Supplementary material

1. InCHEHC study group:

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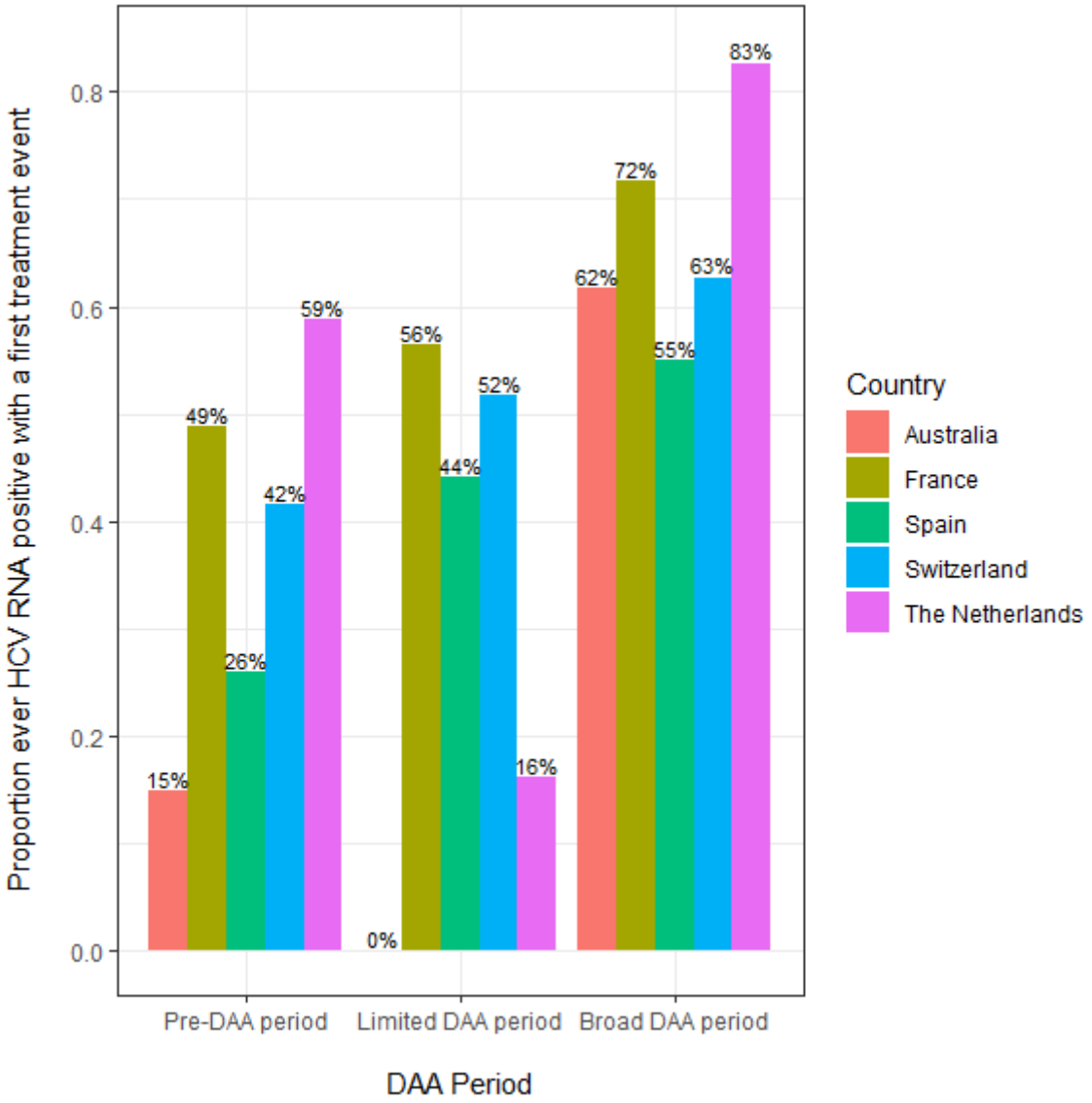
Cohort name abbreviations: ACCESS: Australian Collaboration for Coordinated Enhanced Sentinel Surveillance. ATHENA: AIDS Therapy Evaluation in the Netherlands. AQUITAINE: ANRS CO3 AQUITAINE / AquiVIH-NA - prospective clinical based HIV cohort. CCC: Canadian Co-infection Cohort. CEASE: Control and Elimination within AuStralia of HEpatitis C from people living with HIV. Co-EC: Eliminating hepatitis C transmission by enhancing care and treatment among HIV co-infected individuals. CORIS: The cohort of Spanish HIV research network. HEPAVIH: Clinical Centres Collaborations of Subjects Co-infected with HIV and HCV. MOSAIC: MSM Observational Study of Acute Infection with hepatitis C. SAIDCC: Saint-Antoine Infectious Disease Clinical Cohort. SHCS: Swiss HIV cohort Study.

1.1. Supplementary table 1: Overview of InCHEHC cohorts with data for primary incidence infection and DAA access dates

Site (country)	Study design	Start cohort	Total N in cohort	At least one valid HCV test result n (%)[1]	Official limited DAA access date	Restrictions during the limited DAA access period	Official broad DAA access date
ACCESS (Australia)	Nationwide linked database from 68 primary care, community clinics, hospitals, and pathology laboratories	2009	22,033	17,911 (81.3)	None	NA	March 2016
AQUITAINE (France)	Multi-site prospective hospital-based cohort (13 sites through South-Western France)	1987	9,296	7,849 (84.4)	January 2014	Severe fibrosis, except patients with comorbidities, including HIV coinfection	August 2017
SAIDCC (France)	Single-site (Paris) hospital and clinic-recruited prospective cohort	1992	7,466	3,462 (46.4)	January 2014		August 2017
ATHENA (the Netherlands)	Nationwide prospective cohort	1998	24,785	24,780 (99.9)[2]	November 2014	Moderate to severe fibrosis	November 2015
CoRIS (Spain)	Multicentre cohort study in 28 sites	2004	16,725	16,078 (96.1)	January 2015	Severe fibrosis and those with high risk of transmission such as MSM w/ongoing risk behaviour	June 2017
SHCS (Switzerland)	Nationwide prospective cohort	1988	20,740	16,078 (77.5)	April 2014	Severe fibrosis or defined extrahepatic manifestation.	October 2017

