Mercury exposure and premature mortality in the Grassy Narrows First Nation community: a retrospective longitudinal study

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Summary

Background Little is known about the influence of toxic exposures on reduced life expectancy in First Nations people in Canada. The Grassy Narrows First Nation community have lived with the consequences of one of the worst environmental disasters in Canadian history. In the early 1960s, 10 000 kg of mercury (Hg) was released into their aquatic ecosystem. Although Hg concentration in fish, their dietary staple, decreased over time, it remains high. We aimed to examine whether elevated Hg exposure over time contributes to premature mortality (younger than 60 years) in this community.

Methods We did longitudinal and case-control analyses with data for individuals of the Grassy Narrows First Nation community. In 2019, the community obtained their historical Hg biomarker data from a government surveillance programme, which was then shared with the authors. A matched-pair approach allowed us to compare longitudinal hair Hg concentration between cases (individuals who died aged younger than 60 years) and controls (individuals who lived beyond 60 years). Matching criteria included year of birth (allowing 2 years either side), sex, and a minimum of four hair Hg concentration measures, of which at least two were in the same year. Analyses included change-point detection, interrupted time series, mixed models, and Cox survival models.

Findings We analysed data collected between Jan 1, 1970, and Jan 31, 1997, for 657 individuals (319 women and 338 men, born between 1884 and 1991) for whom we assembled a retrospective database of yearly measures of hair Hg concentration (n=3603). Hair Hg concentration decreased over time. A subgroup of 222 individuals (107 women and 115 men) reached or could have reached 60 years old by August, 2019. There was an increased risk of dying at a younger age among those with at least one hair Hg measure of 15 µg/g or more (adjusted hazard ratio 1·55, 95% CI 1·11–2·16; p=0·0088). Among the deceased individuals (n=154), longevity decreased by 1 year with every 6·25 µg/g (4·35–14·29) increase in hair Hg concentration. Analyses of 36 matched pairs showed that hair Hg concentration of those who died aged younger than 60 years was 4·7 µg/g higher (3·4–5·9) than controls.

Interpretation The consistent findings between our different analyses support an association between long-term Hg exposure from freshwater fish consumption and premature mortality in this First Nation community. There is a need to do risk-benefit analyses of freshwater fish consumption in environmentally contaminated regions.

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Introduction

The Asubpeeschoseewagong Netum Anishinabek (Grassy Narrows First Nation) people have lived with the consequences of one of the worst cases of environmental poisoning in Canadian history. A chloralkali plant, built in Dryden, ON, Canada in 1962, discharged 10 000 kg of mercury (Hg) into the extensive English-Wabigoon water system,[1] destroying the community's livelihood, major food source, and health. Hg concentrations in fish, particularly walleye (*Sander vitreus*), the traditional cultural and dietary mainstay of this community, were among the highest ever reported.[2] Measures to control the discharge were inadequate. In 1975, the chloralkali plant converted to a process that did not use Hg.[3] The concentration of Hg in fish from the rivers and lakes surrounding the Grassy Narrows community decreased until 1985, and since that time has remained relatively stable;[4] however, concentrations are still the highest within the province of ON, Canada.[5]

In the early 1970s, the Medical Service Branch of Health Canada initiated Hg biomarker testing (blood and hair) in two communities living downstream of the plant, Grassy Narrows and Wabaseemoong, also known as Whitedog[6] (appendix p 8). This initiative gave rise to a nationwide surveillance programme for Hg in First Nation communities across Canada. Between 1970 and 1992, 71 842 samples from 38 571 people from 514 First Nation communities were analysed.[6] The highest concentration of blood Hg was 660 µg/L from a person in Grassy Narrows. Although several people in Grassy Narrows

See Online for appendix

Research in context

Evidence before this study

The *Lancet* Series on Canada: global leadership in health, published in February, 2018, raised the issues of inequity and the "unacceptably disproportionate burdens of ill health" among Indigenous people in Canada. Life expectancy is considerably lower in First Nation and Inuit communities, than the rest of the Canadian population. Indeed, data collected by Statistics Canada shows that although life expectancy in Canada is among the highest in the world, for First Nations people, it lags by about 10 years. We searched for publications in English and French from database inception to Sept 7, 2019, on First Nation mortality in Canada, using PubMed and Scopus with the terms: "mortality" or "life expectancy" and "Canada" and "First Nations" or "Aboriginal" or "Indigenous", limited to humans. The search found more than 400 publications, which reported on statistics, methods of analyses, and risk factors, such as poor maternal health, cancer, diabetes, cardiovascular disease, addiction, mental health, and suicide. Some articles have addressed mortality in relation to lifestyle. However, no study has examined the possible contribution of mercury exposure from freshwater fish consumption to shorter life expectancy among First Nation communities in Canada.

