# Pesticides and human health

## Part 2: PEI health and pesticide use

2015

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# 2 Executive summary

Using data from a variety of sources, we focused on identifying the prevalence or incidence rates of health conditions identified in our systematic review (Part 1) as related to pesticides used in quantities greater than 1,000kg per year in Prince Edward Island (PEI). Only health effects that had a Grade A level of association were considered.

After identifying the appropriate rate for the health conditions of interest, the Population Attributable Fraction (PAF) was calculated. The PAF can be defined as the "proportional reduction in average disease risk over a specified time interval that would be achieved by eliminating the exposure of interest from the population while distributions of other risk factors in the population remain unchanged".

We used an adapted risk assessment approach to standardize and quantify the level of risk for Islanders as a population related to pesticide exposure for each outcome considered. The risk was calculated by multiplying the PAF by the average incidence or prevalence rate of the condition on PEI and was then described using standardized terminology.

The health outcomes considered are described below.

## 2.1 Reproductive outcomes

- The incidence of cleft palate in PEI is similar to the Canadian rate.
- The relationship between *maternal occupational agricultural pesticide exposure* and cleft palate has been evidenced in the literature.
- An extremely low reduction in average population cleft palate risk may be achieved by eliminating maternal agricultural exposure to pesticides on PEI.

## 2.2 Neurological outcomes

### 2.2.1 Parkinson's disease

- The prevalence of Parkinson's disease (PD) in PEI is similar to the Canadian prevalence.
- The association between *agricultural employment* and PD has been evidenced in the literature. *Any pesticide exposure* has also been associated with PD in one meta-analysis.
- An extremely low (female) to very low (male) reduction in average population PD risk may be achieved by eliminating agricultural pesticide exposure on PEI. A very low (female to male) to low (male) reduction in average population PD risk may be achieved by eliminating general exposure to pesticides on PEI.

### 2.2.2 Amyotrophic Lateral Sclerosis

- The incidence of Amyotrophic Lateral Sclerosis (ALS) in PEI and Canada does not differ.
- The association between *agricultural pesticide exposure* and ALS was documented in one meta-analysis.
- A negligible reduction in average population ALS risk may be achieved by eliminating agricultural exposure to pesticides on PEI.

## 2.3 Oncological outcomes

### 2.3.1 Adult

#### *2.3.1.1 Lymphohematopoietic cancers*

- Several meta-analyses evidenced the association between lymphohematopoietic cancers and *agricultural occupational pesticide exposure*.
- The incidence of Non-Hodgkin's Lymphoma (NHL) is similar between PEI and Canada.
- A negligible (female) to extremely low (men) reduction in average population NHL risk may be achieved by eliminating agricultural exposure to pesticides on PEI.
- The incidence of leukemia (all types) is similar between PEI and Canada.
- A negligible (female) to extremely low (men) reduction in average population Acute Myeloid Leukemia (AML) risk may be achieved by eliminating agricultural exposure to pesticides on PEI. This is an over estimate of the true risk.
- An extremely low reduction in average male population Chronic Myeloid Leukemia (CML) risk may be achieved by eliminating agricultural exposure to pesticides on PEI. This is also an over estimate of the true risk.

#### *2.3.1.2 Melanoma*

- The average annual incidence of melanoma in PEI is slightly higher than the Canadian incidence.
- Melanoma risk estimates were sourced from a high quality review article and pertains to *agricultural occupational exposure***.**
- A negligible to extremely low reduction (female) and negligible to very low reduction (male) in average population melanoma risk may be achieved by eliminating agricultural exposure to pesticides.

### 2.3.2 Children

- The provincial incidence of childhood cancers is extremely small. Canadian incidence rates have been used as a proxy measure as it is assumed that PEI rates are similar.
- The pediatric risk estimates for childhood cancers have been evidenced from the literature in four meta-analyses.

#### *2.3.2.1 Lymphoma*

- A negligible to extremely low reduction in average population childhood lymphoma risk may be achieved by eliminating exposure to various pesticides.

#### *2.3.2.2 Leukemia*

- A negligible to very low reduction in average population childhood leukemia risk may be achieved by eliminating various exposure to pesticides including *parental occupational agricultural exposure* and *general parental* and *childhood pesticide exposures*.

#### 2.3.2.3 Brain cancer

- A negligible to extremely low reduction in average population childhood brain cancer risk may be achieved by eliminating *exposure to various pesticides*. A negligible reduction in average population childhood brain cancer risk may be achieved by eliminating *paternal occupational agricultural exposure* to pesticides in PEI.

#### 2.3.2.4 Neuroblastoma

- A negligible to extremely low reduction in average population pediatric neuroblastoma risk may be achieved by eliminating *childhood exposure* to pesticides in PEI.

#### 2.3.2.5 Ewing sarcoma

- A negligible reduction in average population pediatric Ewing sarcoma risk may be achieved by eliminating *general childhood* or *paternal agricultural occupational exposure* to pesticides on PEI.

## 2.4 Conclusion

**All health outcomes identified in the systematic review (Grade A association and >1,000 kg/yr pesticide sales) exhibit incidence/prevalence rates in PEI that are similar to Canadian rates.**

The population risk reduction was calculated using the appropriate rate for the health condition and the PAF. The PAF was calculated using risk estimates from high quality studies that had been identified during the systematic review.

**Disease specific risk reduction ranges from *negligible* to *low* with most diseases falling in the *negligible* to *extremely low* classification.**

**Based on the current review, pesticides used in PEI following "labeled-practices" do not pose a significant public health risk.**

The systematic review should be updated periodically to ensure recent evidence is incorporated into assessing risk to Islanders.

# 3 Introduction and methods

In Part 2 of the Pesticides and human health project, we focus on relating the findings from the systematic literature review completed in Part 1 to the health outcomes of Islanders.

Using data from a variety of sources, we focused on identifying the prevalence or incidence rates of conditions identified in Part 1 as related to pesticides used in quantities ≥1,000 kg/year on Prince Edward Island (PEI). Only health effects that had a Grade A level of association were considered.