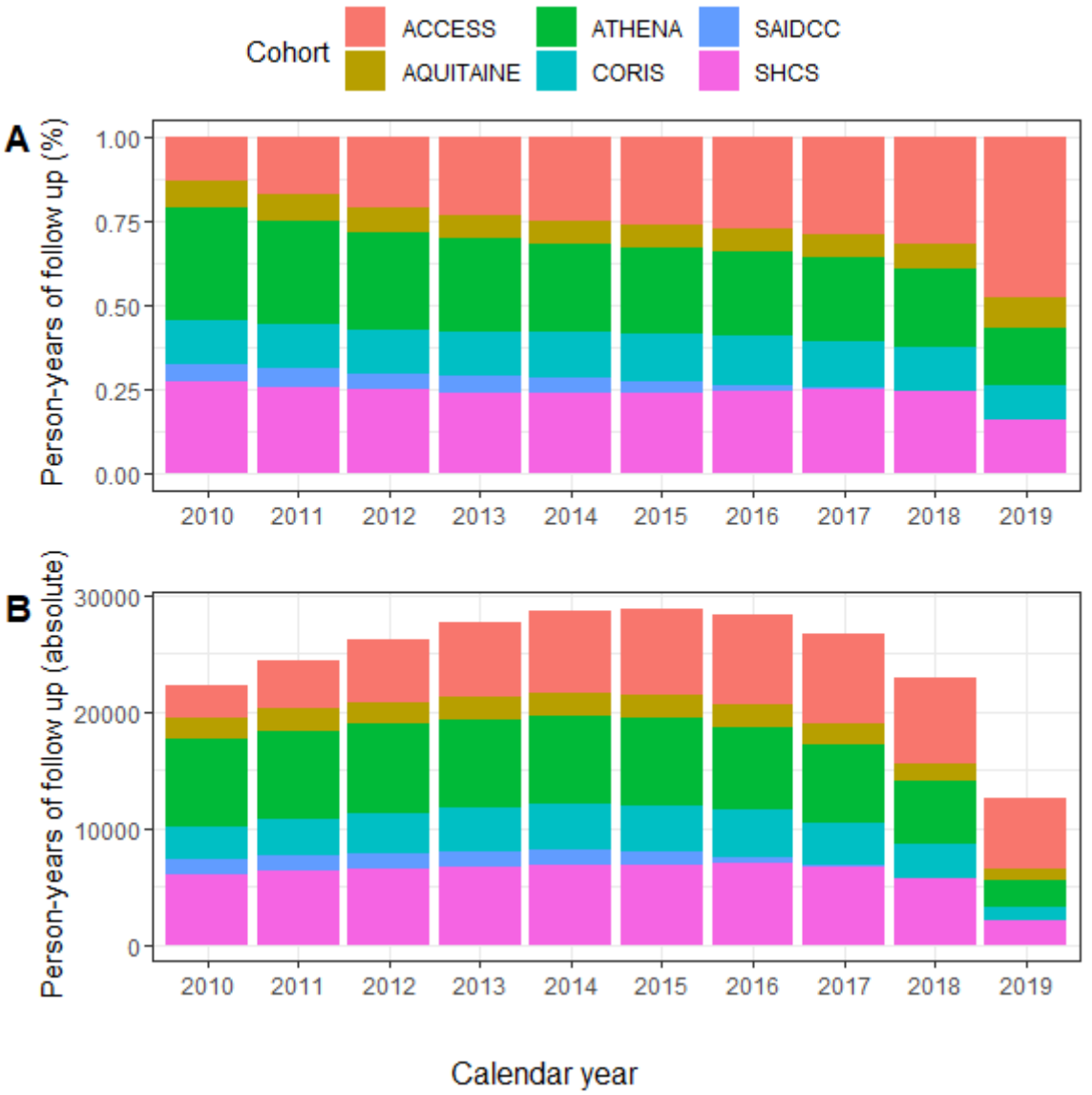
						Later including moderate fibrosis.	

1.2. Supplementary Figure 1: Treatment uptake by DAA access period per country among participants ever testing HCV RNA positive



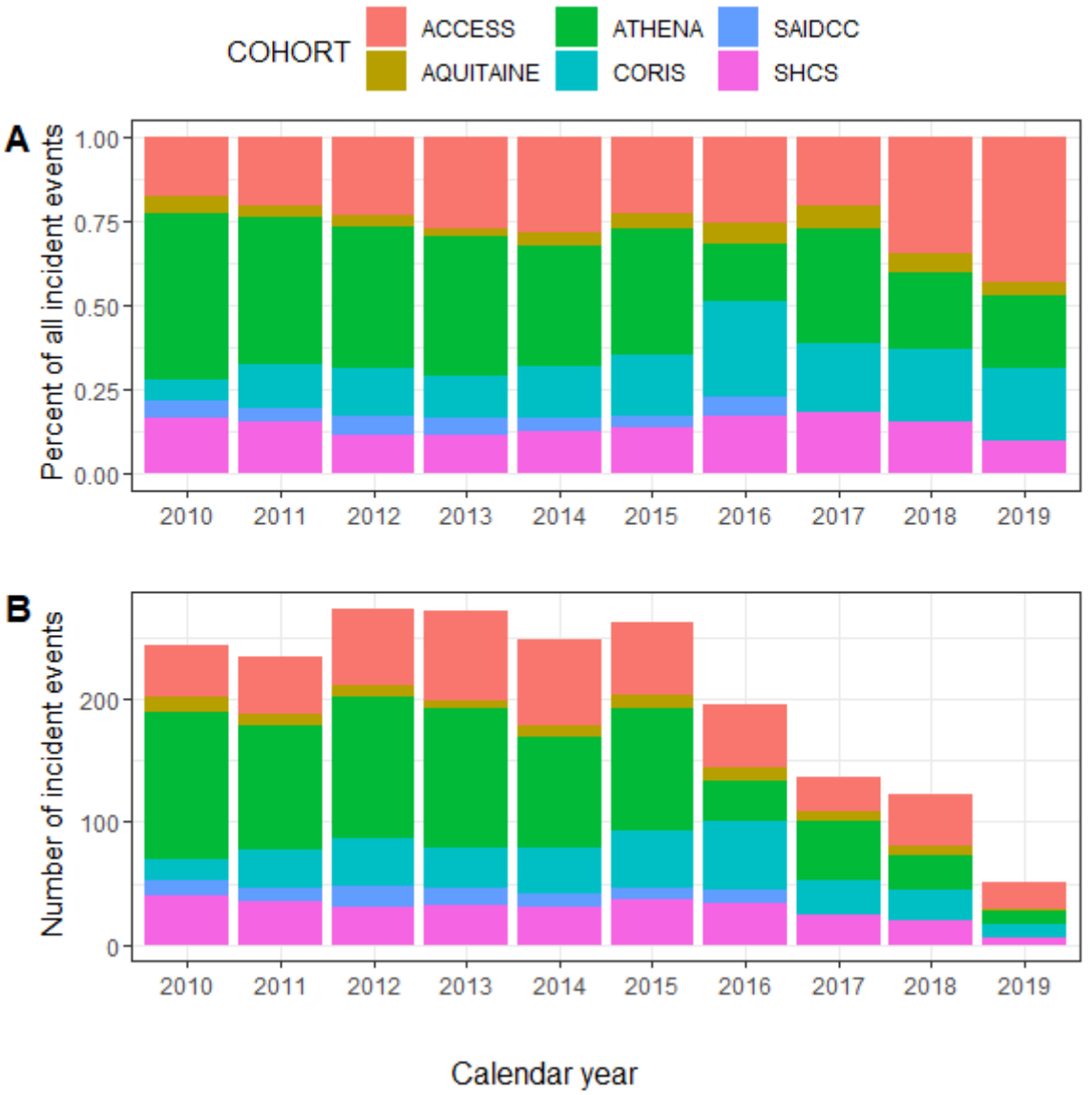
Treatment data are shown is restricted to follow up between 2010 and 2019. Individuals with evidence of HCV clearance (i.e., a negative HCV RNA test at least 28 days after the first positive test) without a treatment episode before the end of the DAA access period were excluded. Individuals were censored after their first HCV treatment episode. Some sites within the ACCESS cohort have missing HCV treatment data and therefore estimates from Australia are an underrepresentation of the true uptake.

