Overcoming Small Numbers in a Small State:
Vermont’s Approach to Cancer Mapping
Overview

- Background
- Purpose
- Methods
- Results
- Conclusions
Background – Reason for the Project
Vermont’s Cancer Landscape

- Small, Mainly Rural (~626,000 pop.)
- Aging Population
  - 2nd oldest state
- 94.3% White Non-Hispanic
- Cancer Incidence
  - 495.2 per 100,000
  - ~3,600 cases per year
  - Statistically higher than U.S. (SEER all races and white rates)
- Vermont Adults Living with Cancer
  - 6% or about 29,000

Data Sources:
- 2010 Census
- Vermont Cancer Registry 2005-2009
- SEER 2005-2009
- VT BRFSS 2010

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CANCER: Clarendon residents seek explanation

Continued from Page 1B

hearing about all this leukemia? They said that because we had leukemia that I just started listening better," Crossman said. "At first I was buying that; "OK, I'm just more aware.' That worked for a few months, but no, that's not it."

Plotting cases

Kayla Webster, who will celebrate her 14th birthday this month, is in remission and starting the eighth grade.

Her mother and Fenner have marked hers and other reports of cancer cases with stickers on a map of local roads. One street immediately catches everyone's attention.

"I don't know anybody who hasn't looked at that map and wondered, 'What the heck is going on on Moulton Avenue?'" said Joe Mark, the academic dean of Castleton State College who is helping the group.

At least eight people living on the street have been treated for some form of cancer. Town records also show 11 others have died from cancer over the past two decades, Crossman said.

Joan Bixby, who was diagnosed with non-Hodgkin's lymphoma in 1995 and is in remission, has known many neighbors with cancer during the 38 years she's lived on Moulton Avenue.

Her dog died from leukemia too, but it wasn't until her husband was diagnosed with colon cancer last year that she became fearful.

"Now that I look at it, seeing as how we both have had it here, it's an awful lot," Bixby said, "but at the time, you didn't think anything of it. Until it's in your home, in your family, and then you..."

Montpelier isn't going to help; it isn't going to change because who knows what you're learning into it.

Crossman doesn't plan to leave, either, but she acknowledged the uncertainty of whether something might have caused the illnesses can be a scary thing. She drinks bottled water and is conscious of everything she eats.

"If we knew what it was, then we could address it and other kids is going to get cancer or I'm going to get cancer; and the only way to deal with it is to face it and try to make changes to stop it," she said.

Cancer concerns raised in Sheldon

Local survivor vows to press on despite Health Department response

By Jedd Kettler

SHELDON- Standing on her front lawn in the mid-October dusk, Jeni Magatno looked up and down the dirt road and felt like she was surrounded by cancer.

She's right, at least literally: all seven of the nearest homes in this quiet rural community have a family member battling cancer. All are reasonably close to Magatno's age — 38 — and all have young children, she said.

Magatno is also a survivor, having been diagnosed with breast cancer a year ago and battling back from the living honor of it. But it is a growing concern that Sheldon has more than its share of cancer victims that troubles her most these days.

"It's very sad, actually. You're looking at a small town... You're looking at neighbors after neighbor after neighbor," Magatno says, sitting inside at her kitchen table.

A map of the town is laid out nearby, colored by small red dots, one for each of the 35 cancer cases she has documented over the last three weeks. All of these dots are within a seven-mile radius and within Sheldon's borders.

Magatno fears that number will continue to grow and has begun to search out possible environmental causes for what she believes is a higher than expected cancer rate, known as the cancer cluster. As an economist, Magatno contacted the Vermont Department of Health in late September.

Families of residents, though, say they looked into Magatno's concerns, analyzing regional and town data, and concluded there is no evidence local cancer rates are elevated here.

See CANCER p15
Example: Concerns from Richmond

- January 2012.
- Development with eight households.
- Five women diagnosed with cancer (female breast cancer and ovarian cancer).
- Farming on land before housing was developed.
- Incidence for county was not elevated.
Cluster Inquiry Protocol

- Level 1
  - Initial responder (IR) communicates with caller and internal team of experts (TAG).

- Criteria to move to Level 2:
  - More cases than expected? Prior concern? Community activation? Politically sensitive? Legal proceedings? Caller thinks there is an environmental cause?
Cluster Inquiry Protocol

- Level 2 - “Yes”
  - Consult with TAG.
  - Compute “observed v. expected.”
What we used to say: “No”

- We do not usually calculate and publish statistics for small geographic areas (such as towns or neighborhoods).
- Rates are unreliable if they are based on small numbers of observations.
- Impossible to distinguish random fluctuation from true changes in the underlying risk of disease.
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The best we could do:

- **Incidence:**
  - U.S., Vermont, and County

- **SIR’s and OR’s**

- **Prevalence:**
  - Vermont and County

**AA cancer incidence rate and number of new cases per year.**

- Statistically Higher
- Statistically Lower
- Not Different

Vermont: 495.2 per 100,000

Data Source:
Needs identified:

- Be able to respond to public concerns in a coordinated, confidential, and efficient way.

