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The Contribution across Three Generations of Mercury Exposure to Attempted Suicide among Children and Youth in Grassy Narrows First Nation, Canada: An Intergenerational Analysis

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Background: For 60 y, the people of Asubpeeschoseewagong Anishinabek (Grassy Narrows First Nation) have endured the effects of massive mercury (Hg) contamination of their river system, central to their traditions, culture, livelihood, and diet. In the years following the Hg discharge into the English–Wabigoon River system by a chloralkali plant in the early 1970s, there was a dramatic increase in youth suicides. Several authors attributed this increase solely to social disruption caused by the disaster.

Objective: This research examined the possible contribution of Hg exposure across three generations on attempted suicides among today's children (5–11 y old) and youth (12–17 y old), using a matrilineal intergenerational paradigm.

Methods: Information from the 2016–2017 Grassy Narrows Community Health Assessment (GN-CHA) survey was merged with Hg biomonitoring data from government surveillance programs (1970–1997). Data from 162 children/youth (5–17 years of age), whose mothers ($n = 80$) had provided information on themselves, their parents, and children, were retained for analyses. Direct and indirect indicators of Hg exposure included *a*) grandfather had worked as a fishing guide, and *b*) mother's measured and estimated umbilical cord blood and childhood hair Hg and her fish consumption during pregnancy with this child. Structural equation modeling (SEM) was used to examine significant links from grandparents (G0) to mothers' exposure and mental health (G1) and children/youth (G2) risk for attempted suicide.

Results: Mothers' (G1) median age was 33 y, 86.3% of grandmothers (G0) had lived in Grassy Narrows territory during their pregnancy, and 52.5% of grandfathers (G0) had worked as fishing guides. Sixty percent of children (G2) were <12 years of age. Mothers reported that among teenagers (G2: 12–17 years of age), 41.2% of girls and 10.7% of boys had ever attempted suicide. The SEM suggested two pathways that significantly linked grandparents (G0) to children's (G2) attempted suicides: *a*) through mothers' (G1) prenatal and childhood Hg exposure and psychological distress, and *b*) through maternal fish consumption during pregnancy (G1/G2), which is an important contributor to children's emotional state and behavior.

Discussion: Despite minimal individual information on G0 and G1 past life experiences, the findings support the hypothesis that Hg exposure over three generations contributes to the mental health of today's children and youth. The prevalence of Grassy Narrows youth ever having attempted suicide is three times that of other First Nations in Canada. https://doi.org/10.1289/EHP11301

Introduction

Since the first public evidence, 52 y ago, of the extent of the mercury (Hg) discharge into the English–Wabigoon River system by a chloralkali plant in Dryden, Ontario (Canada), much has been written about the Asubpeeschoseewagong Anishinabek (Grassy Narrows First Nation) and how the contamination of their waterways disrupted their culture, traditions, and economy.[1–8] For generations, fish provided people of Grassy Narrows with "meaning, social cohesion, and pride."[9] In the early 1960s, a large majority were gainfully employed in fish-based industries.[1–9] Approximately 80% of the households in Grassy Narrows had a least one family member who worked as a fishing guide and many were involved in commercial fishing; employment was 85%–90%.[1–3] During the tourist fishing season, all Grassy Narrows fishing guides reported eating fish every day as part of the customary shore meal for anglers, and almost all (92%) brought fish home to their family.[1]

In 1970, very high Hg levels were reported in fish in the English–Wabigoon River system; inorganic Hg released by the chloralkali plant was being converted into methylmercury (MeHg), a highly toxic compound that bioaccumulates and biomagnifies in the aquatic food chain.[5,10] Hg concentrations in fish reached up to 24 μg/g, almost 50 times the upper limit considered safe for human consumption.[10] Communities received contradictory messages about whether or not they should continue to eat fish. Some lodge owners downplayed the importance of Hg contamination and continued the practice of shore meals, thereby placing fishing guides into the situation of choosing between their health and their livelihood.[1] In 1975, the main fishing lodge had shut down and the commercial fisheries were closed.[1] Over time, fish Hg concentrations declined, stabilizing by around 1985,[10,11] but they have remained to this day higher than in other Ontario lakes and rivers.[12]

In the early 1970s, Canadian government biomonitoring programs for total Hg in hair, blood, and umbilical cord blood were initiated in the First Nation communities affected by the discharge into the English–Wabigoon River system.[13,14] In 1976, annual average individual peak blood total Hg was 23.8 μg/L, with concentrations ranging from 1.5 to 322.9 μg/L.[13] Fishing guides and their families were identified as the groups the most at risk; the highest blood total Hg concentration (660 μg/L) among Indigenous communities in Canada was reported for a Grassy Narrows fishing guide.[15] The biomonitoring programs continued into the 1990s, when average Hg biomarker concentrations declined below the Canadian Hg guidelines, mirroring the decline in fish Hg concentrations.[13,16]

The years following 1970 saw the loss of livelihood and were fraught with social upheaval.[1–5] There was an 8-fold increase of violent deaths from pre- to post-1970 and the prevalence of alcoholism was high.[1–4] Several authors have attributed the social crisis to the loss of traditional lifestyle and the destruction of the very foundation of their society.[1,2,4–6] In Grassy Narrows First Nation, the trauma of cultural dispossession and loss of livelihood was compounded by Hg poisoning from fish consumption. However, the possible direct contribution of high Hg exposure to the

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psychopathology was not considered, despite reports of psychiatric disorders among patients with organic Hg poisoning. As early as 1971, Eyl[17] noted that the symptoms of organic Hg poisoning included a lack of interest in home and work, emotional instability with fits of anger, depression, or rage. In 1968, Tatetsu (cited in Ekino et al. 2007[18]) described the psychiatric profile of many patients with Minamata disease, who had been exposed to MeHg from the consumption of fish and shellfish, contaminated by the wastewater discharge from a chemical plant into the Minamata Bay: "They were egocentric, selfish, and paid little attention to the advice of others. Loss of inhibition was another feature of the disease's personality characteristics. They were often impolite, too friendly to others, easily burst into anger, restless, euphoric, and childish. Some of them spent money as much as they were given and threw away change."

Prior to 1970, no suicide had ever been recorded in Grassy Narrows.[2] Between 1974 and 1978, three of the four persons who took their life were teenagers, and in 1977–1978, 26 young persons between 11 and 19 years of age attempted suicide.[4] Between 1970 and 1977, the incidence of suicide was 3.6 times higher compared with another First Nation community, selected for its pre-1970 socioeconomic similarities to Grassy Narrows.[1] Neurological examinations, carried out in Grassy Narrows in the 1970s, focused primarily on motor and sensory functions, with results that appeared to be "elusive," although there were several signs and symptoms similar to those reported for patients with Minamata disease.[15] In 2010, Harada et al. examined 73 persons from Grassy Narrows using the protocol for the diagnosis of Minamata disease in Japan: 42 (57.4%) were diagnosed with Minamata disease or suspected Minamata disease, 15 (20.5%) exhibited emotional disturbances, and 10 (13.6%) showed intellectual deficits.[19] A recent study in Grassy Narrows reported a positive association between umbilical cord blood total Hg concentration and clustered symptoms of affect/mood disorders in adults.[20]

For the people of Grassy Narrows, the problems associated with Hg exposure may be compounded by the intergenerational consequences of the trauma caused by the Indian Residential School system.[21–24] Children were taken from their communities and sent to government-financed boarding schools, administered by Christian churches. Many children from Grassy Narrows were sent to these schools.[25,26] In 1953, the principal of the Presbyterian school in Kenora, Ontario, wrote: "We must face realistically the fact that the only hope for the Canadian Indian is eventual assimilation into the white race."[26] Mental health issues, particularly emotional well-being, are the most frequently identified intergenerational impacts of residential schools on Indigenous health and well-being in Canada.[27]

Little is known about the consequences of environmental exposures across generations. Depression in parents has been consistently found to be associated with children's behavioral problems and lower cognitive/intellectual/academic performance.[28] During pregnancy, maternal consumption of Hg-laden fish exposes the developing fetus; MeHg is actively transported across the placental barrier and umbilical cord blood MeHg is approximately twice that of maternal blood.[29] Studies of Inuit children in Canada report increased risk for borderline intellectual disability[30] and adolescent anxiety[31] in relation to umbilical cord blood total Hg.

