

Episodes of HIV viremia and the risk of non-AIDS events among successfully treated patients

Shuangjie Zhang
Stichting HIV Monitoring

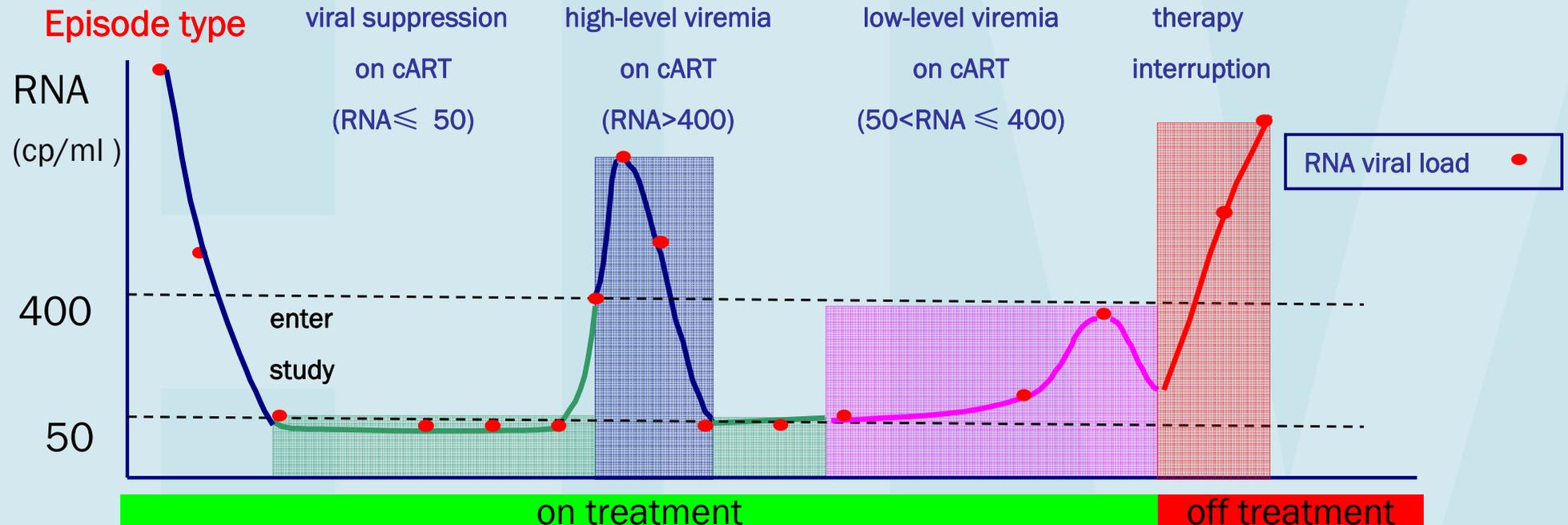
Background and Aim

- Mortality rate has decreased and life expectancy has improved significantly with cART.
- With prolonged survival, mortality is increasingly likely due to non-AIDS causes.
- The occurrence of non-AIDS events appears to be related to the level of immunodeficiency.
- Aim: to investigate the effect of **episodes of viremia (on cART)**, on top of CD4 count, on **non-AIDS events** in successfully treated patients.

Patient selection and endpoint definition

- 6440 patients were selected from the ATHENA cohort, if
 - therapy-naïve
 - treated successfully : RNA \leq 50 cp/ml before 48w of cART
 - no non-AIDS events diagnosed before
 - censored at one year with long interruption
- four non-AIDS endpoints (fatal and non-fatal) were considered:
 - cardiovascular disease (102 events)
myocardial infarction, stroke, invasive coronary procedures
 - renal disease (72 events)
acute and chronic renal failure
 - liver disease (70 events)
fibrosis, cirrhosis
 - overall
combination of non-AIDS events abovementioned

