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

VERMONT DEPARTMENT OF HEALTH

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NAACCR Conference - June 5, 2012

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

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.

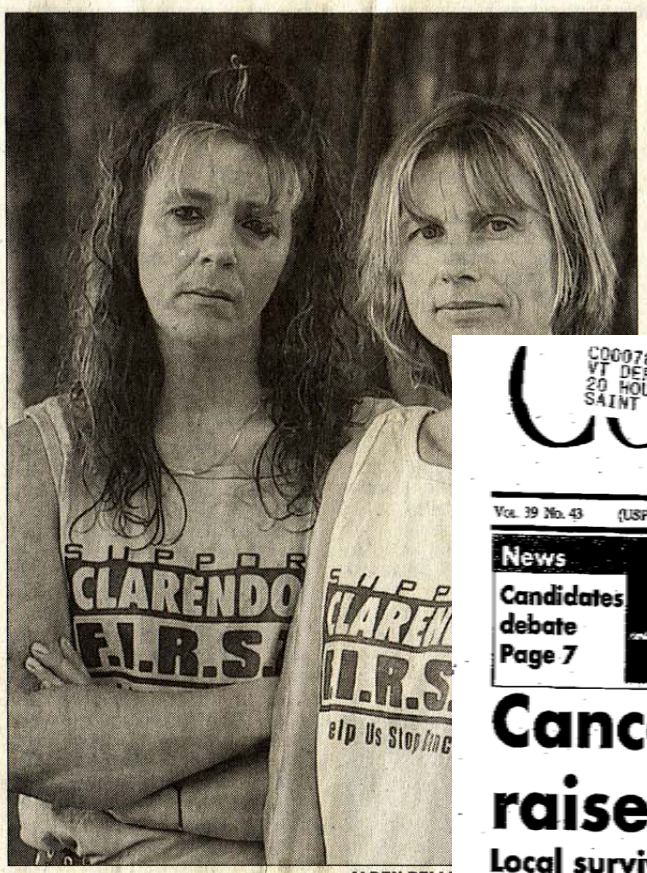
"I don't know anybody who hasn't looked at that map and wondered, 'What the heck is going on on Moulton Avenue?' " said Joe Mark, the academic dean of Castleton State College who is helping the group.

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



ALDEN PELL

Wanda Crossman (left) and Jackie Fenner c formed F.I.R.S.T., Families Interested In Re ness Together, after a number of children i been diagnosed with cancer.

Their group, Clarendon Families Interested in Researching Sickness Together, or Clarendon FIRST, has expanded into a community-wide coalition that includes local businesses, town officials and environmental organizations.

Some in town worry about sludge that was used on a local farm back in the 1980s. Others point to the possibility

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"Just abo organizatio link cancers causes, they to find a lin

Montpelier isn't going to help; it isn't going to change because who knows what you're moving into up there?"

Crossman doesn't plan to leave, either, but she acknowledges that 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.

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COUNTRY COURIER
The Weekly Journal for Northwest Vermont

Vol. 39 No. 43 (USPS 530-560) October 75

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, Jen Magnant looks up and down the dirt road and feels like she is 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 Magnant's age – 38 – and all have young children, she said.

Magnant is also a survivor, having been diagnosed with breast cancer a year ago and battling back from the living horror 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 neighbor after neighbor after neighbor," Magnant 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 38 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.

Magnant 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 a cancer cluster. As her concerns mounted, Magnant contacted the Vermont Department of Health in late September.

Health Department officials, though, say they looked into Magnant's concerns, analyzing regional and town data, and concluded there is no evidence local cancer rates are elevated here.

See CANCER p15

Fog & Light

The Enosburg Opera House is illuminated by early morning sun Saturday, Oct. 18, in Enosburg.

