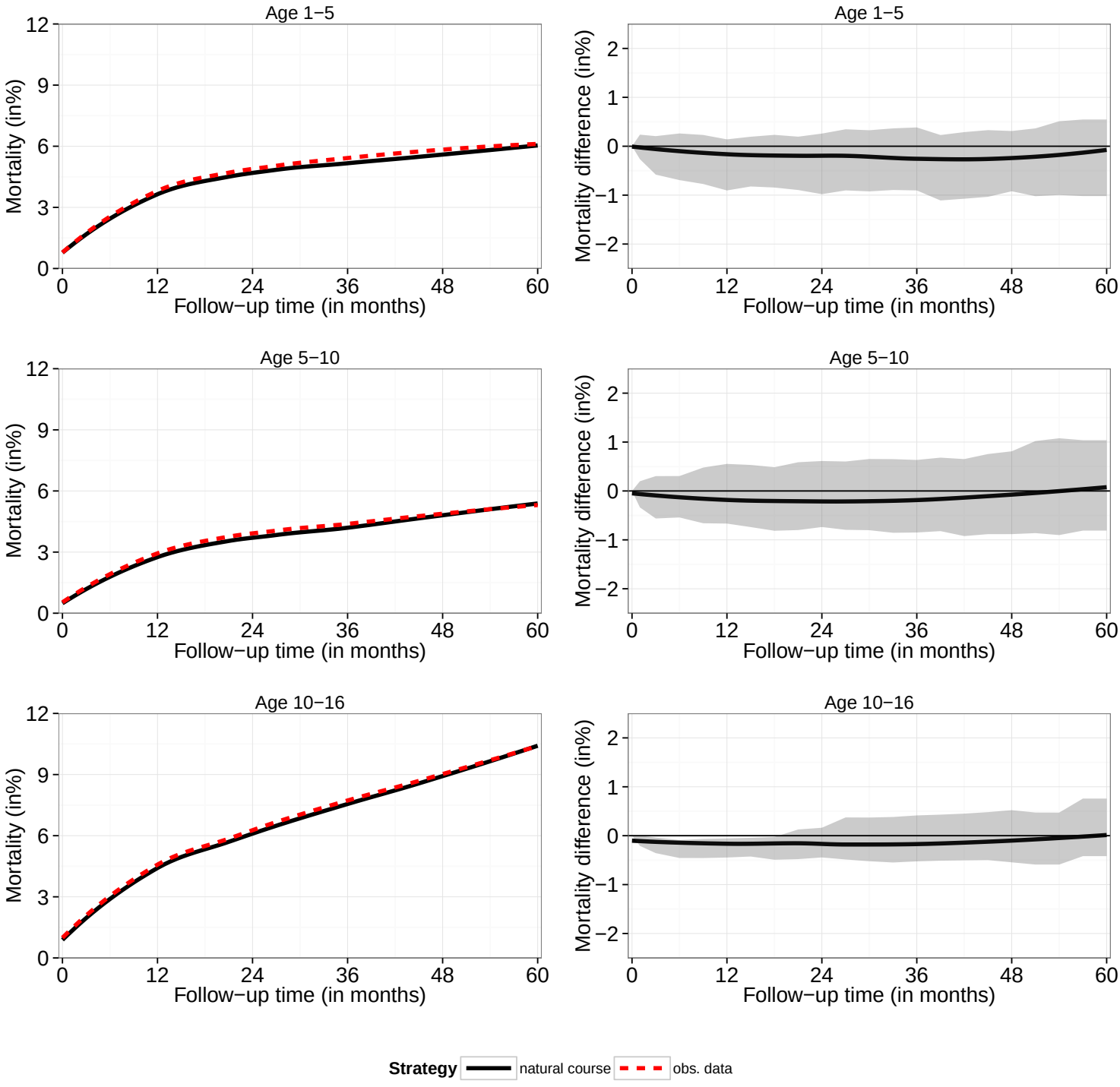
[5]The trajectories are smoothed. The mortality estimates at the first visit may therefore not exactly correspond to 0. The alternative scenario is chosen due its somewhat better performance in the natural course scenario, see eTable 10

Supp. Figure 7. Cumulative incidence of HAZ> −2: an alternative measure to mean HAZ which takes the competing risk of death into account. Results are reported for the main scenario and for different age groups.