By 2016, >90% of the adult population of Grassy Narrows were born since the beginning of the disaster in 1962[32]; most were exposed to Hg *in utero* and their parents experienced the immediate impact of the disaster. Today's children and youth live with this legacy. The present study seeks to explore intergenerational effects of Hg contamination in Grassy Narrows on children's emotions, behavior and attempted suicide, using a maternal-lineage transmission paradigm.

Materials and Methods

Study Design

Between December 2016 and March 2017, Grassy Narrows First Nation carried out a community health assessment, the Grassy Narrows Community Health Assessment (GN-CHA) survey. Participants provided information on themselves, their parents, and their children (0–17 years of age). Information from the GN-CHA on grandparents (G0), mothers (G1), and their children (G2) was merged with a database constructed from archived biomarkers of Hg exposure from a government monitoring program carried out between 1970 and 1997.[16]

GN-CHA Survey

The GN-CHA survey used a systematic house-to-house sampling strategy on-reserve, and convenience sampling off-reserve. Two coordinators from Grassy Narrows devised and supervised the field work, assisted by nine local surveyors. The questionnaire was web-based and participants could fill it out on their own, or with, when needed, the assistance of the surveyor.

The GN-CHA adult (≥18 years of age) survey included 266 questions covering the following areas: demographics, education, generational attendance of residential school, work activities and income, diet, general health status (including diabetes care), mental health and well-being, disabilities, injuries, health care access, physical activity, smoking, drinking and drug use, and participation in community activities. Most questions were taken from the First Nation Regional Health Survey 2008/2010,[33] providing a basis for comparison with other First Nation communities in Canada. Further questions addressed local fish consumption at different periods, as well as specific illnesses and symptoms that have been associated with Hg exposure. The large majority of adult participants filled it out on their own. Those who did not fill it out on their own were older persons for whom English was not their first language. Translation in Anishinabek was available.

Similar to the adult survey, the GN-CHA survey for children and youth included the same questions as the First Nation Regional Health Survey 2008/2010,[33] as well as questions on local fish consumption during mother's pregnancy and the child's current fish consumption (174 questions). Parents or caregivers provided the information on children. In some instances, the youth was present when the questionnaire was being filled out; some youth ≥15 years of age filled out the child questionnaire on their own.

On-reserve, 83.6% of the 213 houses were surveyed (302 persons); 89 persons (22.8%) living off-reserve, from 66 households were likewise surveyed. Data were collected for 391 adult Grassy Narrows Registered Band members and 353 children (0–17 years of age). The age and sex distributions of participants were similar to their distribution in the 2016 Statistics Canada Aboriginal Household Survey.[32] GN-CHA results were presented to and discussed with community members during several small group and community meetings. The final reports were approved by the Chief and Council and made public on 24 May 2018 for adults and on 5 December 2018 for children.

For the present study, we retained information provided for children between 5 and 17 years of age ($n = 162$) and their mothers ($n = 80$). All mothers had filled out the adult and child/youth questionnaires on their own; 17 youth (26.2%), between 13 and 17 years of age, were present when their mother filled out the child/youth questionnaire. The GN-CHA questions retained in the present statistical analyses are classified by generation as described below.

- **Children (G2):** Mothers provided information about each of their children for the following variables: age, sex, physical and mental health status (on a five-point Likert scale), current fish consumption, and diagnosed nervous system disorders [yes/no for at least one of the following: cognitive or mental disabilities, attention-deficit and attention-deficit/hyperactivity disorder (ADD/ADHD), learning disabilities, speech/language difficulties, visual problems that cannot be corrected by glasses, hearing impairment, cerebral palsy, Bell's palsy and movement disorders]. Fetal alcohol spectrum disorder (FASD) was included in the questionnaire, but it was excluded from the list of at least one diagnosed nervous system disorder. Further questions asked whether in the past 6 months the child had more emotional or behavioral problems compared with other children of the same age and sex (yes/no) and whether the child had ever attempted suicide (yes/no). Children's school performance was grouped into three categories: very good/excellent, good, and fair/unsatisfactory.

Several questions addressed the mother's pregnancy with this child. The questions were worded: "If you are the birth mother, did you have …?" Gestational diabetes, hypertension, prematurity and difficulties during childbirth were grouped into yes/no. Questions likewise asked, "If you are the birth mother, did you drink a lot or take drugs during pregnancy?" (yes/no). The child's prenatal Hg exposure was based on mother's reported local fish consumption during her pregnancy with this child, grouped into three categories (less than once a month, once a month, at least once a week).

- **Mothers (G1):** The following variables were retained: age, education (years of education and having received a high school diploma), school success (five-point Likert scale from poor to excellent), having attended a residential school (yes/no), currently working (yes/no), reasons for not working, social support (yes/no), struggle to pay for food over the past 12 months (at least once a month vs. less), current smoking (yes/no), current heavy drinking as defined by the 2008/2010 Regional Health Survey[33] as five drinks in one drinking occasion at least once a month in the past 12 months (yes/no), and obesity categorized using body mass index $\geq 30\,kg/m^2$ (yes/no). Diagnosed nervous system disorders included at least one of the following conditions diagnosed by a health professional: ADHD, Alzheimer's disease, blindness or visual problems that cannot be corrected by glasses, Bell's palsy, cerebral palsy, cognitive/mental disorder, epilepsy, Kennedy's disease, learning disability, muscular dystrophy, Parkinsonism, psychological/nervous disorders, and senile dementia.

  Psychological distress was assessed using the Kessler Psychological Distress Scale (K10)[34] for symptoms of anxiety or depression experienced in the previous month and scored on a scale of 0–40 (0–5: low distress, 6–19: moderate distress, and $\geq$20: high psychological distress).[34] Several GN-CHA questions were about suicidal ideation and attempted suicide; here we retained the answers to the following questions: "In the past 12 months, has a close friend or family member died by suicide?" (yes/no), "Have you ever thought about committing suicide?" (yes/no), and "Have you ever attempted suicide?" (yes/no). "When did the suicide attempt occur?" [during the past year, as an adult, as an adolescent (aged 12–17 y old), as a child (<12 y old)].
- **Grandparents (G0):** From the information mothers (G1) filled out about their parents (G0), the following questions were retained for the present analyses: "Was your father a fishing guide when you were a child"? (yes/no) and "Did (your mother, father, grandmother, grandfather, other family members) attend a residential school?" (yes/no). Mothers provided further information about where their mother (G0) lived when she was pregnant with them and their place of birth.

  For all questions, the GN-CHA survey provided the choices of "I do not know" and "Refused." Although few persons refused to answer, a substantial number of answers were "I do not know," which we considered as missing data.

Biomarkers of Hg Exposure

At the request of the Grassy Narrows Chief and Council, the First Nation and Inuit Health Branch of Indigenous Services, Canada, provided the authors with individual retrospective Hg biomarker data, collected by governmental biomonitoring programs for blood and hair (1970–1997) and umbilical cord blood (1970–1992).[13,16] Blood Hg concentrations were transformed into hair equivalent measures using a hair-to-blood Hg ratio of 1:250.[35] A 28-y Hg biomarker database was created using the highest measurement of equivalent hair Hg concentration for each year sampled (657 persons) and umbilical cord blood Hg concentration (201 persons).[20]

Year-based equivalent hair Hg data were available for 208 individuals of the 391 participants in the GN-CHA (53.2%); 137 had at least one Hg hair sample taken during childhood (between 5 and 15 years of age). Umbilical cord blood Hg concentrations were available for 99 persons, making up (48.5%) of the GN-CHA participants born at the local hospital within the time period.