After identifying the appropriate rate for these health conditions on PEI, we calculated the Population Attributable Fraction (PAF). The PAF can be defined as the "proportional reduction in average disease risk over a specified time interval that would be achieved by eliminating the exposure of interest from the population while distributions of other risk factors in the population remain unchanged".(1)

The PAF was calculated using the following formula

$$PAF = \frac{p_e(RR-1)}{p_e(RR-1)+1}$$

where $p_e$ is the proportion of the source population exposed to the factor of interest and RR[1] is the risk or rate ratio.(1)

We have presented the PAF as a percentage to ease interpretation.

We used an adapted risk assessment approach to standardize and quantify the level of risk for Islanders related to pesticide exposure for each outcome considered.(2)

The population of PEI from 2003 until 2013 was estimated using data from Statistics Canada. Each PAF estimated was based on the applicable population for the year of the estimated incidence rate. When the presented incidence rate was averaged over several years, the PEI population was also averaged over those same years.(3)

Each section will detail how we estimated the proportion of the population at risk for exposure. For occupational exposure data, we used information on employment in agriculture to estimate the number of exposed individuals. This was done because the majority of pesticide exposure, particularly in PEI where there are no large pesticide manufacturing or processing facilities, is in the agricultural sector. Unfortunately, there was no more detailed exposure information available about occupational pesticide exposure. Actual pesticide exposure within the agricultural sector will vary considerably depending on specific farm practices and other factors. Age groupings available for this information were 15 to 24 years, 25 to 54 years and 55 years and up.(4)

[1] RR (Risk Ratio) is the ratio of the risk of disease in the exposed group to the risk of disease in the non-exposed group.

For residential pesticide exposure, the impact of pesticide exposure clearly depends heavily on the individual use by Islanders. For calculation purposes, we have made the assumption that residential pesticide use in PEI is similar to that from a recent Ontario survey by Sritharan et al. (2014). Sritharan et al. (2014) estimated that between 10.9 and 32.7 percent of the population in the Timiskamig and Peel regions used insecticides at their current home or residence.(5) We have calculated the PAF with a range of exposed population from 10.9 to 32.7%.[2]

The level of risk was calculated by multiplying the PAF by the average incidence or prevalence rate of the condition on PEI and was then described using standardized terminology.(6)Table 1 defines the risk descriptions.

**Table 1. Risk definitions**

| Risk | Description |
|---|---|
| 1 in a million ($10^{-6}$) | Negligible |
| 1 in 100,000 ($10^{-5}$) | Extremely Low |
| 1 in 10,000 ($10^{-4}$) | Very Low |
| 1 in 1,000 ($10^{-3}$) | Low |
| 1 in 100 ($10^{-2}$) | Medium |
| 1 in 10 ($10^{-1}$) | High |

## 3.1 Outcomes considered

We considered outcomes in Part 2 that had Grade A evidence for the relationship between pesticide exposure and the outcome. We also limited the outcomes to those related to pesticides used in quantities of more than 10,000kg per year in PEI using the most recent available sales data.(7) Table 2 combines the evidence from the recent literature review with the latest available pesticide sales information from PEI. The underlined outcomes represent pesticides, pesticide classes, types or specific pesticides sold at volumes of more than 10,000kg per year using available data in PEI.

We focused on those underlined outcomes that could be or were previously measured using provincial health data where possible.

Assumptions

- Due to a lack of refined data about agricultural exposure in PEI, ALL agricultural workers were considered exposed to pesticides. This overestimates the number of exposed agricultural workers and could be considered a worst-case scenario. Residential pesticide exposure in PEI was unknown. Results from an Ontario survey were used to estimate the proportion of the population exposed to residential pesticides (10.9-32.7%).
- Rates for pediatric cancers were estimated using national incidence rates as a proxy for provincial data because the PEI incidence rates were so small given the rarity of some of the cancers.
- Consequences for all diseases were not considered in the risk estimate.
- Only human health effects were considered in this review.

[2] There was no information pertaining to residential herbicide or fungicide use. We acknowledge that it is very unlikely that residential fungicide use would fall into the range cited (10.9-32.7%), however it was used as a proxy exposure level due to lack of data. It is likely an over-estimate.

**Table 2. Grade A research findings for any pesticide, pesticide class or pesticide type**

| Exposure | | Outcome | |
|---|---|---|---|
| Any pesticide | Any | Cleft palate | NHL in adults |
| | | PD | Lymphoma, brain cancer, Ewing's sarcoma & neuroblastoma in children |
| | | ALS | |
| | | ML in adults | AML in children |
| | | CML in adult men | Childhood leukemia |
| | | LHC in adults | Cutaneous melanoma |
| Pesticide class | Insecticide | Lymphoma & brain cancer | Childhood leukemia |
| | Herbicide | Childhood leukemia | |
| | Fungicide | Lymphoma & brain cancer | |
| | Solvents | PD | |
| Pesticide type | Organophosphates | Decreased short-term memory, increased reaction time and increased risk of impaired mental development or pervasive developmental problems in children | Increased mental and emotional problems in adolescents |
| | | | Increased number of abnormal reflexes in newborns |
| | | | NHL |
| | Organochlorines | NHL | |
| | Carbamates and thiocarbamates | NHL | |
| | Triazines and triazonines | NHL | |
| | Phenoxys | NHL | |
| Specific pesticides or applications | Paraquat | PD | |
| | Maneb/mancozeb | PD | |
| | Heptachlor | Breast cancer | |
| | Lindane | NHL | |
| | Dicambia | NHL | |
| | 2,4-D | NHL | |
| | Carbaryl | NHL | |
| | Carbofuran | NHL | |
| | Glyphosphate | NHL | |
| | Diazinon | NHL | |
| | Malathion | NHL | |
| | Pentachlorophenol | STS | |
| | Trans-nonachlor | Diabetes | |
| | Oxychlordane | Diabetes | |
| | Specific application (agricultural worker) | Leukemia | |

