Cancer Clusters in the USA: What Do the Last 20 Years of State and Federal Investigations Tell Us?

Michael Goodman, MD, MPH
Department of Epidemiology
Emory University Rollins School of Public Health
Atlanta, GA
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Background

Cancer cluster:

“...a greater-than-expected number of cancer cases that occurs within a group of people in a geographic area over a defined period of time” (CDC 2012)
Cluster types

• Occupational
• Residential - today’s topic
• Other (e.g. linked by common medical factors)
S. 50: Strengthening Protections for Children and Communities From Disease Clusters Act  
Congress: 2013

A bill to direct the Administrator of the Environmental Protection Agency to investigate and address cancer and disease clusters, including in infants and children.
1989: National Conference on Clustering of Health Events: Guidelines

- **Stage 1** Initial contact and response
- **Stage 2a** Evaluation of the area and reported cases
- **Stage 2b** Case verification
- **Stage 2c** Examination of incidence to confirm excess
- **Stage 3** Assessment of feasibility of etiologic study
- **Stage 4** Full scale etiologic study
1989: National Conference: challenges facing cluster investigations

- Limited statistical power
- Vague and heterogeneous case definitions
- Poor exposure characterization
- Inability to account for migration and latency
- “Boundary shrinkage”
Background

Boundary shrinkage

Definite clustering

Definitely no clustering

Random distribution
Study question

Have cancer cluster investigations conducted in the past 20 years (since the 1989 conference) improved our understanding of cancer etiology, or informed cancer prevention and control?
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Michael Goodman¹, Joshua S. Naiman²,³, Dina Goodman⁴, and Judy S. LaKind²,⁵,⁶

¹Department of Epidemiology, Emory University, Rollins School of Public Health, Atlanta, Georgia, ²LaKind Associates, LLC, Catonsville, MD, USA, ³School of Arts and Sciences, University of Pennsylvania, Philadelphia, Pennsylvania, USA, ⁴Emory College of Arts and Sciences, Atlanta, Georgia, ⁵Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, MD, USA, and ⁶Department of Pediatrics, Pennsylvania State University College of Medicine, Hershey, Pennsylvania
Methods

• Contacted health departments of 50 states and DC (phone, e-mail or website) to find publicly-available reports issued since 1990
• Examined available federal documents and peer-reviewed literature
• All investigations categorized with respect to:
  – cancer type(s)
  – hypothesized cause(s)
  – evidence to support perceived increase in incidence
  – conclusions about a link between cancer(s) of concern and hypothesized exposure(s)
Inclusion criteria

Reported or perceived geographic or community cancer cluster

State or federal investigation yielded a written publicly-available report, summary of an investigation, or journal article

Report date: January 1990 - September 2011
Exclusion criterion

- No formal state or federal investigation conducted
- Cluster involved a non-cancer outcome
- Cluster was occupational rather than residential
- Assessment of disease rates was initiated without an *a priori* concern about a cluster
428 investigations evaluating 567 cancers of concern
Three most commonly reported cancer types:

- brain
- breast
- leukemia/myeloma

Three most commonly identified chemicals of concern:

- TCE
- benzene
- dioxin
Brain cancer and exposures of concern

Results

- Not listed (24)
- Unspecified exposures (11)
- Radiation (4)
- PCE (3)
- Dioxin (2)
- TCE (2)
- Pesticides (2)
- CO2
- VOCs
- EMF
- Solvents
- Animal viruses
- N-Nitroso compounds
- 1,2-Dichloroethane
- Vinyl chloride
- Styrene-acrylonitrile trimer
- Chlorinated benzenes
- Pentachlorophenol
- Creosote
- Ammonia Cu Zn arsenate
- Boron
- Benzene
- PCBs
- PAHs
- Lead
- Cadmium
- Barium
Cancers attributed to TCE

Results

- All cancers (15)
- Breast (4)
- Leukemia (4)
- Brain/CNS (2)
- Lung (2)
- Uterus
- Abdomen
- Colon
- Testes
- Kidney
- Pancreas
- Childhood – all
- Astrocytoma
- Sympathetic nervous system
- Neuroblastoma
- Wilm’s tumor
- Bone
- Soft tissue sarcoma
- Lymphoma
- Hodgkin’s disease
- Non-Hodgkin’s lymphoma
Results

