ABSTRACT

Mortality data from Statistics Canada were analyzed to measure the temporal trends and burden of illness attributed to viral hepatitis in Canada. Analysis of age-standardized mortality rates from 1979 to 1997 showed an increasing trend in mortality for both hepatitis B and non-A, non-B hepatitis (NANBH), most of which are attributed to hepatitis C infections. Hepatitis B and NANBH age-standardized mortality rates increased respectively, from 0.03 and 0.12 deaths per 100,000 population in 1979 to 0.26 and 0.41 deaths per 100,000 in 1997. Male mortality rates were consistently higher than female for both diseases. Among deaths from chronic liver disease, over 1,000 deaths were estimated to have been caused by hepatitis B and hepatitis C annually. Although the hepatitis B or NANBH recorded deaths largely underestimate the true burden of HBV and HCV in Canada, the temporal trends are useful as they reflect changes in the impact of both diseases.

ABRÉGÉ

Nous avons analysé les données de Statistique Canada sur la mortalité pour mesurer les tendances temporelles des maladies attribuées à l'hépatite virale au Canada. L'analyse des taux comparatifs de mortalité, de 1979 à 1997, montre une tendance croissante de la mortalité à la fois dans les cas d'hépatite B et dans les cas d'hépatite non A–non B (NANB), dont la plupart sont attribués à l'hépatite C. Les taux comparatifs de mortalité causée par l'hépatite B et l'hépatite NANB ont augmenté, passant respectivement de 0,03 et 0,12 décès pour 100 000 habitants en 1979, à 0,26 et à 0,41 décès pour 100 000 habitants en 1997. Les taux de mortalité chez les hommes étaient constamment plus élevés que chez les femmes, qu'il s'agisse de l'hépatite B ou de l'hépatite NANB. On estime que, sur le nombre total des décès causés par une maladie chronique du foie, plus de 1 000 décès par année sont causés par l'hépatite B et l'hépatite C. Bien que le nombre de décès attribués à l'hépatite B ou à l'hépatite NANB soit bien en deçà du fardeau réel de l'HVB et de l'HVC au Canada, les tendances temporelles sont utiles, car elle reflètent les changements dans l'incidence de ces deux maladies.

Trends of Hepatitis B and Hepatitis C Mortality in Canada, 1979-1997

Gina Pohani, MHSc, Shimian Zou, MD, PhD, Martin Tepper, MD, MHSc, FRCPC

Viral hepatitis is a major public health concern, as it is a source of significant morbidity and mortality worldwide.[1-3] It has been estimated that well over 100,000 Canadians are chronically infected with HBV and an estimated 192,000 are infected with HCV.[4-6] Although death from acute disease is unusual, many patients with HBV and HCV become chronically infected, and a proportion of these progress to chronic liver disease including cirrhosis and hepatocellular carcinoma.[7,8] After acute HBV infection, the risk of developing chronic infection varies inversely with age. Chronic HBV infection occurs in 90% of infants infected at birth, and in 1-10% of persons infected as children or adults. An estimated 15-25% of persons with chronic HBV infection will die prematurely of either cirrhosis or hepatocellular carcinoma.[9] Although initial infection with HCV may appear asymptomatic, approximately 85% will develop chronic HCV infection. Of persons chronically infected with HCV, approximately 20% are at risk of developing cirrhosis and 1-5% will develop hepatocellular carcinoma during the first two decades following initial infection.[10]

Almost 6,000 people in the United States die each year as a consequence of chronic hepatic disease associated with hepatitis B, and 8,000 to 10,000 from hepatitis C.[11] Although no such estimates are currently available for hepatitis B infection in Canada, it has been estimated that 640 hepatitis C deaths occur in Canada each year.[6]

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To understand and evaluate the impact of various intervention programs and other relevant factors on both hepatitis B and hepatitis C, it is important to examine the temporal trends of each disease. Monitoring changes of both diseases over time can help in the prediction of future trends, which is essential for both health care planning and the formulation of prevention strategies. Description of temporal trends for hepatitis C has been difficult, as reporting of hepatitis C in Canada did not start until 1992 and was not nationwide until 1999. As a result, data from the National Notifiable Disease Reporting System are either unavailable or are not adequate to describe the temporal trends of this disease.

