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7 1 **Title:** Chronic Hepatitis C Associated Hospitalizations: A Birth Cohort Analysis with  
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9 2 Implications for Screening  
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19 **Short Title:** Chronic HCV Disease Burden by Birth Cohort

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21 **Word count:** Abstract: 249 Text: 2483

22 Number of Tables: 3

23 Number of Figures: 3

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7 **25 Potential conflicts of interest**  
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9  
10 26 None declared.  
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12  
13 **27 Financial support**  
14

15  
16  
17 28 Third party funding was not sought for this study. LML is supported by a Research Chair  
18  
19 29 from the Manitoba Health Research Council.  
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7 **32 Abstract**  
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10 **33 Background:** Much of the recent increase in chronic hepatitis C (CHC) mortality and  
11 morbidity rates in Canada is believed to be due to higher CHC prevalence among the baby  
12 boom population. We aimed to assess the current and potential future CHC-associated  
13 hospitalization burden by birth cohort and compare the cohort-specific rates.  
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21 **37 Methods:** Hospital records of in-patients with a diagnosis of CHC and liver disease or  
22 liver cancer (CHC-LD) were extracted from the Canadian Discharge Abstract Database  
23 (DAD), for April 2004 to March 2011. Regression was used to estimate the temporal  
24 trend for each 5-year birth cohort from 1915 to 1984. These trends were used to predict  
25 future hospitalizations. Parametric bootstrap methods were used to calculate 95%  
26 confidence intervals (CIs) corresponding to the estimated rate ratios.  
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36 **43 Results:** CHC-LD associated hospitalizations increased an average of 6.0% (95% CI,  
37 4.4%-7.7%) per year over the study period. The CHC-LD associated morbidity burden was  
38 highest for the 1950-54 and 1955-59 birth cohorts at 18 (95%CI, 13-24) and 14 (95%CI,  
39 10.3-18.2) times the rate for the 1970-74 birth cohort in 2010 respectively. Comparing  
40 rates at 75 years of age, the anticipated rate ratios declined to 3.6 (95%CI, 2.3-4.9) and 3.4  
41 (95%CI, 2.1-4.7). Rate ratios at age 75 were statistically elevated for the four 5-year birth  
42 cohorts from 1950-69.  
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7 50 **Conclusions:** Without further interventions, the CHC-LD disease burden will continue to  
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9 51 increase for most birth cohorts, likely peaking after age 70. A significant disease burden is  
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11 52 emerging in younger birth cohorts that should be monitored.  
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18 54 **Keywords:** Epidemiology; Hepatology; Infectious Diseases; Public Health; Statistics and  
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21 55 research methods  
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24 56 **Detailed Keywords:** Birth Cohort; Chronic Hepatitis C; Cohort effect; Disease burden;  
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27 57 Hospitalization; Trends and projections  
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## 59 Introduction

60 In August 2012, the US Center for Disease Control (US CDC) released recommendations  
61 to expand screening for the hepatitis C virus (HCV) to include a one-time blood test for all  
62 persons born between 1945 and 1965 (i.e., baby boom generation). This recommendation  
63 was based in part on estimates that this cohort accounts for three quarters of all HCV  
64 infections in the United States[1] and that of an estimated 4.3% of the population born in  
65 the 1950s who were infected[2], 50% were unaware of their HCV status[3]. Currently in  
66 Canada, screening recommendations for hepatitis C are based on an individual assessment  
67 of risk rather than the patient's age or year of birth[4]. The Canadian Health Measures  
68 Survey, a nationally representative household survey, estimated the seroprevalence for  
69 hepatitis C (HCV) in 2007 to 2011 at 0.5% (95%CI 0.3-0.9). However, only 30% (95% CI  
70 16-51) were aware of their infection status, and prevalence was elevated among persons  
71 aged 50-79 years compared to persons aged 14-49[5].

72 Chronic hepatitis C (CHC) infections have resulted in a considerable morbidity and  
73 mortality burden in Canada[6-8]. Using health-adjusted life-years (HALY), a composite  
74 measure of premature mortality and reduced functioning due to disease, to estimate the  
75 disease burden associated with 51 infectious diseases in Ontario, Kwong and colleagues[9]  
76 found that HCV was the infectious agent that accounted for the largest proportion of the  
77 disease burden, surpassing HIV. Linking diagnostic and mortality data, a study in British  
78 Columbia found significantly elevated standardized mortality ratios (SMR) for both liver