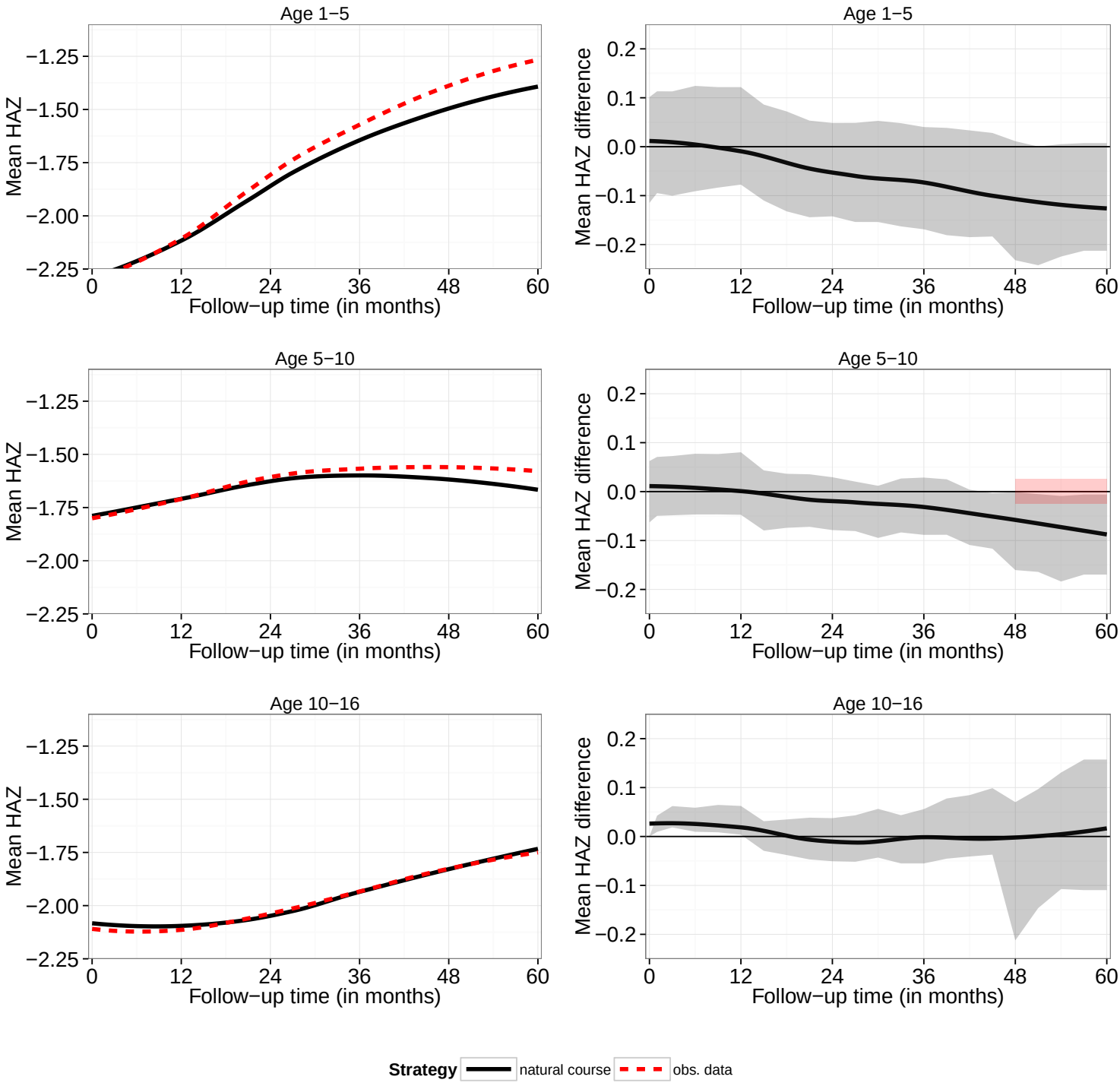


Supp. Figure 8. Comparison of estimated (a) mortality and (b) mean HAZ from the observed data with estimates obtained under the natural course scenario, i.e. the estimates produced with the g-formula under no treatment intervention; see also eTextbox 1 for more details. The difference of observed and simulated estimates, together with 95% bootstrap confidence intervals, is shown in the right panel and expected to be small. The results presented refer to the alternative scenario with infrequent visits as in the real data visits are infrequent too.

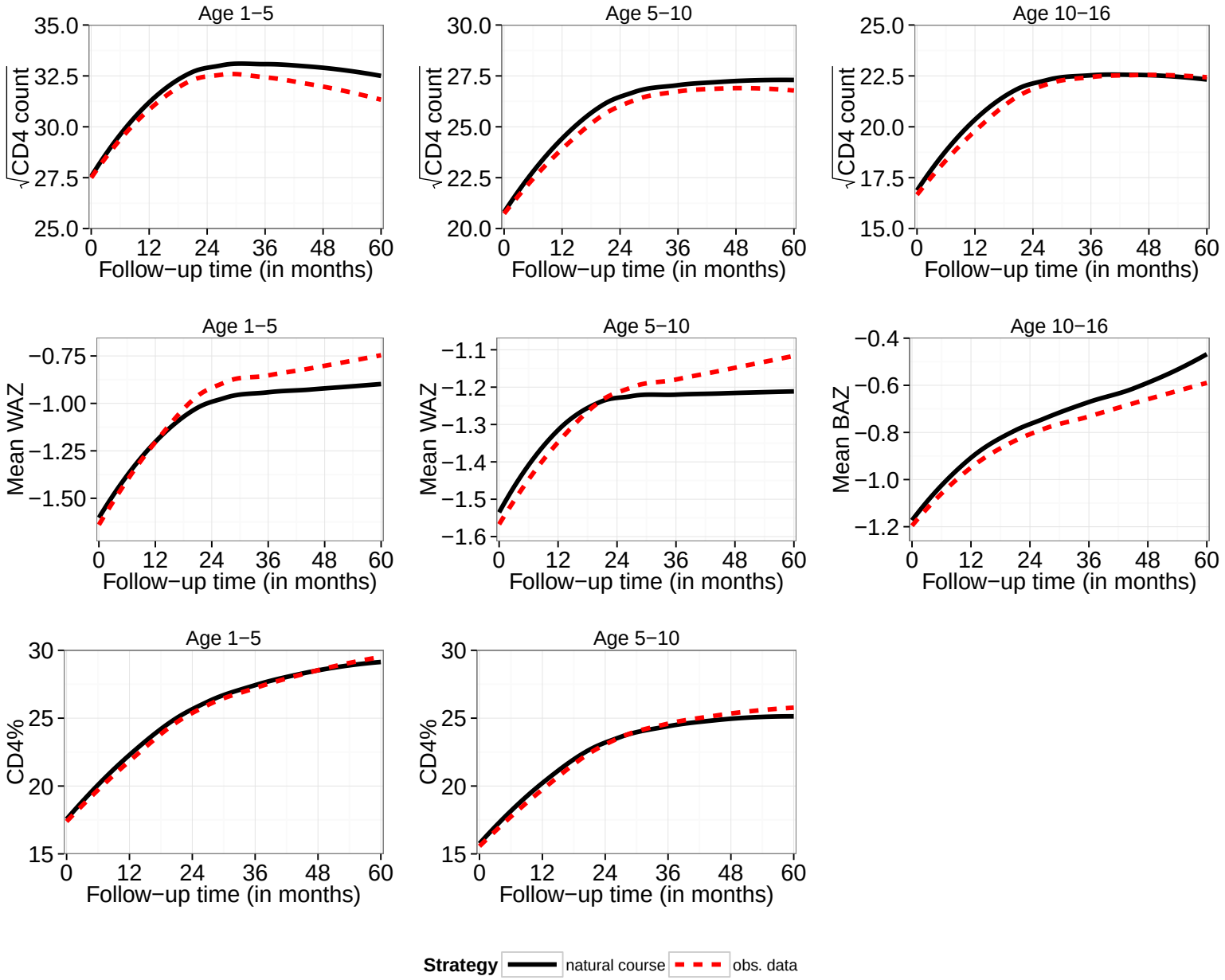
(a)



