

	Deaths (n=4706)	Person-years (n=304 042)	Mortality per 1000 person-years (95% CI)	HR (95% CI)*†	p value	Adjusted HR (95% CI)*†	p value	Adjusted HR (95% CI)*†‡	p value
OAT exposure (time varying)									
On OAT	1832	223 973	8.18 (7.81–8.56)	1 (ref)	..	1 (ref)	..	1 (ref)	..
Off OAT	2244	80 069	28.03 (26.88–29.20)	3.43 (2.79–4.22)	<0.001	3.64 (2.98–4.45)	<0.001	3.37 (1.74–6.53)	<0.001
Sex									
Male	2834	203 776	13.91 (13.40–14.43)	1 (ref)	..	1 (ref)	..	1 (ref)	..
Female	1242	100 266	12.39 (11.71–13.09)	0.89 (0.66–1.19)	0.440	0.94 (0.76–1.17)	0.581	0.94 (0.76–1.17)	0.574
Age group (time-varying), years									
<25	39	6070	6.42 (4.64–8.69)	0.50 (0.08–1.56)	0.325	0.55 (0.20–1.53)	0.252	0.55 (0.20–1.53)	0.251
25–34	658	75 918	8.67 (8.02–9.35)	0.67 (0.45–0.98)	0.045	0.71 (0.53–0.96)	0.024	0.71 (0.53–0.96)	0.024
35–44	1794	139 043	12.90 (12.32–13.51)	1 (ref)	..	1 (ref)	..	1 (ref)	..
45–54	1360	70 699	19.24 (18.23–20.28)	1.49 (1.09–2.03)	0.010	1.36 (1.08–1.71)	0.009	1.36 (1.08–1.71)	0.009
≥55	225	12 312	18.28 (16.00–20.78)	1.42 (0.73–2.49)	0.260	1.21 (0.77–1.90)	0.402	1.21 (0.77–1.90)	0.409
Time period									
2011–12	368	57 890	6.36 (5.73–7.03)	1 (ref)	..	1 (ref)	..	1 (ref)	..
2013–14	500	60 669	8.24 (7.54–8.99)	1.30 (0.73–2.36)	0.385	1.25 (0.81–1.93)	0.316	1.03 (0.53–2.01)	0.924
2015–16	773	61 721	12.52 (11.66–13.43)	1.97 (1.17–3.45)	0.015	1.82 (1.22–2.72)	0.004	1.62 (0.89–2.95)	0.115
2017–18	1117	62 306	17.93 (16.90–19.00)	2.82 (1.72–4.82)	<0.001	2.57 (1.75–3.78)	<0.001	2.45 (1.40–4.30)	0.002
2019–20	1318	61 455	21.45 (20.31–22.63)	3.37 (2.09–5.72)	<0.001	2.83 (1.94–4.13)	<0.001	2.96 (1.70–5.15)	<0.001
Health board									
Other NHS regions in Scotland	2258	179 279	12.60 (12.09–13.13)	1 (ref)	..	1 (ref)	..	1 (ref)	..
Greater Glasgow and Clyde	1430	100 504	14.23 (13.51–14.99)	1.13 (0.84–1.51)	0.414	1.12 (0.89–1.42)	0.328	1.13 (0.89–1.42)	0.320
Tayside	388	24 260	15.99 (14.48–17.67)	1.27 (0.79–2.04)	0.325	1.14 (0.79–1.64)	0.493	1.14 (0.79–1.64)	0.488
SIMD (deprivation index)									
1 (most deprived)	2393	167 507	14.29 (13.73–14.87)	1 (ref)	..	1 (ref)	..	1 (ref)	..
2	982	76 014	12.92 (12.14–13.75)	0.90 (0.65–1.26)	0.548	0.93 (0.73–1.19)	0.554	0.93 (0.73–1.18)	0.544
3, 4, or 5 (least deprived)	701	60 522	11.58 (10.76–12.47)	0.81 (0.56–1.18)	0.269	0.82 (0.62–1.08)	0.166	0.82 (0.62–1.08)	0.163
HIV status (time-varying)									
Never diagnosed	4018	302 034	13.30 (12.90–13.72)	1 (ref)	..	1 (ref)	..	1 (ref)	..
Diagnosed	58	2 009	28.87 (22.32–37.35)	2.17 (0.69–6.82)	0.184	1.44 (0.62–3.35)	0.394	1.44 (0.62–3.34)	0.392
HCV status (time-varying)									
Never diagnosed	1873	178 656	10.48 (10.02–10.97)	1 (ref)	..	1 (ref)	..	1 (ref)	..
Diagnosed with anti-HCV (not chronic)	543	27 362	19.85 (18.24–21.59)	1.89 (1.24–2.89)	0.003	1.78 (1.30–2.43)	<0.001	1.78 (1.31–2.44)	<0.001
Diagnosed ever with chronic HCV infection	1660	98 024	16.94 (16.14–17.77)	1.62 (1.21–2.16)	0.001	1.41 (1.13–1.75)	0.002	1.41 (1.14–1.76)	0.002
Prescriber type									
General practitioner	2520	194 621	12.95 (12.45–13.46)	1 (ref)	..	1 (ref)	..	1 (ref)	..
Other (eg, pharmacists, nurses, and hospitals)	1556	109 422	14.22 (13.53–14.95)	1.10 (0.83–1.45)	0.512	1.02 (0.81–1.29)	0.843	1.02 (0.81–1.29)	0.859
Mental health disorder admission									
No	3466	274 146	12.64 (12.23–13.07)	1 (ref)	..	1 (ref)	..	1 (ref)	..
Yes	610	29 897	18.85 (18.85–22.09)	1.61 (1.10–2.36)	0.014	1.37 (1.02–1.82)	0.034	1.37 (1.02–1.82)	0.033
Non-fatal overdose admission									
No	2966	247 033	12.01 (11.58–12.45)	1 (ref)	..	1 (ref)	..	1 (ref)	..
Yes	1110	57 009	19.47 (18.36–20.65)	1.62 (1.20–2.20)	0.002	1.49 (1.18–1.89)	0.001	1.49 (1.18–1.88)	0.001

A likelihood ratio test indicated that fitting a model that included the interaction term significantly improved model fit ($p < 0.001$). Likelihood-ratio test: $\chi^2 = 19.52$ (df=4); $p = 0.0006$. SIMD=Scottish Index of Multiple Deprivation. HCV=hepatitis C virus. HR=hazard ratio. OAT=opioid-agonist therapy. *HR and adjusted HR modelled using quasi-poisson regression. †95% CIs for rates calculated using the quasi-poisson method. ‡Adjusted HR includes an interaction term for OAT exposure by time period (see table 3 for full model results).

Table 2: Crude mortality rates, HRs, and adjusted HRs for drug-related deaths

further showed the risk of bias over a longer study period with mortality rates of those off and on OAT converging over time (appendix p 5).

Our Greater Glasgow and Clyde specific models, in which CHI coverage is higher, produced generally similar results to the overall models in our main analysis