

Figure S1: Study inclusion criteria. This flow chart shows the selection of infants from 499 infants of the EPPICC who started ART within 6 months after birth. Those subsets considered for our study are grey shaded.

Table S1: Baseline study characteristics.

Variables	Total (n=312)		Suppressor (n=276)		Clean (n=188)		Erratic (n=88)	
	n	%	n	%	n	%	n	%
Gender								
Female	187	59.9	164	59.4	112	59.6	52	59.1
Male	125	40.1	112	40.6	76	40.4	36	40.9
Ethnicity								
White	92	29.5	79	28.6	58	30.9	21	23.9
Black	107	34.3	100	36.2	63	33.5	37	42
Other (Asian)	9	2.9	8	2.9	4	2.1	4	4.5
Unknown	104	33.3	89	32.2	63	33.5	26	29.5
Geographical region								
Central and Western Europe	188	60.3	166	60.1	123	65.4	43	48.9
UK/Ireland	98	31.4	94	34.1	56	29.8	38	43.2
Eastern Europe	21	6.7	12	4.3	8	4.3	4	4.5
Thailand	5	1.6	4	1.4	1	0.5	3	3.4
ART regime								
bPI + ≥ 2 NRTI	129	41.3	105	38	79	42	26	29.5
NNRTI + 2 NRTI	116	37.2	109	39.5	66	35.1	43	48.9
NNRTI + 3 NRTI	67	21.5	62	22.5	43	22.9	19	21.6
Age at ART start (in days)								
median [IQR]	83	[38, 121]	82	[34, 121]	79	[31, 120]	83	[43, 121]
Baseline log₁₀(VL) (copies/ml)^{a,b}								
median [IQR]	145	46.5	128	46.4	87	46.3	41	46.6
median [IQR]	5.4	[4.3, 5.9]	5.3	[4.2, 5.9]	5.4	[4.4, 5.9]	5.0	[4.2, 5.9]
Baseline CD4 counts (cells/μl)^{a,b}								
median [IQR]	117	37.5	104	37.7	72	38.3	32	36.4
median [IQR]	1592	[816, 2350]	1600	[868, 2429]	1648	[1016, 2465]	1530	[529, 2163]
Baseline CD4%^{a,b,c}								
median [IQR]	109	34.9	99	35.9	69	36.7	30	34.1
median [IQR]	33	[22.0, 43.0]	33	[22.5, 42.5]	35	[26.0, 46.0]	29.5	[20.3, 34.0]

bPI, boosted protease inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor

^a baseline measurements within 10 days prior to ART start

^b Number of available data is shown

^c CD4% of total lymphocytes

Figure S2: Continued.

