Evidence of continued injecting drug use after attaining sustained treatment-induced clearance of the hepatitis C virus: implications for reinfection

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ABSTRACT

Background: People who inject drugs (PWID) are at the greatest risk of hepatitis C virus (HCV) infection, yet are often denied immediate treatment due to fears of on-going risk behaviour. Our principle objective was to examine evidence of continued injecting drug use among PWID following successful treatment for HCV and attainment of a sustained viral response (SVR).
Methods: PWID who attained SVR between 1992 and June 2012 were selected from the National Scottish Hepatitis C Clinical Database. Hospitalisation and mortality records were sourced for these patients using record-linkage techniques. Our primary outcome variable was any hospitalisation or death which was indicative of injecting drugs post-SVR.
Results: The cohort comprised 1170 PWID (mean age at SVR 39.6y; 76% male). The Kaplan Meier estimate of incurring the primary outcome after three years of SVR was 10.6% (95% CI, 8.8-12.8) After adjusting for confounding, the risk of an injection related hospital episode or death post-SVR was significantly increased with advancing year of SVR: AHR:1.1 per year (95% CI, 1.0-1.2), having a pre-SVR acute alcohol-related hospital episode: AHR:1.8 (95% CI, 1.3 – 2.6), and having a pre-SVR opiate or injection-related hospital episode: AHR:2.6 (95% CI, 1.9 – 3.7).
Conclusion: Despite attaining the optimal treatment outcome, these data indicate that an increasing significant number of PWID continue to inject post-SVR at an intensity which leads to either hospitalisation or death and potential increased risk of reinfection.

1. Introduction

It is well established that people who inject drugs (PWID) are at the greatest risk of hepatitis C virus (HCV) infection. Globally, there are an estimated 16 million PWID who are currently injecting (Mathers et al., 2008), of which 10 million are estimated to have been infected with HCV (Nelson et al., 2011). Chronic HCV infection is a major cause of liver related morbidity and mortality, but can be cleared with antiviral treatment and establishment of sustained viral response (SVR). Currently, there is low uptake of HCV antiviral treatment among PWID which likely relates to concerns of adherence to, and reinfection post, treatment (Martin et al., 2013; Iversen and Maher 2012). Regardless, a recent meta-analysis found treatment outcomes to be acceptable and risk of HCV reinfection to be relatively low among PWID, albeit based on only a few small scale studies conducted in clinical and harm reduction settings (Aspinall et al., 2013). Modelling work has further demonstrated that treating PWID is cost-effective and has the potential to reduce HCV transmission and prevalence in this population (Martin et al., 2011; Martin et al., 2013). Therefore, recommendations state that treatment is not to be withheld from an individual based on injection status alone (EASL, 2014).

After being deemed one of the greatest public health challenges of our time, HCV was made a priority by the Scottish Government and a comprehensive Action Plan was formulated to curb the predominately injecting-related epidemic (Chisholm, 2004; Scottish Government, 2008). As a result, the overall number of people initiated on antiviral therapy in Scotland more than doubled between 2007 and 2010 with ~1000 now treated per year and the vast majority (>80%) of these report having ever injected drugs (HPA, 2013).

Given this recent, and also anticipated future upscale in treatment provision among PWID, a better understanding is needed of the injecting risk behaviours, and potential for reinfection, post-SVR. Our principle objective, therefore, was to establish evidence, and predictors, of continued engagement in injection drug use post-SVR using a record-linkage approach involving both HCV treatment and injecting-related hospitalisation data for a large nationally representative cohort of over 1000 PWID.

2. Methods

2.1 Study Population, data sources and linkage procedure

This paper utilised a retrospective cohort of Scottish PWID derived from the HCV Clinical Database, using data linked from four, national databases. Health Protection Scotland (HPS) holds and maintains individual patient data for all HCV diagnosed persons who attended a specialist centre for HCV treatment and management across Scotland, referred to as the HCV Clinical Database. This database includes information on patient demographics, virology,

treatment episodes, epidemiological exposures, and liver disease investigations. Inclusion criteria for the study was a history of injection drug use, SVR attained by June 2012, and sufficient identifiers for record-linkage (n=1,259). To enable further database linkage (described below), the HCV Clinical Database was first linked to the Scottish HCV Diagnosis Database, as previously described (Innes, et al., 2011); this linkage also allowed for scrutiny of patient record accuracy, such that patients were dropped if flaws in treatment records were detected (e.g. nonsensical diagnosis and treatment dates).