1.3. Supplementary Figure 2: Follow up during each calendar year per cohort



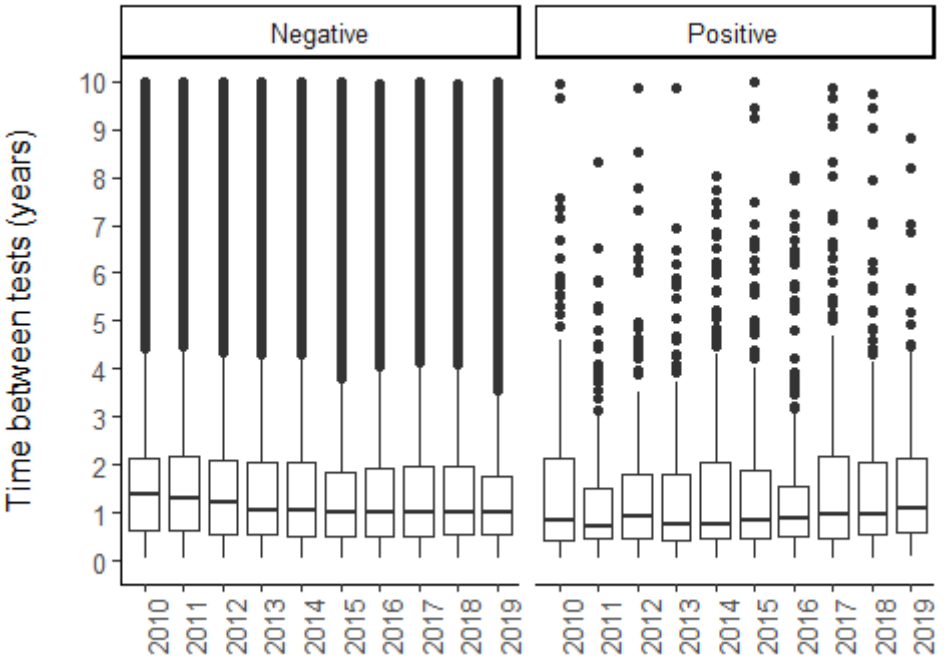
Abbreviations: ACCESS: Australian Collaboration for Coordinated Enhanced Sentinel Surveillance; co-EC: Eliminating hepatitis C transmission by enhancing care and treatment among HIV co-infected individuals; SHCS: Swiss HIV cohort study; ATHENA: AIDS Therapy Evaluation in the Netherlands; SAIDCC: Saint-Antoine Infectious Disease Clinical Cohort; CoRIS: The cohort of Spanish HIV research network. A: Percentage of the total person-years of follow-up within a calendar year from each cohort. Panel B: Absolute number of person-years of follow-up within a calendar year from each cohort.

