Liver cancer and immigration: small-area analysis of incidence within Ottawa and the Greater Toronto Area, 1999 to 2003.

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Population Studies and Surveillance
Outline

- Background
- Objective
- Data, Methods and Tools
- Results
- Implications
- Limitations
- References
- Questions
- Future work
Background

- Liver cancer:
  - Worldwide, sixth most common cancer and third most common cause of cancer mortality (Chen et al, 2008).
  - > 80% of cases and mortality are in developing countries, with majority in sub-Saharan Africa or Eastern Asia, with China accounting for >50% of cases (McGlynn and London, 2005).
  - Hepatocellular carcinoma (HCC) accounts for 75%-90% of liver cancers, and HCC incidence is two-to-four times higher among men (McGlynn and London, 2005).
Background

- **Risk factors:**
  - For HCC, chronic infection with Hepatitis B or C (HBV or HCV)
  - Exposure to aflatoxin B$_1$ (AFB1)
  - Alcohol consumption
    (IARC, 2010; Seitz and Becker, 2007; McGlynn and London, 2005).
Estimated age-standardised incidence rate per 100,000
Liver: male, all ages
Estimated age-standardised incidence rate per 100,000
Liver: female, all ages
Background

- **Liver cancer in Ontario:**
  - 4th most fatal cancer
  - HCC most common.
  - Increasing trend may be related to increasing immigration from areas with endemic HBV infection and exposure to AFB$_1$.
  - **Male incidence increased 3.3% annually from 1980 to 2002.**

(Cancer Care Ontario, 2005 and 2006)
Chen, Yi and Mao (2008)

Standardized incidence ratios for the 35 public health units Ontario

a. Before adjustment for proportion of immigrants, age, sex and geographic location

b. After adjustment for proportion of immigrants, age, sex, and geographic location
## Ottawa, Toronto and York Immigration

<table>
<thead>
<tr>
<th>NAME</th>
<th>Population</th>
<th>Immigrant Pop.</th>
<th>% Immigrant Pop</th>
<th>Chinese born</th>
<th>% Chinese</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toronto Division</td>
<td>2456805</td>
<td>1214625</td>
<td>49.44%</td>
<td>102635</td>
<td>8.45%</td>
</tr>
<tr>
<td>Peel Regional Municipality</td>
<td>985565</td>
<td>424820</td>
<td>43.10%</td>
<td>9970</td>
<td>2.35%</td>
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<tr>
<td>York Regional Municipality</td>
<td>725665</td>
<td>283790</td>
<td>39.11%</td>
<td>22380</td>
<td>7.89%</td>
</tr>
<tr>
<td>Hamilton Division</td>
<td>484385</td>
<td>119810</td>
<td>24.73%</td>
<td>2450</td>
<td>2.04%</td>
</tr>
<tr>
<td>Halton Regional Municipality</td>
<td>372410</td>
<td>83250</td>
<td>22.35%</td>
<td>1105</td>
<td>1.33%</td>
</tr>
<tr>
<td>Ottawa Division</td>
<td>763790</td>
<td>166745</td>
<td>21.83%</td>
<td>12840</td>
<td>7.70%</td>
</tr>
<tr>
<td>Essex County</td>
<td>371085</td>
<td>79775</td>
<td>21.50%</td>
<td>2875</td>
<td>3.60%</td>
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<tr>
<td>Waterloo Regional Municipality</td>
<td>433875</td>
<td>92775</td>
<td>21.38%</td>
<td>2315</td>
<td>2.50%</td>
</tr>
<tr>
<td>Middlesex County</td>
<td>398565</td>
<td>77005</td>
<td>19.32%</td>
<td>1635</td>
<td>2.12%</td>
</tr>
<tr>
<td>Durham Regional Municipality</td>
<td>502905</td>
<td>94890</td>
<td>18.87%</td>
<td>1110</td>
<td>1.17%</td>
</tr>
<tr>
<td>Niagara Regional Municipality</td>
<td>404590</td>
<td>71200</td>
<td>17.60%</td>
<td>905</td>
<td>1.27%</td>
</tr>
<tr>
<td>Wellington County</td>
<td>184840</td>
<td>30470</td>
<td>16.48%</td>
<td>900</td>
<td>2.95%</td>
</tr>
<tr>
<td>Elgin County</td>
<td>80150</td>
<td>11390</td>
<td>14.21%</td>
<td>70</td>
<td>0.61%</td>
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<tr>
<td>Brant County</td>
<td>116750</td>
<td>15230</td>
<td>13.04%</td>
<td>155</td>
<td>1.02%</td>
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<tr>
<td>Frontenac County</td>
<td>135410</td>
<td>16755</td>
<td>12.37%</td>
<td>660</td>
<td>3.94%</td>
</tr>
<tr>
<td>Dufferin County</td>
<td>50360</td>
<td>6130</td>
<td>12.17%</td>
<td>25</td>
<td>0.41%</td>
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<tr>
<td>Simcoe County</td>
<td>372325</td>
<td>43460</td>
<td>11.67%</td>
<td>515</td>
<td>1.18%</td>
</tr>
<tr>
<td>Lambton County</td>
<td>125565</td>
<td>14520</td>
<td>11.56%</td>
<td>155</td>
<td>1.07%</td>
</tr>
<tr>
<td>Haldimand-Norfolk Regional Municipality</td>
<td>103330</td>
<td>11815</td>
<td>11.43%</td>
<td>35</td>
<td>0.30%</td>
</tr>
<tr>
<td>Oxford County</td>
<td>97965</td>
<td>10825</td>
<td>11.05%</td>
<td>25</td>
<td>0.23%</td>
</tr>
</tbody>
</table>

