

Erich Tusch¹, Annegret Pelchen-Matthews², Lars Peters¹, Amanda Mocroft^{1,2}, Daniel Elbirt³, Cristiana Oprea⁴, Huldrych Günthard⁵, Cornelia Staehelin⁶, Robert Zangerle⁷, Colette Smith⁸, Isabelle Suarez⁹, Jörg Janne Vehreschild⁹, Ferdinand Wit¹⁰, Marianna Menozzi¹¹, Antonella d'Arminio Monforte¹², Vincenzo Spagnuolo¹³, Christian Pradier¹⁴, Christina Carlander¹⁵, Paula Suanzes¹⁶, Jan-Christian Wasmuth¹⁷, Andrew Carr¹⁸, Kathy Petoumenos¹⁸, Nikoloz Chkhartishvili¹⁹, Jonathan Carney²⁰, Bastian Neesgaard¹, Nadine Jaschinski¹, Lauren Greenberg¹, Sean R Hosein²¹, Joel Gallant²², Vani Vannappagari²³, Lital Young²⁴, Jens Lundgren¹, Lene Ryom^{1,25}, Joanne Reekie¹

¹CHIP, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; ²Centre for Clinical Research, Epidemiology, Modelling and Evaluation (CREME), Institute for Global Health, University College London, London, UK; ³Allergy, Immunology and HIV Unit, Kaplan Medical Center, Rehovot, Israel; ⁴Victor Babes Clinical Hospital for Infectious and Tropical Diseases, Bucharest, Romania; ⁵Swiss HIV Cohort Study (SHCS), University of Zurich, Zurich, Switzerland; ⁶Department of Infectious Diseases, Bern University Hospital, University of Bern, Bern, Switzerland; ⁷Austrian HIV Cohort Study (AHIVCOS), Medizinische Universität Innsbruck, Innsbruck, Austria; ⁸The Royal Free HIV Cohort Study, Royal Free Hospital, University College London, London, United Kingdom; ⁹University Hospital Cologne, Cologne, Germany; ¹⁰AIDS Therapy Evaluation in the Netherlands (ATHENA) cohort, HIV Monitoring Foundation, Amsterdam, the Netherlands; ¹¹Modena HIV Cohort, Università degli Studi di Modena, Modena, Italy; ¹²Italian Cohort Naive Antiretrovirals (ICONA), ASST Santi Paolo e Carlo, Milano, Italy; ¹³San Raffaele Scientific Institute, Università Vita-Salute San Raffaele, Milano, Italy; ¹⁴Nice HIV Cohort, Université Côte d'Azur et Centre Hospitalier Universitaire, Nice, France; ¹⁵Swedish InfCare HIV Cohort, Karolinska University Hospital; ¹⁶Infectious Diseases Department, Hospital Universitari Vall d'Hebron, Vall d'Hebron Barcelona Hospital Campus, Barcelona, Spain; ¹⁷Medicine Department, Universitat Autònoma de Barcelona, Bellaterra, Spain; ¹⁸University Hospital Bonn, Bonn, Germany; ¹⁹The Australian HIV Observational Database (AHOD), UNSW, Sydney, Australia; ²⁰Georgian National AIDS Health Information System (AIDS HIS), Infectious Diseases, AIDS and Clinical Immunology Research Center, Tbilisi, Georgia; ²¹Frankfurt HIV Cohort Study, Johann Wolfgang Goethe-University Hospital, Frankfurt, Germany; ²²European AIDS Treatment Group (EATG), Brussels, Belgium; ²³Gilead Sciences, Foster City, California, USA; ²⁴Viiv Healthcare, Research Triangle Park, North Carolina, USA; ²⁵Merck Sharp & Dohme, Rahway, New Jersey, USA; ²⁶Department of Infectious Diseases 144, Hvidovre University Hospital, Copenhagen, Denmark

BACKGROUND

- Mortality rates in people living with HIV have declined due to effective antiretroviral treatment (ART) (1). Aging, coinfections, and comorbidities may drive further changes in mortality (2).
- We investigated recent patterns in mortality in the RESPOND cohort consortium to systematically monitor for unexpected trends and identify opportunities to reduce mortality.