Since the 1960s, the Asubpeeschoseewagong Netum Anishinabek (Grassy Narrows First Nation) has lived with the consequences of one of the worst disasters in Canadian history. The community's livelihood, major food source, and health were devastated by the uncontrolled discharge of approximately 10 000 kg of Hg from a chloralkali plant into their river system. Mercury concentrations in walleye (*Sander vitreus*), a fish embedded in their cultural identity, as well as their dietary mainstay, were among the highest every reported, and remain today the highest in the province of ON, Canada. For the past 50 years, Grassy Narrows First Nation has been fighting for river remediation, recognition of the long-term health effects of Hg exposure on their community, and support for appropriate health care. "My people are dying" said Judy Da Silva, an Anishinaabe mother and grandmother, a sentiment shared with other community elders. The present study on premature mortality was done in association with the people of Grassy Narrows.

Added value of this study

This is the first study, to show that in the First Nation community of Grassy Narrows, individuals who died prematurely (aged younger than 60 years) had greater long-term Hg exposure than those who lived longer.

We had the unique opportunity to constitute a retrospective longitudinal database of Hg exposure from freshwater fish consumption for this First Nation community, using biomarker data collected for 657 individuals by government surveillance programmes between 1970 and 1997. From these, we retrieved living status for 96%. Over the 28-year period, blood and hair samples were analysed by the same laboratory, using the same standardised methods, thus providing valid historic measures of Hg exposure. Analyses focused on a subgroup, who could have reached 60 years of age or lived beyond 60 years. The validity of the findings lies in the use of different statistical approaches, which provide consistent results. A matched-pair approach showed that individuals who died when younger than 60 years, had higher Hg exposure over the surveillance period, than those of the same sex, born at the same time. Survival analyses showed a 55% increase in risk of dying for those with at least one hair Hg measure of 15 µg/g or more. For the deceased individuals, longevity decreased by 1 year with every 6·25 µg/g increase in hair Hg concentration.

Implications of all the available evidence

Mercury contamination of freshwater fish is a planetary issue. According to international sources (Food and Agriculture Organization, Work Bank), although freshwater capture fisheries account for only 7% of reported global fish harvests, they are concentrated in low-income countries and among Indigenous peoples in industrialised countries. Consumption of Hg-contaminated freshwater fish over decades can contribute to premature mortality. Risk to benefit analyses from marine fish consumption might not apply to freshwater fish, which have fewer beneficial nutrients. For the community of Grassy Narrows, premature death also means that there are fewer elders to pass on traditional teachings and knowledge. Studies on avoidable mortality in First Nation communities should be encouraged to address environmental contaminants.

with high concentrations of Hg were examined and some presented neurological signs and symptoms consistent with Hg poisoning, a "definite diagnosis remained elusive".[7]

In 1975, Dr Masazumi Harada and his team examined 89 people in Grassy Narrows and Wabaseemoong and reported that no one presented all of the classic signs and symptoms of Minamata disease (a debilitating, neurological disorder caused by Hg poisoning), although many individuals presented with one or more signs.[8] When the team returned to the two communities in 2002 and 2004, they examined 189 individuals; 60 were diagnosed with Minamata disease, a further 54 with Minamata disease and complications due to other diseases, and 25 with suspicion of Minamata disease. Among the examinees, 27 had been previously examined in 1975, and their neurological results indicated that they were "clearly getting worse".[8]

Most knowledge about the long-term consequences of severe Hg poisoning comes from studies of communities living around Minamata Bay, Japan, where methyl Hg was discharged into the wastewater. Minamata disease, has been extensively studied.[9] The standardised mortality rate of individuals with diagnosed Minamata disease was examined between 1970 and 1981 by Tamashiro and colleagues,[10] who found that the sex-specific and

cause-specific standardised mortality rate for patients with Minamata disease was 127 (95% CI 112–141). A further study[11] showed the standardised mortality rate for people living in the Hg-exposed area of Minamata was significantly higher than in the rest of southern Japan for liver diseases, cerebral haemorrhage, and senility.