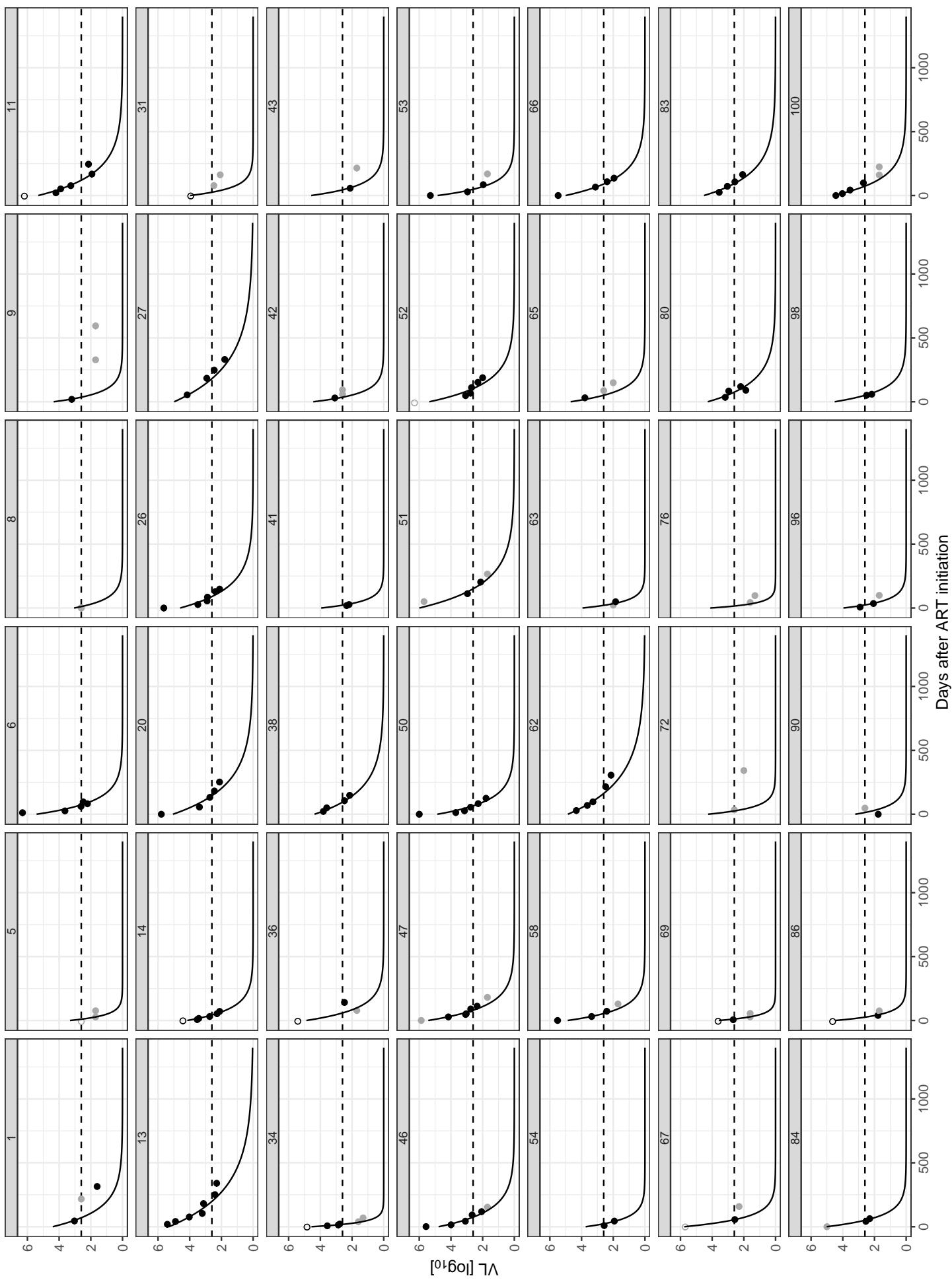
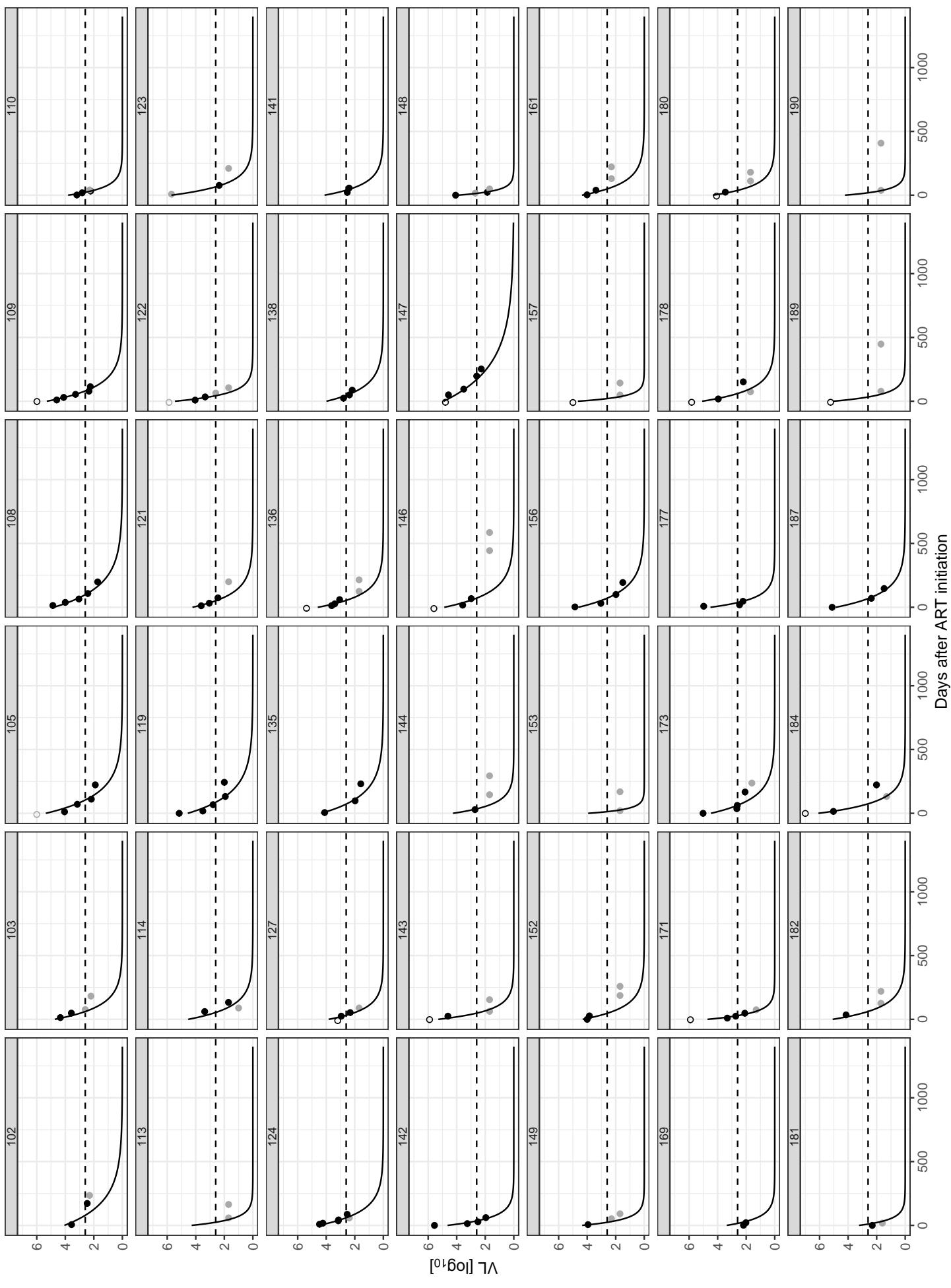


Figure S2: Continued.



