ORIGINAL ARTICLE

The epidemiology of hepatitis C in a Canadian Indigenous population

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BACKGROUND: An estimated 1% to 1.9% of North Americans are infected with the hepatitis C virus (HCV). Although Indigenous peoples are considered to bear the highest burden, there are only limited data regarding the demographic features and epidemiology of hepatitis C in this population.

OBJECTIVES: To document the demographic characteristics, rates of newly diagnosed hepatitis C cases and prevalence of HCV infection in a Canadian First Nations population, and to compare the findings with an infected non-First Nations population.

METHODS: A research database spanning 1991 to 2002 was developed, linking records from multiple clinical and administrative sources. Over a 12-year period, 671 First Nations and 4347 non-First Nations HCV-positive Canadians were identified in the province of Manitoba. Demographics, residence and time trends were compared between infected First Nations and non-First Nations persons.

RESULTS: HCV-infected First Nations individuals were younger (mean [± SD] age 33.0±0.4 years versus 39.7±0.2 years; P<0.0001), more often female (60% versus 40%; P<0.0001) and more often resided in urban centres (73% versus 27%; P<0.001). The rate of newly diagnosed HCV cases was 2.5-fold (91.1 per 100,000 versus 36.6 per 100,000; P<0.000) and prevalence 2.4-fold (801.7 per 100,000 versus 334.8 per 100,000; P<0.000) higher among the First Nations relative to non-First Nations populations.

CONCLUSIONS: The results of the present large population-based study indicate that the First Nations population with hepatitis C is characteristically different from infected non-First Nations persons. The results also describe higher rates of newly diagnosed cases and prevalence of HCV infection in the First Nations population. These findings should serve as an important baseline for future primary prevention and therapeutic intervention strategies in this high-risk population.

Key Words: First Nations populations; Hepatitis C; HCV infection; Incidence; Longitudinal; Population-based; Prevalence

It is estimated that approximately 170 million people worldwide are chronically infected with the hepatitis C virus (HCV) (1). In North America, estimates range between 3.9 million and 4.1 million infected persons in the United States, and between 250,000 and 275,000 in Canada (2-4). While a plethora of data regarding various epidemiological and clinical aspects of hepatitis C in North America has been accumulated, the extent of infection and its burden among Indigenous populations, including Canada's First Nations peoples, remains largely unstudied, this despite recent data suggesting that exposure rates to HCV are higher in Indigenous compared with non-Indigenous populations (5-12).

In Canada, national surveillance data are insufficient for determining the number of cases of hepatitis C among Aboriginal populations, largely because most provinces do not collect information according to ethnicity. As a result, information regarding ethnicity has been confined

L'épidémiologie de l'hépatite C dans une population autochtone canadienne

HISTORIQUE: On estime que de 1 % à 1,9 % des Nord-Américains sont infectés par le virus de l'hépatite C (VHC). Même si on considère que les peuples autochtones en portent le fardeau le plus élevé, on possède seulement des données limitées au sujet des caractéristiques démographiques et épidémiologiques de l'hépatite C au sein de cette population.

OBJECTIFS: Étayer les caractéristiques démographiques, le taux de nouveaux diagnostics d'hépatite C et la prévalence d'infections par le VHC au sein de la population des Premières nations du Canada et comparer les résultats à ceux d'une population infectée ne faisant pas partie des Premières nations.

MÉTHODOLOGIE: Les chercheurs ont mis au point une base de données de recherche couvrant les années 1991 à 2002, reliant les dossiers de multiples sources cliniques et administratives. Sur une période de 12 ans, ils ont recensé 671 Canadiens des Premières nations et 4 347 Canadiens ne faisant pas partie des Premières nations, tous positifs au VHC, dans la province du Manitoba. Ils ont comparé les facteurs démographiques, le lieu de résidence et les tendances dans le temps entre les personnes infectées des Premières Nations et ne faisant pas partie des Premières nations.

