Elvstam O (Lund University, Sweden), Ryom L, Neesgaard B, Tau L, Günthard H, Zangerle R, Vehreschild JJ, Wit F, Sönnerborg A, Abutidze A, Pethoumenos K, Jaschinski N, Hosein S, Bogner J, Grabmeister-Pfistershammer K, Garges H, Rooney J, Young L, Law M, Kirk O, for the RESPOND Study Group

Co-morbidities: The heart of the matter

Detailed modelling of viremia exposure does not independently predict cardiovascular diseases in people with HIV

AIDS 2024

22 – 26 July · Munich, Germany and virtual

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RESPOND International Cohort Consortium of Infectious Diseases

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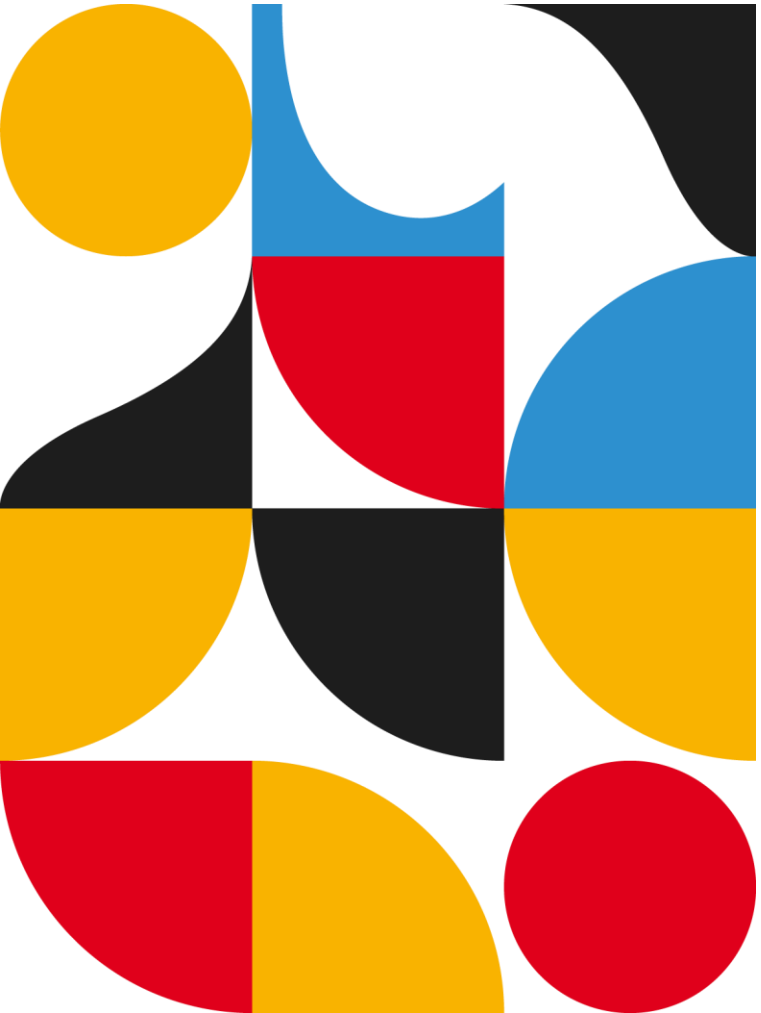
Summary



What is your main question?

Does consideration of HIV viremia improve prediction of cardiovascular diseases (CVD) among people with HIV?

What did you find?

Neither current, pre-antiretroviral therapy (ART), peak during ART, nor cumulative viremia had statistically significant associations with CVD when adjusting for other risk factors.

None of the viremia measures improved predictive capacity.

Why is it important?

Viremia has been associated with incident CVD in previous observational studies. Our study, which could adjust for a wide range of relevant CVD factors, indicates that HIV viremia is not an independent CVD risk factor.

Cardiovascular prevention is an important part of HIV care

People with HIV have around double the risk of CVD, compared with people without HIV.

Shah et al. Circulation 2018;138:1100-1112.