Consequently, mortality was used as an indicator to estimate the overall burden of, and measure temporal trends of hepatitis B and hepatitis C in Canada. This report presents mortality trends for both hepatitis B and hepatitis C in Canada based on the number of recorded deaths caused by hepatitis B or non-A, non-B hepatitis (NANBH) from 1979 to 1997. Further, many cases of HBV and HCV infection progress to chronic liver disease, and subsequent deaths may not be recorded as caused by hepatitis B or hepatitis C. Thus, deaths recorded as caused by chronic liver disease, which are likely caused by hepatitis B or hepatitis C, were also determined to arrive at more accurate estimates of hepatitis B and hepatitis C mortality in Canada.

METHODS

Data on mortality from 1979 to 1997 were obtained from Statistics Canada.[12] Causes of death were selected using the ninth revision of the WHO's International Classification of Disease (ICD-9) which was used for the entire period of study.[13]

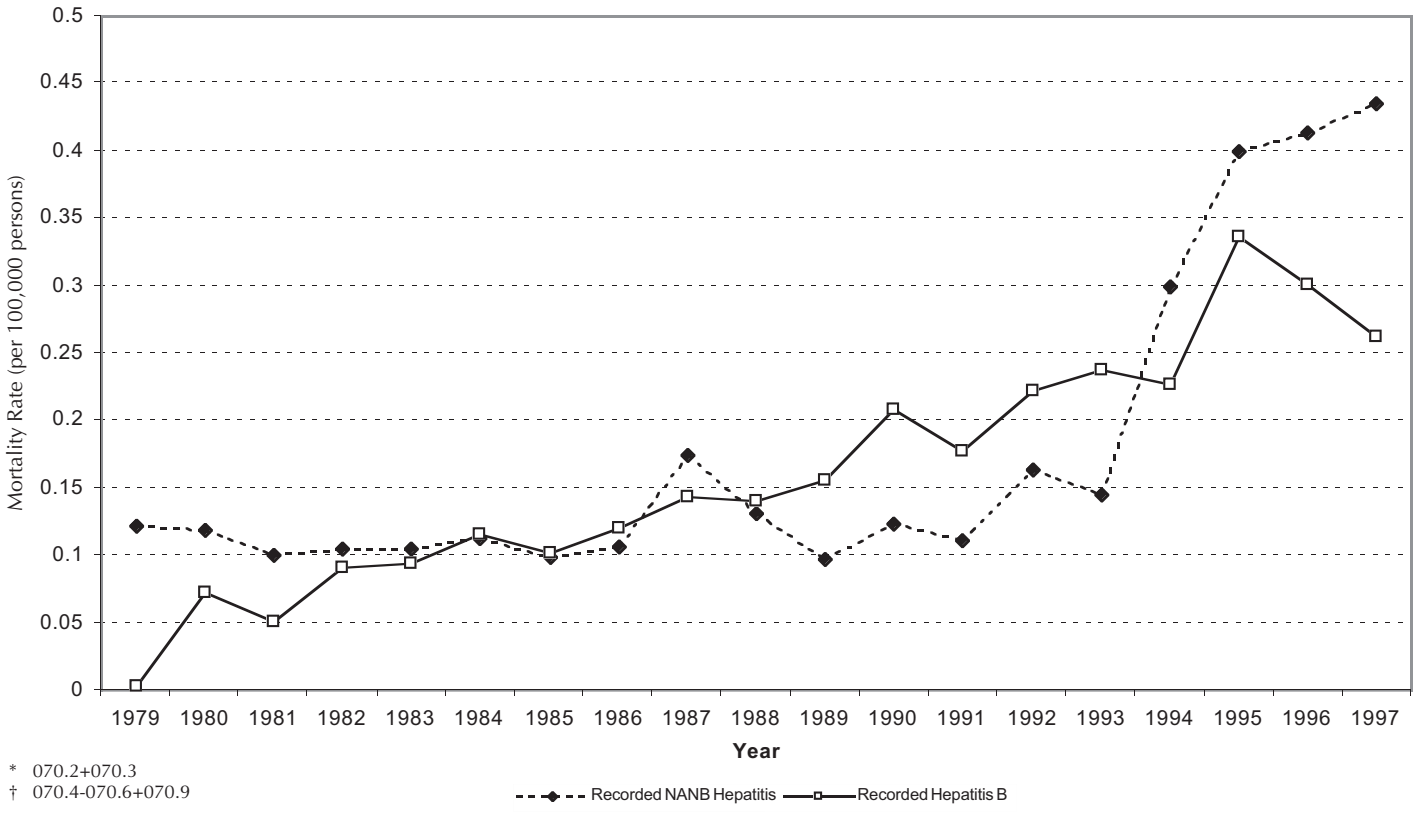

Figure 1. Age-standardized mortality rates for hepatitis B* and NANB hepatitis†, in Canada, 1979-1997

Death certificates are completed by the attending physician and are then transferred to the central vital statistics registry in each province. The underlying cause of death listed on the death certificate is then coded to one of the 17 ICD categories and then to a disease-specific cause of death for use in the compilation of national mortality statistics.[14] A single underlying cause of death is determined, using specific rules depending on both the disease category and the order of diagnoses listed. For the Atlantic provinces and the territories, the cause of death is coded at Statistics Canada.[15]

Mortality rates were calculated for Canada for each cause by age and sex, standardized to the 1991 Canadian population.[16] Viral hepatitis B was identified as ICD-9 codes 070.2 and 070.3, which includes both acute and chronic cases. The term NANBH was applied to cases of viral hepatitis other than hepatitis A (with and without hepatic coma) and hepatitis B (with and without hepatic coma), and includes ICD-9 codes 070.4, 070.5, 070.6 and 070.9. Both acute and chronic cases are classified under the same ICD-9 codes. However, given that death from acute disease is unusual, it is likely that a majority of these are chronic cases. Hepatitis C was not listed in ICD-9, however available data indicate that it was responsible for approximately 90% of NANBH cases.