PD: Parkinson's Disease ALS: Amyotrophic Lateral Sclerosis ML: Myeloid leukemia CML: Chronic Myeloid Leukemia LHC: Lymphohematopoietic Cancer NHL: Non-Hodgkin Lymphoma AML: Acute Myeloid Leukemia STS: Soft Tissue Sarcoma
Pesticides (more than 1,000kg per year sold in PEI) from available data (7)

# 4 Reproductive outcomes

## 4.1 Cleft palate

The association between maternal occupational agricultural pesticide exposure and cleft palate was based on the meta-analysis by Romitti et al. (2007).(8)

The incidence of cleft palate was provided using data from the PEI Perinatal Database. The incidence of cleft lip with or without cleft palate in PEI is 0.71 per 1,000 births and this is similar to the Canadian incidence of 0.82.(9) The incidence of cleft palate alone in PEI is 0.54 per 1,000 births and again is similar to Canada (0.58).(9)

Based on years where data was available, information from 2003, 2008, 2011 and 2012 was considered. To estimate the exposed population, we calculated the average number of females aged 15 to 54 years in PEI in each year of available data. Then we used information about the average number of female agricultural workers aged 15 to 54[3] years in each year of available data to estimate the proportion of the female population 15 to 54 years potentially exposed to pesticides. Finally we multiplied the proportion of the exposed female population by the number of births in each year to obtain the number of potentially exposed births.

**Table 3. PEI cleft palate incidence and maternal agricultural pesticide exposure**

| | | **Inputs** |
|---|---|---|
| Annual births (Average) | | 1400 |
| Annual births exposed (Average) | | 21 |
| Incidence cleft lip +/- cleft palate (per 1,000 births) | PEI | 0.71 |
| | Canada (9) | 0.82 |
| Incidence cleft palate (per 1,000 births) | PEI | 0.54 |
| | Canada (9) | 0.58 |
| Any pesticide(8) (RE[1] [95% CI[2]]) | | 1.37 [1.04-1.81] |
| | | **Output** |
| **PAF[3](%)** | | **0.5** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

The PAF of pesticides and cleft palate is 0.5% in PEI, meaning that 0.5% of the cleft palate in the population was attributable to maternal agricultural pesticide exposure.

An *extremely low reduction* in average population cleft palate risk may be achieved by eliminating maternal agricultural exposure to pesticides on PEI.

[3] It is recognized that this age group is large for the childbearing years, however it was the age grouping from the agricultural dataset.

# 5 Neurological outcomes

## 5.1 Parkinson disease

The association between Parkinson disease (PD) and pesticide exposure was evidenced by several meta-analyses.(10–12) Both Pezzoli and Cereda (2013) and van der Mark (2012) provided estimated risks based on agricultural exposures.(10,11) For these studies, the population at risk was the population employed in agriculture for a given year. The third meta-analysis by Noyce focused on risk estimated for any pesticide exposure.(12)

The prevalence and incidence of PD on PEI was estimated using administrative data for 2011.The prevalence of PD in 2011 on PEI was 1.49 per 1,000 and this was similar to the prevalence of 1.70 per 1,000 in Canada in 2010/2011.(13)

**Table 4. PEI Parkinson disease and agricultural pesticide exposure by sex, 2011**

| | | Inputs | |
|---|---|---|---|
| | | **Men** | **Women** |
| Exposed population (2011) | | 2,900 | 700 |
| Total population (2011) | | 58,530 | 62,334 |
| PEI annual incidence rate per 100,000 population | | 57 | 28 |
| PEI 2011 prevalence (per 1,000 population) – both sexes | | 1.49 | |
| Canada 2010-11 prevalence (per 1,000 population) – both sexes(13) | | 1.70 | |
| Any pesticide (10)(RE[1] [95% CI[2]]) | | 1.58 (1.34-1.86) | |
| Any pesticide (11) (RE[1] [95% CI[2]]) | | 1.62 (1.40-1.88) | |
| Maneb/Mancozeb (10) (RE[1] [95% CI[2]]) | | 2.18 (1.19-3.98) | |
| | | **Output** | |
| | | **Men** | **Women** |
| **PAF[3] (%)** | **Any pesticide (10)** | **2.8** | **0.6** |
| | **Any pesticide (11)** | **3.0** | **0.7** |
| | **Maneb/Mancozeb (10)** | **5.5** | **1.3** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

**Table 5. PEI Parkinson disease and any pesticide exposure by sex, 2011**

| | Inputs | |
|---|---|---|
| | **Men** | **Women** |
| Range of exposed population (2011)* | 6,380-19,139 | 6,794-20,383 |
| Total population (2011) | 58,530 | 62,334 |
| PEI annual incidence rate per 100,000 population | 57 | 28 |
| PEI 2011 prevalence (per 1,000 population) – both sexes | 1.49 | |
| Canada 2010/11 prevalence(per 1,000 population)– both sexes(13) | 1.70 | |
| Any pesticide (12) (RE[1] [95% CI[2]]) | 1.77 (1.48-2.12) | |
| | **Output** | |
| | **Low (10.9%)** | **High (32.7%)** |
| **PAF[3] (%)** | **7.7** | **20.1** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

The PAF varies between 0.6 and 1.3% for women and 2.8 to 5.5% for men for agricultural pesticide exposures, depending on the specific type of pesticide exposure, meaning that between 0.6% and 5.5% of the PD in the population may be attributed to agricultural pesticide exposure. The PAF for general pesticide exposure is estimated to be between 7.7 and 20.1%, meaning that between 7.7 and 20.1% of the PD in the population may be attributed to general pesticide exposure.

An *extremely low* (female) to *very low* (male) reduction in average population PD risk may be achieved by eliminating agricultural exposure to pesticides on PEI. A *very low* (female and male) to *low* (male only) reduction in average population PD risk may be achieved by eliminating general exposure to pesticides on PEI.