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7 79 related and drug related causes of death as well as all-cause mortality among persons who  
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9 80 had tested positive for HCV compared to those who had tested negative for HCV[10].  
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12 81 The natural history of HCV is only partially understood, and the progression to liver  
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14 82 cirrhosis is variable[11-13]. A small portion of persons clear their infection. For others,  
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16 83 symptoms of the chronic infection often emerge 20 or more years after the initial infection.  
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18 84 Disease progression from fibrosis to cirrhosis and hepatocellular carcinoma is not linear in  
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20 85 time, with the rate of progression related to many factors, including time since infection,  
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22 86 age and alcohol consumption.  
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28 87 This long delay from HCV infection to symptoms suggests that cohort-specific differences  
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30 88 in CHC prevalence as well as the aging of these cohorts significantly influenced the  
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32 89 observed trends in morbidity and mortality rates[6]. With access to detailed hospitalization  
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34 90 data, we aimed to explore the effect of birth-cohort on the trends in hospitalizations  
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36 91 associated with CHC and liver disease (CHC-LD); predict the future lifetime  
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38 92 hospitalizations by 5-year birth cohort; and compare the disease burden for different birth  
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40 93 cohorts.  
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7 95 **Methods**  
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10 96 Sources of data:  
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13 97 Hospital discharge records for patients admitted to an acute care hospital with a diagnostic  
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15 98 code of CHC were extracted from the Canadian Institute of Health Information (CIHI)  
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17 99 patient-specific Discharge Abstract Database (DAD)[8] from April 2004 to March 2011, a  
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19 100 period when all DAD participating provinces used the *International Classification of*  
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21 101 *Disease, Tenth Modification (ICD-10)*[14], Canadian version (ICD-10-CA)[15] for  
22  
23 102 diagnostic coding. The province of Quebec does not participate in the DAD, hence the  
24  
25 103 DAD includes approximately 75% of all acute care hospital separations in Canada.  
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27 104 Hospitalizations were stratified by 5-year birth cohorts from 1915 to 1984, year of  
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29 105 discharge (batch year: running from April until March of the following calendar year),  
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31 106 discharge status (alive or deceased) and the presence of a co-diagnosis of liver diseases  
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33 107 (ICD-10 codes K70-K77, R18) including hepatic carcinoma (ICD-10 code C22). CHC  
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35 108 associated hospitalizations were identified by the ICD-10 code B18.2.  
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42 109 Population denominators for rate calculations were obtained from Statistics Canada  
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44 110 population projections, medium growth scenario M1[16].  
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48 111 Analysis:  
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51 112 As a general outline, trends in the number of hospitalizations were estimated by birth  
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53 113 cohort, and then these trends were used to predict the future burden in the younger birth  
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55 114 cohorts as they aged. Next rates and rate ratios with the 1970-74 cohort as a reference  
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7 115 were calculated three different measures of the cohort effect: by year of hospitalization; at  
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9 116 the same age; and future lifetime. Current year and near-term predictions focus on the  
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11 117 visible burden. With new more effective treatments on the horizon, reducing the near-term  
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13 118 burden is a more urgent concern. The same age comparison is a proxy measure of the  
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15 119 relative prevalence. The future lifetime comparison is similar to the comparison used in  
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17 120 cost-effectiveness analysis.

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22 121 The first step was to estimate the trend in the number of CHC-LD associated  
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24 122 hospitalizations for each 5-year birth cohort from 1915-19 to 1980-84. A generalized  
25  
26 123 linear model (GLM) with a log link, Poisson distribution and dispersion parameter  
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28 124 specified[17] was fit to the annual number of hospitalizations stratified by birth cohort with  
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30 125 year of discharge (batch year) and a constant term as the model covariates. The quasi-  
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32 126 Poisson regression model equation to predict the annual number of hospitalizations  
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34 127 ( $Hosp_{i,j}$ ) for birth cohort  $j$  ( $j=1915-19$  to  $1980-84$ ) in batch year  $i$  ( $i=2004$  to  $2010$ ) is  
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36 128 given by:

$$129 \quad \log(Hosp_{i,j}) = \beta_{2,j}Year_i + \beta_{1,j} \quad (1)$$

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45 130 The estimated trend parameter value ( $\beta_{2,j}$ ) and its standard error were converted to an  
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47 131 average annual percentage change ( $e^{\beta_{2,j}} - 1$ ) for each birth cohort. The same model was  
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49 132 used to estimate the overall trend.

