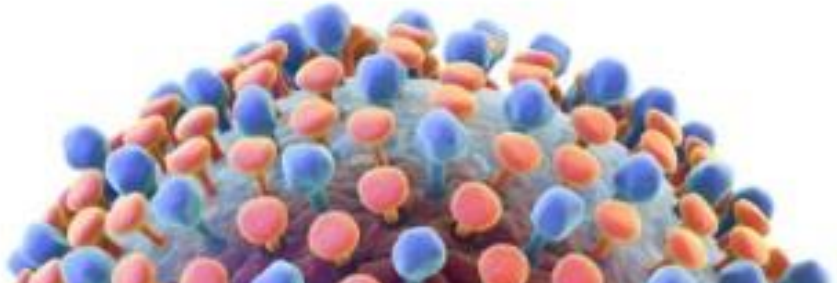
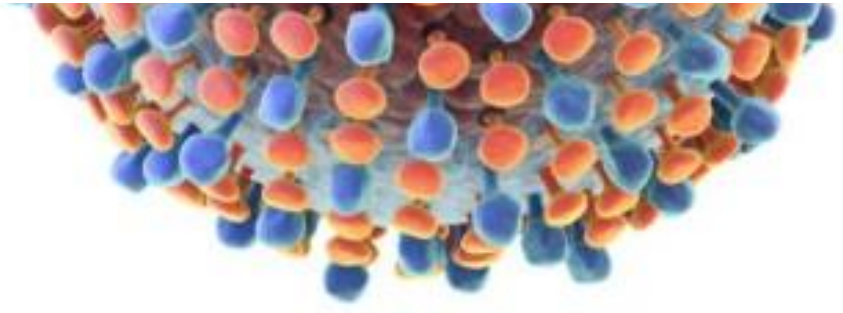


Impact of Hepatitis C treatment on substance use and injecting behaviour: a systematic review



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Hepatitis C (HCV)

- Hepatitis C (HCV) is a blood borne virus which affects around 71 million people globally (World Health Organisation, 2017).
- Around 90% of those infected with hepatitis C acquire the virus through injecting drug use behaviour (sharing needles, syringes and other equipment).
- HCV infection is a major contributor to morbidity and mortality among people who inject drugs (PWID) (Stanaway et al., 2016).
- Hepatitis C is preventable, treatable and curable for the vast majority of people.
- About 1 in 5 people clear the infection spontaneously without treatment.
- The efficacy of pan-genotypic direct acting antivirals (DAA) provide an excellent opportunity to scale up HCV diagnosis and treatment, ultimately achieving the WHO target of HCV elimination by 2030.

Hepatitis C cont.

- Research has supported the treatment of active drug users for Hepatitis C, demonstrating successful adherence to treatment and favourable sustained viral response rates.
- This highlights the feasibility and effectiveness of scaling up treatment services to reduce the prevalence of the disease, using “treatment as prevention” (TasP) models of elimination.
- There is a suggestion that the benefits of engaging with HCV care stretch beyond liver morbidity outcomes. Studies report the positive impact of HCV status notification on reduction in drug use among PWID.
- PWID accessing HCV treatment have the opportunity to develop a therapeutic relationship with healthcare professionals involved in their care, which may facilitate behavioural change.

Objectives

- To examine the literature investigating how, if at all, the behaviour of PWID changes in relation to drug use when undergoing HCV treatment and during follow up, including changes in injecting behaviour, injecting frequency, needle and/or syringe borrowing, and injecting equipment sharing.

Methodology

PICO question (study eligibility)

- Participants= PWID
- Intervention= HCV diagnosis and treatment
- Comparison= participants themselves i.e. behaviour measured before and after treatment; or PWID who did not receive treatment; or PWID who chose to not engage in treatment post HCV diagnosis.
- Outcome= behavioural change in relation to drug use e.g. injecting behaviour, needle and syringe borrowing, sharing of ancillary equipment

Methodology cont.

Search Methods

- Databases= PubMed, EMBASE, CINAHL and PsycINFO
- Search strategy= MeSH/EMTREE terms and keywords for “HCV treatment”, “Behaviour change” and “Drug use”