Hospital episode data were obtained by sourcing Information Services Division (ISD) Scotland's Scottish Morbidity Records (SMR) 01 and 04, which provide general, non-obstetric hospital discharge data and psychiatric hospital admissions data respectively. Hospital episodes are coded using the World Health Organisation's International Classification of Disease (ICD) Ninth Revision for all hospitalisations prior to 1996, and Tenth Revision for hospitalisations thereafter. SMR records include six possible diagnostic fields, all of which were used in analysis.

Mortality data were obtained through sourcing deaths registrations collated by National Records of Scotland. Date, and up to eleven causes of death are recorded for each registered death using ICD-9 and ICD-10 codes.

2.2 Linkage Procedure

ISD Scotland annually link the Scottish HCV Diagnosis Database to SMR and deaths data. This probabilistic linkage technique is estimated to have a rate of false positives or false negatives under 5% (Kendrick & Clarke, 1993); the probabilistic linkage has also been previously described (McDonald et al., 2008).

Thereafter, this linked dataset, containing SMR/deaths data on all HCV diagnosed persons, was transferred to HPS and combined with the Clinical and Diagnosis dataset, via the HCV diagnosis database record number, to enable extraction of hospitalisation and mortality data for all those who had attended a specialist clinic for HCV. The final linked dataset included all relevant demographic, behavioural, morbidity and mortality data for 1170 Scottish PWID who have received antiviral treatment for HCV and attained SVR in the over 20 year period between 1992 and June 2012.

2.2 Outcome Measures

The outcome variable of interest was defined as a hospital event or death indicative of injection drug use. This was identified using the following International Classification of Disease (ICD) codes present in the any diagnosis field indicating hospital discharge diagnosis or death. The

relevant outcome codes comprised opiate-related: *mental and behavioural disorders due to opiate* misuse (ICD-10: F11), *poisoning due to opium* (ICD-9: 965.0; ICD-10: T40.0), *poisoning due to heroin* (ICD-10: T40.1), *accidental poisoning due to heroin* (ICD-9: E8500; ICD-10: X42.4) *accidental poisoning due to opium* (ICD-10: X42.9), *intentional self-poisoning by exposure to opium* (ICD-10: X62.9), *opiate dependence* (ICD-9: 3040), *non-dependent opiate use* (ICD-9: 3055), *finding opiates in blood* (ICD-10: R781),and injection-related as defined in previous literature: *endocarditis* (ICD-9: 421.0; ICD-10: I33), *deep vein thrombosis* (ICD-9: 451, 453 ; ICD-10: I80), *cellulitis /abscesses* (ICD-9: 682; ICD-10: L02, L03), (Lloyd-Smith et al., 2008; Irish et al., 2007).

2.3 Explanatory variables

Behavioural and demographic exposure variables of interest were recorded for each patient pre-SVR and were obtained from clinical and SMR records.

Behavioural variables included presence of an acute alcohol intoxication-related hospital episode, and history of injection indicative hospital episode pre-SVR (using the above listed codes). Alcohol intoxication-related hospital episodes have been previously defined and include hospital episodes due to *problems related to lifestyle alcohol use* (ICD-10: Z72.1), *mental and behavioural disorders due to use of alcohol* (ICD-10: F10), *toxic effect of alcohol (ethanol, methanol, unspecified)*(ICD-9: 980.0, 980.1, 980.9; ICD-10: T51.0, T51.1, T51.9), *blood alcohol level 100-240+/ 100 ml* (ICD-9: 790.3; ICD-10: Y90.5 – Y90.9), *evidence of alcohol involvement determined by level of intent* (ICD-10: Y91), *finding of alcohol in blood* (ICD-10: R78.0), *poisoning by and exposure to alcohol*(ICD-9: E8600-02, E8609; ICD-10: X45, X65, Y15), *alcohol deterrents* (ICD-10: Y57.3), *alcohol abuse counselling and surveillance* (ICD-10: Z71.4), *non-dependent alcohol abuse* (ICD-9: 305.0).