(b)


Age 1−5
Mean HAZ
−1.25
−1.50
−1.75
−2.00
−2.25
0
12
24
36
48
60
Follow−up time (in months)
Age 1−5
Mean HAZ difference
0.2
0.1
0.0
−0.1
−0.2
0
12
24
36
48
60
Follow−up time (in months)
Age 5−10
Mean HAZ
−1.25
−1.50
−1.75
−2.00
−2.25
0
12
24
36
48
60
Follow−up time (in months)
Age 5−10
Mean HAZ difference
0.2
0.1
0.0
−0.1
−0.2
0
12
24
36
48
60
Follow−up time (in months)
Age 10−16
Mean HAZ
−1.25
−1.50
−1.75
−2.00
−2.25
0
12
24
36
48
60
Follow−up time (in months)
Age 10−16
Mean HAZ difference
0.2
0.1
0.0
−0.1
−0.2
0
12
24
36
48
60
Follow−up time (in months)
Strategy
natural course
obs. data

Supp. Figure 9. Natural course comparisons for secondary (non-outcome) variables, i.e. CD4%, CD4 count, WAZ, and BAZ.



Supplementary Textbox 1. Details on our specification of the g-computation algorithm.

Background and Setting:

Notation: Consider n subjects studied at baseline ($t = 0$) and during discrete follow-up times ($t = 1, \ldots, T$). The data consists of the outcome Y_t, an intervention variable A_t, q time-dependent covariates $\mathbf{L}_t = \{L_t^1, \ldots, L_t^q\}$, an indicator for administrative censoring C_t, and a censoring due to loss to follow-up (drop-out) indicator M_t. The covariates may also include baseline variables $V = \{L_0^1, \ldots, L_0^{q_V}\}$. The treatment and covariate history of an individual i up to and including time t is represented as $\bar{A}_{t,i} = (A_{0,i}, \ldots, A_{t,i})$ and $\bar{L}_{t,i}^s = (L_{0,i}^s, \ldots, L_{t,i}^s)$, $s \in \{1, \ldots, q\}$, respectively. C_t equals 1 if a subject gets censored administratively in the interval $(t-1, t]$, and 0 otherwise. Therefore, $\bar{C}_t = 0$ is the event that an individual remains administratively uncensored until time t. The same notation is used for M_t and $\bar{M}_t$.

Let $\mathbf{L}_{t+1}^*$ be the covariates which had been observed under a deterministic dynamic intervention rule $d_t^* = d_t^*(\bar{\mathbf{L}}_t)$ which assigns treatment $A_{t,i} \in \{0, 1\}$ as a function of the covariates $\bar{L}_{t,i}^s$. The counterfactual outcome $Y_{(\bar{a}^*,t,i)}$ refers to the hypothetical outcome that would have been observed at time t if a subjects had received, likely contrary to the fact, the treatment history $\bar{A}_t = \bar{a}_t^*$ related to rule d_t^*.

Note that $\mathbf{L}_t$ may contain indicator variables which describe whether $L_{t,i}^s$ has been measured at time t or not.

The g-computation formula: If the outcome is binary (and can occur only once, such as death) we can write the cumulative probability of $Y = 1$ at time T, under no administrative censoring and no loss to follow-up, as

$$\sum_{t=1}^{T} \mathbb{P}(Y_t = 1 | \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0) =$$

$$\sum_{t=1}^{T} \int_{\bar{\mathbf{l}} \in \bar{\mathbf{L}}_t} \sum_{\bar{\mathbf{a}} \in \bar{\mathbf{A}}_t} \left\{ \begin{array}{l} \mathbb{P}(Y_t = 1 | \bar{A}_t = \bar{a}_t^*, \bar{\mathbf{L}}_t = \bar{\mathbf{l}}_t, \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0) \times \\ \prod_{t=1}^{T} \left[\begin{array}{l} \mathbb{P}(C_t = 0 | \bar{A}_{t-1} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_{t-1} = \bar{\mathbf{l}}_{t-1}, \bar{C}_{t-1} = 0, \bar{M}_{t-1} = 0, \bar{Y}_{t-1} = 0) \times \\ \mathbb{P}(M_t = 0 | \bar{A}_{t-1} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_{t-1} = \bar{\mathbf{l}}_{t-1}, \bar{C}_{t-1} = 0, \bar{M}_{t-1} = 0, \bar{Y}_{t-1} = 0) \times \\ f(\mathbf{L}_t | \bar{A}_{t-1} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_{t-1} = \bar{\mathbf{l}}_{t-1}, \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0) \times \\ \mathbb{P}(\mathbf{A}_t = \bar{a}_t^* | \bar{A}_{t-1} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_t = \bar{\mathbf{l}}_t, \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0) \times \\ \mathbb{P}(\mathbf{Y}_{t-1} = 0 | \bar{A}_{t-2} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_{t-2} = \bar{\mathbf{l}}_{t-2}, \bar{C}_{t-1} = 0, \bar{M}_{t-1} = 0, \bar{Y}_{t-2} = 0) \end{array} \right] \end{array} \right\} d\bar{\mathbf{l}} \tag{1}$$

For ordered $\mathbf{L}_t = \{L_t^1, \ldots, L_t^q\}$ we can write $f(\mathbf{L}_t | \bar{A}_{t-1} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_{t-1} = \bar{\mathbf{l}}_{t-1}, \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0)$ in (1) as

$$\prod_{s=1}^{q} f(L_t^s | \bar{A}_{t-1} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_{t-1} = \bar{\mathbf{l}}_{t-1}, L_t^1 = l_t^1, \ldots, L_t^{s-1} = l_t^{s-1}, \bar{C}_t = 0, \bar{M}_t = 0) \,. \tag{2}$$