Marine fish have higher concentrations of beneficial nutrients, such as omega-3 fatty acids, than freshwater fish.[12] Studies on fish consumption and reduced mortality have, for the most part, focused on populations who eat marine fish.[13,14] A mortality study of regular consumers of Great Lakes sport fish and a reference population showed positive effects of eating store-bought fish (primarily marine fish), but not Great Lakes freshwater fish.[15] The authors suggest that, unlike marine fish, freshwater fish do not contain high concentrations of nutrients, such as omega-3 fatty acids and selenium.

Reduced lifespan in Canadian First Nations people is well known,[16,17] but the contribution of toxic exposures to premature mortality remains to be elucidated. We aimed to examine whether Hg exposure between 1970 and 1997 from freshwater fish consumption in the Grassy Narrows First Nation community was associated with premature mortality.

Methods

Partnership

This study was done in partnership with the Grassy Narrows community, according to the First Nations Principles of OCAP, a registered trademark of the First Nations Information Governance Centre (ie, ownership, control access and possession of data)[18] and guidelines of the Canadian Institutes of Health Research.[19] The Chief and Council of Grassy Narrows obtained the data that form the basis of this study, invited the collaboration with the authors, and approved the grant application and the submitted and final manuscript. Community members participated in the conception of the project, data collection, and interpretation. The preliminary results were presented at a community meeting for discussion.

Study design and participants

We used a retrospective longitudinal design to determine whether individuals of the Grassy Narrows First Nation community who died prematurely had higher hair Hg over the time of the government surveillance programme, which extended from 1970 to 1997, than those who lived longer, using 60 years as a cutoff for premature mortality. Life expectancy is lower among First Nations people in Canada than non-Indigenous Canadians; between 1991 and 2006, the probability of survival from age 25 to 60 years for non-Indigenous Canadians was 91% for men and 94% for women, while for First Nations people it was 80% for men and 87% for women.[20]

Figure 1 presents the flow chart for the selection of subgroups. All individuals were included in the descriptive analyses to illustrate the variations in Hg exposure between 1970 and 1997. Further analyses included only individuals who lived or could have lived to 60 years by Aug 3, 2019. A matched-pair case-control design (36 pairs) was also used to ensure homogeneity. Each prematurely deceased person (case) was matched with a living or deceased person, who lived to 60 years or older (control). The matching criteria included year of birth (allowing 2 years either side), sex, and a minimum of four hair Hg concentration measures, of which at least two were in the same year. When a case died before the end of the sampling period, his or her control was removed at the same time to prevent bias.

Ethics certificates were obtained from the Université du Québec à Montréal (2016_e_1350) and from Health Canada (REB 2017-0006). The study used historical data, collected between 1970 and 1997. Informed consent forms were signed at the time of sampling. The data were transferred to the researchers by the First Nations and Inuit Health Branch of the Ministry of Indigenous Services Canada at the request of the Grassy Narrows First Nation Chief and Council, in accordance with the Canadian Privacy Act. The use of the data is consistent with the purpose for which it was originally obtained.

Procedures

Hg biomarker (hair and blood) and date of birth and sex of all Registered Grassy Narrows First Nation members tested between 1970 and 1997, were obtained from the First Nations and Inuit Health Branch of the Ministry of Indigenous Services Canada and the Ontario Ministry of Health and Long-term Care (657 individuals, born between Jan 1, 1884, and Dec 31, 1991). The original information was gathered as part of surveillance programmes for Hg exposure in Canadian Aboriginal people.[6] Sampling was not equally repeated over time, and each person was not necessarily present at the time of the programme's visits to the community. The Band List of Registered Grassy Narrows First Nation members, which contains the date of birth and death of all registered Band members, was used to identify those who had died and their date of death. Personal historical biomarkers of Hg were provided and individually explained to all community members who signed a request form.

A retrospective longitudinal database was assembled, using the highest measure of equivalent hair Hg concentration for each year sampled. Since fish consumption varied throughout the year,[7] the corresponding month was also recorded. Most Hg biomarkers available were hair-based and we converted blood Hg into corresponding hair Hg, using a hair-to-blood ratio of 250:1.[21] The source database included 319 women and 338 men with at least one hair Hg measure.

Statistical analysis

Using the source database (n=657), change-point detection analysis was applied to detect changes in mean hair Hg concentrations between 1970 and 1997.