- Provide increased access to cancer data.

- Better understand the cancer burden in communities statewide.
  - Evaluate observed/expected.
Purpose – Scope of the Project
# Methods Evaluated – Workflow

<table>
<thead>
<tr>
<th>SaTScan</th>
<th>Smoothed SIR</th>
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</thead>
<tbody>
<tr>
<td>Summarize registry data by census block groups or census blocks.</td>
<td>Summarize registry data by census blocks.</td>
</tr>
<tr>
<td>Prep multiple SaTScan input files (difficult for census blocks).</td>
<td>Calculate state AA cancer rates.</td>
</tr>
<tr>
<td>Choose SaTScan analysis settings (tricky business!).</td>
<td>Calculate expected cases for each census block.</td>
</tr>
<tr>
<td>Map SaTScan outputs.</td>
<td>Establish a statewide grid of analysis points.</td>
</tr>
<tr>
<td></td>
<td>Utilize spatial adaptive filtering technique to deal with small case numbers in rural areas.</td>
</tr>
<tr>
<td></td>
<td>Calculate observed to expected ratio (SIR) for each grid point.</td>
</tr>
<tr>
<td></td>
<td>Generate final smoothed SIR map.</td>
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</table>

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Methods Evaluated – Pros and Cons

**SaTScan**
- Well-documented.
- Sophisticated geostatistical screening methodologies.
- Customization options.
- Difficult to understand or explain.
- Difficult to use without considerable expertise.

**Iowa’s Smoothed SIR**
- Relatively straightforward.
- Easily explained.
- Visually intuitive results.
- Significance? (multiple comparisons problem).

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Methods Evaluated – Conclusions

- SaTScan was difficult to understand and interpret. The software, though functional, was time-consuming to use.

- Smoothed SIR mapping was more promising, but significance testing for areas identified with higher than expected rates was needed.

  - Manage the issue of “multiple comparisons”.

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Methods – How We Approached the Project
Geography

- Required areas as small as possible but still statistically workable.
  
  - From 251 towns in Vermont, 107 analysis areas were identified as a result of the process.
    
    - Census tracts.
    - Towns.
    - Paired towns or groups of towns.

  - Total populations 3,500 – 10,000.
Data

- Vermont Cancer Registry.
  - Diagnosis years 2001-2008.
  - Address at diagnosis geocoded to corresponding latitude and longitude coordinates.
  - Some addresses excluded.

- Census – demographics.
Vermont Geocoding

- Street names changed when E911 street name/number standardization protocols went into effect.
- Old names and numbers continued to be used.
- PO Boxes, Rural Route #s ("RR"), Lot #'s, building or facility names.
  - Livingston and Cross Town Road, Cedar View Apartments, Foot of Elm Street, MVMP.
- Paired towns.
  - "Barre" Is it Barre Town or Barre City?
- Unresolved address results in assignment to a town centroid.

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Calculations

- Age-Adjusted Expected Cases.
  - Age-specific rates, then expected cases based on local age structure (not displayed).

- Standardized Incidence Ratios (SIR).

- Byar’s Z and Byar’s P-values (not displayed).

- “Statistical Comparison to State.”
  - 2-stage False Discovery Rate (FDR) calculations.
Standardized Incidence Ratio (SIR)

SIR = Observed Cases/Expected Cases

- Age-Adjusted Expected Cases
  - Statewide age-specific rates.
  - Multiply local age group populations by Statewide rate for that age group.
  - Expected cancer cases are aggregated for all age groups in each analysis area.
Statistical Significance Testing

- A Z-value is computed based on the observed and expected numbers of cases.

If observed cases exceeds expected cases then:

Byar’s Z = \sqrt{9 \times \text{Observed}} \times (1 - \frac{1}{9/\text{Observed}} - \left(\frac{\text{Expected}}{\text{Observed}}\right)^{1/3})

Otherwise:

Byar’s Z = \sqrt{9 \times (\text{Observed}+1)} \times (1 - \frac{1}{9/(\text{Observed}+1)} - \left(\frac{\text{Expected}}{(\text{Observed}+1)}\right)^{1/3})

- The Z-value is converted to a P-value based on the normal distribution.