G0/G1 prenatal exposure. For the 80 mothers retained for the present study, direct umbilical cord blood Hg measurements were used where available. For the missing umbilical cord blood data, we estimated Hg concentration from the complete umbilical cord blood Hg database ($n = 201$). For those born between 1970 and 1992, the umbilical cord blood Hg–predicted arithmetic mean for their year of birth was attributed as described in Philibert et al. (2022).[20] For those born between 1962 and 1970, the predicted arithmetic mean cord blood Hg in 1970 was used (65.1 $\mu g/L$). For women whose mother had spent her pregnancy and delivered elsewhere, umbilical cord blood Hg was set at 1.0 $\mu g/L$, which corresponded to the lowest 2.5th percentile of measured cord blood values. The correlation between measured and estimated values for umbilical cord blood Hg concentrations was rho $= 0.22$; $p = 0.023$.[20]

G1 childhood Hg exposure. Direct hair Hg concentration measurements, taken between 5 and 15 years of age, were available for 39 mothers. For the remaining mothers, childhood estimated Hg was derived from the overall arithmetic mean hair Hg in the year in which they turned 10 y old and then adjusted on the basis of reported child fish consumption and having attended a residential school, as previously described.[20] The correlation between measured and estimated childhood hair Hg concentrations was rho $= 0.73$; $p < 0.001$.[20]

No Hg measurements were available for the G0 or G2 generations. For the former, the G1 answer to the question: "Was your father a fishing guide when you were a child?" was used as an indicator of higher Hg exposure, and for children (G2), mother's fish consumption during this pregnancy (G1/G2) and child's current fish consumption, were used.

Statistical Analyses

Complex networks with causal pathways between variables are the essence of intergenerational analyses. Structural equation modeling (SEM) provides an appropriate framework for illustrating pathways and testing statistical associations. SEM allows for simultaneous consideration of multiple exposures and outcomes[36] while providing direct and indirect relations and flexibility in modeling covariances.[37–40] The SEM path diagrams illustrate and quantify the contribution of variables and transmission of effects.

Using SEMs, we tested the pathways relevant to Hg exposure between G0, G1, and G2 with respect to the final outcomes of children and youth's emotional status and behavior and attempted suicide. The correlations between error terms of the different variables were verified and taken into account in the models. The pathways used a time order based on the premise of chronological occurrences (causes precede their effects). To control for confounding, we ensured that all backdoor paths on the SEM were closed (adjustment of covariates). Covariates along pathways were kept in the model at a $p \leq 0.10$ or if they substantively altered the model ($\geq 20\%$ change). Based on underlying assumptions, mediation (i.e., the chain of events) was tested by examining direct and indirect effects. The moderating effects of mothers' age or age at birth were tested.

Model goodness of fit was verified using the comparative fit index (CFI),[39,41] Tucker–Lewis index (TLI),[40] and global fit index (GFI),[38] as well as chi-square divided by the degrees of freedom ($\chi 2/\text{df}$), root mean square error of approximation (RMSEA),[39,41] standardized root mean square residual (SRMR),[42] and Schwarz's Bayesian information criterion (BIC).[39,41,43] To improve goodness of fit, we tested the addition/deletion of variables, using modification indices (MIs).[39] The sequence of initial fit, modification, and refitting were repeated until we obtained the SEM with the best fit.

To support the SEM, in parallel, a series of directed acyclic graphs (DAGs) were performed to confirm the structure of relations between variables and to prevent misspecification or misinterpretation from possible biases. DAGs are useful for representing conditional independency among variables by evaluating data consistency and for controlling backdoor paths with minimal sufficient adjustment sets.[43,44] To support the nature and size of the relationship between two variables along the SEM pathways, a series of logistic regression models were used to examine the direct associations and provide an indication of the magnitude of effects.

Given the potential for errors associated with creating Hg exposure estimates from data based on surveillance programs with no precise sampling strategy,[13] as well as the inherent variance in blood to hair conversion[45,46] where possible, we examined the associations between measured Hg concentrations and reported fish consumption. We reran the SEM using reported G1 fish consumption during childhood in the place of estimated Hg exposure during childhood.

To ensure that the database of 80 mothers and their 162 children was sufficient to run SEM, two types of power analyses were performed: *a*) to detect model misspecification, and *b*) to detect target effects between associations.[39,41,43] Post hoc power analyses were run to detect model misspecification based on likelihood-ratio (LR) chi-square and RMSEA tests of close and not-close fit.[47–51] The power for detecting specific target effect for direct and indirect pathways was determined with simulated data in SEM for 100 and 500 simulations on the 162 children.[51] Because some children shared the same mother, we tested the nonindependent sample using clustering (mother), with the lavaan.survey R package.[52]

To reduce bias introduced by missing data, the full-information maximum likelihood (FIML) technique in the lavaan R package was used to handle missing data.[39,53] Even though several authors[54,55] consider that logit FIML can accommodate missing categorical data with unbiased errors and fit parameters, we verified the model with the weighted least squares (WLS) mean- and variance-adjusted chi-square test of model fit (WLSMV) estimator, which handles nonnormal and categorical variables, based on complete cases after multiple imputation.[39,56] When using FIML, we ran the maximum likelihood with robust standard errors (MLR), as well as the maximum likelihood estimation with Huber–White standard errors (Hubert–White sandwich), because it supports complete and incomplete data.[39]

Hg estimates for umbilical cord blood and childhood hair concentrations were calculated from exposure prediction models,[20] which included averaged year-based measured Hg exposure. Our assumption was that true Hg exposure varied randomly around the year-based average (Berkson type error). The Berkson type error would have the effect of lowering the power of analyses.[57] To control for this, we corrected with bootstrap confidence intervals (CIs) for relative risks.

Bootstrap standard errors and *p*-values analyses were carried out to increase SEM accuracy and its reliability (lavaan R package). The Bollen.stine technique, where data is first transformed such that the null hypothesis holds exactly in the resampling space, was verified to extract fit parameters from a fitted lavaan object.[58,59] We used the false discovery rate (FDR) measure for controlling type I error of multiple comparisons.[60]

We compared the performance of SEM by comparing the fit parameters, point estimates, and standard errors to the complex sampling design (cluster-based), which takes into account multiple children. In the case of small differences between non clustered-based and cluster-based analyses, we preferred to use the conventional analysis using FIML[53] rather than data imputation as required by the mother-clustered–based model (lavaan.survey R package).[39,61]

Variables with a skewed distribution were log (base 10) transformed. Threshold of statistical significance in all analyses was set at $p \leq 0.05$.

Database management and descriptive statistical analyses were performed using JMP Professional (version 16.0; Statistical Analysis Hardware; SAS Institute Inc.). All other analyses used the R statistical software (version 3.6.1; R Development Core Team). SEMs were computed with the lavaan R package.[39,62] Further analyses with DAGs used dagitty and ggdag R packages. Power analyses for model misspecification were computed using the semPower R package. An online tool[51] was used to assess power for detecting target effects. The clustering (mother) effect was tested with the lavaan.survey R package along with mice and mitools R packages for data imputation.

Results

The characteristics reported by mothers ($n = 80$) for themselves (G1) and their parents (G0) are presented in Table 1. The large majority of grandmothers (G0) resided in Grassy Narrows territory during their pregnancy ($n = 69$), and half of grandfathers (G0; $n = 42$) had been fishing guides. Many grandparents (G0) had attended residential schools; for all mothers (G1) ≥ 35 years of age ($n = 31$), at least one parent (G0) had been taken to a residential school.