Study selection

- Screening of search strategy results was conducted by two reviewers

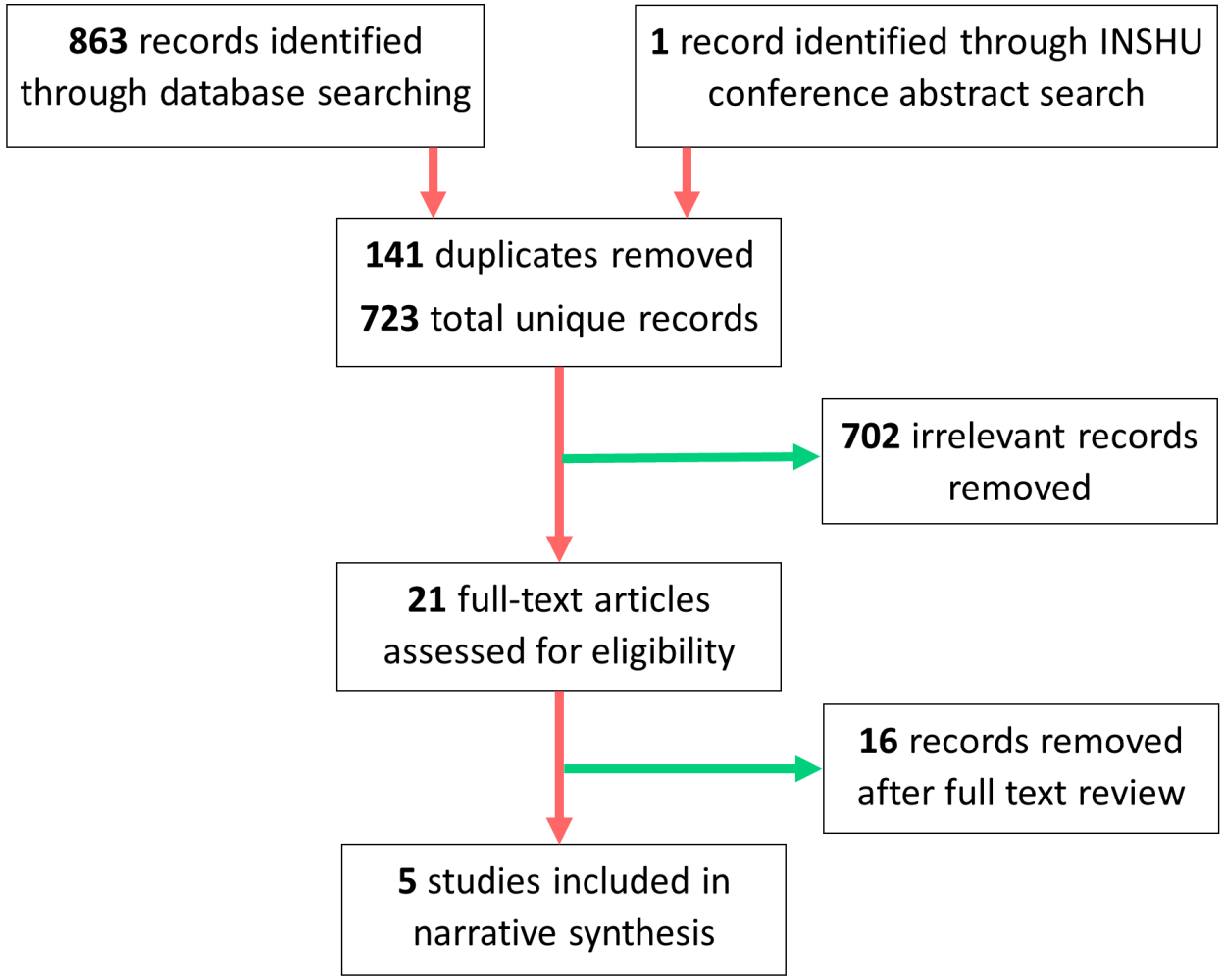
Data collection

- Standardised data collection form
- 2+ independent reviewers
- Quality assessed using the Quality Appraisal Checklist for quantitative intervention studies by NICE public health guidance

Analysis

- Narrative Synthesis

Study Selection Process



Results- Characteristics of Selected Studies

- Studies evaluated impact of treatment on drug use in various settings including tertiary hospitals; GP and primary care clinics; drug and alcohol treatment clinics; and injecting equipment provision services.
- Studies were conducted in various countries including Australia, Canada, France, Germany and the UK.
- There were four prospective cohort studies and one retrospective cohort study.
- Two studies included comparison groups in their study design.
- Four studies involved treatment with pegylated interferon and/or ribavirin, with only one study involving treatment with direct acting antivirals (DAAs).
- Four studies investigated past month injecting drug use; two studies investigated injecting frequency; two studies investigated needle and syringe borrowing; and three studies investigated ancillary injecting equipment sharing.
- The majority of participants were Caucasian males, with a mean age ranging from 32-47 years old, who had injected drugs in the last 6 months prior to study enrolment.
- Follow up times ranged from 6 months to 2 years.

Results- Risk of bias in individual studies

- Studies scored highly on external validity
- Issues of internal validity
  - Losses to follow up- selection bias
  - Lack of comparison groups

Results- individual studies

- Three of the four studies assessing impact of treatment on past month injecting frequency found treatment significantly reduced the odds of participants reporting past month injecting at follow up.
- One study found that there was significant reduction in weekly injecting frequency between enrolment, treatment and follow up.
- No association was found between treatment engagement and needle and syringe borrowing.
- Two out of three studies reported a significant decrease in injecting equipment sharing between enrolment, treatment and follow up.

Discussion

- There is dearth of research on the impact of engaging in treatment on behavioural change in relation to drug use.
- Engaging in treatment may result in a possible reduction in injecting- implications for treatment accessibility for PWID.
- Supports notion that treatment engagement may lower risk of HCV transmission within PWID population.
- Although no significant decrease in needle and syringe borrowing was observed, the fact that such risk behaviours remain stable throughout treatment and follow up has meaningful implications for risk of reinfection and onward transmission.

