Guidelines for the Investigation of Clusters of Non-Communicable Health Events

June 2011
Guidelines for the investigation of clusters of non-communicable health events were developed through collaboration between the Surveillance and Assessment Branch, Alberta Health and Wellness, and Surveillance and Health Status Assessment, Population and Public Health, Alberta Health Services.

For additional information, contact

Surveillance and Assessment
Alberta Health and Wellness
P.O. Box 1360 Stn Main
Edmonton, AB T5J 2N3

Phone: 1.780.427.4518
Toll Free: 310-0000 (in Alberta only)
Fax: 1.780.427.1470
Email: Health.Surveillance@gov.ab.ca

Cancer Surveillance Department
Surveillance and Health Status Assessment
Alberta Health Services
Suite 1400 10123 99 St
Edmonton, AB T5J 3H1

Phone: 1.780.643.4496
Fax: 1.780.643.4380
Email: shsa@albertahealthservices.ca or acb.surveillance@albertahealthservices.ca

Internet: www.health.alberta.ca
ISBN: 978-0-7785-8299-1 (Print)
ISBN: 978-0-7785-8300-4 (PDF)
# Table of Contents

Executive Summary ....................................................................................................................... 4
Background...................................................................................................................................... 5
Methods.......................................................................................................................................... 6
Guideline Descriptions.................................................................................................................. 6

Figure 1: Non-communicable disease cluster investigation ........................................................ 7

Primary Evaluation: Phase 1 ........................................................................................................ 8

Figure 2: Primary evaluation (Phase 1) of the non-communicable disease cluster investigation process ................................................................................................................. 8

P1S1........................................................................................................................................ 8
P1S2........................................................................................................................................ 9
P1D1 ....................................................................................................................................... 9
P1S3........................................................................................................................................ 9

Secondary Evaluation: Phase 2 .................................................................................................. 10

Figure 3: Secondary evaluation (Phase 2) of the non-communicable disease cluster investigation process ......................................................................................................................... 10

P2S1........................................................................................................................................ 10
P2S2........................................................................................................................................ 11
P2D1 ....................................................................................................................................... 11
P2S3........................................................................................................................................ 12
P2D2 ....................................................................................................................................... 12
P2S4........................................................................................................................................ 12

Tertiary Evaluation: Phase 3 ....................................................................................................... 12

Figure 4: Tertiary Evaluation (Phase 3) of the non-communicable disease cluster investigation process ......................................................................................................................... 12

P3 ........................................................................................................................................ 13

Discussion .................................................................................................................................... 13

Appendix A – Glossary.................................................................................................................. 15

Appendix B – Figures 1–4.............................................................................................................. 16

Figure 1: Non-communicable disease cluster investigation process ........................................... 16
Figure 2: Primary evaluation (Phase 1) of the non-communicable disease cluster investigation process ...................................................................................................................................... 17
Figure 3: Secondary evaluation (Phase 2) of the non-communicable disease cluster investigation process ...................................................................................................................................... 18
Figure 4: Tertiary evaluation (Phase 3) of the non-communicable disease cluster investigation process ...................................................................................................................................... 19

Appendix C – P2S2 (Gather and Evaluate Evidence) Analytic Approaches.............................. 20
Epidemiologic Dimensions........................................................................................................... 20
Potential Measures....................................................................................................................... 20
Analytic Considerations........................................................................................................ 21
Examine Community’s Experience .................................................................................. 21
Examine Province’s Experience...................................................................................... 21
Statistical Considerations.............................................................................................. 21
Synthesis of Evidence..................................................................................................... 22
Appendix D – References................................................................................................. 23
Executive Summary

Guidelines for the investigation of a non-communicable disease cluster were developed to apply recognized investigative processes within an Alberta-specific context. Alberta Health and Wellness and Alberta Health Services collaborated to perform an analysis of provincial practice and needs, a detailed literature review and established the guidelines presented here. The guidelines account for data access and data quality available in Alberta, as well as communication processes mandatory for the success of any non-communicable disease cluster investigation.

The overall investigation is separated into three phases that mark the primary, secondary and tertiary evaluation components of an investigation. Decision points indicated within each phase highlight considerations about whether further action is required. Guidelines and considerations are also provided for the analytic and communication actions of relevant investigative steps or decision points.