Additional explanatory variables for each PWID included age at SVR, gender, year of SVR (date of SVR was defined as negative HCV RNA reading 24 weeks post-treatment completion), presence of cirrhosis at treatment initiation. Age at SVR was categorised into three groups (<30, 30-44, ≥45). Year of SVR was categorised for descriptive analysis (1992-2004, 2005-2012), and kept continuous for statistical modelling. Patients who were cirrhotic at time of treatment initiation were identified by the Clinical Database, based on a combination of (i) clinical examination; (ii) radiology (ultrasound, transient elastography, computed tomography, or magnetic resonance imaging); or (iii) liver biopsy, as previously described (Innes, et al., 2012).

2.4 Statistical Analyses

All statistical analyses, data storage, and manipulation were conducted using STATA version 12 (College Station, TX, USA).

2.4a Analysis of first-time opiate or injection related hospital event or death

Firstly, Kaplan Meier survival estimates were used to calculate the estimated proportion of the cohort who had an opiate or injection-related hospital episodes or death at three years post-SVR attainment.

Secondly, we used multivariate Cox regression to determine predictors for the first time to first injecting related hospital episode or death. Time at risk was calculated in person years (PY) from date of SVR attainment to first injection-related hospital episode, death, or end of follow up (30th June 2012). Adjusted hazard-ratios of an opiate or injection-related hospital episode or death post-SVR were generated using a multivariate Cox regression analysis, with inclusion of all covariates irrespective of univariate association.

2.4b Analysis of multiple opiate or injection related hospital events and/or death

Risk of multiple hospital episodes associated with behavioural and demographic covariates were analysed using Poisson regression. Time at risk was censored at either death of end of follow up(30 June 2012), but was not censored for periods in hospital. Crude, unadjusted rates of multiple hospital episodes due to opiate or injection-related reasons were measured per 100 PY of follow-up.

3. Results

3.1 Sample Characteristics (Table 1)

Table 1 displays the demographic and behavioural characteristics of the cohort with regards to injection indicative hospital episodes or deaths post-SVR. The average age at SVR was 39.6 years (standard deviation ± 8.2 years; range 19.0-67.7 years), and the majority were male (76%). The majority of the cohort (76%) attained SVR between 2006- June 2012. 37% of the cohort had been in hospital for an opiate or injection related episode pre-SVR. 13% had at least one opiate or injection-related hospital episode or death during an average follow up of 4.1 years.

Kaplan Meier estimates of incurring our primary outcome at three years are presented in Table 1. The overall estimate was 10.6% (95%CI 8.8-12.8%). This proportion varied by demographic/behavioural factors and was highest among those with an opiate or injection-related hospital event/death pre-SVR (19.2%, 95%CI 15.2% - 24.2%). While the lowest estimated proportion of opiate or injection-related hospital event or death was observed for

those who had attained SVR between 1992-2000 (2.2%, 95% CI 0.3-14.7%). A Kaplan Meier curve of those PWID who remain free of injection related hospitalisation over 8 years is illustrated in Figure 1.

3.2 First-time opiate or injection-related hospital episode post-SVR

The overall crude rate of injection indicative hospital episodes post-SVR was 3.12 per 100 PY (Table 2), with the highest incidence rate noted in PWID who had an opiate or injection-related hospital episode pre-SVR (6.04 per 100 PY). Within the respective exposure variable groups, those aged 30 or younger at SVR had the highest incidence (3.92 per 100 PY) when compared with those aged 45 and older, along with females (3.75 per 100 PY), and those with an alcohol intoxication-related hospital episode pre-SVR (5.7 per 100 PY).