[17] Age-specific mortality rates were stratified as follows: i) 5-year intervals from 0 to 84 years, and 85 years and older were used for calculation of age-standardized mortality, and ii) collapsed intervals 0-19, 20-44, 45-69, and 70 years and older were used for trends in age-specific mortality. Age-specific mortality rates were calculated as the number of deaths per age interval, per 100,000 persons.

Chronic liver disease (CLD) includes primary liver cancer, alcoholic cirrhosis, alcoholic liver disease, chronic hepatitis, cirrhosis without alcohol, chronic hepatitis without alcohol, other chronic hepatitis, hepatic coma, portal hypertension, hepatorenal syndrome and other sequelae of chronic liver disease (identified as ICD-9 codes 155.0, 571.2-571.5, 571.8, 571.9, 572.2-572.4 and 572.8), and excludes acute alcoholic, fatty liver-alcoholic and primary biliary cirrhosis (ICD-9 codes 571.0, 571.1 and 571.6). Estimated annual deaths from chronic liver disease that were attributable to hepatitis B and hepatitis C were calculated from proportions obtained from an unpublished population-based study conducted in Jefferson County, Alabama by the Centers for Disease Control and Prevention (CDC) in the US. Proportions were applied as follows: 14% and 40% of total deaths from CLD were attributed to HBV and HCV respectively (CDC: unpublished data).

RESULTS

Recorded deaths, hepatitis B

Overall, 855 deaths attributed to hepatitis B were recorded in Canada from 1979 to 1997, of which males and females accounted for 70% and 30% of deaths respectively. There has been a progressive increase in the trend of mortality recorded as caused by hepatitis B over time, as the age-standardized mortality rate increased from 0.03 deaths per 100,000 population in 1979 to 0.34 deaths per 100,000 in 1995 followed by a decrease to 0.26 deaths per 100,000 in 1997 (Figure 1).