1.4. Supplementary Figure 3: Number of incident events during each calendar year per cohort



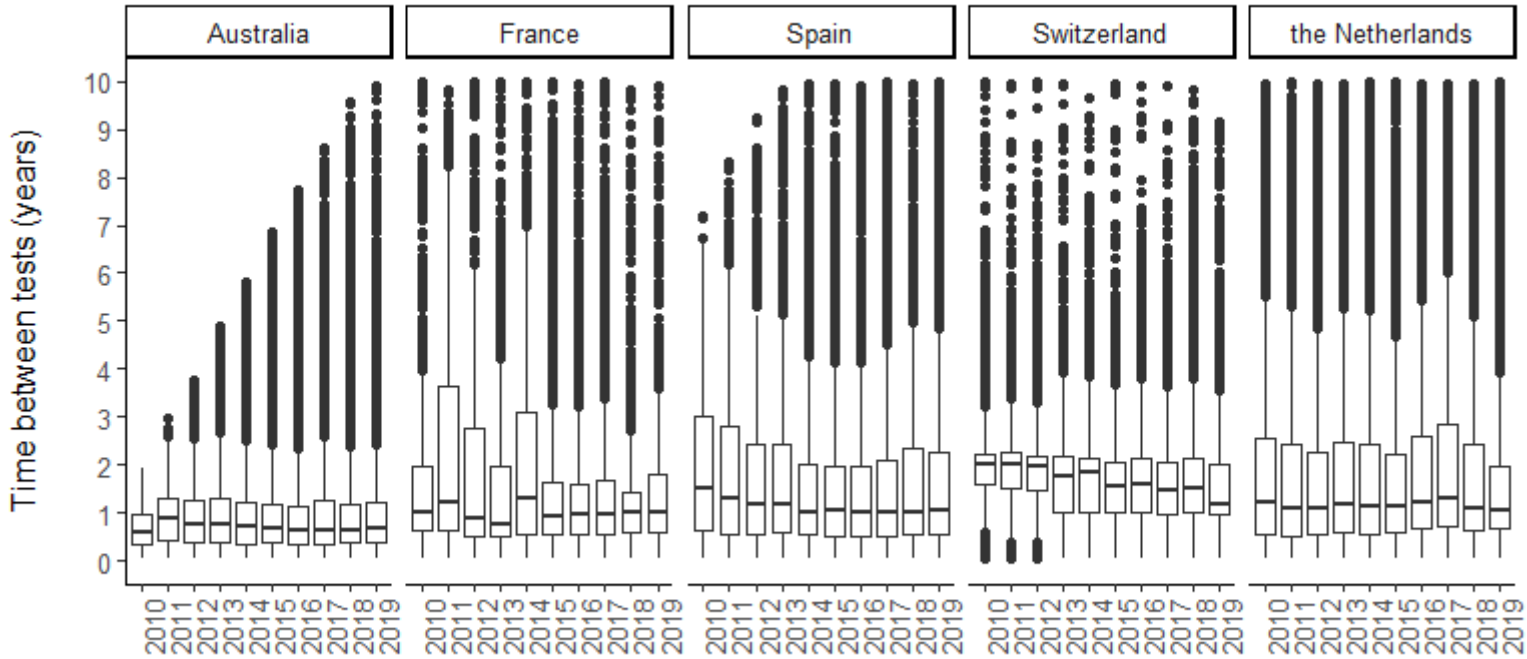
Abbreviations: ACCESS: Australian Collaboration for Coordinated Enhanced Sentinel Surveillance; co-EC: Eliminating hepatitis C transmission by enhancing care and treatment among HIV co-infected individuals; SHCS: Swiss HIV cohort study; ATHENA: AIDS Therapy Evaluation in the Netherlands; SAIDCC: Saint-Antoine Infectious Disease Clinical Cohort; CoRIS: The cohort of Spanish HIV research network. Panel A: Percentage of the total number of events within a calendar year from each cohort. Panel B: Absolute number of events within a calendar year from each cohort.

1.5. Supplementary Figure 4: Time since previous test by HCV test status result in the pooled dataset



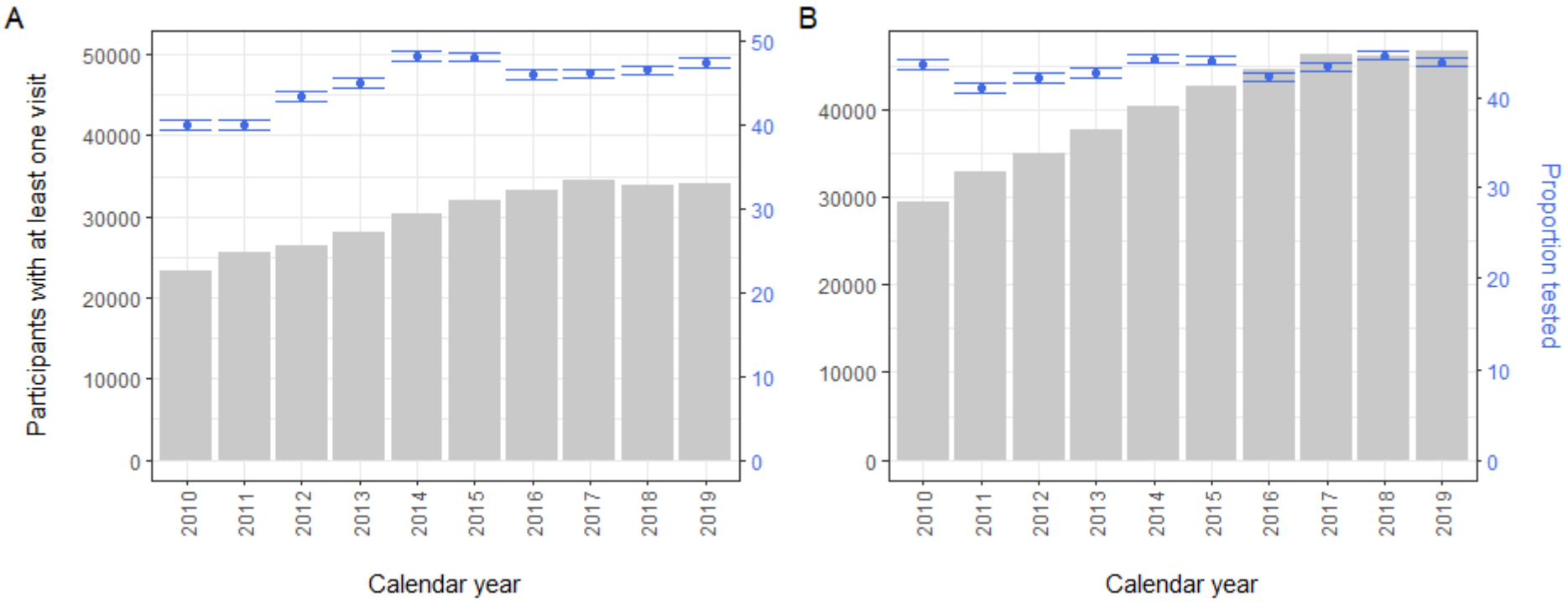
This graph shows all positives tests during 2010 and 2019 without accounting for the midpoint date of HCV seroconversion, hence more positives test may be represented in this graph than included in the analysis.

