

# Population-level estimates of hepatitis C reinfection post scale-up of direct-acting antivirals among people who inject drugs

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**Table S1** PWID cohort in Scotland by time of initiating treatment for HCV, NHS board of treatment and treatment setting.

	<b>2000-2009</b> n (% within NHS board)	<b>2010-2014</b> n (% within NHS board)	<b>2015-2016</b> n (% within NHS board)	<b>2017-2018</b> n (% within NHS board)
<b>Greater Glasgow and Clyde</b>	<b>410</b>	<b>863</b>	<b>854</b>	<b>1102</b>
Hospital	26 (6.3%)	679 (78.7%)	722 (84.5%)	731 (66.3%)
Community	0 (0.0%)	30 (3.5%)	64 (7.5%)	303 (27.5%)
Prison	0 (0.0%)	70 (8.1%)	66 (7.7%)	68 (6.2%)
Other/Not Known	384 (93.7%)	84 (9.7%)	2 (0.2%)	0 (0.0%)
<b>Grampian/Lothian</b>	<b>331</b>	<b>421</b>	<b>346</b>	<b>341</b>
Hospital	179 (54.1%)	348 (82.7%)	264 (76.3%)	200 (58.7%)
Community	7 (2.1%)	56 (13.3%)	70 (20.2%)	120 (35.2%)
Prison	11 (3.3%)	17 (4.0%)	11 (3.2%)	21 (6.2%)
Other/Not Known	134 (40.5%)	0 (0.0%)	1 (0.3%)	0 (0.0%)
<b>Tayside</b>	<b>145</b>	<b>303</b>	<b>226</b>	<b>344</b>
Hospital	1 (0.7%)	82 (27.1%)	73 (32.3%)	52 (15.1%)
Community	0 (0.0%)	141 (46.5%)	125 (55.3%)	259 (75.3%)
Prison	0 (0.0%)	38 (12.5%)	28 (12.4%)	33 (9.6%)
Other/Not Known	144 (99.3%)	42 (13.9%)	0 (0.0%)	0 (0.0%)

NHS = National Health Service.

**Table S2** Characteristics of the PWID cohort treated for HCV in Scotland and the numbers that were followed up for reinfection.

	Number achieved SVR N1 (col %)*	Number with confirmatory negative SVR test N2 (% of N1)**	Number with at least one follow-up test post-SVR N3 (% of N1)**
Total	5686	5145 (90.5)	4126 (72.6)
<b>Time of Treatment Initiation</b>			
2000-2009	886 (15.6)	694 (78.3)	588 (66.4)
2010-2014	1587 (27.9)	1372 (86.5)	1137 (71.6)
2015-2016	1426 (25.1)	1354 (95.0)	1185 (83.1)
2017-2018	1787 (31.4)	1725 (96.5)	1216 (68.0)
<b>NHS Board of Treatment</b>			
Greater Glasgow and Clyde	3229 (56.8)	3053 (94.5)	2624 (81.3)
Grampian/Lothian	1439 (25.3)	1229 (85.4)	990 (68.8)
Tayside	1018 (17.9)	863 (84.8)	512 (50.3)
<b>Treatment Setting</b>			
Hospital	3357 (59.0)	3090 (92.0)	2589 (77.1)
Community	1175 (20.7)	1103 (93.9)	778 (66.2)
Prison	363 (6.4)	323 (89.0)	252 (69.4)
Other/Not Known	791 (13.9)	629 (79.5)	507 (64.1)
<b>Gender</b>			
Female	1355 (23.8)	1201 (88.6)	920 (67.9)
Male	4331 (76.2)	3944 (91.1)	3206 (74.0)
<b>Age (Years)</b>			
50+	1218 (21.4)	1157 (95.0)	955 (78.4)
35-49	3286 (57.8)	2989 (91.0)	2383 (72.5)
<35	1182 (20.8)	999 (84.5)	788 (66.7)
<b>Cirrhosis at Time of Treatment</b>			
No	4544 (79.9)	4074 (89.7)	3203 (70.5)
Yes	1142 (20.1)	1071 (93.8)	923 (80.8)
<b>Opioid/Injection Hospital Admission</b>			
>3 Years Pre-Treatment/Never Pre-Treatment	4452 (78.3)	4032 (90.6)	3245 (72.9)
During Treatment/In the 3 Years Pre-Treatment	1234 (21.7)	1113 (90.2)	881 (71.4)

\*Achieved SVR according to the Scottish HCV clinical database. Patients can achieve SVR more than once if they were reinfected.