Episode definition and statistical model

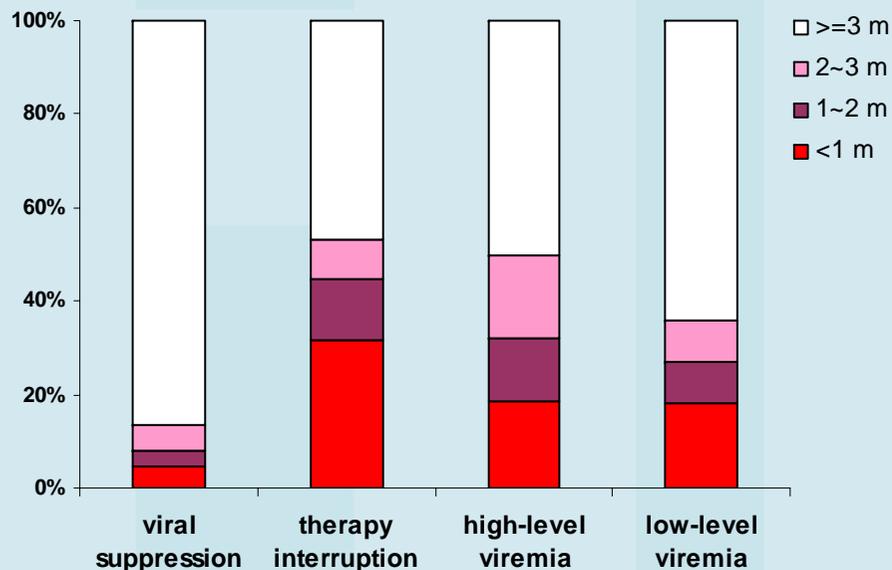


- The effect of **episodes of viremia and CD4**, as time-updated variables, on **non-AIDS events** was studied with time-discrete Cox regression model.
- Both univariate and multivariate analysis were conducted. The latter was adjusted for relevant covariates:
 - demographic (age, gender)
 - clinical (diabetes, HBV/HCV co-infection, CDC Stage)
 - lifestyle (smoking, alcohol abuse)
 - transmission risk group