In univariate analysis, all covariates with the exception of sex and cirrhosis at treatment initiation were associated with an injection indicative hospital episode or death post-SVR (Table 2). Significant predictors of an opiate or injection-related hospital episode or death post-SVR identified in multivariate Cox regression include: year of SVR (AHR: 1.07, 1.01 – 1.14), alcohol-related hospital episode pre-SVR (AHR: 1.83, 1.29 – 2.60), and opiate or injection-related hospital episode pre-SVR (AHR: 2.59, 1.84 – 3.64). Age at SVR did not retain its significance after adjusting for other covariates.

3.3 Multiple opiate and injection-related hospital episodes post-SVR

There were a total of 236 post-SVR injection indicative hospital episodes and 11 (1%) opiate or injection-related deaths among 1170 PWID, ranging from 0-8 episodes per patient (Table 3). In univariate analysis, all factors with the exception of cirrhosis at treatment initiation were associated with incidence of injection indicative hospital episodes or death post-SVR. In multivariate analysis significant predictors of increased incidence of opiate or injection related hospital episodes post-SVR include sex, history of alcohol intoxication-related hospital episode pre-SVR, and history of opiate or injection-related hospital episode pre-SVR. When compared to males, females had an increased incidence of opiate or injection-related hospital episodes post-SVR (adjusted incidence rate ratio [AIRR]: 1.32, 1.00 – 1.73). History of an alcohol intoxication-related hospital episode (AIRR: 2.59, 1.99 – 3.36), and of opiate of injection-related hospital episode (AIRR: 2.95, 2.24 – 3.89) were shown to significantly predict increased incidence of injection indicative hospital episodes/death post-SVR after adjusting.

4. Discussion

With highly effective but costly HCV treatments on the horizon, and potential demand for treatment to increase, particularly among the population who injects drugs, it is essential that

the behaviours which pose a risk of re-infection post-SVR are well understood. There have been a few small studies examining engagement in injection drug use post-HCV antiviral treatment induced SVR, and these have relied on participation and accurate self-report by PWID, and have varied in respect of recruitment setting; thus, rates of continued injection drug use ranged considerably from 12-100% post-SVR (Marco et al., 2013; Page et al., 2009). Results obtained from our study were derived from a large anonymous record-linkage exercise of routine administrative data on all PWID undergoing therapy, thereby increasing cohort size and avoiding participation bias. This study estimated that 10.6% of the Scottish cohort of 1170 PWID had been in hospital for or had died from an opiate or injection-related cause in the first three years post-SVR, which suggests that in excess of this proportion were injecting drugs during the early years following successful therapy.

A relatively low risk of HCV reinfection post-SVR has so far been reported from studies involving PWID (pooled rate of 2 per 100 PY from recent meta-analysis), however these were predominately centred in settings with considerable harm reduction support and thus may not reflect the wider injecting population (Aspinall et al., 2013). Risk of HCV reinfection has certainly been demonstrated to be far higher, by thirteen-fold, among people who report actively injecting drugs post-SVR when compared with those who do not (Marco et al., 2013). The result here show that the risk of an opiate or injection=related hospital episode or death was rising over time with increasing year of SVR attainment likely reflects the expansion of treatment among the population who have ever injected drugs in Scotland, having increased nine-fold between 2001-2 and 2009-10 (McDonald et al., 2014), and broadening to not just those who have injected in the distant past, but to those who have injected recently and continue to do so. The expansion of therapy in this population group was consistent with the aims of the Scottish Government's Action Plan on HCV and now also the European and Global guidelines which endorse treatment of patients with ongoing drug use. Thus, our proxy injection indicative hospitalisations/deaths data would suggest that reinfection post therapy will rise in Scotland, and could well increase in other countries as they scale-up therapy in their PWID populations.

Individuals found to have been hospitalised for either an injection indicative or alcohol-related cause prior to therapy, being 30% of our cohort, were at significantly increased risk of being admitted or died post-therapy or an opiate/injection-related cause. So the hospitalisation data may help point to a group who are particularly prone to re-engaging with risk behaviours. Likewise, those younger compared to older in age, although not significant in multivariate analysis, were more likely to engage in injecting practices post-treatment, as indicated by an

estimated 15% and 7% of those aged under 30 and over 45 years, respectively, having been in hospital or died from an opiate/injection-related cause within three years of SVR attainment.