RÉSULTATS: Les personnes infectées par le VHC faisant partie des Premières nations étaient plus jeunes (âge moyen [±ÉT] de 33,0±0,4 ans par rapport à 39,7±0,2 ans; P<0,0001), étaient plus souvent de sexe féminin (60 % par rapport à 40 %; P<0,0001) et habitaient plus souvent dans un centre urbain (73 % par rapport à 27 %; P<0,001). Le taux de nouveaux diagnostics de VHC était 2,5 fois plus élevé (91,1 cas sur 100 000 habitants par rapport à 36,6 cas sur 100 000 habitants; P<0,000) et la prévalence 2,4 fois élevée (801,7 cas sur 100 000 habitants, par rapport à 334,8 cas sur 100 000 habitants; P<0,000) chez les populations des Premières nations que chez les populations n'en faisant pas partie.

CONCLUSIONS: D'après les résultats de la présente étude en population d'envergure, la population des Premières nations atteinte d'hépatite C diffère de manière caractéristique des populations infectées n'en faisant pas partie. Les résultats font également foi de taux plus élevés de nouveaux diagnostics et d'une plus forte prévalence d'infection par le VHC au sein de la population des Premières nations. Ces observations devraient constituer une base importante pour les prochaines stratégies de prévention et d'intervention thérapeutique auprès de cette population à haut risque.

to population groups already at high risk for acquisition of bloodborne pathogens (such as prison inmates and the injection drug use [IDU] population). For example, the prevalence of antibodies to HCV (anti-HCV) among attendees of a First Nations alcohol and drug rehabilitation program in British Columbia was 18% (5), while the Enhanced Hepatitis Surveillance of Canadian Street Youth study (6) revealed 6% of self-identified Aboriginals to be anti-HCV positive. A study examining street-involved youth in Winnipeg (Manitoba) (7) found the anti-HCV prevalence among self-identified Aboriginal youth to be 20.1% compared with 14.4% among non-Aboriginal ethnicities. Finally, a high prevalence of hepatitis C (25% to 40%) and over-representation of HCV-infected individuals of Aboriginal heritage has also been documented among populations of prison inmates in Canada (8-12).

Thus, the objective of the present study was to provide detailed population-based data on the demographic features, rates of newly

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diagnosed cases and prevalence of HCV infection in a large Canadian Indigenous First Nations population.

METHODOLOGY

Data sources

The data used for the present study were derived from Manitoba Public Health and administrative databases. Universal health insurance is available to all residents of Manitoba; consequently, almost all (>98%) resident's physician visits, hospitalizations, prescription drug use and vital statistics are accurately recorded (13,14). The developed study database contains a longitudinal record for Manitoba residents who tested positive for hepatitis C by the Cadham Provincial Laboratory and were, therefore, reported to the Public Health Unit of Manitoba Health. The Cadham Provincial Laboratory is the only laboratory performing HCV testing for the province of Manitoba. There were two distinct periods for HCV testing. From 1991 to 1995, no RNA assays were available and only first- and second-generation immunoassays were used to detect HCV infection. Consequently, cases diagnosed between 1991 and 1995 would include those infected with HCV at the time of testing as well as those previously infected who spontaneously cleared the virus. Subsequent to 1995, when RNA assays were introduced, specimens were considered to be positive only if both anti-HCV screening and HCV-RNA tests were positive (15). The study database includes records for the period between January 1, 1991 and December 31, 2002.

The Manitoba Health population registry was used to identify individuals belonging to a First Nations population. As part of the process for registration within the Manitoba Health insurance system, First Nations affiliation is recorded in the population registry. However, for a variety of historical and political reasons, some individuals of Aboriginal ancestry are not eligible for registration under the Indian Act of Canada. These individuals (an estimated 30%) were, therefore, not identified as First Nations in the present study (16,17). The anonymous linkage of Manitoba Health databases was possible via scrambled health numbers, thereby allowing for the creation of a deidentified longitudinal record of health services. The detailed description of the study database is provided elsewhere (18).

Definitions

For the purpose of the present study, the term 'incidence' was used to emphasize that the study was concerned with all new cases of HCV diagnosed in Manitoba (18). Therefore, all newly reported cases were regarded as incident cases, although they may not necessarily represent a newly acquired infection. The date of such 'incident' cases was based on the date of the first positive blood test recorded in the provincial Viral Hepatitis Surveillance Database, and cases were only counted once.

The term 'prevalence' was used to describe the accumulation of previously diagnosed and newly diagnosed cases of hepatitis C each year in the province among residents whose health coverage had not been terminated by death or migration out of province (18). A prevalent case was counted annually from the incident year, provided the resident maintained provincial health care coverage.