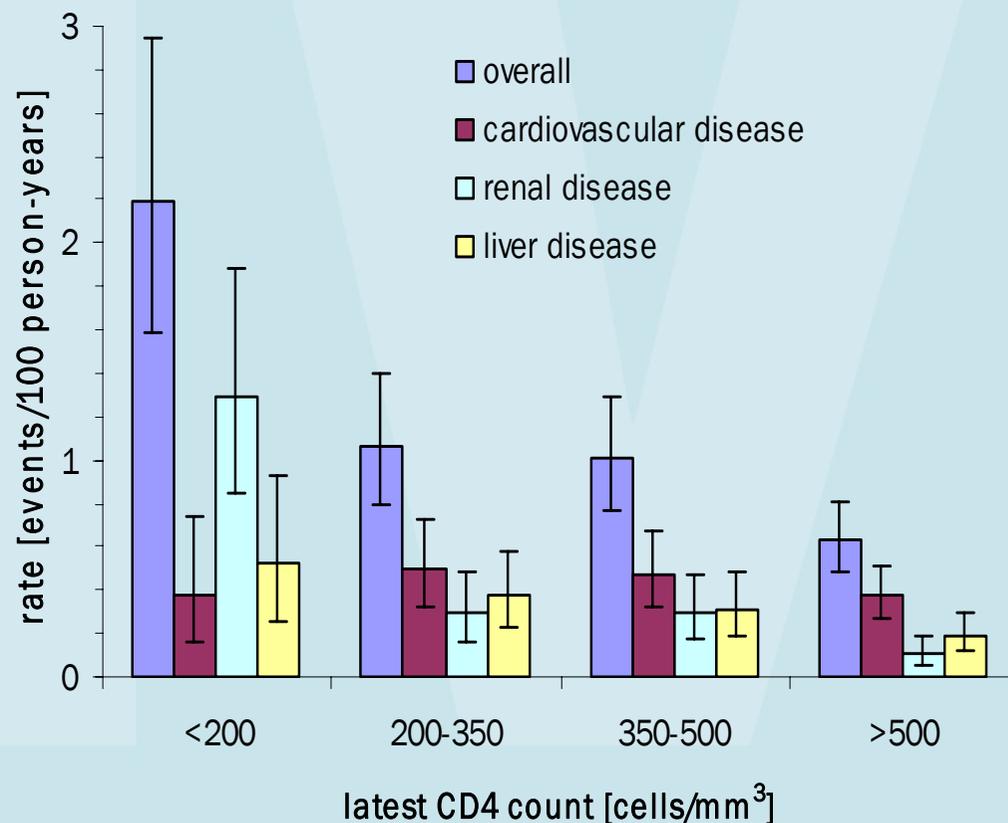
characteristics of episodes

non-AIDS rate across CD4 count

duration distribution of 4 types of episodes

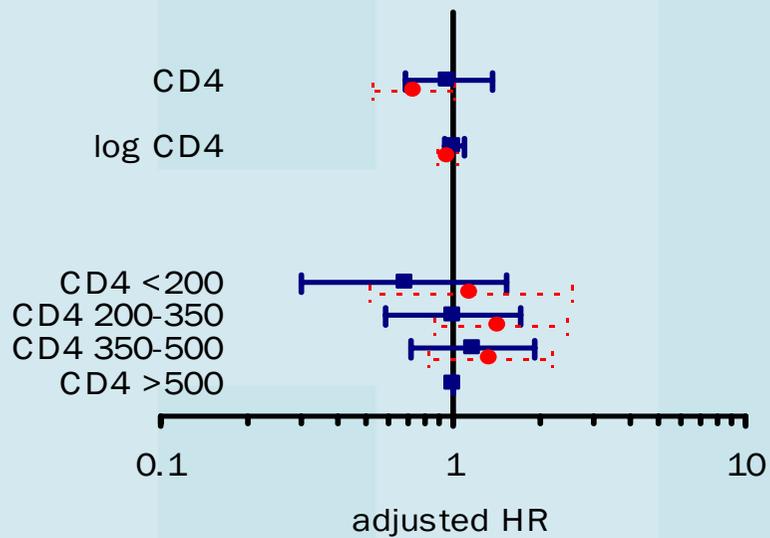


	viral suppression	therapy interruption	high-level viremia	low-level viremia
duration (median)	15.3	2.5	4.3	3.0
<1 m	4.7%	31.7%	18.4%	18.2%
Frequency	10672	1629	3793	1269
	(61.5%)	(9.4%)	(21.8%)	(7.3%)