- Age-standardized incidence of CVD has decreased rapidly the last 20 years.
- The total burden of CVD among HIV is increasing (as the average age of people with HIV increases).
- Guidelines recommend **estimation of CVD risk** to guide preventive interventions.
- Observational studies indicate association between HIV viremia and CVD – but many studies could not adjust for relevant CVD risk factors.

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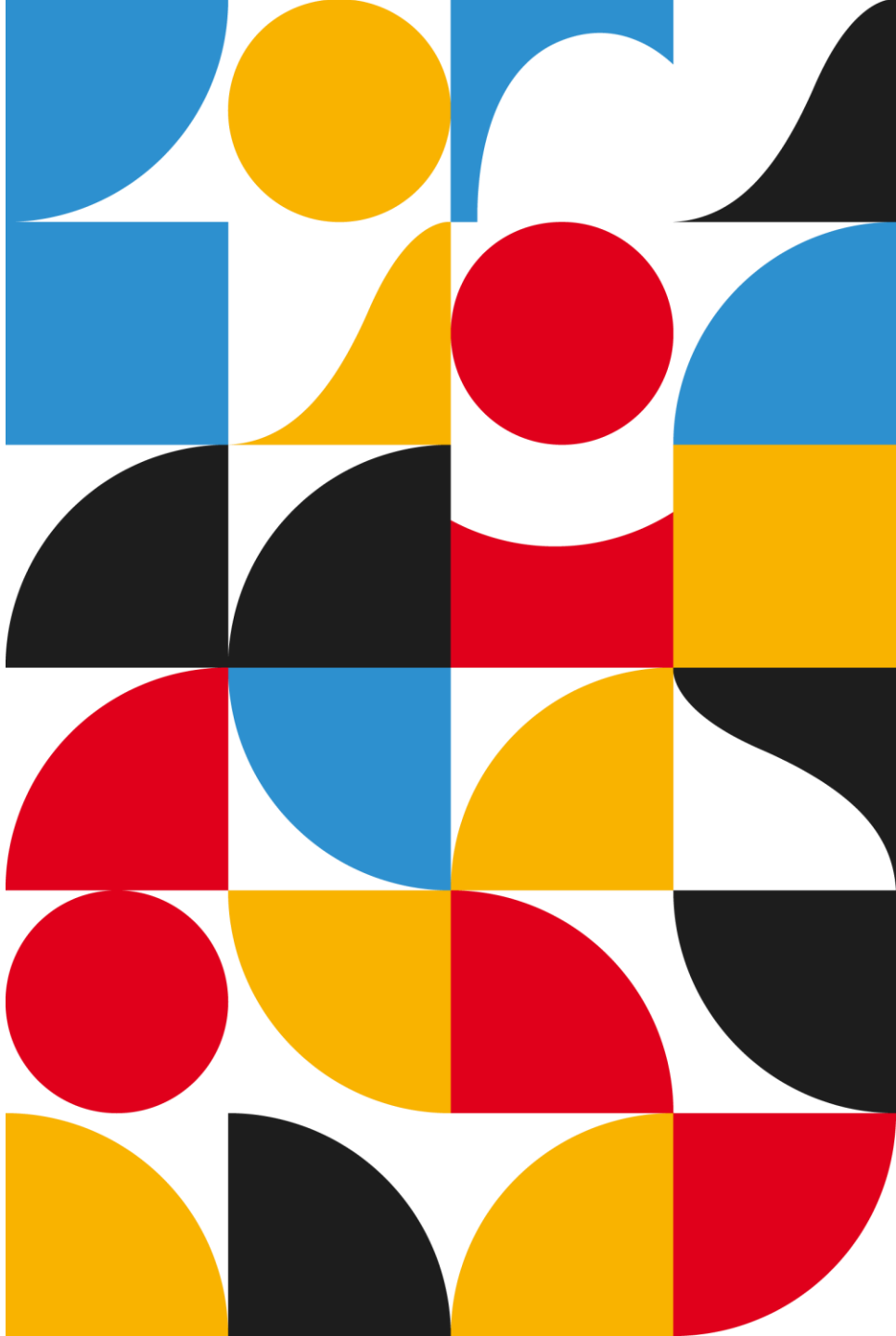
Aim