These guidelines can be used province wide in the event that a suspected cluster of non-communicable health events is reported and can also serve as a guide for other provinces or areas that have access to high quality population-based data sources.
Background

A cluster is defined as a greater than expected number of health events in a group of people, geographic area and time period.\(^1\) Suspected clusters of non-communicable or chronic disease health events such as birth defects, multiple sclerosis, or cancer are often reported by community members or representatives and typically result from a perceived environmental or occupational association. Following the report of a suspected cluster, public health officials evaluate the situation and initiate a response.

Many public health agencies worldwide have published guidelines and protocols for investigations into clusters of non-communicable health events. Previous non-communicable disease cluster investigations in Alberta have been performed on a case-by-case basis; each has typically followed a process similar to that outlined by the internationally-recognized Centers for Disease Control (CDC).\(^1\) The CDC protocol is a useful guide; however, it does not account for data access and data quality available in Alberta, nor does it address Alberta-specific communication needs.

The absence of a standardized Alberta-specific document has occasionally created confusion making stakeholder communication and education very difficult. Established provincial guidelines will standardize the process to promote efficient and informed communication among all stakeholders including provincial and local public health professionals, provincial and federal health agencies, as well as the general public. Additionally, the guidelines will help instruct, support and educate individuals completing surveillance analytic work required in such investigations.
Methods

Alberta Health Services and Alberta Health and Wellness collaborated to develop these guidelines for the investigation of clusters of non-communicable health events. The initial assessment of provincial needs and practice was performed through discussions and interviews with provincial public health officials, as well as an analysis of former non-communicable disease investigations undertaken by provincial public health agencies.

In addition to the provincial assessment, a detailed literature review was performed. This included a review of guidelines and protocols that have been published by public health agencies such as the internationally-recognized Centres for Disease Control (CDC)\(^1\) and in countries worldwide; New Zealand,\(^2\) Europe,\(^3\) and seven states within the United States.\(^4\)\(^\text{-10}\) Each document outlined the region-specific protocol followed in the event of a suspected cluster of non-communicable health events.

The in-depth literature review also included peer-reviewed journal publications that outlined issues related to non-communicable disease cluster investigations. These included discussions and recommendations about the use of statistical tools and analyses required for small numbers,\(^1\)\(^\text{-13}\) methodological problems to be expected,\(^1\)\(^\text{-17}\) communication concerns,\(^1\)\(^\text{-20}\) as well as risk communication strategies that should be considered.\(^2\)\(^\text{-24}\)
Guideline Descriptions

Figure 1: Non-communicable disease cluster investigation

In these guidelines overall investigative steps of the non-communicable disease cluster investigation are separated into three phases that reflect the progress of the investigation over time (P1–P3, Figure 1).

- The aims of the primary evaluation, Phase 1, are to establish an open dialogue with the person or organization reporting a suspected cluster of health events and to determine the likely scope of the investigation (Figure 1, P1; Figure 2). The person or organization reporting the cluster is the requestor, who could be for example, a member of the public or a concerned health care provider.

- The secondary evaluation, Phase 2, is pursued if warranted and involves further in-depth investigation, as well as an assessment of the necessity and feasibility of further action (Figure 1, P2; Figure 3).

- If justified, a tertiary evaluation involving on-going surveillance or etiologic investigation is executed in Phase 3 (Figure 1, P3; Figure 4).
The three investigative phases (P1–P3) are further broken down into steps (S) and decision points (D); each of these will be described further in subsequent sections. In Figures 1–4 the steps and decision points are accompanied by communication and analytic actions for consideration. The communication and analytic actions are essential components of the guidelines for cluster investigations. The investigative process is presented in a stepwise fashion although some analytic steps may occur concurrently and may be repeated as information needs evolve.