1.6. Supplementary Figure 5: Time since previous HCV test by country



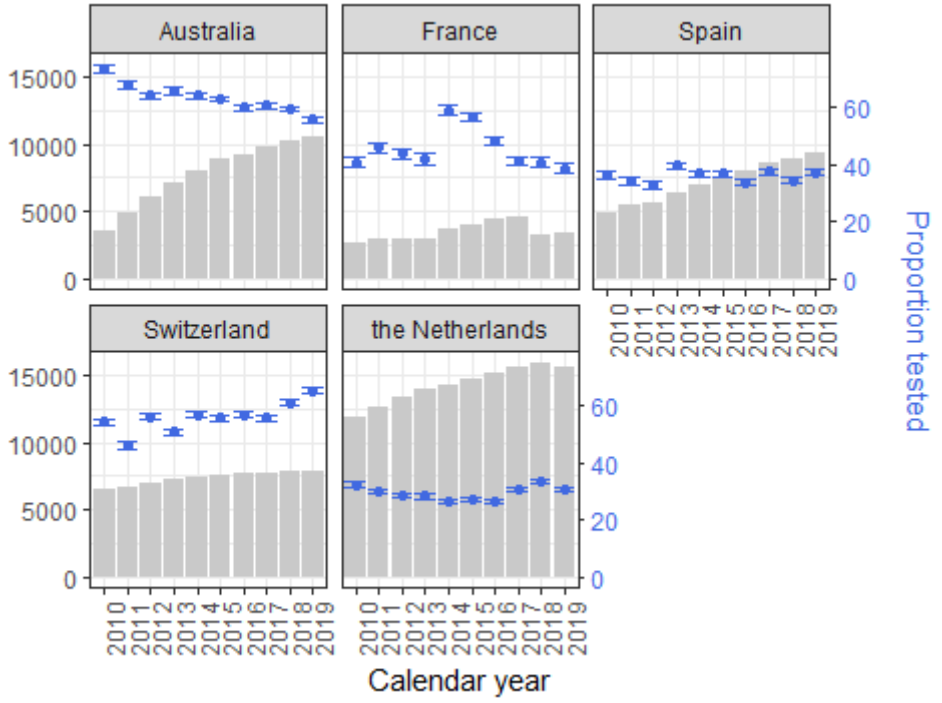
This graph shows all positives tests during 2010 and 2019 without accounting for the midpoint date of HCV seroconversion, hence more positives test may be represented in this graph than included in the analysis.

1.7. Supplementary Figure 6: Number of participants with a study visit and an HCV test per calendar year (2010-2019)

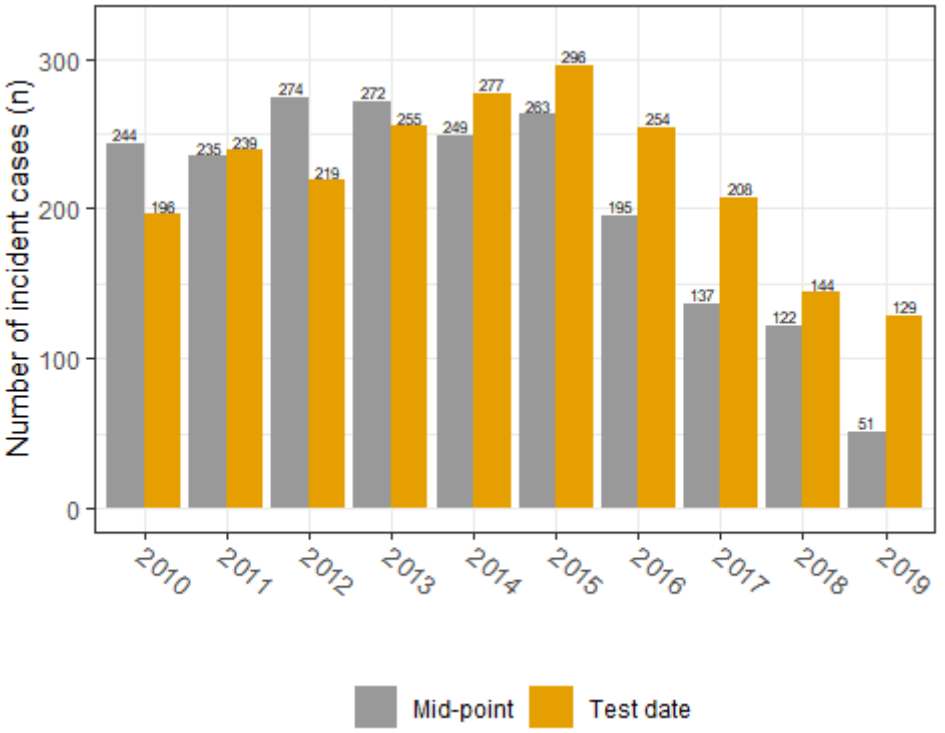


A) Among individuals with an unknown (i.e., no recorded HCV test) or negative HCV antibody status B) Among individuals with a negative HCV antibody status. The ATHENA cohort was excluded from panel A as data among untested was not available for this cohort within InCHEHC.

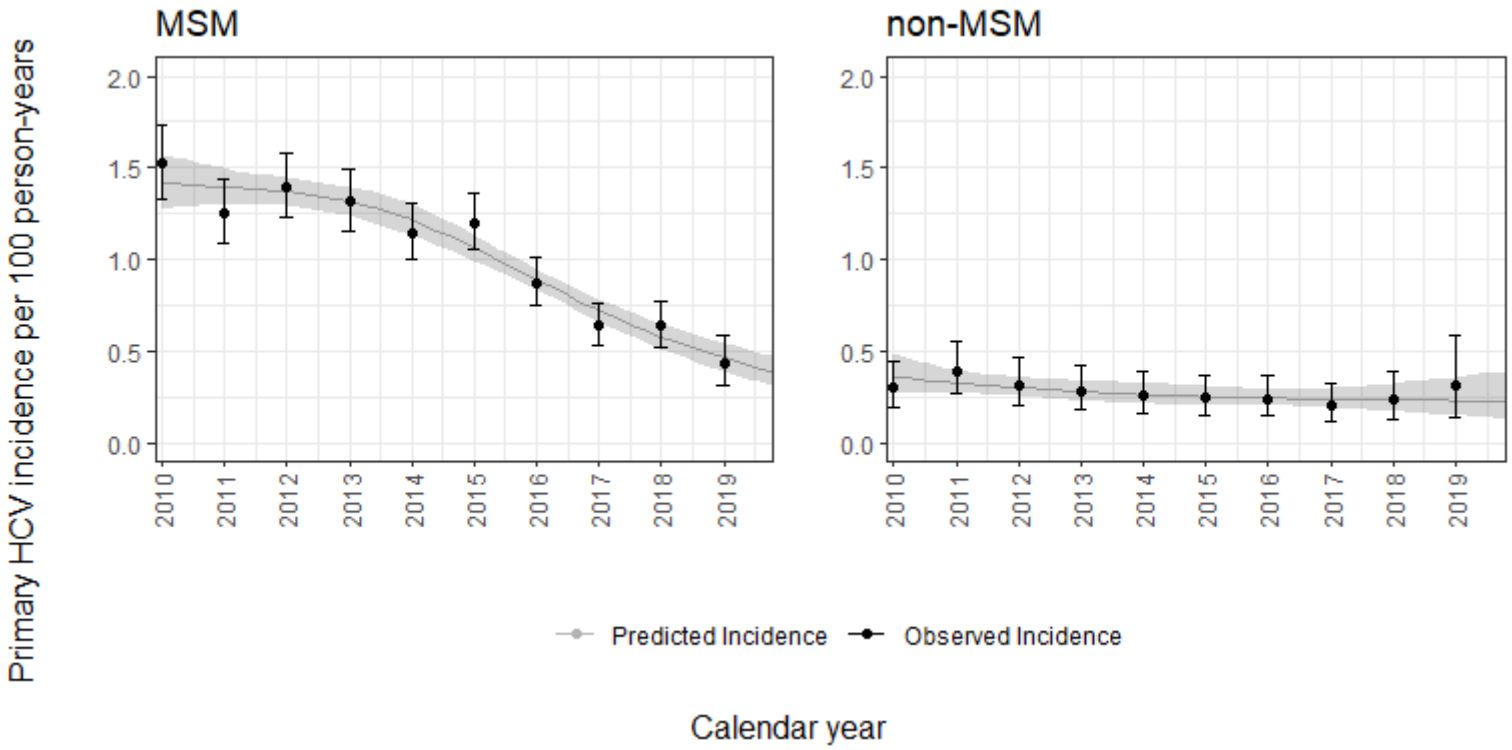
1.8. Supplementary Figure 7: Number of participants with HCV antibody negative HCV status with a visit and a HCV test per country and calendar year (2010-2019)