## 5.2 Amyotrophic Lateral Sclerosis

The association between Amyotrophic Lateral Sclerosis (ALS) and agricultural pesticide exposure was based on one meta-analysis.(14)

The PEI incidence rate was not available because the incidence was less than 10 cases per year. The Canadian prevalence is 10 cases per 100,000.(13) The calculations below were completed assuming 5 cases per year in PEI.

**Table 6. Estimated PEI ALS and agricultural pesticide exposure, 2011**

| | **Inputs** |
|---|---|
| Exposed population (2011) | 3,600 |
| Total population (2011) | 120,864 |
| PEI incidence rate per 100,000 population | 4.0 |
| Canada prevalence rate per 100,000 population (13) | 10 |
| Any pesticide (14) (RE[1] [95% CI[2]]) | 1.9 (1.1-3.1) |
| | **Output** |
| **PAF[3] (%)** | **2.6** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction ALS:Amyotrophic Lateral Sclerosis

The PAF for ALS was 2.6% meaning that 2.6% of ALS in the population may be attributed to pesticide exposure.

An *negligible* reduction in average population ALS risk may be achieved by eliminating agricultural exposure to pesticides on PEI.

# 6 Oncological outcomes

Cancer incidences for adult cancers in PEI were available from the Canadian Cancer Society's annual Canadian Canada Statistics publications from 2004 to 2013. These publications were accessed and the actual incidence rates (2004, 2005, 2006, 2008, and 2010) and estimated incidence rates (2007, 2009, 2011, 2012 and 2013) were used to calculate 10-year average incidence rates for NHL, melanoma and leukemia.(15–25) A 10-year average was used to smooth out the large variations in rates of cancers that exist in a small population. The average PEI population during the 10-year period from 2004 to 2013 was also used in the PAF calculation. All incidence reported in the oncological outcome section are age standardized to the 1991 Canadian population.

## 6.1 Adults

Three meta-analyses reviewed the association of adult lymphoma and leukemia and pesticide exposure and were the source of the adult risk estimates. (26–28)

### 6.1.1 Lymphohematopoietic cancers

The overall incidence of Lymphohematopoietic Cancers (LHC), which includes all types of lymphoma and leukemia, was not available for PEI or for Canada. Specific LHC cancer PAFs are considered within the next three sections: Non-Hodgkin Lymphoma (NHL), Acute Myeloid Leukemia (AML) and Chronic Myeloid Leukemia (CML).

#### *6.1.1.1 Non-Hodgkin lymphoma*

Based on recent PEI health trend reports, NHL accounts for 3% of all incident cancers among men.(29) The 10-year average annual incidence rate in PEI is 19.4 per 100,000 for men and 12.9 for women, similar to the Canadian rates (19.7 and 14.3).

**Table 7. PEI adult NHL and agricultural pesticide exposure by sex, 2004-2013**

| | | | Inputs | |
|---|---|---|---|---|
| | | | **Men** | **Women** |
| Average exposed population | | | 2,840 | 760 |
| Total average population | | | 56,674 | 60,378 |
| Annual incidence rate per 100,000 population | | PEI | 19.4 | 12.9 |
| | | Canada | 19.7 | 14.3 |
| Any pesticide (26) (RE[1] [95% CI[2]]) | | | 1.3 (1.2-1.5) | |
| Organophosphate insecticides (27) (RE[1] [95% CI[2]]) | | | 1.6 (1.0-1.4) | |
| Triazine herbicides (27) (RE[1] [95% CI[2]]) | | | 1.5 (1.0-2.1) | |
| Glyphosphate herbicides (27) (RE[1] [95% CI[2]]) | | | 1.5 (1.1-2.0) | |
| 2,4-D (27) (RE[1] [95% CI[2]]) | | | 1.4 (1.0-1.9) | |
| Carbofuran (27) (RE[1] [95% CI[2]]) | | | 1.6 (1.2-2.3) | |
| Diazinon (27) (RE[1] [95% CI[2]]) | | | 1.6 (1.2-2.2) | |
| | | | **Output** | |
| | | | **Men** | **Women** |
| **PAF[3] (%)** | **Any pesticide (26)** | | **1.7** | **0.4** |
| | **Organophosphate insecticides (27)** | | **2.9** | **0.7** |
| | **Triazine herbicides (27)** | | **2.4** | **0.6** |

| | | |
|---|---|---|
| **Glyphosphate herbicides (27)** | **2.4** | **0.6** |
| **2,4-D (27)** | **2.0** | **0.5** |
| **Carbofuran (27)** | **2.9** | **0.7** |
| **Diazinon (27)** | **2.9** | **0.7** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction NHL: Non-Hodgkin Lymphoma

The PAF for various agricultural pesticide exposures ranges from 0.4 to 0.7% for women and 1.7 to 2.9% for men. This means that up to 0.7% and 2.9% of the NHL in the female and male populations may be attributed to agricultural pesticide exposure.

A *negligible* (female) to *extremely low* (male) reduction in average population NHL risk may be achieved by eliminating agricultural exposure to pesticides on PEI.

#### *6.1.1.2 Leukemia (including acute and chronic myeloid leukemias)*

Based on recent PEI health trend reports, leukemia (all types) accounts for 3% of incident cancers among men. From 1980 to 2009, leukemia incidence rates have been increasing by 1.8% per year in men and decreasing by 0.8% per year in women.(29)

For leukemia overall, the average annual incidence per 100,000 in PEI from 2004-2013 was 17.0 for men and 8.1 for women, similar to the Canadian rates of 15.1 for men and 9.2 for women.

As the incidence of AML and CML for PEI was not available, the incidence of all types of leukemia was used for calculation purposes. This would over-estimate the risk because all cases of leukemia are counted instead of just the AML and CML cases.

**Table 8. PEI acute myeloid leukemia and agricultural pesticide exposure by sex, 2004-2013**

| | **Inputs** | |
|---|---|---|
| | **Men** | **Women** |
| Average exposed population | 2,840 | 760 |
| Total average population | 56,674 | 60,378 |
| PEI annual incidence rate per 100,000 population[4] | 15.1 | 9.2 |
| Any pesticide (28) (RE[1] [95% CI[2]]) | 1.38 (1.06-1.79) | |
| | **Output** | |
| | **Men** | **Women** |
| **PAF[3] (%)** | **1.9** | **0.5** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction 4- Incidence rate for all types of leukemia

The PAF is 0.5% for women and 1.9% for men, meaning that 0.5% and 1.9% of AML in the female and male population may be attributed to agricultural pesticides.

