Can health risk behaviours explain the excess mortality rate for adults with chronic hepatitis C in the United States? A population cohort study

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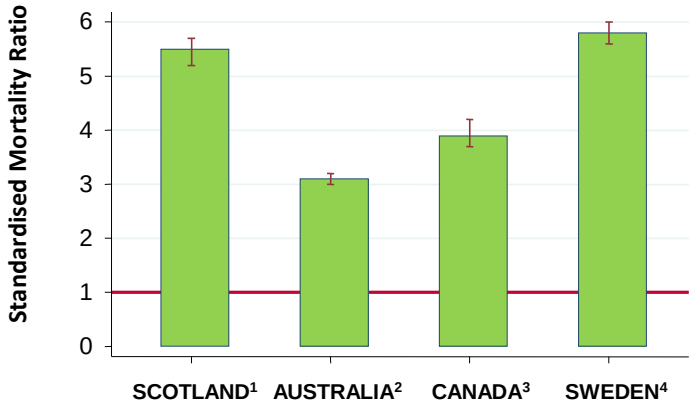
BACKGROUND

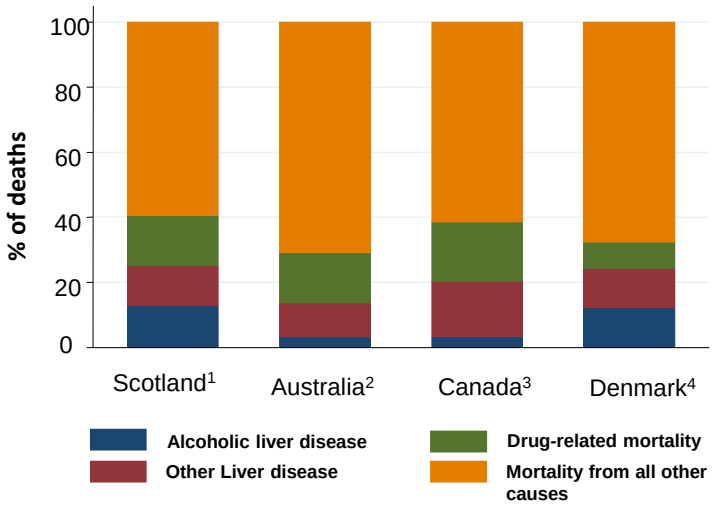
Standardised Mortality Ratios for individuals diagnosed with hepatitis C antibodies(adjusted for age/sex/calendar period)



[1]McDonald et al. Stat Methods Med Res 2009; 18:271-283.
[2]Amin et al. Lancet 2006;368:938-945.
[[3] Aspinall et al. J Hepatol 2015;62:269-77.
[4] Duberg et al J Viral Hepat 2008; 15: 538-550.

BACKGROUND

Cause of death among diagnosed HCV decedents



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[3] Aspinall et al. J Hepatol 2015;62:269-77.
[4] Omland et al. J Hepatol 2010; 53: 36-42.

Study question

What portion of excess mortality in hepatitis C infected persons can be explained by the five major health risk behaviours? (alcohol; smoking; illicit drug use, physical inactivity; and unhealthy diet),

The U.S National Health and Nutritional Examination Survey (NHANES)

- Designed to assess the health and nutritional status of adults and children in the US
- *continuous NHANES* began in 1999 and interviews a sample of ~5000 a year
- NHANES sample is representative of US general population (albeit excludes prisoners and homeless)
- Survey comprises interviews and physical examinations carried out at the participants homes and/or in a purpose-built mobile examination centre
- Data on all five HRBs collected through self-report questionnaires
- Participants tested for HCV antibodies and those testing positive are further tested for HCV RNA.
- Mortality data on NHANES participants to Dec 2011 available via linkage to National Death Index.
- Annonymised data are available to researchers free-of-charge and can be downloaded online