If we intervene upon treatment assignment and censoring our quantity of interest is the cumulative probability of $Y = 1$ under the assigned treatment rule and no censoring due to any reason for the follow-up time of T years:

$$\sum_{t=1}^{T} \mathbb{P}(Y_{(\bar{a}^*,t)} = 1 | \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0) = {}^{1}$$

$$\sum_{t=1}^{T} \int_{\bar{\mathbf{l}} \in \bar{\mathbf{L}}_t} \left\{ \begin{array}{l} \mathbb{P}(Y_t = 1 | \bar{A}_t = \bar{a}_t^*, \bar{\mathbf{L}}_t = \bar{\mathbf{l}}_t, \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0) \times \\ \prod_{t=1}^{T} \left[\begin{array}{l} 1 \times 1 \times f(\mathbf{L}_t | \bar{A}_{t-1} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_{t-1} = \bar{\mathbf{l}}_{t-1}, \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0) \times 1 \times \\ \mathbb{P}(\mathbf{Y}_{t-1} = 0 | \bar{A}_{t-2} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_{t-2} = \bar{\mathbf{l}}_{t-2}, \bar{C}_{t-1} = 0, \bar{M}_{t-1} = 0, \bar{Y}_{t-2} = 0) \end{array} \right] \end{array} \right\} d\bar{\mathbf{l}} \tag{3}$$

[1]The equality holds under assumptions such as *consistency* (if $\bar{A}_{t,i} = \bar{a}_{t,i}$, then $Y_{(\bar{a},t)} = Y_t$ for $\forall t, \bar{a}$), *no unmeasured confounding* (conditional exchangeability, $Y_{(\bar{a}^*,t)} \perp A_t | \bar{\mathbf{L}}_t, \bar{A}_{t-1}$ for $\forall t, \bar{a}$), *positivity* ($\mathbb{P}(\bar{A}_t = \bar{a}_t | \bar{\mathbf{L}}_t = \mathbf{l}_t) > 0$ for $\forall t, \bar{a}, \mathbf{l}$), as well as correctly specified models etc. – see Robins and Hernan (2009), Daniel et al. (2013, 2011), Young et al. (2011) and Robins et al. (2004) for more details and interpretations.

The equality of (1) and (3) follows because the probability of remaining uncensored due to any reason is 1 as per our specification. Similarly, we assign the treatment rule and can therefore replace the distribution in (1) with 1. It follows that, under the assumptions listed in footnote 1, the quantity of interest can be calculated by integrating $\mathbf{L}$ out (i.e. by simulation) and evaluating Y at each time point conditioned on those observations which did not experience an event yet. We assume time points to represent intervals and thus both covariates and a fatal event like death can be measured at the same time t.

Our setting: In our setting we study 8665 children aged 1-5 (7358 aged 5-10, 4553 aged 10-16) for $t = 0, 1, 3, 6, 9, \ldots, 60$ months. The follow-up time points refer to the intervals $(0, 1.5)$, $[1.5, 4.5)$, $[4.5, 7.5)$, $[7.5, 10.5)$, $[10.5, 13.5)$, $[13.5, 16.5)$, $[16.5, 19.5)$, $[19.5, 22.5)$, $[22.5, 25.5)$, $[25.5, 28.5)$, $[28.5, 31.5)$, $[31.5, 34.5)$, $[34.5, 37.5)$, $[37.5, 40.5)$, $[40.5, 43.5)$, $[43.5, 46.5)$, $[46.5, 49.5)$, $[49.5, 52.5)$, $[52.5, 55.5)$, $[55.5, 60)$ months respectively. Follow-up measurements, if available, refer to measurements closest to the middle of the interval. In our data

- Y_t refers to death at time t (i.e. occurring during the interval $(t-1, t]$)
- A_t refers to antiretroviral treatment (ART) taken at time t
- $\mathbf{L}_t = (L_t^1, L_t^2, L_t^3, L_t^4, L_t^5, L_t^6)$ refer to CD4 count, CD4%, and weight for age z-score (WAZ)[2] as well as indicator variables whether these three variables have been measured at time t or not. In the main scenario we assume regular measurements and thus intervene upon the measurement frequency. In the alternative scenario we use the distribution of measurement frequency to resemble the visit pattern in the data[3].
- $V = \mathbf{L}_0^V$ refers to baseline values of CD4 count, CD4%, WAZ (BMIAZ for age 10-16), height for age z-score (HAZ) as well as sex, age, year of treatment initiation and region
- $d_{t,j}(\mathbf{L}_t)$ refer to dynamic treatment rules assigning treatment based on CD4 count, CD4%, and WAZ, see eTable 4 for a comprehensive list

We want to estimate cumulative mortality (under no administrative censoring and loss to follow-up) after T months, that is $\sum_{t=1}^{T} \mathbb{P}(Y_{(\bar{a}^*,t)} = 1 | \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0) \quad \text{for} \quad T = 1, 3, 6, \ldots, 60\,.$

[2]Note that weight for age-z-scores serve as a proxy for WHO stage because most stage-defining events relate to a child's WAZ, such as tuberculosis or persistent diarrhoea, see Schomaker et al. (2013) for more details. For the oldest age group BMIAZ was used instead of WAZ, see also the explanations in the main text.

[3]Main scenario: we estimate all counterfactual outcomes under no administrative censoring, no loss to follow-up, full adherence to the regime, immediate ART initiation after reaching eligibility, and regular (three monthly) follow-up. Alternative Scenario: we do not assume regular follow-up, but rather infrequent follow-up which we model based on the visit frequency in our data. In addition, we assume that treatment is started at one visit after reaching eligibility.

a) Detailed algorithm to estimate the g-formula for outcome "death":

Step 1: Modelling.

a) Time dependent confounders: We used additive linear models to estimate the association of the time-dependent confounders (CD4 count, CD4 percentage, weight for age z-score (age 1-10), BMI for age z-score (age 10-16) at time t) with disease progression history (CD4 count, CD4 percentage, weight for age z-score, BMI for age z-score, height for age-z-score at time $t-1$), demographics (age, sex, region, year of treatment initiation), and the intervention (ART at times $t-1$ and $t-2$) for $\forall t$. This corresponds to fitting 3 models (relating to the 3 time-dependent confounders[3]) for 20 points in time. In more detail, we initially fit the linear models:

