Special Report: An Archive of the Cluster Advisory Service Content of the EUROCAT Website

(August 2014)

EUROCAT Central Registry
Room 12L09
University of Ulster
Newtownabbey, Co Antrim
Northern Ireland, BT37 0QB
Tel: +44 (0)28 90366639
Fax: +44 (0)28 90368341
Email: eurocat@ulster.ac.uk
Web: www.eurocat.ulster.ac.uk

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The EUROCAT Website underwent a period of cleaning and revision in preparation for EUROCAT's transition to the Joint Research Centre, post 2014. In August 2014 the Cluster Advisory Service section of the website was removed and the content found within this section of the web has been included below for archiving purposes. Some of the links within were found to be redundant and replacement links to the same material were sought where possible.

Cluster Advisory Service

This webpage was accessed via http://www.eurocat-network.eu/clustersandtrends/clusteradvisoryservice/introduction

Introduction

One of the objectives of the annual Statistical Monitoring conducted by EUROCAT is to co-ordinate the detection of, and response, to clusters and early warning of teratogenic exposures.
Most EUROCAT member registries have had the experience that clusters of birth defects detected in their routine surveillance or by others (health services or general public) may attract general interest, including considerable attention in the media. In some cases the disentangling of a cluster and its conclusion may represent a great challenge involving a high number of interested parties and with important consequences even for the community at large. Thus, the registry involved may feel a need to consult with a "neutral" body to have a second opinion on the interpretation of a cluster.
The Cluster Advisory Service was originally developed by the EUROCAT Cluster Advisory Working Group in 2003. The working group built on EUROCAT's prior experience in the investigation of clusters and environmental exposure incidents.

A new committee has now been formed under Work package 6 of the EUROCAT Joint Action (WP6: Investigation of Trends, Clusters and New Exposures). The EUROCAT Taskforce for Evaluation of Clusters (TEC) has been established to serve as such a "neutral" body. In addition TEC may be requested to comment on the routine cluster investigation conducted by EUROCAT including its presentation and possible use. Details of the work of the TEC and any associated investigations will be reported in future Statistical Monitoring reports.

TEC Mandate proposal (Version 2 - 29th August 2011)
1 TEC (Taskforce for Evaluation of Clusters) is a committee reporting to the EUROCAT Project Management Committee and established in connection with the EU financed project EUROCAT: Surveillance of Congenital Anomalies in Europe as an activity under Work Package 6: 6.2:.Investigation of Trends, Clusters and New Exposures.

2 TEC has the following functions:
2.1 On request by the PMC to comment on the output of cluster investigations conducted by EUROCAT including its presentation and possible uses.
2.2 Serve as a consulting unit in cases of clusters, commissioned by EUROCAT or individual member registries.
2.3 In the assessment of a cluster the TEC may:
2.3.1 Correspond and get written information and data from the registers involved
2.3.2 Pay site visits for meetings with the registries involved and, if considered expedient, with other parties.
2.3.3 Propose and advise on ad hoc studies aiming at clarification of a cluster.

3 TEC members are:
Lorentz M Irgens (EUROCAT Bergen, Chair)
Ingeborg Barisic (EUROCAT, Zagreb)

Petter Kristensen (Oslo)
Rolv Terje Lie (Bergen)
Nichola McCullough (EUROCAT Central Registry, secretary)
Vera Nelen (EUROCAT Antwerp)
Helen Dolk (EUROCAT Project Leader, ad hoc member)
Additional members may be appointed by TEC in ad hoc situations according to needs for further expertise in relevant specialities.

The Cluster Advisory Service was developed by the EUROCAT Cluster Advisory Working Group in 2003.

This Working Group has built on EUROCAT's twenty years of experience in the investigation of clusters and environmental exposure incidents. This has included investigation of clusters detected by routine surveillance at Local Registry or Central Registry level, assessment of the impact of the Chernobyl accident on the prevalence of congenital anomalies in EUROCAT regions, local and multi-regional assessments of the risk of residence near waste sites, contaminated land or industrial areas including the EUROHAZCON project, and in 1997 an international workshop on cluster assessment (EUROCAT Technical Report "Cluster Assessment Strategy for Europe").

