

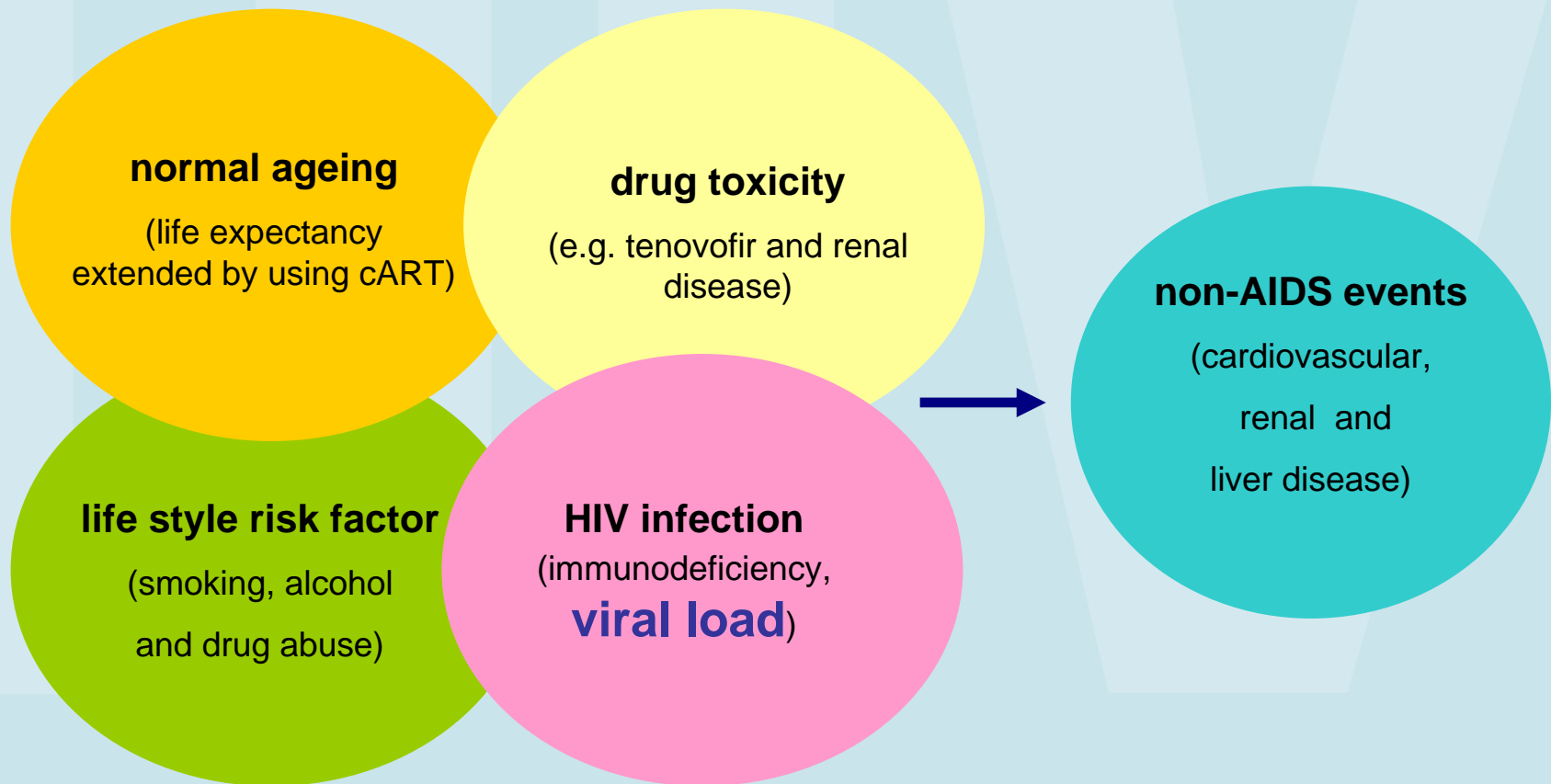
Limited impact of episodes of viremia on the risk of non-AIDS events among successfully treated patients

Shuangjie Zhang
HIV Monitoring Foundation

Background

- In the era of combination antiretroviral therapy (cART), AIDS related disease and death has declined greatly.
- With prolonged life expectancy, non-AIDS related disease and death are observed at an increasing rate in HIV-infected patients.
- Viremia, as a risk factor of AIDS related disease, could be observed even in patients who initially reach treatment success.