Photograph by Gregory J. Lamoureux

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

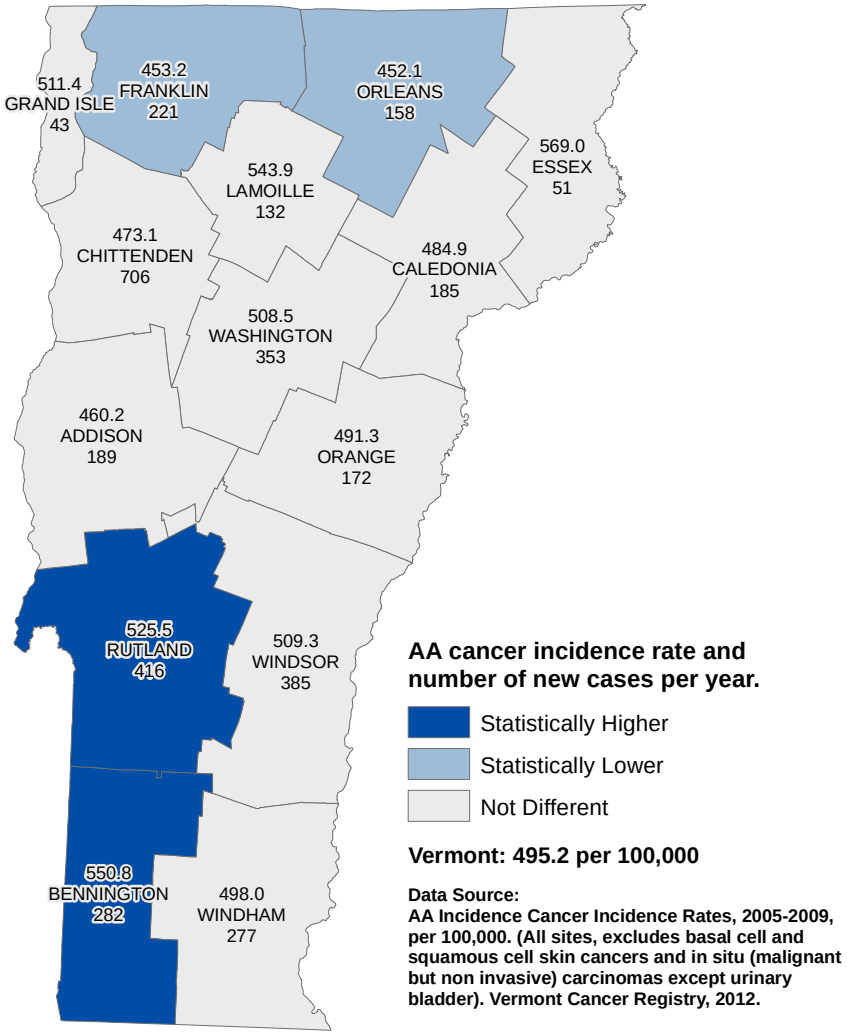
- Level 2 - **“Yes”**
  - Consult with TAG.
  - **Compute “observed v. expected.”**

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.

The best we could do:

- Incidence:
  - U.S., Vermont, and County
- SIR's and OR's
- Prevalence:
  - Vermont and County