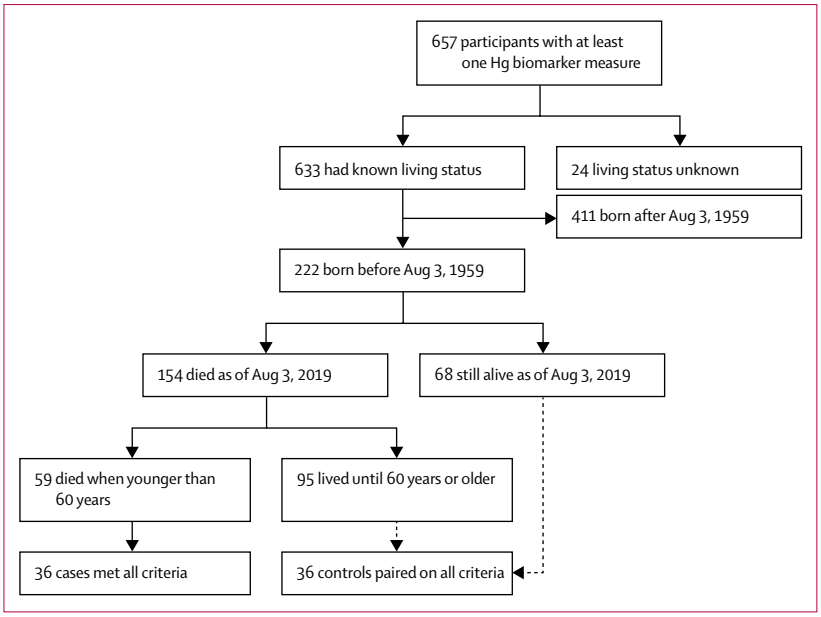

Figure 1: **Study profile**

In change-point detection, observations are processed in order, starting with the first, and a decision is made after each observation whether a change-point has occurred. Once a change is detected, the change detector restarts from the following observation in the sequence.[22] Because the biomarker data are not normally distributed, non-parametric statistics (Mann-Whitney, Kolmogorov-Smirnov, Cramér-von Mises) were applied.

Interrupted time series analyses (ITSA) were used with the matched pairs to determine whether the cases and controls displayed similar hair Hg distribution along sequences of time, identified by the change-point detection analysis. Immediate and over time shifts in mean hair Hg were tested after each change-point. The Durbin-Watson's alternative test was used to verify serial autocorrelations. We used an extended ordinary least-squares regression model divided into pre-event and post-event segments, while adjusting for the variance estimation by the Newey-West Standard Errors method that corrects for serial correlation in residuals. The maximum lag to be considered in the autocorrelation structure was determined by visual inspection and with CIs calculated using a SE of 1 divided by the square root of *n*. The segmented regression analysis in ITSA is shown in the appendix (p 9).

The ITSA model uses the following equation[23]:

$$YY_t = \beta_0 + \beta_1 TT_{tt} + \beta_2 XX_{tt} + \beta_3 XX_{tt} TT_{tt} + \beta_4 Z + \beta_5 ZZTT_{tt} + \beta_6 ZZXX_{tt} + \beta_7 ZZXX_{tt} TT_{tt} + \varepsilon_{tt}$$

In which: Y_t is the aggregated outcome measure along time t; T_t is a time variable from the point when the study began; X_t is a dummy variable representing the change-point, indicated as 0 before and 1 after the change-point year; Z is a dummy variable for assignment to 0 to controls and 1 to cases; and ZT_t, ZX_t, and ZX_tT_t are interaction terms between variables.

Longitudinal mixed-effects models (LMEMs) were applied to the matched pairs to determine whether hair Hg concentrations over the entire period were higher among cases than controls. LMEM enables partitioning of the covariance structure into fixed and random effects and handling of missing data. The intra-class correlation coefficient was used to quantify the proportion of variance accounted for by a random effect in the intercept-slope LMEM. The normality of residuals was tested with a q-q plot. The most appropriate LMEM was identified by the Akaike information criterion, the Bayesian information criteria, and the likelihood ratio test at $p<0·05$.

LMEM was also used to examine whether Hg exposure over this period was associated with reduced longevity. For this analysis, we used a subset of the 154 deceased individuals (figure 1) with at least four measures of hair Hg concentration over the sampling period (n=105).

Cox's Proportional Hazards Model (CPHM) was used to evaluate the relative risk (hazard) at different point concentrations of hair Hg and complement the findings of the LMEMs. The CPHM was applied to the 222 individuals who could have reached 60 years old by Aug 3, 2019 (figure 1). Cutoff criteria were hair Hg concentration of at least one measure of 3, 5, 10, 15, and 20 µg/g or more over the sampling period. Non-adjusted and adjusted models (covariates: hair Hg concentration, sex, and year of birth) were compared. The proportional hazards assumption was verified with visual inspection and statistical tests on the scaled Schoenfeld residuals. Time-varying effect was used when the proportional hazards assumption was not fulfilled. The significance of the final CPHM was confirmed using three tests (likelihood ratio test, Wald, and score [log rank test]).