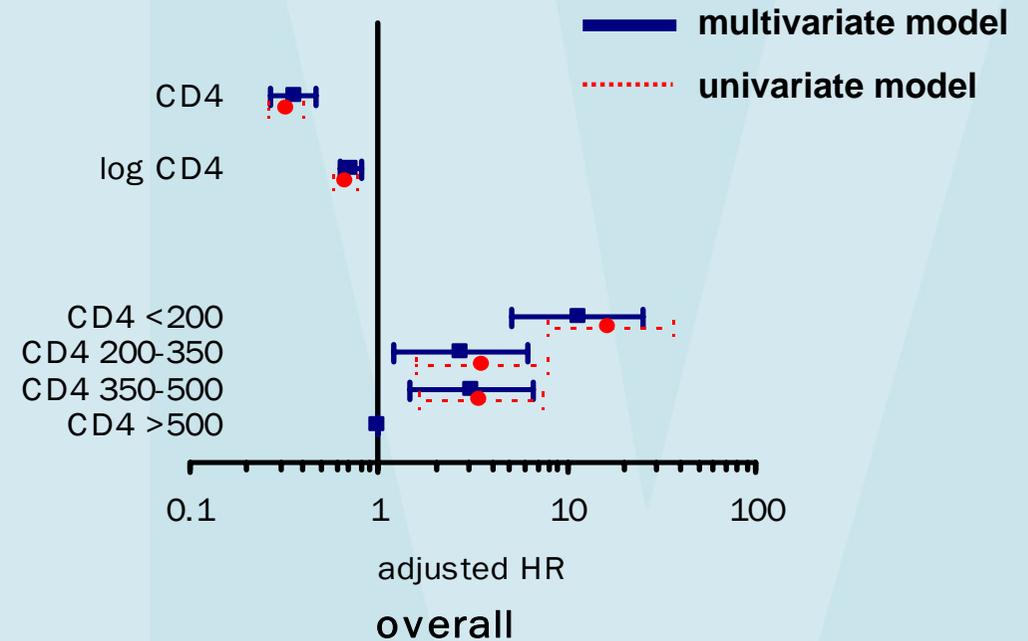


CD4 and risk of non-AIDS events

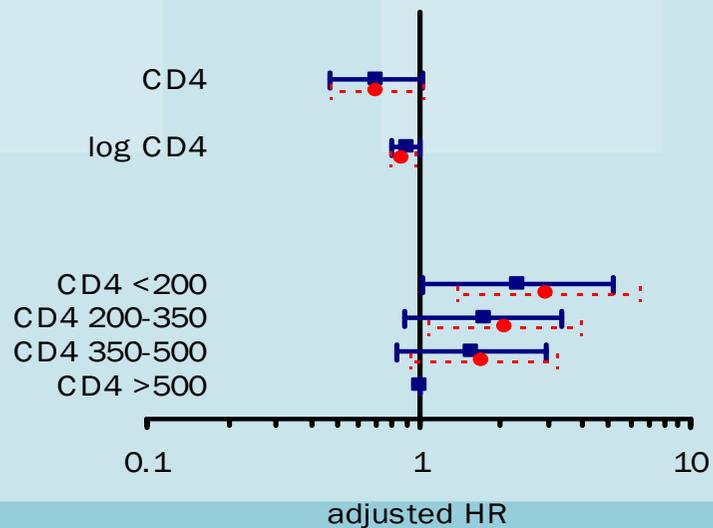
cardiovascular disease



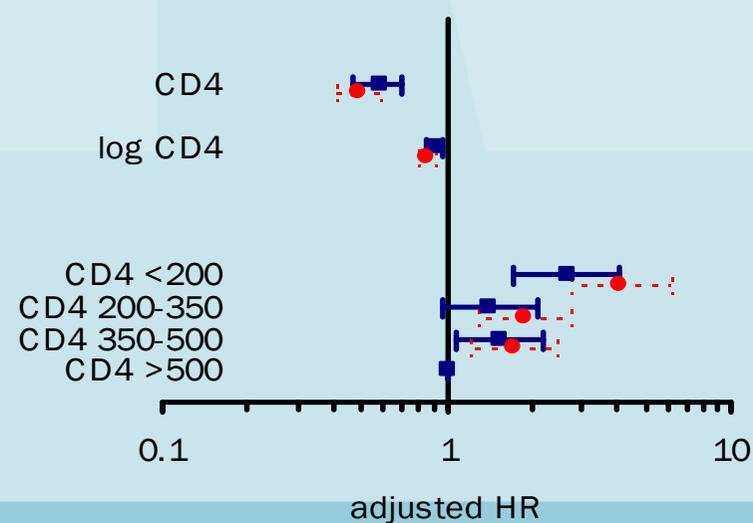
renal disease



liver disease

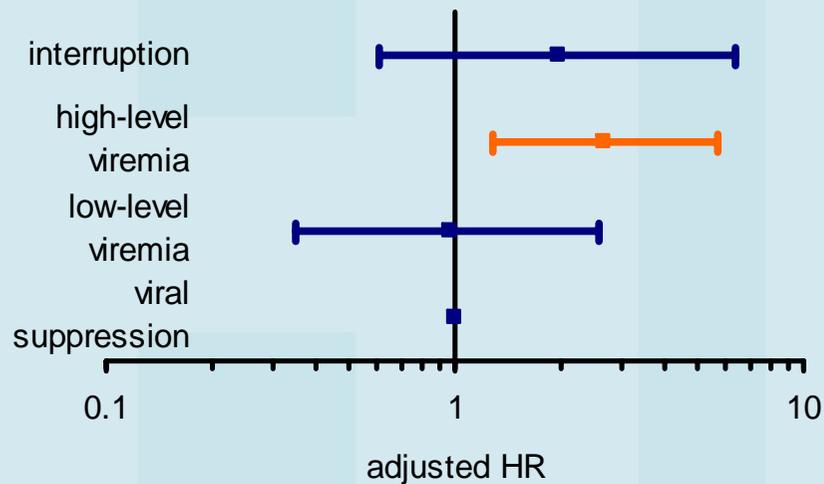


overall

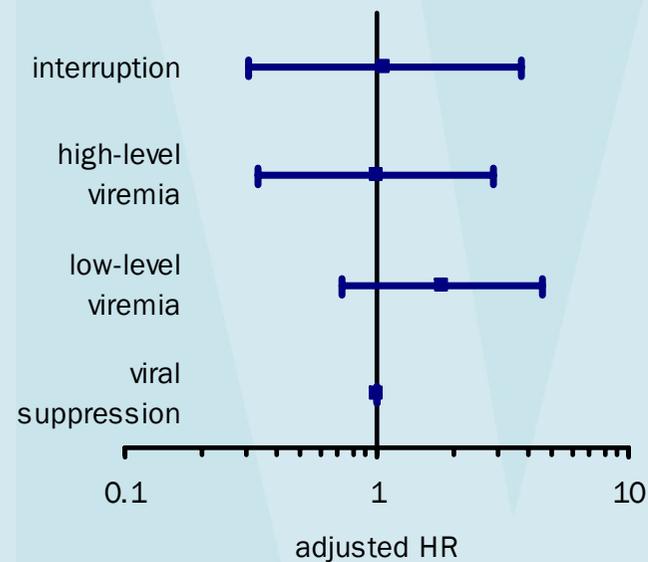


Viremia and risk of non-AIDS events