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53 133 The second step was to use a parametric bootstrap approach, which involves generating  
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55 134 simulated values of the parameters, to facilitate the calculation of confidence intervals (CI)

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7 135 for the projected rate ratios. The bootstrap is a computationally intensive statistical  
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9 136 technique that allows the researcher to make inferences from data with complex  
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11 137 distributions (in this case, the ratios of projected rates)[17-19]. Random values were  
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13 138 generated using the normal distribution with the mean and standard deviation given by the  
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15 139 trend ( $\beta_{2,j}$ ) and standard error estimated in the quasi-Poisson regression model in the first  
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17 140 step. The number of hospitalizations for each birth cohort in the last year of available data  
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19 141 ( $Hosp_{2010,j}$ ) was also simulated from the distribution of uncertainty (standard error)  
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21 142 associated with model predicted value for 2010. In the third step, the average age at  
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23 143 hospitalization over the study period was calculated for each birth cohort and the  
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25 144 simulated values for the cohort-specific trends ( $\beta_{2,j}$ ) were interpolated linearly to obtain  
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27 145 trend estimates for each single year of age[17]. The fourth step was to project the number  
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29 146 of hospitalizations until age 90 for each 5-year birth cohort and then sum the predicted  
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31 147 number of hospitalizations for the time period of interest (for example, next 10 years, at  
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33 148 age 75, or future lifetime) and calculate hospitalization rates. Future lifetime  
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35 149 hospitalizations were calculated by summing the projected values from 2011 until age 90  
36  
37 150 and rates were calculated by dividing by the population in 2010. The 1970-74 birth cohort  
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39 151 was selected as the reference for the rate ratios. Same-age rate ratios were reported for age  
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41 152 75, though with the methodology used same-age rate ratios would not be sensitive to this  
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43 153 choice of age. The final step was to calculate the mean and standard deviation of the rate  
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45 154 ratios from the previous step. Results from steps 1 (trends), 4(projections) and 5 (rate  
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47 155 ratios) are reported. SAS Enterprise Guide 5.1 [17] was used for the analysis.  
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7 **157 Results**  
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11 158 The number of CHC-associated hospitalizations in the study area increased approximately  
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13 159 5% per year from 4700 in 2004/05 to 6400 in 2010/11. The rate of increase was more  
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15 160 pronounced for CHC-LD associated hospitalizations at 6.0% (95% CI, 4.4%-7.7%) per  
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17 161 year. The proportion of CHC-LD associated hospitalizations increased with increasing age  
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19 162 from 5% for patients less than 30 years of age, reaching 60% by age 65. The fatality rate  
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21 163 also increased with increasing age from 10% of CHC-LD associated hospitalizations for  
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23 164 patients under the age of 30 years to 18% by age 65. The 'baby boom' cohort accounted  
24  
25 165 for 75% of all CHC-LD associated hospitalizations in 2010, though by 2010 the number of  
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27 166 CHC-LD associated hospitalizations among the 1965-69 birth cohort had already increased  
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29 167 to levels seen 5 years earlier in the 1960-64 birth cohort (Figure 1).  
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35 168 Trends:  
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38 169 Statistically significant increases in the number of CHC-LD associated hospitalizations  
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40 170 over the study period were detected for birth cohorts from 1950-54 to 1975-79,  
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42 171 corresponding to an approximate age range of 25 to 60 years and statistically significant  
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44 172 declines were detected for the 1920-24 and 1925-29 birth cohorts (Table 1). The rate of  
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46 173 increase was highest at approximately 30 years of age (Table 1 and Figure 2).  
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50 174 Projections:  
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53 175 Applying these estimated trends to the historic hospitalization data produced a status quo  
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55 176 projection which suggests that the 1950-54 and 1955-59 birth cohorts will continue to  
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7 177 experience the highest annual number of CHC-LD associated hospitalizations well past  
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9 178 2020 (Table 2, Figure 3a). The number of annual hospitalizations is projected to peak  
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11 179 around age 70 to 80 (Table 1, Figure 3b). The 6.0% (95%CI, 4.1%-7.9%) annual increase  
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13 180 observed over the study period for all 5-year birth cohorts (1915-1984) combined is  
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16 181 projected to decline to 3% per year by 2020 and eventually plateau approximately 10 years  
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18 182 later.

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22 183 Ratio Ratios:

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25 184 Over the next 10 years, the morbidity rate for the 1950-54 and 1955-59 cohorts is predicted  
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27 185 to remain high at approximately 10.7 (95% CI, 6.7 -14.7) and 9.1 (95% CI, 5.8 – 12.4)  
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29 186 times the rate for persons born between 1970 and 1974 respectively in 2020 (Table 2). The  
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31 187 estimated rate ratios at age 75 can be considered a proxy for the relative prevalence of  
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33 188 CHC in different cohorts, since age effects have been controlled for. The same-age ratios  
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35 189 suggest that the CHC prevalence is approximately 3.6 (95% CI, 2.3 – 4.9) times higher for  
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37 190 the 1950-54 birth cohort compared to the 1970-74 cohort, while the estimated ratio for the  
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39 191 future lifetime morbidity burden is slightly lower at 2.4 (95% CI, 1.5 – 3.4). Though the  
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41 192 disease burden for both 1960s birth cohorts is currently lower than for the two 1950s birth  
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43 193 cohorts, the future lifetime burden is predicted to be similar for all four birth cohorts. It is  
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45 194 uncertain whether the decline in prevalence seen in successive 5-year birth cohorts from  
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47 195 1955-59 to 1970-74 will continue with younger cohorts, though the future lifetime burden  
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49 196 for persons born after 1970 is possibly elevated compared to persons born before 1944  
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7 197 (Tables 2). Table 3 provides summary classification of the relative disease burden by birth

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9 198 cohort.