Background and aim



Aim: To investigate the impact of **episodes of viremia on treatment and treatment interruptions** on the risk of **non-AIDS events** in initially successfully treated patients.

Methods

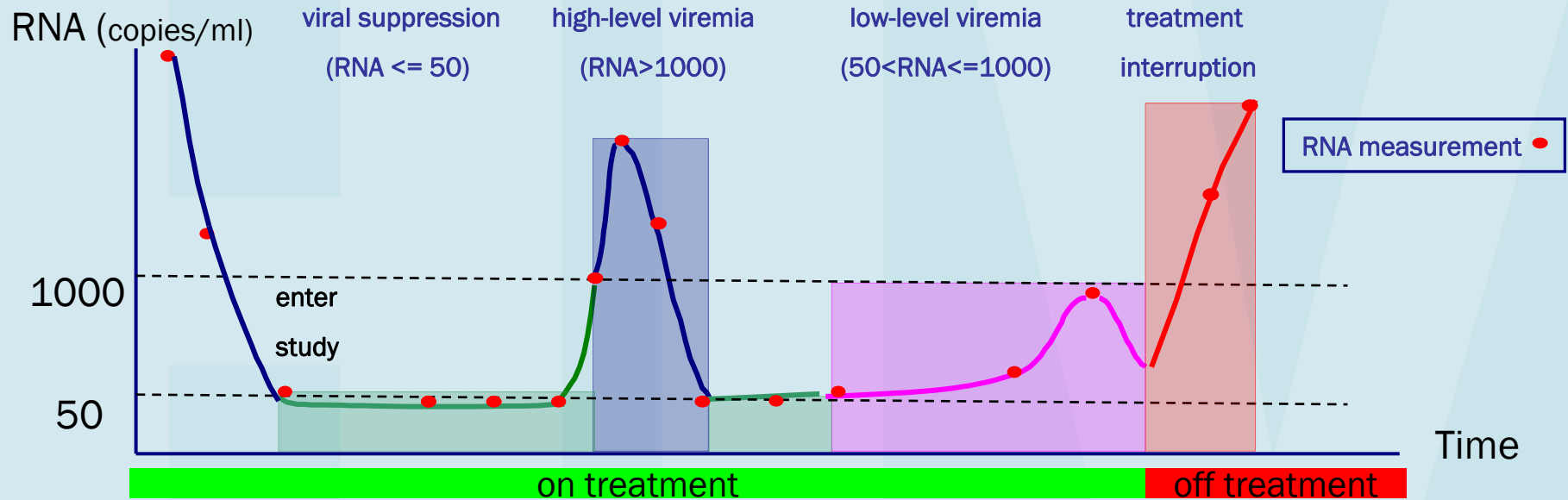
- 5891 patients, 23621 person-years of follow-up (Feb 2009):
 - selected from the ATHENA national observational cohort in the Netherlands.
 - therapy-naïve at start of cART.
 - successfully treated: achieved RNA ≤ 50 copies/ml before 48w of cART.
 - exclude patients who had a non-AIDS event before initial success.
- Three non-AIDS (fatal and nonfatal) endpoints were considered:
 - cardiovascular disease (96 events)
myocardial infarction, stroke, invasive coronary procedures
 - renal disease (64 events)
renal failure, dialysis, kidney transplantation
 - liver-related events (68 events)
fibrosis, cirrhosis, liver carcinoma

Characteristics at study entry

N=5442		N / Median	% / IQR
age		38.9	32.4 - 46.0
gender, male		4430	75.2
CDC Stage C		1584	26.9
transmission	MSM	3027	51.4
	Heterosexual	2238	38.0
	IVD	155	2.6
hepatitis	C	316	5.4
	B	462	7.8
diabetes		128	2.2
current/ever smoking*		1924	32.7
CD4 (cells/ml)	at start of cART	200	90 - 290
	at study entry	330	210 - 460
RNA (log ₁₀ copies/ml)	at start of cART	5.0	4.5 - 5.3
follow-up time (years)		3.7	1.6 - 6.1

*43.7% patients with smoking history missing

Statistical models



- The association between each of the **4 types of episodes** and **non-AIDS events** was studied with Poisson regression models.
- Two modelling approaches (episodes included as time-updated variables):
 - most recent episode was included as a dichotomous variable.
 - cumulative follow-up time spent in each type of episode as a continuous variable.
- All models adjusted for age, gender, diabetes, smoking, alcohol abuse, HBV/HCV co-infection, transmission risk group, CDC stage, and time-updated CD4.