Limitations

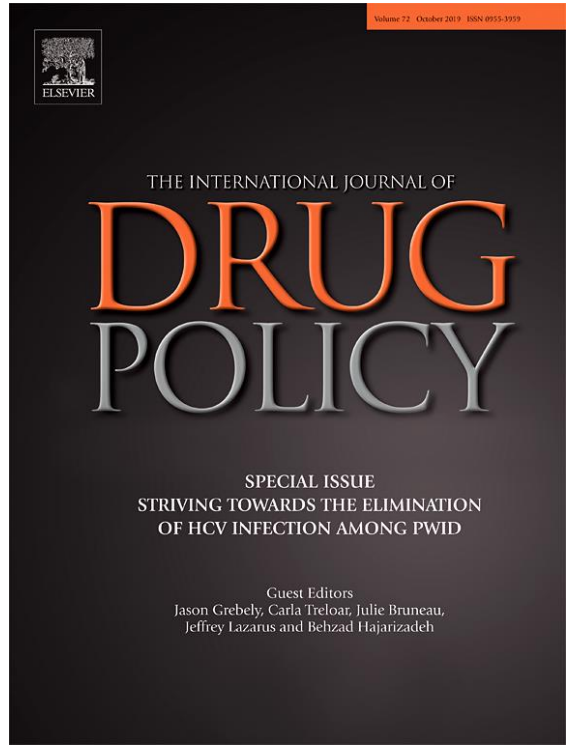
- Limited number of selected studies
- Lack of comparability between studies
- Four of 5 studies were conducted during interferon era of treatment- generalisability to DAA era?

Conclusions

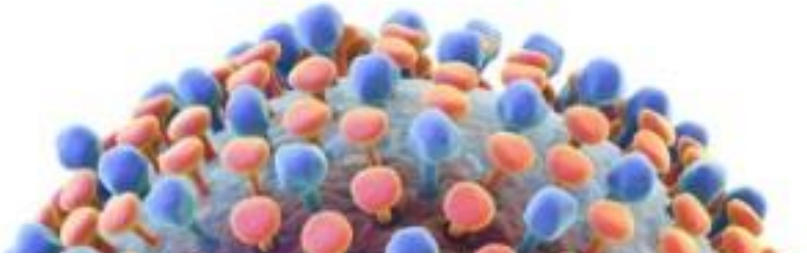
- Comparison and synthesis of results was challenging due to heterogeneity between studies.
- However, it is likely that engaging in treatment has a positive impact upon patients' injecting drug use and injection equipment sharing behaviour, with the health benefits of engaging with HCV care stretching beyond liver morbidity outcomes.
- HCV treatment engagement may provide an opportune time to implement targeted interventions to reduce injecting behaviours and promote further harm reduction measures.

Publication

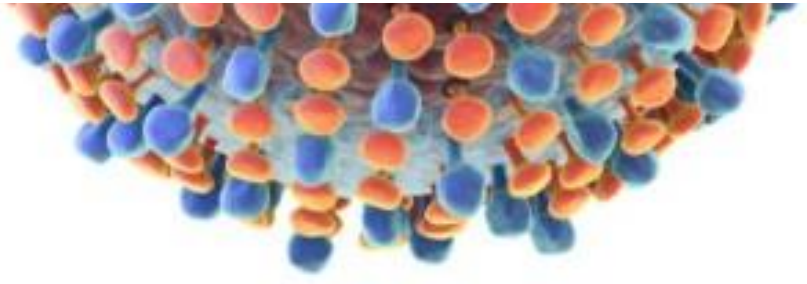
Caven, M., Malaguti, A., Robinson, E., Fletcher, E., & Dillon, J. F. (2019). Impact of Hepatitis C treatment on behavioural change in relation to drug use in people who inject drugs: A systematic review. *International Journal of Drug Policy*, *72*, 169-176. https://doi.org/10.1016/j.drugpo.2019.05.011



Questions?



HCV Diagnosis and Treatment, Impact on Engagement and Behaviour of People Who Inject Drugs, a service evaluation, the Hooked C project



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Drug related deaths in Scotland

- The causes of death among PWID are strongly associated with active drug use.
- Scotland has observed a two fold increase in drug related deaths between 2008 and 2018, with Tayside experiencing the highest number of drug deaths ever recorded in the region in 2018.
- The introduction of Multidisciplinary Managed Care Networks (MCN) in Hepatitis C treatment for PWID has increased access to services and reduced all- cause mortality (Tait et al., 2016).
- The associated increased speed of access into care and focus on HCV treatment for this population may have led to a greater degree of engagement with health services and may have had a stabilizing effect on drug- using behavior.
- However, there is concern around the potential impact of reduction in intensity of staff contact when transitioning from the interferon era to the DAA era of treatment.

Current Project

- Does HCV diagnosis and engagement in HCV treatment services reduce a) all-cause mortality, b) drug related death?

- Does any change observed in a) all-cause mortality, b) drug related death depend on if the treatment is interferon based or DAA based, and intensity of engagement with staff?

Methodology

Data sources and linkage

- Tayside Hepatitis C Clinical Database
- Tayside Drug Deaths Database
- Linkage using CHI numbers

Selected cohort

- Risk factor= intravenous drug use
- Postcode within Tayside
- Not co-infected with other BBVs
- Tested/initiated treatment between January 2008 and November 2017

Definition of drug related death

“A death where the underlying cause is: drug abuse or drug dependence; or drug poisoning (intentional or accidental) that involves any substance controlled under the Misuse of Drugs Act 1971.”

Methodology cont.