- Association between viremia variables and CVD when adjusting for established risk factors
- Prediction of CVD with and without viremia variables



Methods

Study design

RESPOND consortium – 19 cohorts across Europe and Australia

>18 years

Data from 2012–2021

Outcome: CVD (myocardial infarction, stroke, invasive cardiovascular procedures)

Variables in the D:A:D CVD risk score: age, gender, smoking, family history, diabetes, cumulative PI and NRTI, recent abacavir, CD4 count, blood pressure, cholesterol, high-density lipoprotein (HDL)

Viremia classification	
1. Most recent viral load (VL)	
2. Pre-ART VL	
3. Peak viremia category during ART	
	Suppression ≤200 c/mL
	Low-level viremia 201–999 c/mL
	Non-supression ≥1000 c/mL
Cumulative viremia (viremia-copy-years)	
	4. Including all available VLs
	5. During ART (>12 months after start of ART)
	6. Recent (sliding 3-year window)

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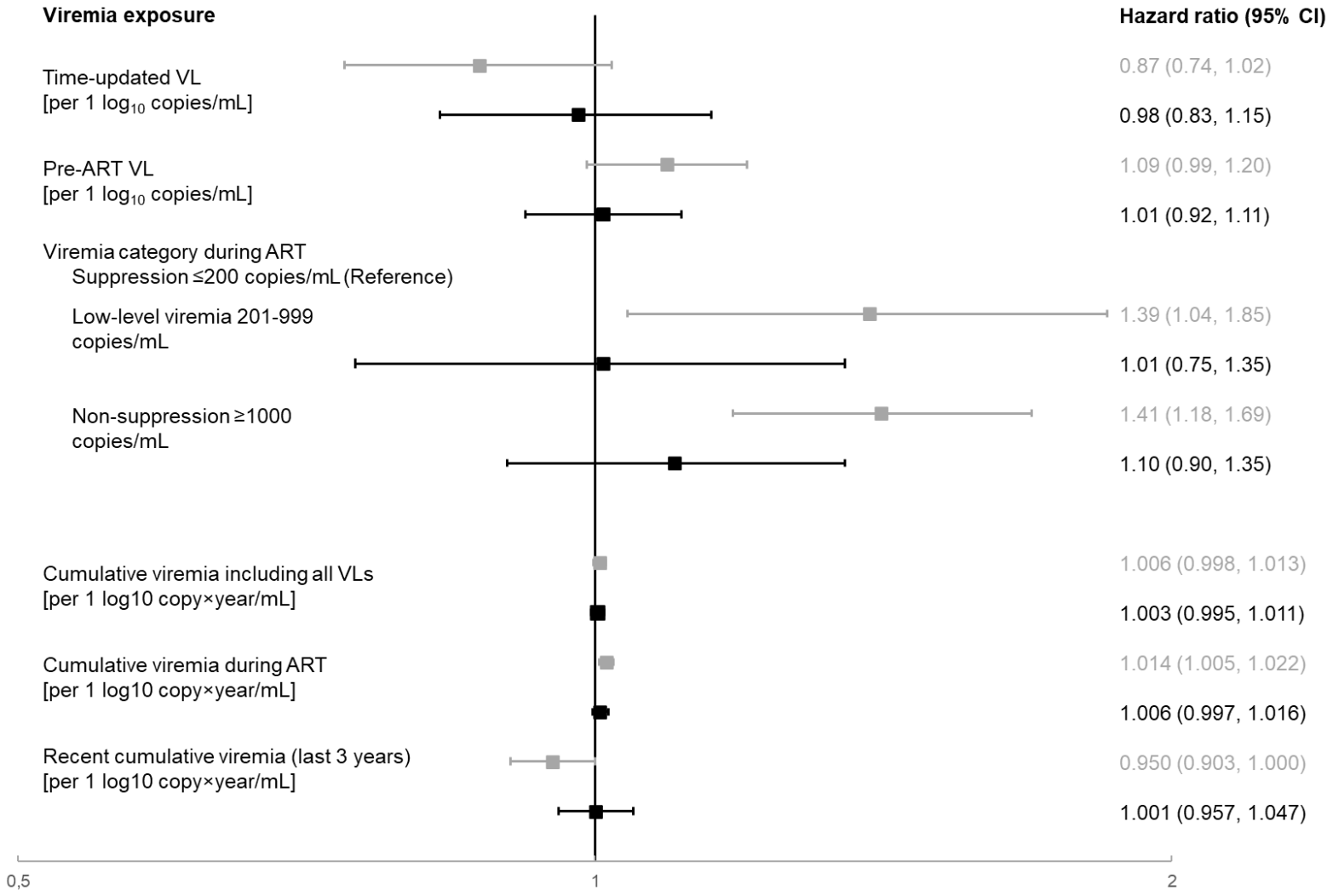
Study population