Top 20 Ontario Census Divisions sorted by immigrant population (in descending order).  
Source: 2001 Census of Canada, Statistics Canada
Objective

- Follow-up on the findings of Chen, Yi and Mao (2008) to determine if the association of liver cancer and immigrant population exists at the small-area level.
Data Sources, Methods and Tools

**Liver Cancer data**
- Ontario Cancer Registry, 1999-2003

**Statistics Canada Census 2001**
- Census geography
- Population by 5 year age group and sex
- Immigrant birth place

**Link data**
- Postcode - DA
  - CT, CMA/CA
  - CSD, CD boundaries
  - PCCF+

**Tools**
- Rapid Inquiry Facility -> SIRs
- ArcGIS -> mapping/spatial
- WinBUGS -> Bayesian inference
- Besag, York, Mollié (BYM) model
- SaTScan -> corroboration

**Methods**
RESULTS
Total: 173 CTs
Overall SIR: 1.25 (95% CI: 1.02, 1.50)
WinBUGS fracspatial: 0.84 (95% CI: 0.14, 0.99)

* indirectly standardized incidence ratios (SIRs), all ages, using Ontario age-specific rates, 1999-2003, adjusted for % of immigrants born in China (2001 Census CTs). Full Bayesian smoothing using the Besag, York and Molié (BYM) model (1991). Excludes 1.4% of male primary liver cancer cases having missing or invalid postal code residence at diagnosis and 0.6% of cases due to suppressed immigrant birthplace data for the 2001 Census.

Data sources:
Ontario Cancer Registry, CCO and 2001 Census, Statistics Canada
Male Primary Liver Cancer Incidence 1999-2003 (127 observed cases), Ottawa Division
Full Bayesian Smoothing and Adjusted for % of Immigrants born in China Quintiles, by 2001 Census Tract (CT)

O/E = 32/12.92 = 2.48, p=0.008

Total: 173 CTs
Overall SIR: 1.07 (95% CI: 0.88, 1.28)
WinBUGS fracspatial: 0.71 (95% CI: 0.04, 0.99)

* indirectly standardized incidence ratios (SIRs), all ages, using Ontario age-specific rates, 1999-2003, adjusted for % of immigrants born in China (2001 Census CTs). Full Bayesian smoothing using the Besag, York and Mollié (BYM) model (1991). Excludes 1.4% of male primary liver cancer cases missing or invalid postal code residence at diagnosis and 0.6% of cases due to suppressed immigrant birthplace data for the 2001 Census.

Data sources:
Ontario Cancer Registry, CCO and 2001 Census, Statistics Canada
Female Primary Liver Cancer Incidence 1999-2003 (30 observed cases), Ottawa Division
Full Bayesian Smoothing, by 2001 Census Tract (CT)

Total: 173 CTs
Overall SIR: 0.91 (95% CI: 0.61, 1.27)
WinBUGS fracspatial: 0.76 (95% CI: 0.05, 0.99)

* indirectly standardized incidence ratios (SIRs), all ages, using Ontario age-specific rates, 1999-2003, adjusted for % of immigrants born in China (2001 Census CTs). Full Bayesian smoothing using the Besag, York and Mollié (BYM) model (1991). Excludes 1.2% of female primary liver cancer cases having missing or invalid postal code residence at diagnosis and 0.6% of cases due to suppressed immigrant birthplace data for the 2001 Census.

Data sources:
Ontario Cancer Registry, CCO and 2001 Census, Statistics Canada
Female Primary Liver Cancer Incidence 1999-2003 (30 observed cases), Ottawa Division
Full Bayesian Smoothing and Adjusted for % of Immigrants born in China Quintiles, by 2001 Census Tract (CT)

Total: 173 CTs
Overall SIR: 0.79 (95% CI: 0.53, 1.10)
WinBUGS fracspatial: 0.79 (95% CI: 0.06, 0.99)
* indirectly standardized incidence ratios (SIRs), all ages, using Ontario age-specific rates, 1999-2003, adjusted for % of immigrants born in China (2001 Census CTs). Full Bayesian smoothing using the Besag, York and Mollié (BYM) model (1991). Excludes 1.2% of female primary liver cancer cases missing or invalid postal code residence at diagnosis and 0.6% of cases due to suppressed immigrant birthplace data for the 2001 Census.

