

PROTOCOL FOR RESPONDING TO COMMUNITY CONCERNS FOR UNUSUAL PATTERNS OF CANCER



TEXAS
Health and Human
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Purpose of this Document

This document details the Texas Department of State Health Services (DSHS) protocol for responding to community cancer cluster concerns. This protocol was adapted from the Centers for Disease Control and Prevention (CDC) Agency for Toxic Substances and Disease Registry (ATSDR) 2022 *Guidelines for Examining Unusual Patterns of Cancer and Environmental Concerns* [1].

Background

CDC defines unusual patterns of cancer as “a greater than expected number of the same or etiologically related cancer cases that occurs within a group of people in a geographic area over a defined period of time” [1].

In accordance with its mission, the DSHS Environmental Epidemiology & Disease Registries Section (EEDRS) is tasked with addressing community concerns about unusual patterns of cancer, and has done so since 1984. Within EEDRS, the Environmental Surveillance and Toxicology Branch (ESTB) and Texas Cancer Registry (TCR) collaborate to respond to these concerns. Since 1995, TCR has been responsible for the collection, maintenance, and dissemination of high-quality Texas population-based cancer data. TCR meets national CDC timeliness and other data quality standards, as well as North American Association of Central Cancer Registry certification standards and National Cancer Institute’s (NCI) Surveillance, Epidemiology, and End Results (SEER) program standards.

Over the past 37 years, DSHS has responded to hundreds of inquiries about community concerns for unusual patterns of cancer. Inquiries have come directly from citizens and from state and local government agencies. While some of the analyses conducted in Texas have identified statistically significantly higher-than-expected cancer, none have resulted in the identification of an association between environmental contaminants and the cancers observed. In fact, of all investigations of suspected cancer clusters conducted in the United States (1990-2011), only one such investigation was able to definitively identify a causal link with environmental exposures occurring in a community setting [2, 3]. However, investigations into unusual patterns of cancer are important, as they provide concerned community members with information about the occurrence of cancer in their area.

Proactive Evaluation and Routine Monitoring of Cancer Data

Making Cancer Rates Publicly Available

Strong partnerships between population-based cancer registries and other public health professionals can aid in addressing community concerns and questions about unusual patterns of cancer within certain geographic areas. One-way TCR does this by making sub-state level cancer rates publicly available. TCR provides:

- Age-adjusted incidence rates of cancer across the state at the county level to the public through a web query tool. The web query tool can provide incidence rates for specific cancer sites whilst stratifying for year, sex, and race/ethnicity (<https://www.cancer-rates.com/tx/>).
- Data on CDC's National Environmental Public Health Tracking Program Tracking Network Data Explorer (<https://ephtracking.cdc.gov/DataExplorer/>).
- Statistical reports and annual data summaries for the state of Texas for different types of cancers and populations. These are available on TCR Cancer Statistics website (<https://www.dshs.texas.gov/texas-cancer-registry/cancer-statistics>).

Phased Approach to Respond to Community Inquiries

DSHS follows a phased approach when responding to community inquiries. The phased approach will help with the following:

- Initiating communication with the inquirer and community members
- Examining data and criteria aimed at evaluating the occurrence of cancer
- Exploring further epidemiological studies

Information about the phased approach is outlined in the remainder of this document, and additional details can be found in the appendices. This approach only addresses the response to concerns about unusual patterns of cancer in the community context. For concerns related to a suspected unusual pattern of cancer in an occupational setting, please see Appendix A.

Phase 1. Initiating Lines of Communication

Purpose: To gather information from the concerned individual or group reporting a suspected unusual pattern of cancer, and to provide education about cancer.

Information Gathering

When report of a community concern for an unusual pattern of cancer is first received, DSHS collects additional information to determine the

appropriate response. At a minimum, the following will be collected:

- **Inquirer information:** Name, residential address, email address, telephone number, length of residence at current location, organization affiliation (if any).
- **Inquirer information about the patterns of cancer:** number of and types of cancer cases; age of diagnosis of people with cancer, geographic area of concern (zip codes or census tracts), time period over which cancers were diagnosed, and how the inquirer learned of the possible unusual pattern
- **Other information:** suspected exposure(s) of concern, and timeframe during which they may have occurred, any specific environmental concerns, other risk factors (e.g., family history of cancer); other government agencies previously or currently involved in responding to this concern, and the outcome of their involvement.