1.9. Spplementary Figure 8: Annual number of incident HCV cases by positive test date and midpoint date estimation between 2010 and 2019

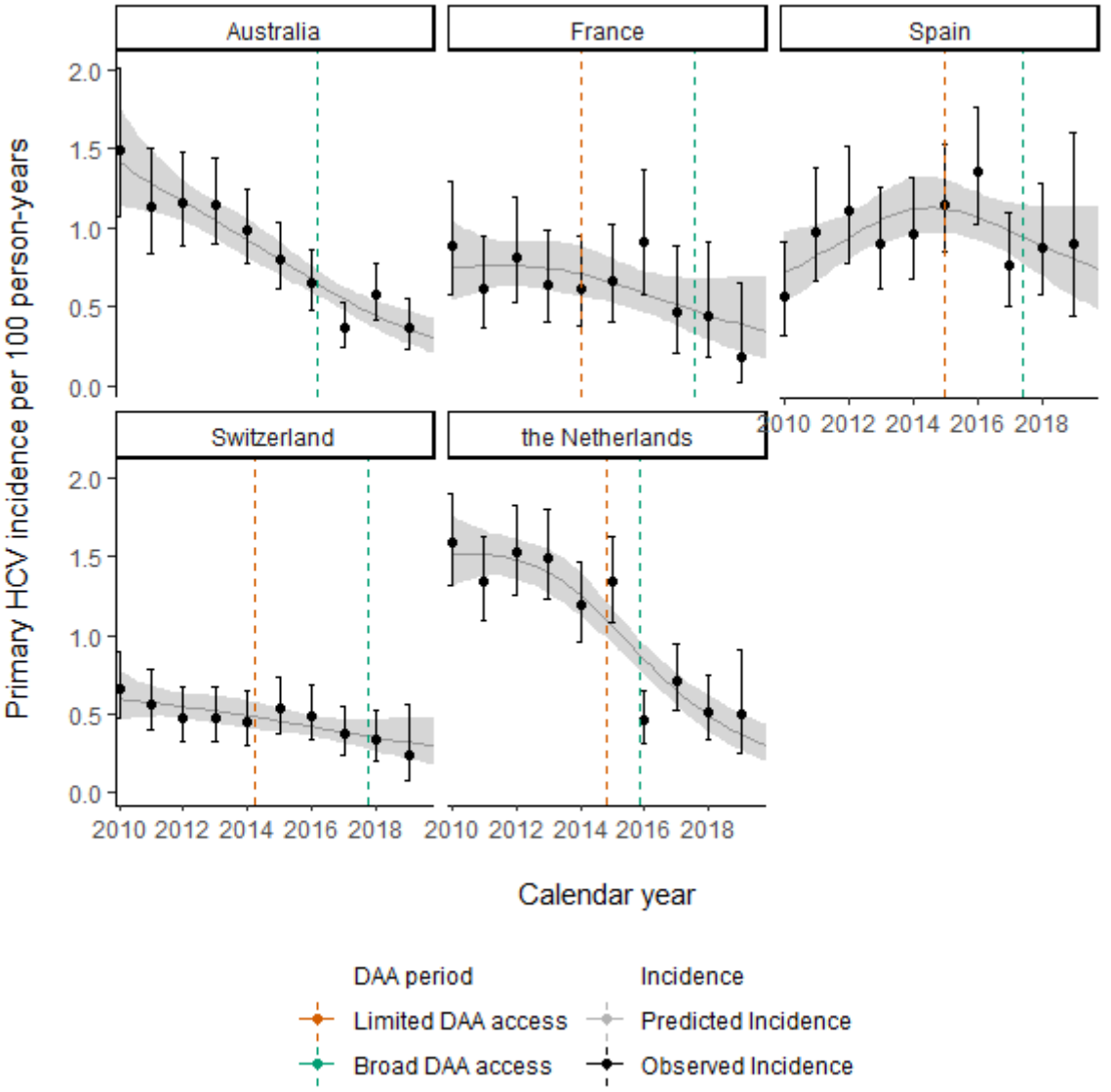


1.10. Supplementary Figure 9: Overall HCV incidence per calendar year in the pooled dataset among MSM (2010-2019)



Black dots and bars represented the observed incidence and its 95%CI. Grey line and band represent the predicted incidence and its 95%CI using Poisson regression modelling calendar year using restricted cubic splines.