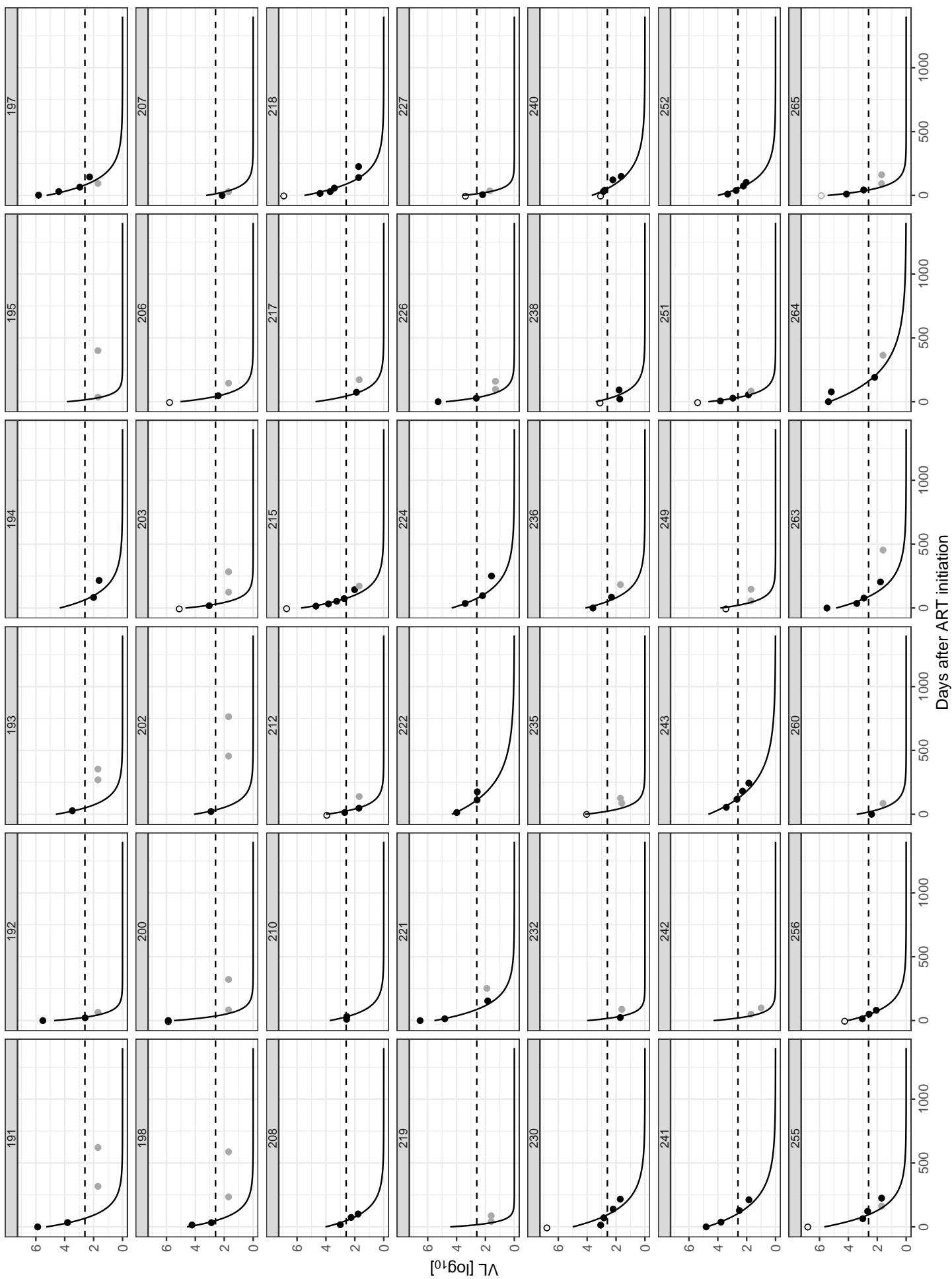
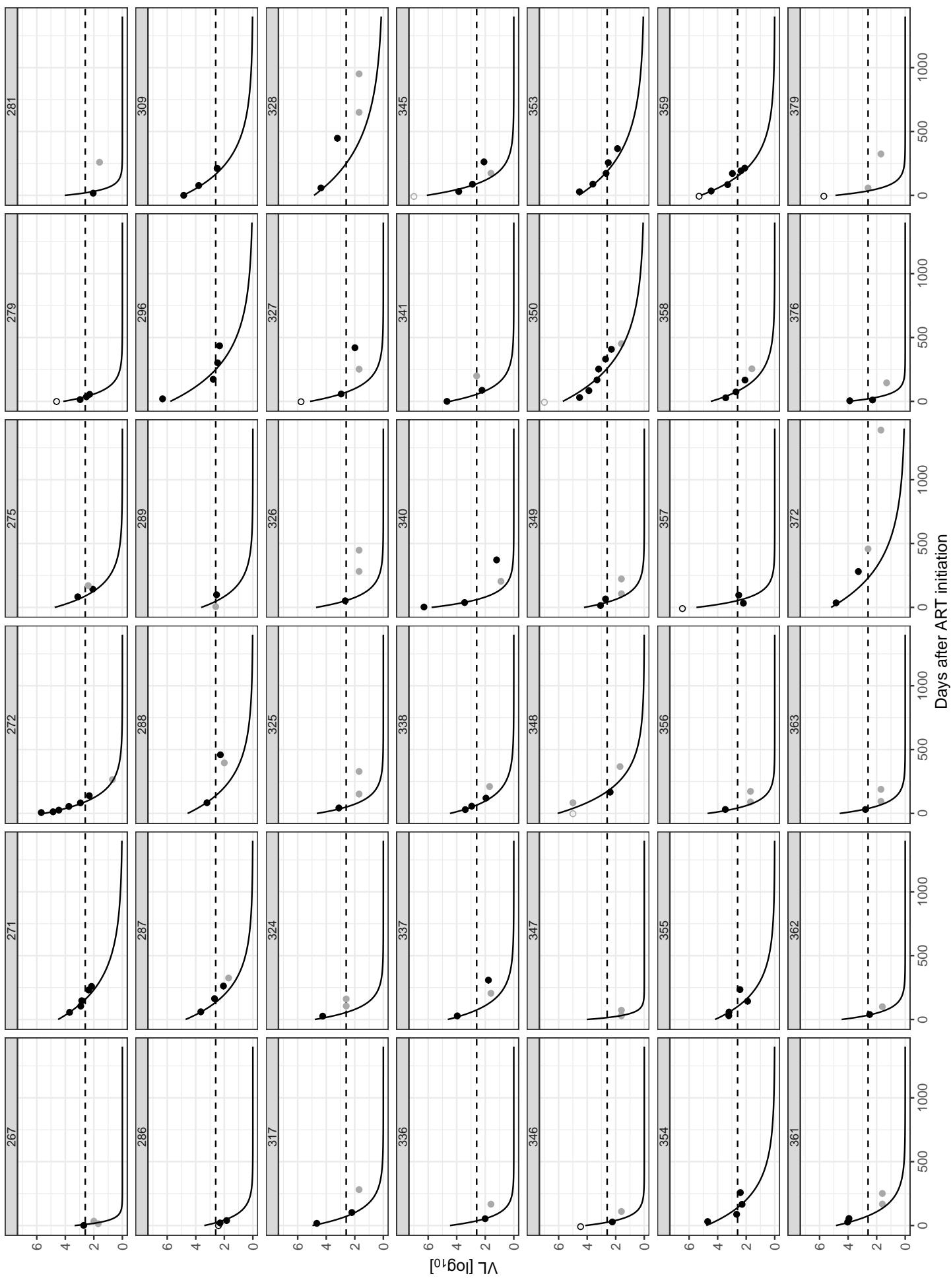


Figure S2: Continued.