A *negligible* (female) to *extremely low* (male) reduction in average population AML risk may be achieved by eliminating agricultural exposure to pesticides on PEI.

**Table 9. PEI chronic myeloid leukemia and agricultural pesticide exposure in men, 2004-2013**

| | **Inputs** |
|---|---|
| | **Men** |
| Average exposed population | 2,840 |
| Total average population | 56,674 |

| | |
|---|---|
| PEI annual incidence rate per 100,000 population[4] | 15.1 |
| Any pesticide (28) (RE[1] [95% CI[2]]) | 1.39 (1.03-1.88) |
| | **Output** |
| | **Men** |
| **PAF[3] (%)** | **1.9** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction 4- Incidence rate for all types of leukemia

The PAF is 1.9% for men, meaning that 1.9% of CML in the male population may be attributed to agricultural pesticides.

An *extremely low* (male) reduction in average population CML risk may be achieved by eliminating agricultural exposure to pesticides on PEI.

### 6.1.2 Melanoma

Melanoma risk estimates were sourced from a high quality review article and pertain to agricultural occupational exposures that met our systematic review inclusion criteria.(30)

Melanoma accounts for 4% of male and 5% of female incident cancers. From 1980 to 2009, melanoma incidence rates have been increasing at a yearly rate of 4.4% in men and 3.6% in women. (29) The average annual incidence rate in PEI is 20.9 per 100,000 for men and 16.9 for women, slightly higher than the Canadian average of 14.0 for men and 11.2 for women.

**Table 10. PEI melanoma and agricultural pesticide exposure by sex, 2004-2013**

| | | | |
|---|---|---|---|
| | | **Inputs** | |
| | | **Men** | **Women** |
| Average exposed population | | 2,840 | 760 |
| Total average population | | 56,674 | 60,378 |
| Annual incidence rate per 100,000 population | PEI | 20.9 | 16.9 |
| | Canada | 14.0 | 11.2 |
| Any pesticide, male agricultural(30)(RE[1][p-value]) | | 4.80 (p<0.01) | |
| Any pesticide, male and female agricultural (30)(RE[1] [95% CI[2]]) | | 3.60 (1.50-8.30) | |
| Any pesticide, male and female agricultural(30)(RE[1] [95% CI[2]]) | | 1.12 (1.00-1.24) | |
| | | **Output** | |
| | | **Men** | **Women** |
| **PAF[3] (%)** | **Any pesticide, male agricultural** | **16.0** | **NA** |
| | **Any pesticide, male and female agricultural** | **11.5** | **3.2** |
| | **Any pesticide, male and female agricultural** | **0.6** | **0.2** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction NA- Not Applicable

The PAF for male agriculture is between 0.6% and 16.0%, meaning that between 0.6% and 16.0% of the melanoma in the male population may be attributed to agricultural pesticide exposure. The PAF for female agriculture is between 0.2% and 3.2%, meaning that between 0.2% and 3.2% of the melanoma in the female population may be attributed to agricultural pesticide exposure.

A *negligible* to *extremely low* (female) and *negligible* to *very low* (male) reduction in average population melanoma risk may be achieved by eliminating agricultural exposure to pesticides.

## 6.2 Children

The pediatric risk estimates for lymphoma, leukemia, brain cancer, neuroblastoma and Ewing sarcoma came from four meta-analyses. (31–34)

Pediatric cancer data was not available at a provincial level because of the low incidence of disease. Canadian statistics were used as a proxy for PEI data and the Canadian incidence rates were applied at the provincial level. The provincial incidence rate for pediatric cancer was assumed to be the same as the Canadian rate. The Canadian data presented represents 5-year averages of pediatric cancers.(17,21)

### 6.2.1 Lymphoma

The Canadian average incidence rate per 100,000 for pediatric lymphoma was 1.8 for those aged 0 to 14 years from 2006-2010 and 2.6 for those aged 0 to 19 years from 2003-2007.

**Table 11. PEI pediatric lymphoma and pesticide exposure, 2003-2007 and 2006-2010**

| | | Inputs | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| Range of exposed population | | 2,546-7,639 | 3,761-11,284 |
| Total average population | | 23,360 | 34,508 |
| Canada annual incidence rate per 100,000 population | | 1.8 | 2.6 |
| Any pesticide, childhood (33) (RE[1] [95% CI[2]]) | | 1.37 (1.22-1.54) | |
| Any pesticide, maternal prenatal (33) (RE[1] [95% CI[2]]) | | 1.53 (1.22-1.91) | |
| Any pesticide, maternal home and garden use (33) (RE[1] [95% CI[2]]) | | 1.48 (1.23-1.80) | |
| Insecticide (33) (RE[1] [95% CI[2]]) | | 1.46 (1.20-1.78) | |
| Fungicide (33) (RE[1] [95% CI[2]]) | | 1.45 (1.06-1.99) | |
| | | **Output** | |
| | | **Low (10.9%)** | **High (32.7%)** |
| **PAF[3] (%)** | **Any pesticide, childhood (33)** | **3.9** | **10.8** |
| | **Any pesticide, maternal prenatal (33)** | **5.5** | **14.8** |
| | **Any pesticide, maternal home and garden use (33)** | **5.0** | **13.6** |
| | **Insecticide (33)** | **4.8** | **13.1** |
| | **Fungicide (33)[4]** | **4.7** | **12.8** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

The PAF for the low exposure scenario ranged from 3.9 to 5.5% and for the high exposure scenario from 10.8 to 14.8%, meaning that between 3.9 and 14.8% of pediatric lymphoma in the population may be attributed to various pesticide exposures.

[4] Please see footnote 2 (page 8).

