The impact of injecting drug use and hepatitis C on mortality.

A register based cohort study on 5350 persons connected to drug use treatment 1996-2014.

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Poster 57

Objective

To evaluate overall mortality and cause of death and the impact of hepatitis C on mortality in people connected to drug treatment services

Background

Hepatitis C (HCV) is prevalent among people with current or former drug use (PWUD) and mainly among people who inject drugs (PWID). An estimated 52% of PWID in Western Europe has been exposed to the HCV. The impact of chronic hepatitis C(CHC) on mortality in PWUD and PWID is difficult to elucidate due to the high mortality from competing causes of 1-4% pr. years(1). It takes several decades of infection to develop liver cirrhosis and even longer to develop end-stage liver disease and hepatocellular carcinoma.

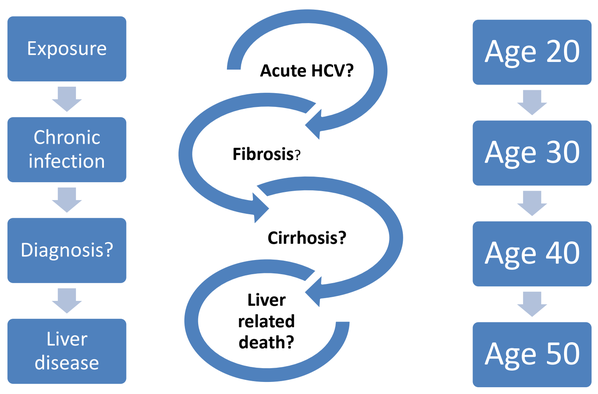

Figure 1. Simple diagram of hepatitis C and development of liver disease

Investigations into the impact HCV has on mortality in PWID is challenged by several epidemiological difficulties including testing bias, healthy survivor bias and limited follow-up time. Previous studies in small populations with long follow-up has found a possible impact after 30 years of infection(2). As test for HCV is often years after exposure and symptoms years after diagnosed infection following persons from year of entry into drug treatment and stratifying for drug use and hepatitis C status might be informative on impact of HCV status on all cause and liver related mortality.

This study is part of the Odense-Drugusers-HEPatitis(ODD-HEP) cohort study aiming at using available registers to identify barriers in the treatment cascade and impact of Hepatitis C.

Method

Register based retrospective cohort study.

Baseline cohort:

Registered in the Danish National Drug use Treatment database(SIB) since 1996-2014 in the region of Funen, Denmark.

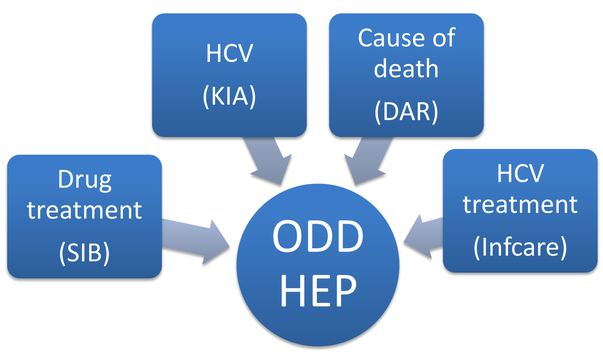

Figure 2: ODD-HEP Cohort data sources.
SIB: National drug use treatment database. KIA: Regional test database. DAR: Danish Death Certificate Register. Infcare : Regional hepatitis care database.

Method and measures

- *Time measures*

All data censored at December 31st 2014 end of follow-up
Follow-up time from date of entry into the SIB to date of death or end of follow-up

- *Hepatitis C results*

Categories: Not tested, HCV negative, anti-HCV+, HCV-RNA+

- *Date and cause of death*

Categories: Liver-related , non-natural , other.
Derived from the DAR and validated in Infcare

- *Drug treatment and use history*

Categories: High risk use; ever on opioid substitution therapy(OST) or disclosed injecting. Alcohol use

- *Mortality*

Standardized mortality ratios(SMR) were calculated using sex, age and year of death matched mortality rates(MR) from the Danish National Statistics Bureau.
Cox regression reporting hazard rations performed on all cause and liver related only in PWID subpopulation

Results

The cohort comprised 5350 individuals ever in drug use treatment

ODD-HEP Mortality cohort	Total Cohort	Low risk Never on OST and no disclosed injecting	High risk Ever on OST or disclosed injecting	P#
Individuals n (% of group)	5350	2652(49.6)	2698(50.4)	
Females n (% of group)	1329 (24.8)	694 (26.2)	635 (23.5)	0.026
Age at entry Median(IQR)	24 (20-32)	21 (18-26)	27 (22-36)	<0.001
Disclosed injecting n (% of risk group)	2398 (44.8)	NA	2398 (88.9)	NR
Ever on OST n (% of risk group)	1838(34.3)	NA	1838(68%)	NR
Hepatitis C				
Tested HCV ever n (% of risk group)	2879 (53.8)	801 (30.2)	2078 (77.0)	<0.001
Anti-HCV+ n (% of tested)	1334 (46.3)	35 (4.4)	1299 (62.5)	<0.001
HCV-RNA+ n (% of tested)	794 (59.4)	15 (1.9)	779 (37.5)	<0.001

Table 1: Cohort characteristics and hepatitis C results at end of follow-up.

Mortality

Cohort followed for 49,403 person years(PY) with a crude mortality rate of 1.15/100 PY.