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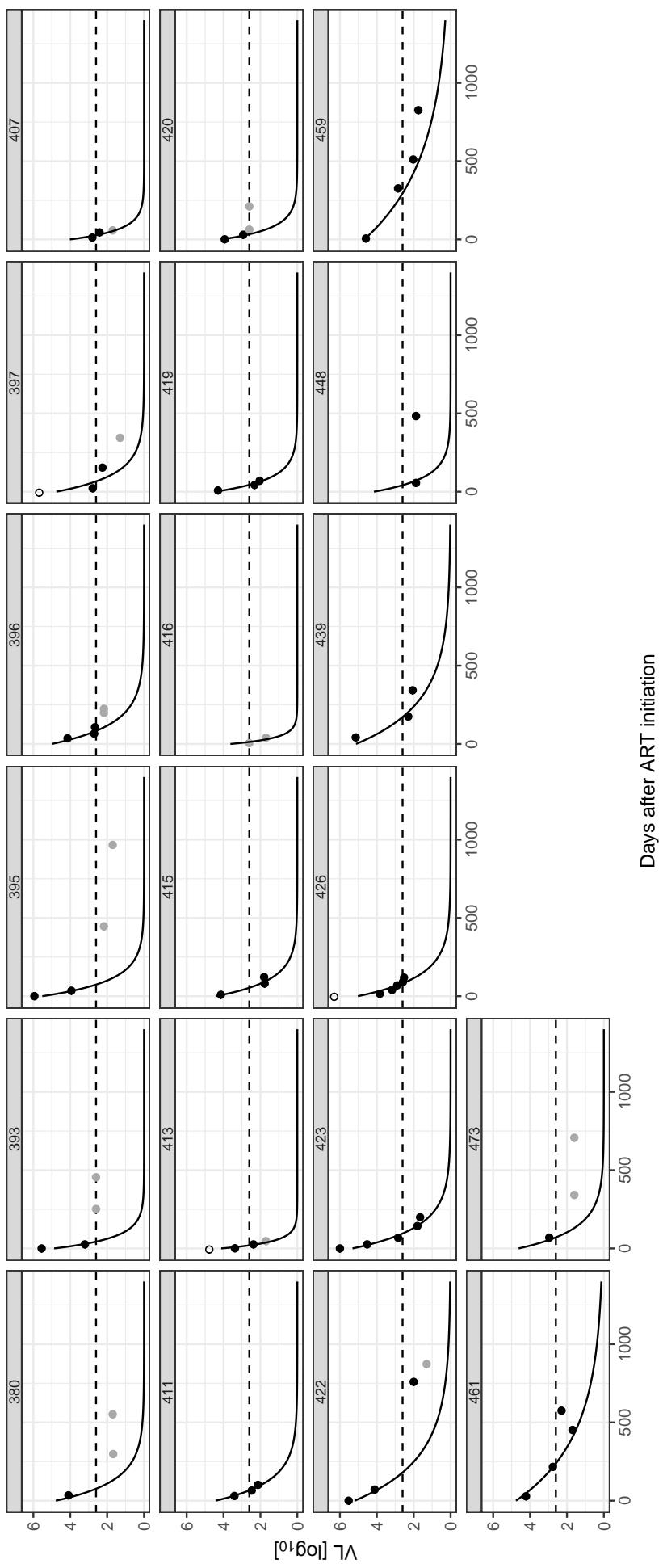


Figure S2: Non-linear mixed effect model fits “clean” VL decay of 188 infants. Each panel represents a different infant labelled with its ID. Dots represent VL measurements: black dots are exact measurements; grey dots are censored and below or above the RNA-assay detection threshold. Open circles indicated that the baseline measurements are extrapolated from the closest measurements within 10 days prior to ART initiation. The solid black lines represent the model fit and the horizontal dashed line marks the threshold criteria for VL suppression (400 RNA copies/ml).