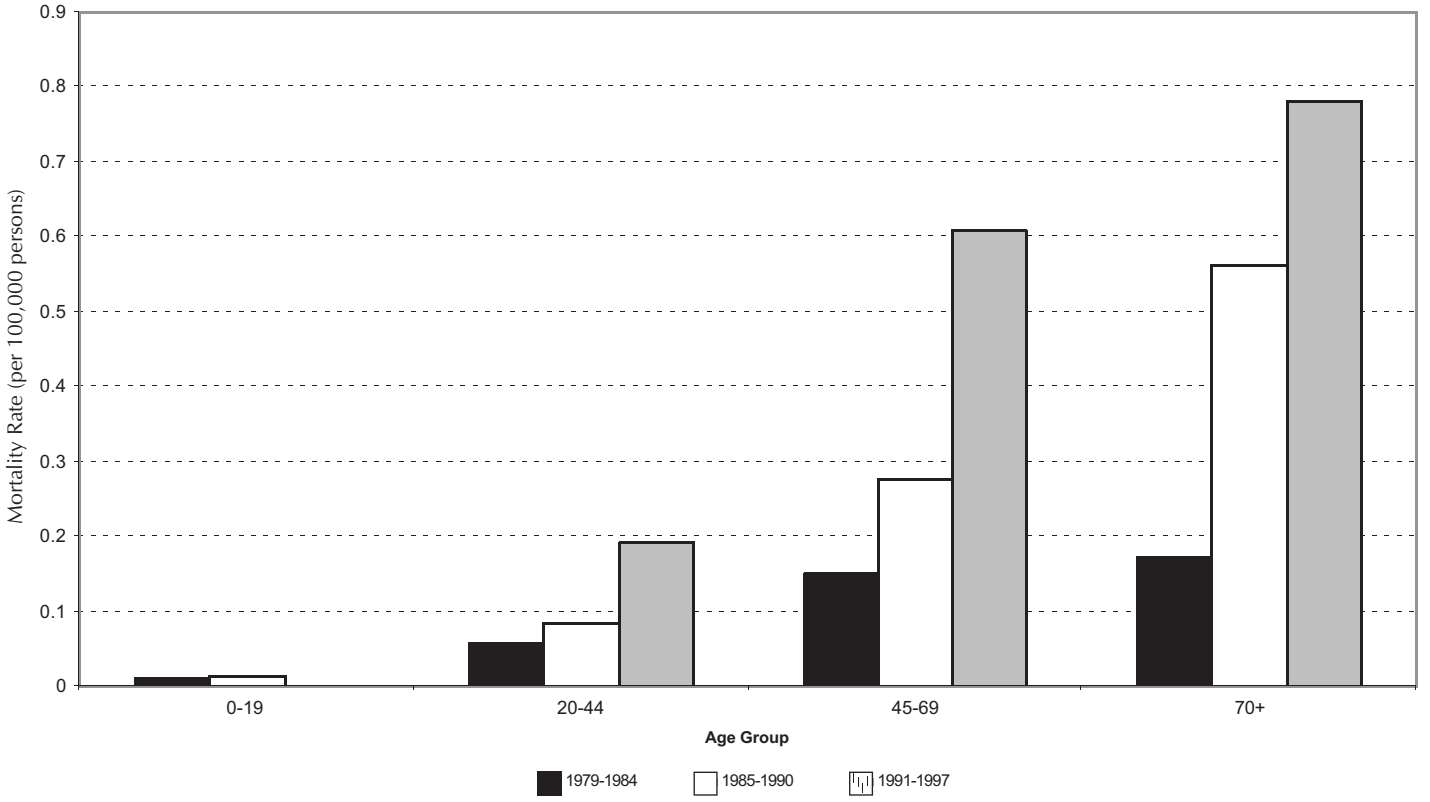

Figure 2. Hepatitis B in Canada, age-specific mortality rates, 3 time periods (collapsed age-intervals)

After 1979, the age-standardized mortality rates for males were higher in most years than those for females. Both male and female age-standardized rates increased over time until 1995. Males had a range of 0.03 deaths per 100,000 in 1979 to 0.53 deaths per 100,000 in 1995 and 0.38 deaths per 100,000 in 1997. Females showed less of an increase over time, with 0.03 deaths per 100,000 in 1979 and 0.15 deaths per 100,000 in 1997. Figure 2 presents age-specific mortality rates with collapsed age-intervals over three time periods. All age groups over 19 years contributed to the increase over time, with a pronounced increase in mortality in 1991-1997.