A *negligible* to *extremely low* reduction in average population childhood lymphoma risk may be achieved by eliminating exposure to various pesticides.

### 6.2.2 Leukemia

The Canadian average incidence rate per 100,000 for pediatric leukemia was 5.3 for those aged 0 to 14 years from 2006-2010 and 4.6 for those aged 0 to 19 years from 2003-2007.

The various exposures scenarios surrounding pesticides and childhood leukemia are abundant and built on many assumptions. The results should be interpreted with caution and the specific exposure scenario in mind.

**Table 12. PEI pediatric leukemia and pesticide exposure, 2003-2007 and 2006-2010**

| | | Inputs | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| **Range of exposed population** | | 2,546-7,639 | 3,761-11,284 |
| **Total average population** | | 23,360 | 34,508 |
| **Canada annual incidence rate per 100,000 population** | | 5.3 | 4.6 |
| **Any pesticide, during pregnancy (31)(RE[1] [95% CI[2]])** | | 1.54 (1.13-2.11) | |
| **Any pesticide, childhood (31)(RE[1] [95% CI[2]])** | | 1.38 (1.12-1.17) | |
| **Insecticide, during pregnancy (31)(RE[1] [95% CI[2]])** | | 2.0 (1.80-2.32) | |
| **Insecticide, childhood (31)(RE[1] [95% CI[2]])** | | 1.61 (1.33-1.95) | |
| **Herbicide, during pregnancy (31)(RE[1] [95% CI[2]])** | | 1.61 (1.20-2.16) | |
| **Any pesticide, maternal prenatal (32)(RE[1] [95% CI[2]])** | | 2.09 (1.51-2.88) | |
| **Any pesticide, maternal prenatal (33)(RE[1] [95% CI[2]])** | | 1.48 (1.26-1.75) | |
| **Any pesticide, maternal postnatal (33)(RE[1] [95% CI[2]])** | | 2.12 (1.17-3.84) | |
| **Any pesticides, paternal and maternal postnatal (33)(RE[1] [95% CI[2]])** | | 1.84 (1.39-2.44) | |
| **Any pesticide, maternal home and garden use (33) (RE[1] [95% CI[2]])** | | 1.56 (1.21-2.02) | |
| **Any pesticide, paternal postnatal (33)(RE[1] [95% CI[2]])** | | 1.33 (1.07-1.66) | |
| **Any pesticide, childhood (33) (RE[1] [95% CI[2]])** | | 1.23 (1.14-1.32) | |
| **Herbicide, any (33)(RE[1] [95% CI[2]])** | | 1.26 (1.14-1.39) | |
| **Herbicide, maternal prenatal (32)(RE[1] [95% CI[2]])** | | 3.62 (1.28-10.3) | |
| **Insecticide, any (33)(RE[1] [95% CI[2]])** | | 1.17 (1.03-1.33) | |
| **Insecticide, maternal prenatal (32)(RE[1] [95% CI[2]])** | | 2.72 (1.47-5.04) | |
| | | **Output** | |
| | | **Low (10.7%)** | **High (32.7%)** |
| **PAF[3] (%)** | **Any pesticide, during pregnancy (31)** | **5.6** | **15.0** |
| | **Any pesticide, childhood (31)** | **4.0** | **11.1** |
| | **Insecticide, during pregnancy (31)** | **9.8** | **24.0** |
| | **Insecticide, childhood (31)** | **6.2** | **16.6** |
| | **Herbicide, during pregnancy (31)[5]** | **6.2** | **16.6** |
| | **Any pesticide, maternal prenatal (32)** | **10.6** | **26.3** |
| | **Any pesticide, maternal prenatal (33)** | **5.0** | **13.6** |
| | **Any pesticide, maternal postnatal (33)** | **10.9** | **26.8** |
| | **Any pesticides, paternal and maternal postnatal (33)** | **8.4** | **21.5** |

[5] Please see footnote 2 (page 8).

| | | | |
|---|---|---|---|
| | **Any pesticide, maternal home and garden use (33)** | **5.8** | **15.5** |
| | **Any pesticide, paternal postnatal (33)** | **3.5** | **9.7** |
| | **Any pesticide, childhood (33)** | **2.4** | **7.0** |
| | **Herbicide, any (33)[5]** | **2.8** | **7.8** |
| | **Herbicide, maternal prenatal (32)[5]** | **22.2** | **46.1** |
| | **Insecticide, any (33)** | **1.8** | **5.3** |
| | **Insecticide, maternal prenatal (32)** | **15.8** | **36.0** |

**1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction**

For the PAF for maternal exposure to pesticides, the low exposure situation ranged from 5.0% to 22.2% and the high exposure situation ranged from 13.6% to 46.1%, meaning that up to 46.1% of the pediatric leukemia in the pediatric population may be attributed to maternal pesticide exposure. For paternal pesticide exposure, the low exposure PAF is 3.5% and the high exposure PAF is 9.7%, meaning that up to 9.7% of the pediatric leukemia in the pediatric population may be attributed to paternal pesticide exposure. For childhood pesticide exposure, the PAF at the low end ranged from 2.4% to 6.2% and at the high end from 7.0% to 16.6%, meaning that up to 16.6% of the pediatric leukemia in the pediatric population may be attributed to childhood pesticide exposure. Estimates for any exposure indicated a range of PAFs from 1.8% to 7.8% meaning that up to 7.8% of the pediatric leukemia in the pediatric population may be attributed to pesticide exposure.

A *negligible* to *very low* reduction in average population childhood leukemia risk may be achieved by eliminating exposures to pesticides.