[3]only two time-dependent confounders (CD4 count and BMIAZ) for age 10-16 since CD4% is not meaningful for adolescents

$$\begin{aligned}\sqrt{\text{CD4 count}_t} &= f_1(\text{CD4 count}_{t-1}) + f_2(\text{CD4\%}_{t-1}) + f_3(\text{WAZ}_{t-1}) + f_4(\text{HAZ}_{t-1}) \\ &+ f_5(\text{CD4 count}_0) + f_6(\text{CD4\%}_0) + f_7(\text{WAZ}_0) + f_8(\text{HAZ}_0) + f_9(\text{Age}) \\ &+ \beta_0 + \beta_1\text{Region1} + \beta_2\text{Region2} + \beta_3\text{Sex} + \beta_4\text{Year} + \beta_5\text{ART}_{t-1} + \beta_6\text{ART}_{t-2} + \epsilon \qquad (4)\end{aligned}$$

$$\begin{aligned}\text{CD4\%}_t &= f_1(\text{CD4 count}_t) \\ &+ f_2(\text{CD4 count}_{t-1}) + f_3(\text{CD4\%}_{t-1}) + f_4(\text{WAZ}_{t-1}) + f_5(\text{HAZ}_{t-1}) \\ &+ f_6(\text{CD4 count}_0) + f_7(\text{CD4\%}_0) + f_8(\text{WAZ}_0) + f_9(\text{HAZ}_0) + f_{10}(\text{Age}) \\ &+ \beta_0 + \beta_1\text{Region1} + \beta_2\text{Region2} + \beta_3\text{Sex} + \beta_4\text{Year} + \beta_5\text{ART}_{t-1} + \beta_6\text{ART}_{t-2} + \epsilon \qquad (5)\end{aligned}$$

$$\begin{aligned}\text{WAZ}_t &= f_1(\text{CD4\%}_t) + f_2(\text{CD4 count}_t) \\ &+ f_3(\text{CD4 count}_{t-1}) + f_4(\text{CD4\%}_{t-1}) + f_5(\text{WAZ}_{t-1}) + f_6(\text{HAZ}_{t-1}) \\ &+ f_7(\text{CD4 count}_0) + f_8(\text{CD4\%}_0) + f_9(\text{WAZ}_0) + f_{10}(\text{HAZ}_0) + f_{11}(\text{Age}) \\ &+ \beta_0 + \beta_1\text{Region1} + \beta_2\text{Region2} + \beta_3\text{Sex} + \beta_4\text{Year} + \beta_5\text{ART}_{t-1} + \beta_6\text{ART}_{t-2} + \epsilon \qquad (6)\end{aligned}$$

These models estimate the conditional densities from equation (2) for $\forall s, t$, and therefore the second part of the right hand side of equation (3) for $\forall t$.

Note: The models (4)-(6) are restricted to those subjects who survived until time t and were not censored (administratively or due to LTFU). The functions f_j are estimated via penalized regression splines (with smoothness determined by generalized cross validation [GCV, Golub et al., 1979]). All model specifications implicitly assume that time-dependent risk factors measured before or on time $t-2$ do not predict the respective outcome. All models are updated based on model selection, see item d) below. For age 10-16 WAZ is replaced by BMIAZ. The implicit ordering is clear from the above specifications: L_1 = CD4 count, L_2 = CD4%, L_3 = WAZ (BMIAZ). We assume $\epsilon \sim N(0, \sigma^2 I)$. The ordering was based on the thought that the outcomes at time t should make use of WAZ, CD4 count and CD4% at time (interval) t; and that WAZ, a strong predictor of death and HAZ, should be informed by CD4 count and CD4% at t.

For the alternative scenario we fit 3×20 models more, i.e. additive logistic regression models the estimate the probability that L_t^s is measured at time t:

$$\begin{aligned}\log\left(\frac{\mathbb{P}(\text{CD4 count}_t = \text{m})^4}{1 - \mathbb{P}(\text{CD4 count}_t = \text{m})}\right) &= f_1(\text{CD4 count}_{t-1}) + f_2(\text{CD4\%}_{t-1}) + f_3(\text{WAZ}_{t-1}) + f_4(\text{HAZ}_{t-1}) \\ &+ f_5(\text{CD4 count}_0) + f_6(\text{CD4\%}_0) + f_7(\text{WAZ}_0) + f_8(\text{HAZ}_0) + f_9(\text{Age}) \\ &+ \beta_0 + \beta_1\text{Region1} + \beta_2\text{Region2} + \beta_3\text{Sex} + \beta_4\text{Year} + \beta_5\text{ART}_{t-1} + \beta_6\text{ART}_{t-2} \\ &+ \epsilon \qquad (7)\end{aligned}$$

$$\begin{aligned}\log\left(\frac{\mathbb{P}(\text{CD4\%}_t = \text{m})}{1 - \mathbb{P}(\text{CD4\%}_t = \text{m})}\right) &= f_1(\text{CD4 count}_t) \\ &+ f_2(\text{CD4 count}_{t-1}) + f_3(\text{CD4\%}_{t-1}) + f_4(\text{WAZ}_{t-1}) + f_5(\text{HAZ}_{t-1}) \\ &+ f_6(\text{CD4 count}_0) + f_7(\text{CD4\%}_0) + f_8(\text{WAZ}_0) + f_9(\text{HAZ}_0) + f_{10}(\text{Age}) \\ &+ \beta_0 + \beta_1\text{Region1} + \beta_2\text{Region2} + \beta_3\text{Sex} + \beta_4\text{Year} + \beta_5\text{ART}_{t-1} + \beta_6\text{ART}_{t-2} \\ &+ \beta_7\text{CD4 count measured} + \epsilon \qquad (8)\end{aligned}$$

[4] m = measured

$$\log\left(\frac{\mathbb{P}(\text{WAZ}_t = \text{m})}{1-\mathbb{P}(\text{WAZ}_t = \text{m})}\right) = f_1(\text{CD4\%}_t) + f_2(\text{CD4 count}_t) + f_3(\text{CD4 count}_{t-1}) + f_4(\text{CD4\%}_{t-1}) + f_5(\text{WAZ}_{t-1}) + f_6(\text{HAZ}_{t-1}) + f_7(\text{CD4 count}_0) + f_8(\text{CD4\%}_0) + f_9(\text{WAZ}_0) + f_10(\text{HAZ}_0) + f_{11}(\text{Age}) + \beta_0 + \beta_1\text{Region1} + \beta_2\text{Region2} + \beta_3\text{Sex} + \beta_4\text{Year} + \beta_5\text{ART}_{t-1} + \beta_6\text{ART}_{t-2} + \beta_7\text{CD4 count measured} + \beta_8\text{CD4\% measured} + \epsilon \quad (9)$$