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

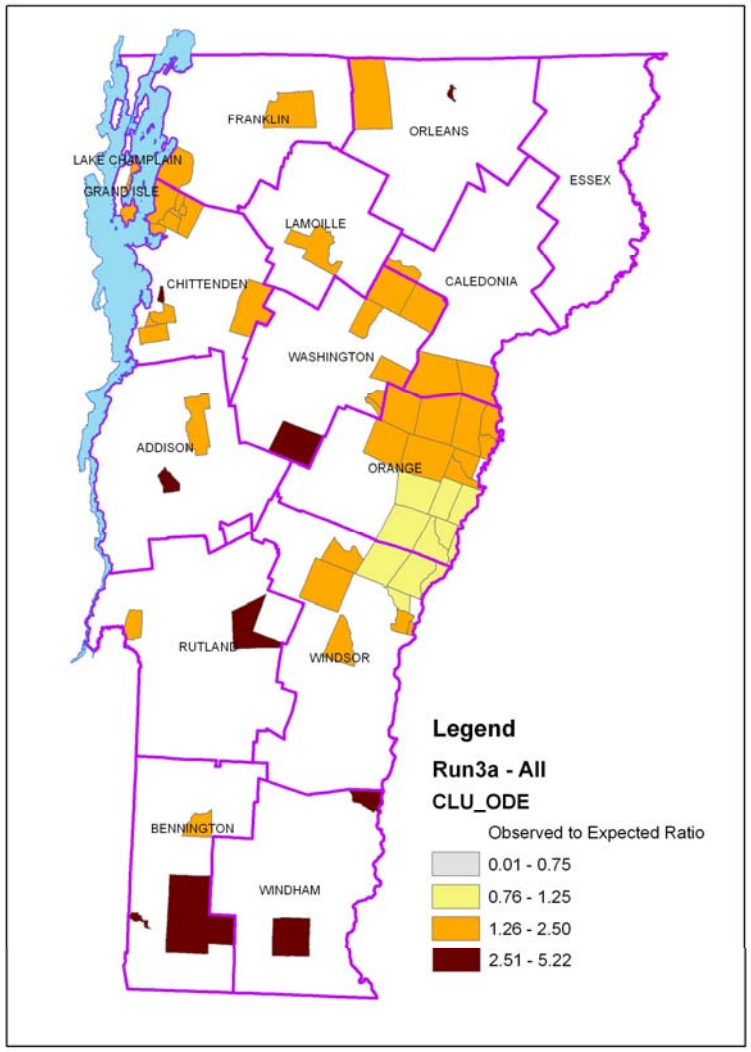
SaTScan

- Summarize registry data by census block groups or census blocks.
- Prep multiple SaTScan input files (difficult for census blocks).
- Choose SaTScan analysis settings (tricky business!).
- Map SaTScan outputs.

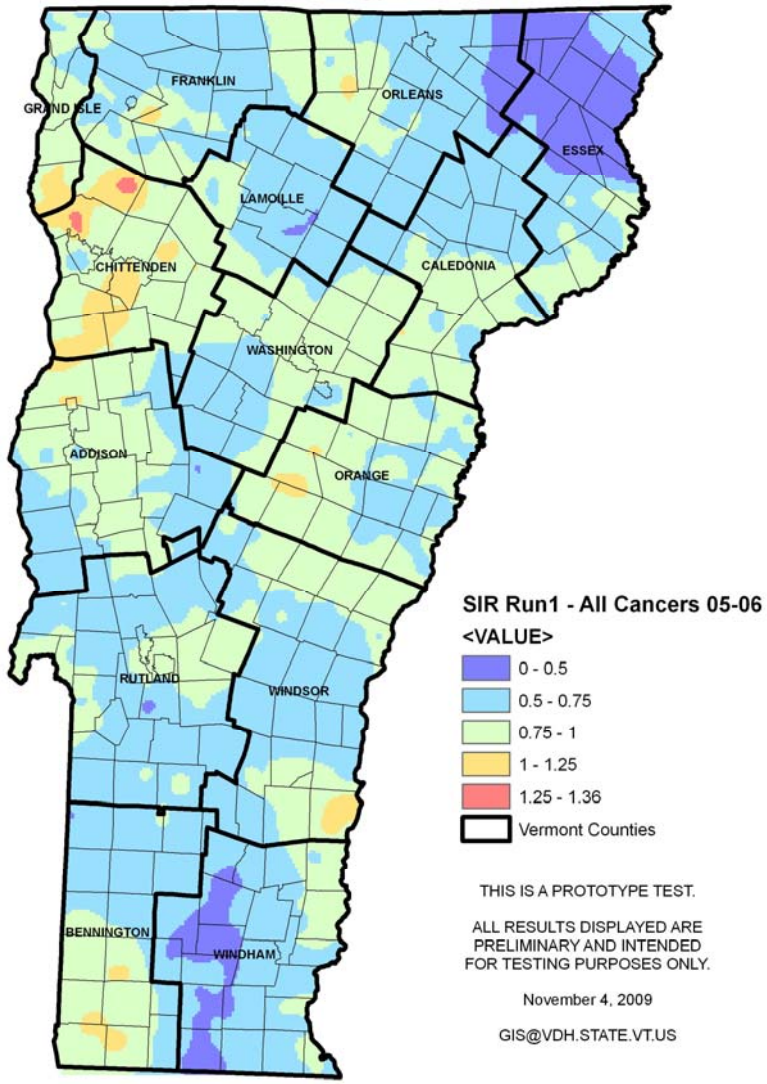
Smoothed SIR

- Summarize registry data by census blocks.
- Calculate state AA cancer rates.
- Calculate expected cases for each census block.
- Establish a statewide grid of analysis points.
- Utilize spatial adaptive filtering technique to deal with small case numbers in rural areas.
- Calculate observed to expected ratio (SIR) for each grid point.
- Generate final smoothed SIR map.