Database management and descriptive statistical analyses were done with JMP professional 14.0 statistical analysis hardware. ITSA and LMEMs were done with Stata 16 software. All other multivariate statistical analyses were done using the R statistical computing software version 3.6.1. We used the CPM R package for change-point analysis. CPHM and survival curves were run with both survival and survminer R packages. When necessary, multiple imputation was done to handle missing values. Thresholds of statistical significance were set at $p<0·05$.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study. Final responsibility for the decision to submit for publication was made by the corresponding author, after review and approval by the

Grassy Narrows First Nation community, in conformity with Canadian Institutes of Health Research guidelines for health research involving Indigenous people. All authors approved the submission of the final manuscript.

Results

The descriptive analyses included 657 individuals (319 women and 338 men) for whom we had Hg biomarker data, sampled between Jan 1, 1970, and Jan 31, 1997. Living status was identified for 633 (96%); 308 women and 325 men, born between October, 1884, and June, 1991. Of these, 249 (39%, 113 women and 136 men), had died between August, 1972, and June, 2019. Further analyses were done on 222 individuals (107 women and 115 men) born before Aug 3, 1959. Figure 2 shows the mean hair Hg time series sequence for each year, using the entire source database (n=657). Change-point detection detected two change-points; the first occurred in 1977 and the second in 1987. The mean hair Hg concentrations for each year are presented in the appendix (p 2). The mean hair Hg temporal progression was similar for the 222 individuals, who were born between October, 1884, and June, 1959 (appendix pp 3, 10). Overall, men presented higher mean hair Hg concentrations than women, although the highest hair Hg measure in women was 183 µg/g and in men was 145 µg/g.

Deceased individuals (n=154) presented with higher hair Hg concentrations than living individuals as of Aug 3, 2019, (n=68) for most of the time period (appendix p 4). This result might be because they were born earlier and experienced the highest Hg exposure period between 1970 and 1977. For the deceased individuals, the earliest year of birth was 1884 (median 1938, IQR 1922–1948), whereas for those still alive as of Aug 3, 2019, the earliest year of birth was 1921 (median 1952, 1948–1956). The matched-pair approach allowed us to overcome this discrepancy.

With the matched-pair approach, the 36 case-control pairs included 17 pairs of women and 19 pairs of men, born between 1926 and 1959. Among the controls, 21 were still alive on Aug 3, 2019, and 15 were deceased. The mean age of cases at death was 48·1 years (SD 10·0, median 52·5 years, IQR 40·3–56·0). No difference was observed in the number of hair samples between cases (median 9, 5·3–18·5) and controls (median 10, 7·0–12·8).

The ITSA plot and results for cases and controls with the 1977 and 1987 change-points are presented in figure 3. The hair Hg intercept was significantly higher for cases compared with controls (p<0·0001). Between 1970 and 1977, hair Hg declined significantly for cases (p<0·0001), but not for controls (p=0·40). Between 1977 and 1986, there was a tendency for decline in hair Hg (p=0·066), while controls remained stable (p=0·50). After 1987, cases showed a significant decline in hair Hg concentrations (p=0·0022) and controls showed a tendency for decline (p=0·056). The parameter estimates of ITSA are presented in the appendix (p 5). Comparison of mean hair Hg between pairs for the three time sequences is shown in the table. In each sequence, cases have significantly higher hair Hg concentrations than controls.

