



Cancer Cluster Investigation Protocol

Cancer Clusters: Background Information

The Centers for Disease Control and Prevention (CDC) and the National Cancer Institute (NCI) define a cancer cluster as a greater-than-expected number of cancers diagnosed among a population in a particular geographic area, over a given period of time.

Some cancer clusters occur simply by chance. In these situations, clusters are not the result of a single, external cause; instead, the cluster simply reflects coincidental spatial grouping among individuals who have been diagnosed with cancer.

Other cancer clusters may be due to environmental exposure. Health officials may more easily trace the origin of a cancer cluster to an environmental cause if the cluster involves one or more of the following three traits: (1) the cluster contains a large number of *one* type of cancer, as opposed to several cancer types; (2) the cluster involves a *rare* type of cancer, as opposed to more commonly diagnosed cancers; and (3) the cluster involves a large number of cases of a type of cancer in an age group that is usually not affected by that cancer type.

Cancer clusters may also reflect better access to health care. Residents from one geographic area may be more likely to be screened for cancer compared to residents from another area. In these situations, cancer clusters exist because more cases of cancer are being diagnosed earlier than in other areas. As such, these cancer clusters do not reflect a truly elevated cancer risk in a geographic area.

Finally, cancer clusters may be due to clustering of lifestyle behaviors. Tobacco use, regular physical activity, diet, and other behaviors strongly impact cancer risk. If residents in one geographic area are more likely to engage in unhealthy lifestyle behaviors, the cancer incidence rate for that area may be elevated compared to other areas.

Steps to Investigating a Cancer Cluster

1. Make contact with requester (person initiating investigation)
 - a. Contact requester within one week of original inquiry
 - b. Verify requester contact information
 - i. Name, street address, zip code, preferred contact phone number and email address
 - c. Discuss specific cancer type(s) of concern
 - d. Discuss geographic area to be investigated
 - i. Determine if requester is concerned about rates in their zip code, or in a smaller area, such as their specific neighborhood or several streets
 - e. Determine if requester is personally aware of any cases
 - i. If so, obtain information about specific cancer cases, including patient's last name and date of birth
 - f. Record requester's perceived environmental risk factors (if any)
 - g. Inform requester of DPH's cancer cluster investigation protocol
 - i. Discuss prospective timeline
 - ii. Inform requester that investigation may take several months to complete

- h. Provide investigator's contact information (email address and direct office phone number)
 - i. Encourage requester to contact investigator with any concerns or questions about the investigation process
- 2. Establish a case definition
 - a. Case definition: a standard set of criteria to help DPH identify all cases that should be included in cluster analyses
 - b. Case definition parameters: cancer type; residence at diagnosis; year of diagnosis; age at diagnosis
- 3. Submit data request to Delaware Cancer Registry
 - a. Verify that specific cases provided by requester (if any) represent actual cancer diagnoses
 - i. Obtain record-level abstracts for review
 - b. Request all site file (2000-present) for the specified area under investigation
 - c. Required variables:
 - 1. Date of dx
 - 2. Age at dx
 - 3. Race
 - 4. Gender
 - 5. Primary Site
 - 6. Histology
 - 7. Behavior
 - 8. Address at dx
 - 9. Zip Code at dx
 - 10. Census Tract at dx
 - 11. County at dx
 - 12. Vital Status
 - 13. Other variables as needed
- 4. Calculate Expected Number of Cases
 - a. Calculate appropriate population denominators for area under investigation
 - i. Calculate census-based estimates of the ratio of the area population to total Delaware population
 - ii. Apply census-based ratios to total population estimates published annually by the Delaware Population Consortium (DPC) to derive DPC-based area population estimates
 - b. Perform basic cancer analyses
 - i. Calculate total number of cancers for area
 - ii. Identify distribution of cancer cases by type (using 25 broad cancer categories)
 - 1. Compare area distribution to state distribution
 - iii. Identify cancers contributing to "Other" category
 - 1. Verify breakdown of "other" cases follows expected proportions (i.e., not all "other" cases belong to same primary site)
 - c. Calculate area-specific incidence rates for comparison
 - i. Calculate age-adjusted rates for requested cancers
 - 1. If distribution of cancers indicates abnormalities, also calculate incidence rates for all other 25 cancer types
 - 2. If requester is especially concerned about environmental hazards, also calculate rates for known associated cancers
 - ii. Calculate rates using most recently available five-year period of data
 - iii. Compare area-specific incidence rates to rates for larger geographic regions

1. Zip code vs. county vs. Delaware vs. United States
 2. If cancer type under investigation is monitored via the I&M Report, obtain county- and state-level rates from I&M Report
 3. If cancer type is more specific, and not represented in the 25 categories monitored via the I&M Report, obtain county- and state-level rates from a national cancer surveillance organization (e.g., NAACCR)
5. Analyze Age of Diagnosis Trends for Requested Cancers
- a. Verify average age of diagnosis occurs within the expected age group
 - b. Determine number of outliers (cases diagnosed at a much younger or older age than expected)
 - i. Perform chi-square analysis to test for significant differences in the age of diagnosis distribution (zip code-level (or census tract-level) vs. state-level)
 - ii. Perform t-test to test for significant differences between mean age of diagnosis (zip code-level (or census tract-level) vs. state-level)
6. Observed vs. Expected Cases
- a. Determine if significant differences exist between area and state rates
 - i. Calculate 95% confidence intervals (CIs) for area-specific rates
 1. For incidence rates based on fewer than 100 cases, calculate 95% CIs using a modified methodology endorsed by the National Center for Health Statistics
 - a. Modified methodology accounts for underlying Poisson probability distribution assumptions
 2. For incidence rates based on greater than 100 cases, calculate 95% CIs using traditional methodology
 - ii. Compare CIs for area-specific rates to CIs for state-level rates to determine if statistically significant differences in rates exist
 1. If area-specific rates are significantly higher than state rates, calculate race- and gender-specific incidence rates for the area under investigation
 - b. Calculate standardized incidence ratios (SIRs) for cancers that are significantly elevated at the zip code (or census tract) level compared to the state rate

Outcomes

1. Post completed cluster investigations to the DPH website (exclude requester's identity)
 - a. Cluster investigation chart updated with respect to investigation findings
2. Adopt "watchful waiting" annual surveillance under the following two circumstances: (1) rarer or unusual cancers are non-significantly elevated in the area under investigation or (2) common cancers (with typical age of diagnosis distributions) are significantly elevated in the area under investigation
 - a. Add indicated cancer type and area to surveillance list
 - b. Calculate five-year rates annually using most recently available DCR data
 - c. Maintain contact with original requester and provide updated rates on a yearly basis
 - d. Re-evaluate need for continued surveillance annually
3. Provide educational materials or seminars to residents in the area under investigation
4. Target Screening for Life services in the area under investigation, if applicable
5. Discuss the utility for an in-depth investigation under the following two circumstances: (1) rarer or unusual cancers are significantly elevated or (2) a cancer with an unusual age of diagnosis pattern is non-significantly elevated

Prepare Response Letter

1. Provide general background information on cancer clusters
2. Explain how DPH investigates suspected clusters
3. Review findings related to requested cancers
 - a. If rates for non-requested cancer types were found to be significantly elevated, also include this information in the response letter
4. Discuss risk factors for cancer type(s) mentioned in original inquiry
 - a. When appropriate, include educational brochures (e.g., cancer-specific information from ACS, NCI) and information on free cancer-related services for (e.g., Screening for Life; Delaware Cancer Treatment Program)
5. Discuss how DPH plans to proceed based on findings
6. If applicable, mail a copy of the response letter to local legislators within requester's immediate area