Mothers' (G1; $n = 80$) median age was 33 y old, ranging from 23 to 55 [interquartile range (IQR): 29–37 y]. Most mothers (G1; $n = 77$) had some high school education, but only 21% ($n = 17$) had received a high school diploma (Table 1). At the time of the survey, approximately half of the mothers (G1; $n = 41$) were working; those who were not looking for work at the time of the survey were either an at-home parent, in poor health or disabled, or a student. The most prevalent nonneurologic chronic health conditions were allergies ($n = 25$; 33%), eczema ($n = 19$; 24%), arthritis ($n = 11$; 15%), and diabetes ($n = 11$; 15%). Diagnosed neurologic disorders were reported by 14 mothers (Table 1); all scored in the moderate/high K10 Psychological Distress Scale compared with 56% ($n = 34$) of those who reported no diagnosis.

A third of mothers ($n = 27$) reported that a family member or close friend had committed suicide, and half ($n = 40$) reported

Table 1. Descriptive characteristics for grandparents (G0) and mothers (G1) as reported by mothers (G1) in the Grassy Narrows Community Health Assessment (GN-CHA) survey; $n = 80$.

Characteristics	Yes [n (%)]	No [n (%)]	Missing [n (%)][a]
Generation grandparents (G0)			
Grandmother pregnant in GN territory	69 (86.25)	8 (10.00)	3 (3.75)
Grandfather a fishing guide	42 (52.50)	24 (30.00)	14 (17.50)
Grandmother attended a residential school	47 (58.75)	29 (36.25)	4 (5.00)
Grandfather attended a residential school	46 (57.50)	25 (31.25)	9 (11.25)
Generation mother (G1)			
Age <35 y	46 (57.50)	34 (42.50)	0
Education (high school diploma)	17 (21.25)	61 (76.25)	2 (2.50)
School success (very good/excellent)	28 (35.00)	49 (61.25)	3 (3.75)
Childhood fish consumption (≥several times a week)	38 (47.50)	36 (45.00)	6 (7.50)
Currently working	41 (51.25)	37 (46.25)	2 (2.50)
Unemployed but looking for work	19 (51.35)	16 (43.24)	2 (5.41)
Struggle to pay for food (at least once a month)	43 (53.75)	27 (33.75)	10 (12.50)
Health perception: thriving (very good/excellent)	17 (21.25)	63 (78.75)	0
At least one chronic health condition	56 (70.00)	23 (28.75)	1 (1.25)
At least one diagnosed nervous system disorder	14 (17.50)	65 (81.25)	1 (1.25)
Obesity $\geq 30\,kg/m^2$	44 (55.00)	34 (42.50)	2 (2.50)
Current heavy drinker	44 (55.00)	32 (40.00)	4 (5.00)
Family or close friend has died from suicide last 12 months	27 (33.75)	48 (60.00)	5 (6.25)
Suicidal ideation	40 (50.00)	34 (42.50)	6 (7.50)
Ever attempted suicide	31 (38.75)	43 (53.75)	6 (7.50)
K10 (moderate/high)	49 (61.25)	27 (33.75)	4 (5.00)

[a]For each question in the GN-CHA, persons could provide the reply "I don't know," "I can't recall," or "Refused", which were grouped as "Missing."

that they themselves had thought about suicide (Table 1). Among those who had ever thought about suicide, 31 (77.5%) had attempted suicide at least once in their lives; for over half of these ($n = 19$; 61.2%), the first suicide attempt occurred during childhood/adolescence. More mothers who had thought about suicide scored in the moderate-high range of the K10 Psychological Distress Scale compared with those who had not ($n = 31$; 81.6% vs. $n = 13$; 40.6% LR chi-square = 12.82; Fisher exact test: $p < 0.001$).

Some mothers (G1) did not know whether their father (G0) had been a fishing guide or not ($n = 14$; 17.5%). Comparison of the characteristics of mothers who reported that their father had been a fishing guide ($n = 42$) and those who reported that their father had not been a fishing guide ($n = 24$) are presented in Table S1. No difference was observed with respect to their parents (G0) having been placed a residential school; however, all mothers (G0) of the 42 women whose father had been a fishing guide, resided on Grassy Narrows territory during their pregnancy, compared with 75% for the mothers of the 24 women whose father had not been a fishing guide (Table S1).

For the mothers who knew whether their father had been a fishing guide (G1) ($n = 66$), no significant differences were observed with respect to the father (G0) having been a fishing guide or not for sociodemographic and health characteristics (Table S1), with the exception of diagnosed neurologic disorders: 23.8% ($n = 10$ of 42) of those who knew that their father had been a fishing guide and none of those who knew that he had not been a fishing guide (Table S1). Childhood fish consumption and suicidal ideation were higher among the women who reported that their father had been a fishing guide ($n = 24$; $n = 25$ of 42, respectively), but the difference was just above the significance threshold (Table S1). More women whose father had been a fishing guide scored in the high range of the K10 Psychological Distress Scale ($n = 11$; 26.8%) compared with only one for the others.

Table 2 contains the measured and estimated mean, median, and IQR values for mothers' umbilical cord blood and hair Hg. There was no difference in measured umbilical cord Hg between mothers who reported that their father had been a fishing guide compared with those who indicated that their father had not been a fishing guide [median = 8.5 μg/L; 75th percentile: 8.7 μg/L ($n = 17$) vs. median = 5.7 μg/L; 75th percentile: 17.5 μg/L ($n = 7$); Wilcoxon/Kruskal–Wallis tests (rank sums): $S = 108$; $p = 0.204$], but their measured childhood hair Hg was significantly higher [median = 0.77 μg/g; 75th percentile: 1.1 μg/g vs. median = 0.5 μg/g; 75th percentile: 0.7 μg/g; Wilcoxon/Kruskal–Wallis tests (rank sums): $S = 140$; $p = 0.045$], paralleling their reported fish consumption.

Table 3 contains information, reported by the mothers, for each pregnancy and the child's health and well-being (G2; $n = 162$). Mothers filled out the questionnaire for an average of two children, ranging from one to seven children. For almost 20% of children ($n = 31$), mothers reported eating fish at least once a week during their pregnancy (Table 3). Mothers' fish consumption during pregnancy reflected her own childhood fish consumption [Kendall's Tau-b: 0.46 (95% CI: 0.33, 0.57) Fisher's exact test: $p < 0.001$] and was higher among those whose father (G0) was a fishing guide [Kendall's Tau-b: 0.355 (95% CI: 0.210, 0.510) Fisher's exact test: $p < 0.001$]. Indeed, 21 mothers (28.4%), whose father (G0) had been a fishing guide reported eating fish at least once a week or more compared with only 2 (4.5%) among those whose father had not been a fishing guide (LR chi-square: 20.78; Fisher exact test: $p < 0.001$). No associations were observed for mothers' age, maternal age at pregnancy, or child's age with respect to G1/G2 fish consumption during pregnancy [Wilcoxon/Kruskal–Wallis tests (rank sums) one-way test chi-square = 3.39, $p = 0.188$; 2.15, $p = 0.342$; and 1.97, $p = 0.374$, respectively].

Table 2. Measured and estimated mothers' (G1) umbilical cord blood and childhood hair mercury (Hg).

	n	Mean	Median	IQR	Min–max
Measured umbilical cord blood Hg (μg/L)	29	7.65	5.70	2.35–8.80	1.5–35.7
Estimated umbilical cord blood Hg (μg/L)	51	15.15	5.25	3.59–16.86	1.0–65.2
Measured childhood hair Hg (μg/g)	39	1.50	0.50	0.50–0.90	0.50–11.4
Estimated childhood hair Hg (μg/g)	38	1.52	0.92	0.72–2.60	0.50–5.64

Note: IQR, interquartile range; max, maximum; min, minimum.

Table 3. Descriptive characteristics for pregnancy (G1/G2) and children/youth (G2), as reported by mothers (G1) in the Grassy Narrows Community Health Assessment (GN-CHA) survey: $n = 162$.