This information will then be entered into the DSHS community cancer concerns inquiry database.

DSHS will notify appropriate local, state and federal environmental agencies about the concern for suspected unusual pattern of cancers and any potential environmental hazards. When collecting information about the suspected unusual pattern of cancers, DSHS staff will provide any available information about unusual patterns for cancer(s) of concern as well as the DSHS protocol for responding to such concerns, to the inquirer or concerned entities. If the concerned individual/entity requests for DSHS to consider proceeding with a statistical analysis related to the unusual pattern, they will be provided with the information on next steps, including an estimated timeframe within which a response to their request will be provided. DSHS will provide information to the concerned individual/entity about how an investigation into an unusual pattern of cancer is conducted and any potential limitations of the resulting data and study.

Phase 2. Criteria to Determine Continued Assessment of a Report of an Unusual Pattern of Cancer

Purpose: To determine if a report of suspected unusual pattern of cancer meets the criteria for continued assessment to examine whether the observed number of cancer cases in the area of concern is statistically significantly greater than expected.

Determination of next steps

After initial information has been collected, details about the cancers and the geographic area of concern will be gathered and reviewed internally to determine appropriate next steps. The following criteria

are meant to assess the cancer(s) of concern and related environmental risk factors. These criteria promote further assessment of unusual patterns of cancer that may not always meet the formal definition of a cancer cluster.

Factors that indicate a possible unusual pattern of cancer include:

- The concern described could plausibly meet the definition of a cancer cluster.
- The cancers of concern are all the same type or may share a common etiology. Frequently, not enough is known to rule out the possibility of a common etiology.
- The concern described involves a rare cancer or an atypical demographic distribution (such as breast cancer in men).
- There is a known or suspected environmental issue in the area, and the scientific literature supports an association between the environmental issue and cancer of concern. [Note: Information about known or a suspected environmental issue will be collected from the concerned citizen and stakeholders, such as local health jurisdictions, Texas Commission of Environmental Quality (TCEQ), Texas Department of Agriculture (TDA), Railroad Commission of Texas (RRC) and/or other community partners as appropriate].

Inquiries involving an unusual pattern of cancer at a school (including preschool or daycare) setting

- Cancer concerns among school staff (e.g., teachers) will be considered as an occupational concern and referred to NIOSH. For concerns related to a suspected unusual pattern of cancer in an occupational setting, please see [Appendix A](#).
- Cancer concerns that include a school and its surrounding neighborhood will be considered as a community inquiry and addressed per protocol for unusual patterns of cancer in a community setting.
- Cancer concerns among children attending a school, will be addressed on a case-by-case basis. At a minimum additional information from the school is needed (such as names of children) and a memorandum of understanding with TCR is needed. DSHS will seek technical assistance from appropriate state or federal agency to further examine environmental exposure concerns in the area of school and expertise on children's environmental health.

Factors that do not point to the existence of an unusual patterns of cancer:

- Cancer cases occurred within genetically-linked family members

(especially when cancers are known to be strongly genetically related).

- Reported cases include a few cases of a common cancer.
- Reported cases included many different cancers.
- The cases did not all live in the area of concern during the time during which they would have been exposed to a common carcinogen.

DSHS will review the concern and relevant additional data to determine if the inquiry may meet the definition of an unusual pattern of cancer, and whether an assessment of the occurrence of cancer is appropriate. Based on this review, DSHS will either:

Close the Inquiry

If the concern clearly doesn't fit the definition of an unusual pattern of cancer (i.e. the concern involves many different types of common cancer), the inquiry will be closed. A follow-up email or letter will be sent to the concerned individual(s) summarizing the inquiry, and outlining next steps. If there are known or suspected environmental hazards in the area of concern, then additional information including appropriate contacts at environmental or other government agencies (e.g., EPA, TCEQ, local health department) will be provided to the inquirer.

Proceed with an assessment of the occurrence of cancer

At least one of following must be met to proceed with an assessment:

- The cancers of concern are all of the same type or may share a common etiology;
- The concern described involves a rare cancer or an atypical demographic distribution;
- There is widespread community concern.