ODD-HEP Mortality cohort	Total Cohort	Low risk Never on OST and no disclosed injecting	High risk Ever on OST or disclosed injecting	P#
Death rate n(% of group)	1.15/100 py 571(10.7)	0.4/100 py 77(2.9)	1.6/100 py 494(18.3)	<0.001
Years to death Median (IQR)	8.2 (4.0-12.5)	3.7(1.5-7.6)	8.7(4.7-13.1)	<0.001
Age at death Median(IQR)	42(34-51)	36(27-44)	43(35-51)	<0.001
Liver related rate n (% of deaths)	0.13 /100 py 63(11.0)	0.01/100 py 2(2.6)	0.2/100 py 61(12.3)	0.011
Non-natural rate n (% of deaths)	0.8 100/py 386(67.6)	0.3/100 py 59(76.6)	1.1 100/py 327(66.2)	0.08
Other causes rate n (% of deaths)	0.25/100 py 122(21.4)	0.09/100 py 16(20.8)	0.3 100/py 106(21.5)	0.89

Table 2. Deaths in cohort

Mortality rates and ratios by risk group

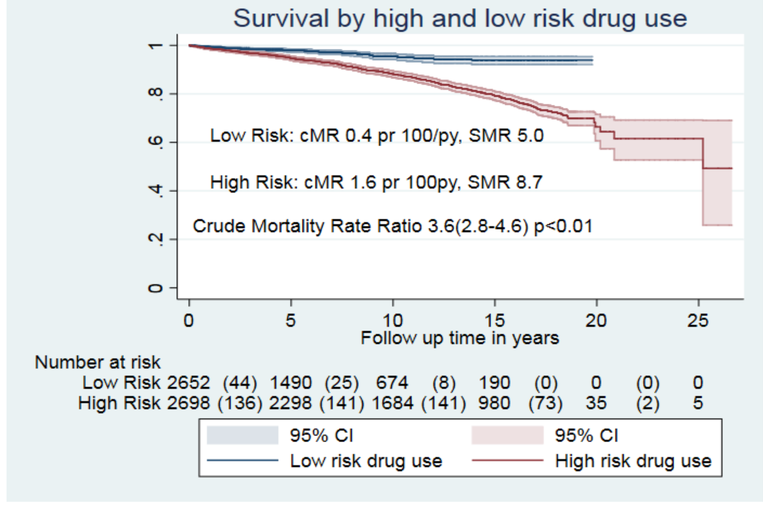

Figure 3: Mortality by high and low risk drug use.
Note: Crude mortality rate(cMR), Standardized mortality rate (SMR)

Mortality by Hepatitis C test category

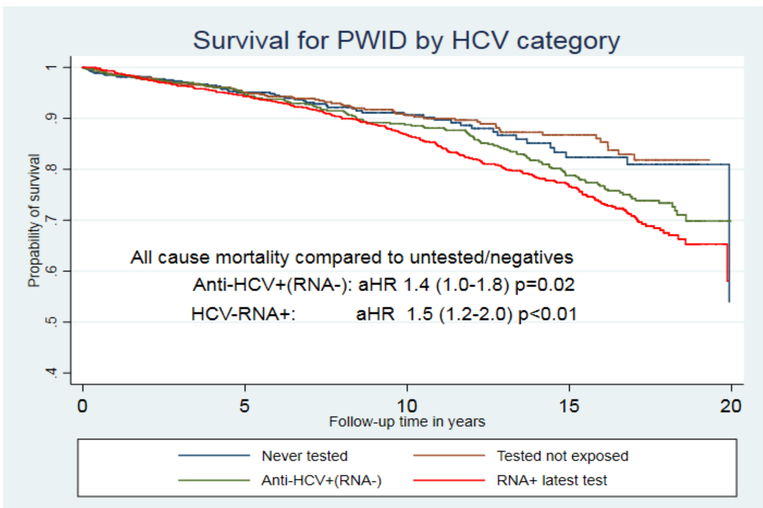

Figure 5. PWID only population. Cox regression adjusted for sex, age at entry, age, sex and OST. Difference between anti-HCV+ and RNA+ was not significant

Liver Related Mortality

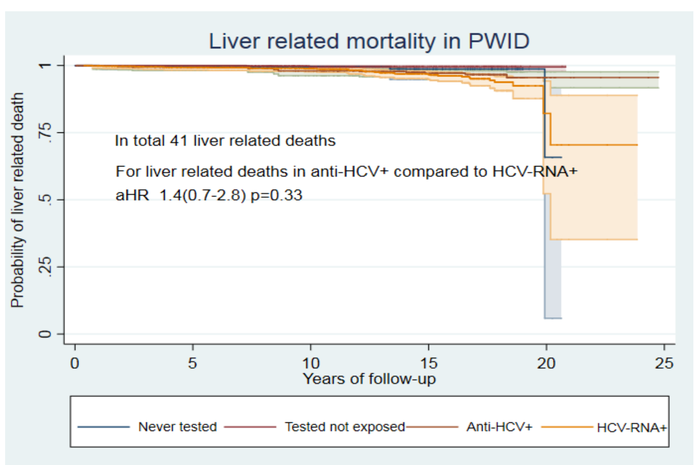

Figure 5 . PWID only population. Cox regression adjusted for sex, age at entry, age, sex and alcohol. Difference between anti-HCV+ and RNA+ was not significant

Conclusion

- We found a high mortality among PWUD compared to the general population both in low and high risk users.
- Liver-related death was common in high risk users (12.3 % of deaths)
- For PWID liver related mortality and overall mortality was numerical highest in the HCV-RNA+ group but not significantly different from the anti-HCV+ / HCV-RNA- in adjusted analysis.

Disclosures

This study was partly supported by a Gilead Sciences Nordic Fellowship Grant. Gilead Sciences have not been involved in the design, data analysis or writing of this paper

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