Characteristics	Yes [n (%)]	No [n (%)]	Missing [n (%)][a]
Pregnancy (G1/G2)			
Mother's age at birth of child (≥22 y)	93 (57.41)	69 (42.59)	0
Maternal fish consumption during pregnancy (≥once a week)	31 (19.14)	125 (77.16)	6 (3.70)
Problems during pregnancy/childbirth	33 (20.37)	125 (77.16)	4 (2.47)
Mother's drinking/drugs during pregnancy	24 (14.81)	134 (82.72)	4 (2.47)
Generation children/youth (G2)			
Age (≥12 y)	66 (40.74)	96 (59.26)	0
Sex (girls)	89 (54.94)	73 (45.06)	0
Grandfather was a fishing guide	74 (45.68)	49 (30.24)	39 (24.07)
Fish consumption past year (often)	25 (15.40)	121 (74.69)	16 (9.88)
Overall health (very good/excellent)	129 (79.63)	33 (20.37)	0
Mental health (very good/excellent)	98 (60.49)	62 (38.27)	2 (1.23)
Speech/language disorder	17 (10.49)	139 (85.80)	6 (3.70)
Anxiety or depression	16 (9.88)	134 (82.72)	12 (7.40)
Emotional or behavioral problems	42 (25.93)	102 (62.96)	18 (11.11)
Emotional or behavioral problems (12–17 y)	24 (36.36)	31 (49.97)	11 (16.67)
Ever attempted suicide (all children)	22 (13.58)	133 (82.10)	7 (4.32)
Ever attempted suicide (12–17 y)	17 (27.42)	45 (72.58)	4 (6.45)

[a]For each question in the GN-CHA, persons could provide the reply "I don't know," "I can't recall," or "Refused", which were grouped as "Missing."

Seventeen mothers (21.3%) reported drinking or taking drugs for 24 pregnancies (Table 3), representing 15.1% of pregnancies for which this information was available ($n = 158$). Mothers who reported drinking alcohol or taking drugs during pregnancy for their child (G0/G1) were significantly younger at childbirth compared with those who reported not drinking or taking drugs (median = 19 y; IQR: 18–21 y and median = 23 y; IQR: 20–27 y, respectively; Wilcoxon/Kruskal–Wallis chi-square: 11.83; Fisher exact test: $p = 0.001$). The proportion of pregnancies for which the mother reported drinking or taking drugs was higher for those whose father (G0) had been a fishing guide compared with those who reported that their father had not been a fishing guide ($n = 14$, 19.7% vs. $n = 2$, 4.2%). No association was observed between drinking or taking drugs during pregnancy and the mother's current drinking habits (LR chi-square: 0.06; Fisher exact test: $p = 0.801$). Few children ($n = 4$, 2.5%) had a diagnosis of FASD.

GN-CHA mothers' (G1) reports about their children (G2) are presented in Table 3. Children's median age was 10 y (IQR: 8–14). For almost one quarter ($n = 39$), their mothers did not know if their grandfather had worked as a fishing guide. Most children (74.7%; $n = 121$) had not eaten local fish often over the year prior to the survey (Table 3). The First Nations Regional Health Survey 2008/2010 defined a measure for conditions that "may have an impact on learning ability" as at least one of the following diagnosed conditions: cognitive or mental disabilities, ADD/ADHD, learning disabilities, speech/language difficulties[33]; 24 children (14.8%) fell into this category. No difference was observed between boys ($n = 14$) and girls ($n = 10$) (LR chi-square: 2.27; Fisher exact test: $p = 0.132$).

Mothers' perceived the mental health of almost 40% ($n = 62$) of their children as less than very good or excellent (Table 3), and for 25% of children, the mother reported that the child had more emotional or behavioral problems compared with other children of the same age and sex (Table 3). The prevalence of emotional or behavioral problems was twice as high in youth (≥12 years of age) compared with younger children (36.7%; $n = 24$ vs. 18.8%; $n = 18$; LR chi-square: 8.87; Fisher exact test: $p = 0.003$). Among younger children (<12 years of age), no difference was observed between boys and girls [$n = 9$ of 41 (22.95%) vs. $n = 9$ of 48 (18.75%), respectively; LR chi-square: 4.65; Fisher exact test: $p = 0.794$]. However, more adolescent girls (≥12 years of age) presented emotional or behavioral problems compared with boys [$n = 17$ of 30 (56.67%) vs. $n = 7$ of 25 (28.00%), respectively; LR chi-square: 4.65; Fisher exact test: $p = 0.031$].

Mothers reported that 13% ($n = 22$) of children/youth had attempted suicide, but the percentage rose to 27% ($n = 17$) when considering only those ≥12 years of age (Table 3). Among adolescents (≥12 years of age), suicide attempts were higher among girls ($n = 14$ of 34; 41.18%) compared with boys ($n = 3$ of 28; 10.71%; Fisher exact test LR chi-square: 7.70; $p = 0.006$). None of the children with a diagnosis of FASD had attempted suicide.

The SEM in Figure 1 presents the intergenerational pathways for children and youth attempted suicide, with the corresponding fit parameters in Table 4 and estimates of sequential mediations in Table 5. The pathways began with mothers' year of birth, which represented not only her age, but also accounted for the change in Hg exposure over time. Different pathways linked G0 through G1 with an increased risk for G2 attempted suicide.

One modeled pathway originated from mothers' umbilical cord blood Hg (G0/G1), a reflection of (G0) grandmothers' fish consumption, as well as maternal prenatal exposure, and grandfather having worked as a fishing guide (G0), both of which are seen to contribute to mothers' childhood Hg (G1) (Figure 1). Mothers' childhood Hg (G1) was then associated with her being diagnosed with at least one neurological disorder, which in turn, was associated with current psychological distress, to which suicidal ideation, over her lifetime, also contributed. The model further suggested an association between mothers' K10 psychological distress score (G1) and child's mental health status (G2), which was linked to the child's emotional state and behavioral problems, which, in turn, may contribute to an increased risk for attempted suicide, particularly among older girls.

A second modeled pathway lead from the father as a fishing guide (G0) (Figure 1) to daughters' fish consumption during pregnancy (G1) and consequently her children's prenatal Hg exposure (G1/G2). Maternal fish consumption during pregnancy (G1/G2) contributed to children's (G2) poor mental health and emotional and behavioral problems, the latter of which was directly associated to attempted suicide.

Another pathway showed associations between the grandfather having been a fishing guide (G0) and mothers' drinking or taking drugs during pregnancy (G1/G2) (Figure 1). The association between mothers' drinking and drugs during pregnancy and child's emotional and behavioral problems was not significant ($p = 0.14$).

For the SEM (Figure 1), power analyses on model misspecification showed that a sample size of 162 children was associated with a power of 71.8%, which was acceptable. Table 4 shows the SEM fit parameters for the final model and the sensitivity analyses