Members of the group were:

Ben Armstrong (EUROCAT Central Registry)

Fabrizio Bianchi (EUROCAT Tuscany)

Araceli Busby (EUROCAT Central Registry)

Helen Dolk (EUROCAT Project Leader, Chair)

Marjon Drijver (Amsterdam)

Judith Greenacre (EUROCAT Wales)

Vera Nelen (EUROCAT Antwerp)

Elisabeth Robert (EUROCAT Central East France)

Paul Wilkinson (London)

How Unusual is an Observed Cluster?
Direct link to this page was: http://www.eurocat-network.eu/clustersandtrends/clusteradvisoryservice/howunusualisanobservedcluster

These pages give some simple statistical aids and comments on addressing this question. We provide a calculator for a simple statistical test, but there are major difficulties of interpretation of such tests, so we start with some explanation of these.

This is a simple guide to a complex problem. References to more comprehensive guides are given at the end.

What is a Cluster?
There are many different definitions of a cluster. EUROCAT has adopted the following definition of a cluster as:

'An aggregation of cases of congenital anomaly in time and/or space which appears to be unusual' (EUROCAT Working Group on the Management of Clusters and Environmental Exposure Incidents, 2003). The Working Group also noted that the definition of space here employed should include space as defined by a common activity such as a place of work/education/recreation etc. and not just space as defined by residence.

Types of Cluster Investigation
It is important to distinguish two contexts:

1. A causal hypothesis in search of a cluster
2. A cluster in search of a causal hypothesis

Statistical methods employed in contexts 1 and 2 are often similar, but interpretation of their results should be very different.

A Causal Hypothesis in Search of a Cluster
An example of this is a study of anomalies in relation to proximity of residence to a waste dump site (the clustering of anomalies around the site), instigated because animal experiments or other independent evidence have suggested exposure around such sites may carry a risk of anomaly. These kinds of studies raise some methodological problems, mainly those common to all geographical epidemiology, but do not suffer from the major interpretational problems arising in cluster investigations of the second type.

A Cluster in Search of a Causal Hypothesis
An example is when a local newspaper or residents association perceives an apparently unusually high number of cases of disease occurring in an area. A cause (a local factory, power lines, or similar) is often then hypothesised. This is the context that is usually referred to as a **cluster report**. Interpretation of cluster reports are extremely problematic, and often controversial.

Stages of Investigation
The classic Guidelines for Investigating Clusters of Health Events, published by the Centers for Diseases Control, USA, identified three preliminary stages in the further investigation of reported clusters:

1. A preliminary evaluation to provide a quick rough estimate of the likelihood that an important excess of cases has occurred.
2. Case evaluation to verify diagnosis.
3. Occurrence evaluation to ensure all relevant cases have been recorded.

The process is one of screening. At each stage, it can be decided that there is insufficient evidence to warrant the resources required to go further.

Preliminary Evaluation
We usually need to establish:
1. How many cases in the cluster?
2. How many cases would you expect, on average?

Once these are established, it may be useful to carry out a statistical test.

How Many Cases in the Cluster?

This might seem simple, but is often not. Tricky points are:

1. What geographical and time boundaries are appropriate?
2. What types of anomaly should be included?

Where possible, the cluster should be defined in relation to the hypothesised exposure. For example, if the concern is a waste landfill site, cases before the site started are not relevant. For choosing which types of anomaly to include, keep in mind that the more homogeneous the cluster is, the more common the cause. For example, it would not usually be sensible to pool chromosomal and non-chromosomal anomalies.

How Many Cases Would you Expect, on Average?

If you know how many births there were in the population from which the cluster arose, then an expected number can be calculated by applying an appropriate reference rate (for example, that for the registry overall). Ideally this would take account of the distribution of maternal age (particularly for chromosomal anomalies) and any other risk factor, but his may not be available.

If number of births is not known, a rougher number may be obtained by some less formal means, for example, noting that the population under investigation comprises about 20% of the population covered by the registry, so one would expect about 20% of the total cases found by the registry.

A Simple Statistical Test and Calculator

This webpage provided a link to the following statistical test and calculator which could be accessed by the following direct link http://www.eurocat-network.eu/pagecontent.aspx?tree=Asimplestatisticaltest

A simple statistical test and calculator

It is almost impossible to decide definitively whether chance is a plausible explanation of a cluster, but this statistical test might help somewhat.

Confidence interval and p-value for an excess of cases given observed O and expected E

Observed (O) number of cases:

Expected (E) number of cases:

Reset Calculate

One-sided p value:

Ratio of observed to expected cases (O/E):

95% confidence intervals for the O/E ratio:

Maximum numbers of cases that can easily be explained by chance (p>0.05):

The p-value tells us how likely it is to have an excess of the size observed by chance alone. For example, chance would give rise to excesses giving p-values of 0.01 in one in every 100 communities. However, interpretation of p-values in clusters is more complex.