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## 200 **Interpretation**

201 The disease burden associated with CHC is significantly elevated for the 1950-54 and  
202 1955-59 birth cohorts. Without further interventions, CHC-LD hospitalizations for these  
203 cohorts are expected to continue increasing before peaking at approximately 1.5 times the  
204 2010 rate around 2025 to 2030. Despite the apparent lower prevalence of CHC among  
205 persons born in the 1960s, the potential to reduce the disease burden over a longer life span  
206 in younger cohorts suggests that the 60s cohorts could also benefit from earlier detection  
207 and treatment to stop disease progression. It is too early to fully assess the relative CHC  
208 prevalence and disease burden for persons born after 1974, though this analysis suggests  
209 continued monitoring of these younger birth cohorts would be appropriate. Both age and  
210 year of birth as a proxy for exposure contribute to the level of severe disease.

211 The rate of increase in CHC- and CHC-LD-associated admissions over the study period is  
212 considerably less than earlier estimates of 15% to 30% annual increases[6, 20]. The higher  
213 trends of the earlier studies can be explained in part by the combined effects of aging and  
214 differences in prevalence by birth cohort. In contrast to the increase in the disease burden,  
215 the number of new HCV diagnoses have been declining in recent years for most birth  
216 cohorts over the age of 30[21, 22]. Though the natural history of an infection with HCV is  
217 difficult to study and disease progression rates vary depending on the cohorts studied[11-  
218 13, 23], estimates of the rate of increase in disease burden by age alone are emerging.  
219 Zalesak and colleagues[24], in examining a Medicare claims database from the US, found  
220 that CHC patient populations have already started to decline for persons born before 1945

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7 221 (aged 65+ in 2010). Our age-specific estimates of the rate of increase in patient  
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9 222 populations followed by birth cohort are in close agreement, though we do not detect a  
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11 223 statistically significant decline in the number of CHC-LD associated hospitalizations  
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14 224 except for persons born before 1925.

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17 225 Estimates from an American household survey found that persons born in the 1950s had  
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19 226 the highest anti-HCV prevalence at 4.3 times that of persons born in the 1970s[2], whereas,  
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22 227 we predict a CHC-LD burden for Canadians born in the 1950s of 3.5 times that for  
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24 228 Canadians born between 1970 and 1974. The Canadian anti-HCV prevalence estimates  
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26 229 from recent household surveys are however lower than the American estimate by a factor  
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29 230 of 3 (0.5% versus 1.6%)[2, 5]. Our estimates of relative prevalence, combined with the  
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31 231 CHMS estimate[5], suggest an anti-HCV Canadian household prevalence of approximately  
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33 232 1.1% for persons born in the 1950s and 0.5% and 0.3% for Canadians born in 1945-49 and  
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36 233 the 1970s respectively. Household prevalence is, however, considered an underestimate  
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38 234 of the national prevalence as groups such as the homeless and inmates are at high risk for  
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41 235 HCV and were not included in the household surveys.

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44 236 Limitations:

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47 237 The primary limitation of this study is that to project the future disease burden, we  
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49 238 assumed that the main driver of the birth-cohort specific trends in the annual number of  
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51 239 CHC-LD associated hospitalizations was age combined with time since infection. As time  
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53 240 since infection was not observed, it could be an important confounder. The relationship  
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56 241 between age and time since infection is expected to be consistent across younger birth  
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7 242 cohorts for whom injection drug use is considered the primary risk factor for HCV  
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9 243 infections. However, this may not be the case for older birth cohorts for whom blood  
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11 244 transfusion, blood products, or organ transplant before 1992 are recognized sources of  
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13 245 infection in Canada[4]. Later age at acquisition has been associated with a higher  
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16 246 prevalence of cirrhosis 20 years later and faster rates of progression to cirrhosis[12, 25].  
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18 247 The source of the HCV infection is also known to influence the all-cause mortality  
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21 248 rate[10]. As a result, the disease burden for persons born after 1950 may peak somewhat  
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23 249 earlier and decline faster than suggested in Figure 3. Although improvement in treatment  
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25 250 options over the study period have likely influenced the historic trends, significant future  
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28 251 improvements in treatment options or the development of drug resistance could  
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30 252 significantly alter the future disease burden and rate ratios. These sources of additional  
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33 253 uncertainty were not included in the estimated confidence intervals for the rate ratios.  
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36 254 Conclusions:

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39 255 In summary, this analysis has demonstrated an increasing burden of CHC-LD associated  
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41 256 hospitalizations from 2004 to 2010. It is clear that without additional interventions, the  
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43 257 disease burden of the 1950-54 and 1955-59 birth cohorts is especially high and will  
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46 258 continue to be noticeably elevated over many years. The potential to reduce the disease  
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48 259 burden over a longer life span in younger cohorts suggests that the potential benefits of  
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50 260 earlier detection and treatment should be considered for younger birth cohorts as well.  
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53 261 Analysis of birth cohort-specific trends has provided additional insight into the emerging  
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55 262 disease burden due to CHC at the population level.  
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7 **263 Acknowledgements**  
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10 264 The authors acknowledge the support of the Canadian Institute of Health Information and  
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12 265 all those involved in the collection and compilation of the Discharge Abstract Database.  
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15 266 As well, the authors wish to thank the Data Coordination and Access Program of the Public  
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17 267 Health Agency of Canada for providing access to this database. The cooperation of all  
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19 268 involved in these activities is gratefully acknowledged.  
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270 **Notes**

271 Financial support

272 Third party funding was not sought. LML is supported by a Research Chair from the  
273 Manitoba Health Research Council.

274 Potential conflicts of interest

275 None declared.

276 Author contributions

277 DLS performed the analysis and drafted the manuscript. All contributed to the concept and  
278 design of the study, to the interpretation and presentation of study results. All authors  
279 revised the manuscript critically and all approved the final version submitted for  
280 publication.

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282 **Tables:**283 Table 1: Birth-cohort specific Average Annual Percentage Change in the Number of CHC-  
284 LD associated Hospitalizations from 2004/05 to 2010/11<sup>1</sup>  
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Birth Cohort	Average Age	Rate in 2010 (100,000) (95% CI)	Average Annual %Change	95% CI	p-value	Stat Sig.
1915 - 1919	89	8.9 (4.8, 16.6)	-6.8%	(-20.9, 9.4)	0.3902	
1920 - 1924	83	6.7 (4.5, 10.1)	-13.9%	(-22.0, -5.1)	0.0028	*
1925 - 1929	79	12.4 (9.8, 15.8)	-6.6%	(-12.3, -0.6)	0.0314	*
1930 - 1934	74	17.1 (14.2, 20.6)	3.5%	(-1.9, 9.1)	0.2095	
1935 - 1939	69	14.9 (12.5, 17.8)	1.1%	(-3.9, 6.2)	0.6786	
1940 - 1944	64	16.4 (14.1, 19.1)	1.6%	(-2.6, 5.9)	0.4715	
1945 - 1949	59	24.4 (21.9, 27.1)	2.2%	(-0.8, 5.3)	0.1594	
1950 - 1954	54	48.2 (45.0, 51.8)	6.6%	(4.4, 8.9)	<.0001	*
1955 - 1959	50	36.5 (33.9, 39.4)	8.9%	(6.5, 11.4)	<.0001	*
1960 - 1964	45	15.8 (14.2, 17.7)	11.5%	(7.7, 15.4)	<.0001	*
1965 - 1969	40	9.1 (7.8, 10.6)	12.7%	(7.4, 18.4)	<.0001	*
1970 - 1974	35	2.6 (1.9, 3.5)	10.1%	(0.7, 20.6)	0.0361	*
1975 - 1979	30	1.6 (1.0, 2.4)	33.6%	(14.3, 57.8)	0.0004	*
1980 - 1984	25	0.4 (0.2, 0.9)	25.0%	(-5.1, 69.3)	0.1244	
<b>All Birth Cohorts: 1915-1984</b>	55	8.9 (4.8, 16.6)	6.0%	(4.1, 7.9)	<.0001	*

286 Notes:

287 <sup>1</sup> Results from regression model

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289 Table 2: Average Projected Ratios of Hospitalizations Rates Associated with CHC-LD with 95% Confidence Intervals

