Government of **Western Australia**
Department of **Health**

Guidelines for the Investigation of Cancer Clusters in Western Australia

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This publication can be accessed from the cancer clusters webpage below:
https://www.health.wa.gov.au/Articles/A_E/Cancer-clusters

Summary

A cancer cluster is the occurrence of a greater than expected number of the same or aetiologically related cancer cases that occur within a geographically or otherwise definable group of people over a defined time period.

Cancer cluster investigation is a scientific process to determine if there is an increased number of aetiologically related cancer cases in the suspected cluster and if there is a biologically plausible causal agent(s) that could have caused the cluster.

The purpose of this document is to provide a clear step-by-step guide to investigating suspected cancer clusters in Western Australia. *Guidelines for the Investigation of Cancer Clusters in Western Australia*, "The Guidelines" in short, outline the various settings in which cancer clusters can occur, which entity takes responsibility in each setting, and the key roles to be discharged in an investigation.

Five evaluation phases for investigation are described with detailed procedures provided to move through each phase, as required. The five phases of investigation are:

1. **Initial assessment** (initial information collection and general assessment)
2. **Primary evaluation** (collection of further information and broad assessments)
3. **Secondary evaluation** (epidemiological and environmental assessments)
4. **Tertiary evaluation** (detailed epidemiological and environmental health assessments)
5. **Research evaluation and surveillance** (optional phase; assess if a research investigation and/or ongoing surveillance are necessary and feasible).

The Guidelines were developed in alignment with established guidelines from other Australian jurisdictions and international health agencies and are informed by current scientific best-practice for investigating cancer clusters.

The Guidelines provide a structured investigation process that is specific to Western Australia in terms of the Department of Health's involvement, data quality and access, and state-specific communication needs.

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Abbreviations

Terms	Definitions
ABS	Australian Bureau of Statistics
IA	Initial assessment
PE	Primary evaluation
RE	Research evaluation
SA1	Statistical Area 1
SA2	Statistical Area 2
SE	Secondary evaluation
TE	Tertiary evaluation
WA	Western Australia

1. Introduction

1.1 Purpose

The Guidelines aim to provide an efficient, multidisciplinary approach to responding to expressions of concern from the community, health professionals or other interested parties about a possible cancer cluster in Western Australia (WA). The Guidelines provide a systematic process for conducting a cancer cluster investigation and aim to be accessible to all whom such clusters affect, including communities in which clusters are suspected or have been observed.

While the Guidelines specifically address investigating a cancer cluster, the principles can also be applied to the clustering of non-infectious diseases other than cancer.

Clustering of infectious diseases is not covered in these Guidelines.

1.2 Structure of the Guidelines

The Guidelines are structured as below:

- **Section 1** outlines this document's purpose and structure and provides background information for cancer cluster investigations.
- **Section 2** outlines how to move through the Guidelines, including a user list that provides easy navigation to relevant sections for each potential user's role in investigating a cancer cluster.
- **Section 3** provides key information about the different settings in which cancer clusters may arise, the key roles in an investigation, and how to determine the roles and responsibilities of the WA Department of Health and other entities.
- **Section 4** outlines the five phases of an investigation as listed in Figure 1 below, and the detailed process for each.
- **Section 5** Describes the WA Department of Health cluster investigation database.

Phase 1	• **Initial assessment:** general information collection and assessment to determine whether further investigation is required.
Phase 2	• **Primary evaluation:** case definition and verification, and broad epidemiological and environmental assessment.
Phase 3	• **Secondary evaluation:** epidemiologic and environmental assessment.
Phase 4	• **Tertiary evaluation:** detailed epidemiologic assessment and environmental health risk assessment.
Phase 5 (optional)	• **Research evaluation:** Assessment of value and feasibility of research into the suspected cancer-causing agent and observed clustering, and the need for ongoing surveillance.

Figure 1: Outline of the five phases of a cancer cluster investigation

The **Appendices** contain key supporting documents:

- **Appendix 1** provides a glossary of terms used.
- **Appendix 2** to **Appendix 6** detail the tasks, actions, and roles responsibilities of each investigation phase.
- **Appendix 7** outlines decision-making criteria for the end of each evaluation phase.
- **Appendix 8** details how to close an investigation for Department of Health led investigations.
- **Appendix 9** details how to close an investigation for non-Department of Health led investigations.

1.3 Background to cancer clusters

Cancer encompasses a large group of diseases with a range of different causes, though all share the defining characteristic of uncontrollable multiplication of abnormal cells that have the potential to spread beyond their tissue of origin to other parts of the body (metastasis)[1]. It is very common, with approximately two in five Australians being diagnosed with cancer in their lifetime[2].

A cancer cluster is the occurrence of a greater than expected number of cancer cases of the same type or cause (i.e. aetiologically related) within a geographically or otherwise definable group over a defined period of time[3]. Cancer clusters appear as an unusual pattern of cancer which may or may not be due to chance alone.

A perceived cancer cluster is more likely to be confirmed as a cluster if it has the following features[4]:

- An unusual number of one type of cancer or aetiologically related cancers (i.e. cancers of the same type, within the same family of tumours, or have a known or suggested link to the same specific environmental exposures).
- A rare type of cancer.
- An unusual number of cases with an age at diagnosis that is typically not observed.
- Cases that share a common occupational or environmental exposure that is a known or suspected cause of cancer.

Most perceived clusters turn out not to be true clusters and do not require extensive investigation due to most reported clusters having no identifiable cause[5]. For the purposes of investigation, a coincidental cluster is a clustering of cancer cases that has likely occurred from one or a combination of the following:

- **Chance**: Some communities may have higher rates of cancer than others simply due to chance. This may appear as a cancer cluster but as there is no opportunity for remediation of exposure to a causal agent, cancer clusters due to chance are not considered true clusters.
- **Differential access to health care**: Residents in one geographic area may be more likely to undergo cancer screening or have differential access to health services compared to residents from another area[3]. In these circumstances, clustering may be observed because cases of cancer are being diagnosed earlier in one area than in others. Such cancer clusters would not reflect a truly elevated cancer risk in a specific area and therefore are not considered true clusters.

- **Lifestyle behaviours**: Numerous common behaviours that increase the risk of cancer are more prevalent in some communities or groups than in the whole population, such as tobacco use, high alcohol consumption, lack of physical activity and an unhealthy diet. Cancer clusters attributable to the clustering of lifestyle factors are not considered true clusters in the context of investigation, though may indicate opportunities for lifestyle changes in the higher risk population through public health and/or health promotion measures.
- **Genetics**: Certain groups are known to be at an increased risk of having an inherited susceptibility to cancer from associated genetic mutations. The clustering of genetic causes of cancer can also occur by chance in a group that is not known to be at an increased risk of cancer. Both types of genetic clustering, known or by chance, are not considered true clusters for the purposes of investigation. If such a group is identified during a cluster investigation, it would be appropriate to advise them of this risk and provide access to genetic services.