**Table 13. PEI pediatric leukemia and agricultural pesticide exposure, 2003-2007 and 2006-2010**

| | | **Inputs** | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| Average exposed population | | 1,307 | 2,000 |
| Total average population | | 23,360 | 34,508 |
| Canada annual incidence rate per 100,000 population | | 5.3 | 4.6 |
| Any pesticide, paternal (33)(RE[1] [95% CI[2]]) | | 1.37 (1.23-1.52) | |
| Insecticides, paternal (32)(RE[1] [95% CI[2]]) | | 1.43 (1.06-1.92) | |
| | | **Output** | |
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| **PAF[3] (%)** | **Any pesticide, paternal (33)** | **2.0** | **2.1** |
| | **Insecticides, paternal (32)** | **2.3** | **2.4** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

The PAF for paternal agricultural pesticide exposure is near 2%, meaning that between 2.0% and 2.4% of the pediatric leukemia in the pediatric population may be attributed to paternal agricultural pesticide exposure.

A *negligible* reduction in average population childhood leukemia risk may be achieved by eliminating paternal agricultural occupational exposure to pesticides (including insecticides).

### 6.2.3 Acute myeloid leukemia

The Canadian average incidence rate per 100,000 for pediatric Acute Myeloid Leukemia (AML) was 0.7 for those aged 0 to 14 years from 2006-2010 and 0.7 for those aged 0 to 19 years from 2003-2007.

**Table 14. PEI pediatric acute myeloid leukemia and maternal agricultural pesticide exposure, 2003-2007 and 2006-2010**

| | | Inputs | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| Average exposed population | | 353 | 586 |
| Total average population | | 23,360 | 34,508 |
| Canada annual incidence rate per 100,000 population | | 0.7 | 0.7 |
| Any pesticide, maternal prenatal (34)(RE[1] [95% CI[2]]) | | 1.94 (1.19-3.18) | |
| | | **Output** | |
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| **PAF[3] (%)** | **Any pesticide, maternal prenatal (34)** | **1.4** | **1.6** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

The PAF for maternal agricultural pesticide exposure is 1.4 to 1.6%, meaning that approximately 1.5% of the pediatric AML in the pediatric population may be attributed to maternal agricultural pesticide exposure.

A *negligible* reduction in average population childhood AML risk may be achieved by eliminating maternal agricultural occupational exposure to pesticides.

### 6.2.4 Acute lymphoblastic leukemia

The Canadian average incidence rate per 100,000 for pediatric Acute Lymphoblastic Leukemia (ALL) was 4.2 for those aged 0 to 14 years from 2006-2010 and 3.4 for those aged 0 to 19 years from 2003-2007.

**Table 15. PEI pediatric acute lymphoblastic leukemia and paternal agricultural pesticide exposure, 2003-2007 and 2006-2010**

| | | Inputs | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| Average exposed population | | 1,307 | 2,000 |
| Total average population | | 23,360 | 34,508 |
| Canada annual incidence rate per 100,000 population | | 4.2 | 3.4 |
| Any pesticide, paternal around conception (34) (RE[1] [95% CI[2]]) | | 1.20 (1.06-1.38) | |
| | | **Output** | |
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| **PAF[3] (%)** | **Any pesticide, paternal around conception (34)** | **1.1** | **1.1** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

The PAF for paternal agricultural pesticide exposure around conception is 1.1%, meaning that 1.1% of the pediatric ALL in the pediatric ALL population may be attributed to paternal agricultural pesticide exposure around conception.

A *negligible* reduction in average population childhood ALL risk may be achieved by eliminating paternal agricultural occupational exposure to pesticides.

### 6.2.5 Brain cancer

The average Canadian incidence rate per 100,000 for pediatric brain cancer is 3.1 for those aged 0 to 14 years from 2006-2010 and 2.7 for those aged 0 to 19 years from 2003-2007.

**Table 16. PEI pediatric brain cancer and pesticide exposure, 2003-2007 and 2006-2010**

| | | **Inputs** | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| Range of exposed population | | 2,546-7,639 | 3,761-11,284 |
| Total average population | | 23,360 | 34,508 |
| Canada annual incidence rate per 100,000 population | | 3.1 | 2.7 |
| Any pesticide, paternal before birth (33) (RE[1] [95% CI[2]]) | | 1.49 (1.23-1.79) | |
| Any pesticide, paternal after birth (33) (RE[1] [95% CI[2]]) | | 1.66 (1.11-2.49) | |
| Any pesticide, childhood (33) (RE[1] [95% CI[2]]) | | 1.22 (1.13-1.31) | |
| Any pesticide, paternal residential (33) (RE[1] [95% CI[2]]) | | 1.48 (1.22-1.80) | |
| Insecticide (33) (RE[1] [95% CI[2]]) | | 1.18 (1.06-1.33) | |
| Fungicide (33) (RE[1] [95% CI[2]]) | | 1.32 (1.06-1.65) | |
| | | **Output** | |
| | | **Low (10.7%)** | **High (32.7%)** |
| **PAF[3] (%)** | **Any pesticide, paternal before birth (33)** | **5.1** | **13.8** |
| | **Any pesticide, paternal after birth (33)** | **6.7** | **17.8** |
| | **Any pesticide, childhood (33)** | **2.3** | **6.7** |
| | **Any pesticide, paternal residential (33)** | **5.0** | **13.6** |
| | **Insecticide (33)** | **1.9** | **5.6** |
| | **Fungicide (33)[6]** | **3.4** | **9.5** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

Paternal pesticide exposure had PAFs ranging from 5 to 17.8%, meaning that between 5% and 17.8% of the pediatric brain cancer in the pediatric population may be attributed to paternal pesticide exposure. Childhood and non-specific exposures had PAFs ranging from 1.9 to 9.5%, meaning that between 1.9% and 9.5% of the pediatric brain cancer in the pediatric population may be attributed to childhood and non-specific various pesticide exposures.

A *negligible to extremely low* reduction in average population childhood brain cancer risk may be achieved by eliminating exposure to various pesticides.

[6] Please see footnote 2 (page 8).