There are some limitations to our study. Using hospital diagnosis records does not capture the total amount of injecting occurring post-SVR. Hospitalisations represent extreme cases of injecting (poisoning, overdose, severe injury), and thus likely underestimate the extent to which PWID are continuing to inject, as most injecting episodes do not result in hospitalisation. Additionally, utilising hospitalisation records relies on using ICD codes as a measure of current-diagnosis. ICD codes indicating opiate use or injection drug use do not always necessarily indicate acute injecting episodes and could thus include historical events, or non-injecting opiate abuse, which could have caused an overestimation of the true rate of hospitalisation for post-SVR injection drug use.

This study did not explore engagement in other reinfection risk factors (e.g. tattooing, sexual practices) post-SVR, although these are unlikely to pose the same population risk as continued injecting drug use. Further, we did not consider specifically the risk of reinfection here, as it required follow-up laboratory data on HCV RNA testing, but that is now the focus of a subsequent study. This risk behaviour research has, however, informed the need to fully understand the extent of testing and diagnosis of PWID post-SVR. Additionally, SVR patients account for roughly 60% of the overall treated population, and we therefore did not report on the behaviours of remaining 40% who were treated and did not attain the optimal outcome (Innes, et al., 2012). This leaves scope for further research using such a comparison group.

Implications and Recommendations

While treatment induced viral clearance is well known to improve health outcomes, it does not completely remove the risk of liver related morbidity and mortality. Lifestyle factors- that can either accelerate the rate of liver disease progression (e.g. alcohol consumption) or cause re-infection- pose a significant excess risk of liver disease among patients who have attained SVR (Innes, et al., 2013).This study indicates that the risk of HCV reinfection post-SVR through continued injection drug use could increase as treatment is expanded and scaled up in populations who inject drugs. Therefore for patients who successfully complete treatment and would ordinarily be discharged from care, continued monitoring with RNA testing would be advised for those with on-going risk behaviour, in line with recent European guidelines (EASL, 2014). Harm reduction interventions aimed at reducing the risk of HCV transmission should continue to be promoted once treatment ceases.

Role of Funding Source

This project was supported by funding from the Scottish Government.

Contributors

HV performed the data analysis and interpretation under the supervision JL, and drafted the paper under the supervision of SH. SH and DG conceived, proposed, and oversaw the scope of the project. AW deterministically linked hospitalisation and mortality data with HCV Clinical and Diagnosis databases. All other authors provided revisions, and approved the paper for final submission.

Conflict of interest

None declared

Acknowledgements

Health Protection Scotland, Information Services Division, Scotland, who hold all Scottish morbidity (hospitalisation) and mortality data, and who made the linkage between the two databases. Clinical Database Monitoring Committee, Clinical Database Managers, and Data Entry Clerks, who routinely monitor data which are entered onto the database.

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Characteristics	N(%)	Opiate or injection related hospital episode/death post-SVR, n (%N)	Estimated proportion of opiate or injection hospital episodes/deaths at 3 years post-SVR % (95% CI)
Total	1170 (100)	149 (13)	10.59 (8.75 – 12.79)
Age at SVR			
<30	142 (12)	23 (16)	13.71 (8.53 – 21.62)
30-44	738 (63)	103(14)	11.28 (8.93 – 14.21)
≥45	290 (25)	23(8)	7.19 (4.50 – 11.39)
Sex			
Male	889 (76)	104 (12)	10.26 (8.20 – 12.80)
Female	281 (24)	45 (16)	11.65 (8.07 – 16.66)
Year of SVR			
1992-2000	45 (4)	8 (18)	2.22 (0.32 – 14.75)
2001-2005	236 (20)	48 (20)	8.50 (5.57 – 12.86)
2006-2012	889 (76)	93 (10)	12.03 (9.67 – 14.93)
Cirrhosis diagnosis at treatment initiation			
No	1081 (92)	137 (13)	10.28 (8.40 – 12.56)
Yes	89 (8)	12 (13)	14.65 (8.05 – 25.73)
Alcohol intoxication-related hospital episode pre-SVR			
No	912 (78)	98 (11)	8.69 (6.84 – 11.02)
Yes	258 (22)	51 (20)	17.58 (12.81 – 23.87)
Opiate or injection-related hospital episode pre-SVR			
No	743 (63)	63 (8)	6.04 (4.38 – 8.31)
Yes	427 (37)	86 (20)	19.24 (15.22 – 24.16)

Table 1. Description of cohort of 1,170 PWID who attained a sustainedviral response (SVR) in Scotland, 1992-2012.