Investigation is required when a perceived cluster meets all or most of the key features of a cancer cluster. Investigation is also required in situations where a perceived cluster does not have many of the key features of a cancer cluster but there is plausible concern regarding exposure to a known or suspected carcinogen.

There are rare instances where cluster investigations have led to the discovery of new cancer-causing exposures, such as with angiosarcoma of the liver[6], bladder cancer[7] and vaginal clear cell adenocarcinoma[8]. Importantly, all these instances involved the clustering of rare cancer types and in people with prolonged exposure to high levels of an occupational or pharmaceutical causal agent which was identified at the time or shortly after the first report of the cluster.

1.4 Investigating a suspected cancer cluster

A cancer cluster may be suspected when an individual (the informant) reports that several family members, friends, neighbours, or co-workers have been diagnosed with cancer. Following the report of a perceived cluster to a state or local health service, health officials evaluate the situation and may initiate a response (cluster investigation).

Perceived clustering of cancer can generate a great deal of anxiety and stress in the community involved and it is common for concerned communities to assume an environmental hazard is responsible for the apparent clustering. Investigations continue to be an important and necessary public health responsibility, with good risk communication forming an essential component of a cluster investigation.

It is imperative that the team investigating the cluster maintains communication and an ongoing collaborative relationship with the informant and the study population (i.e. population within which the suspected cluster has arisen) throughout the process.

1.4.1 Cluster investigation

Cluster investigation is the scientific process used to determine whether there is evidence of an increased number of cancer cases and exposure to a biologically plausible causal agent(s) associated with a specific type of cancer or aetiologically related cancers.

Cluster investigation comprises two main components:

- Epidemiological assessment
- Environmental health assessment

All evaluation phases in the investigation process undertake some form of epidemiological and environmental health assessment. Each successive phase requires the completion of a more detailed epidemiological and environmental health assessment to facilitate the collection of evidence to confirm the presence or non-presence of a true cancer cluster. The investigation is usually formally terminated when there is sufficient evidence to establish the non-presence of a cluster and the outcomes of the investigation have been communicated with the informant and concerned parties.

1.4.2 Cluster management

Cluster management is the process of identifying and evaluating the actions to be taken in response to cluster investigation findings and the implementation of these actions.

Cluster management and cluster investigation are interdependent and may have different objectives. Cluster management is the responsibility of the cluster manager, who is typically a representative of the setting of the cluster.

1.4.3 Evidence underpinning the Guidelines

The development of the first version of the Guidelines (2017) was informed by guidelines established by other agencies worldwide and various state health agency guidelines[3, 4, 9-15].

A detailed review of peer-reviewed publications on cancer cluster investigations was also undertaken, alongside discussion with relevant experts on statistical analyses required for small case numbers, methodological issues, and risk communication strategies[16-36].

This revised version of the Guidelines (2024) was informed by the first version of the Guidelines[37] and updated versions of cancer cluster investigation guidelines published by Queensland Health[38], the New South Wales Ministry of Health[39], the US Centers for Disease Control and Prevention[3], current epidemiological practice[30] and expert advice.

2. How to use the Guidelines

The Guidelines are structured for easy navigation when undertaking a cluster investigation.

Step 1: The setting (**Section 3.1**) and entity with primary responsibility for the investigation (**Sections 3.2** and **Section 3.3**) are determined.

Step 2: The roles of the Guideline users are identified (**Section 3.4**).

Step 3: Each Guideline user takes the steps required of them. The navigation table (**Table 1**) below lists the key roles in a cancer cluster investigation and the relevant sections for each user of the Guidelines.

Table 1: Guideline user list and navigation table

User's role	Relevant guideline sections
Initial responder	Section 3.4.2
Department of Health representative	Section 3.4.3
Cluster manager	Section 3.4.4
Epidemiologic assessor	Section 3.4.7
WA Cancer Registry adviser	Section 3.4.8
Environmental health assessor	Section 3.4.9
Communications adviser	Section 3.4.10

3. Determining the cluster context and investigation roles

This section details the following:

- Settings in which a cancer cluster could occur in WA
- The entity responsible for investigating the suspected cancer cluster in each setting
- The roles of specific individuals in investigating the potential cluster
- An overview of the five phases of cluster investigations

3.1 Cancer cluster settings

For the purposes of investigation, we define three settings for suspected cancer clusters:

- Workplace setting
- Non-workplace setting
- Complex setting

The cluster settings are defined to assist in evaluating the potential involvement and subsequent role of the Department of Health in a cluster investigation and to identify which entity has ultimate responsibility for the investigation. Different settings will affect the definition of the population, investigation stakeholders, management responsibilities and cluster investigation team members.

- **Workplace setting**: A setting where clusters are primarily defined by employment (including volunteering) in a workplace. Three types of workplace settings are defined for the purposes of this document:
    - WA Government (Department of Health and non-Department of Health)
    - Other government (local or Commonwealth)
    - Private (non-government)
- **Non-workplace setting**: A setting where clusters are primarily defined in a context other than a workplace. These include, but are not limited to, suspected clusters defined primarily by occurring in a specific geographical area (e.g. a suburb or in an adjoining set of suburbs) or involving people attached to an institution of which they are not an employee of (e.g. students of an educational facility/institution, patrons of a shopping centre or community gathering place).
- **Complex setting**: A setting in which two or more distinct population groups are affected (e.g. employees and non-employees in a care facility, students and staff in a school, and people living and working in regional/remote communities etc.).

Table 2 outlines examples of the different types of settings and who has responsibility for each. Further detail is provided in **Section 3.2** and **Section 3.3**.

Table 2: Examples of cancer cluster settings and responsible entities

Setting	Examples of setting	Responsible entity
Workplace		
WA Government (Department of Health and non-Department of Health)	• Royal Street, East Perth offices • Health Service Provider hospital, clinic, or office (if related to staff only) • Public school (if related to staff only) • WA government department (non-Department of Health) offices	Department of Health
Other government (local or Commonwealth)	• Local or Commonwealth government offices	Owner and/or manager of entity setting
Private (non-government)	• Corporate office of a private business • Private childcare centre • Private school • Private healthcare facility • Privately owned factories/workshops • Not for profit organisations	Owner and/or manager of entity setting
Non-workplace		
Specific geographical area	• Community facility (garden, hall etc.) • Private residences in reasonable proximity to one another (e.g. suburb or adjoining set of suburbs)	Health Service Provider (if expertise exists) **or** Department of Health
People attached to an institution of which they are not an employee	• Public school (if related to students only) • University (if related to students only) • Shopping centre (if related to patrons only)	Health Service Provider (if expertise exists) **or** Department of Health

Setting	Examples of setting	Responsible entity
Complex		
Various community services (settings that have employees *and* in which people gather)	• Shopping centre (if related to staff and patrons) • Care facility (if related to staff and patients) • Public School (if related to staff and students) • Regional/remote communities	Health Service Provider (if expertise exists) **or** Department of Health

3.2 Role of the Department of Health

The role of the Department of Health must be clarified as soon as possible for any cluster investigation that has the potential for Department of Health involvement, as per **Table 2**.