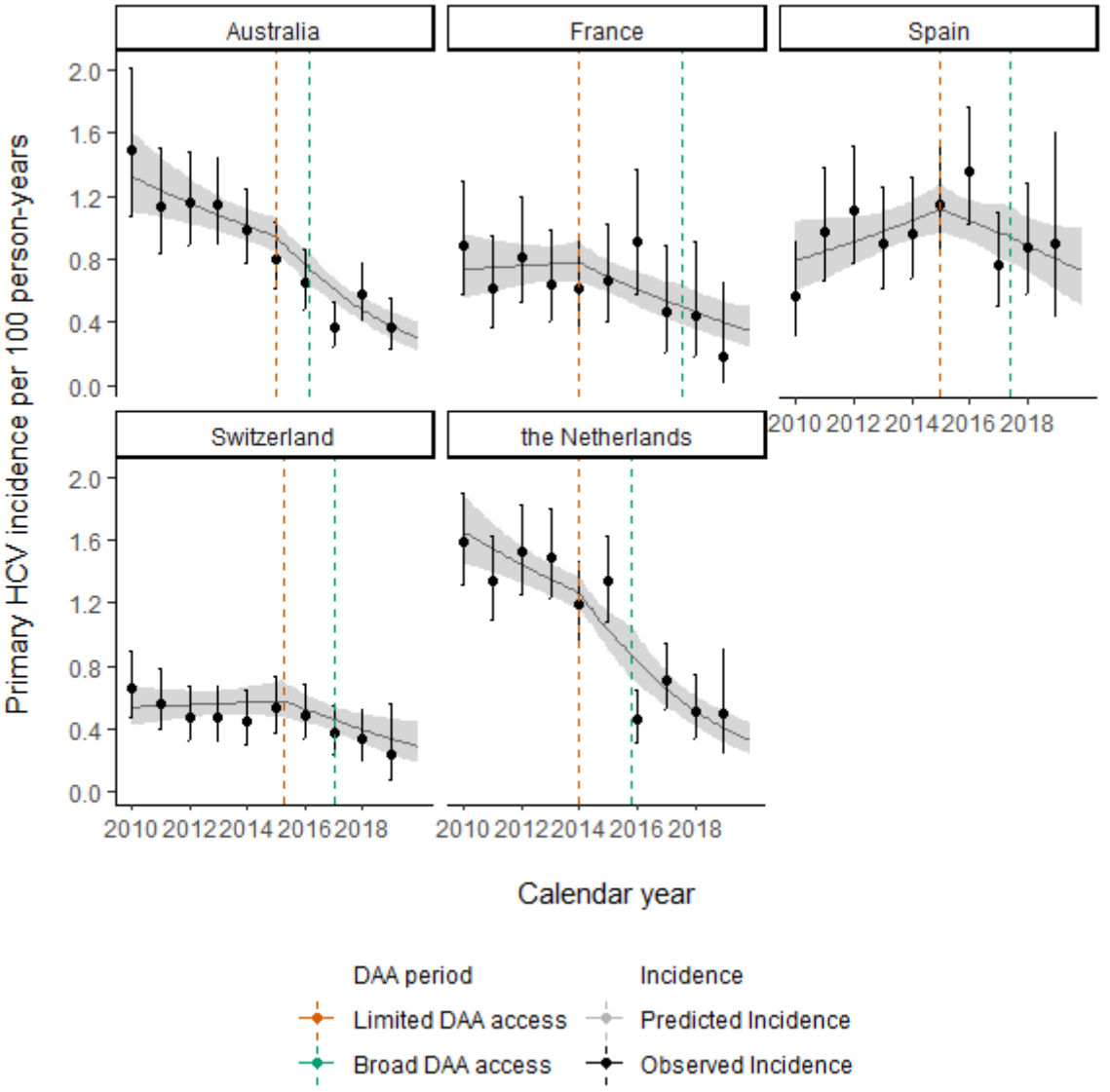
1.11. Supplementary Figure 10: Observed and predicted trends in primary HCV incidence by country (2010-2019)



Trends in primary HCV incidence over calendar time shown in this graph were calculated using Poisson regression models where HCV incidence was allowed to vary smoothly over calendar years using restricted cubic splines with three knots (at the 10th, 50th and 90th percentiles of follow up time). Analyses were stratified per country.

2. Sensitivity analyses

2.1. Supplementary Figure 11: Treatment as prevention effect of DAA access on HCV primary incidence, sensitivity analysis including a DAA restricted period for Australia



Abbreviations: HCV: hepatitis C virus; DAA: direct-acting antiviral. Predicted incidence based on the linear spline model.

2.2. Table 2: Piecewise exponential survival model of primary incidence prior to and during DAA access excluding Spain

	Piecewise exponential survival model
Limited DAA access: IRR (95% CI)	0.91 (0.79-1.05)
Broad DAA access: IRR (95% CI)	0.44 (0.39-0.50)
Intercept: IR (95% CI)	0.01 (0.01-0.01)