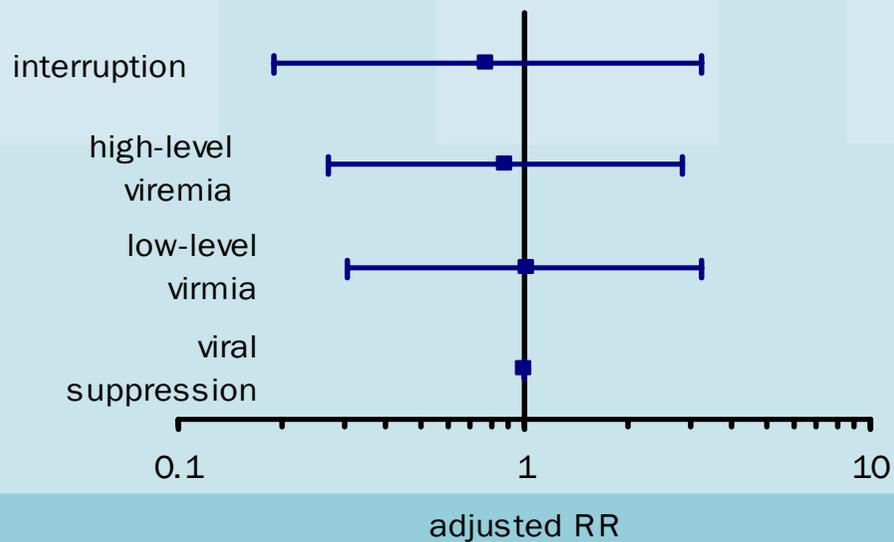
cardiovascular disease



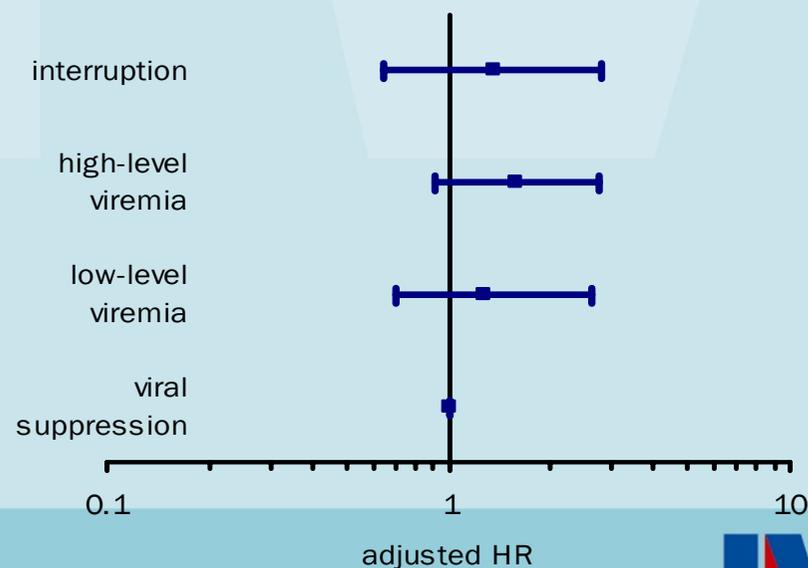
renal disease



liver disease



overall



Conclusions

- Episodes of high-level viremia were associated with cardiovascular disease.
- Lower CD4 counts were associated with an increased risk of renal and liver disease.
- However, the power to detect an association of viremia may have been small given the limited amount of follow-up time spent in episodes of viremia.
- The extent to which RNA levels affect the risk of non-AIDS events could be investigated further in cohorts of untreated patients.

Acknowledgements

Treating physicians (*Site coordinating physicians)