For cluster investigations where a non-WA government entity has primary responsibility, the Department of Health will provide ongoing expert advice and a point of contact, however, will not have direct involvement in the investigation or management of a cluster.

3.3 Role of other organisations

The role of other organisations involved in cluster investigations will vary depending on the setting of the cluster.

It is recognised that most entities outside of the Department of Health and the Health Service Providers will not have the expertise to conduct the investigation themselves. The expectation is that these entities would engage third-party experts to undertake the investigation following these Guidelines, with the entity being responsible for the overall management of the cluster. The appointment of a qualified and trusted third-party for investigation purposes ensures that the interests of the responsible entity in a suspected workplace/workforce cluster, have no impact on the quality or the outcomes of the investigation. Advice should be sought from the Department of Health regarding data access and the potential need for research ethics and governance approval. The entity conducting the investigation is requested to keep the Department regularly informed on the progress and findings of each evaluation phase of the investigation. The Department of Health may request that reports be peer reviewed to ensure transparency and robustness.

3.4 Roles of specific individuals or organisations[1]

3.4.1 Informant

The informant is the person or organisation reporting a suspected cancer cluster. Suspected clusters can be identified by anyone, including members of the public, media, health care professionals or a local, regional, or national entity.

3.4.2 Initial responder

The initial responder is the person who receives the notification of a potential cluster from the informant and collects the necessary information to perform the initial assessment. The individual undertaking the initial responder role differs depending on the entity with overall responsibility for the investigation:

- **Where the Department of Health has primary responsibility**: This will be an Epidemiology Directorate staff member responsible for cancer cluster investigations (see Department of Health representative, **Section 3.4.3**).
- **Where another entity has primary responsibility**: The initial responder is a nominated person from the cluster setting entity management.

Where another entity has primary responsibility, a Department of Health representative will be available to advise on or assume the role of the initial responder (e.g. if contacted first by the informant or by a representative from the setting on behalf of the informant), if necessary. In such circumstances, the Department of Health representative will return primary responsibility for the cluster investigation to the entity in which the suspected cluster has been observed as soon as is reasonably possible.

3.4.3 Department of Health representative

The Department of Health representative will be a contact person in the Epidemiology Directorate and is responsible for providing advice on all matters related to the cancer cluster investigation. This may be the Director of the Epidemiology Directorate or a nominated cancer cluster investigator within the Directorate.

The Department of Health representative role differs depending on the entity with overall responsibility for the investigation:

- **Where the Department of Health has primary responsibility**: The Department of Health representative will take primary responsibility for the investigation.

  The role includes responding to the initial inquiry, conducting the primary evaluation, and undertaking the role of cluster manager in any subsequent evaluation phases or delegating these roles to other suitably trained staff, as required.

- **Where another entity has primary responsibility**: The Department of Health representative should provide advice and maintain broad oversight of all cancer cluster investigations that the Department is made aware of. The Department of

[1] Individuals or organisations specified may fulfil more than one of the roles or functions listed.

Health representative is responsible for maintaining the cluster investigation database for all investigations, regardless of who holds primary responsibility.

3.4.4 Cluster manager

A cluster manager is appointed to take the lead in secondary, tertiary and research evaluation phases if further investigation is required**.** A cluster manager is not required for the initial assessment or primary evaluation.

The individual undertaking the cluster manager role differs depending on the investigation setting:

- **Workplace setting**: The cluster manager will be a representative from the workplace of the suspected cluster.
    - **For WA Government workplace settings**: the cluster manager will be appointed from the setting in which the suspected cluster has occurred or may be appointed from the Department of Health.
    - **For non-WA Government workplace settings and private (non-government) settings**: the cluster manager will be a representative from the workplace and appointed by the management of that workplace.

- **Non-workplace setting**: The cluster manager will be a representative from the Health Service Provider responsible for that setting.

In default of any other option, the Department of Health representative will be the cluster manager. They may delegate this role in any investigation with Director Epidemiology approval.

The cluster manager will lead the investigation and holds primary responsibility for the following:

- Engaging a cluster investigation team to conduct the investigation, through consultation with the Department of Health representative or the management representative.
- Convening a Cluster Investigation Advisory Committee, if required.
- Assigning tasks and overseeing the operations of the cluster investigation team, as described in the secondary, tertiary and research evaluation phases.
- Reporting progress and findings of the investigation according to established Department of Health reporting protocols.
- Communicating with other agencies as needed.
- Overseeing public communication, education, and coordination of local educational events relevant to the cluster.
- Documenting all aspects of the investigation and sending the required details to the Department of Health representative for entry into the cancer cluster investigation database.
- Compiling reports for the Chief Health Officer at the end of each evaluation phase.

3.4.5 Cluster investigation team

A cluster investigation team must be formed by the cluster manager for the secondary, tertiary and research evaluation and surveillance phases of the investigation.

The cluster investigation team will generally include, but is not limited to, an epidemiologist (the epidemiologic assessor), an environmental or occupational hygienist or other environmental health professional (the environmental health assessor), a public health physician, a communications adviser, and a representative from the WA Cancer Registry.

When the Department of Health has primary responsibility for the investigation, the team should also include a representative of the cluster setting. Additional advisers may be appointed depending on the cluster setting and population group involved.

3.4.6 Cluster Investigation Advisory Committee

The Cluster Investigation Advisory Committee serves to provide additional external expertise to determine and/or validate the most appropriate approach to investigating complex or atypical suspected clusters.

The Chief Health Officer may appoint a Cluster Investigation Advisory Committee if there are complexities to the investigation due to the nature of the entities involved. For example, if it is in a complex setting or the suspected cancer cluster involves a high-profile group.

3.4.7 Epidemiologic assessor

The role of the epidemiologic assessor/s includes:

- Conducting literature reviews on the cancer(s) in question and the known or suspected causes of the cancer(s) and evaluating the demographic characteristics of people with the reported cancer(s).
- Providing epidemiological advice and technical support to setting management, investigation partners, and other stakeholders of the cluster setting.
- Determining whether a probable excess of cases has occurred in the population in which the cluster has been reported.

3.4.8 WA Cancer Registry adviser

If there is a requirement to use routinely collected cancer data as part of epidemiological analyses or case verification, a WA Cancer Registry adviser will be appointed, regardless of the entity responsible for the investigation. The WA Cancer Registry adviser is responsible for advising on:

- availability, completeness, and accuracy of cancer data
- cancer data access and use allowed by relevant legislation or regulation
- interpretation of findings from cancer data analyses.

3.4.9 Environmental health assessor

An environmental health assessor/s must be appointed for any investigation where there is a plausible cause (e.g. exposure to a known or suspected causal agent) for the clustered cancers in the affected population or if the type(s) of cancers reported are rare.

The role of the environmental health assessor/s includes:

- finding and reviewing existing, relevant environmental data for the setting (historical and current data)

- identifying the possibility of exposure, past and present, to environmental agent(s) that are plausible causal agent(s)
- providing advice on environmental testing for the measurement of plausible causal agents
- conducting relevant health risk assessments, including exposure and toxicity assessment.