Characteristics of study participants (n=17,479)	
Sex/gender	
Male	13,265 (76%)
Female	4,232 (24%)
Age [median (IQR) years]	45 (37,52)
Ethnicity	
White	13,297 (76%)
Black	1,489 (9%)
Other	894 (5%)
Unknown or missing	1,817 (10%)

Associations between viremia variables and CVD



- 109,381 person-years; 547 events of CVD
- Variables related to viremia exposure during ART had statistically significant associations in univariable analyses.
- No viremia variable had statistically significant association when adjusting for established risk factors.

No statistically significant association when adjusting for CVD risk factors

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	Model 1 Unadjusted	**Model 2** Adjusted for age, gender, CD4 count	**Model 4 (Adjusted for all D:A:D variables)** Further adjusted for smoking, blood pressure, cholesterol, HDL, family history, abacavir, PI, NRTI	**Model 5** Extended model further adjusted for CKD, BMI, risk group, ethnicity, INSTI
Time-updated VL[a]	0.87 (0.74, 1.02)	0.98 (0.83, 1.16)	0.98 (0.83, 1.15)	0.98 (0.83, 1.16)
Pre-ART VL[a]	1.09 (0.99, 1.20)	1.01 (0.93, 1.11)	1.01 (0.92, 1.11)	1.01 (0.92, 1.10)
Viremia category during ART				
Low-level viremia 201-999 copies/mL	**1.39 (1.04, 1.85)**	1.08 (0.81, 1.43)	1.01 (0.75, 1.35)	1.01 (0.75, 1.35)
Non-suppression ≥1000 copies/mL	**1.41 (1.18, 1.69)**	1.18 (0.98, 1.41)	1.10 (0.90, 1.35)	1.10 (0.90, 1.35)
Cumulative viremia including all VLs[b]	1.006 (0.998, 1.013)	1.006 (0.998, 1.013)	1.003 (0.995, 1.011)	1.003 (0.995, 1.011)
Cumulative viremia during ART[b]	**1.014 (1.005, 1.022)**	**1.010 (1.001, 1.019)**	1.006 (0.997, 1.016)	1.006 (0.997, 1.016)
Recent cumulative viremia[b]	0.950 (0.903, 1.000)	1.005 (0.962, 1.051)	1.001 (0.957, 1.047)	1.000 (0.956, 1.047)

Data are hazard ratio (95% CI). [a]per 1 $\log_{10}$ copies/mL. [b]per 1 $\log_{10}$ copy×year/mL.