SaTScan Clusters
(all cancers 2005-2006 using 19 age group classes as covariat)



SIR Mapping using Spatial Adaptive Filtering technique
(similar to methodology used in Iowa)



analysis based on underlying geocoded cancer data (2005-2006) summarized by census blocks

Vermont Department of Health

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 straight-forward.
- Easily explained.
- Visually intuitive results.
- Significance? (multiple comparisons problem).

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”.

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.

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 x Observed) x (1-1/9/Observed - (Expected/Observed)^(1/3))

Otherwise:

Byar's Z = SQRT(9 x (Observed+1)) x (1-1/9/(Observed+1) - (Expected/(Observed+1))^(1/3))

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

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".

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.

Yoav Benjamini, Abba M. Krieger and Daniel Yekutieli. Adaptive linear step-up procedures that control the false discovery rate. *Biometrika* (September 2006) 93 (3): 491-507.

False Discovery Rate (FDR) - Example

- 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:

  3/107 = 0.028, 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

FDR: **0.05**

Area	observed	expected	SIR	Byar's Z-value	Byar's P-value	rank	1=Significant stage1_YN	1=Significant stage2_YN	Final: Significant_YN
Burlington	16	24.20	0.661	-1.626	0.1042	5	0	0	
Bennington	25	14.75	1.695	2.353	0.0184	4	0	1	yes
Wht Rvr Jct	15	11.93	1.258	0.769	0.4415	9	0	0	
Rutland	36	20.85	1.727	2.940	0.0030	2	1	1	yes
Springfield	12	10.03	1.197	0.508	0.6109	10	0	0	
Newport	22	12.03	1.830	2.495	0.0123	3	1	1	yes
St. Johnsb.	8	12.25	0.653	-1.085	0.2779	7	0	0	
Barre	14	16.13	0.868	-0.370	0.7114	11	0	0	
Brattleboro	21	9.23	2.276	3.224	0.0011	1	1	1	yes
St. Albans	20	21.00	0.952	-0.073	0.9419	12	0	0	
Middlebury	7	10.00	0.700	-0.773	0.4393	8	0	0	
Morrisville	8	12.63	0.634	-1.186	0.2358	6	0	0	
total:	204	175.0							

Results – Findings and Publications

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 Cancer Incidence Report

Lung Cancer 2001-2008

VERMONT
DEPARTMENT OF HEALTH
Vermont Cancer Registry

Cancer Type | Data Notes | Screen Capture | Print | Export Data | Help

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

Area	Observed Cases	Expected Cases	SIR	Statistically Compared to
Washington County South	13	30.1	0.43	Statistically Lower
Windham County South	18	35.7	0.50	Statistically Lower
Bennington City - Downtown	65	42.9	1.51	Statistically Higher
Orange County NW	45	27.9	1.61	Statistically Higher
Addison County Central	45	40.2	1.12	Not Different
Middlebury	41	47.8	0.86	Not Different
Bennington County Central	29	25.7	1.13	Not Different
Bennington County South	15	14.8	1.02	Not Different
Addison County West	24	35.3	0.68	Not Different

Statewide	SIR	Observed Cases
VERMONT	1.00	3,742

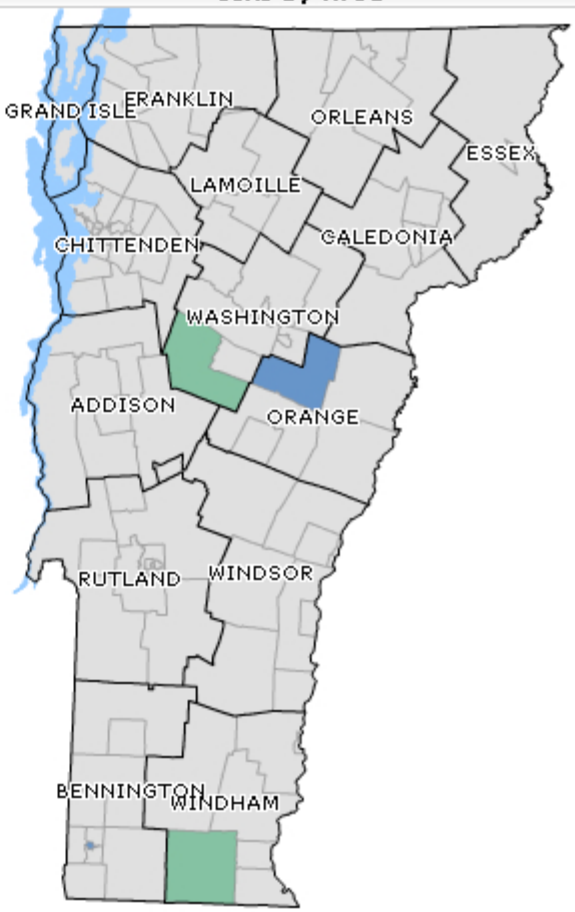
Data not shown in areas with fewer than 6 observed cases. Statistical comparison to state based on multiple comparisons correction.