\*\*HCV RNA or antigen test.

NHS = National Health Service. SVR = sustained virological response.

**Table S3** Retreatment for HCV among PWID with reinfections diagnosed between 2015-2017.

	Reinfections diagnosed 2015-2017	Number retreated	% retreated	Time to retreatment (Years; Median, IQR)	Number not retreated
Total	79	49	62%	1.2 (0.6-1.8)	30
<b>NHS Board of Treatment</b>					
Greater Glasgow and Clyde	42	19	45%	0.8 (0.6-1.5)	23
Grampian/Lothian	9	6	67%	1.1 (0.4-2.1)	3
Tayside	28	24	86%	1.4 (0.8-2.1)	4
<b>Treatment Setting</b>					
Hospital	31	14	45%	0.8 (0.6-1.4)	17
Community	35	28	80%	1.5 (0.8-2.1)	7
Prison	13	7	54%	1.2 (0.6-1.6)	6
<b>Gender</b>					
Female	17	10	59%	1.3 (0.6-2.1)	7
Male	62	39	63%	1.2 (0.6-1.6)	23
<b>Age (Years)</b>					
50+	12	7	58%	1.1 (0.9-1.9)	5
35-49	50	31	62%	0.8 (0.5-1.5)	19
<35	17	11	65%	2.1 (1.4-2.4)	6
<b>Cirrhosis at Time of Treatment</b>					
No	62	42	68%	1.4 (0.7-1.8)	20
Yes	17	7	41%	0.6 (0.5-0.8)	10
<b>Opioid/Injection Hospital Admission</b>					
>3 Years Pre-Treatment/Never Pre-Treatment	43	25	58%	1.3 (0.6-1.8)	18
During Treatment/In the 3 Years Pre-Treatment	36	24	67%	1.1 (0.5-1.5)	12

IQR = interquartile range. NHS = National Health Service.

**Table S4** HCV reinfection rates for PWID treated between 2015-2018 within the first, second and third years of follow-up since SVR.

Year of Follow-up Since SVR	Time of Treatment Initiation	Reinfections	Person-Years	Reinfection Rate per 100 PY
1	2015-2016	36	906	4.0 (2.8-5.4)
	2017-2018	65	693	9.4 (7.3-11.9)
	2015-2018	101	1,599	6.3 (5.2-7.6)
2	2015-2016	45	520	8.7 (6.4-11.5)
	2017-2018	9	144	6.3 (3.1-11.4)
	2015-2018	54	663	8.1 (6.2-10.5)
3	2015-2016	13	287	4.5 (2.5-7.5)
	2017-2018	0	5	0.0 (0.0-46.5)
	2015-2018	13	292	4.5 (2.5-7.4)

PY = person-years. SVR = sustained virological response.

**Table S5** Number of SVR events for PWID treated for HCV between 2015-2018 and tested for HCV within different time intervals following SVR.

Time of treatment initiation	No. tested 0-11 months post-SVR / No. with SVR*	No. tested 12-23 months post-SVR / No. with $\geq 12$ months follow-up possible*	No. tested $\geq 24$ months post-SVR / No. with $\geq 24$ months follow-up possible*	No. tested any time post-SVR / No. with SVR*
2015-2016	1067/1426 (75%)	468/1389 (34%)	484/1342 (36%)	1242/1426 (87%)
2017-2018	1133/1787 (63%)	349/1372 (25%)	37/331 (11%)	1252/1787 (70%)
2015-2018	2200/3213 (68%)	817/2761 (30%)	521/1673 (31%)	2494/3213 (78%)

\*HCV RNA/Ag test; follow-up time possible starts from the date of their confirmatory SVR test (or 12 weeks post-treatment where a SVR test was not identified) up to the earliest of the end of 2019, death or migration.