Characteristics of Episodes in the Population

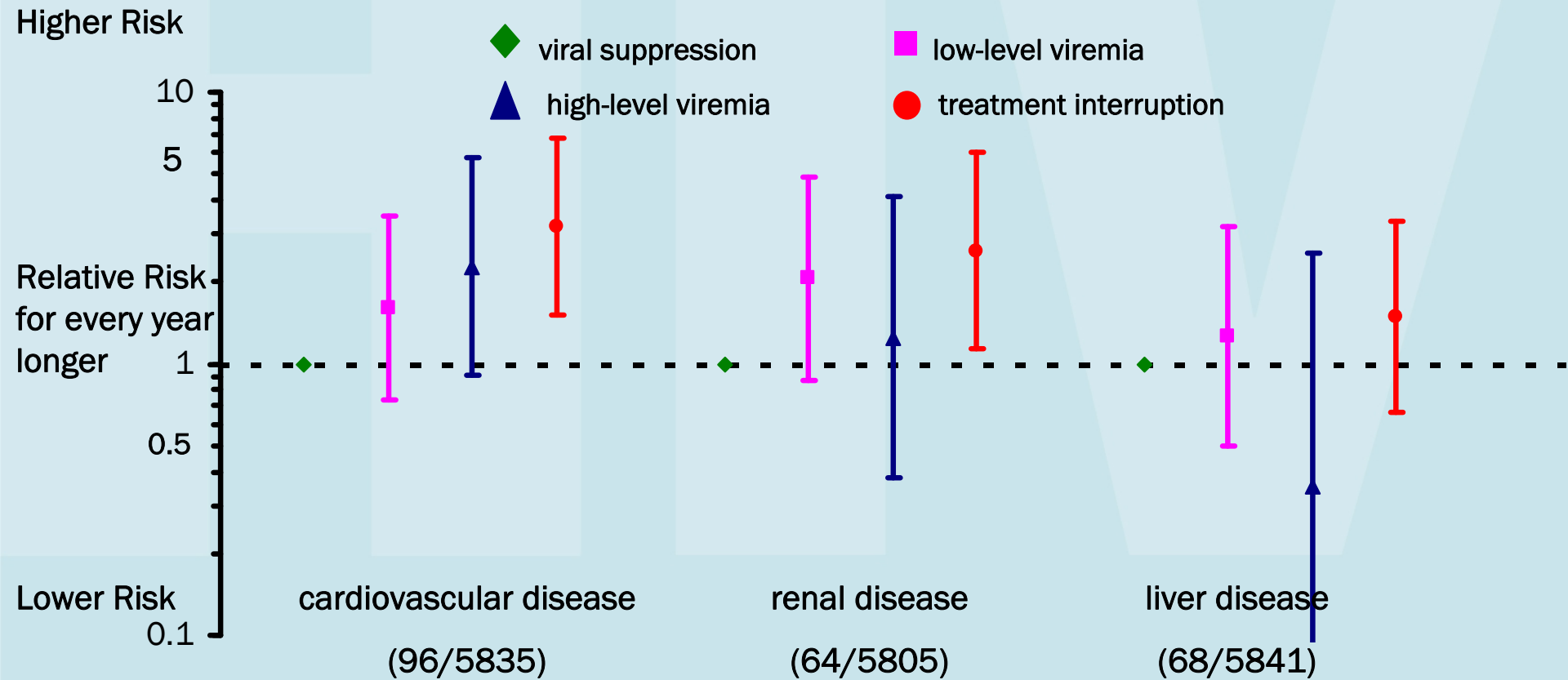
3100 (52.6%) patients were on treatment and always virally suppressed.

1012 (17.2%) patients experienced one or more episodes of interruption.