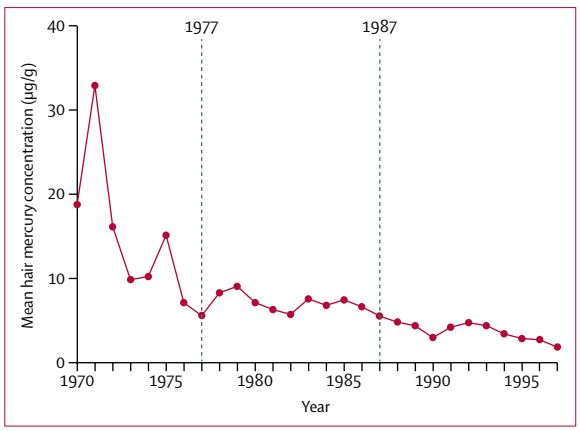

Figure 2: **Distribution of yearly mean hair mercury concentrations, 1970–97**

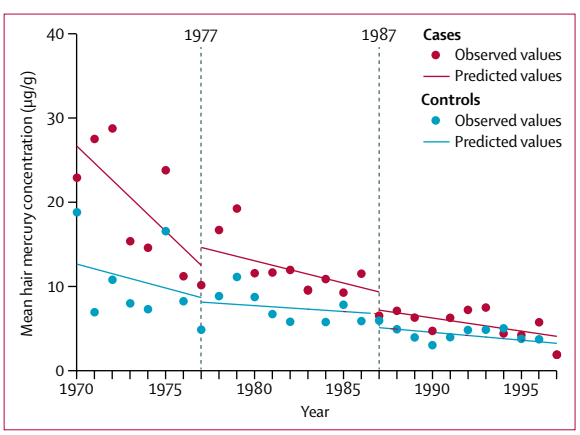

Figure 3: **Comparison of trends in mean hair mercury concentration**
Data are for cases (n=36) and controls (n=36) in a double-group interrupted time series analysis. Regression with Newey-West Standard Errors lag 2. Cases were prematurely deceased individuals and controls were individuals who lived to 60 years or older.

The retrospective longitudinal trend of yearly based hair Hg concentration between 1970 and 1997 for the matched pairs was analysed using LMEM. After adjustment for covariates, the LMEM, which follows a linear function for hair Hg, was assigned as the most appropriate (all assumptions confirmed: Akaike information criterion, Bayesian information criteria, likelihood ratio test, intra-class correlation criterion, and residual distribution). The model revealed a fixed effect of sampling year, sampling season, year of birth, sex, and premature death, and a hierarchical random effect (age of sampling nested in sampling year and sampling season). Retrospective longitudinal hair Hg concentration decreased with sampling year and is 4·7 µg/g higher (95% CI 3·4–5·9) in cases than controls (appendix p 6). Compared with women, men's hair Hg concentration was 7·2 µg/g higher (95% CI 5·6–8·8) over the sampling period. Hair Hg concentrations during summer and

	Hair mercury concentration (µg/g)		Wilcoxon or Kruskal-Wallis p value
	Cases	Controls	
1970–76	22·2 (13·6–27·0)	7·1 (6·1–15·7)	0·022
1977–86	10·5 (8·9–12·1)	6·1 (4·5–7·9)	0·0008
1987–97	5·0 (3·1–5·9)	2·6 (2·4–3·6)	0·0067

Data are median (IQR). Cases were prematurely deceased individuals and controls were individuals who lived to 60 years or older.