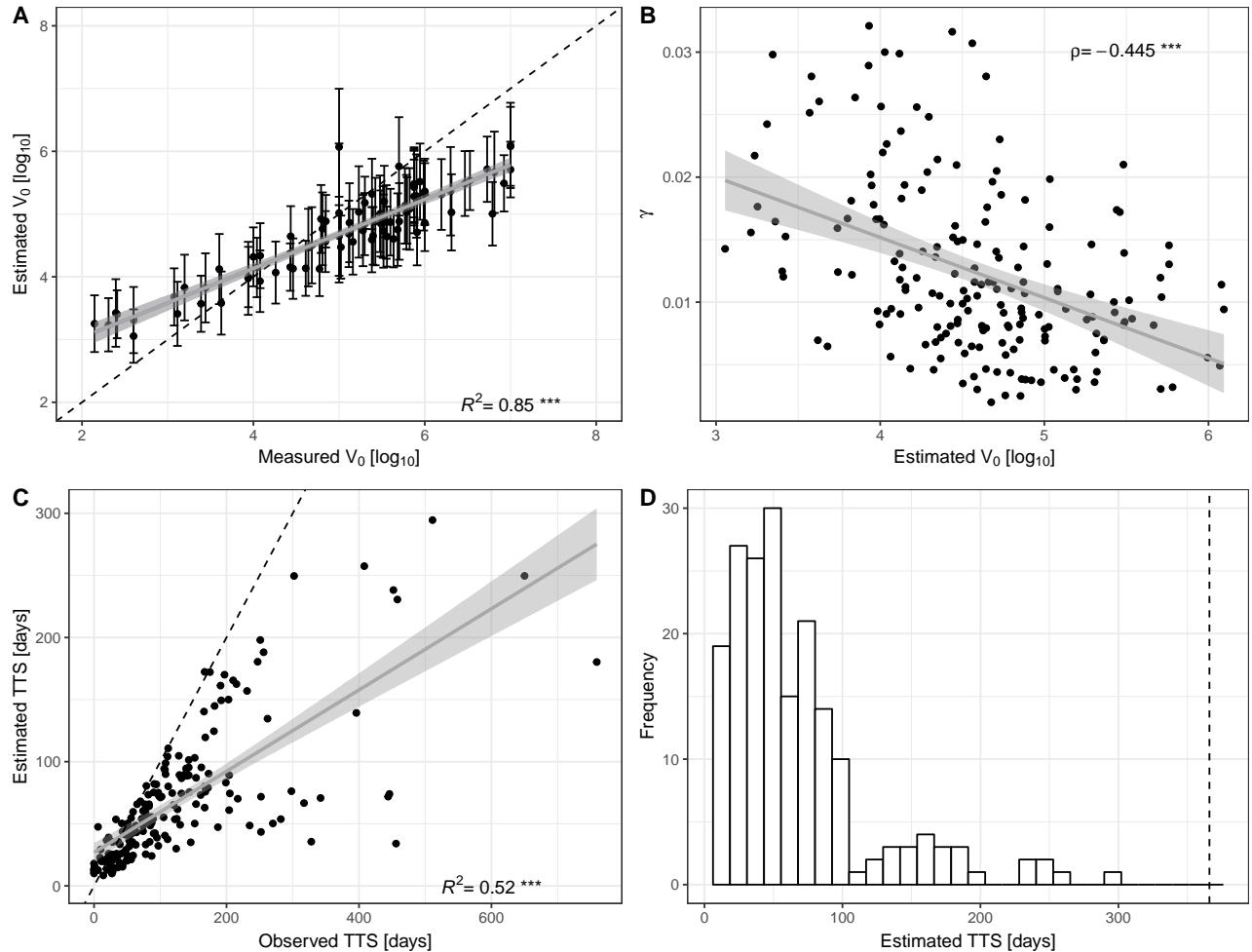


Figure S3: Estimated TTS of “clean” mVL decays is shorter than observed TTS. Sensitivity check of model parameters: Correlation plots between (A) measured and mean estimated baseline viral load V_0 and (C) observed and predicted time to viral suppression (TTS) are shown. The dashed lines present the diagonal. The linear regression lines and the 95% confidence intervals are shown in grey. We performed a Pearson correlation test and the R^2 are given (***, p-value < 0.001). In (A) the error bars represent the standard derivation of the estimated V_0 . In (B) the correlation between the mean estimated V_0 and the slope parameter γ is shown. Spearman’s correlation coefficient ρ is given (***, p-value < 0.001). (D) shows the distribution of the estimated times to viral suppression (TTS) in a histogram. The dashed line represents one year.

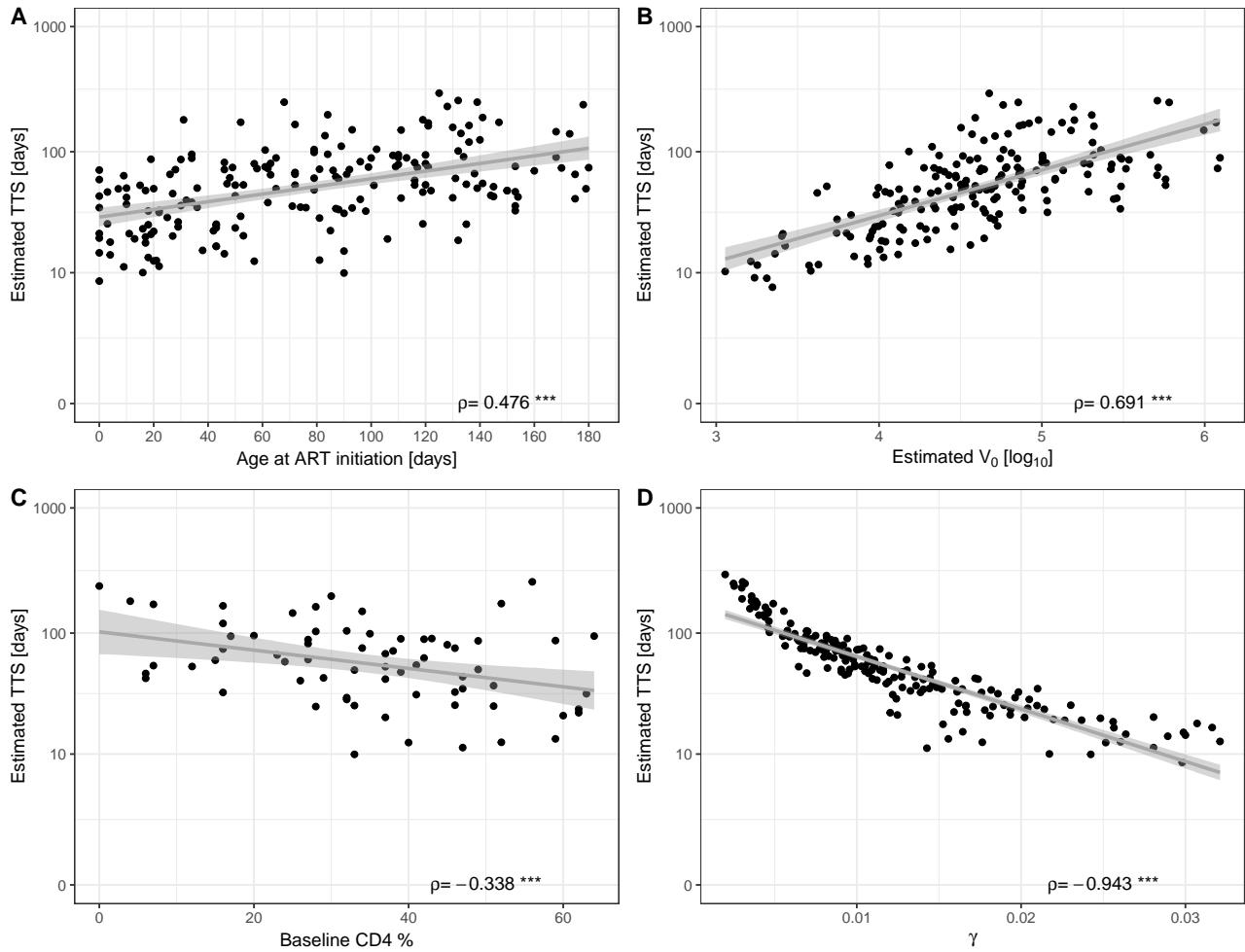


Figure S4: TTS correlates with baseline measurements and model parameters. Plots show estimated time to viral suppression (TTS) as a function of (A) age at ART initiation, (B) mean estimated baseline viral load V_0 , (C) measured baseline CD4% at ART initiation, and (D) the slope parameter γ . The linear regression lines with their 95% confidence intervals are shown in grey. Spearman's correlation tests were performed and correlation coefficients ρ are given (***, p-value < 0.001).