Viremia does not improve CVD prediction

	Calibration (mean predicted 5-year risk)	Discriminiation (Harrell's C)
Kaplan-Meier estimate of 5-year CVD risk (95% CI)	2.44% (2.20%, 2.71%)	
D:A:D model	2.34%	0.75
D:A:D model + time-updated VL	2.34%	0.75
D:A:D model + pre-ART VL	2.20%	0.75
D:A:D model + peak viremia category	2.35%	0.75
D:A:D model + cumulative, all VLs	2.34%	0.75
D:A:D model + cumulative, during ART	2.35%	0.75
D:A:D model + cumulative, recent	2.32%	0.75

Sensitivity analyses

Our conclusions remained the same in the following sensitivity analyses:

1. Considering the three components of the composite CVD endpoint separately.
2. Also including people with a known prior CVD.
3. Excluding the variable “Family history”.
4. Using 50 c/mL as the threshold for suppression.
5. Modelling with restricted cubic splines to allow for non-linear relationships between viremia and CVD.

Limitations and strengths

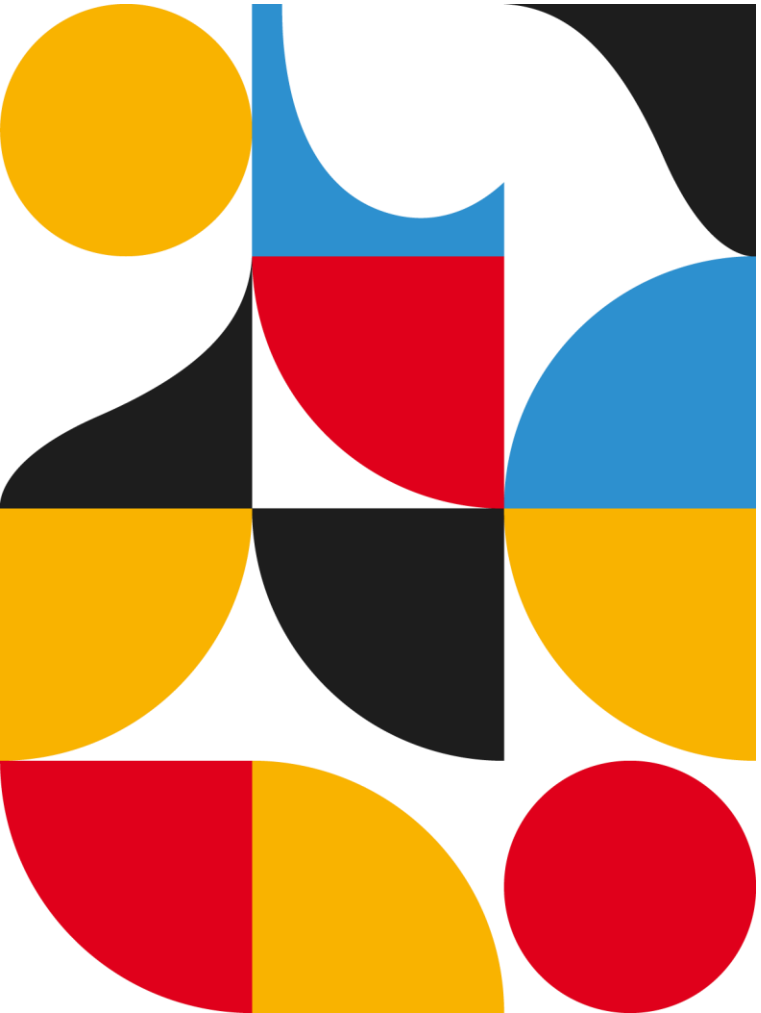
Limitations

- Limited median follow-up (5-year risk)
- HIV viremia before diagnosis is unknown
- Generalizability
  (high CD4 counts, high degree of viral suppression, relatively few non-white people with HIV, Europe/Australia)
- Excluded 51% of the cohort (and excluded individuals had higher CVD risk)
  - Main reason (35%), cohort with low reporting of CVD events or risk factors
- Lack data on e.g. recreational drug use

Strengths

- Large cohort
- Rigorously validated endpoints
- Rich data on CVD risk factors

Conclusions



Exposure to HIV viremia was not associated with higher CVD risk.

Consideration of viremia history did not improve CVD prediction.