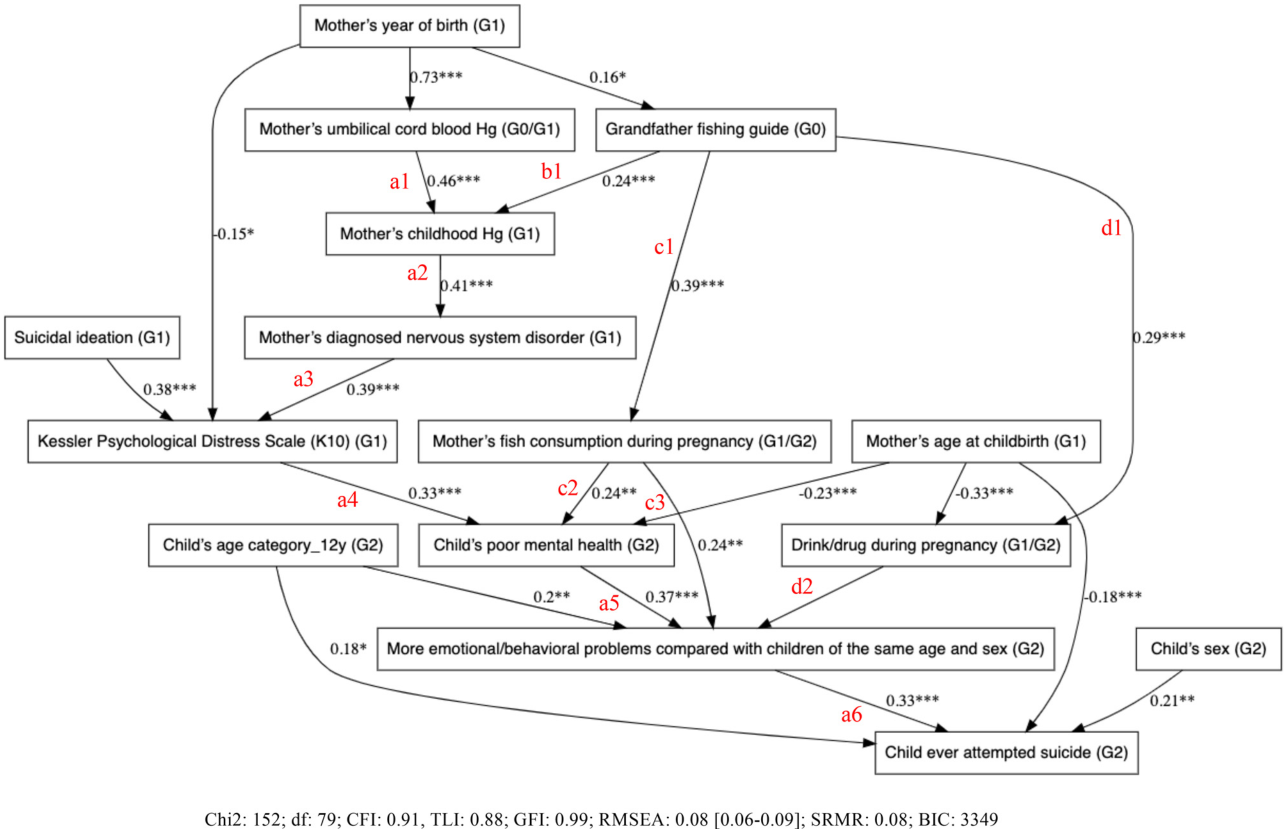

Figure 1. Structural equation model pathway diagram on the psychological impact of Hg exposure through a matrilineal lens across three generations. Intergenerational information, provided by mothers ($n = 80$) for the Grassy Narrows Community Health Assessment provided for 162 children. Mothers' umbilical cord Hg and childhood hair Hg concentrations were estimated from a 1970–1997 biomarker database. Note: BIC, Schwarz's Bayesian information criterion; CFI, comparative fit index; Chi2, chi-square; df, degrees of freedom; GFI, global fit index; Hg, mercury; RMSEA, root mean square error of approximation; SRMR, standardized root mean square residual; TLI, Tucker–Lewis index. p-Values: significance of pathway coefficient estimates: $^{*}p \leq 0.05$; $^{**}p \leq 0.01$; $^{***}p \leq 0.001$.

using maternal childhood fish consumption and a mother-clustered–based model. The performance of the SEM models that *a*) replaced estimated maternal childhood Hg exposure by her reported fish consumption at ∼10 years of age (G1), and *b*) used a mother-clustered–based model, with imputation, were similar.

Estimates of sequential mediation at different stages in the SEM pathways are presented in Table 5, with target effects power analyses simulation for each link. For all pathways toward children and youth (G2) attempted suicide, effects diminished over generations, but remained significant (Table 5). The strongest contributions passed through fish consumption during pregnancy. The pathway that passed through mothers' drinking or taking drugs during pregnancy ($d1 \times d2 \times a6$ in Figure 1) to children's attempted suicide was not significant (coefficient estimate = 0.01; $p = 0.17$).

Finally, children's risk of attempting suicide was significantly influenced by mothers' age at childbirth (Figure 1). The median age at childbirth for mothers of children who attempted suicide was 19.5 y (75th percentile: 22 y), whereas the median age at childbirth of mothers whose child had never attempted suicide was 23 y (75th percentile: 27 y) (Wilcoxon/Kruskal–Wallis chi-square: 12.2; $p = 0.001$).

Tables 1 and 3 include several characteristics that were tested in the SEM, but which were not retained in the final model. For G0, residential school attendance (grandmother and grandfather) did not enter the model ($p > 0.1$). A total of 59 mothers (78.7%) reported that at least one of their parents had attended a residential school; these mothers were significantly older than those whose parents had not been taken to a residential school [median = 36 y (IQR: 31–39 y) vs. median = 28.5 y (IQR: 25–30 y); Wilcoxon chi-square = 19.7; $p < 0.0001$]. For G1, the following variables were tested but did not enter the model ($p > 0.1$): education and school success, currently working, struggle to pay for food, heavy drinking, general health, obesity, at least one chronic health condition, and current fish consumption; for G1/G2: health issues during pregnancy, prematurity, and difficulties during childbirth; for G2: physical health, fish consumption over the past year, and school performance.

Table 4. SEM Fit parameters for the final model, the model with maternal childhood fish consumption and the mother-clustered–based model.

SEM model	Chi2	df	CFI	TLI	GFI	RMSEA (95% CI)	SRMR	BIC
Final model (Figure 1)	161	80	0.90	0.87	0.99	0.08 (0.06, 0.10)	0.09	3,352
Maternal childhood fish consumption	153	80	0.90	0.88	0.99	0.08 (0.06, 0.10)	0.09	3,793
Mother-clustered	201	80	0.86	0.82	0.99	0.10 (0.08, 0.11)	0.09	3,753

Note: BIC, Schwarz's Bayesian information criterion; CFI, comparative fit index; Chi2, chi-square; CI, confidence interval; df, degrees of freedom; GFI, global fit index; RMSEA, root mean square error of approximation; SEM, structural equation model; SRMR, standardized root mean square residual; TLI, Tucker–Lewis index.

Table 5. Estimates of sequential mediation in SEM pathways for Hg exposure across three generations to attempted suicide in children and youth.

	Pathways	Estimate	(95% CI)	p-Value	Power target simulations	
					$n=100$	$n=500$
Toward psychological distress (G1)						
Umbilical cord blood Hg (G0/G1)	a1 × a2 × a3	0.07	(0.02, 0.12)	0.017	1.00	1.00
Childhood Hg (G1)	a2 × a3	0.16	(0.07, 0.25)	0.000	1.00	1.00
Father fishing guide (G0)	b1 × a2 × a3	0.04	(0.01, 0.06)	0.000	0.87	0.91
Toward decreased child's mental health (G2)						
Umbilical cord blood Hg (G0/G1)	a1 × a2 × a3 × a4	0.02	(0.01, 0.04)	0.017	0.99	0.99
Childhood Hg (G1)	a2 × a3 × a4	0.05	(0.02, 0.09)	0.000	0.99	0.99
Fish consumption during pregnancy (G1/G2)	c2	0.24	(0.09, 0.39)	0.000	0.95	0.96
Father fishing guide (G0)	(b1 × a2 × a3 × a4) + (c1 × c2)	0.11	(0.03, 0.18)	0.000	0.90	0.92
Toward child's emotional or behavioral issues (G2)						
Umbilical cord blood Hg (G0/G1)	a1 × a2 × a3 × a4 × a5	0.01	(0.00, 0.02)	0.000	0.95	0.95
Childhood Hg (G1)	a2 × a3 × a4 × a5	0.02	(0.00, 0.04)	0.028	0.96	0.97
Fish consumption during pregnancy (G1/G2)	(c2 × a5) + c3	0.33	(0.15, 0.50)	0.000	0.99	0.99
Father fishing guide (G0)	(b1 × a2 × a3 × a4 × a5) + (c1 × c2 × a5) + (d1 × d2) + c3	0.17	(0.07, 0.27)	0.000	0.99	0.99
Toward child's attempted suicide (G2)						
Umbilical cord blood Hg (G0/G1)	a1 × a2 × a3 × a4 × a5 × a6	0.00	(0.00, 0.01)	0.010	0.73	0.77
Childhood Hg (G1)	a2 × a3 × a4 × a5 × a6	0.01	(0.00, 0.01)	0.044	0.83	0.85
Fish consumption during pregnancy (G1/G2)	(c2 × a5 × a6) + (c3 × a6)	0.11	(0.03, 0.19)	0.017	0.96	0.97
Father fishing guide (G0)	(b1 × a2 × a3 × a4 × a5 × a6) + (c1 × c2 × a5 × a6) + (d1 × d2 × a6) + (c1 × c3 × a6)	0.06	(0.01, 0.10)	0.017	0.97	0.99

Note: Pathways with "a" originated from mothers' umbilical cord blood Hg; Pathways with "b," "c," or "d" originated from grandfather a fishing guide. Hg, mercury; SEM, structural equation modeling. p-Values adjusted on bootstrap: significance of pathway coefficient estimates: $^{*}p \le 0.05$; $^{**}p \le 0.01$; $^{***}p \le 0.001$.