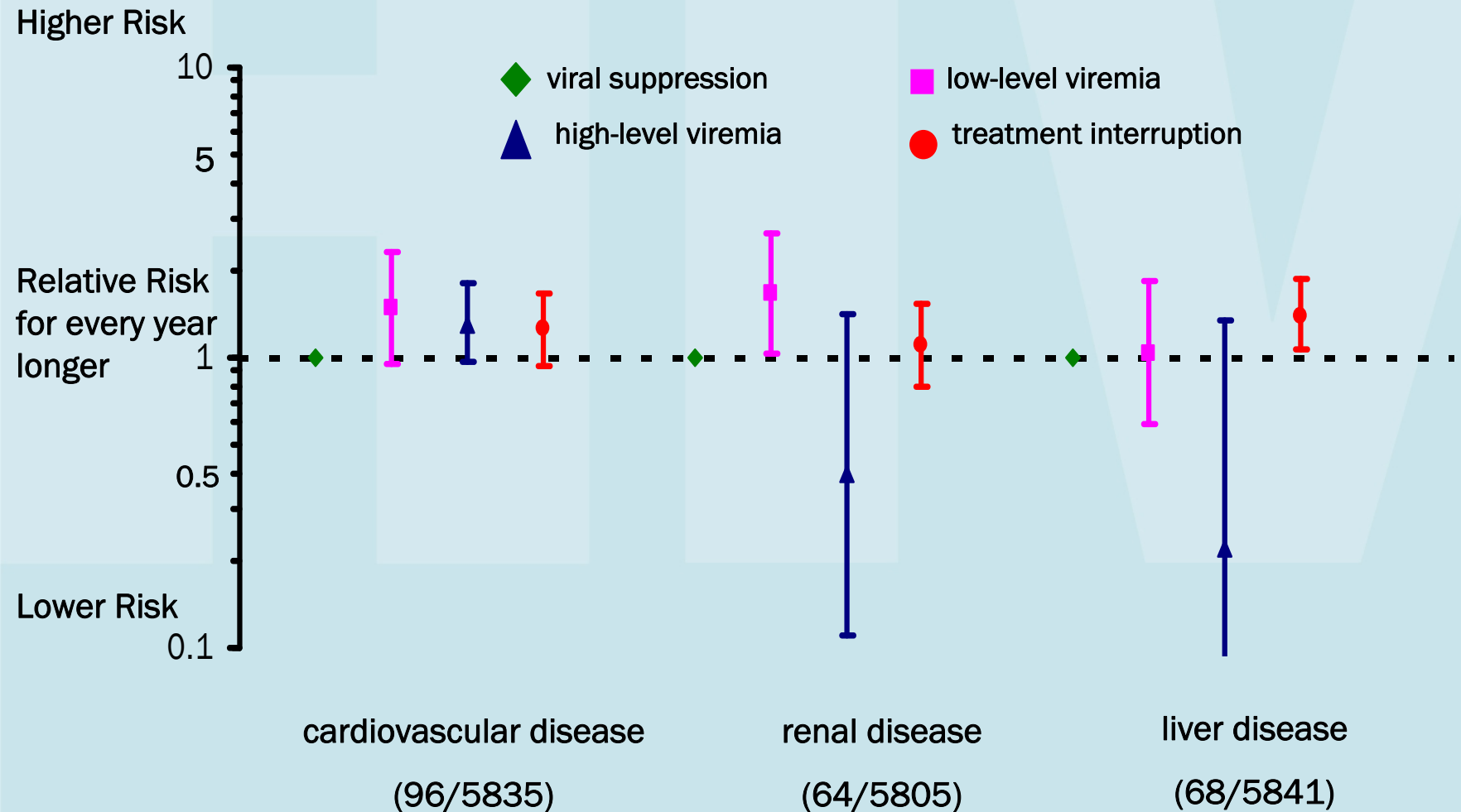
2594 (44.0%) had at least one episode of viremia, of which 861 (33,2%) experienced at least one episode of high-level viremia.

Type of episode	Number of episodes (%)	Follow-up time (person-years)	Median duration (IQR, years)
treatment interruption	1712 (9.8%)	1156 (4.9%)	0.21 (0.06-0.87)
viral suppression	10579 (60.6%)	20208 (85.6%)	1.31 (0.45-3.12)
low-level viremia	3864 (22.1%)	1182 (5.0%)	0.26 (0.13-0.38)
high-level viremia	1306 (7.5%)	1073 (4.5%)	0.41 (0.15-1.03)
All	17461 (100%)	23621 (100%)	0.60 (0.24-2.08)