In the alternative scenario the ordering of $\mathbf{L_t}$ is $L^1 =$ CD4 count measured, $L^2 =$ CD4 count, $L^3 =$ CD4% measured, $L^4 =$ CD4%, $L^5 =$ WAZ measured, $L^6 =$ WAZ. Note that in the alternative scenario models (4)-(6) contain additional terms related to whether L_t^s was measured or not.

b) Outcome: We used a logistic additive model to estimate the association of the outcome (death) with the time dependent confounders at time t, disease progression history, baseline characteristics, demographics, and intervention for $t = 1, 3, 6, ..., 36$. This corresponds to fitting 1 (non-pooled) model for 20 points in time.

$$\log\left(\frac{\mathbb{P}(Y_t = 1)}{1-\mathbb{P}(Y_t = 1)}\right) = f_1(\text{CD4 count}_t) + f_2(\text{CD4\%}_t) + f_3(\text{WAZ}_t) + f_4(\text{HAZ}_t) + f_5(\text{CD4 count}_{t-1}) + f_6(\text{CD4\%}_{t-1}) + f_7(\text{WAZ}_{t-1}) + f_8(\text{HAZ}_{t-1}) + f_9(\text{CD4 count}_0) + f_{10}(\text{CD4\%}_0) + f_{11}(\text{WAZ}_0) + f_{12}(\text{HAZ}_0) + f_{13}(\text{Age}) + \beta_0 + \beta_1\text{Region1} + \beta_2\text{Region2} + \beta_3\text{Sex} + \beta_4\text{Year} + \beta_5\text{ART}_{t-1} + \beta_6\text{ART}_{t-2} + \epsilon \quad (10)$$

These models estimate the first part of the right hand side of equation (3) for $\forall t$.

Note that in the alternative scenario model (10) contains additional terms related to whether L_t^s was measured or not

c) Treatment: In the natural course scenario (see also Step 2 below and eFigures 8 and 9) treatment is not assigned deterministically based on a rule or function of $\mathbf{L_t^s}$ but rather stochastically assigned as observed in the data. Thus $\mathbb{P}(\mathbf{A}_t = \bar{a}_t^* | \bar{A}_{t-1} = \bar{a}_{t-1}^*, \bar{\mathbf{L}}_t = \bar{\mathbf{l}}_t, \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0)$ in (1) is not 1 but rather estimated from the data. For this scenario we use the following model:

$$\log\left(\frac{\mathbb{P}(A_t = 1)}{1-\mathbb{P}(A_t = 1)}\right) = f_1(\text{CD4 count}_t) + f_2(\text{CD4\%}_t) + f_3(\text{WAZ}_t) + f_4(\text{HAZ}_t) + f_5(\text{CD4 count}_{t-1}) + f_6(\text{CD4\%}_{t-1}) + f_7(\text{WAZ}_{t-1}) + f_8(\text{HAZ}_{t-1}) + f_9(\text{CD4 count}_0) + f_{10}(\text{CD4\%}_0) + f_{11}(\text{WAZ}_0) + f_{12}(\text{HAZ}_0) + f_{13}(\text{Age}) + \beta_0 + \beta_1\text{Region1} + \beta_2\text{Region2} + \beta_3\text{Sex} + \beta_4\text{Year} + \beta_5\text{ART}_{t-1} + \beta_5\text{ART}_{t-2} + \epsilon \quad (11)$$

Note that in the alternative scenario model (11) contains additional terms related to whether L_t^s was measured or not.

d) Model selection (for all models from above):

i) To allow for flexible disease progression depending on how sick children are when they present at their first visit, interactions of baseline characteristics (represented in categories)[5] with all other variables were added. Depending on the functional form of the covariates these interactions were either linear or non-linear. If an interaction improved the GCV score the interaction was kept in the model, otherwise it was removed again.

ii) After adding interactions to the respective models in a forward selection, variables and interactions were removed in a backward selection if this again improved the GCV score. If the plotted nonlinear interactions showed signs of volatility they were removed as well.

[5]categories for first visit CD4 count are '$[0, 50), [50, 200), > 200$', for CD4% '$[0, 20), [20, 30), > 30$', and for WAZ '$< -3, [-3, -1.5), > 1.5$'

iii) The order in which variables and their interactions were first added and then removed corresponds to the order of the variables listed in equations (3)-(6).

iv) The procedure was not automated and each model was checked individually for stability and interpretability. The chosen variables were used in the bootstrap samples too. The smoothing parameters of the penalized splines, modeling the non-linear relationships between variables, were re-fitted in each bootstrap sample.

↓

Step 2: Intervention choice and repetition. For children aged 1-5 we choose one of the following four interventions:

i) Give a child ART immediately, irrespective of his/her CD4 count:

$$d^*_{t,i,1}(\text{CD4 count}_{t,i}, \text{CD4\%}_{t,i}, WAZ) = \begin{cases} a^*_{t,i} = 1 & \text{always} \\ a^*_{t,i} = 0 & \text{never} \end{cases}$$

ii) Give a child ART when his/her absolute CD4 count falls below 750 cells/mm^3 or his/her CD4 percentage falls below 25%:

$$d^*_{t,i,2}(\text{CD4 count}_{t,i}, \text{CD4\%}_{t,i}, WAZ) = \begin{cases} a^*_{t,i} = 1 & \text{if} \quad \text{CD4 count}^*_{t,i} < 750 \quad \text{or} \quad \text{CD4\%}^*_{t,i} < 25 \text{or} \quad \text{WAZ}^*_{t,i} < -2 \\ a^*_{t,i} = 0 & \text{otherwise} \end{cases}$$

iii) Give a child ART when his/her absolute CD4 count falls below 350 cells/mm^3 or his/her CD4 percentage falls below 15%:

$$d^*_{t,i,3}(\text{CD4 count}_{t,i}, \text{CD4\%}_{t,i}, WAZ) = \begin{cases} a^*_{t,i} = 1 & \text{if} \quad \text{CD4 count}^*_{t,i} < 350 \quad \text{or} \quad \text{CD4\%}^*_{t,i} < 15 \text{or} \quad \text{WAZ}^*_{t,i} < -2 \\ a^*_{t,i} = 0 & \text{otherwise} \end{cases}$$

iv) Never give a child ART:

$$d^*_{t,i,4}(\text{CD4 count}_{t,i}, \text{CD4\%}_{t,i}, WAZ) = \begin{cases} a^*_{t,i} = 1 & \text{never} \\ a^*_{t,i} = 0 & \text{always} \end{cases}$$