SVR = sustained virological response.

**Table S6** Number of SVR events observed between 2015-2018 and person-time contributed to estimate reinfection as well as the number of SVR events and person-time that could not be observed due to incomplete retesting for HCV.

	Observed SVR events	Observed PY	Unobserved SVR events*	Unobserved PY**
Total	2401	2646	678	3997
<b>Greater Glasgow and Clyde</b>	<b>1649</b>	<b>1870</b>	<b>251</b>	<b>2168</b>
Hospital	1225	1477	180	1754
Community	313	281	49	282
Prison	109	109	22	128
Other/Not Known	2	3	0	4
<b>Grampian/Lothian</b>	<b>485</b>	<b>477</b>	<b>174</b>	<b>1096</b>
Hospital	341	337	107	801
Community	117	112	63	254
Prison	26	28	4	39
Other/Not Known	1	0	0	3
<b>Tayside</b>	<b>267</b>	<b>299</b>	<b>253</b>	<b>732</b>
Hospital	64	54	42	218
Community	180	215	179	434
Prison	23	31	32	80

\*PWID who attained SVR according to the HCV clinical database and had a confirmatory SVR test identified on the HCV test database but could not be followed up for reinfection because they had no follow-up HCV RNA/Ag test.

\*\*For patients that could be followed up for reinfection, unobserved person-time is the time between their latest HCV RNA/Ag test and the end of the study period; for patients that could not be followed up, unobserved person-time is the amount of time between their confirmatory SVR test and the end of the study period.

PY = person-years. SVR = sustained virological response.

**Table S7** HCV reinfection rates per 100 person-years for observed data and observed data supplemented with simulated data to give complete follow up for PWID initiating treatment in 2015-2018. Reinfection rates used in simulations were halved to account for the possibility of reduced reinfection risk for unobserved periods. An additional 678 patients with a confirmatory SVR test identified on the HCV test database but no follow-up test post-SVR were included in simulations.

	Observed Data			Estimated from Simulation				
	SVR events	Diagnosed reinfections	PY	Reinfection rate per 100 PY (95% CI)*	Undiagnosed reinfections (Median, 95% CI)*	Total reinfections (Median, 95% CI)*	PY (Median)*	Reinfection rate per 100 PY (Median, 95% CI)
<b>Total</b>	2401	169	2646	6.4 (5.5-7.5)	104 (87-125)	273 (256-294)	6484	4.2 (3.5-5.1)
<b>Time of Treatment Initiation**</b>								
2015-2016	1185	95	1803	5.3 (4.3-6.5)	52 (39-66)	147 (134-161)	4099	3.6 (2.7-4.6)
2017-2018	1216	74	843	8.8 (7.0-11.1)	53 (40-66)	127 (114-140)	2386	5.3 (4.0-6.9)
<b>Treatment Setting</b>								
Hospital	1633	68	1871	3.6 (2.8-4.6)	42 (30-55)	110 (98-123)	4566	2.4 (1.8-3.2)
Community	610	66	608	10.9 (8.5-13.9)	43 (31-56)	109 (97-122)	1531	7.1 (5.2-9.6)
Prison	158	35	167	20.9 (14.8-29.5)	19 (12-28)	54 (47-63)	388	14.0 (8.8-21.0)
<b>NHS Board of Treatment</b>								
Greater Glasgow and Clyde	1649	110	1870	5.9 (4.9-7.1)	51 (38-64)	161 (148-174)	3960	4.1 (3.2-5.1)
Grampian/Lothian	485	11	477	2.3 (1.3-4.3)	13 (7-21)	24 (18-32)	1549	1.5 (0.7-2.9)
Tayside	267	48	299	16.1 (12.0-21.6)	41 (30-53)	89 (78-101)	976	9.1 (6.3-12.6)
<b>Age (Years)</b>								
50+	730	25	724	3.5 (2.3-5.1)	19 (12-28)	44 (37-53)	1960	2.2 (1.3-3.5)
35-49	1414	110	1612	6.8 (5.6-8.3)	60 (47-76)	170 (157-186)	3774	4.5 (3.5-5.7)
<35	257	34	310	11.0 (7.8-15.5)	25 (16-35)	59 (50-69)	751	7.9 (5.0-11.6)

\*Median and 95% confidence intervals estimated from 1000 simulations.