Table: **Hair mercury concentrations before and after the change-points**

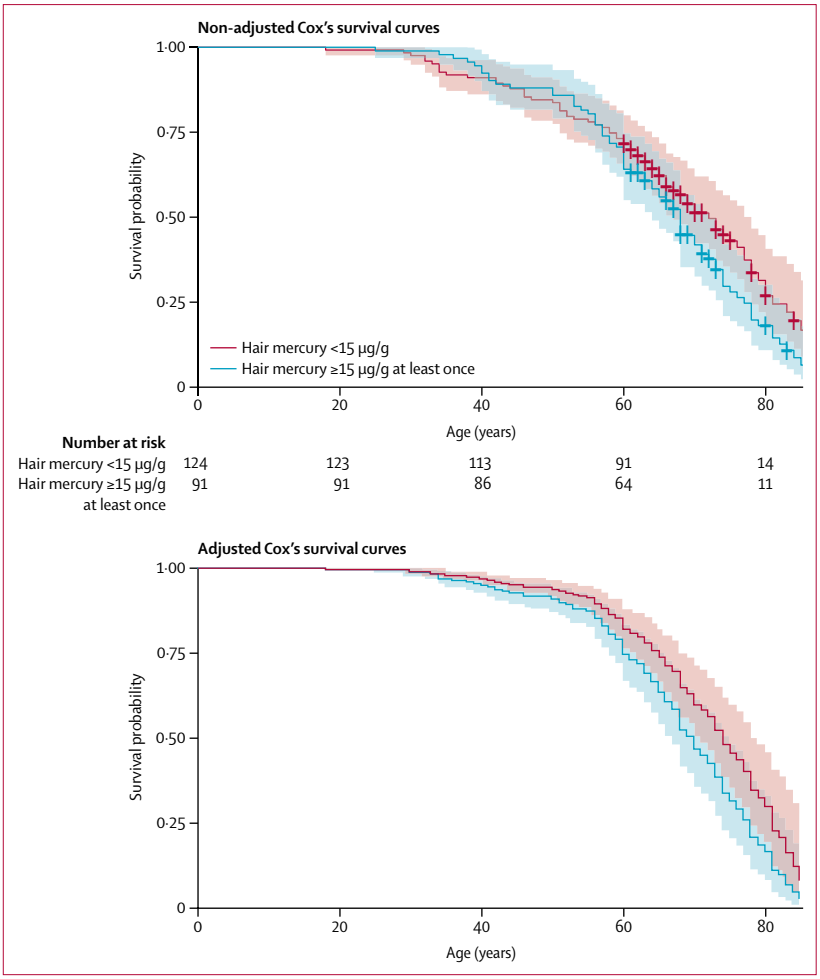

Figure 4: **Non-adjusted and adjusted Cox's survival curves for individuals who could have reached 60 years old by Aug 3, 2019**

autumn (July to December) were significantly higher than the rest of the year.

The non-adjusted CPHM respected the assumptions for proportional hazards; however, the adjusted CPHM required time-varying coefficients for year of birth (cuts at 55 years and 80 years at death). Goodness of fit was satisfied at the cutoff of at least one hair Hg measure at 15 µg/g or more. Non-adjusted hazard ratios (HRs; 1·30, 95% CI 0·98–1·90; p=0·058) and adjusted HRs (1·55, 1·11–2·16; p=0·0088) were similar for the increase in risk of dying at a younger age among those with at least one hair Hg measure of 15 µg/g or more. 91 (42%) of 215 individuals had hair Hg concentrations of 15 µg/g or greater at least once between 1970 and 1997. Figure 4 shows the non-adjusted and adjusted survival curves and the forest plot is shown in the appendix (p 11). Visual inspection shows that the non-adjusted and adjusted curves separate at different ages. In the adjusted models, the curves begin to separate at about 30 years, while in the non-adjusted model, differences were not observed until individuals were in their late-50s. When stratifying by sex, CPHM was significant for men at hair Hg cutoff at 15 µg/g (HR 1·68, 95% CI 1·05–2·68; p=0·033) and 20 µg/g (HR 1·58, 1·00–2·47; p=0·051). No significant differences were observed for women in the CPHM.

LMEM analyses of longevity showed that age at death decreased by 1 year for every 6·25 µg/g (95% CI 4·35–14·29) increase in hair Hg concentration over the surveillance period of 1970–97 (appendix p 7).

Discussion

This is the first study, to our knowledge, to show a significant association between longitudinal Hg exposure from freshwater fish consumption and premature mortality. In the First Nation community of Grassy Narrows, individuals who died prematurely before reaching 60 years old, had significantly higher Hg exposure between 1970 and 1997 than those who lived longer. The matched-pair approach revealed that Hg exposure, measured as hair Hg, was almost 5 µg/g higher for those who died before the age of 60 years, compared with those who lived beyond this age. The risk of dying increased by 55% when hair Hg was greater than or equal to 15 µg/g at least once over the sampling period. Among deceased individuals, there was a 1-year decrease in age at death with each increase of 6·25 µg/g hair Hg concentration.

Although population surveys in Canada classify premature mortality as dying when younger than 75 years,[24] in the present study, we used 60 years, as there were few individuals older than 60 years. The 2016 Canadian census reported that only 4% of individuals from the Grassy Narrows First Nation (English River 21, ON, Canada) were 65 years or older. In the present study, for those who were at least 21 years old at the beginning of the sampling period, 88 (77%) of 115 men and 75 (70%) of 107 women lived beyond 60 years. A survival study of Hg-exposed patients with Minamata disease in Japan[10] reported that by 1981, the probability of survival to 60 years was 75% for women and 55% for men, compared with 95% for women and 88% for men in the general Japanese population.

Over the period of the surveillance programme, mean hair Hg concentration decreased significantly between 1970 and 1976 and continued to decline until 1986, after which it stabilised. This pattern parallels fish Hg

concentrations, reported by Neff and colleagues,[4] who examined long-term (1970–2010) fish Hg monitoring data to assess temporal trends in lakes located in the area around the community of Grassy Narrows. These authors showed a strong decline in total Hg in walleye, the fish most consumed in Grassy Narrows, from 1974 to the early-1980s in all lakes, stabilising between 1990 and 2005 in most lakes.