3.4.10 Communications adviser

The communications adviser role differs depending on the investigation setting:

- **Where the setting is a Department of Health site**: a cluster communications adviser will be appointed from the Communications Directorate who will support the cluster manager in preparing and releasing all official Department of Health communications regarding the cluster investigation.
- **Where the setting is a Health Service Provider site**: a cluster communications adviser should be appointed who will support the cluster manager in preparing and releasing all official communications in close liaison with the Department of Health Communications Directorate.
- **Where the setting is a WA Government site (non-Department of Health) or a private, non-government workplace**: These entities will be responsible for all public communications regarding the cluster and investigation. It is recommended that these entities consult with and keep the Department of Health informed about all forthcoming public communications.

3.5 Governance

Department of Health led cluster investigations are to be conducted according to the Guidelines and will follow established Department reporting and advisory pathways, as detailed in **Figure 2**.

Cluster investigations conducted by entities other than the Department of Health will generally have similar reporting and advisory pathways.

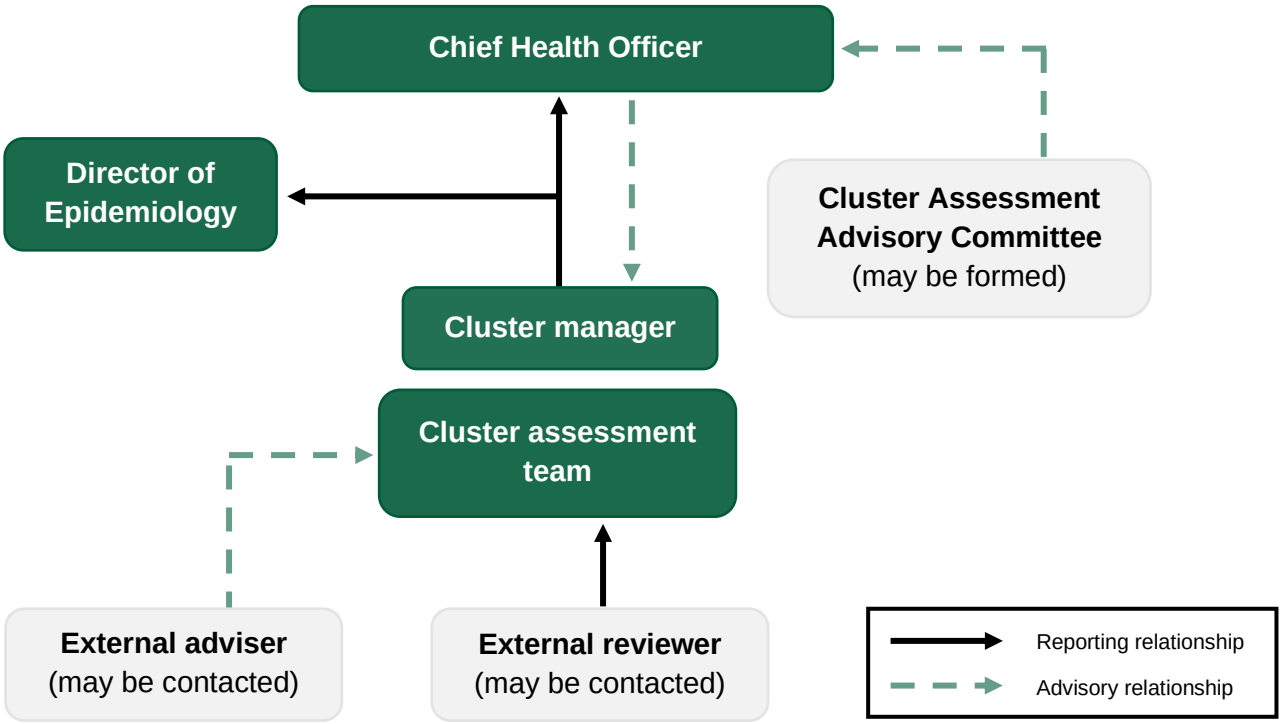

Figure 2: Reporting and advisory relationships of cluster investigations conducted by the Department of Health

3.6 Overview of evaluation phases

These Guidelines describe five phases of evaluation for the process of investigating suspected cancer clusters (**Figure 3**).

Each evaluation phase begins by identifying the issues and concerns of the informant and the community they represent. The relevant personnel are assembled and the roles and responsibilities for each are defined.

Findings are reviewed at the completion of each phase and a decision regarding whether to conclude or continue the investigation is recommended and approved by the relevant decision maker for the phase. Certain criteria must be met to proceed to the next phase and are described in **Appendix 7**.

The Chief Health Officer should approve each phase of investigation except the initial assessment and primary evaluation phases, which can be approved by the Director of Epidemiology. This format aims to achieve standardisation of the investigation process and an optimal allocation of resources.