\*\*Estimates of undiagnosed reinfection were based on observed data on diagnosed reinfection multiplied by half; estimates for those initiating treatment in 2015-16 were based on observed data from those treated during 2014-16, and estimates for those initiating treatment in 2017-18 were based on observed data from those treated during 2014-18.

CI = confidence interval. NHS = National Health Service. PY = person-years.

**Table S8** HCV reinfection rates per 100 person-years for observed data and observed data supplemented with simulated data to give complete follow up for PWID initiating treatment in 2015-2018. Reinfection rates used in simulations were increased by 50% to account for the possibility of increased reinfection risk for unobserved periods. An additional 678 patients with a confirmatory SVR test identified on the HCV test database but no follow-up test post-SVR were included in simulations.

	Observed Data			Estimated from Simulation				
	SVR events	Diagnosed reinfections	PY	Reinfection rate per 100 PY (95% CI)*	Undiagnosed reinfections (Median, 95% CI)*	Total reinfections (Median, 95% CI)*	PY (Median)*	Reinfection rate per 100 PY (Median, 95% CI)
<b>Total</b>	2401	169	2646	6.4 (5.5-7.5)	285 (257-315)	454 (426-484)	6356	7.1 (6.1-8.4)
<b>Time of Treatment Initiation**</b>								
2015-2016	1185	95	1803	5.3 (4.3-6.5)	138 (119-159)	233 (214-254)	4021	5.8 (4.6-7.2)
2017-2018	1216	74	843	8.8 (7.0-11.1)	146 (126-168)	220 (200-242)	2336	9.4 (7.4-11.7)
<b>Treatment Setting</b>								
Hospital	1633	68	1871	3.6 (2.8-4.6)	120 (102-141)	188 (170-209)	4502	4.2 (3.2-5.3)
Community	610	66	608	10.9 (8.5-13.9)	117 (99-135)	183 (165-201)	1486	12.3 (9.4-15.6)
Prison	158	35	167	20.9 (14.8-29.5)	48 (38-58)	83 (73-93)	367	22.7 (15.4-31.7)
<b>NHS Board of Treatment</b>								
Greater Glasgow and Clyde	1649	110	1870	5.9 (4.9-7.1)	142 (123-163)	252 (233-273)	3902	6.4 (5.2-7.9)
Grampian/Lothian	485	11	477	2.3 (1.3-4.3)	36 (26-48)	47 (37-59)	1531	3.1 (1.7-4.9)
Tayside	267	48	299	16.1 (12.0-21.6)	107 (90-125)	155 (138-173)	923	16.7 (12.5-21.8)
<b>Age (Years)</b>								
50+	730	25	724	3.5 (2.3-5.1)	54 (41-67)	79 (66-92)	1932	4.1 (2.7-5.9)
35-49	1414	110	1612	6.8 (5.6-8.3)	165 (143-188)	275 (253-298)	3701	7.4 (6.0-9.0)
<35	257	34	310	11.0 (7.8-15.5)	66 (52-79)	100 (86-113)	724	13.8 (9.6-18.8)

\*Median and 95% confidence intervals estimated from 1000 simulations.

\*\*Estimates of undiagnosed reinfection were based on observed data on diagnosed reinfection multiplied by 1.5; estimates for those initiating treatment in 2015-16 were based on observed data from those treated during 2014-16, and estimates for those initiating treatment in 2017-18 were based on observed data from those treated during 2014-18.

CI = confidence interval. NHS = National Health Service. PY = person-years.