Recorded deaths, NANBH

From 1979 to 1997, 940 deaths were reported in Canada with NANB viral hepatitis coded as the cause of death; of this total number, males and females accounted for 56% and 44% of deaths respectively. There has been a progressive increase in the trend of mortality over time, as the age-standardized mortality rate in 1997 was 3.7 times that of 1979 (0.12 deaths per 100,000 population in 1979 to 0.44 deaths per 100,000 in 1997). The most notable increase was after 1993 (0.15 deaths per 100,000 in 1993 to 0.44 deaths per 100,000 in 1997) (Figure 1).

Both male and female mortality rates were relatively stable until the 1990s with a sizeable increase from 1993 to 1996. Male age-standardized mortality rates ranged from 0.10 deaths to 0.52 deaths per 100,000 persons in 1980 and 1997 respectively. Female age-standardized mortality rates ranged from 0.13 deaths per 100,000 persons in 1979 to 0.35 deaths per 100,000 in 1997. Figure 3 presents age-specific mortality rates over three time periods. A significant increase in mortality was observed in 1991-1997 in persons 45 years and older.

Recorded deaths, chronic liver disease

In 1997, 2,555 deaths were attributed to chronic liver disease (CLD) as defined in the Methods section. Applying the estimated CDC proportions, of these 2,555 deaths ascribed to CLD in 1997, 358 and 1,022 deaths were estimated to have been caused by hepatitis B and hepatitis C respectively.

DISCUSSION

Hepatitis B and hepatitis C have become increasingly important public health concerns in Canada. However, the impact of these two diseases has not been well documented given the chronic nature of some hepatitis B and most hepatitis C cases and the large proportion of asymptomatic infections for both diseases. Many deaths resulting from unrecognized chronic hepatitis B or hepatitis C infections are likely not recorded as caused by either hepatitis B or NANBH. Thus, the deaths recorded as caused by hepatitis B or NANB hepatitis underestimate the true number of deaths attributable to these two diseases. Nevertheless, the trend in mortality specifically recorded as hepatitis B or NANB hepatitis should reflect the changing pattern of both hepatitis B and hepatitis C.

In terms of testing practices for HBV infection, there have been no major changes in diagnostic methods as the sensi-