Statistical analysis

Statistical analyses were performed using SAS version 9.1 (SAS Institute, USA) for Windows (Microsoft Corporation, USA). Both crude and age/sex-adjusted rates of newly diagnosed cases per 100,000 population were calculated to correct for the demographic differences between the First Nations and non-First Nations populations in Manitoba. Direct standardization was used for calculating adjusted rates, with the 2001 Canadian population (census data) as the standard (19). First Nations to non-First Nations, and female to male ratios of adjusted rate of newly diagnosed cases with 95% CIs were calculated. Annual rates of newly diagnosed cases of HCV infection were calculated using the population of Manitoba for the corresponding year. The cumulative rates of newly diagnosed cases for 1992 to 2002 were computed by

TABLE 1
Demographic characteristics of hepatitis C cases in
Manitoba. 1991 to 2002

Characteristic	First Nations	Non-First Nations
Total	671 (13.4)	4347 (86.6)
Female sex	392 (58.4)*	1575 (36.2)*
Female:male ratio	1.41	0.57
Age group, years		
<18	25 (3.7)*	65 (1.5)*
18–39	506 (75.4)*	2278 (52.4)*
40–59	129 (19.2)*	1682 (38.7)*
>60	11 (1.6)*	322 (7.4)*
Age, years, mean ± SD (median)	33±0.4* (33)	39.7±0.2* (39)
Female	32±0.5* (32)	39±0.4* (39)
Male	34±0.5* (34)	40±0.2* (39)
Residence		
Urban (Winnipeg, Manitoba)	530 (79.0)†	3651 (84.0) [†]
Rural south	87 (13.0)	609 (14.0)
Rural north	54 (8.0)*	87 (2.0)*

Data presented as n (%) unless otherwise indicated. First Nations versus non-First Nations: *P<0.0001; †P<0.001

summing all new cases and the mid-year population at risk for those years. The point prevalence at December of each year was estimated by determining the number of cases that had previously been diagnosed with hepatitis C and whose health coverage had not ended due to death or outmigration from the province according to the Manitoba Health population registry at that time.

RESULTS

Demographics

During the 12-year study period, a total of 5018 cases of HCV infection were reported, of which 671 (13.4%) were First Nations. This represents more than twice the proportion of First Nations persons registered with the Manitoba Health Plan Registry (20). The demographic features of the hepatitis C-diagnosed individuals are summarized in Table 1.

First Nations subjects were younger than their non-First Nations counterparts, with 79% of First Nations persons testing positive for HCV before 40 years of age, compared with 54% of non-First Nations individuals (P<0.00001). Almost 60% of HCV-infected First Nations persons were female (female to male ratio 1.4:1). Conversely, there was a male predominance in the non-First Nations group (64%) (female to male ratio = 0.6:1).

Overall, 26% of all First Nations and 59% of non-First Nations Manitobans reside in Winnipeg. However, 79% of cases occurred among 26% of urban First Nations (ratio 3.7), whereas 84% of cases occurred in the 59% of urban non-First Nations (ratio 1.4). Rural residents, both First Nations and non-First Nations, were less often infected with HCV, with 21% of cases occurring among 78% of rural First Nations (ratio 0.3), and 16% of cases occurring in the 41% of rural non-First Nations (ratio 0.4).

Rate of newly diagnosed HCV infection

Since 1991/1992 (31 reported HCV cases), the annual number of cases increased to more than 500 new cases per year by 1995 (Table 2). The highest rates of HCV infection were observed among First Nations females, followed by First Nations males, non-First Nations males and non-First Nations females (Figure 1). The cumulative rate of newly diagnosed HCV among First Nations females was 4.1 times higher than the rate of newly diagnosed cases among non-First Nations females. The cumulative rate of newly diagnosed HCV infection among First Nations males was 1.6 times that of non-First Nations males.