Birth Cohort	2010 (last year of Data)	2011 (1 year projection)	5 years <sup>1</sup>	2015	10 years <sup>1</sup>	2020	At age 75	Until Age 90 <sup>1</sup>
1915 - 1919	2.9 (1.4, 6.1)	2.7 (0.9, 4.5)						
1920 - 1924	2.4 (1.4, 4.1)	2.1 (1.5, 2.8)	1.6 (0.5, 2.7)	1.2 (<2.3)				
1925 - 1929	4.4 (3.0, 6.4)	3.7 (2.3, 5.2)	2.4 (1.3, 3.6)	1.6 (0.6, 2.7)	1.6 (0.5, 2.6)	0.8 (<2.1)		
1930 - 1934	7.0 (5.0, 9.7)	6.1 (3.8, 8.3)	3.5 (2.0, 5.0)	2.2 (1.0, 3.4)	2.0 (1.0, 3.0)	0.8 (0.2, 1.4)		0.2 (0.1, 0.3)
1935 - 1939	4.7 (3.4, 6.6)	5.8 (3.4, 8.2)	4.1 (2.6, 5.7)	3.1 (1.8, 4.5)	2.6 (1.5, 3.7)	1.1 (0.4, 1.8)	0.8 (0.4, 1.2)	0.3 (0.1, 0.4)
1940 - 1944	6.3 (4.6, 8.6)	6.0 (4.3, 7.8)	4.7 (3.0, 6.4)	3.9 (2.3, 5.6)	3.5 (2.1, 5.0)	2.3 (1.1, 3.4)	1.0 (0.5, 1.5)	0.5 (0.2, 0.7)
1945 - 1949	8.8 (6.5, 11.8)	9.3 (6.2, 12.4)	6.9 (4.5, 9.4)	5.7 (3.5, 8.0)	5.3 (3.2, 7.4)	3.8 (2.0, 5.6)	1.6 (0.9, 2.3)	0.9 (0.5, 1.4)
1950 - 1954	17.6 (13.2, 23.5)	17.8 (10.9, 24.7)	14.0 (9.3, 18.6)	11.7 (7.3, 16.0)	10.7 (6.7, 14.7)	7.5 (4.0, 10.9)	3.6 (2.3, 4.9)	2.4 (1.5, 3.4)
1955 - 1959	13.7 (10.3, 18.2)	13.9 (9.7, 18.1)	11.5 (7.7, 15.3)	10.0 (6.3, 13.6)	9.1 (5.8, 12.4)	6.6 (3.7, 9.4)	3.4 (2.1, 4.7)	2.6 (1.6, 3.6)
1960 - 1964	5.6 (4.2, 7.6)	6.2 (4.5, 7.9)	5.6 (3.7, 7.5)	5.2 (3.2, 7.1)	4.8 (3.0, 6.6)	3.8 (2.2, 5.5)	2.2 (1.4, 3.1)	1.9 (1.2, 2.6)
1965 - 1969	3.4 (2.5, 4.7)	3.7 (2.5, 5.0)	3.4 (2.2, 4.6)	3.3 (2.1, 4.6)	3.2 (2.0, 4.4)	3.0 (1.8, 4.1)	2.1 (1.3, 2.8)	1.9 (1.2, 2.6)
1970 - 1974 (Reference)								
1975 - 1979	0.7 (0.4, 1.0)	0.7 (0.4, 1.0)	0.6 (0.3, 1.0)	0.6 (0.2, 1.0)	0.6 (0.2, 1.0)	0.6 (0.2, 1.1)	1.1 (0.4, 1.8)	1.1 (0.4, 1.8)
1980 - 1984	0.1 (0.1, 0.3)	0.1 (<0.3)	0.3 (<0.6)	0.3 (<0.8)	0.3 (<0.7)	0.3 (<0.8)	0.7 (< 1.5)	1.0 (<2.5)

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291 Notes:  
292 <sup>1</sup> From 2011

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293 Table 3: Classification of Disease Burden by Birth Cohorts

<b>Relative Burden</b>	<b>Next 10 years</b>	<b>Lifetime</b>
High	1950-59	1950-69
Medium High	1960-69	
Medium	1945-49, 1970-84	1945-49, 1970-84
Low	1925-44	1925-44