Table S2 presents a series of multiple regression models for the various components of the SEM pathways, without mediating variables. The results support the direct associations computed by the SEM.

Discussion

This study, which examined a matrilineal linkage over three generations, suggests an intergenerational impact of Hg exposure on Grassy Narrows First Nation children's emotions and behavior and attempted suicides. Mothers who participated in the GN-CHA provided information on their parents and children. Most of these women, born between 1962 and 1993, were exposed to Hg prenatally and as children, teenagers, and adults. During the years when Hg exposure was at its highest, their families suffered the dramatic consequences of the loss of their Indigenous culture and values, as well as their traditional food and livelihood.[1–6] In the absence of information on exposure of the grandparent generation (G0), we used the maternal father's occupation as a fishing guide as a proxy for grandfathers' high Hg exposure, based on biomonitoring data.[13,14] Maternal umbilical cord blood Hg (G0/G1) reflected grandmothers' Hg exposure through fish consumption during pregnancy.

The point of departure for the study was the prevalence of attempted suicide among today's children and youth. Mothers reported that 27.4% of adolescents ($n=17$) had attempted suicide at least once: girls ($n=14$; 41.2%) and boys ($n=3$; 10.7%). These prevalences are considerably higher than those reported in the most recent First Nation and Regional Health Survey,[63] administered to 4,639 First Nation youth at the same period as the GN-CHA, in which 10.3% reported ever attempting suicide (15.6% of girls and 5.2% of boys).

In the SEM of the present study, several pathways linked grandparents (G0) Hg to an increased risk of attempted suicide for G2 children and youth. The pathway through mothers' (G1) childhood Hg exposure was mediated by her umbilical cord blood Hg concentration (G0/G1) and having a father a fishing guide (G0), both of which likely reflect grandparents fish consumption and Hg exposure. Mothers' (G1) childhood Hg exposure was directly associated with having at least one nervous system disorder, which, in turn, was associated with her current psychological distress. These findings are consistent with studies that have examined Hg exposure and psychological distress. Using the General Health Questionnaire (GHQ), a study in Japan reported a high prevalence of psychological distress among 86% of 133 women ≥40 years of age living in the Minamata area, where they were exposed to Hg as children.[64] In a recent study of an Indigenous community in the Brazilian Amazon, hair Hg among persons 12–72 years of age [mean age 27.4 y ($n=109$)] was associated with depressive symptoms, as assessed with the Geriatric Depression Scale Short Form; persons with hair Hg ≥10 μg/g were 1.8 times more likely to manifest depressive symptoms.[65] In the GN-CHA, one mother in five reported a high level of psychological distress on the Kessler Psychological Distress Scale. This is consistent with Harada's observations in 2010 where 20% of 73 Grassy Narrows examinees manifested signs and symptoms of emotional disturbances.[19] In the present study, maternal psychological distress score was associated with child's poorer health. This association has been observed in many studies that have linked mothers' psychological distress to their children's mental health status.[66,67]

Based on the SEM, the strongest contribution of G0 on G2 was through grandfather's influence on mothers' fish consumption during pregnancy, suggesting that the tradition of fish consumption is passed on from father to daughter. Indeed, women who consumed fish as children, tended to consume fish as adults. Grassy Narrows elder J.D.S., co-investigator on the present study, notes that: "fish has always played a vital role in Anishinaabek natal traditions. The grandmothers used to say, 'Eat fish broth, and the breast milk will come out.'" In 2005, Chan et al.[68] reported a very high correlation between local fish consumption and hair Hg concentrations in Grassy Narrows; for women of child-bearing age (18–40 y), the average fish intake varied by season and was highest during the summer months (~ 28 g/d) and lowest during the winter months (~ 2 g/d). In 2010, Neff et al.,[10] who analyzed Hg concentrations in fish in the English–Wabigoon River system, indicated that they had not declined significantly since the mid-1980s and may still present a potential health risk to humans.

In the SEM, maternal fish consumption during pregnancy (G1/G2), an indicator of prenatal MeHg exposure, was the major contributor to children's mental health and emotional state and behavior, suggesting that at recent fish Hg concentrations, MeHg was affecting fetal development. MeHg is actively transported across the placenta and its concentration in umbilical cord blood has been measured to be ~ 1.7 times (95th percentile: 3.4) that of maternal blood.[29,69,70] Several studies have reported an association between prenatal Hg exposure and anxiety-related symptoms in children or adolescents.[18,31,71–73] These findings are supported by recent imaging studies of prefrontal brain areas of Inuit adolescents.[74] For the children and youth in the present study, there was a direct association between emotional state and behavioral problems and attempted suicide.

The SEM results suggested that despite the absence of specific information on G0 or about the trauma suffered by mothers (G1) during their own childhood or adolescence, a pathway linked grandfather having been a fishing guide to mothers' drinking or taking drugs during pregnancy. The vivid descriptions of life in Grassy Narrows in the years of the highest Hg exposures and the socioeconomic and cultural trauma suggest that the context in which these women were raised would be an important determinant of their adolescent and early adult behavior. Negative childhood experiences have been associated with early alcohol drinking.[75] In the present study, drinking alcohol or taking drugs was more prevalent during pregnancies at a younger age [≤ 20 years of age; $n = 14$ of 44 (31.82%)], compared with 10 of 114 (8.8%) for pregnancies at an older age. Although the GN-CHA did not specify the quantity of alcohol or drugs absorbed during pregnancy, the percentage of children whose mother drank or took drugs during her pregnancy (15.2%, $n = 24$) was inferior to the prevalence for First Nations' pregnancies in Canada, estimated in a systematic review of six studies[76]: 36.5% for drinking and 22.1% for binge drinking during pregnancy.

The possible interaction between MeHg and ethanol has been examined in animal models.[77–80] In one study, ethanol lowered Hg accumulation in the prefrontal and motor cortex of mice that were administered chronic low doses of MeHg and ethanol equivalent to binge drinking; the authors suggest that ethanol intake could reduce central nervous system Hg levels associated with psychiatric and cognitive disorders in MeHg-intoxicated individuals.[80] Future studies in communities with high Hg exposure might consider addressing whether drinking might relieve or aggravate Hg-related symptoms.

In the present study, an inverse relation was observed between mothers' age at childbirth and children's attempted suicide. This is consistent with the findings of a systematic review and meta-analysis of attempted suicide in relation to *in utero* and perinatal factors, in which teenage pregnancy was identified as an important risk factor.[81] The review did not include environmental toxic exposures.