METHODS

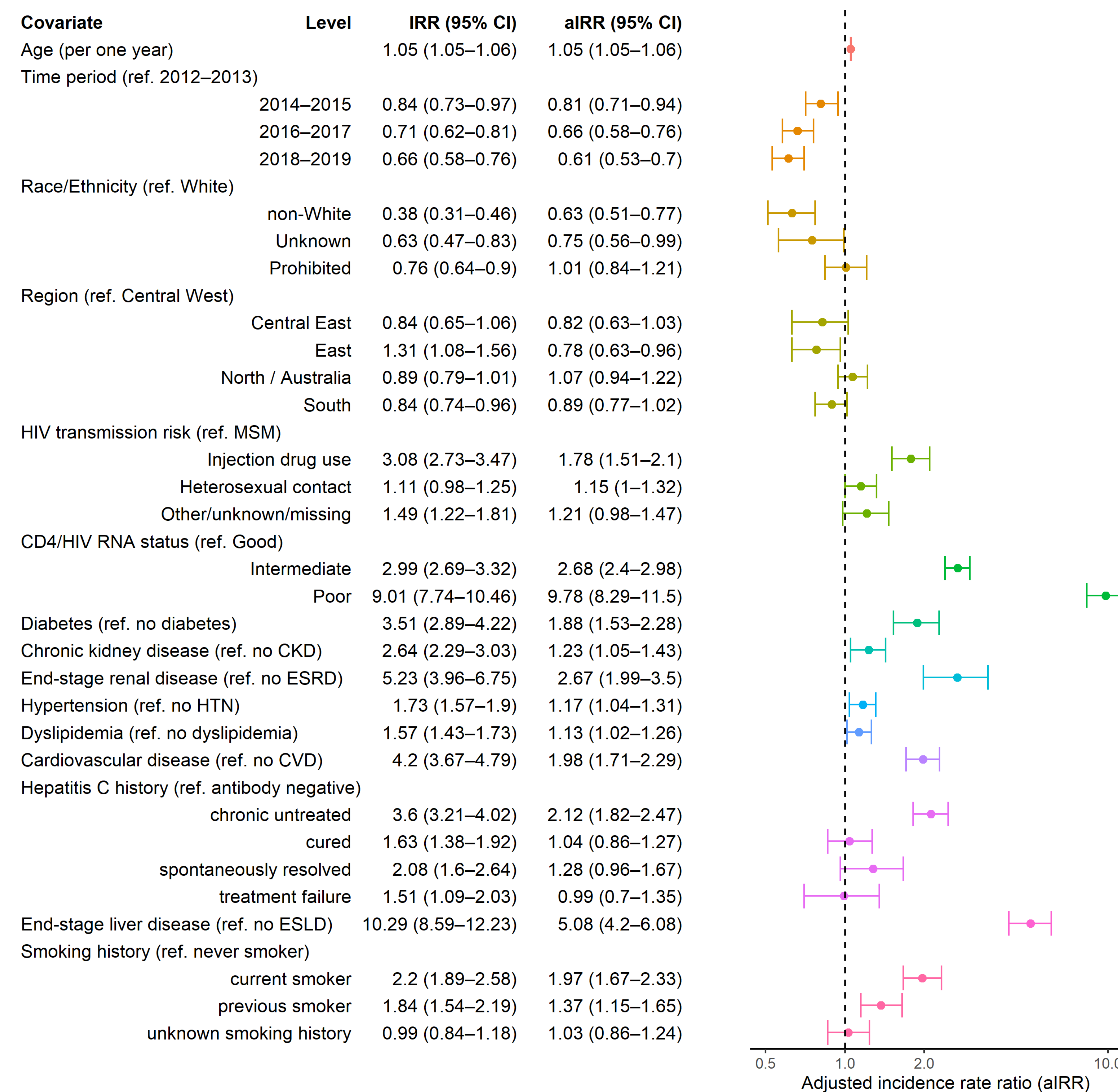
- The RESPOND cohort consortium was initiated in 2017 and includes over 30,000 people living with HIV from 17 cohorts across Europe and Australia.
- Prospective follow up from 2012 through 2019. Participants before 2017 enrolled retrospectively.
- Mortality classified by the Coding Causes of Death in HIV (CoDe) methodology (3).
- Age-standardized mortality rates were compared over time.
- Multivariable Poisson regression was used to investigate risk factors for all-cause mortality.

RESULTS

- 33,598 participants, 167,930 PYFU (median 4.8 years; IQR 3.1–8.0); 1700 (5.1%) died.
- Crude, all-cause mortality rate decreased over time.
 - 2012–13: 13.0/1000 PYFU (95%CI 11.8–14.4)
 - 2018–19: 8.6/1000 PYFU (95%CI 7.9–9.5)
- Median age at death increased over time:
 - 2012–13: 52 (IQR 45–62); 2018–19: 56 (IQR 48–65)
- Highest cause-specific crude mortality rate was due to non-AIDS defining malignancy (NADM); see Table 1.
- Age-adjusted Poisson regression showed decreasing mortality from 2012–13 to 2018–19 for deaths due to NADM, AIDS, cardiovascular disease (CVD), liver disease, and other causes, but not unknown/missing (see Figure 2).
- In multivariable analysis including all risk factors where $p < 0.1$ in univariable analysis (Figure 1), the strongest predictors of all-cause mortality were poor immunologic/virologic status (current CD4 ≤ 350 cells/mm³ + HIV viral load (VL) > 200 cp/mL) vs. good immunologic/virologic status (CD4 ≥ 500 cells/mm³ + VL < 200 cp/mL) and other modifiable risk factors.

In the RESPOND cohort from 2012 through 2019, cause-specific age-adjusted mortality rates declined. Immunologic/virologic status was the strongest predictor of mortality.