TABLE 2
Annual age- and sex-adjusted rates of newly diagnosed cases and prevalence of hepatitis C virus infection (per 100,000 population) among First Nations and non-First Nations persons, Manitoba, 1991 to 2002

Year	Newly diagnosed cases					Prevalent cases					
	First Nations		Non-First Nations		_	First Nations		Non-First Nations		Prevalence	
	Cases, n	Rate	Cases, n	Rate	Rate ratio	Cases, n	Prevalence	Cases, n	Prevalence	ratio	
1991/1992	*		30	2.71		*		30	2.80		
1993	7	19.61	80	7.34	2.7	7	11.41	110	10.23	1.1	
1994	22	37.01	217	19.85	1.9	29	46.08	325	30.01	1.5	
1995	87	141.56	478	43.8	3.2	116	180.95	792	73.14	2.5	
1996	71	107.93	479	43.95	2.5	184	281.23	1219	112.95	2.5	
1997	87	140.66	503	46.21	3.0	263	394.95	1671	154.76	2.6	
1998	94	160.51	582	53.59	3.0	352	521.42	2161	201.03	2.6	
1999	87	144.96	485	44.53	3.3	433	629.49	2551	237.16	2.7	
2000	57	88.29	477	43.69	2.0	471	656.34	2915	270.37	2.4	
2001	89	146.85	596	54.36	2.7	539	733.84	3364	311.62	2.4	
2002	69	101.53	420	38.32	2.6	598	801.71	3621	334.77	2.4	
Cumulative	671	91.10	4347	36.63	2.5						

^{*}Suppressed due to small number

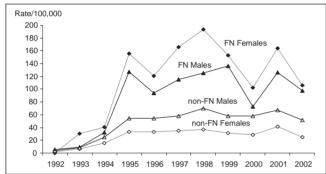


Figure 1) Annual age-adjusted rate of newly diagnosed hepatitis C virus infection according to sex among First Nations (FN) versus non-FN persons, Manitoba, 1992 to 2002 (per 100,000 population)

The age-specific rates of newly diagnosed HCV infections were higher among First Nations than non-First Nations individuals in most age groups (Table 3). In First Nations, the rates of newly diagnosed hepatitis C among females were higher compared with males in all age groups except 40 to 44 years. In contrast, the rates of newly diagnosed HCV infection among non-First Nations males were higher than in females in all age groups beginning at 25 years of age.

The difference in age-specific rate of newly diagnosed HCV infection was particularly large in women, with the cumulative rate of newly diagnosed cases in First Nations females four times that of non-First Nations females, while the cumulative rate of newly diagnosed cases of hepatitis C in First Nations males was 1.6 times higher than in non-First Nations males.

Prevalence

The age-adjusted prevalence of hepatitis C among Manitoba residents increased steadily between 1991/1992 and 2002 for First Nations and non-First Nations. There was a 4.5-fold increase in age-adjusted prevalence from in 2002 compared with 1995 (Figure 2). At the end of the study period, 89% of all HCV-infected First Nations persons and 83% of infected non-First Nations remained in the province (Table 2), illustrating the significant burden of chronic HCV infection. Throughout the 12-year study period, First Nations males had an average prevalence of HCV infection 1.5 times that of non-First Nations males, whereas First Nations females had an average prevalence of HCV 3.9 times that of non-First Nations females.

In 2002, the age-specific prevalence of hepatitis C was higher among First Nations than non-First Nations individuals in almost all age groups (Table 3). The highest age-specific prevalence was in the

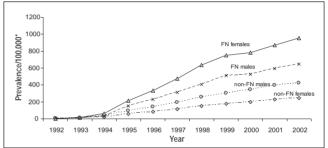


Figure 2) Annual age-adjusted prevalence of hepatitis C in Manitoba, 1992 to 2002. FN First Nations

30 to 34 years of age group among females (both First Nations and non-First Nations), and in the 35 to 39 years of age group for males (also both First Nations and non-First Nations).

In First Nations persons, the age-specific prevalence of hepatitis C was higher among females than males in all groups except the 40 to 44 years of age group. Conversely, the prevalence of hepatitis C was higher among non-First Nations males than females in all age groups except those zero to 24 years of age.