The purpose of such an assessment is to determine whether the observed number of cases is statistically significantly greater than expected. It is not intended to identify the cause of the observed cancers or identify possible associations with any risk factors. If it is determined that an assessment of cancer can be conducted, a follow-up email or letter will be sent to the concerned individual(s) summarizing the inquiry, and outlining next steps.

Assessment of the Occurrence of Cancer

If DSHS has determined that an assessment of the occurrence of cancer is appropriate, the inquirer must submit a written request for the assessment to proceed. DSHS will then collaborate with the inquirer to confirm the cancers of interest, and the demographic, geographic, and temporal

boundaries to be included in the investigation. These parameters will reflect the population the inquirer believes to be or have been at risk of a common exposure of concern, if known.

Before proceeding, DSHS will notify local or regional public health officials of DSHS's intent to conduct an assessment. DSHS may also notify elected officials and other state agencies as appropriate.

Data Sources

All cancer data will be obtained from the TCR. For each cancer type, the number of cases observed during the indicated timeframe and area included in the investigation will be calculated. For the same age range and timeframe, rates for each cancer for the state of Texas will be identified from TCR data. All-ages or adult cancers will be defined according to International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3), while childhood cancers will be defined according to the International Classification of Childhood Cancer (ICCC).

The census tract is the smallest geographic area that can be reliably analyzed. If the geographic area of investigation is defined by census tracts, census tract certainty will be calculated to determine proportion of cases that cannot be reliably coded to a census tract for reasons such as having a post office box address instead of a street address.

Population estimates for the area investigated will be calculated using linear interpolation based on population counts obtained from the United States Decennial Census, when possible. This method, outlined by the United States Census Bureau, assumes population growth has occurred in a linear manner [4].

Statistical analysis

To determine if a statistically significant excess of cancer exists in the area of investigation, the number of observed cancer cases will be compared to what would be expected for the area based on cancer rates in Texas.

Standardized incidence ratios (SIRs) will be calculated to determine if an excess of cancer exists in the area. The SIR is the number of observed cases compared to (divided by) the number of expected cases for each cancer type. The expected number of cancer cases will be calculated by multiplying the age-, sex-, and race-specific cancer incidence rates of Texas residents (reference population) by the number of people in the corresponding demographic groups in the area of investigation. Additionally, 95 percent confidence intervals (CI) will be calculated for the SIRs based on the Poisson distribution. If a 95 percent CI (range) includes 1.00, no statistically significant excess (or reduction) of cancer is indicated.

If a 95 percent CI does not contain 1.00, the SIR is outside the expected range and is statistically significant. A narrower confidence interval indicates a more precise estimate [5].

The size of the SIR estimate indicates the magnitude of the difference between observed and expected cases. Larger SIRs are sometimes thought to indicate that it is more likely that there is a “real” cluster that can be studied. However, there is no specific threshold that constitutes a “large” or “small” SIR, and interpretation has to be context-specific. Recommendations for the interpretation of SIR effect sizes vary widely. For example, Neutra, *et al.*, suggest that an effect size of 20 might be an acceptable threshold indicating further investigation is warranted [6]. Still others suggest that a “large” effect size is a ratio of about four [7, 8]. There is not a consensus on what effect size should be the threshold for concern.

For any cancer type with less than or equal to five observed cases for the time period included in the analysis, SIRs will not be calculated, and case counts will be suppressed. Displaying case counts of less than six jeopardizes patient confidentiality. Furthermore, SIRs calculated with such small numbers are likely to be unreliable estimates. Although larger observed case counts may also result in unreliable SIR estimates, five observed cases is a threshold that balances statistical limitations with data transparency. For details on standardized incidence ratio, and challenges and limitations of investigating cancer clusters see additional resources in Appendix C.

Summary Report

DSHS will produce a summary report of the assessment. The report will include the following sections:

- Executive Summary
- Background
 - Pertinent information about the concern will be provided.
- Methods
 - Specifies the data sources and statistical methods used in the analysis.
- Results
 - A written summary of results as well as data tables will be provided.
- Discussion
 - Provides detailed information on the limitations of cancer cluster assessments in general, and any additional limitations of the analysis conducted, including latency, residential history, and

multiple comparisons.