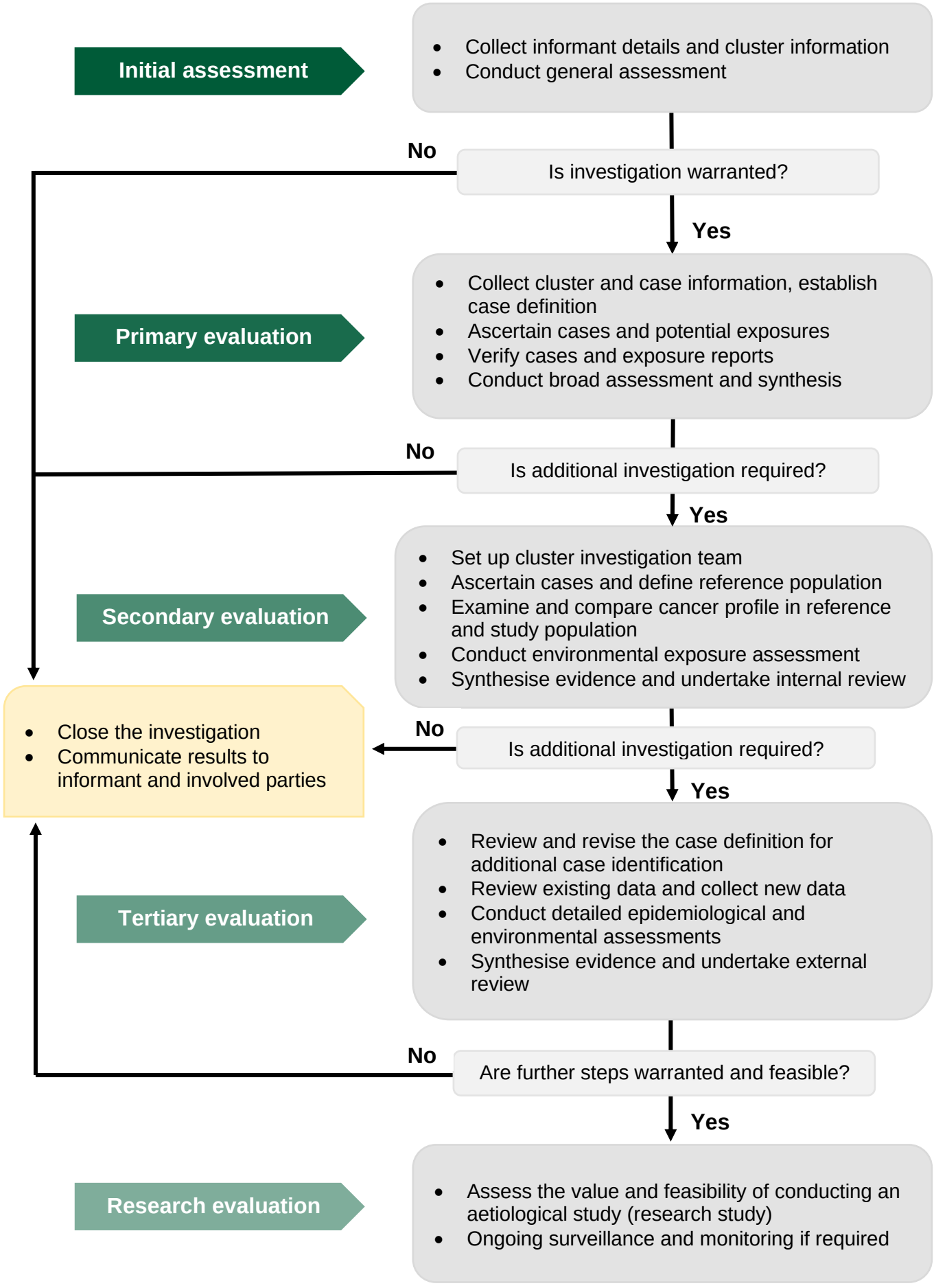

Figure 3: Overview of the cluster investigation process

4. Implementing the Guidelines

This section describes the cancer cluster investigation process in terms of Department of Health led investigations. However, it is intended to be easily generalisable to circumstances when an entity other than the Department of Health has primary responsibility for the investigation.

It should be noted that the investigation process as presented in the Guidelines is not necessarily a linear process in practice. Some investigations may require a mix of elements from different phases and analytic steps may occur concurrently or repeatedly. Some analytical steps may not be possible depending on the availability and quality of the required data.

Phase 1 – Initial assessment

All reports of suspected cancer clusters should be directed to the Epidemiology Directorate for initial assessment at cluster.assessments@health.wa.gov.au. The initial assessment is conducted by the initial responder (usually a senior officer of the Epidemiology Directorate, e.g. the Department of Health representative: see **Section 3.4.3**) and typically takes a few days to complete, with most initial assessments resolved after the first phone call with the informant. A detailed list of the required information and necessary processes for this evaluation phase are in **Appendix 2**. The features of an initial assessment are summarised in **Table 3**.

Table 3 – Summary of initial assessment phase

Initial assessment summary	
Purpose	Collect and assess initial information regarding a suspected cancer cluster to determine whether investigation is warranted
Decision maker	Director – Epidemiology Directorate
Research components, data collection and analysis	Use information provided by the informant on cancer(s), possible exposure(s) and setting of concern
Responsible person(s)	Department of Health representative
Likely duration	Days

4.1 Overview, procedures, and details

For most suspected cancer clusters, no plausible explanation is found due to the high likelihood of chance clustering (**Section 1.3**). Regardless of the initial assessment outcome, it is important to address the informant's questions and concerns during the initial assessment phone call as this conversation will determine whether further assessment is sought by the informant.

Assessing and responding to potential cancer clusters is time consuming. It is therefore crucial that the initial assessment carefully documents and addresses all aspects of the initial report of a suspected cluster.

The following steps guide all initial assessments:

IA1 Collect contact details of the informant for the initial assessment phone call. Responses to suspected cancer cluster reports must be prompt, with the report acknowledged within a few days of receiving the report.

IA2 Prior to the initial assessment phone call, prepare sufficient information to answer likely questions from the informant. This should include plain English explanations on the nature of cancer clusters and the factors that go into determining whether a

suspected cluster is a true cluster or due to chance (i.e., a coincidental cluster), as well as general information on cancer and cancer statistics in WA.

Overall, the information given to the informant must be sufficient to help them understand that most clusters are chance clusters, that further investigation is complex, and that most often no actionable explanation for the cluster can be found.

IA3 Make the initial assessment phone call, ensuring the conversation is empathetic and informative.

Request the following information on the suspected cluster from the informant:

- number of cases and types of cancer(s)
- age at diagnosis of each case (or age of cases if age at diagnosis information is not readily available)
- setting of concern
- any specific environmental or occupational exposure concerns

IA4 Make an initial assessment based on the information provided.

If the outcome of the initial assessment is that no further investigation is required (i.e. the suspected cluster does not align with the features of a cancer cluster), the informant is informed of the outcome and all relevant information collected will be entered into the cluster investigation database (**Section 5**).

If further investigation is required, the assessment progresses to the primary evaluation phase.

IA5 Send a follow-up email soon after the phone call and initial assessment that provides a summary of the information discussed as well as resources on cancer clusters (e.g. cancer cluster guidelines, fact sheets, relevant cancer statistics) to assist the informant with their concerns.

4.2 Decision point

The decision to initiate investigation after the initial assessment is made by the Department of Health representative in conjunction with and upon approval from the Director of Epidemiology.

This decision must be based on the assessment of available information against the key features of a cancer cluster (**Section 1.3**) and follow the decision point criteria in **Appendix 7**.

4.3 Outcome

Communication with the informant is an essential part of the investigation process, regardless of whether the decision for further investigation is made or not. The informant must be notified of the decision and given clear explanation of the reasons for the decision.

Phase 2 – Primary evaluation

If the initial assessment determines that further investigation of a suspected cancer cluster is warranted, the formal cancer cluster investigation process will begin with a primary evaluation.

A detailed list of the required information and necessary processes for this evaluation phase are in **Appendix 3**. Criteria to guide decision making at the conclusion of all evaluation phases are outlined in **Appendix 7**. The features of a primary evaluation are summarised in **Table 4**.

Table 4 – Summary of primary evaluation phase

Primary evaluation summary	
Purpose	Collect and assess informant provided data to define and verify cases to assess if further investigation is warranted
Decision maker	Director – Epidemiology Directorate
Research components, data collection and analysis	• Use informant data on cases and exposures • Use standard literature and texts • Potential use of additional existing data, e.g. WA Cancer Registry
Responsible person(s)	• Department of Health representative • +/- Senior officers of: - Public Health (physicians) - Epidemiology and/or - Environmental Health and/or - Public Health Regulation and/or - WA Cancer Registry and/or - Media and Communications • +/- other relevant experts
Likely duration	Days to weeks

4.4 Overview, procedures, and details

The primary evaluation phase is conducted by the Department of Health representative, who is typically the initial responder from the initial assessment phase. Expert advice may be sought from public health physicians, environmental health practitioners, and other relevant experts as required. The purpose of the primary evaluation is to assess information collected from the informant to determine whether a more detailed investigation is required.