**Primary Evaluation: Phase 1**

**Figure 2: Primary evaluation (Phase 1) of the non-communicable disease cluster investigation process**

<table>
<thead>
<tr>
<th>COMMUNICATION ACTIONS</th>
<th>INVESTIGATION STEPS</th>
<th>ANALYTIC ACTIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Establish open communication with the requestor and inform other agencies as necessary</td>
<td>P1 – Primary Evaluation</td>
<td></td>
</tr>
<tr>
<td><strong>S1</strong> Assess the Situation</td>
<td>Collect initial information and form initial case definition (disease; illness or symptoms; people; number of cases; place; geographic area/time)</td>
<td></td>
</tr>
<tr>
<td><strong>S2</strong> Review the Information</td>
<td>Collect general information on disease and community risk factors</td>
<td></td>
</tr>
<tr>
<td>Consideration: Is there intense community concern?</td>
<td><strong>D1</strong> Decision Point 1: Is Further Investigation Warranted?</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td><strong>S3</strong> Update the Requestor</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Begin Phase 2</td>
<td></td>
</tr>
<tr>
<td>Provide education (process, general disease information)</td>
<td>Consideration: Is there an apparent high number of cases and/or biologic plausibility?</td>
<td></td>
</tr>
</tbody>
</table>

**P1S1**

Following the initial report of a suspected clustering of health events, open communication must be established between the person reporting the suspected cluster and a representative of the investigating team. This relationship is vital to the maintenance of transparent and trusting two-way communication throughout the entire investigation and should involve regular updates about the process and employed steps.

A situational assessment where the needs of the requestor are clarified is an important component of this communication. Clarifying and gathering information will help inform the analytic aspects of the investigation. These include an establishment of a preliminary case definition (disease and parameters) and evaluation of the feasibility of determination and attainment of epidemiologic variables. Epidemiologic variables include the number of persons affected by the disease (person), geographic location (place), and period of time the illness has been observed (time). General information about the disease and risk factors that are relevant to the community should be collected. If necessary, other agencies should be notified about the suspected cluster.
In these communications privacy and confidentiality should be considered; however, it is also important to consider that the good of the community may override the rights of the individual during a cluster investigation. This may involve notifying others such as Alberta Health Services, Alberta Health and Wellness, or appropriate medical officers of health (MOH; dependent on location of requestor; Health Canada for on-reserve investigations and designates in health zones for other locations). In all cases disclosures made by all parties would be consistent with relevant legislation. Finally, a timeline for responding to the requestor should be agreed to with the requestor.

P1S2
The investigating team should now compile and review the information gathered in P1S1. This will ensure that analysts and other team members are familiar with the relevant topic(s) of investigation. Further gathering and review should be undertaken if a more in depth understanding is necessary and may include additional academic and grey literature review, or discussions with public health content experts.

P1D1
Following review of the obtained information, an evaluation of whether or not further investigation is warranted will be made by the investigating team. Each of the following should be considered:

• Is there intense community concern?
• Are there an apparent high number of cases?
• Is there biologic plausibility between the reported disease and potential environmental or occupational exposure?
• Are cases in a specific geographic area and within a certain time period?
• Are there a large number of cases of one type of disease? Is that disease type rare or common? Are the persons diagnosed in age groups commonly affected by that type of disease?
• Is further investigation feasible?
• If further investigation is not warranted or feasible, what other actions could be undertaken to address community concerns?

P1S3
Following the information review and preliminary decision-making steps, the requestor should be notified about any conclusions or next steps. This may include education about general disease information, results of the primary evaluation and expectations for Phase 2 (if applicable). This communication with the requestor should occur at the agreed upon time with any potential delays having been communicated to the requestor as they occurred. The outcome of this update (i.e., community response) may inform the investigative team about whether or not a re-evaluation of P1D1 is necessary.
Secondary Evaluation: Phase 2

Figure 3: Secondary evaluation (Phase 2) of the non-communicable disease cluster investigation process

P2S1

When the investigation involves multiple agencies, an investigative lead and requestor liaison should be identified. These may continue to be representatives from the initial agency contacted. If possible, the requestor liaison should remain the same as the original person who maintained contact with the requestor. At this step it should be determined whether the requestor will take an active or passive role in the investigation. In some cases the lead and liaison roles may be designated to public health professionals responsible for the health of the community, such as the appropriate MOH.