- Conclusions
 - A summary of the findings and guidance for the interpretation of these findings will be provided.
- Recommendations and Next Steps
 - Recommendations and next steps to be taken by DSHS will be described.
- Additional Information
 - Additional resources, such as facts about cancer risk factors, links to other cancer information resources, and DSHS contact information, will be provided.

Results Communication

The final report will be sent by letter or an email to the requester, local health jurisdiction, state and/or federal agencies and elected official(s) as appropriate. The report will also be posted on the DSHS website for the public. DSHS will also develop a plain language document summarizing the cancer assessment report in English and Spanish languages, and any other languages as needed. The plain language summary document for each assessment report will be posted with the DSHS website (<https://www.dshs.texas.gov/environmental-surveillance-toxicology/cancer-cluster-investigations>).

Determine Appropriate Next Steps

After completion of the assessment, DSHS will determine how to proceed, taking into consideration several factors. DSHS will consider the magnitude and direction (greater or less than one) of the calculated SIRs, along with additional details. For example, when using a 95 percent CI, five percent of SIR values calculated are expected to be statistically significantly higher or lower than the state average simply due to random chance. Therefore, if many different cancer types are evaluated in several geographic areas, the statistical issue of multiple comparisons must be taken into consideration. DSHS may also consider issues such as the number of observed cases, population growth and migration patterns in the area of investigation, and the rate of disease in the reference population.

Based on a review of relevant information, there are several possible next steps that may be recommended:

- **No further action needed.**

If none of the cancers were statistically significantly higher than expected, DSHS may recommend no further action related to the assessment of the

occurrence cancer. The investigation will be closed at this point.

- **Continue monitoring cancers in the area investigated.**

If any SIRs were statistically significant, but SIRs were small, or estimates were not reliable due to small numbers, DSHS may recommend continuing monitoring cancer in the community by updating the unusual pattern of cancer assessment, upon request, as new years of data are completed in the TCR.

- **Assess the feasibility of conducting an epidemiologic study.**

In considering the factors mentioned above, there is no single rule that applies to every situation. However, a recommendation to proceed with a feasibility assessment could be made under circumstances such as:

- SIRs are statistically significant and are greater than or equal to 10; and,
- There are enough cases to sufficiently power an epidemiologic study; and,
- There is a suspected or known environmental hazard in the area, and there is evidence in the scientific literature that this hazard may be associated with cancer.

Establishing Strong Relationships and Partnerships with the Community

When further assessment activities are warranted, DSHS will develop and implement a community engagement plan in consultation with the relevant local health jurisdiction.

Phase 3. Considerations for Epidemiologic Studies

Purpose: To determine the feasibility of conducting an epidemiologic study of the associations between specific cancers and environmental contaminants in the area investigated.

If DSHS recommends proceeding to this step, there are multiple factors that must be considered during the process to determine if an epidemiologic study of the associations between specific cancers and environmental contaminants is feasible. This process will be carried out transparently and in collaboration with the community, environmental agencies, and other partners.

Information Gathering

During the process of determining the feasibility of an epidemiological

study, DSHS will gather additional information to be considered along with results of the previously-conducted assessment of cancer. This may include examination of any relevant existing data sources, such as additional clinical or environmental data.

Environmental exposures

DSHS will gather additional information about any exposures of concern identified by concerned community members. Existing literature, reports, and other documentation will be reviewed. DSHS will consult with other government agencies that may have knowledge of the area investigated.

Community concerns

DSHS will engage with community members to ask for input regarding what outcomes the community would like to see, and how those outcomes might be met.

Public health interventions

A list of public health interventions that may help achieve outcomes desired by concerned community members will be compiled. Interventions may include health risk assessments, cancer screenings, smoking cessation programs, or other targeted interventions.

Feasibility Assessment

The feasibility of designing and conducting an epidemiologic study is dependent upon a variety of factors. For that reason, a feasibility assessment should be conducted to determine whether it is practical to conduct a study that would provide meaningful answers. The feasibility assessment should address multiple issues, including, but not limited to, data availability, adequate sample size to detect meaningful differences or associations, staff capacity, and other resources.