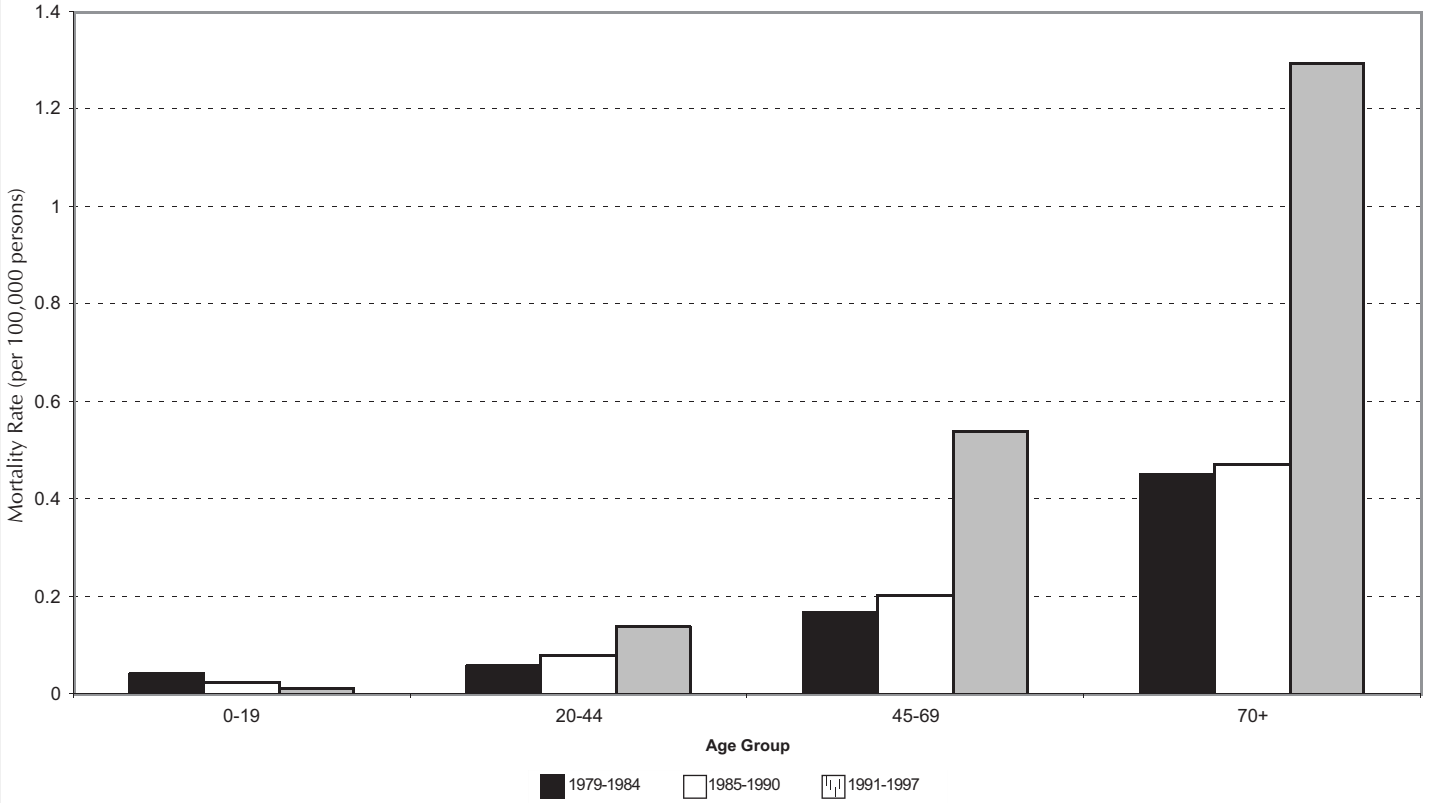

Figure 3. NANB in Canada, age-specific mortality rates, 3 time periods (collapsed age-intervals)

tivity of laboratory tests for HBV has not changed significantly over the study period.[18] Thus, it is unlikely that the observed increase in HBV mortality is solely due to artifact. These findings are corroborated by data from the National Notifiable Diseases Registry System (NNDRS) from 1986 onwards, which indicate that incidence rates remained relatively stable until 1996.[19]

Previous reports indicate that immigrants from regions where hepatitis B is highly endemic (e.g., East Asians, Sub-Saharan Africans), Alaskan Eskimos and Canada's First Nations, are at high risk for infection.[20,21] There was a significant increase in the number of immigrants into Canada from Eastern, Southeast and Southern Asia during the period of 1971 to 1996 (a total of 109,385 persons prior to 1971 as compared to 1,242,530 persons after 1971), which may account for some of the observed increase in mortality.[22,23]

Previous reviews have shown that in areas with a low endemicity of infection such as Canada and the United States, most of indigenously acquired HBV infections occur among high-risk adult populations that include parenteral drug users, persons with multiple sexual partners, homosexual men, and health care workers.[3,5] The increase in HBV mortality observed could also be attributed to a period of increased intravenous drug use during the 1960s and early 1970s, and unsafe sexual practice.[21] Our results indicate that mortality rates for males are 2.4 times that for females, reflecting a higher case fatality and prevalence of chronic hepatitis B in men than in women. These findings may also be the result of overrepresentation of males in groups at high risk of acquiring HBV infection (i.e., parenteral drug users, homosexual men).

Hepatitis B vaccination and the implementation of 'universal precautions' have reduced the rates of HBV infection among some at-risk groups over the past decade.[3] The decrease in hepatitis B mortality after 1995 may reflect the impact of these measures. Prior to the licensing of the vaccine, however, there was presumably a large pool of persons infected with the virus. Thus, due to the chronic nature of the virus, and the lag time between infection and death, the increased mortality rate over time may be attributed to the infections which occurred prior to availability of the vaccine.