**Table 17. PEI pediatric brain cancer and agricultural pesticide exposure, 2003-2007 and 2006-2010**

| | | Inputs | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| Average exposed population | | 1,307 | 2,000 |
| Total average population | | 23,360 | 34,508 |
| Canada annual incidence rate per 100,000 population | | 3.1 | 2.7 |
| Any pesticide, paternal occupational (33) (RE[1] [95% CI[2]]) | | 1.40 (1.20-1.62) | |
| | | **Output** | |
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| **PAF[3] (%)** | **Any pesticide, paternal occupational (33)** | **2.2** | **2.3** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

Paternal agricultural pesticide exposure has a PAF of 2.2% to 2.3%, meaning that between 2.2% and 2.3% of the pediatric brain cancer in the pediatric brain cancer population may be attributed to paternal agricultural pesticide exposure.

A *negligible* reduction in average population childhood brain cancer risk may be achieved by eliminating paternal agricultural occupational exposure to pesticides in PEI.

### 6.2.6 Neuroblastoma

The annual age-standardized Canadian incidence rate for pediatric neuroblastoma was 0.9 per 100,000 in children 0 to 19 years from 2002 to 2006 and was 1.3 per 100,000 in children 0 to 14 years from 2006-2010.

**Table 18. PEI pediatric neuroblastoma and pesticide exposure, 2003-2007 and 2006-2010**

| | | Inputs | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| Range of exposed population | | 2,546-7,639 | 3,761-11,284 |
| Total average population | | 23,360 | 34,508 |
| Canada annual incidence rate per 100,000 population | | 1.3 | 0.9 |
| Any pesticide, childhood (33)(RE[1] [95% CI[2]]) | | 1.70 (1.14-1.51) | |
| | | **Output** | |
| | | **Low (10.7%)** | **High (32.7%)** |
| **PAF[3] (%)** | **Any pesticide, childhood (33)** | **7.1** | **18.6** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

The PAF of childhood pesticide exposure for neuroblastoma is between 7.1 and 18.6%, meaning that up to 18.6% of neuroblastoma in the population may be attributed to childhood pesticide exposure.

A *negligible* to *extremely low* reduction in average population pediatric neuroblastoma risk may be achieved by eliminating childhood exposure to pesticides on PEI.

### 6.2.7 Ewing sarcoma

The annual incidence rate for Ewing sarcoma in Canadian children was 0.3 per 100,000 in those aged 0 to 14 years from 2006-2010 and 0.3 per 100,000 in those aged 0 to 19 years from 2003-2007.

**Table 19. PEI pediatric Ewing sarcoma and pesticide exposure, 2003-2007 and 2006-2010**

| | | Inputs | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| Range of exposed population | | 2,546-7,639 | 3,761-11,284 |
| Total average population | | 23,360 | 34,508 |
| Canada annual incidence rate per 100,000 population | | 0.3 | 0.3 |
| Any pesticide, childhood (33)(RE[1] [95% CI[2]]) | | 2.01 (1.45-2.79) | |
| | | **Output** | |
| | | **Low (10.7%)** | **High (32.7%)** |
| **PAF[3] (%)** | **Any pesticide, childhood (33)** | **9.9** | **24.8** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

The PAF for pediatric Ewing sarcoma is between 9.9 and 24.8% for childhood pesticide exposure, meaning that up to 24.8% of the Ewing sarcoma in the pediatric population may be attributed to childhood pesticide exposure.

**Table 20. PEI pediatric Ewing sarcoma and agricultural pesticide exposure, 2003-2007 and 2006-2010**

| | | Inputs | |
|---|---|---|---|
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| Average exposed population | | 1,307 | 2,000 |
| Total average population | | 23,360 | 34,508 |
| Canada annual incidence rate per 100,000 population | | 0.3 | 0.3 |
| Any pesticide, paternal occupational (33) (RE[1] [95% CI[2]]) | | 2.34 (1.33-4.12) | |
| | | **Output** | |
| | | **0 to 14 years, 2006-2010** | **0 to 19 years, 2003-2007** |
| **PAF[3] (%)** | **Any pesticide, paternal occupational (33)** | **7.0** | **7.2** |

1- Risk Estimate 2- 95% Confidence Interval 3- Population Attributable Fraction

The PAF for pediatric Ewing sarcoma and paternal agricultural pesticide exposure is between 7.0 and 7.2%, meaning that up to 7.2% of the Ewing sarcoma in the pediatric population may be attributed to paternal agricultural pesticide exposure.

A *negligible* reduction in average population pediatric Ewing sarcoma risk may be achieved by eliminating general childhood or paternal agricultural occupational exposure to pesticides on PEI.

# 7 Conclusion

**All health outcomes identified in the systematic review (Grade A association and >1,000 kg/yr pesticide sales) exhibit incidence/prevalence rates in PEI that are similar to Canadian rates.**

The population risk reduction was calculated using the appropriate rate for the health condition and the PAF. The PAF was calculated using risk estimates from high quality studies that had been identified during the systematic review.

**Disease specific risk reduction ranges from *negligible* to *low* with most diseases falling in the *negligible* to *extremely* low classification.** The specific risk estimates are listed in the table shown below.

**Table 21. Disease specific risk reduction**

| Outcome | RA |
|---|---|
| Cleft palate | EL |
| Parkinson disease | EL-L |
| ALS | N |
| Adult lymphohematopoietic cancer | |
| NHL in men | EL |
| NHLin women | N |
| AML in men | EL |
| AML in women | N |
| CML in men | EL |
| Adult melanoma | |
| Men | N to VL |
| Women | N to EL |
| Pediatric lymphohematopoietic cancer | |
| Lymphoma | N to EL |
| Leukemia | N to VL |
| AML | N |
| ALL | N |
| Brain cancer | N to EL |
| Neuroblastoma | N to EL |
| Ewing sarcoma | N |

RA: Risk Assessment N: Negligible EL: Extremely Low VL: Very Low L: Low
ALS: Amyotrophic Lateral Sclerosis NHL: Non-Hodgkin Lymphoma
AML: Acute Myeloid Leukemia CML: Chronic Myeloid Leukemia
ALL: Acute Lymphocytic Leukemia

**Based on the current review, pesticides used in PEI following "labeled-practices" do not pose a significant public health risk.** The systematic review should be updated periodically to ensure recent evidence is incorporated into assessing risk to Islanders.

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