Establish a Community Advisory Committee

Internal and external experts will be involved in assessing the feasibility of an epidemiologic study. An advisory committee comprised of subject matter experts may be comprised to address specific environmental, study design, statistical, or other issues. This group may include scientists with relevant expertise, including environmental protection specialists, toxicologists, epidemiologists, biostatisticians, and clinicians. Additionally, at least one community-designated representative will be included. DSHS will work with this group to determine if a follow-up epidemiologic study of the associations between specific cancers and environmental contaminants is feasible, and if it would be likely to identify the cause of the higher-than-expected cancer rates. Issues that may be considered during the feasibility

assessment can be found in Appendix B.

If a review of relevant information shows that additional study is not feasible, the investigation will be closed. If epidemiologic study is deemed feasible and likely to lead to the identification of associations between environmental contaminants and cancers, DSHS will proceed to coordinate necessary resources. The agency will most likely need to seek external funding, and may need to partner with external entities to complete the study. In either case, a summary document describing the feasibility assessment, final determination, and additional actions to be taken will be provided to community members and the public. If further epidemiologic study will be conducted, DSHS will work to ensure ongoing communication with the community throughout the process.

In a situation where the agency decides to move forward with conducting an epidemiologic study, the following steps will be taken into consideration in alignment with the 2022 CDC/ATSDR guidelines:

- Establishing a community advisory committee
- Developing and designing an appropriate protocol and study
 - Generating a formal case definition
 - Forming a hypothesis
 - Defining a population of interest
 - Assessing latency
 - Considering other environmental data, additional health data, and contributing risk factors

Other considerations for a potential epidemiologic study should also include:

- Funding
- Outreach i.e., reaching out to other states
- Communication.

Appendix A

Response to Occupational Cluster Concerns

DSHS does not currently have the appropriate data or resources to investigate occupational cancer concerns. Individuals concerned about potential exposures in the workplace will be referred to contact the National Institute for Occupational Safety and Health (NIOSH). Through its Health Hazard Evaluation (HHE) Program, NIOSH investigates concerns of hazardous working conditions when employers, authorized employee representatives, or employees request it. More information about the HHE Program is available at the NIOSH website at <https://www.cdc.gov/niosh/hhe/default.html>, or by contacting 513-841-4382 or HHERequestHelp@cdc.gov.

Appendix B

Feasibility Assessment Considerations

Environmental Exposures

- Are there any documented or suspected exposures to environmental contaminants?
 - Are there any known completed exposure pathways?
- Does the literature support a possible association between these potential exposures and the cancers with elevated SIRs?
- Would the dose and duration of exposure to any known contaminant be sufficient to make an association biologically plausible?
- Is the time sequence of exposure consistent with the latency period of these particular cancers?

Hypothesis

- Is there a testable hypothesis?

Study design

- What type of study would be appropriate to test this hypothesis?
- What cancer types/sites would be included in the study?
- What is the source population? How would the study population be selected? What would the inclusion criteria be?
- What sample size would be needed to conduct such a study?
- Is there an appropriate comparison group?
- What additional data (e.g., residential history, demographics, risk factors, exposures) would be needed to conduct a study?
- Can this data be obtained for both the cases and comparison group?
- Can environmental exposures be characterized accurately at the individual level?

Resource Requirements

- What resources would be needed to complete this study?
- Who will provide these resources?
- Is this the best use of these resources, or could they be used in other ways resulting in more benefit to the community?
- Who will lead the study?
- How long would this study take?
- What would the potential public health benefits of further study be?

Community Concerns

- What outcomes would the community like to see?
- What public health actions will contribute to the achievement of those outcomes?

Appendix C

Additional Resources

- 1 Centers for Disease Control and Prevention (CDC). Investigating Cancer Clusters and Unusual Patterns of Cancer: Challenges and Limitations. <https://www.cdc.gov/nceh/cancer-environment/pdfs/Challenges-and-Limitations-508.pdf>.
- 2 Centers for Disease Control and Prevention (CDC). Standardized Incidence Ratio (SIR). A Math-based Approach to Evaluating Unusual Patterns of Cancer. <https://www.cdc.gov/nceh/cancer-environment/pdfs/Standardized-Incidence-Ratio-Fact-Sheet-508.pdf>.

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