Our results have shown an increasing trend in NANBH from 1979 to 1997, with a 267% increase in mortality over time (0.12 deaths per 100,000 in 1979 and 0.44 deaths in 1997), principally confined to 1993-1997. In 1990, the development of serological tests for HCV infection indicated that this virus has been the primary etiologic agent of parenterally transmitted non-A, non-B hepatitis.[17,24] Prior to HCV testing, NANBH was strictly a diagnosis of exclusion, and then only in symptomatic patients or those found to have elevated transaminase levels.[25] Since it is now known that most HCV patients are asymptomatic early on, it has become clear that many NANBH cases may have been missed or misdiagnosed, contributing to an underestimate of the actual number of NANBH infections. Recognition of this disease may have been delayed because of lack of accurate testing, and fewer deaths

would have been attributed to NANBH. This may be reflected in the relatively stable mortality rates seen from 1979 to 1990. The increase in mortality rates from 1990 onward may be partially attributed to artifact because more deaths could have been ascribed to HCV due to the increased availability of accurate diagnostic tests, and increased awareness of the disease.

The increasing trend in mortality of HCV subsequent to 1990 could also arise from infections that occurred as a result of increased intravenous drug use in the 1960s and early 1970s. Considering the chronic nature and slow progression of HCV, it is likely that infections acquired in previous decades would have a significant effect on the mortality rates now seen. Although part of the observed increase in mortality can be attributed to artifact, we do suspect that there was an increase in mortality that occurred as a result of previous high rates of transmission. The sex distribution (males:females, 0.52:0.35 deaths per 100,000 persons in 1997) is likely related to patterns of exposure (i.e., injection drug use in young adult males).

There are inherent biases and limitations to consider in figures obtained from the Statistics Canada mortality database. Generally, the coding of death certificate diagnoses is believed to be relatively objective and accurate and not a major source of error in the compilation of mortality statistics. However, errors in certifying the underlying cause of death may result in coding misclassifications.[14] Given the lag-time between the onset of HBV or NANBH and subsequent death, mortality data are likely subject to unavoidable errors. However, national mortality statistics obtained from Statistics Canada are a convenient and constant source of data, and can serve to approximate the changing patterns of mortality attributable to HBV and NANBH in Canada.

The findings of a study conducted in Jefferson County, Alabama, suggest that viral hepatitis may be responsible for at least 50% of all chronic liver disease in the United States and HCV may be as important as alcohol as a cause of chronic liver disease (CDC: unpublished data). In the study, among patients who died of chronic liver disease, 14% had evidence of HBV infection, 40% HCV infection, and for 17% no cause could be determined (CDC: unpublished data). While cautious interpretation is prudent, applying U.S. projections to the Canadian situation predicts that of the recorded 2,555 deaths in 1997 from chronic liver disease, approximately 358 and 1,022 deaths may have been related to chronic hepatitis B and hepatitis C respectively. If the 1997 recorded deaths from hepatitis B (82) and NANBH (139) are added to those estimated from chronic liver disease associated with hepatitis B (358) and hepatitis C (1,022), a total of 440 and 1,161 people would have died from hepatitis B and hepatitis C in 1997 respectively.

Of interesting note, while HBV and HCV mortality have increased over the study period, the CLD mortality has steadily and significantly declined in the same time period (CIDPC, unpublished data). It is plausible that the observed decrease in CLD mortality is attributable to a decrease in alcohol-related CLD, which has declined significantly since 1979 (CIDPC, unpublished data).

Nevertheless, our findings clearly indicate the significant impact of hepatitis B and hepatitis C on the health of Canadians, and the increasing burden of these two diseases. These results are in line with data from other sources and studies that show that sequelae of hepatitis C in Canada will likely double or triple in the coming decade,[6,26] and that each year thousands of new cases of hepatitis B and hepatitis C will be added to the existing pool of infected patients.[27] All aspects of prevention – primary, secondary and tertiary – are essential for the effective control of these two diseases.

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Received: August 17, 1999
Revise/Resubmit: December 10, 1999
Revised MS Received: February 21, 2001
Accepted: March 8, 2001