The following steps guide all primary evaluations:

PE1 Collect general information about the suspected cancer cluster (listed in **Appendix 3**). For example, the following epidemiological variables are usually required to complete a thorough primary evaluation:

- type(s) of cancer
- number of cancer cases (both confirmed and unconfirmed)
- age and sex of cancer cases
- setting of the clustered cancer cases
- period during which cancer cases were diagnosed.

PE2 Collect initial case information from the informant or any other relevant person to whom the informant might refer and establish a preliminary case definition that includes demographic characteristics of the cases and the population to which they belong.

PE3 Collect information on any significant exposure(s) to occupational or environmental agents (physical, chemical, or biological), and likely frequency and duration of exposure(s). Also collect information on other risk factors such as age, genetic or biological factors (e.g. family history of cancer or related diseases, infections), and lifestyle behaviours (e.g. diet, smoking, alcohol consumption) that may have a confounding effect and lead to a spurious association between the suspected exposure and outcome (i.e. cancer)[40]. Any known, suspected, or suggested biologically plausible causative agent(s) should be considered.

PE4 Review literature on the epidemiology of the types of cancer(s) reported, exposures (both exposures suspected and known to be associated with the cancer types reported) and setting.

PE5 Assess the reliability of the information gathered in PE2 and PE3. Where possible, review appropriate records to verify case and exposure reports to confirm the accuracy of the reported cancer diagnoses[2] (e.g. WA Cancer Registry) and the potential for exposure to cancer causing agents (e.g. desktop review of occupational health and safety incident records, hazardous materials storage records, land use records etc).

PE6 Compile and review the information gathered in PE1-PE5 to make a judgement on whether further investigation is warranted using the decision point criteria (**Appendix 7**).

4.5 Decision point

The decision to finalise the investigation at the end of the primary evaluation is made by the Department of Health representative in conjunction with and upon approval from the Director of Epidemiology. To progress to the secondary evaluation phase of investigation, approval from the Chief Health Officer is required.

The decision to progress to the next phase of investigation (i.e. secondary evaluation) must be based on the assessment of available information against the key features of a

[2] While individual cancer cases may be verified using the WA Cancer Registry, no individual case validation will be provided back to cases, informants or other entities. The information will only be used by Department of Health staff to form general conclusions on whether to close or continue the investigation.

cancer cluster (see **Section 1.3**) and follow the decision point criteria in **Appendix 7**. This includes the consideration of both epidemiological and environmental aspects, and the level of community concern. The Department of Health representative will consult colleagues with relevant expertise on the decision before informing the Chief Health Officer and responding to the informant.

4.6 Outcome

Following the primary evaluation decision, the informant must be notified of any conclusions or next steps. This includes information about the process followed (i.e. primary evaluation steps), the results, reasons for closure, and/or expectations for the next phase of evaluation if the decision to progress the investigation is made.

The actions required to appropriately close the investigation are described in **Appendix 8** (Department of Health led investigation) and **Appendix 9** (other entity led investigation).

Phase 3 – Secondary evaluation

The secondary evaluation aims to determine whether there is an excess of cancer cases (of the same type or aetiologically related types) in the study population and plausible exposure to a known or suspected causal agent.

A detailed list of the required information and necessary processes for this evaluation phase is provided in **Appendix 4**. Criteria to guide decision making at the conclusion of any evaluation phase are outlined in **Appendix 7**. The features of a secondary evaluation are summarised in **Table 5**.

Table 5 – Summary of secondary evaluation phase

Secondary evaluation summary	
Purpose	Determine whether there is an excess number of aetiologically related cancer cases and whether there is evidence of exposure to a plausible causal agent
Decision maker	Chief Health Officer
Research components, data collection and analysis	• Use existing data • Consult literature • Quantify study population and reference population • Determine expected case numbers from reference population and the observed/expected ratio for study population • Conduct an environmental exposure assessment (if required)
Responsible person(s)	Cluster investigation team: • Cluster manager • Department of Health representative • Public health physician • Senior officers of: - Epidemiology and/or - Environmental Health and/or - Public Health Regulation and/or - WA Cancer Registry and/or - Media and Communications • +/- other relevant experts • Setting representative
Likely duration	Weeks to months

4.7 Overview, procedures, and details

The secondary evaluation involves a more in-depth analysis of previously collected information from the initial assessment and primary evaluation phases and expands data collection and analysis to other appropriate existing data sources to assess the need for and feasibility of further investigation.

This phase is led by a cluster manager with expert advice sought from epidemiologists, public health physicians, environmental health practitioners and other relevant experts as required. The purpose of the secondary evaluation is to determine if there are more aetiologically related cancer cases in the study population than expected and exposure to a causal agent that could have caused the cancer(s).

The following steps guide all secondary evaluations:

SE1 Appoint a cluster manager and set up the cluster investigation team.

SE2 Consult with the study population to:

- discuss any remaining issues from the primary evaluation phase
- elicit any new relevant information (cases, exposures, potential causal agents, etc.).

SE3 Re-examine the information obtained during primary evaluation alongside any additional information collected from consultation with the study population in SE2.

Consult relevant experts and review the case definition, inclusion and exclusion criteria, and exposure data. Amend as necessary.

SE4 Determine and describe the reference population by establishing the geographical area and the demographic composition of the reference population.

For non-workplace settings, the reference population will be defined by the largest geographical boundary that contains a population demographically similar to the study population. Ideally, the study population will lie within the geographic boundaries of the reference population.

For a workplace setting, if the suspected cluster is localised to a specific part of the workplace, the reference population will likely be the entire workforce of the organisation. If the suspected cluster is not localised to a specific part of the workplace, the reference population will likely be the industry of the affected workplace.

SE5 Conduct a literature review of potential risk factors for the cancer type(s) in the suspected cluster. These may include lifestyle factors, genetic and biological factors, and/or known or suspected environmental exposures.

As part of the literature review, review epidemiological information on the study population to assess patterns in incidence or trends over time for the cancer types(s) and/or exposure(s) of concern. This may identify other factors (e.g. differential access to health care, differences in screening practices, etc.) that could affect or explain any observed excess in cancer cases. Sources for this data include the Australian Institute of Health and Welfare and WA Cancer Registry reports.

SE6 Using WA Cancer Registry data, determine cancer incidence rates for the reference population for comparison with study population rates.

SE7 Assess the likelihood of an excess of cancer(s) in the study population by comparing the cancer incidence rates of the reference population to the incidence rates of the study population. This is done by comparing the observed number of cases in the study population to the number of cases that would be expected to occur in the study population, if it experienced the same cancer rates as in the reference population.

Note that this is a logical assessment. No tests for statistical significance are performed as these tests contribute to establishing causal relationships in situations when there is a prior cause and effect hypothesis. For many suspected cancer cluster investigations, the presence of a causal agent and/or frequency and duration of exposure are unknown or undetermined, therefore limiting the utility of statistical significance testing in these situations. For the rare instance where a causal agent and exposure to it are known, and a cause-and-effect relationship between this exposure and a particular cancer(s) has been established, significance testing is appropriate.