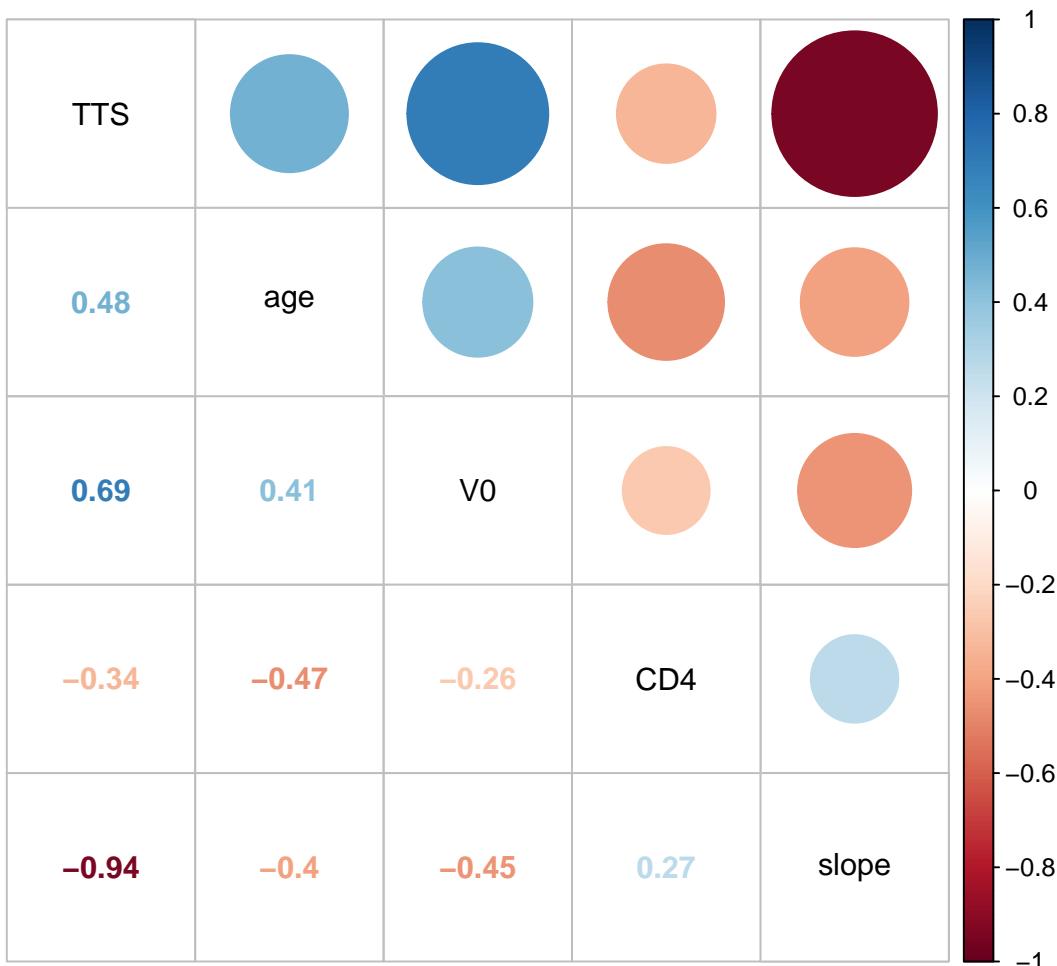


Figure S5: Parameters determining TTS highly intercorrelate. Correlation matrix of time to viral suppression (TTS), age at ART initiation, estimated baseline V_0 , estimated slope parameter γ and measured baseline CD4%. We performed Spearman's correlation tests, the correlation coefficients ρ are given in the lower triangular. The strengths of the correlation are represented by the size of the circle and their colour intensity in the upper triangular. A negative correlation is shown in red, a positive correlation is shown in blue. All correlations have a p-values < 0.05 .