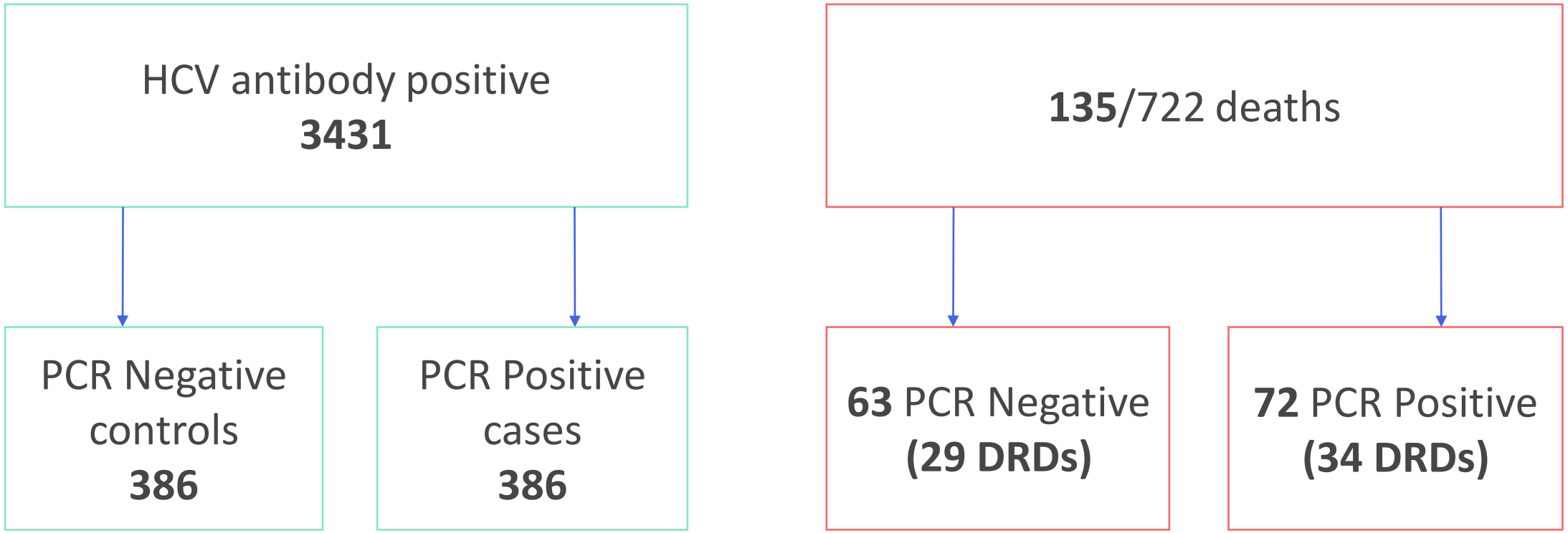
Case control studies (1:1 matching by age and sex):

- PWID with active HCV infection (PCR Positive) vs PWID who were HCV infected but cured spontaneously (PCR Negative)- elucidate whether knowledge of HCV status impacted risk of mortality
- PCR Positive patients who engaged vs did not engage with treatment services- assess if outcomes were dependent on engagement
- Pegylated interferon alpha treated patients vs Direct acting antiviral patients- explore the effect of intensity of HCV therapy provider interaction on outcomes