The interventions used for other age groups (5-10, 10-16) can be found in eTable 4. To investigate for potential problems in our implemenation we also assign a further intervention in each age group, i.e. the natural intervention as observed in the data, see Young et al. (2011) for more details. Here, we assign treatment based on a draw from a Bernoulli distribution with the probability obtained from the logistic additive model fitted in (11). Under this intervention the observed data and the data obtained by the g-formula (see below) should yield approximately the same results if there is no informative censoring, no model mis-specification, and no unmeasured confounding. In the alternative scenario treatment is only assigned one visit after reaching eligibility.

↓

Step 3: Monte-Carlo Simulation. We simulate data for the children for each specific intervention rule *forward in time* based on the estimated conditional distributions from Step 1.

At the first visit, $t = 0$, the data corresponds to the observed data of *all* children.

a) Simulation of the covariates $\mathbf{L}_t^* = (\text{CD4 count}_t^*, \text{CD4\%}_t^*, \text{WAZ}_t^*)$[6] for $t = 1, 3, 6, 9, \ldots$:

- Applying the chosen treatment rule from step 2[7] (i.e. $d_{t,j}^*$) to the models (4)-(6) yields predicted square root CD4 counts ($\hat{L}_t^1$), CD4% ($\hat{L}_t^2$), and WAZ ($\hat{L}_t^3$).
- Drawing from the conditional distributions in (2) relates to drawing from normal distributions with mean $\hat{L}_t^1$ and variance $\hat{\sigma}_{\mathcal{M}}^2$ (which is the estimated residual variance from the respective model):

$$\tilde{L}_t^s \quad \text{drawn from} \quad N(\hat{L}_t^s, \hat{\sigma}_{\mathcal{M}}^2)$$

- The simulated counterfactual covariates related to the chosen treatment rule are therefore $\mathbf{L}_t^{s*} = \tilde{\mathbf{L}}_t^s$.
- The simulated values of CD4 count, CD4% and WAZ at time $t-1$ ($\tilde{\mathbf{L}}_{t-1}$) are used when predicting CD4 count, CD4% and WAZ at time t ($\hat{\mathbf{L}}_t$ and $\tilde{\mathbf{L}}_t$).

b) As in a), we apply the chosen treatment rule from step 2. The hypothetical outcome (death) is simulated based on a draw from a Bernoulli distribution with the probability obtained from the logistic additive model fitted in Step 1b), that is $\hat{p}_t$.

$$\tilde{Y}_t \quad \text{drawn from} \quad B(\hat{p}_t)$$

If the simulated outcome for an individual at time t is equal to 1 (death), then there will be no more follow-up at time t+1. This reflects the condition specified in the third part of the right hand side of equation (3).

Note that we intervene on administrative censoring and loss to follow-up by setting $\bar{C}_t = 0$ and $\bar{M}_t = 0$ and therefore simulate a dataset with no administrative censoring and drop-out.

By applying a) and b) over time (from $t = 1$ onwards) a simulated dataset, consisting of $(\tilde{Y}, \tilde{\mathbf{L}})$, is generated for each particular treatment rule. Repeating this for all interventions yields $(\tilde{Y}, \tilde{\mathbf{L}})^d = \{(\tilde{Y}, \tilde{\mathbf{L}})^{d_1}, (\tilde{Y}, \tilde{\mathbf{L}})^{d_2}, (\tilde{Y}, \tilde{\mathbf{L}})^{d_3}, (\tilde{Y}, \tilde{\mathbf{L}})^{d_4}\}$

c) For the alternative scenario we also need to simulate whether a L_t^s has been measured or not. Thus we use draws from Bernoulli distributions with probabilities obtained from (7)-(9) to determine whether L_t^s, $s = 1, 2, 3$, has been measured at time t or not. If the simulated value is 1 we set $L_{t,i}^{s*} = \tilde{L}_{t,i}^s$, otherwise $L_{t,i}^{s*} = L_{t-1,i}^{s*}$.

d) Under the natural course intervention we also simulate whether treatment has been assigned or not, see Step 2 for more details.

The simulation procedure approximates the integral in (3) for a specific treatment rule with the aim to estimate cumulative mortality as defined in (3).

[6] Again, BMIAZ and CD4 count are used for the age group 10-16

[7] For example, setting $\text{ART}_t = 0$ in all models if $d_{t,4}$ [never give a child ART] is applied

↓

Step 4: Estimation of mortality. We estimate the cumulative relative mortality $\omega_T = \sum_{t=1}^{T} \mathbb{P}(Y_{(\bar{a}^*,t)} = 1 | \bar{C}_t = 0, \bar{M}_t = 0, \bar{Y}_{t-1} = 0)$ for $T = 1, 3, 6, \ldots, 60$ months: the cumulative proportion of children who die at the different time points in the simulated dataset $(\tilde{Y}, \tilde{\mathbf{L}})^{d_i}$ from Step 3 equates to the g-computation formula estimate of the cumulative mortality under intervention rule d_i.

↓

Step 5: Multiple Imputation. Steps 1 to 4 are implemented for 10 imputed sets of data. Multiple imputation was utilized for missing baseline data using the `Amelia II` package in R (Honaker et al., 2011). The imputation model included all measured baseline and follow-up variables, mortality, follow-up time, a variable indicating which observations were carried forward completely, all indicators on whether the confounders were measured at time t or not, and the region (West Africa, Southern Africa, Europe).