Abbreviations; SVR, sustained viral response; CI, confidence interval

Covariate	Person Years	Unadjusted crude rate per 100 PY (95% CI)	Opiate or injection-related hospital episode/death post-SVR			
			Univariate (HR, 95%CI)	p-value	Multivariate (AHR, 95% CI)	p-value
Study Population	4764	3.12 (2.66 – 3.67)				
Age at SVR						
<30	586	3.92 (2.61 – 5.90)	2.07 (1.17 – 3.66)	0.013	1.51 (0.83 – 2.73)	0.179
30-44	3023	3.41 (2.81 – 4.13)	1.65 (1.02 – 2.67)	0.041	1.48 (0.93 – 2.35)	0.099
≥45	1155	1.99 (1.32 – 2.99)	1.00 (Baseline)		1.00 (Baseline)	
Gender						
Male	3564	2.92 (2.41 – 3.54)	1.00 (Baseline)		1.00 (Baseline)	
Female	1200	3.75 (2.89 – 5.02)	1.29 (0.91 – 1.83)	0.155	1.28 (0.90 – 1.83)	0.164
Year of SVR			1.10 (1.03 – 1.16)	0.006	1.07 (1.01 – 1.14)	0.025
Cirrhosis diagnosis at time of treatment initiation						
No	4376	3.13 (2.64 – 3.70)	1.00 (Baseline)		1.00 (Baseline)	
Yes	388	3.09 (1.76 – 5.45)	1.05 (0.58 – 1.90)	0.876	1.03 (0.56-1.89)	0.966
Alcohol intoxication-related hospital episode pre-SVR						
No	3864	2.54 (2.08 – 3.09)	1.00 (Baseline)		1.00 (Baseline)	
Yes	900	5.67 (4.31 – 7.46)	2.17 (1.54 – 3.05)	<0.001	1.83 (1.29 – 2.60)	0.001
Opiate or injection-related hospital episode pre-SVR						
No	3342	1.88 (1.47 – 2.41)	1.00 (Baseline)		1.00 (Baseline)	
Yes	1422	6.04 (4.90 – 7.47)	3.08 (2.22 – 4.27)	<0.001	2.59 (1.84 – 3.64)	<0.001

Table 2. Risk of firstopiate or injection-related hospital episode or death among 1170 PWID who attained SVR in Scotland, 1992-2012.

Abbreviations; SVR, sustained viral response; HR, hazard ratio; AHR, adjusted-hazard ratio; CI, confidence interval

Covariate	*N*	PY	Unadjusted crude rate per 100 PY (95% CI)	Opiate or injection-related hospital episode/death post-SVR			
				Univariate (IRR, 95%CI)	p-value	Multivariate (AIRR, 95%CI)	p-value
Study Population	236	5319	22.05 (29.83 – 23.35)				
Age at SVR							
<30	37	771	22.97 (29.83 – 26.62)	1.77 (1.13 – 2.79)	0.012	1.32 (0.83 – 2.09)	0.239
30-44	160	3456	21.62 (20.12 – 23.22)	1.48 (1.04 – 2.11)	0.027	1.22 (0.85 – 1.74)	0.280
≥45	39	1092	22.79 (20.12 – 25.81)	1.00 (Baseline)		1.00 (Baseline)	
Gender							
Male	159	3977	22.43 (21.00 – 23.95)	1.00 (Baseline)		1.00 (Baseline)	
Female	77	1342	20.95 (18.64 – 23.55)	1.48 (1.13 – 1.95)	0.005	1.32 (1.00 – 1.73)	0.048
Year of SVR				1.05 (1.01 – 1.08)	0.015	1.03 (0.99 – 1.07)	0.107
Cirrhosis diagnosis at treatment initiation							
No	213	4849	22.34 (21.04 – 23.71)	1.00 (Baseline)		1.00 (Baseline)	
Yes	23	470	19.15 (15.58 – 23.54)	1.24 (0.81 – 1.91)	0.327	1.03 (0.66 – 1.60)	0.894
Alcohol intoxication-related hospital episode pre-SVR							
No	111	4223	21.64 (20.29 – 23.09)	1.00 (Baseline)		1.00 (Baseline)	
Yes	125	1096	23.63 (20.92 – 26.69)	2.85 (2.19 – 3.71)	<0.001	2.59 (1.99 – 3.36)	<0.001
Opiate or injection related hospital episode pre-SVR							
No	88	3621	20.54 (19.12 – 22.07)	1.00 (Baseline)		1.00 (Baseline)	
Yes	148	1698	25.27 (22.99 – 27.78)	3.79 (2.89 – 4.97)	<0.001	2.95 (2.24 – 3.89)	<0.001