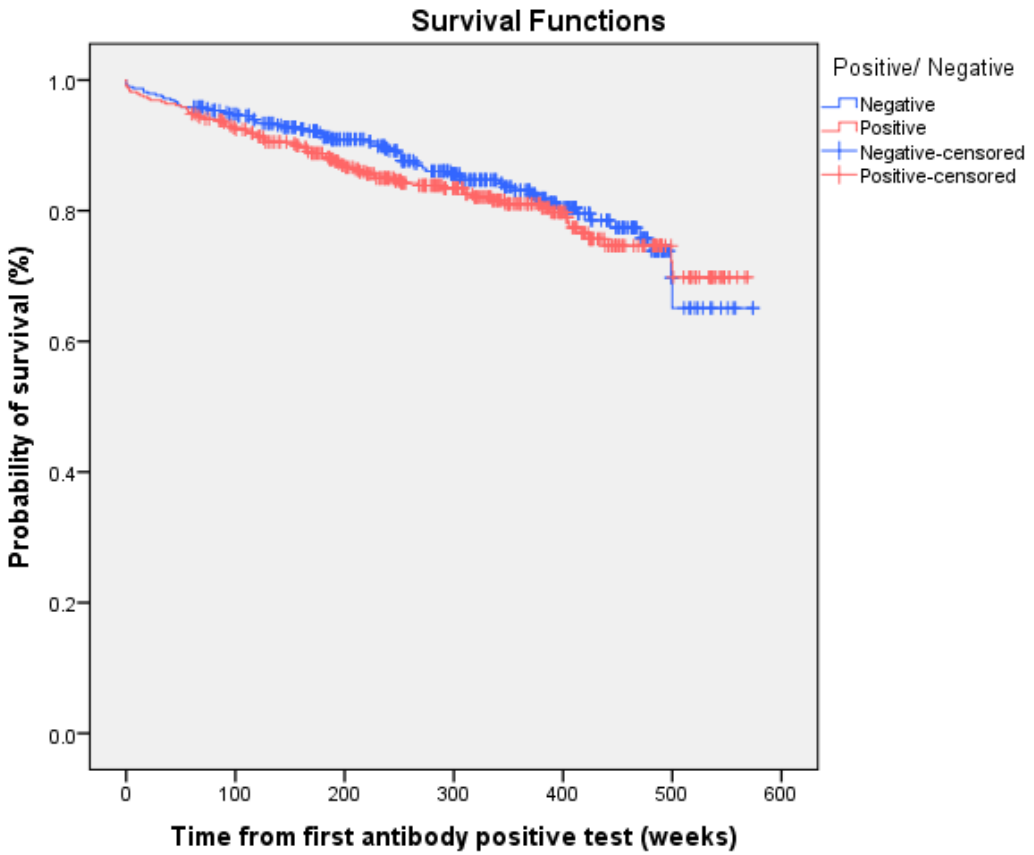
Statistical Analysis

- Kaplan Meier survival analysis
- Binary logistic regression

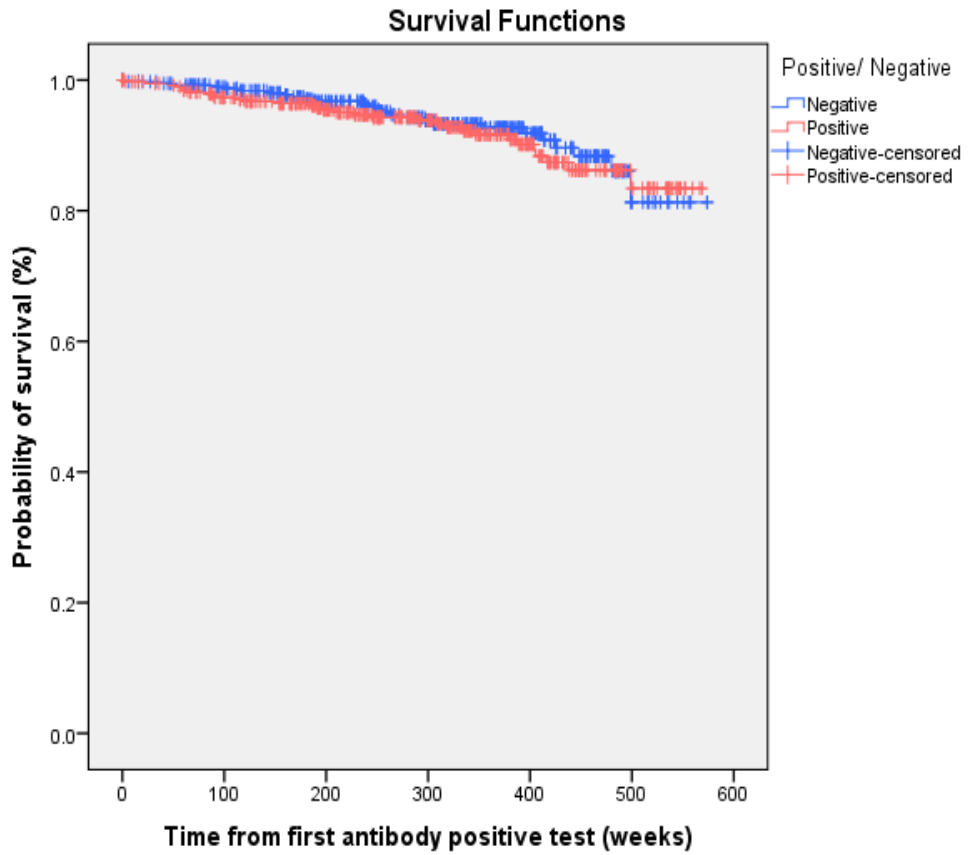
Results- PCR Positive vs PCR Negative



Results- PCR Positive vs PCR Negative



Kaplan Meier survival curve for time from first antibody positive to all-cause mortality comparing PCR Positive cases and PCR Negative controls



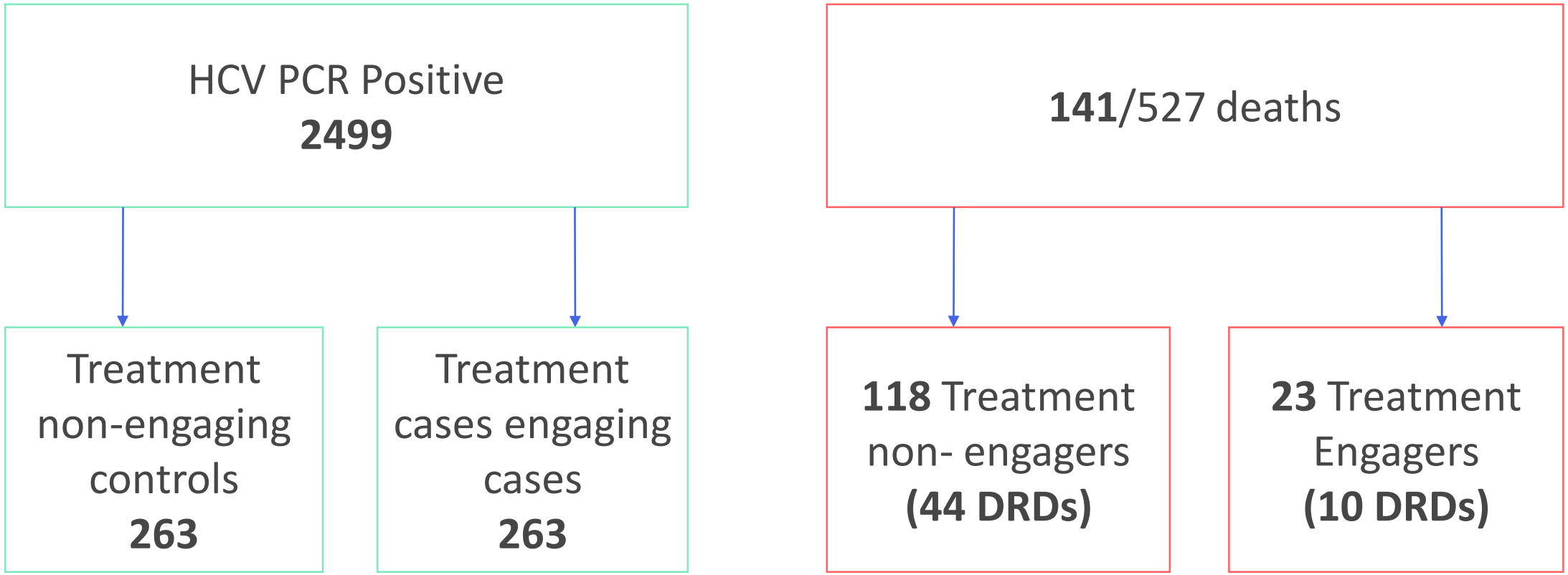
Kaplan Meier survival curve for time from first antibody positive to drug related death comparing PCR Positive cases and PCR Negative controls