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7 296 **Figure Legends:**  
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10 297 Figure 1: Annual chronic hepatitis C and liver disease associated hospitalizations by 5-year  
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12 298 birth cohort, DAD participating hospitals (Canada, excluding the province of  
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14 299 Quebec). Each data point corresponds to the annual number of hospitalizations with a  
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16 300 contributing diagnosis of CHC and liver disease for the 5-year birth cohort identified  
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18 301 in the legend (by batch year running from April to March). Data points are plotted  
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20 302 against the average age at time of admission for the 5-year birth cohort on the x-axis.  
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22 303 Data points corresponding to the same birth cohort have been joined. Each time  
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24 304 series corresponds to years 2004/05-2010/11. The first data point in a time-series  
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26 305 corresponds to the batch year of 2004/05. For successive birth cohorts, there is an  
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28 306 overlap of two data points with the same age. The vertical space between the cohort-  
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30 307 specific series at the same age is an indication of a cohort effect due to different  
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32 308 levels of exposure to HCV as well as differences in the availability of treatments.  
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39 309 Figure 2: Rate of change in the number of chronic hepatitis C and liver disease associated  
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41 310 hospitalizations, estimated by 5-year birth cohort and plotted by the average age of  
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43 311 the cohort. The 95% confidence intervals are indicated by the vertical bars and were  
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45 312 calculated by the regression model. The age indicated on the x-axis corresponds to  
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47 313 the average age for the birth-cohort over the study period. (See Table 1)  
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52 314 Figure 3: Status quo projection of the number of chronic hepatitis C and liver disease  
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54 315 associated hospitalizations. This is one of the simulated projections that illustrates  
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56 316 the underlying cohort structure. In the calculations of rate ratios, the 1970-74 birth  
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7 317 cohort was used as the reference (dotted brown line). a) Projections are plotted  
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9 318 against calendar year on the x-axis. For near term measures of disease burden, rate  
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11 319 ratios were calculated for: the last year of data (2010); 1 year projection (2011); over  
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13 320 the next 5 years (2011-2015); in 5 years (2015); over the next 10 years (2011-2020);  
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15 321 and in 10 years (2020). b) Projections are plotted against the average age of the birth  
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17 322 cohort on the x-axis. Rate ratios calculated for the same age (age 75 was used in the  
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19 323 text) provide a measure of relative exposures closely related to the relative CHC  
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21 324 prevalence. Future lifetime hospitalizations were calculated as the area under the  
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23 325 curve from 2011 to age 90.  
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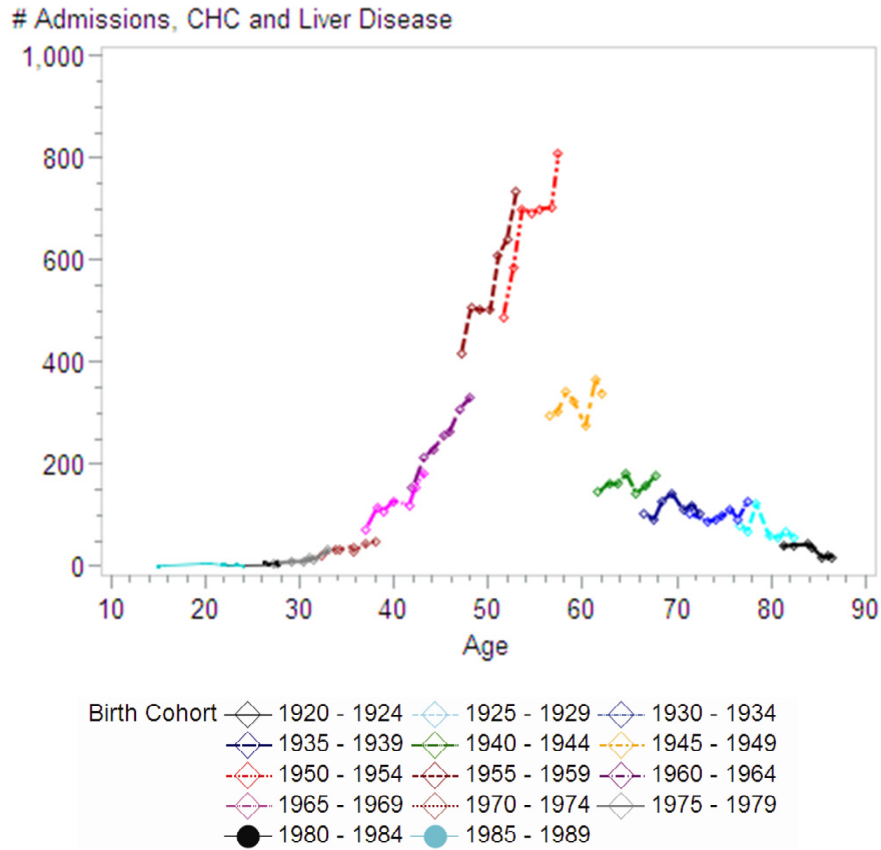


Figure 1

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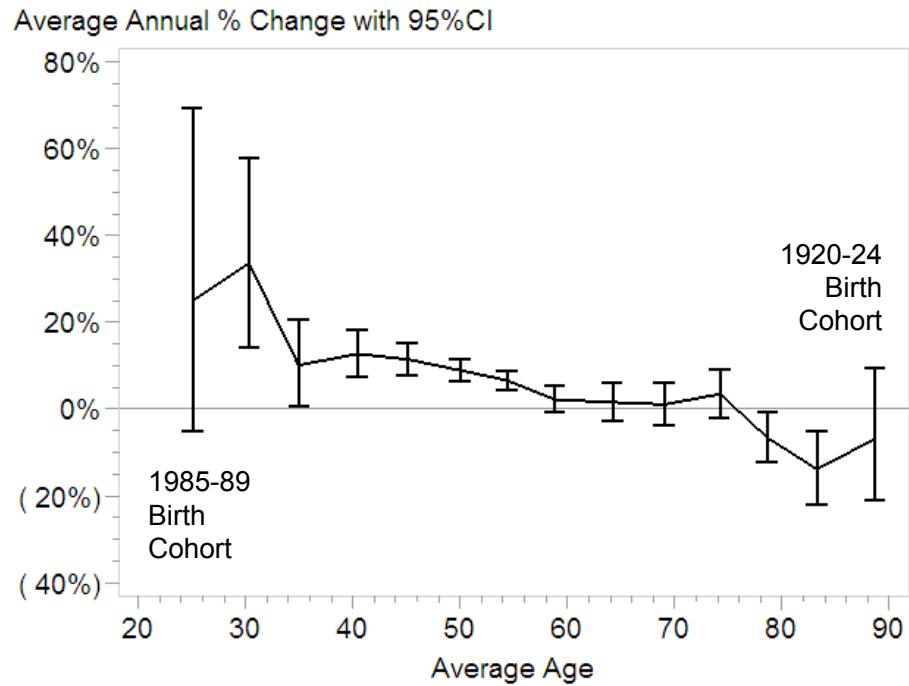