SIRs by Area

Legend

- Statistically Lower
- Statistically Higher
- Not Different
- < 6 Cases
- Vermont Counties
- Vermont Towns
- Lake Champlain

SIRs by Area



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http://healthvermont.gov/prevent/cancer/incidence_reports_IA/VCR_SIRs_5Cancers0108_Suppressed_L - Windows Internet Explorer

SORT	Area_ID	Area_Name	Statistical Comparison to Stat	SIR	Observed Cases	Expected Cases	Byars P	Significant after multiple comparisons correctio
5	50001090250	Bristol	: Not Different	0.89	18	20.13	0.7411	no
2	50001100000	Addison County East	: Not Different	1.21	19	15.76	0.4755	no
3	50001200000	Addison County North	: Not Different	0.84	37	43.98	0.3286	no
4	50001300000	Addison County West	: Not Different	0.68	24	35.30	0.0583	no
1	50001400000	Addison County Central	: Not Different	1.12	45	40.15	0.4830	no
6	50001443500	Middlebury	: Not Different	0.86	41	47.78	0.3656	no
11	50003100000	Bennington County Central	: Not Different	1.13	29	25.65	0.5580	no
12	50003200000	Bennington County North	: Not Different	0.82	32	39.18	0.2832	no
13	50003300000	Bennington County South	: Not Different	1.02	15	14.75	0.9838	no
14	50003428500	Manchester	: Not Different	0.94	34	36.13	0.8059	no
15	50003570250	Pownal	: Not Different	0.99	21	21.12	0.9053	no
16	50003635500	Shaftsbury	: Not Different	0.93	23	24.83	0.8140	no
8	50003970900	Bennington City - NE	: Not Different	1.56	18	11.57	0.0964	no
10	50003971000	Bennington City - West	: Not Different	1.15	28	24.35	0.5093	no
9	50003971100	Bennington City - SE	: Not Different	1.34	53	39.58	0.0479	no
7	50003971200	Bennington City - Downtown	: Statistically Higher	1.51	65	42.91	0.0018	yes
17	50005100000	Caledonia County North	: Not Different	0.86	19	22.17	0.5871	no
18	50005200000	Caledonia County South	: Not Different	0.96	37	38.65	0.8742	no
19	50005300000	Caledonia County West	: Not Different	1.02	44	43.17	0.9392	no
20	50005417250	Lyndon	: Not Different	1.23	42	34.27	0.2216	no
22	50005957400	St Johnsbury - West	: Not Different	1.13	33	29.22	0.5305	no
21	50005957500	St Johnsbury - East	: Not Different	0.72	21	29.33	0.1373	no
23	50007000001	Burlington - Downtown	: Not Different	1.01	52	51.68	0.9987	no
24	50007000002	Burlington - Hill	: Not Different	1.01	25	24.68	0.9975	no
25	50007000003	Burlington - New North End	: Not Different	0.79	57	72.54	0.0701	no
26	50007000004	Burlington - Old North End	: Not Different	1.31	44	33.57	0.0960	no
29	50007002200	Colchester - East	: Not Different	0.88	23	26.09	0.6296	no
30	50007002300	Colchester - West	: Not Different	0.99	40	40.32	0.9567	no
33	50007002701	Essex Town - West	: Not Different	0.79	19	23.94	0.3664	no
32	50007002702	Essex Town - East	: Not Different	0.95	17	17.90	0.9566	no
39	50007003200	South Burlington - NE	: Not Different	1.06	56	53.03	0.7189	no

Lung Cancer 2001-2008 / Non-Hodgkin Lymphoma 2001-2008 / Prostate Cancer 2001-2008 / Notes

Vermont Department of Health

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

Vermont Department of Health

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?

Acknowledgments:

Peter Young, Ali Johnson, Moshe Braner, and Bill Apao all contributed significantly to the completion of this project.

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