Academisch Medisch Centrum bij de Universiteit van Amsterdam - Amsterdam: Dr. J.M. Prins*, Drs. J.C. Bos, Dr. J.K.M. Eeftinck-Schattenkerk, Dr. S.E. Geerlings, Dr. M.H. Godfried, Prof. dr. J.M.A. Lange, Dr. J.T.M. van der Meer, Dr. F.J.B. Nellen, Drs. D.P. Olszyna, Dr. T. van der Poll, Prof. dr. P. Reiss, Drs. S.U.C. Sankatsing, Drs. R. Steingrover, Drs. M. van der Valk, Drs. J.N. Vermeulen, Drs. S.M.E. Vrouwenraets, Dr. M. van Vugt, Dr. F.W.M.N. Wit. Academisch Ziekenhuis Maastricht - Maastricht: Dr. G. Schreij*, Dr. S. van der Geest, Dr. A. Oude Lashof, Dr. S. Lowe, Dr. A. Verbon. Catharina Ziekenhuis - Eindhoven: Dr. B. Bravenboer*, Drs. M.J.H. Pronk. Emma Kinderziekenhuis - AMC Amsterdam: Prof. dr. T.W. Kuijpers, Drs. D. Pajkt, Dr. H.J. Scherpbier. Erasmus MC - Rotterdam: Dr. M.E. van der Ende*, Drs. H. Bax, Drs. M. van der Feltz, Dr. L.B.S. Gelinck, Drs. Mendoca de Melo (until September 1, 2008), Dr. J.L. Nouwen, Dr. B.J.A. Rijnders, Dr. E.D. de Ruiter, Dr. L. Slobbe, Drs. C.A.M. Schurink, Dr. T.E.M.S. de Vries. Erasmus MC - Sophia - Rotterdam: Dr. G. Driessen, Dr. M. van der Flier, Dr. N.G. Hartwig. Flevoziekenhuis - Almere: Dr. J. Branger. Haga Ziekenhuis, locatie Leyenburg - Den Haag: Dr. R.H. Kauffmann*, Drs. K. Pogány (until August 1, 2008), Dr. E.F. Schippers (from May 1, 2008). Isala Klinieken - Zwolle: Dr. P.H.P. Groeneveld*, Dr. M.A. Alleman. Kennemer Gasthuis - Haarlem: Prof. dr. R.W. ten Kate*, Dr. R. Soetekouw. Leids Universitair Medisch Centrum - Leiden: Dr. F.P. Kroon*, Dr. S.M. Arend, Drs. M.G.J. de Boer, Prof. dr. P.J. van den Broek, Prof. dr. J.T. van Dissel, Drs. C. van Nieuwkoop. Maasstadziekenhuis - locatie Clara - Rotterdam: Dr. J.G. den Hollander*. Medisch Centrum Alkmaar - Alkmaar: Dr. W. Bronsveld*. Medisch Centrum Haaglanden -locatie Westeinde - Den Haag: Dr. R. Vriesendorp*, Dr. F.J.F. Jeurissen, Dr. E.M.S. Leyten. Medisch Centrum Leeuwarden - Leeuwarden: Dr. D. van Houte*, Dr. M.B. Polée. Medisch Spectrum Twente - Enschede: Dr. C.H.H. ten Napel*, Dr. G.J. Kootstra. Onze Lieve Vrouwe Gasthuis - Amsterdam: Prof. dr. K. Brinkman*, Drs. G.E.L. van den Berk, Dr. W.L. Blok, Dr. P.H.J. Frissen, Drs. W.E.M. Schouten. St. Medisch Centrum Jan van Goyen - Amsterdam: Dr. A. van Eeden*, Dr. D.W.M. Verhagen. Slotervaart Ziekenhuis - Amsterdam: Dr. J.W. Mulder*, Dr. E.C.M. van Gorp, Dr. A.T.A. Mairuhu, Drs. R. Steingrover, Dr. J. Wagenaar. St. Elisabeth Ziekenhuis - Tilburg: Dr. J.R. Juttman*, Dr. M.E.E. van Kasteren. St. Lucas Andreas Ziekenhuis - Amsterdam: Dr. J. Veenstra*, Dr. W.L.E. Vasmeel. Universitair Medisch Centrum St. Radboud - Nijmegen: Dr. P.P. Koopmans*, Drs. A.M. Brouwer, Dr. A.S.M. Dofferhoff, Prof. dr. R. de Groot, Drs. H.J.M. ter Hofstede, Dr. M. Keuter, Dr. A.J.A.M. van der Ven. Universitair Medisch Centrum Groningen - Groningen: Dr. H.G. Sprenger*, Dr. S. van Assen, Dr. J.T.M. van Leeuwen, Dr. C.J. Stek. Universitair Medisch Centrum Groningen - Beatrix Kliniek - Groningen: Dr. R. Doedens, Dr. E.H. Scholvinck. Universitair Medisch Centrum