Methods

1. IDENTIFICATION OF RELEVANT VARIABLES: four main categories of fields from survey interviews/examinations extracted
   - Socio-demographics: age, gender, education, race, income
   - Medical history: heart disease, stroke, COPD, cancer, diabetes, HBV/HIV co-infection, BMI/obesity
   - Health risk behaviours: recent and past alcohol consumption, current and past cigarette smoking, portions of fruit/veg eaten in past 24 hours; recent physical activity, history of using illicit drugs, history of injecting illicit drugs, and recent injection of illicit drugs
   - Chronic hepatitis C status: HCV antibody positivity, HCV RNA positivity
2. DOWNLOAD DATA AND MERGE INTO ONE DATASET
3. INCLUSION CRITERIA: a) adults (20+ years) ;who b) completed NHANES interview; and who c) had a determinant result for chronic hepC

Methods… cont

4. PREVALENCE OF HRBS: Calculated the % with each HRB in persons with CHC, and compared to the adjusted % in persons without CHC assuming the same socio-demographic background.
5. CONTRIBUTION OF HRBs
   - Determine the mortality rate ratio (MRR) in individuals with CHC versus individuals without after adjustment for socio-demographic factors
   - Assess the extent to which the MRR attenuates following adjustment for the five major HRBs (premise= that the level of attenuation would reflect the % HRB contribution to mortality excess)
6. SUBGROUP ANALYSES: Carried out the above analyses for the full cohort, and also for individuals aged 45-70 years (to approximately mirror the target population for US birth cohort screening)

Results: description of final sample:

- 28,691 individuals identified met inclusion criteria (388 with CHC; 28,303 without CHC)
- Socio-demographic characteristics of sample:
  - Mean age: 47 years
  - 52% female
  - 55% educated beyond high school
  - Race: 71% white non-hispanic; 11% non hispanic black
  - 15% living below US poverty line
- Individuals with CHC more likely to be older; be male; be non-hispanic black, be living below the poverty threshold, and to not have more than a high school education
- Average follow-up per participant: 6.2 years
- 2785 deaths observed (50 among participants with CHC).

Prevalence of HRBs according to CHC: full cohort

		With CHC	Without CHC*	P-value
1. Heavy Alcohol use	Recent alcohol consumption ≥5 drinks/day	**7.6%**	**1.7%**	**0.002**
	History of drinking ≥5 drinks/day?	**41.0%**	**18.5%**	**<0.001**
2.Cigarette smoking	Current smoker	**63.0%**	**28.4%**	**<0.001**
3. Physical inactivity	No moderate/vigorous activity in a typical week	**41.2%**	**31.5%**	**0.04**
4.Unhealthy diet	< 3 portions of fruit/veg a week	**67.7%**	**58.7%**	**0.003**
5.Illicit drug use	Ever injected drug use	**46.4%**	**1.6%**	**<0.001**

*N.B. prevalence in "without CHC" population adjusted to reflect the same socio-demographic composition present in the CHC-infected population

Prevalence of HRBs according to CHC: aged 45-70yrs at baseline

		With CHC	Without CHC*	P-value
1. Heavy Alcohol use	Recent alcohol consumption ≥5 drinks/day	**5.4%**	**1.8%**	**0.04**
	History of drinking ≥5 drinks/day?	**44.9%**	**19.5%**	**<0.001**
2.Cigarette smoking	Current smoker	**61.0%**	**26.8%**	**<0.001**
3. Physical inactivity	No moderate/vigorous activity in a typical week	**42.0%**	**32.9%**	**0.09**
4.Unhealthy diet	< 3 portions of fruit/veg a week	**69.5%**	**56.3%**	**<0.001**
5.Illicit drug use	Ever injected drug use	**47.7%**	**1.6%**	**<0.001**

*N.B. prevalence in "without CHC" population adjusted to reflect the same socio-demographic composition present in the CHC-infected population