Number of cancer clusters investigated: 567

Number of confirmed cancer clusters associated with an environmental exposure: 72

Number of cancer clusters with established cause: 3

Number of cancer clusters with established cause: 1
Evidence for cluster/environmental association

**Woburn, MA**
Pediatric leukemia
Association with exposure to water from two wells G and H (boys only)

**Toms River, NJ**
Pediatric acute lymphocytic leukemia (ALL) and brain cancers
Associations with several air and water exposure metrics for ALL (girls only)
Evidence of causal link between exposure and cluster

Many pleural cancers noted in a single ZIP code in S. Carolina
Close aggregation of cases in a tri-county area around Charleston area, SC
Twelve of the 19 cases worked at the Charleston naval shipyard with evidence of exposure to asbestos
22 years after the National Conference on Clustering of Health Events, it is fair to state that an extensive nationwide effort to find environmental causes of community cancer clusters has not been successful.

Investigations of reported residential clusters rarely (if ever) provide answers about disease etiology.

Not the fault of the researchers and state or federal agencies conducting these investigations, but rather a reflection of fundamental methodological problems.
At a time when cancer research funding is scarce, we pose the following questions:

Given the outcomes of community cancer cluster investigations over the past 50 years (since 1960s):

Is it appropriate to devote more resources to staying on the same path we have been following, using the same hypotheses and tools?

If we do, can we expect a different outcome when we look back 20 years from now?
What’s Next?

Need to:

• recognize the shortcomings of the current approach to investigating cancer clusters investigations that originate with a perception of increased rates of cancer in a community.

• begin a multi-disciplinary national dialogue on more creative, innovative approaches towards understanding why cancer and other chronic diseases cluster in time and space.
Investigating Suspected Cancer Clusters and Responding to Community Concerns

Guidelines from CDC and the Council of State and Territorial Epidemiologists
CDC 2013 guidelines

• Continue to recommend the four-stage approach
• Highlight data sources and statistical techniques
• Emphasize effective communication strategies

Goals of updated guidelines “to provide needed decision support to public health agencies in order to promote sound public health approaches, facilitate transparency and build community trust”
What’s Next?

Workshop, April 2013, Baltimore

Advancing the Science and Communication of Cancer Cluster Investigations

Donald R. Mattison (chair), Risk Sciences International, U Ottawa
Michael Goodman, Emory U
Judy S. LaKind
Jerald A. Fagliano, NJ Dept Health and Senior Services
Timothy L. Lash, Emory U
Joseph L. Wiemels, UC, San Fransisco
Deborah M. Winn, NCI
Chirag Patel, Stanford U
Juliet VanEenwyck, Washington State Dept Health
Betsy A. Kohler, North American Association of Central Cancer Registries
Enrique F. Schisterman, NICHD
Paul Albert, NICHD
Baruch Fischhoff, Carnegie Mellon U.
Cancer Cluster Investigations: Review of the Past and Proposals for the Future

Michael Goodman ¹, Judy S. LaKind ²,³,⁴,⁵, Jerald A. Fagliano ⁵, Timothy L. Lash ¹, Joseph L. Wiemels ⁶, Deborah M. Winn ⁷, Chirag Patel ⁸, Juliet Van Eenwyk ⁹, Betsy A. Kohler ¹⁰, Enrique F. Schisterman ¹¹, Paul Albert ¹¹ and Donald R. Mattison ¹²,¹³
Proposed Approaches: technology

- Rapid case ascertainment
- Reconstructing residential history
- Spatial statistics untethered by administrative boundaries
Proposed Approaches: biology

• Use biomarkers of carcinogenesis to overcome latency problem

• Reclassify and re-group cases based on common mechanism of carcinogenesis rather than site

• Look for new and test under-explored hypotheses
Example of an underexplored hypothesis: infection and pediatric leukemia

- Leukemia incidence shows “epidemic patterns”
- In Fallon, NV all cases occurred within 3 years (most in one year), but age of children ranged between 2 and 19
- “Population mixing” theory has been around for over 30 years, but usually is not addressed in cluster investigations (including Woburn and Toms River)
Questions?