Figure 1. All-cause mortality univariable and multivariable time-updated Poisson regressions

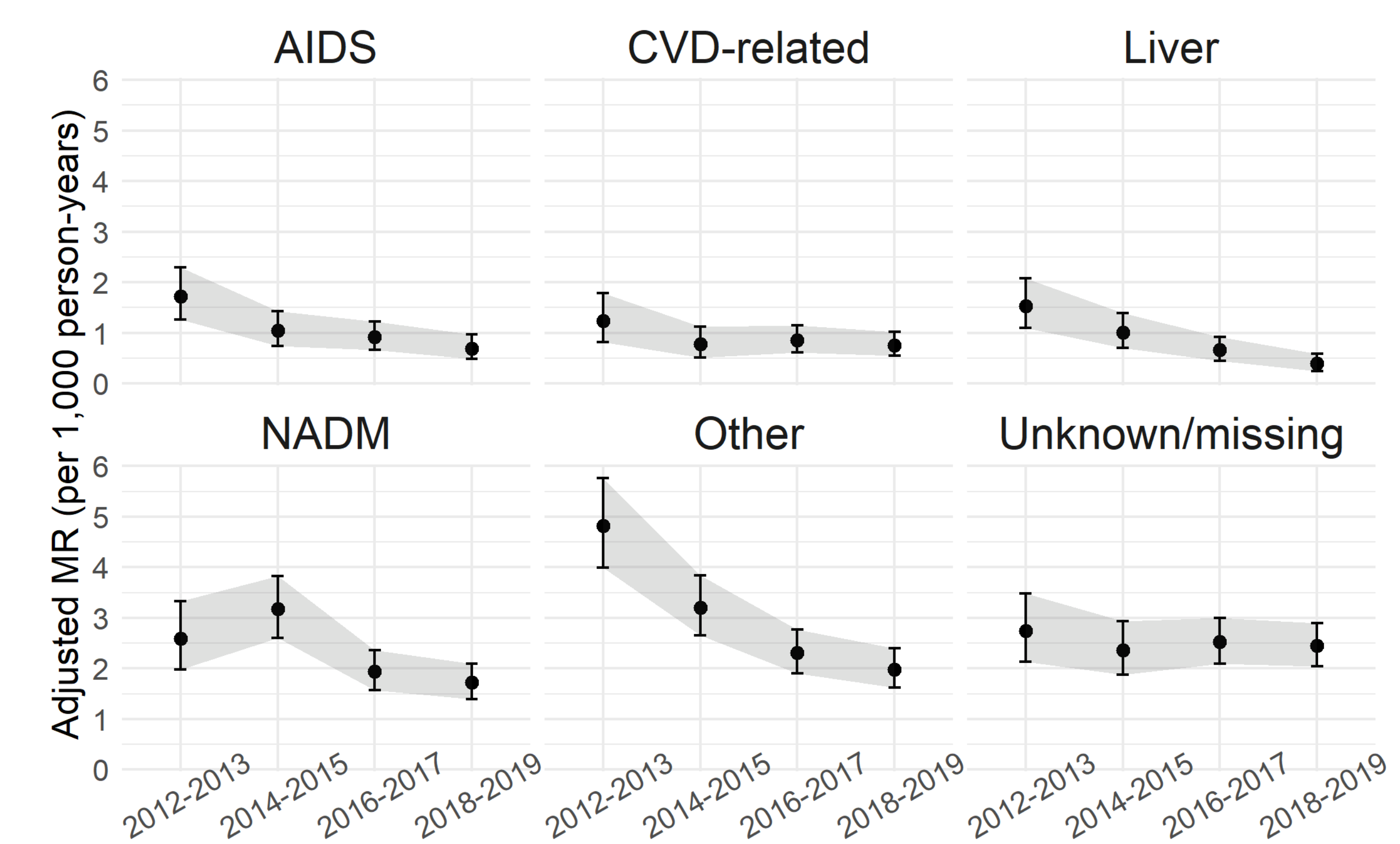


Multivariable analysis also adjusted by Gender, Hepatitis B; aIRR n.s.

Table 1: Cause-specific crude mortality rates (MR) per 1000 person-years

	N events	crude MR (95%CI)
NADM	370	2.20 (1.98 - 2.44)
AIDS	169	1.01 (0.85 - 1.16)
CVD	142	0.85 (0.71 - 1.00)
Liver	133	0.79 (0.66 - 0.94)
Other	469	2.79 (2.55 - 3.06)
Unknown/missing	417	2.48 (2.25 - 2.73)

Figure 2: Age-standardized mortality rates (MR)



LIMITATIONS

- Many unknown/missing causes of death.
- Retrospective enrollment may lead to selection bias.

CONCLUSIONS

- Age-adjusted mortality rates due to specific causes declined from 2012–13 to 2018–19.
- Mortality due to NADM was greater than AIDS-, CVD-, or liver-related mortality.
- Median age at death has increased over time but is still relatively young compared to the background population.
- All-cause mortality was strongly associated with modifiable risk factors, especially immunologic/virologic status and chronic conditions, indicating areas for improvement.

(1) Smith CJ, et al. The Lancet. 2014; (2) Pelchen-Matthews A, et al. AIDS. 2018; (3) Kowalska JD, et al. Epidemiology. 2011