Utrecht - Utrecht: Prof. dr. I.M. Hoepelman*, Dr. M.M.E. Schneider, Prof. dr. M.J.M. Bonten, Dr. P.M. Ellerbroek, Drs. C.A.J.J. Jaspers, Drs. L.J. Maarschalk- Ellerbroek, Dr. J.J. Oosterheert, Dr. E.J.G. Peters, Dr. T. Mudrikova, Drs. M.W.M. Wassenberg, Dr. S. Weijer. Wilhelmina Kinderziekenhuis - UMC Utrecht: Dr. S.P.M. Geelen, Dr. T.F.W. Wolfs. VU Medisch Centrum - Amsterdam: Prof. dr. S.A. Danner*, Dr. M.A. van Agtmael, Drs. W.F.W. Bierman, Drs. F.A.P. Claessen, Drs. M.E. Hillebrand, Drs. E.V. de Jong, Drs. W. Kortmann, Dr. R.M. Perenboom, Drs. E.A. bij de Vaate. Ziekenhuis Rijnstate - Arnhem: Dr. C. Richter*, Drs. J. van der Berg, Dr. E.H. Gisolf. Ziekenhuis Walcheren - Vlissingen: Dr. A.A. Tanis*. St. Elisabeth Hospitaal/Stichting Rode Kruis Bloedbank - Willemstad, Curaçao: Dr. A.J. Duits, Dr. K. Winkel. Virologists: Academisch Medisch Centrum bij de Universiteit van Amsterdam - Amsterdam: Dr. N.K.T. Back, Dr. M.E.G. Bakker, Dr. H.L. Zaaijer. Prof. dr. B. Berkhout, Dr. S. Jurriaans. CLB Stichting Sanquin Bloedvoorziening - Amsterdam: Dr. Th. Cuijpers. Onze Lieve Vrouwe Gasthuis - Amsterdam: Dr. P.J.G.M. Rietra, Dr. K.J. Roozendaal; Slotervaart Ziekenhuis - Amsterdam: Drs. W. Pauw, Drs. P.H.M. Smits, Dr. A.P. van Zanten. VU Medisch Centrum - Amsterdam: Dr. B.M.E. von Blomberg, Dr. A. Pettersson, Dr. P. Savelkoul; Ziekenhuis Rijnstate - Arnhem: Dr. C.M.A. Swanink. Haga, ziekenhuis, locatie Leyenburg - Den Haag: Dr. P.F.H. Franck, Dr. A.S. Lampe; Medisch Centrum Haaglanden, locatie Westeinde - Den Haag: Drs. C.L. Jansen.; Streeklaboratorium Twente - Enschede: Dr. R. Hendriks. Streeklaboratorium Groningen - Groningen: Dr. C.A. Benne; Streeklaboratorium Volksgezondheid Kennemerland - Haarlem: Dr. J. Schirm, Dr. D. Veenendaal. Laboratorium voor de Volksgezondheid in Friesland - Leeuwarden: Dr. H. Storm, Drs. J. Weel, Drs. J.H. van Zeijl; Leids Universitair Medisch Centrum - Leiden: Dr. H.C.J. Claas, Prof. dr. A.C.M. Kroes. Academisch Ziekenhuis Maastricht - Maastricht: Prof. dr. C.A.M.V.A. Bruggeman, Drs. V.J. Goossens. Universitair Medisch Centrum St. Radboud - Nijmegen: Prof. dr. J.M.D. Galama, Dr. W.J.G. Melchers, Dr. Verduyn-Lunel. Erasmus MC - Rotterdam: Dr. G.J.J. van Doornum, Dr. H.G.M. Niesters, Prof. dr. A.D.M.E. Osterhaus, Dr. M. Schutten. St. Elisabeth Ziekenhuis - Tilburg: Dr. A.G.M. Buiting. Universitair Medisch Centrum Utrecht - Utrecht: Dr. C.A.B. Boucher, Dr. E. Boel, Dr. R. Schuurman. Catharina Ziekenhuis - Eindhoven: Dr. A.F. Jansz, Drs. M. Wulf; Pharmacologists: Medisch Centrum Alkmaar - Alkmaar: Dr. A. Veldkamp. Slotervaart Ziekenhuis - Amsterdam: Prof. dr. J.H. Beijnen, Dr. A.D.R. Huitema. Universitair Medisch Centrum St. Radboud - Nijmegen: Dr. D.M. Burger. Academisch Medisch Centrum bij de Universiteit van Amsterdam - Amsterdam: Drs. H.J.M. van Kan.

HIV Monitoring Foundation

Ard van Sighem

Luuk Gras

Colette Smit

Frank de Wolf

Academic Medical Centre

Peter Reiss

Jan Prins

HAGA Hospital

Robert Kauffmann

Rijnstate Hospital

Clemens Richter