Viral suppression undoubtedly remains an important goal – though not associated with CVD.

Underscores complex pathogenesis of CVD among people with HIV.

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Cohort principal investigators:
S De Wit (St. Pierre), R Zangerle (AHICOS), K Petoumenos (AHOD), F Wit (ATHENA) J Kowalska (EuroSIDA), N Chkhartishvili (IDACIRC), C Pradier (Nice HIV cohort), A d'Arminio Monforte (ICoNA), C Mussini (Modena), H Günthard (SHCS), A Sönnerborg (Swedish InfCare), F Burns (Royal Free HIV cohort), J Begovac (Croatia, HIV cohort), A Castagna (San Raffaele, Milano), JC Wasmuth (Bonn, HIV cohort), JJ Vehreschild (Cologne, HIV cohort), J Vera (Brighton HIV cohort).

Cohort coordinator, operational team members and data management:
C Necsoi, M Delforge (St. Pierre, Brussels), H Appoyer, G Leierer (AHIVCOS), J Hutchinson, D Rupasinghe, W Min Han (AHOD), M Van der Valk, M Hillebregt, D Bergsma (ATHENA), O Chokoshvili, E Karkashadze (IDACIRC), E Fontas, K Dollet, C Caissotti (NICE, HIV cohort), J Fanti, A Tavelli, A Rodanò (ICoNA), V Borghi, M Menozzi, A Cervo (Modena), K Kusejko (SHCS), C Carlander, P Nowak, J Vesterbacka, L Mattsson, K Stigsäter, D Carrick (Swedish InfCare), M Johnson, F Lampe, C Smith, C Chaloner (Royal Free, HIV cohort), C Elisabetta, R Lolatto, A Lazzarin, A Poli, S Nozza (San Raffaele, Milano), J Rockstroh (Bonn, HIV cohort), M Scherer, C Lehmann, N Schulze, B Franke (Cologne HIV cohort).

RESPOND Scientific Steering Committee:
J Lundgren*, H Günthard*, L Ryom, M Law, D Raben, L Peters, J Rockstroh, O Kirk, D Podlekareva, A Volny-Anne, N Dedes, ED Williams, J Kowalska, N Chkhartishvili, R Zangerle, K Petoumenos, F Wit, C Necsoi, C Pradier, A D'Arminio Monforte, C Mussini, A Sönnerborg, JJ Vehreschild, JC Wasmuth, F Burns, A Castagna, J Vera, J Begovac, J Rooney, M Dunbar, V Vannappagari, H Garges, L Young, R Campo ***Chairs**

Community representatives:
A Volny-Anne, N Dedes, L Mendão (European AIDS Treatment Group), E Dixon Williams (UK)

RESPOND Executive Committee:
L Ryom*, M Law*, J Rooney, F Bognar, V Vannappagari, H Garges, K Petoumenos, J Kowalska, R Zangerle, C Mussini, S De Wit, J Lundgren, H Günthard, L Young, R Campo ***Chairs**

External Clinical Reviewers:
K Lærum Sibilitz (Clinical Cardiology), P Meidal Petersen (Clinical Oncology)

RESPOND coordination office, data management and quality assurance:
N Jaschinski, A Timiryasova, B Neesgaard, O Fursa, L Ryom, JF Larsen, ML Jacobsen, O Valdenmaiier, T Elsing, S Shahi, L Ramesh Kumar, M Gardizi, B Pepa, L Peters, D Raben

Members of the Scientific Interest Groups:
Hepatitis/Viral Coinfection, Public Health, Outcomes with Antiretroviral Treatment, Tuberculosis, Gender specific outcomes

Members of the Working Groups:
Cancer, Weight Gain on INSTI, Two-drug vs three-drug, Heavy treatment experience, Cardiovascular Disease, Causes of death, Ageing/multimorbidity, Methodology, Long-acting ART, Liver disease and NASH, Resistance

Statistical Staff:
L Greenberg, K Petoumenos, W Min Han, A Roen, E Tusch, W Bannister, J Reekie

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