There must be a distinction at this stage between the roles of the investigative lead and support services. The MOH may be leading the overall investigation, but primary analyses and/or communication supports may be undertaken by a relevant group such as cancer surveillance, and supported by other agencies such as the Public Health Agency of Canada and Alberta Health and Wellness. In larger investigations a formal committee or working group may be formed to ensure effective collaboration and communication among involved groups.
P2S2

The purpose of this step is to determine if there is any evidence to support a clustering of health events in the area of concern. Using the information obtained in Phase 1 and through consultation with clinical or surveillance experts as necessary, the following characteristics should be defined and, where applicable, obtained from administrative data:

- case definition;
- study population(s);
- reference population(s);
- geographic area of interest and;
- study time period.

Considerations that may restrict these definitions include accessibility of relevant administrative data as well as the availability and limitations of existing data. It is also necessary to set parameters that have the potential to capture the suspected cluster without dilution of the possible observed health effects. For example, it may be necessary to select a geographic area large enough to capture all potential cases but small enough to be able to detect any localized difference in outcome.

To examine the community’s experience it is important to evaluate whether the number of cases observed in the study population is different than what would be expected. This evaluation is based on what was observed in an appropriate reference population. An examination of the community’s experience in a larger context should be performed to understand whether the results observed differ substantially from other communities across the province. This might include a ranking of the observed incidence rates by community across the province, a spatial scan to identify clusters in the province, or a point source cluster analysis. At this stage of the investigation it may be useful to consider potential explanatory risk factors (lifestyle, occupation, environment).

If an environmental or occupational contaminant is suspected, an expansion of the case definition to include un-reported health events based on biologic plausibility may be necessary. This information will likely be more difficult to obtain than the administrative data used to examine the community situation. At this point in the investigation it may be appropriate to initiate a community health assessment. Potential etiologic considerations, such as potential occupational or environmental exposures, may be further investigated in a tertiary evaluation (Phase 3).

Qualitative and quantitative evidence should be synthesized and an overall assessment and evaluation performed. For more information on suggested analytic approaches in P2S2, see Appendix A.

P2D1

Once the evidence to-date has been compiled the investigating team must determine if the results are definitive or if other information is needed before an evaluation of the evidence can take place. For example, it may have been determined that there are a higher than expected number of incident cases in a small area; however, to better understand if a reported point source could be involved, returning to P2S2 and assessing a potential dose-response effect could be useful.
P2S3
A quality assurance review of the results should occur after all valid evidence is gathered. The quality assurance review may include reviews of the methodology, results and report by intra-agency peers not involved in the investigation or peer-reviews by external professionals.

P2D2
Following review of the information obtained in Phase 2, the investigating team will evaluate whether or not further investigation is warranted. Each of the following should be considered:

- What does the evidence suggest in terms of the existence of a cluster? For example, is there evidence that the number of observed cases is higher than expected or that there is a sudden increase over time?
- If there is evidence of a cluster, is there a biologically plausible mechanism?
- Have the concerns of the requestor been addressed?
- Have necessary public health actions been taken?
- Is further investigation feasible and likely to answer any remaining questions?
- If further investigation is not warranted or feasible, what other actions could be undertaken to address community concerns?

P2S4
On going documentation of all events must be maintained throughout the investigation. As a final stage in the analytic process of Phase 2 a report should be completed that documents the methods used, results obtained and recommended next steps. Following the completion of the report a repeat of the quality assurance stage (P2S3) may be necessary. A summary of the main investigation points should also be presented to the requestor through an executive summary or in-person presentation. The requestor should receive the results before they are released publicly. In the case of media involvement, a person designated to speak on behalf of the investigating team should be provided with a summary of the investigation process, methods, results and next steps.

Tertiary Evaluation: Phase 3

Figure 4: Tertiary Evaluation (Phase 3) of the non-communicable disease cluster investigation process

© 2011 Government of Alberta
P3

If further investigation is warranted following an assessment of the necessity and feasibility of further investigation in Phase 2 (P2D2), Phase 3 will take the form of ongoing surveillance or epidemiologic investigation.

Surveillance activities might be continued if the results of Phase 2 are not definitive, if an epidemiologic investigation is not feasible, or if there is continued strong interest from the community.

If the results of Phase 2 are indicative of an excess an epidemiologic investigation may be initiated to successfully reveal a potential etiology or help to define the scope of the problem. This may be undertaken by parties external to the investigative team for example, international experts and academic experts in the relevant fields. If the members involved in the investigation change or expand, it is imperative that ongoing communication be maintained among all relevant stakeholders.