Women had lower hair Hg concentrations than men up until the early 1990s and there was a sex difference in the pattern over time. Many of the men who were sampled worked in the fishing trades and had a regular diet of fish.[6] These jobs were lost when commercial and recreational fishing activities were closed down, resulting in the initial sharp slope of diminishing hair Hg concentration. Over the period, women might have eaten less fish than men. A study of First Nation individuals, living on reserve in Ontario, reported that freshwater fish intake (g/day) for women of childbearing age (19–50 years) was about half of that for men.[25] Moreover, during pregnancy, women lose Hg to the fetus due to active placental transport.[26,27] The plateau observed for hair Hg concentrations in women suggests that, unlike men, women did not greatly reduce their fish consumption, but Hg concentrations in the fish that they were eating decreased over time. Segmental analyses of individual hair strands in this population by Wheatley and Paradis,[6] showed important annual seasonal variations, which we confirmed on a population level.

The major strengths of this study lie in the retrospective 28-year hair Hg database and the use of multiple statistical approaches. Samples had been collected by a government surveillance programme and analysed by the same laboratory, using the same standardised analytical techniques throughout the period.[28] Efforts were made to take samples from fishing guides and those with previous high Hg biomarkers, in addition to sampling individuals concerned about their Hg exposure.[28] The matched-pair approach for longitudinal analyses allowed us to circumvent possible sampling bias. Because a strong correlation is seen between year of birth and hair Hg concentration, and men had higher hair Hg concentration than women, matching allowed us to create pairs of men and women, born at the same time in this community. LMEM allowed us to handle missing data and take into account random effects, while Cox's survival models provided an adjusted HR and time-varying coefficients, to take into account covariates that change over time. The findings were supported by the longevity analyses, which showed that higher hair Hg concentrations were associated with a decrease in lifespan.

A further strength of the study is that all participants were Registered Indians of Grassy Narrows First Nation. Under the Canadian Indian Act, the date of birth and death of Registered Indians are recorded in their Band Lists and provided to the community. Our database contains Hg hair and blood measurements from all 657 Grassy Narrows members, who were tested as part of the 1970–97 government surveillance programme. For these, we were able to ascertain the living status for 633 (96%) individuals.

There are important limitations to the study. The first concerns biomarker sampling, which was only initiated in 1970, while the discharge of approximately 1000 kg per year of Hg into the English-Wabigoon River system began in 1962.[1] No data are available for the period before 1970, when fish consumption was higher because there were no advisories to limit fish consumption.[6]

A second limitation is the absence of information on the specific cause of death for each individual. The contribution of long-term methyl-Hg exposure to early mortality is probably not direct. The neurotoxic properties of methyl-Hg are well known and the resulting neurological and neuropsychiatric dysfunction could lead directly or indirectly to premature death. In addition, methyl-Hg exposure is associated with several known risk factors for reduced longevity, including diabetes,[29,30] hypertension,[31] and myocardial infarction.[32] Other studies suggest that methyl-Hg could have a synergistic effect on liver damage in heavy drinkers.[33] By contrast, NHANES (2007–10) data showed inverse relations for the risk factors of obesity and smoking with blood Hg.[34] In the present study, independently of the cause of death, individuals who died prematurely had considerably higher Hg exposure over the 28 years of the surveillance programme. Cause-specific mortality in relation to long-term Hg exposure would require a much larger population study, such as linking the entire Canadian Hg biomarker surveillance database[6] with databases for mortality in First Nation communities.

Our findings cannot be generalised to all fish-eating populations as the community in the present study ate freshwater fish and had very high Hg exposures. Several studies on Canadian lakes have reported that freshwater fish do not have high concentrations of omega-3 fatty acids[15,35] and found no association between fish intake from these lakes and serum omega-3 fatty acids.[36,37] Many studies have shown the beneficial effects of omega-3 fatty acids on longevity.[12–14]

Reduced longevity has deprived the Grassy Narrows community of elders, who play an important role in the transmission of knowledge and traditions. The present study focused on community members who were born before the onset of the Hg discharge into the English-Wabigoon river system in the early 1960s. It did not include individuals born since that time, who were exposed to Hg in utero and early childhood, a critical period for developmental programming, particularly for the nervous system. Further studies are needed to investigate the health and social consequences of these early and life-time exposures.

Contributors
DM obtained the data and AP created the longitudinal data base. AP and DM designed the study. AP developed the statistical methods and did

statistical analyses. All authors contributed to data interpretation, writing, critical revision, final approval, and were involved in community collaboration.

Declaration of interests

We declare no competing interests.

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