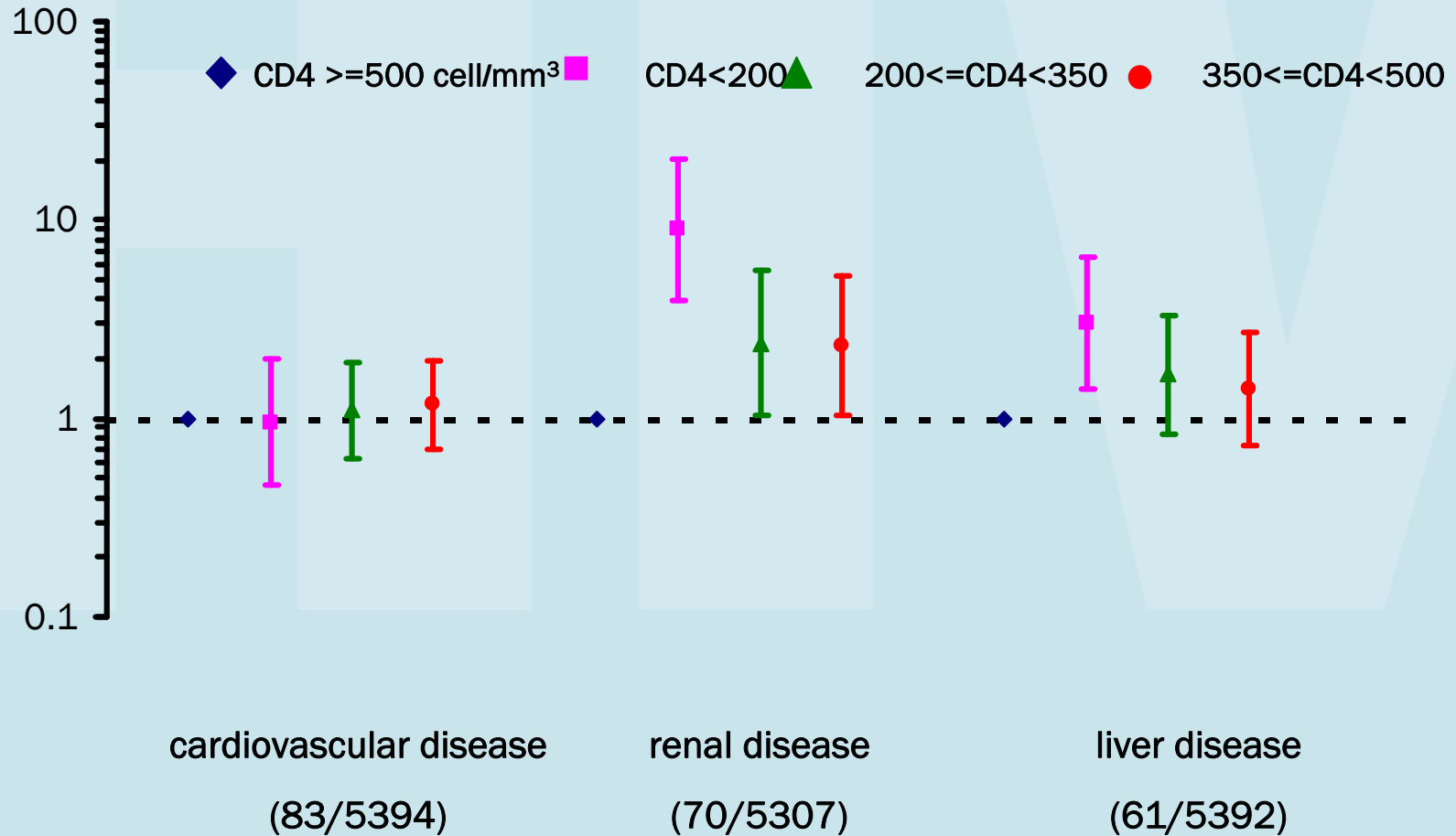
Risk of non-AIDS events by most recent episode



Risk of non-AIDS events by cumulative time spent in each type of episode



Risk of non-AIDS events by most recent CD4 count



Conclusions

- Episodes of viremia were a common phenomenon in patients achieving initial virological suppression on cART.
- Most recent episode of treatment interruptions were associated with cardiovascular disease and renal disease.
- Longer exposure to low-level viremia increased the risk of renal disease.
- CD4 counts lower than 200 cell/mm³ were associated with a higher risk of renal and liver disease.
- But the number of non-AIDS events was small.