A followup plan and communication strategy should be arranged to foster continued collaboration and risk communication for the surveillance or epidemiology team, original investigative team, requestor and other concerned parties.

Discussion

Requests for investigations into suspected clusters of non-communicable health events such as birth defects, multiple sclerosis, and cancer are made on a regular basis to various health agencies worldwide. It was reported that there were over 1,000 cancer cluster investigation requests in the United States in both 1989 and 1997. Despite many requests for cluster investigations the majority (70–95%) end at the time of initial contact with the requestor. Potential methodological issues that arise in these investigations, such as small incident cases that yield results with low statistical power and potential post-hoc bias as described by the Texas sharpshooter fallacy, have raised some debate about whether or not non-communicable disease cluster investigations are worth the resources that they require. Because a perceived clustering of health events is usually associated with a great deal of anxiety and stress from involved communities, these investigations continue to be a very important and necessary public health responsibility.

It is recommended that respondents maintain communication with the requestor throughout the process. This on-going collaborative relationship with the local community should be established at the beginning stages of the investigation, not at the end of the process. It has also been noted that it is important to listen to the requestor, recognize and legitimize their emotions, as well as to be transparent and open about the process and results. Although many other health agency non-communicable disease cluster investigation protocols mention communication activities with the requestor, few expand on the communication aspects of the investigation. These guidelines include suggested communication key milestones in addition to the recommended analytic actions provided because they are important to a successful risk communication strategy.

The documentation and implementation of established guidelines provides a common resource that can instruct and guide all stakeholders involved in an investigation. Along with increased stakeholder education, a common document can also increase effective collaboration among public health officials, support agencies, media, and the general
public. These non-communicable disease cluster investigation guidelines can be used as part of the joint Alberta Health Services - Alberta Health and Wellness strategy for the investigation of clusters of non-communicable health events. The guidelines can also serve as a guide for any other provinces or areas that have access to high quality population-based data.
## Appendix A – Glossary

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biologic plausibility</td>
<td>The likelihood that a given factor can cause a biological effect within an individual that leads to disease. It is based on current knowledge of biological processes.</td>
</tr>
<tr>
<td>Data dredging</td>
<td>Exploring data through repeated significance tests until you find something significant, without appropriately accounting for all of the exploratory tests that have taken place.</td>
</tr>
<tr>
<td>Dose-response effect</td>
<td>The idea that larger doses will result in larger observable effects.</td>
</tr>
<tr>
<td>Epidemiology</td>
<td>The study of diseases and their risk factors (in humans). It has its origins in the study of epidemics but now broadly encompasses infectious diseases, chronic diseases, injury and determinants of health.</td>
</tr>
<tr>
<td>Funnel plots</td>
<td>A method of displaying rates for a large number of small communities at the same time. Funnel plots take into account the variability expected from different population sizes.</td>
</tr>
<tr>
<td>Grey literature</td>
<td>Non-academic literature, often in the form of government and not-for-profit reports.</td>
</tr>
<tr>
<td>Point source</td>
<td>A fixed potential source of exposure that is localized to a small geographic area. A point source cluster analysis would examine health outcomes around the point source.</td>
</tr>
<tr>
<td>Post-hoc bias</td>
<td>The potential bias that can occur when investigations are started because of a random clustering of events. Also known as the Texas sharpshooter fallacy, which describes a Texan shooting at the side of the barn and afterwards drawing a bull’s eye around the biggest clustering of shots.</td>
</tr>
<tr>
<td>Spatial scan</td>
<td>A statistical method that searches a large geographic area for smaller geographic clusters of higher or lower rates.</td>
</tr>
<tr>
<td>Temporal trends</td>
<td>Changes in the incidence and/or prevalence of a disease or risk factors that occur over time.</td>
</tr>
</tbody>
</table>
Appendix B – Figures 1–4

Figure 1: Non-communicable disease cluster investigation process

**COMMUNICATION ACTIONS**
- Establish open communication with the requestor and inform other agencies as necessary
- Provide education (process, general disease information)
- Identify role of the requestor in the investigation
- Identify investigation lead
- Identify working group/committee
- Identify requestor liaison (ongoing communication with requestor)
- Perform an inter-agency evaluation and/or external peer-review