The longitudinal structure of the data was explicitly considered in the EMB algorithm, nonlinear time trends were allowed and lag- and lead-variables of CD4 count, CD4%, WAZ, and HAZ were added to the imputation model. Imputation diagnostics (comparing imputed and observed densities, overimputation, convergence of EM chains, time-series plots; see also Honaker et al., 2011) were evaluated to ensure the convergence of the algorithm and the appropriateness of the imputations.

The procedure yields 10 different mortality estimates related to the 10 imputed sets of data ($\hat{\omega}_T^{(m)}; m = 1, \ldots, 10$). The final point estimate for the cumulative mortality is therefore

$$\hat{\omega}_T^{\text{MI}} = \frac{1}{10} \sum_{m=1}^{10} \hat{\omega}_T^{(m)} \quad \text{for} \quad T = 1, 3, 6, \ldots . \tag{12}$$

Step 6: Bootstrap repetitions. We repeat steps 1 to 5 for 200 bootstrap samples to obtain 95% confidence intervals. Each bootstrap sample includes missing data and needs to be multiply imputed. Thus, for each bootstrap sample we estimate $\hat{\omega}_T^{MI}$ which yields 200 cumulative mortality estimates $\hat{\omega}_T^{b,d_i}, b = 1, \ldots, 200$ for each intervention. The bounds of the 95% confidence intervals are set at the 2.5^{th} and 97.5^{th} percentiles of the distribution of these 200 estimates.

b) G-computation algorithm for outcome "growth": The algorithm corresponds to the above algorithm for outcome "death", but with the following additions:

Background: The main quantity of interest for this analysis is the expected height-for-age z-score of all survivors under no loss to follow-up and no administrative censoring for different time points and interventions. Consider the notation from the analysis above, but let Y_t be the height-for-age z-score at time t and S_t an indicator variable which is 1 if a patient is still alive at time t and 0 otherwise. Then the g-computation formula from (3) can be re-written as

$$\begin{aligned}&\mathbb{E}(Y_{(\bar{a}^*,t)}|\bar{C}_t=0,\bar{M}_t=0,S_t=1)=\\&\sum_{t=1}^{T}\int_{\bar{\mathbf{l}}\in\bar{\mathbf{L}}_t}\left\{\begin{array}{l}\mathbb{E}(Y_t=1|\bar{A}_t=\bar{a}_t^*,\bar{\mathbf{L}}_t=\bar{\mathbf{l}}_t,\bar{C}_t=0,\bar{M}_t=0,S_t=1)\times\\\prod_{t=1}^{T}\left[\begin{array}{l}f(\mathbf{L}_t|\bar{A}_{t-1}=\bar{a}_{t-1}^*,\bar{\mathbf{L}}_{t-1}=\bar{\mathbf{l}}_{t-1},\bar{C}_t=0,\bar{M}_t=0,S_t=1)\times\\\mathbb{P}(S_t=1|\bar{A}_{t-1}=\bar{a}_{t-1}^*,\bar{\mathbf{L}}_{t-1}=\bar{\mathbf{l}}_{t-1},\bar{C}_t=0,\bar{M}_t=0,S_{t-1}=1)\end{array}\right]\end{array}\right\}d\bar{\mathbf{l}}\end{aligned}\tag{13}$$

To estimate (13) the algorithm for the outcome death can be used, with the following additions and changes:

Step 1: We used an additive linear model to also model the association of (the outcome) height for age z-score with disease progression history, baseline variables, demographics, and the intervention:

$$\begin{aligned}\text{HAZ}_t &= f_1(\text{CD4\%}_t)+f_2(\text{CD4 count}_t)+f_3(\text{WAZ}_t)\\&\quad+f_4(\text{CD4 count}_{t-1})+f_5(\text{CD4\%}_{t-1})+f_6(\text{WAZ}_{t-1})+f_7(\text{HAZ}_{t-1})\\&\quad+f_8(\text{CD4 count}_0)+f_9(\text{CD4\%}_0)+f_{10}(\text{WAZ}_0)+f_{11}(\text{HAZ}_0)+f_{12}(\text{Age})\\&\quad+\beta_0+\beta_1\text{Region1}+\beta_2\text{Region2}+\beta_3\text{Sex}+\beta_4\text{Year}+\beta_5\text{ART}_{t-1}+\beta_6\text{ART}_{t-2}+\epsilon\end{aligned}\tag{14}$$

Following (7) - (9) we also model the measurement process of height in the alternative scenario. Model (10) is used to model survival.

Step 2: as in a)

Step 3: We simulate height for age z-score data for all children for a specific intervention forward in time. The predictions are based on a random draw from a normal distribution where mean and standard error are obtained from the prediction of the additive linear model (14) fitted in Step 1, i.e. $\tilde{Y}_t$ drawn from $N(\hat{Y}_t,\hat{\sigma}^2_{\mathcal{M}})$. The probability of death is simulated as in a), i.e. as specified in (10), and $\tilde{S}_t$ is drawn from $B(\hat{p}_t)$. Note that we still intervene on administrative censoring and loss to follow-up by setting $\bar{C}_t=0$ and $\bar{M}_t=0$ and therefore simulate a dataset with no administrative censoring and no drop-out. However, we do not intervene upon S_t which implies that if the simulated outcome for an individual at time t is equal to 1 (death), then there will be no more follow-up at time $t+1$. Consequently, the number of individuals in the simulated datasets $(\tilde{Y},\tilde{\mathbf{L}})^d$ varies with respect to time and intervention.

Step 4: We estimate the expected height-for-age z-score of all survivors under no loss to follow-up and no administrative censoring, $\mathbb{E}(Y_{(\bar{a}^*,t)}|\bar{C}_t=0,\bar{M}_t=0,S_t=1)$, for $t=1,3,6,...$ months: the mean HAZ at time t in the simulated dataset $(\tilde{Y},\tilde{\mathbf{L}})^{d_i}$ from Step 3 equates to the g-computation formula estimate of the expected HAZ under intervention rule d_i.

Step 5 and 6: as in a)

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Supplementary Textbox 2. Steering Groups of IeDEA-SA, IeDEA-WA, and COHERE in EuroCoord.

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