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False Discovery Rate (FDR)

- Allows significance levels for multiple comparisons to be determined based on the whole group of comparisons.

Areas are ranked (1-107) by Byar's P-values (low to high).

**FDR Stage 1:** If (Byar's P < (Rank / 107 x 0.1)) then “Yes”, Otherwise “No”.

**FDR Stage 2:** If (Byar’s P < (Rank x 0.1 / (1 + 0.1) / (107 – (sum of FDR Stage 1 “Yes” results))) then “Yes”, Otherwise “No”.

**Final significance testing algorithm:** If FDR Stage 1 are all “No” then “No”; If FDR Stage 1 are all “Yes” then “Yes”; If FDR Stage 2 is “Yes” then “Yes”; Otherwise “No”.

If SIR > 1.0 and FDR significance = “Yes” then “Statistically Higher”; If SIR < 1.0 and FDR significance = “Yes” then “Statistically Lower”; Otherwise “Not Different”.

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False Discovery Rate (FDR)

- Attempts to reduce the “false discovery rate”.

- Balances false positives v. false negatives to maximize the power of the test.

- Not as “conservative” as Bonferroni.

- Not as “liberal” as doing no correction for multiple comparisons at all.

FDR Approach to correcting the multiple comparisons problem. An example:

- “Milo’s Gore” has 11 observed cases and 23.64 expected cases.
- SIR = 0.465
- P-Value of .006
- Rank of 3 (ranked by P-values)
False Discovery Rate (FDR) - Example

- Stage 1 Formula:

  \[ \frac{3}{107} = 0.028, \quad P=0.006 < 0.028 \]
  therefore it is "significant" (at Stage 1)
## False Discovery Rate (FDR) - Example

Compute P-values based on observed/expected, and significance using 2-stage adaptive FDR method

<table>
<thead>
<tr>
<th>Area</th>
<th>observed</th>
<th>expected</th>
<th>SIR</th>
<th>Byar's Z-value</th>
<th>Byar's P-value</th>
<th>rank</th>
<th>1=Significant stage1_YN</th>
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**FDR:** 0.05

**Total:** 204 175.0
Results – Findings and Publications

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Results

- SIR’s were calculated at the community level for:
  
  - Non Hodgkin Lymphoma
  - Colorectal Cancer
  - Breast Cancer (female)
  - Prostate Cancer
  - Lung Cancer

http://healthvermont.gov/prevent/cancer/cancer_programs.aspx#stats

If You’re Concerned about Cancer Rates in Your Community

Vermont Department of Health
Vermont Cancer Incidence Report
Lung Cancer 2001-2008

Standardized Incidence Ratio (SIR) = Observed Cases / Expected Cases

<table>
<thead>
<tr>
<th>Area</th>
<th>Observed Cases</th>
<th>Expected Cases</th>
<th>SIR</th>
<th>Statistically Compared to</th>
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Statewide

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SIRs by Area

Data not shown in areas with fewer than 6 observed cases. Statistical comparison to state based on multiple comparisons.
### Vermont Department of Health

#### Table of Data

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<th>Area ID</th>
<th>Area_Name</th>
<th>Statistical Comparison to Stat SIR</th>
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<td>Not Different</td>
<td>0.96</td>
<td>17.90 0.9566 no</td>
</tr>
<tr>
<td>32</td>
<td>50003710000</td>
<td>Essex Town - West</td>
<td>Not Different</td>
<td>1.08</td>
<td>56.03 0.7188 no</td>
</tr>
</tbody>
</table>

Unknown Zone
Conclusions – Lessons Learned
Findings Applied to Richmond

- May 2012.
- Analyzed town-level cancer statistics for Richmond.
- No statistically significant differences found.
- Multidisciplinary collaboration (VDH, DEC, Ag).
- VDH recommends homeowners test drinking water for total coliform bacteria (Kit A) once a year and inorganic chemicals and mineral radioactivity (Kits C and RA) once every five years.
- Biggest delay to response related to Hurricane Irene.
Waterbury State Complex
Conclusions – Why this works for Vermont

- Able to do analysis at the community level for the whole state.

- Able to show significant differences that were not due to chance alone.

- Geographic and population size were conducive to the right number of analysis areas to make FDR method useful.
Lessons Learned

- Larger states with greater numbers of analysis areas would have trouble with the FDR multiple comparisons correction.

- Figuring out analysis geography is time consuming and requires multiple drafts.
Future Directions

- Excel works but it is cumbersome.
  - SQL Server for future iterations.
- Instant Atlas Desktop.
  - Move to Instant Atlas Server.
- Possible EPHT enhanced/ongoing activity with VCR.
Any Questions?

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