**INVESTIGATION STEPS**
- **P1 – Primary Evaluation**
  - S1: Assess the Situation
  - S2: Review the Information
  - D1: Is Further Investigation Warranted?
  - S3: Update the Requestor

- **P2 – Secondary Evaluation**
  - S1: Define roles
  - S2: Gather and Evaluate Evidence
  - D1: Is Further Context Required?
  - S3: Quality Assurance
  - D2: Are Further Steps Warranted? Are they Feasible?
  - S4: Communicate Results to the Requestor

- **P3 – Tertiary Evaluation**
  - Surveillance or Epidemiologic Investigation

**ANalytic ACTIONS**
- Collect initial information and form initial case definition (disease, person, place and time)
- Collect general information on disease and community risk factors
- Obtain administrative data based on case definition, disease, person, place and time
- Examine community’s experience, province’s experience and consider potential explanatory risk factors
- Synthesize the evidence
- Review of intra-agency evaluation and/or peer-review results
- Complete a report
- Coordinate ongoing activities if warranted and feasible
Figure 2: Primary evaluation (Phase 1) of the non-communicable disease cluster investigation process

**COMMUNICATION ACTIONS**

- Establish open communication with the requestor and inform other agencies as necessary

**ANALYTIC ACTIONS**

- Collect initial information and form initial case definition (disease; illness or symptoms/people; number of cases/place; geographic area/time)
- Collect general information on disease and community risk factors

**INVESTIGATION STEPS**

- **S1** Assess the Situation
- **S2** Review the Information
- **S3** Update the Requestor

**Decision Point 1:** Is Further Investigation Warranted?

- **No** Begin Phase 2
- **Yes**

**Consideration:** Is there an apparent high number of cases and/or biologic plausibility?
Figure 3: Secondary evaluation (Phase 2) of the non-communicable disease cluster investigation process

**COMMUNICATION ACTIONS**
- Identify role of the requestor in the investigation
- Identify investigation lead
- Identify working group/committee
- Identify requestor liaison (ongoing communication with requestor)

**INVESTIGATION STEPS**

**P2 – Secondary Evaluation**

**S1** Determine Roles and Responsibilities

**S2** Gather and Evaluate Evidence

**D1** Decision Point 1: Is Further Context Required?
   - No
   - Yes → Back to S2

**S3** Quality Assurance

**D2** Decision Point 2: Are Further Steps Required? Are they Feasible?
   - No
   - Yes → Begin Phase 3

**S4** Communicate Results to the Requestor

**ANALYTIC ACTIONS**

- Case definition, time period, geographic area, population, etc.
- Examine community’s experience
- Examine province’s experience
- Examine potential risk factors (lifestyle, occupation, environment)
- Synthesize the evidence
- Considerations: Are the results definitive? Are the potential risk factors a concern?
- Review of intra-agency evaluation and/or peer-review results
- Considerations: Is there evidence of an excess? Is there a sudden increase over time? Is there a biologically plausible exposure?
- Complete a report

Present results to the requestor
Figure 4: Tertiary evaluation (Phase 3) of the non-communicable disease cluster investigation process

**COMMUNICATION ACTIONS**

Communicate with requestor and implement follow-up plan

**INVESTIGATION STEPS**

Based on Phase 2, Decision Point 2:

- Surveillance
- Epidemiologic Investigation

**ANALYTIC ACTIONS**

Coordinate on-going activities if warranted and feasible
Appendix C – P2S2 (Gather and Evaluate Evidence) Analytic Approaches

Epidemiologic Dimensions

The Gather and Evaluate Evidence step is the primary analysis step in these guidelines. The goal is to provide evidence regarding the possibility of a cluster, context to place the community’s experience within the provincial experience, and information to inform decisions and future actions. The basic epidemiologic dimensions of disease, person, place, and time are considered, as are the approaches to analyses and evidence synthesis.

The information obtained in Phase 1 regarding the disease or condition of interest will be crucial to the creation of a case definition. A case definition is the operational definition used to obtain case observations from information systems. In registry based data the case definition will centre on the coding rules used. However, with administrative data, in addition to coding rules, the case definition will include considerations regarding disease course and contact with the health care system. The relationship between the disease of interest and any relevant coding rules must be considered in the development of the case definition, as should the impact of any community situation that may affect case definitions or ascertainment.