PCR Positive vs PCR Negative- Regressions

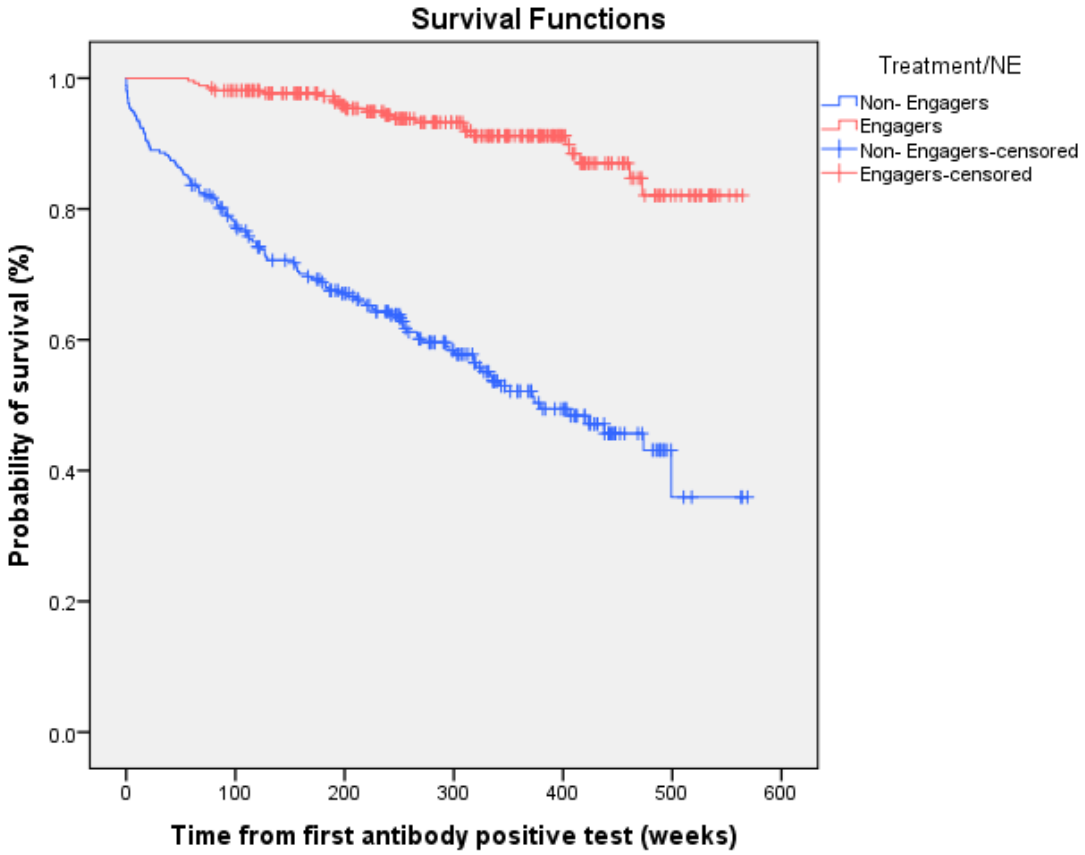
- Binary logistic regression revealed that there was no difference in risk of all-cause mortality between PCR Negative controls and PCR Positive cases (aOR 1.18, 95% CI 0.80- 1.73, *p* = .40), after adjustment for age and sex.

- Binary logistic regression revealed that there was no difference in risk of drug related death between PCR Negative controls and PCR Positive cases (aOR 1.19, 95% CI 0.71- 2.00, *p* = .512), after adjustment for age and sex.

