Competing risks of mortality among people with hepatitis C: a population-based linkage study, 1993-2012

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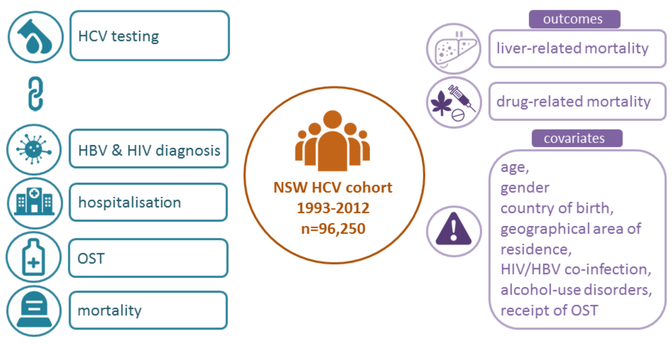
Introduction

Compared to the general population, people with hepatitis C virus (HCV) infection have higher mortality rates. Increased uptake of highly effective direct-acting antiviral therapies is expected to lower liver-related mortality over the coming years. However, reducing the burden of mortality among HCV cohorts will not be feasible without developing strategies to lower the impact of other health risk behaviors, including drug and alcohol use. The aim of this study was to assess cause-specific mortality trends and associated factors among people with an HCV notification in New South Wales (NSW), Australia.

Methods

NSW HCV notifications (1993-2012) were linked to cause-specific mortality records (1993-2013) and other databases. Liver- and drug-related deaths were coded in the underlying field of a linked record, using ICD-10.



Age-standardised incidence rates [per 100 person-years (PY)] were calculated using the Poisson distribution, by all cause-, other cause-, liver-, and drug-related mortality. The Australian Standard Population 2001 was used for standardisation. The strength of association between risk factors and liver-, and drug-related mortality were assessed by unadjusted and adjusted competing risk regressions, using the Fine and Gray method.

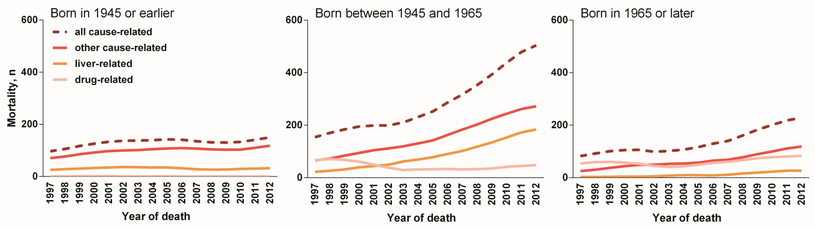
Results

Table 1. Demographic characteristics among NSW people with an HCV notification 1993-2012, n=96,250

	Alive	%	Deceased	%
Characteristics, n %	n=86,549		n=9,701	
Birth cohort[α]				
≥1965	45,807	53	2,426	25
1945-1965	37,252	43	5,056	52
<1945	3,465	4	2,219	23
Male gender[α]	53,337	62	6,909	71
Country of birth[α]				
Australia	35,284	78	4,202	71
Asia-Pacific	4,418	10	549	9
Other	5,663	12	1,181	20
Year of HCV notification				
1993-2000	44,450	51	6,275	65
2001-2006	24,375	28	2,392	25
2007-2012	17,724	20	1,034	11
HBV co-infection	3,232	4	480	5
HIV co-infection	812	1	153	2
HBV/HIV co-infection	50	<1	14	<1
Area of residence at the time of HCV notification[α]				
Rural NSW	29,443	35	3,094	32
Outer metropolitan NSW	28,071	33	3,362	35
Metropolitan NSW	27,264	32	3,192	33
Alcohol-related disorders	13,489	16	2,820	29
Receipt of OST	25,869	30	2,765	31

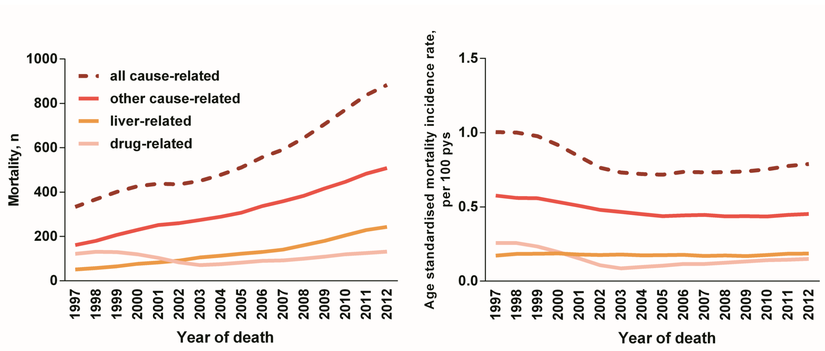
[α]among people with available information: n=25 had missing date of birth; n=349 had missing gender; n=44,953 had missing country of birth and; n=1,824 had missing area of residence at the time of HCV notification

Figure 1. Mortality numbers among NSW people with an HCV notification 1993-2012, by birth cohort, n=96,250



- Between 2002 and 2012, liver-related mortality numbers increased among those born during 1945-1965 (*P*<0.001) and in or after 1965 (*P* 0.020).
- Between 2002 and 2012 , drug-related mortality numbers increased among those born in or after 1965 (*P* <0.001).