Potential differences between the clinical and the data-based case definitions should be considered. A clinical definition may be more focused or may be broader than the resolution reliably available from administrative or registry data. Some general principles would be to ensure that the administrative case definition captures the relevant cases and that case definitions err on the side of inclusion. Consultation with both clinical experts and surveillance experts early in the process can help assure that an appropriate case definition is used.

It is important to ensure that an appropriate time period be selected for study. This period should neither be so long that it dilutes an emerging cluster nor so short that it cannot provide useful information. One approach is to include a longer period of study and account for time in the analyses. Data availability is a potential constraint in choosing the time period.

The finest unit of geography routinely available in health data in Alberta is the postal code. Therefore geographic-based analyses are often constrained to postal code boundaries. The definition of the geography of interest will depend on available information regarding the area/population allegedly affected and on information concerning homogeneous communities in that area. The population within the geographic area is significant to the investigation. If the population is too small there will be little statistical evidence available; conversely, an area too large has the potential to conceal any cluster effect.

Potential Measures

Data availability and the type of cluster being investigated are likely to determine the types of measures available for analysis in the first phases of an investigation. Potential measures include:
• **Incidence** – The number of newly diagnosed cases of a given health condition. This provides an indication of how many new cases are being diagnosed and whether this is changing over time.

• **Prevalence** – The proportion of a given population currently having a given health condition.

• **Treated Prevalence** – The proportion of a given population seeking care and receiving a diagnosis of interest.

• **Mortality** – The number of people dying.

• **Survival** – The number of people living following a particular diagnosis.

• **Screening rates** – Screening activities have a direct influence on the number of cases of a given disease that are detected within a community. Differences in screening rates can influence the interpretation of findings, of higher or lower levels, of a specific disease in a community.

### Analytic Considerations

#### Examine Community’s Experience

The goal of examining the community’s experience is to obtain evidence that can help determine whether there is an excess of cases grouped in space or time. The most common approach is to compare the observed number of cases with the expected. For example, computing an SIR (standardized incidence ratio) with the expected, coming from provincial data, examines this for the small area of interest. Simulation and modeling methods are also useful. The small areas typically involved in cluster investigations will usually limit the amount of evidence that this type of statistical hypothesis testing can provide.

#### Examine Province’s Experience

The goal of examining the province’s experience is to put the community experience in a larger context. This involves looking at the province as a whole and examining where the community of interest lies within the province. There are a number of techniques for examining this; small area spatial or spatial-temporal scan statistics can identify clusters, and funnel plots or rankings of communities can show the placement of the community relative to all other communities in the province.

#### Statistical Considerations

The Texas sharpshooter fallacy, finding a cluster in randomness because the area examined was a randomly occurring cluster, should be considered during the analysis and interpretation phases. Cluster investigations by nature are often iterative processes and can lead to substantial searching. Finding “significant” results by chance because of a large number of comparisons is a possibility and caution should therefore be exercised with multiple testing.
If an examination of a large number of diseases, geographies or other subgroups (e.g., age groups, sex, ethnicities) is necessary, interpretation of the results should be made with acknowledgement of the potential effect of multiple comparisons. Discussions with the community early in the process and maintenance of the case definition can protect against data dredging. Similarly, public health professionals must enter the investigation from an unbiased standpoint; there could be less disease, more disease, or no difference in disease rates in an area. If multiple diseases or subgroups are examined, results that are significantly lower should be reported with as much dedication as significantly higher results.

Statistics can be daunting to many members of the community. Public health professionals must take care to ensure that any statistics presented are understandable and do not lose their meaning. It is also important to note that statistical modeling and analysis are only one component informing the cluster investigation; therefore, statistical evidence must be synthesized with all other available evidence.

**Synthesis of Evidence**

The totality of evidence and context of the results must be evaluated; biologic plausibility between identified diseases and risk factors, statistical significance, and epidemiologic considerations are all important. The following questions should be addressed:

- If dealing with a point source, is there a dose-response relationship?
- Are some rates higher than expected and others lower?
- Do temporal trends support a cluster?
Appendix D – References