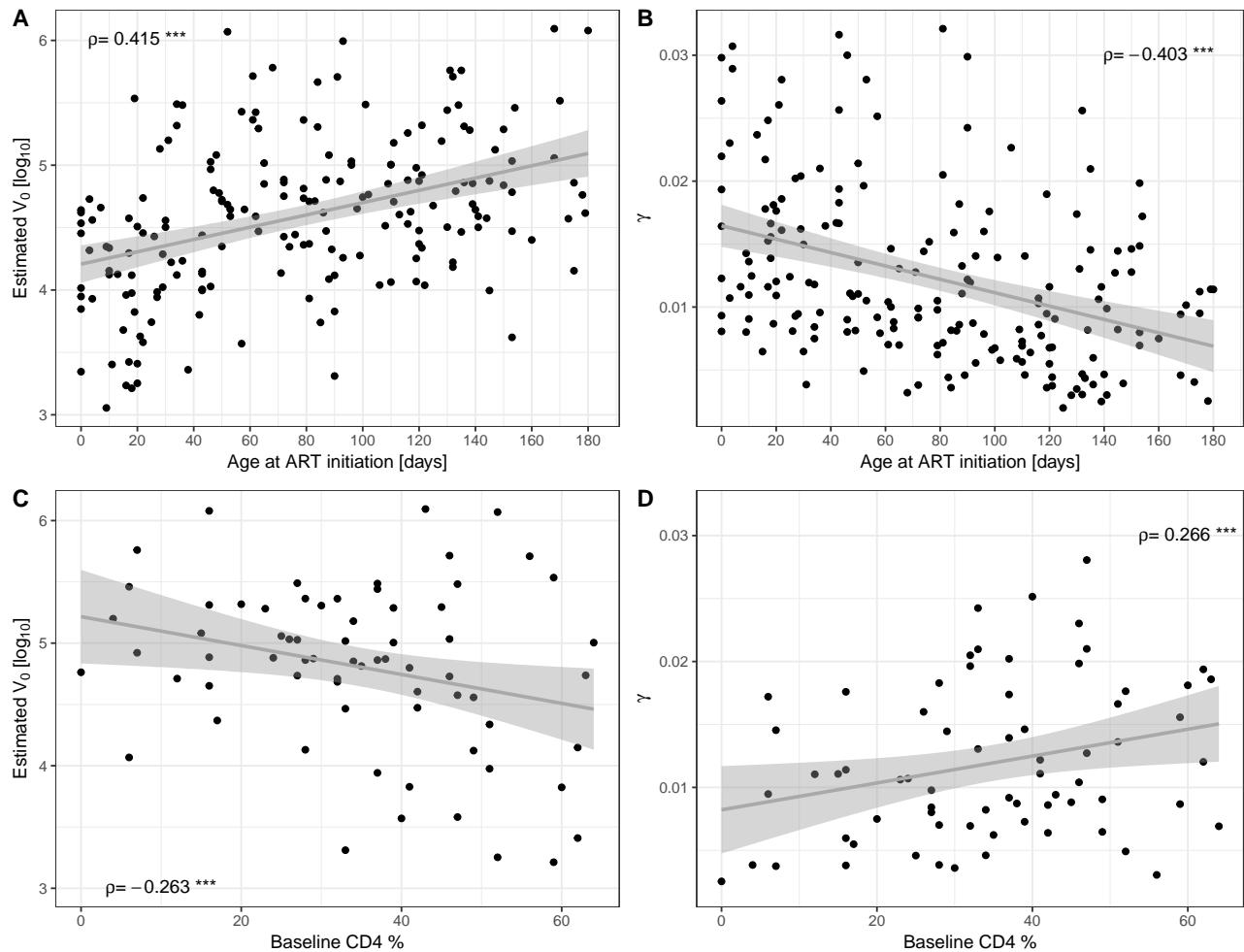


Figure S6: Parameters associated with TTS highly intercorrelate. Panel (A) shows mean estimated V_0 and (B) shows the slope parameter γ for each infant against age at ART initiation. The correlation of measured baseline CD4% with mean estimated V_0 is shown in (C) and with slope parameter γ is shown in (D). The linear regression lines with their 95% confidence interval are shown in grey. Spearman's correlation tests were performed and correlation coefficients ρ are given (***, p-value < 0.001).

APPENDIX

The EPPICC cohorts:

Belgium: Hospital St Pierre Cohort, Brussels: Tessa Goetghebuer, MD, PhD; Marc Hainaut, MD PhD; Evelyne Van der Kelen, Research nurse; Marc Delforge, data manager.

France: French Perinatal Cohort Study/Enquête Périnatale Française, ANRS EPF-CO10. Coordinating center, INSERM U1018, team 4: Josiane Warszawski, Jerome Le Chenadec, Elisa Ramos, Olivia Dialla, Thierry Wack, Corine Laurent, Lamya Ait si Selmi, Isabelle Leymarie, Fazia Ait Benali, Maud Brossard, Leila Boufassa. *Participating sites (hospital name, city, main investigator):* Hôpital Louis Mourier, Colombes, Dr Corinne Floch-Tudal; Groupe Hospitalier Cochin Tarnier Port-Royal, PARIS, Dr Ghislaine Firtion; Centre Hospitalier Intercommunal, Creteil, Dr Isabelle Hau; Centre Hospitalier Général, Villeneuve Saint Georges, Dr Anne Chace; Centre Hospitalier Général-Hôpital Delafontaine, Saint-Denis, Dr Pascal Bolot; Groupe Hospitalier Necker, Paris, Pr Stéphane Blanche; Centre hospitalier Francilien Sud, Corbeil Essonne, Dr Michèle Granier; Hôpital Antoine Béclère, Clamart, Pr Philippe Labrune; Hôpital Jean Verdier, Bondy, Dr Eric Lachassine; Hôpital Trousseau, Paris, Dr Catherine Dollfus; Hôpital Robert Debré, Paris, Dr Martine Levine; Hôpital Bicêtre, Le Kremlin Bicêtre, Dr Corinne Fourcade; Centre Hospitalier Intercommunal, Montreuil, Dr Brigitte Heller- Roussin; Centre Hospitalier Pellegrin, Bordeaux, Dr Camille Runel-Belliard; CHU Paule de Viguier, Toulouse, Dr Joëlle Tricoire; CHU Hôpital de l'Archet II, Nice, Dr Fabrice Monpoux; Groupe Hospitalier de la Timone, Marseille; CHU Hôpital Jean Minjoz, Besancon, Dr Catherine Chirouze; CHU Nantes Hotel Dieu, Nantes, Dr Véronique Reliquet; CHU Caen, Caen, Pr Jacques Brouard; Institut d'Hématologie et Oncologie Pédiatrique, Lyon, Dr Kamila Kebaili; CHU Angers, Angers, Dr Pascale Fialaire; CHR Arnaud de Villeneuve, Montpellier, Dr Muriel Lalande; CHR Jeanne de Flandres, Lille, Dr Françoise Mazingue; Hôpital Civil, Strasbourg, Dr Maria Luisa Partisan.

Germany: German Paediatric & Adolescent HIV Cohort (GEPIC): Dr Christoph Königs, Dr Stephan Schultze-Strasser. *German clinical centers:* Hannover Medical School, Dr. U. Baumann; Pediatric Hospital Krefeld, Dr. T. Niehues; University Hospital Düsseldorf, Dr. J. Neubert; University Hospital Hamburg, Dr. R. Kobbe; Charite Berlin, Dr. C. Feiterna-Sperling; University Hospital Frankfurt, Dr. C. Königs; University Hospital Mannheim, Dr. B. Buchholz; Munich University Hospital, Dr. G. Notheis.