DISCUSSION

Unlike the sex distribution of HCV infection described in the literature and noted in the non-First Nations populations of the present study, the majority of First Nations persons with HCV infection are female. HCV-infected First Nations persons are also significantly younger than non-First Nations individuals. Collectively, these findings are consistent with the Enhanced Hepatitis Strain Surveillance System report, which demonstrated that Aboriginal patients with newly acquired HCV infection were more often female (55% of Aboriginal versus 38% non-Aboriginal persons) and significantly younger than non-Aboriginal persons (21). The most likely explanation for these findings is the predominance of First Nations females of younger age in the IDU population, which has been described in several North American studies (3,20-25). For example, the Winnipeg Injection Drug Epidemiology (WIDE) study found a clear trend toward younger drug users being female, with 41% of Aboriginal females versus 25% of males <30 years of age and the overall proportion of Aboriginal females in the study's IDU cohort being 52% (22). Callaghan et al (23) documented that among Canadian Aboriginal individuals admitted to an inpatient substance abuse detoxification program in Prince George, British Columbia, females were younger than males, received proportionately higher rates of cocaine and

TABLE 3
Age-specific cumulative rate of newly diagnosed cases and prevalence of hepatitis C virus infection infection according to sex

	Age-s _l	pecific rate	of newly dia	gnosed case	s, 1991 to 2002	Age-specific prevalence, 2002					
Age group,	First Nations		Non-First Nations			First Nations		Non-First Nations			
	Rate per			Rate per	Rate ratio*		Rate per		Rate per	Rate ratio*	
years	Cases, n	100,000	Cases, n	100,000	(95% CI)	Cases	100,000	Cases	100,000	(95% CI)	
Female											
0–17	19	10.6	36	2.3	4.6 (2.5-7.8)	17	103.1	31	25.0	4.1 (2.1-7.2)	
18–24	61	119.1	166	27.2	4.4 (3.2-5.8)	59	1313.2	148	298.7	4.4 (3.2-5.8)	
25-29	68	192.8	199	43.7	4.4 (3.3-5.7)	63	2159.8	175	511.8	4.2 (3.1-5.5)	
30-34	95	296.6	278	55.5	5.3 (4.2-6.7)	87	2904.8	239	672.0	4.3 (3.3-5.5)	
35-39	76	290.3	270	51.3	5.7 (4.3-7.2)	66	2381.0	231	561.6	4.2 (3.1-5.5)	
40-44	39	199.0	216	43.3	4.6 (3.1-6.2)	36	1604.3	190	431.0	3.7 (2.5 -5.1)	
45-49	18	125.1	142	32.4	3.9 (2.1-5.9)	17	1036.0	133	319.8	3.2 (1.7-5.0)	
≥50	16	41.3	268	13.5	3.1 (1.6-4.6)	12	305.6	210	117.4	2.6 (1.1-4.2)	
Total	392	98.8	1575	24.0	4.1 (3.7-4.6)	357	953.0	1357	247.1	3.9 (3.4-4.3)	
Male											
0-17	6	3.2	31	1.9	1.7 (0.4-3.4)	6	35.3	28	21.4	1.6 (0.4-3.4)	
18–24	32	63.6	129	20.5	3.1 (2.0-4.4)	27	593.7	104	203.8	2.9 (1.8-4.3)	
25-29	44	133.9	300	65.3	2.1 (1.4-2.7)	42	1564.8	240	694.0	2.3 (1.5-3.0)	
30-34	69	229.6	425	83.7	2.7 (2.1-3.5)	57	2106.4	351	985.0	2.1 (1.6-2.8)	
35-39	61	246.5	510	95.9	2.6 (1.9-3.3)	55	2164.5	433	1062.4	2.0 (1.5-2.6)	
40-44	41	215.2	510	101.7	2.1 (1.5-2.8)	36	1662.8	419	933.1	1.8 (1.2-2.4)	
45-49	12	81.6	424	96.5	0.8 (0.4-1.3)	12	791.6	356	855.5	0.9 (0.4-1.5)	
≥50	14	34.8	443	26.4	1.3 (0.6-2.0)	6	150.2	333	217.2	0.7 (0.1-1.3)	
Total	279	70.0	2772	43.5	1.6 (1.4–1.8)	241	649.1	2264	425.1	1.5 (1.3-1.7)	

*First Nations/non-First Nations

opiate detoxification diagnoses (highest among females 18 to 25 years of age), and more often reported having hepatitis C compared with male clients (29% versus 21%, respectively). Finally, in the Cedar Project from British Columbia (24), 65% of community-based young Aboriginal women between 14 and 30 years of age used injection drugs for periods of between 0.1 and 13 years; the proportion of HCVinfected individuals was 43.6% in women compared with 25.4% in men. Restricting analysis to young injection drug users resulted in the same trend in that the proportions who were HCV-positive were significantly higher among Aboriginal females (25). Our results are also consistent with data from American Indian populations in which 3% of women screened during routine prenatal care were anti-HCV positive compared with 1.6% in the general population (26). On the other hand, Armstrong et al (3) and McMahon et al (27) reported the prevalence of HCV in an Alaskan Native community-based population to be 0.82%, which is below the estimated United States national prevalence of 1.6%. Nonetheless, the investigators also found that the majority of HCV-infected persons were female (55%) and most resided in urban areas.