Figure 2. Mortality numbers and age-standardised incidence rates among NSW people with an HCV notification 1993-2012, n=96,250



- Between 2002 and 2012, overall, liver- and drug-related mortality numbers increased (*P* <0.001 and *P* 0.001, respectively).
- Between 2002 and 2012 , age-standardised liver-related mortality incidence remained stable (*P* 0.213); however, drug-related mortality incidence increased (*P* 0.002)

Table 2. Adjusted analysis of factors associated with liver-related mortality among NSW people with an HCV notification 1993-2012, n=96,250

	Deceased[α]	%	aSHR[β]	95% CI	*P*
Characteristics, n %	n=2,088				
Birth cohort					
≥1965	207	<1	1.00	-	-
1945-1965	1,416	3	7.20	6.20, 8.37	<0.001
<1945	465	8	26.43	22.14, 31.54	<0.001
Gender					
Female	524	1	1.00	-	-
Male	1,561	3	1.48	1.34, 1.64	<0.001
Missing	3	1	0.64	0.21, 2.02	0.451
Country of birth					
Australia	888	2	1.00	-	-
Asia-Pacific	136	3	1.17	0.97, 1.42	0.102
Other	276	4	1.33	1.15, 1.54	<0.001
Missing	788	2	1.03	0.93, 1.15	0.582
Year of HCV notification					
1993-2000	1,377	3	1.00	-	-
2001-2006	511	2	1.38	1.24, 1.54	<0.001
2007-2012	200	1	2.46	2.11, 2.88	<0.001
HBV co-infection					
No	1,969	2	1.00	-	-
Yes	119	3	1.59	1.32, 1.93	<0.001
Area of residence at the time of HCV notification					
Rural NSW	645	2	1.00	-	-
Outer metropolitan NSW	719	2	1.16	1.04, 1.30	0.006
Metropolitan NSW	707	2	1.04	0.93, 1.16	0.513
Missing	8	<1	0.54	0.27, 1.08	0.081
Alcohol-use disorders					
No	1,088	1	1.00	-	-
Yes	1,000	6	6.80	6.19, 7.47	<0.001
Receipt of OST [γ]					
No	1,619	2	1.00	-	-
Yes	469	2	0.85	0.75, 0.95	0.005

[α]drug- and other cause-related mortality considered to be competing risk events. Mortality records included in analysis 1997-2013, [β]adjusted subhazard ratio, [γ]included as a time-dependent variable

Table 2. Adjusted analysis of factors associated with drug-related mortality among NSW people with an HCV notification 1993-2012, n=96,250

	Deceased[α]	%	aSHR[β]	95% CI	*P*
Characteristics, n %	n=1,622				
Birth cohort[γ]					
<1965	699	1	1.00	-	-
≥1965	923	2	1.20	1.08, 1.33	<0.001
Gender					
Female	451	1	1.00	-	-
Male	1,170	2	1.48	1.33, 1.65	<0.001
Missing	1	<1	0.45	0.60, 3.20	0.423
Country of birth					
Australia	607	2	1.00	-	-
Asia-Pacific	37	1	0.65	0.46, 0.90	0.010
Other	80	1	0.66	0.52, 0.84	0.001
Missing	898	2	0.83	0.75, 0.93	0.001
Year of HCV notification					
1993-2000	1,144	2	1.00	-	-
2001-2006	372	1	0.84	0.76, 0.95	0.006
2007-2012	106	1	0.88	0.71, 1.08	0.215
HBV co-infection					
No	1,522	2	1.00	-	-
Yes	100	3	1.39	1.11, 1.67	0.003
Area of residence at the time of HCV notification					
Rural NSW	470	1	1.00	-	-
Outer metropolitan NSW	606	2	1.24	1.09, 1.40	0.001
Metropolitan NSW	538	2	1.16	1.02, 1.31	0.019
Missing	8	<1	0.48	0.24, 0.98	0.044
Alcohol-use disorders					
No	1,172	1	1.00	-	-
Yes	450	3	1.59	1.42, 1.77	<0.001
Receipt of OST[δ]					
No	521	1	1.00	-	-
Yes	1,101	4	4.70	4.20, 5.27	<0.001

[α]liver- and other cause-related mortality considered to be competing risk events. Mortality records included in analysis 1997-2013, [β]adjusted subhazard ratio, [γ]birth cohort categories ≤1945 and 1945-1965 were combined due to small numbers (n=9) in the ≤1945 age group, [δ]included as a time-dependent variable

Discussion

- Liver-related mortality numbers have continued to rise during the 2000s and early 2010s, underlining the ageing cohort effect and limited impact of HCV treatment programs on population-level HCV-related liver disease.
- Although declined compared to 1990s, drug-related mortality has remained one of the main causes of death among younger HCV cohorts during the study period.
- Given the strength of the association between alcohol use and liver- and drug-related mortality, alcohol-use disorders are ikely to have a major impact on the mortality burden among people with HCV infection, particularly liver-related mortality.
- These findings highlight the need for developing multilateral public health plans against the hepatitis C epidemic, including strategies to reduce the impact of drug and alcohol, those facilitating access to HCV antiviral treatment and, other interventions to prevent HCV infection and its sequelae.

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