SE8 If the number of cases observed is higher than expected, there is a notable number of rare cancers, or there is an unusual age and/or sex distribution of cases identified from SE7, conduct an environmental exposure assessment of the cases.

An environmental exposure assessment examines agents and exposures (frequency and duration) in the cases to assess whether they have been exposed to a biologically plausible causal agent(s) for the cancer(s) of interest. This assessment requires the appointment of an environmental health/exposure assessor or an occupational hygienist. The assessment usually involves:

- review/update desktop study from primary evaluation phase
- conducting a site inspection and/or interviews with relevant personnel
- limited environmental or biological sampling and analysis (if possible or required).

The information gathered from an environmental exposure assessment is used to develop an initial exposure profile for the cases reported in the suspected cluster.

SE9 Synthesise information and prepare a report (refer to **Appendix 8** or **9**, as applicable).

SE10 Undertake an internal review of the report. In the case of Department of Health led investigations, the quality assurance review is conducted by internal department advisors, such as key staff from the Epidemiology Directorate, Environmental Health Directorate, public health physicians, the WA Cancer Registry advisor, and/or the Cluster Investigation Advisory Committee (if appointed).

4.8 Decision point

The decision to progress to the next phase of investigation (i.e. tertiary evaluation) is made by the cluster investigation team guided by the decision point criteria in **Appendix 7** and is

reviewed by the Director of Epidemiology. The decision must also consider whether there is evidence to support further investigation, and if such evidence exists, the feasibility of undertaking such investigation.

For scenarios where exposure to a known or suspected causal agent(s) is suspected but not confirmed (e.g. there is limited evidence of agent carcinogenicity or limited/incomplete exposure data), the lack of evidence should not preclude further investigation if there is other evidence suggestive of a cancer cluster (refer to features of cancer clusters, **Section 1.3**).

However, if no biologically plausible causal agents are identified, or there are no likely or sufficient exposure pathways to a known or suspected causal agent(s), progression to tertiary evaluation is not appropriate or feasible.

If evidence and feasibility requirements are met and the decision to progress the investigation is made, approval from the Chief Health Officer is required prior to commencing the tertiary evaluation phase.

4.9 Outcome

The cluster investigation team decides whether to continue or close the investigation with final approval required from the Chief Health Officer. The actions required to appropriately close the investigation and communicate outcomes to involved parties are described in **Appendices 8** and **9**, depending on which entity is responsible for the investigation.

Phase 4 – Tertiary evaluation

The tertiary evaluation aims to further validate the excess of aetiologically related cancer cases observed in the secondary evaluation and undertake a detailed assessment of exposure to physically and biologically plausible causal agents.

A detailed list of the required information and necessary processes for this evaluation phase is provided in **Appendix 5**. Criteria to guide decision making at the conclusion of any evaluation phase are outlined in **Appendix 7**. The features of a tertiary evaluation are summarised in **Table 6**.

Table 6 – Summary of tertiary evaluation phase

Tertiary evaluation summary	
Purpose	Validate excess of aetiologically related cancer cases and undertake detailed assessment of exposure to biologically plausible causal agent(s)
Decision maker	Chief Health Officer
Research components, data collection and analysis	• Use existing and newly collected data • Use standard literature and texts • Identify missing cases and new data sources • Verify cases and exposure reports • Conduct health risk assessment
Responsible person(s)	Cluster investigation team: • Cluster manager • Department of Health representative • Public health physician • Senior officers of: - Epidemiology and/or - Environmental Health and/or - Public Health Regulation and/or - WA Cancer Registry and/or - Media and Communications • +/- other relevant experts
Likely duration	Months to years

4.10 Overview, procedures, and details

If clustering remains evident following the secondary evaluation, the cluster investigation team will expand the investigation and undertake additional case ascertainment to define cluster characteristics in more detail. This involves an active search for additional cases that were not discovered in the previous evaluations.

The tertiary evaluation phase uses information from the primary and secondary evaluation phases and expands the investigation of cases and suspected exposures in finer detail. As this will likely require collection of new data either via surveys or data linkage, research ethics and governance approval should be sought before commencing the tertiary evaluation phase.

The following steps guide all tertiary evaluations:

TE1 Establish the tertiary evaluation cluster investigation team. This will likely comprise the members of the secondary evaluation cluster investigation team with the addition of any other required roles.

TE2 Re-engage with the study population to discuss concerns from the previous evaluations and identify any new community concerns that may have arisen.

TE3 Review and revise the case definition and determine if greater sensitivity and specificity are required for the following:

- case definition
- study period
- study population

Tracking putative cases lost to follow-up in the secondary evaluation may be important to the epidemiological analysis and should be considered. Cases already counted may not be members of the study population at the time of diagnosis, and data on the length of residence or time of employment in a particular setting are also important, where known exposure may not have occurred in a period in which it could have caused the cancer.

TE4 Re-ascertain all potential cases using the revised case definition from TE3.

Basic information can be collected from the review of existing data collected in previous evaluation phases. For the ascertainment of cases lost to follow-up and missed cases not originally reported, new data sources will be required. Examples of these sources can be found under TE4 in **Appendix 5**.

TE5 After all cases have been ascertained under the revised case definition, identify new data sources for the collection of more complex case-related information. Assess the availability and quality of these sources in terms of providing more detailed exposure and case-related information for both the cases and the population at risk.

For the sources, proactive methods of data collection can be used, such as conducting surveys to identify unknown cases or undertaking an environmental health assessment to determine exposure levels. These data collection methods may be done independently or in conjunction with other responsible persons, depending on investigation requirements.

If access to the source(s) is feasible, obtain the additional information.

TE6 Evaluate the degree of association between the identified exposure(s) and the type(s) of cancer by conducting a detailed health risk assessment of the presumed exposure site using the Health Risk Assessment[41] guidance documents prepared by the WA Department of Health Environmental Health Directorate.

The health risk assessment involves the collection of new information and/or re-examination of existing information, as well as an updated review of the literature to evaluate whether any suspected association is epidemiologically and pathologically possible, based on the latest evidence. For more details, see TE6 in **Appendix 5**.

Environmental testing should be carried out only when there is a clear scientific rationale, including when there is concern that the agent is still present in the setting. Due to the long latency periods of most cancers, the utility of environmental testing is limited in providing accurate data on historical exposure for most causal agents. If available, most additional data will be collected from historical records of relevant agencies, such as the Department of Water and Environmental Regulation, local councils, or the organisation itself in the context of workplace settings.

In the absence of a suspected aetiologic agent(s), it is typically not recommended to engage in a general or open-ended inquiry to identify potential contaminants in a setting. However, if the setting currently has, or previously had, exposure to an agent not known or suspected to be a carcinogen and at levels not seen in the natural environment, a paucity of data may prompt the need for further research into that agent.

TE7 Using the revised case definitions, new data, and additional information, repeat the epidemiological assessments done in the secondary evaluation and consider new analyses to assess the likelihood of the clustered cancer cases being associated (temporally and pathologically) with the potential exposure(s). Incorporate environmental exposure evidence obtained in this assessment.