Greece: Greek cohort: Vana Spoulou.

Italy: Italian Register for HIV infection in Children. Coordinators: Maurizio de Martino (Florence), Pier Angelo Tovo (Turin). Participants: Osimani Patrizia (Ancona), Domenico Larovere (Bari), Maurizio Ruggeri (Bergamo), Giacomo Faldella, Francesco Baldi (Bologna) Raffaele Badolato (Brescia), Carlotta Montagnani, Elisabetta Venturini, Catiuscia Lisi (Florence), Antonio Di Biagio, Lucia Taramasso (Genoa), Vania Giacomet, Paola Erba, Susanna Esposito, Rita Lipri, Filippo Salvini, Claudia Tagliabue (Milan), Monica Cellini (Modena), Eugenia Bruzzese, Andrea Lo Vecchio (Naples), Osvaldo Rampon, Daniele Donà (Padua), Amelia Romano (Palermo), Icilio Dodi (Parma), Anna Maccabruni (Pavia), Rita Consolini (Pisa), Stefania Bernardi, Hypolite Tchidjou Kuekou, Orazio Genovese (Rome), Paolina Olmo (Sassari), Letizia Cristiano (Taranto), Antonio Mazza (Trento), Clara Gabiano, Silvia Garazzino (Turin), Antonio Pellegatta (Varese).

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Coordinating Centre: Director: P. Reiss; Data analysis: D.O. Bezemer, A.I. van Sighem, C. Smit, F.W.M.N. Wit, T.S. Boender; Data management and quality control: S. Zaheri, M. Hillebregt, A. de Jong; Data monitoring: D. Bergsma, S. Grivell, A. Jansen, M. Raethke, R. Meijering; Data collection: L. de Groot, M. van den Akker,

Y. Bakker, E. Claessen, A. El Berkaoui, J. Koops, E. Kruijne, C. Lodewijk, L. Munjishvili, B. Peeck, C. Ree, R. Regtop, Y. Ruijs, T. Rutkens, M. Schoorl, A. Timmerman, E. Tuijn, L. Veenenberg, S. van der Vliet, A. Wisse, T. Woudstra; Patient registration: B. Tuk.

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Portugal: Centro Hospitalar do Porto: Laura Marques, Carla Teixeira, Alexandre Fernandes. Hospital de Santa Maria/CHLN: Filipa Prata.

Romania: "Victor Babes" Hospital Cohort, Bucharest: Dr Luminita Ene.

Russia: Federal State-owned Institution "Republican Clinical Infectious Diseases Hospital" of the Ministry of Health of the Russian Federation, St Petersburg: Liubov Okhonskaia, Evgeny Voronin, Milana Miloenko, Svetlana Labutina.

Spain: CoRISPE-cat, Catalonia: Financial support for CoRISPE-cat was provided by the Instituto de Salud Carlos III through the Red Temática de Investigación Cooperativa en Sida. Members: Hospital Universitari Vall d'Hebron, Barcelona (Pere Soler-Palacín, María Antoinette Frick and Santiago Pérez-Hoyos (statistician)), Hospital Universitari del Mar, Barcelona (Antonio Mur, Núria López), Hospital Universitari Germans Trias i Pujol, Badalona (María Méndez), Hospital Universitari Josep Trueta, Girona (Lluís Mayol), Hospital Universitari Arnau de Vilanova, Lleida (Teresa Vallmanya), Hospital Universitari Joan XXIII, Tarragona (Olga Calavia), Consorci Sanitari del Maresme, Mataró (Lourdes García), Hospital General de Granollers (Maite Coll), Corporació Sanitària Parc Taulí, Sabadell (Valentí Pineda), Hospital Universitari Sant Joan, Reus (Neus Rius), Fundació Althaia, Manresa (Núria Rovira), Hospital Son Espases, Mallorca (Joaquín Dueñas) and Hospital Sant Joan de Déu, Esplugues (Clàudia Fortuny, Antoni Noguera-Julian).

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Funding: This work has been partially funded by the Fundación para la Investigación y Prevención de SIDA en España (FIPSE) (FIPSE 3608229/09 , FIPSE 240800/09, FIPSE 361910/10), Red Temática de Investigación en SIDA (RED RIS) supported by Instituto de Salud Carlos III (ISCIII) (RD12/0017/0035 and RD12/0017/0037), project as part of the Plan R+D+I and cofinanced by ISCIII- Subdirección General de Evaluación and Fondo Europeo de Desarrollo Regional (FEDER), Mutua Madrileña 2012/0077, Gilead Fellowship 2013/0071, FIS PI15/00694, CoRISPe (RED RIS RD06/0006/0035 y RD06/0006/0021).

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Funding: the Swiss HIV Cohort Study is supported by the Swiss National Science Foundation (grant #148522), and by the SHCS research foundation.

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Funding acknowledgement: PENTA Foundation.

UK & Ireland: Collaborative HIV Paediatric Study (CHIPS): CHIPS is funded by the NHS (London Specialised Commissioning Group) and has received additional support from Bristol-Myers Squibb, Boehringer Ingelheim, GlaxoSmithKline, Roche, Abbott, and Gilead Sciences. The MRC Clinical Trials Unit at UCL is supported by the Medical Research Council (<https://www.mrc.ac.uk>) programme number MC_UU_12023/26. CHIPS Steering Committee: Hermione Lyall, Alasdair Bamford, Karina Butler, Katja Doerholt, Caroline Foster, Nigel Klein, Paddy McMaster, Katia Prime, Andrew Riordan, Fiona Shackley, Delane Shingadia, Sharon Storey, Gareth Tudor-Williams, Anna Turkova, Steve Welch. MRC Clinical Trials Unit: Intira Jeannie Collins, Claire Cook, Siobhan Crichton, Donna Dobson, Keith Fairbrother, Diana M. Gibb, Lynda Harper, Ali Judd, Marthe Le Prevost, Nadine Van Looy.

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