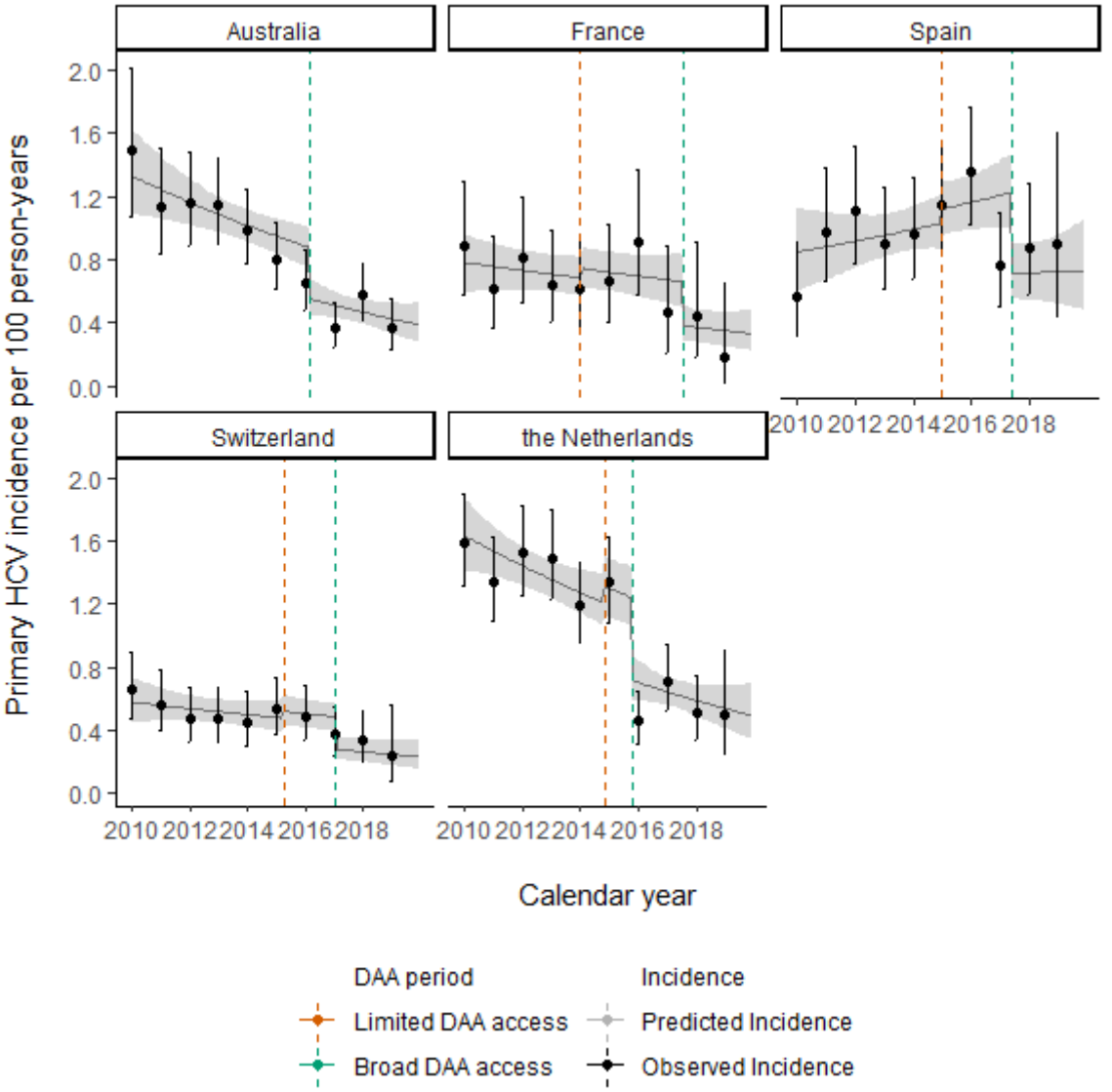
CI: Confidence interval

IRR: Incidence rate ratio

IR: Incidence rate

Random effect variance for the intercept was 0.13 (standard error=0.36).

2.3. Supplementary Figure 12: Treatment as prevention effect of DAA access on HCV primary incidence using an interrupted time series analysis approach



Abbreviations: HCV: hepatitis C virus; DAA: direct-acting antiviral.

2.4. Supplementary Table 3: Treatment as prevention effect of DAA access on HCV primary incidence using an interrupted time series analysis approach

	ITSA
Intercept: IR (95% CI)	0.01 (0.01-0.01)
Slope: IRR (95% CI)	0.97 (0.92-1.02)
Change in slope associated with limited DAA access: IRR (95% CI)	1.00 (0.90-1.10)
Change in slope associated with broad DAA access: IRR (95% CI)	0.97 (0.85-1.10)
Immediate change in incidence after limited DAA access: IRR (95% CI)	1.09 (0.92-1.29)
Immediate change in incidence after broad DAA access: IRR (95% CI)	0.63 (0.49-0.81)
Intraclass correlation	0.55

Abbreviations: DAA: direct-acting antiviral; HCV: hepatitis C virus; IR: Incidence rate; CI: Confidence interval; IRR: Incidence rate ratio; ITSA: interrupted time series analysis.

3. Ethics and fundings per cohort

3.1. Ethics committees

Ethics approval for the coordinating centre was granted by the Alfred Hospital Human Research Ethics Committee. Ethics approval for each cohort has been granted by the following committees: ACCESS and Co-EC: Alfred Hospital Human Research Ethics Committee. ANRS CO13 HEPAVIH: CPP Ile de France III. ANRS CO3 AQUITAINE: CPP Sud-Ouest et Outre-mer III. ATHENA cohort: At initiation, the cohort was approved by the institutional review board of all participating centres. People entering HIV care receive written material about participation in the ATHENA cohort and are being informed by their treating physician of the purpose of collection of data, after which they can consent verbally or elect to opt-out. Data are pseudonymised before being provided to investigators and may be used for scientific purposes. A designated quality management coordinator safeguards compliance with the European General Data Protection Regulation. Canadian Coinfection Cohort: McGill University Health Centre Research Ethics Board. CEASE: St Vincent's Hospital Human Research Ethics Committee. CoRIS: Comité Ético de Investigación Clínica del Hospital General Universitario Gregorio Marañon. MOSAIC: Institutional Review Board of the Academic Medical Center and ethical committees/board of directors of each institute recruiting participants SAIDCC: Registre général des traitements de l'APHP.

3.2. Funding

ACCESS is funded by the Australian Department of Health. The ATHENA database is maintained by Stichting HIV Monitoring and supported by a grant from the Dutch Ministry of Health, Welfare and Sport through the Centre for Infectious Disease Control of the National Institute for Public Health and the Environment. The Canadian Co-infection Cohort is supported by the Canadian Institutes of Health Research (CIHR FDN-143270), the CIHR Canadian HIV Trials Network (CTN222) and the Fonds de recherche du Québec - Santé (FRQ-S): Réseau SIDA/maladies infectieuses. The CEASE study is supported by an investigator initiated grant from Gilead. Co-EC is supported by an investigator initiated grant from Bristol-Myers-Squibb. The RIS cohort (CoRIS) is supported by the Instituto de Salud Carlos III through the Red Temática de Investigación Cooperativa en Sida (RD06/006, RD12/0017/0018 and RD16/0002/0006) as part of the Plan Nacional R+D+I and cofinanced by ISCIII-Subdirección General de Evaluación y el Fondo Europeo de Desarrollo Regional (FEDER). The MOSAIC study is financially supported by the 'Aidsfonds' Netherlands (grant numbers 2008.026 and 2013.037) ; the Research and Development Foundation of the Public Health Service of Amsterdam; Gilead Sciences Netherlands BV and AbbVie BV. The Saint-Antoine Infectious Disease Clinical Cohort is funded by the Saint-Antoine hospital. The Swiss HIV cohort studies are supported by the Swiss National Science Foundation (grant #177499). The ANRS CO13 Hepavih cohort is supported by the French national Agency for HIV and Hepatitis Research (ANRS). The ANRS CO3 Aquitaine cohort is supported by the ANRS | MIE and the CHU de Bordeaux.