N, Number of observed hospital episodes; PY, person years (does account for time spent in hospital); Rate, fitted number of hospital episodes per 100 person-years; SVR, sustained viral response; IRR, incidence rate ratio; AIRR, adjusted-incidence rate ratio; CI, confidence interval

Table 3. Incidence and risk of multiple opiate or injecting-related hospital episodes among 1170 PWID who attained SVR in Scotland, 1992-2012.

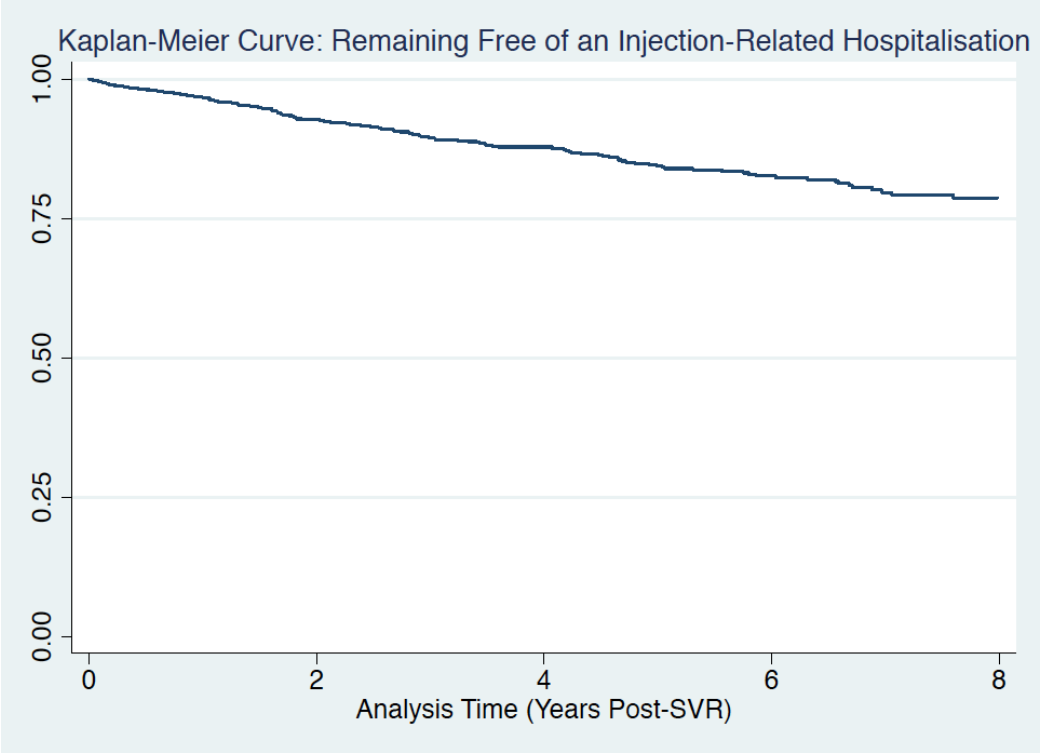

Figure1: Kaplan Meier Curve estimating the proportion of patients remaining free of in injection-related hospitalisation among 1170 PWID who attained SVR in Scotland, 1992-2012.