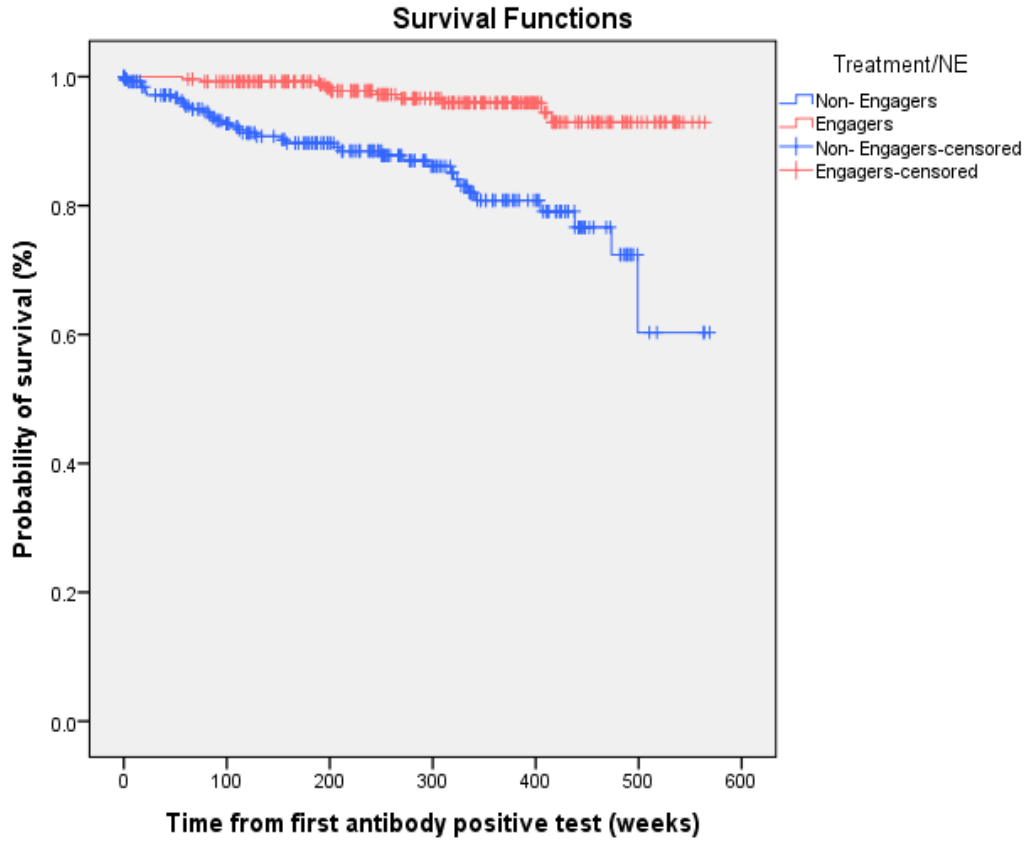
Results-Treatment Engagers vs Non- Engagers



Results- Treatment Engagers vs Non- Engagers



Kaplan Meier survival curve for time from first antibody positive to all-cause mortality comparing treatment engaging cases and treatment non-engaging controls



Kaplan Meier survival curve for time from first antibody positive to drug related death comparing treatment engaging cases and treatment non-engaging controls

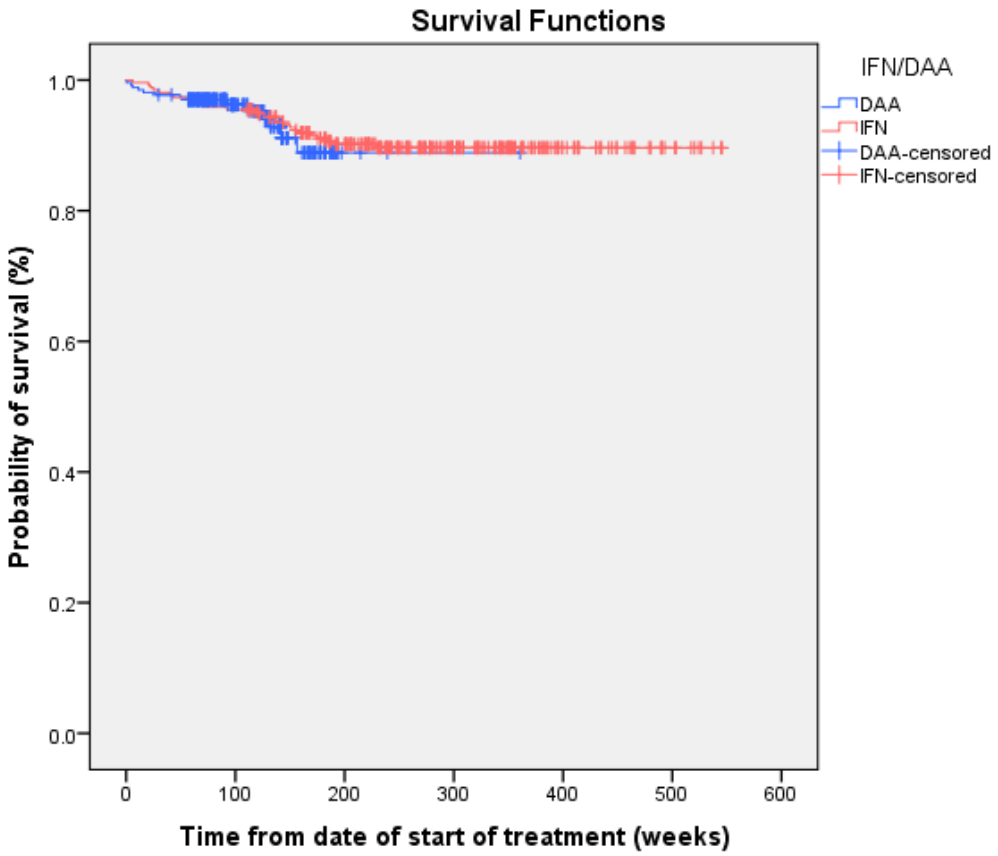
Treatment Engagers vs Non- Engagers- Regressions

- Binary logistic regression revealed that the odds of all-cause mortality was 12.2 times higher amongst treatment non- engaging controls, (aOR 12.15, 95% CI 7.03- 20.99, $p < 0.001$) compared to treatment engaging cases, after adjustment for age, sex and OST.