TE8 Synthesise information and prepare a report (refer to **Appendix 8** or **9**, as applicable).

TE9 Undertake an internal review of the report. In the case of Department of Health led investigations, the quality assurance review is conducted by internal department advisors, such as key staff from both the Epidemiology Directorate and Environmental Health Directorate, public health physicians, the WA Cancer Registry advisor, and/or the Cluster Investigation Advisory Committee (if appointed).

If considered necessary by the cluster investigation team and/or the Cluster Investigation Advisory Committee (if established), undertake an external quality assurance review of the report. Investigations where an external reviewer may be required include more complex investigations and/or investigations where results may have social, political and/or economic implications.

4.11 Decision point

The decision to finalise the tertiary evaluation is made by the cluster investigation team guided by the decision point criteria in **Appendix 7** and reviewed by the Director of Epidemiology.

If an excess of cancer(s) is not confirmed or is confirmed but with no plausible association to the presumed exposure(s), the cluster investigation team will give the Chief Health Officer a summary report with the recommendation to close the investigation.

If an excess of cancer(s) is observed and there is compelling evidence for an association between the suspected exposure(s) and excess cancer(s), the Department of Health will recommend exposure mitigation to the highest degree possible. This may include removal of the identified causal agent(s) from the setting or elimination of known or likely pathways to exposure. The agency and/or regulator responsible must ensure that exposure has been successfully mitigated and the hazard removed or contained/managed.

It is unlikely that any cancer cluster will comprise enough cases to conduct a full aetiological study. However, if case numbers are sufficient, the feasibility of a study and progressing to the research evaluation and surveillance phase of investigation should be considered. Permission from the Chief Health Officer is required to both close a tertiary evaluation and to progress to the research evaluation and surveillance phase.

4.12 Outcome

The cluster investigation team decides whether to continue or close the investigation with final approval required from the Chief Health Officer. The actions required to appropriately close the investigation and communicate outcomes to involved parties are described in **Appendices 8** and **9**, depending on which entity is responsible for the investigation.

Phase 5 – Research evaluation and surveillance

The purpose of the research evaluation and surveillance phase is to consider whether an epidemiological study should be conducted to further investigate the aetiology of the cluster, and/or whether surveillance of the setting for additional cancer cases should be implemented, if not already in place.

The research evaluation component of the phase is optional and is not a successive continuation of investigation after the tertiary evaluation.

A detailed list of the required information and necessary processes for this evaluation phase is provided in **Appendix 6**. The features of the research evaluation and surveillance phase are summarised in **Table 7**.

Table 7 – Summary of research evaluation and surveillance phase

Research evaluation and surveillance summary	
Purpose	Determine whether a research study is justifiable and if setting surveillance is required
Decision maker	Chief Health Officer
Research components, data collection and analysis	• Assess value and feasibility of conducting an aetiologic research study • Prepare research brief • Assess need for, and methods of, ongoing surveillance
Responsible person(s)	Cluster investigation team
Likely duration	Weeks to months

4.13 Overview, procedures, and details

The research evaluation and surveillance phase assesses the need for and feasibility of performing an aetiological study. An aetiological study should only be considered if the research is deemed highly important from either a public health or scientific perspective, and if there may be funds available for it.

The aim of an aetiological study is to determine if there is a causal association between a specific occupational or environmental exposure present in a particular setting and the development of cancer in people within that setting.

In circumstances where the suspected cluster does not meet the criteria for further investigation (see **Appendix 7**), the recommendation of ongoing surveillance as further action should be considered.

The following steps guide all research evaluations and surveillance:

RE1 Consider the criteria in RE1 in **Appendix 6** to determine the need for and feasibility of conducting an aetiologic research study.

If further investigation in the form of a research study is deemed necessary and feasible, the cluster investigation team will prepare a research brief and source appropriate research personnel through a formal tender process. An external party (e.g. academic experts in fields relevant to the study) will typically undertake the research and be responsible for submitting an ethics application to an appropriate research ethics committee. The Department of Health will have a peripheral role in conducting the research, if any.

RE2 In circumstances where the suspected cluster does not meet the criteria for further investigation, surveillance on the setting to detect any increases in cancer rates may be recommended.

Community concern alone may be a sufficient reason to initiate surveillance. Recommendations for public health interventions (e.g. smoking cessation programs, cancer screening, environmental hazard mitigation) may coincide with surveillance, if relevant.

The cluster investigation team will be responsible for recommending the mode of surveillance and the cluster manager will be responsible for its implementation. The key components of cancer cluster surveillance include:

- establishment of a suitable reporting system
- maintaining contact with study population
- annual re-evaluation of the need for surveillance.

4.14 Decision point

Approval from the Chief Health Officer is required both to proceed with conducting a research study and to initiate surveillance.

The decision to conduct a research study must be based on information from previous evaluation phases and from the feasibility and needs assessment described in RE1. The decision is made by the cluster investigation team and recommended in a report to the Chief Health Officer for approval.

4.15 Outcome

For conducting a research study, Chief Health Officer approval must be obtained prior to commencing the tender process for appointment of an external research team. Regarding study outcomes, it is important to note that a demonstration of association between an exposure(s) and cancer may not be sufficient to prove causation, as determining causation relies on evidence from epidemiological studies and from experimental animal and biological studies.[42] Regardless, the results of the study, if conducted, should be published in a recognised peer-reviewed journal as the findings will contribute to epidemiological and public health knowledge, whatever the results may be.

For surveillance, the decision to continue or end surveillance must be made in consultation with the Chief Health Officer following annual review. The outcomes of this review,

including the decision to continue or cease surveillance and findings from the surveillance program, should be regularly communicated to the informant and population of interest.

5. Cluster investigation database

The Epidemiology Directorate maintains a cluster investigation database containing summary details of all cancer cluster investigations the Directorate is aware of. The database contains personal information related to individuals' health status and therefore must remain confidential.

The database includes information on all investigations, including reported suspected clusters that did not progress past the initial assessment stage. An Epidemiology Directorate representative will update the database at the beginning and end of each evaluation phase.

5.1 Information recorded

The types of information contained in the database serve as a governance mechanism, reporting source, and a reference to use for any similar suspected clusters that may occur in future.

The database contains the following information:

- Administrative information: information on investigation name, key dates, investigation level and individuals involved in the investigation.
- Informant details: information on informant name, agency (if applicable), and contact details.
- Cluster investigation details: information on setting, cancer type(s), case demographic information, suspected exposure(s), and population at risk.
- Assessment summary: information on study period, WA Cancer Registry verification, assessment status, notable comments and completion date.
- Actions taken: summary of communication strategies implemented.
- Data entry information: administrative information for data governance, including cluster ID number and name of data entrant.

5.2 Access and database management

The cluster investigation database, along with all documents pertaining to each cluster investigation, is stored on the department's secure records management system. Access to the database and documents is limited to the Director of Epidemiology and key Department of Heath staff involved in cancer cluster investigations. All updates to and management of the database will be made by one of the approved Epidemiology Directorate staff members, including for all non-Department of Health led investigations.

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