Attenuation in Mortality Rate Ratio (MRR): Results for full cohort

#	MODEL ADJUSTMENT	MRR	% attenuation
1	socio-demographics only	2.54 (1.83-3.52)	\
2	Socio-demographics+ medical history		
3	Socio-demographics+ alcohol		
4	Socio-demographics+ cigarette smoking		
5	Socio-demographics+ physical inactivity		
6	Socio-demographics+ diet		
7	Socio-demographics+ illicit drug use		
8	**Socio-demographics+ all five HRBs**		

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1	socio-demographics only	2.54 (1.83-3.52)	\
2	Socio-demographics+ medical history	2.45 (1.78-3.38)	6%
3	Socio-demographics+ alcohol		
4	Socio-demographics+ cigarette smoking		
5	Socio-demographics+ physical inactivity		
6	Socio-demographics+ diet		
7	Socio-demographics+ illicit drug use		
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2	Socio-demographics+ medical history	2.45 (1.78-3.38)	6%
3	Socio-demographics+ alcohol	2.14 (1.52-3.01)	26%
4	Socio-demographics+ cigarette smoking		
5	Socio-demographics+ physical inactivity		
6	Socio-demographics+ diet		
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4	Socio-demographics+ cigarette smoking	2.05 (1.49-2.82)	32%
5	Socio-demographics+ physical inactivity	2.36 (1.70-3.29)	12%
6	Socio-demographics+ diet		
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6	Socio-demographics+ diet	2.50 (1.81-3.47)	3%
7	Socio-demographics+ illicit drug use		
8	**Socio-demographics+ all five HRBs**		

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6	Socio-demographics+ diet	2.50 (1.81-3.47)	3%
7	Socio-demographics+ illicit drug use	2.33 (1.64-3.30)	14%
8	**Socio-demographics+ all five HRBs**	**1.77 (1.24-2.53)**	**50%**

Attenuation in Mortality Rate Ratio (MRR): aged 45-70yrs at baseline

#	MODEL ADJUSTMENT	MRR	% attenuation
1	socio-demographics only	1.77 (0.99-3.15)	\
2	Socio-demographics+ medical history	1.83 (1.04-3.22)	-8%
3	Socio-demographics+ alcohol	1.38 (0.78-2.45)	51%
4	Socio-demographics+ cigarette smoking	1.34 (0.77-2.36)	56%
5	Socio-demographics+ physical inactivity	1.63 (0.92-2.89)	18%
6	Socio-demographics+ diet	1.69 (0.95-3.00)	10%
7	Socio-demographics+ illicit drug use	1.83 (0.92-3.66)	-8%
8	**Socio-demographics+ all five HRBs**	**1.32 (0.80-2.48)**	**58%**

Conclusion:

- In a relatively unselected cohort approximating the general infected population in the US, about half of the excess mortality dissolves after accounting for HRBs
- considerable prevalence differences in smoking and alcohol appear particularly to drive this attenuation.
- Suggests that high all-cause mortality rates in individuals with HCV (see slide 1) are a compound problem that requires a compound solution.

ANTIVIRAL THERAPY

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STRATEGY TO ADDRESS HRBs

REVERSAL OF MORTALITY EXCESS

Research activity on HRB interventions has been limited thus far.

- Abundance of activity on antiviral therapy front – six hundred RCTs evaluating HCV antiviral therapy in 2000-2011 alone (J Natl Med Assoc 2016; 108:24-9)
- In contrast, activity on HRBs more limited
  - A recent systematic review could identify only two RCTs and three small observational studies for an alcohol reduction intervention in patients with hepatitis C. (see Doyle et al, Hepatol 2014; 60:S314-S315)
  - In a systematic search of our own, we couldn't identify a single intervention study relating to smoking in patients with CHC

Limitations/caveats

- No longitudinal data on HRBs (cross-sectional data may particularly underestimate contribution of poor diet and physical inactivity- see: JAMA 2010; 303:1159-66)
- No data on SVR attainment (but uptake low over the time frame of this study ~ 1.5% SVR attainment per year)
- NHANES excludes homeless and prisoner populations – where prevalence of HCV is particularly high
- Limited data on cause-specific mortality and limited power to examine this (with only 50 deaths in total among individuals with CHC)

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