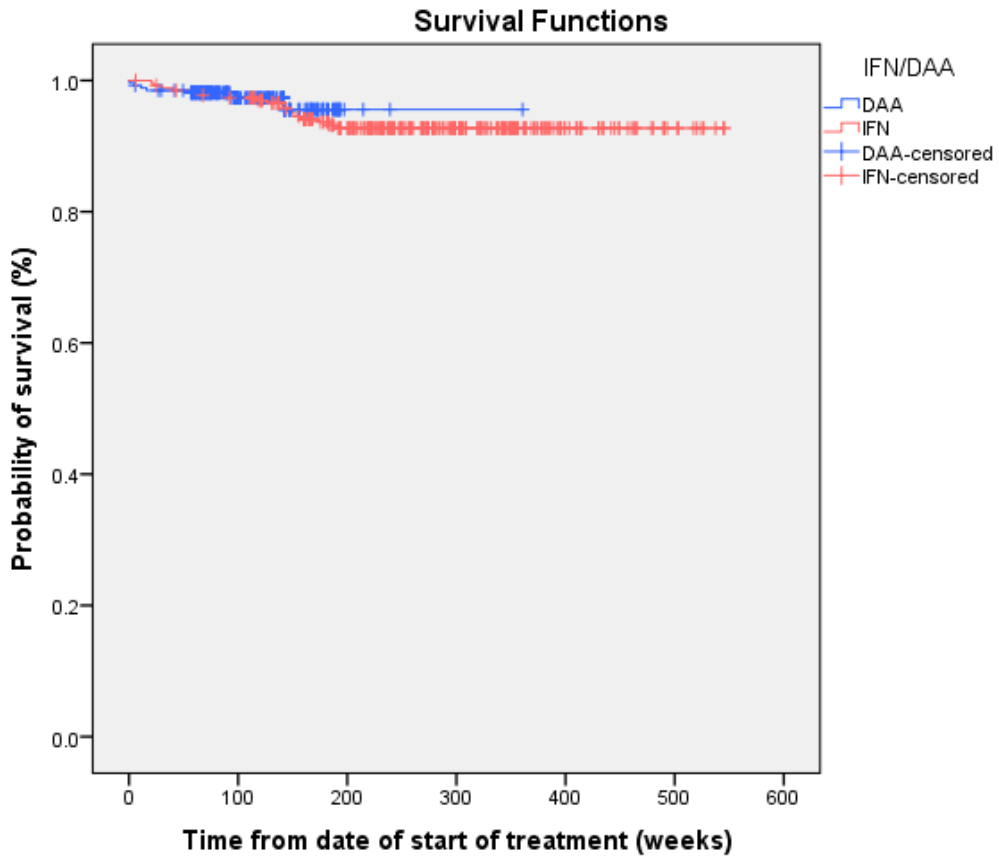
- Binary logistic regression revealed that the odds of a drug related death was 5.5 times higher amongst treatment non- engaging controls, (aOR 5.52, 95% CI 2.67- 11.44, $p < 0.001$) compared to treatment engaging cases, after adjustment for age, sex and OST.

Results- Interferon treated vs DAA treated

Results- IFN treated vs DAA treated



Kaplan Meier survival curve for time from treatment commencement to all-cause mortality comparing interferon treated cases and direct antiviral agent treated controls



Kaplan Meier survival curve for time from treatment commencement to drug related death comparing interferon treated cases and direct antiviral agent treated controls

IFN treated vs DAA treated- Regressions

- Binary logistic regression revealed that there was no difference in risk of all-cause mortality between DAA treated controls and interferon treated cases (aOR 1.45, 95% CI 0.70- 2.98, p = .37), after adjustment for age, sex, SVR, OST, and cirrhosis.

- Binary logistic regression revealed that there was no difference in risk of drug related death between DAA treated controls and interferon treated cases (aOR 2.06, 95% CI 0.80- 5.23, p = .13), after adjustment for age, sex, SVR, OST, and cirrhosis.

Discussion

- Our results suggest that awareness of HCV infection status makes no difference to risk of morality.
- Our findings provide evidence that HCV treatment engagement is a significant protective factor against both all-cause mortality and drug related death amongst PWID.
- Our results suggest that this engagement effect is independent of treatment regimen, with no differences in risk of mortality between interferon and DAA treated patients.
- It could be argued that patients engaging with HCV treatment services are self-selecting individuals who are more willing to engage with services in general, and that we have observed a generalised engagement effect, rather than a specific HCV treatment effect.
- This finding also has significant implications for addressing ongoing concern around the change in intensity of staff contact when transitioning from the interferon era to the DAA era of treatment.

Discussion

Limitations

- Retrospective data analysis- quality of available data
- Lack of differentiation between engagers vs non-engagers

Future research

- Underlying mechanisms of engagement effect- what is it about engaging in the HCV treatment process that enables behaviour change and lowers risk of mortality amongst PWID?
- Promotion of HCV care and engagement strategies, highlighting the psychological, social and physical health benefits of achieving a cure, as well as treatment options

Conclusions

- Our results suggest that awareness of HCV infection status makes no difference to mortality, either all cause or drug related.
- HCV treatment engagement is significantly protective against all-cause mortality and drug related death.
- This engagement effect is independent of treatment regimen, with the introduction of DAA therapies not increasing the risk of drug related death, suggesting intensity of engagement with staff is not an important factor.
- Further evidence of the importance of HCV diagnosis and treatment amongst PWID, reducing their risk of mortality, beyond liver related outcomes.

Thank you for listening!

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