The GN-CHA focused primarily on current health, socioeconomic conditions, and well-being and as a result, no specific information was available on each mother's (G1) possible adverse experiences earlier in her life. The descriptions of psychological suffering in this community following the Hg discharge[1–9] resemble those of other environmental disasters, such as the *Deepwater Horizon* spill, where an increase in domestic partner fights, depression, memory loss, and inability to concentrate was reported for wives of clean-up workers 2 y after the spill.[82] Palinkas et al.[83] reported that the decline in subsistence activities was an important risk factor for post-traumatic stress disorder in Alaska Natives affected by the *Exxon Valdez* oil spill. Furthermore, children who lived closer to the *Hebei Spirit* oil spill in Korea, presented a higher prevalence of depressive symptoms compared with those who lived farther away.[84] The authors mention that adult suicides increased following the spill and suggested that parent psychopathology subsequent to a disaster influences children's psychological health.[84]

At the time of the GN-CHA, Statistics Canada reported that suicide risk among First Nation adults was three times higher than among the non-Indigenous population.[62] The GN-CHA use of the same questions as the First Nations Regional Health Survey 2008/2010,[33] administered to 11,043 First Nation adults from 216 communities in Canada, allowed us to compare Grassy Narrows with other First Nation communities. In the First Nations Regional Health Survey 2008/2010,[33] 11.8% of participants reported that a close friend or family member had committed suicide in the previous year. In the GN-CHA, 27 (36%) of the 75 mothers (G1) who answered this question responded in the affirmative. The prevalence of both suicidal ideation and attempted suicide during one's lifetime for mothers in the present study was also considerably higher compared with those of other First Nations in Canada who were 18–39 y old at the time of the survey[33]: Fifty percent ($n = 40$) among the mothers of Grassy Narrows, compared with 22% in First Nation communities in Canada, and 40% ($n = 32$) vs. 13.1%, respectively.[33]

Although prenatal Hg exposure was associated with emotional and behavioral problems and attempted suicide in today's children and youth (G2), this relation was not observed for their mothers (G1). Several reasons possibly explain this difference. For the mothers (G1), no individual information was available for other lifetime factors that could have contributed to suicidal ideation or attempted suicide, notably the breakdown of the mother's family in the years following the discharge; some families would have had more difficulty coping than others. Many historic descriptions of Grassy Narrows underline the high prevalence of successful suicides,[1,2,4,5] but no studies were performed on their possible relation to prenatal or childhood Hg exposure or whether their fathers (G0) had been fishing guides. A previous study in Grassy Narrows has linked higher lifetime Hg exposure with premature death ($n = 154$ of 222).[16] It is possible that women with higher exposures may have died prior to the GN-CHA.

Although we cannot go back in time, we can certainly ask about the possible contribution of very high concentrations of prenatal and childhood Hg to the dramatic increase in youth suicide during the 10–12 y following the discharge of extremely high levels of Hg. Erikson,[4] who visited Grassy Narrows in 1979, reported that in the 11 months between 1977 and 1978, 26 young people between the ages of 11 and 19 years had attempted suicide.[4] In the same chapter, he provided a description of Hg poisoning that included "depression and apathy, memory loss and . . . explosive shifts in mood", but then went on to explain how alcohol and "the way in which the Ojibway raise their children" accounted for the striking disorder in this community. In all the accounts of social disruption in the Grassy Narrows disaster, no one seriously considered whether Hg exposure may be a contributing factor, and no one considered whether drinking might relieve or aggravate Hg-related symptoms.

In the present study, we examined the possible contribution of family members having been placed in a residential school, but these variables were not retained in the SEM pathways. This may be due to the lack of variance given that almost 80% ($n = 59$) of 75 mothers reported that at least one of their parents had attended a residential school and they were significantly older than those whose parents had not been placed in a residential school.

There are important limitations to the present study owing to limited data availability. Generational SEM is inherently complex and, in the present study, this was compounded by the small size of the population, paucity of information on G0 and G1's early childhood experiences, and missing data. This is, indeed, a relatively small community; the census data for 2016 indicates that in Grassy Narrows, there were 160 women between the ages of 20 and 54 y and 175 children 5–19 years of age.[32] No specific information was available on individual grandfather's (G0) Hg exposure and behavior in the years following the discharge, and we relied on published reports and descriptions.[1–6,14] Information on mothers' childhood (G1) was limited to her childhood fish consumption, her father working as a fishing guide, and schooling and school performance. Missing Hg exposure data were handled using estimates, based on larger measurements.[16,20] Children's mental health was not assessed, but relied on mothers' perception. All of these factors contributed to limiting model performance. To ensure the performance of the SEM, we used a series of statistical techniques to address different types of error, and power analyses. We tested the reliability of the pathways, using a different childhood exposure variable (maternal fish consumption at 10 years of age) and mother-clustered–based modeling. The strengths of the associations were verified using logistic regression models without mediating variables. Although not perfect, the final SEM provided a plausible portrait of the contribution of Hg effects over three generations.

Although social disruption certainly played an important role in the psychological well-being of the people of Grassy Narrows First Nation following the disaster,[1–6] the findings of the present study suggest that Hg exposure over three generations likewise contributed to their mental health. However, to our knowledge, no study has carefully addressed the possible positive psychological impact on this community's fortitude and resilience over the past decades. In the mid-1970s, Grassy Narrows initiated demonstrations and then legal proceedings to obtain compensation for the harm that was done to their community.[1–3] In 1975, community members worked with M. Harada and his team from Japan to document their neurological health,[19] and since that time the community has maintained close relations with the Japanese physicians, who have carried out several series of examinations.[85] Over the past 50 y, successive Chiefs and Council and grassroots Grassy Narrows people have worked with scientists for Hg remediation[86,87] and protection of their territory.[9] Their actions are marked by memoirs to federal and provincial parliaments, demonstrations, a hunger strike, and the longest blockade in Canada to stop logging on their territory.[79] Willow, writing about the blockade, stated: "The story of the Grassy Narrows blockade cannot be understood apart from the community's multigenerational struggle to endure in the face of political, cultural, and environmental colonization."[88]

After several years of community lobbying of government ministries, Grassy Narrows First Nation obtained funding for their community health assessment, as well as access to their own historic Hg exposure data. This study was only possible through the leadership of Grassy Narrows First Nation and collaboration with an academic research team, based on the principles of ownership, control, access, and possession of First Nations' data [OCAP, a registered trademark of the First Nations Information Governance Centre (FNIGC)].[89] Several authors have aptly pointed out that Indigenous leadership throughout the research process is key to decolonizing health research.[90,91]

Understanding the intergenerational harm that was done to the people of Grassy Narrows should serve to support efforts to restore the health and well-being that this community enjoyed prior to the discharge of Hg into the river system of their traditional territory. From a public health perspective, a community-based interdisciplinary approach[92,93] would be useful to understand and act upon the social, economic, historical, cultural, physiological, and psychological consequences of this and other environmental disasters.

Acknowledgments

D.M. was invited by the Grassy Narrows First Nation as scientific advisor for the GN-CHA. She collaborated on study design, questionnaire content, data analyses, and preparing reports. She is principal investigator and main author of the present research. A.P. created the database, determined the statistical approaches and performed the analyses. She co-wrote the manuscript with D.M. M.F. participated in the analyses and dissemination of the GN-CHA. She participated in the writing and editing of the manuscript. J.D.S. is the initiator and organizer of the GN-CHA survey. She shared information on the history and context across generations and participated in data interpretation. All authors read and approved the final manuscript.

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Ethics approval for the GN-CHA was obtained from the Manitoulin Anishinaabek Research Review Committee (MARRC), who issued an ethics certificate on 11 November 2016. The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the institutional review board of the Université du Québec à Montréal (2016_e_1350; 6 September 2016) and Health Canada Research Ethics Board (REB 2017–0006; 3 August 2017).

Informed consent forms were signed by all participants. Consent included survey participation and the linking of the information from the GN-CHA to data obtained from previous surveillance programs or studies of Hg exposure.

The data sets generated and analyzed in the present study are the property of the Grassy Narrows First Nation. Permission for use of the data lies with the Grassy Narrows Chief and Council.

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