The present study also documented significantly higher and increasing rates of newly diagnosed HCV infection among the First Nations compared with non-First Nations population. Similar findings have been reported in which HCV infection rates among First Nations populations accounted for 0.4% to 29.3% of all reported cases within various provinces (6,28). Similarly, a 2010 Epi-Update also demonstrated that between 2002 and 2008, the overall reported rate of newly diagnosed HCV was 4.7 times higher among Aboriginal Canadians than among those of other ethnicities (29). Wu at al (21) described the incidence of newly acquired HCV infection to be 6.7 times higher in Aboriginal than non-Aboriginal Canadians (18.9 versus 2.8 cases per 100,000 population, respectively). Similarly, the incidence of hepatitis C among American Indians/Alaska Natives was 2.8 times higher than among the Caucasian population (30).

There have been no published reports describing hepatitis C prevalence among First Nations populations nationally. However, Remis (28) estimated the prevalence of hepatitis C in the First Nations of Canada to be 3%, an estimate supported by our results.

The present study had several strengths. Population-based data regarding HCV infection in North America is largely limited to the two National Health and Nutrition Examination Survey (NHANES) conducted in the United States from 1988 to 1994, and 1999 to 2002, which reported the prevalence of HCV infection to be 1.8% and 1.6%, respectively (2,3). Even more limited are population-based data regarding hepatitis C in North American Indigenous populations. The majority of studies published to date involve either specific high-risk populations (IDU, prison inmates, etc) or are based on various clinical settings with highly selected populations. To our knowledge, the present study was the first to use large population-based data on HCV infection in an Indigenous population. Using a combination of public health and administrative data created a comprehensive database of HCV infection in a defined and stable population. The relatively long time interval of 12 years also permitted an examination of time trends in rates of newly diagnosed hepatitis C and prevalence data.

The present study was, however, not without limitations. First, the data were derived from a public health database for estimates of rate of newly diagnosed HCV infection and prevalence of hepatitis C. This approach underestimates the actual incidence and prevalence of hepatitis C because it is contingent on infected persons being tested, diagnosed and reported to the public health department through interaction with the health care system, and is not based on a population-based sampling. Therefore, the results of the present study are not directly comparable with the results of seroepidemiological surveys such as NHANES-derived data. What is reported here is the lowest bound of the epidemic and the true number of cases may only be greater. As suggested by Sherman et al (31), upwards of one-third of cases in Canada remain undiagnosed. Second, it is unknown what proportion of the provinces' population had undergone HCV testing in addition to the rates of HCV testing in different demographic groups. The differential rates of testing across population subgroups will influence the number of cases found and reported. However, the surveillance data capture only positive test results and, in absence of data on actual numbers of persons tested or those who tested negative, our reported estimates represent demographics of hepatitis C cases that are diagnosed and enter the health care system in Manitoba. Third, the restriction of

First Nations designation in the present study to individuals registered under the Indian Act of Canada and the under-recording of First Nation status in the Manitoba Health Registry likely diminished the observed differences between the First Nations and non-First Nations populations. Finally, the estimated prevalence of hepatitis C was based on the balance of incoming incident and outgoing cases due to death or moving out of province (data reliably provided by the population registry); however, a small number of persons with chronic hepatitis C who were successfully treated for their infection (estimated to be <5%) could not be identified from the administrative sources and, therefore, would have been retained within the prevalence calculations.

CONCLUSION

The present large population-based study spanned a 12-year period of data accrual and described a North American Indigenous population in which HCV infections occur in a significantly younger age group, that are more often female and residents of urban communities. It also described a burden of hepatitis C that is increasing at a greater rate than in the non-First Nations population. These findings should serve as an important baseline for future primary prevention and therapeutic intervention strategies.

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