Figure 2

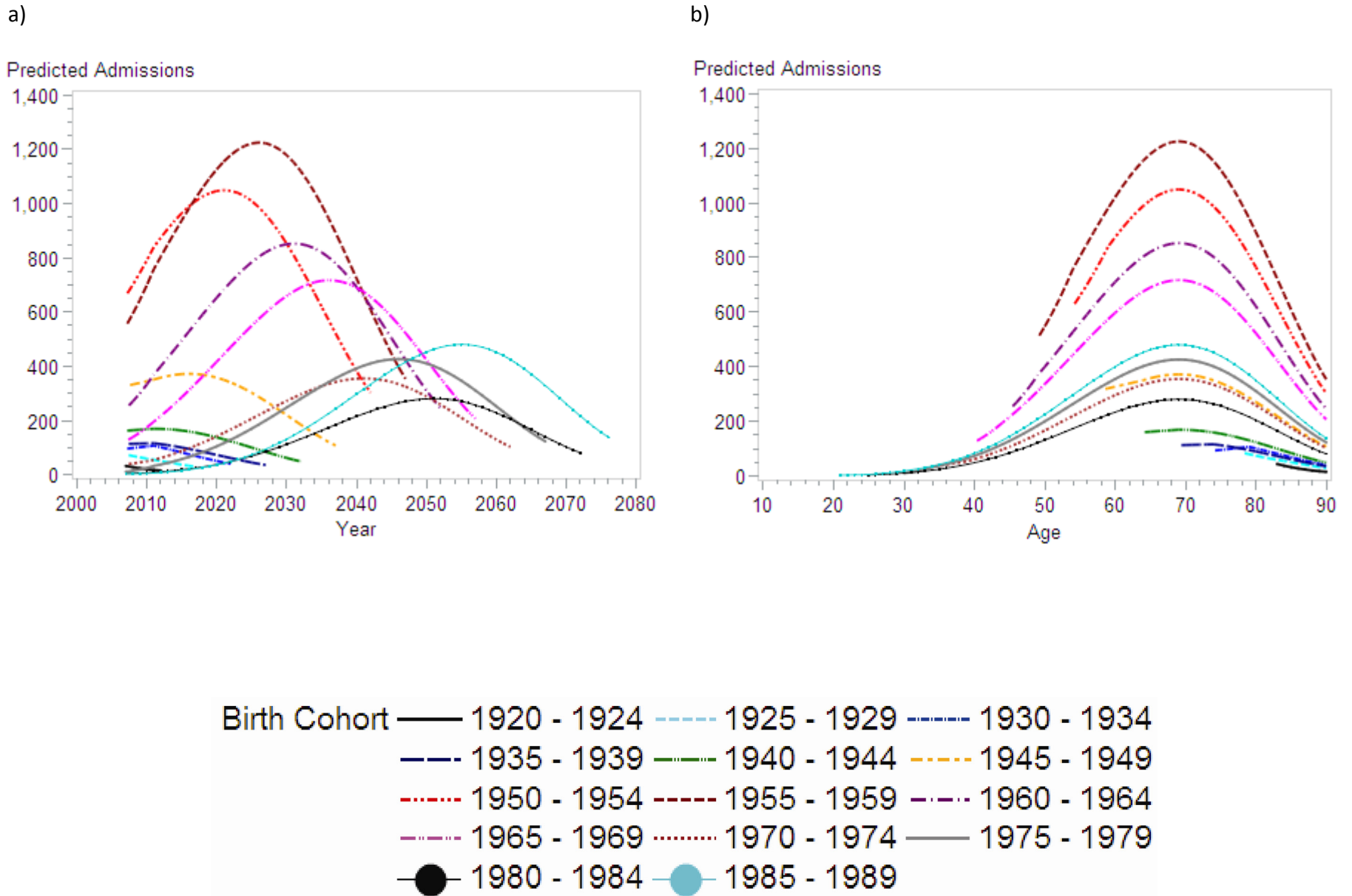


Figure 3