Acknowledgements

HIV Monitoring Foundation

Ard van Sighem

Luuk Gras

Colette Smit

Frank de Wolf

Academic Medical Centre

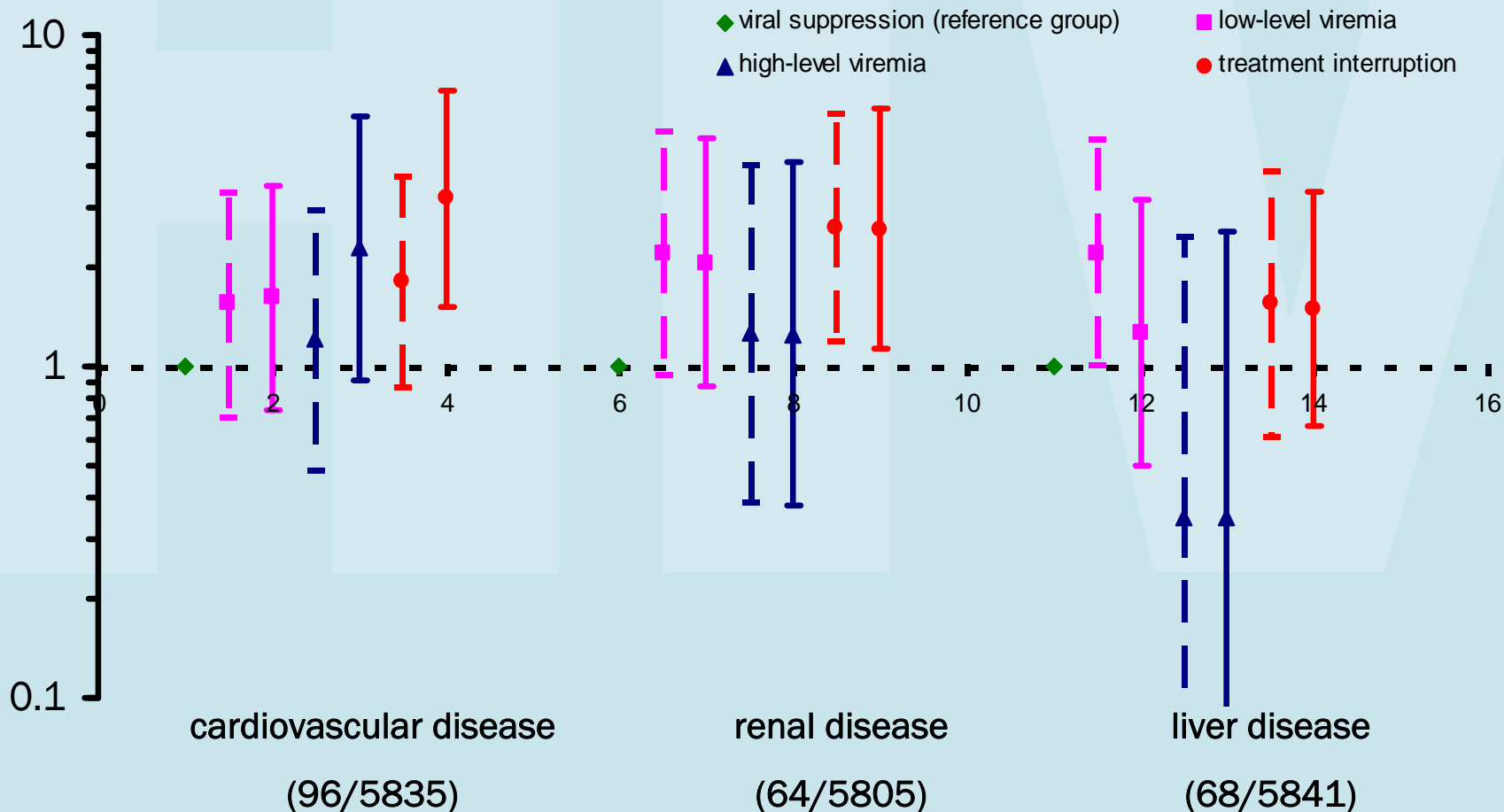
Peter Reiss

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. Pajkrt, Dr. H.J. Scherpier. 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. Vasmel. 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. Zaaier. 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. van 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. Huijtema. 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.

Answers for possible Question:

Risk of non-AIDS events by most recent episode (Univariate v.s. Multivariate)



Answers for possible Question:

Risk of non-AIDS events by RNA>50 v.s. RNA<=50 with different measurement scales