Data sources:
Ontario Cancer Registry, CCO and 2001 Census, Statistics Canada
Male Primary Liver Cancer Incidence 1999-2003 (690 observed cases), Toronto and York Regions
Full Bayesian Smoothing, by 2001 Census Tract (CT)

Total: 647 CTs
Overall SIR: 1.53 (95% CI: 1.40, 1.67)
WinBUGS fracspatial: 0.97 (95% CI: 0.79, 0.99)
* indirectly standardized incidence ratios (SIRs), all ages, using Ontario age-specific rates, 1999-2003.
Full Bayesian smoothing using the Besag, York and Mollie (BYM) model (1991). Excludes 1.4% of male primary liver cancer cases having invalid or missing postal code residence at diagnosis and 0.9% of cases due to suppressed income data for the 2001 Census.

Data sources:
Ontario Cancer Registry, CCO and 2001 Census, Statistics Canada
Male Primary Liver Cancer Incidence 1999-2003 (690 observed cases), Toronto and York Regions
Full Bayesian Smoothing and Adjusted for % of Immigrants born in China Quintiles, by 2001 Census Tract (CT)

Total: 647 CTs
Overall SIR: 1.15 (95% CI: 1.05, 1.25)
WinBUGS fracspatial: 0.94 (95% CI: 0.57, 0.99)
* indirectly standardized incidence ratios (SIRs), all ages, using Ontario age-specific rates, 1999-2003, adjusted for % of immigrants born in China (2001 Census DAs).
Full Bayesian smoothing using the Besag, York and Mollie (BYM) model (1991). Excludes 1.4% of male primary liver cancer cases missing postal code residence at diagnosis and 0.9% of cases due to suppressed income data for the 2001 Census.

Data sources:
Ontario Cancer Registry, CCO and 2001 Census, Statistics Canada

O/E = 160/91.14 = 1.76, p=0.001
Female Primary Liver Cancer Incidence 1999-2003 (206 observed cases), Toronto and York Regions
Full Bayesian Smoothing, by 2001 Census Tract (CT)

O/E = 37/15.62 = 2.37, p=0.036

Total: 647 CTs
Overall SIR: 1.42 (95% CI: 1.16, 1.66)
WinBUGS frac.spatial: 0.56 (95% CI: 0.01, 0.99)
* indirectly standardized incidence ratios (SIRs), all ages, using Ontario age-specific rates, 1999-2003.
Full Bayesian smoothing using the Besag, York and Mollie (BYM) model (1991). Excludes 1.2% of female primary liver cancer cases having invalid or missing postal code residence at diagnosis and 0.9% of cases due to suppressed income data for the 2001 Census.

Data sources:
Ontario Cancer Registry, CCO and 2001 Census, Statistics Canada
Female Primary Liver Cancer Incidence 1999-2003 (206 observed cases), Toronto and York Regions
Full Bayesian Smoothing and Adjusted for % of Immigrants born in China Quintiles, by 2001 Census Tract (CT)

Total: 647 CTs
Overall SIR: 1.12 (95% CI: 0.94, 1.29)
WinBUGS fracspatial: 0.37 (95% CI: 0.01, 0.99)

* indirectly standardized incidence ratios (SIRs), all ages, using Ontario age-specific rates, 1999-2003, adjusted for % of immigrants born in China (2001 Census DAs).
Full Bayesian smoothing using the Besag, York and Mollie (BYM) model (1991). Excludes 1.2% of female primary liver cancer cases missing postal code residence at diagnosis and 0.9% of cases due to suppressed income data for the 2001 Census.

Data sources:
Ontario Cancer Registry, CCO and 2001 Census, Statistics Canada

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Summary

- Spatial clustering of elevated rates of primary liver cancer incidence exists for the 1999-2003 period for males in Ottawa, and for both sexes in the Toronto-York regions.
- % of population that were Chinese-born attenuates elevated SIRs overall, but does not account for all variations in local-area spatial patterns.
- Continue investigation...
Implications

- Planning for service utilization
- Collaboration with Public Health to promote HBV immunization targeted to areas with high risk for liver cancer.
Limitations

- % immigrant population by birth place covariate:
  - not sex-specific;
  - for use in the RIF, converted to ordinal data (quintiles) and not possible to quantify effect as a coefficient

- Ecological analysis -> associations not causality
References


References


References

  - SaTScanTM is a trademark of Martin Kulldorff. The SaTScanTM software was developed under the joint auspices of (i) Martin Kulldorff, (ii) the National Cancer Institute, and (iii) Farzad Mostashari of the New York City Department of Health and Mental Hygiene.


QUESTIONS?
Future work

- Implement BYM model using R and WinBUGS using Bayesian inference with immigrant birth place as continuous covariate to quantify the association and significance;
- Examine ethnicity, SES as covariates;
- Examine different time periods: 1984-1988 and 2004-2008 to explore temporal and spatial persistence of these clusters;
- Include estimates of HBV and HCV prevalence (if possible);
- Utilize birth place of individual from mortality file linked to OCR.