The O / E ratio is called the relative risk, and expresses how many times more cases were observed than expected.

The confidence interval (CI) for the O / E ratio gives an idea of uncertainty around it, due to chance.

The last row of the table gives the maximum number of cases occurring in 95% of populations of your size.

Formulae for p-value and CI

We assume that O > E.
The (one-sided) p-value is the probability of observing O or more cases if E are expected. The probability of observing r cases if E are expected is given by the Poisson distribution:

$$P(R = r \mid E) = e^{-E} E^r / r!$$

The one-sided p-value is thus:

$$p(1-sided) = 1 - \sum_{r=0..O-1} \Pr(R = r \mid E) = 1 - \sum_{r=0..O-1} [e^{-E} E^r / r!]$$

An approximate formula for a 95% confidence interval for the O/E ratio is:

$$(\sqrt{O} \pm 1.96/2)^2/E$$

eg. if O = 5 and E = 2.4
p(1-sided) = 1 - 0.904 = 0.096
p(2-sided) = 2 × 0.096 = 0.192

$$95\%\ CI: (\sqrt{O} \pm 1.96/2)^2/E = (\sqrt{5} \pm 1.96/2)^2/2.4 = (0.66, 4.31)$$

Finally, the largest number of cases giving p > 0.05 is given by:

$$\text{Largest } R \text{ such that } \sum_{r=0..R} [e^{-E} E^r / r!\ ] < 0.95$$

eg. E = 2.4, R = 5

Difficulties in interpreting p-values in cluster reports

P-values were designed for scientific experiments, not cluster reports. The key difficulty is usually referred to as the Texas sharp-shooter phenomenon.

Some epidemiologists and statisticians consider the Texas sharp-shooter problem so severe that p-values or confidence intervals have no value at all in these contexts. We do not take such a strong view. Clusters with p-values above 0.10 would only very rarely merit further follow-up. The reverse is unfortunately not true, because of the interpretation difficulties. Along with the p-value, stakeholders might usefully consider the plausibility that the exposure could have caused the excess, the degree of concern in the population, and the extent of the potential public health problem.

The Texas sharp-shooter

American humour has it that the "Texas sharp-shooter" (why Texas?) first fires his gun at the barn, then paints a target on the barn with the bulls-eye where most bullet-holes have clustered. He then shows this to his friends to show what a good shot he is.

We should interpret cluster reports with something of the same caution that we should interpret the sharp-shooter's claims of marksmanship. The local area in which the cluster is situated has come to your attention precisely because there were a lot of anomalies there. Anomaly occurrence rates will always vary randomly between areas. Has the "target" been drawn around the area with high rates (there must be some), after the bullets have been fired?

Systematic searching for clusters

Anomaly register data-bases can be systematically searched for clusters. Such systematic searches can adjust appropriately for "Texas sharp-shooting" with more complex statistical methods, identifying only excesses unusual GIVEN THE LARGE NUMBER of populations implicitly considered. However, for this investigator's need to decide formally exactly what sorts of patterns represent "clusters". We do not consider this further here.

Summary

1. Most cluster investigations are carried out because an unusual occurrence of anomalies has come to light. In these cases statistical tests are hard to interpret.
2. A preliminary investigation can be made by identifying the number in the cluster, and the number expected on average.
3. A test of how unusual this is straightforward.
4. Interpretation of the test is difficult because of the "Texas sharp-shooter" phenomenon.

Further reading on clusters

NCI: Cancer Clusters
http://www.cancer.gov/cancertopics/factsheet/Risk/clusters

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Cluster Investigation Protocols

Direct link to this page was: http://www.eurocat-network.eu/clustersandtrends/clusteradvisoryservice/clusterinvestigationprotocols

Classification of Cluster Types

We consider four situations where different investigative strategies apply:

1. A reported cluster of congenital anomalies with a putative environmental cause
2. A reported cluster of congenital anomalies with no suggested environmental cause
3. A cluster of congenital anomalies identified as a results of routine surveillance
4. A reported environmental exposure which is of concern in relation to its capacity to cause a cluster of congenital anomalies

A Summary of Existing Cluster Investigation Protocols

Existing protocols are generally aimed at clusters of Type 1 and 2. The EUROCAT Working Group recommends the Dutch Triple Track approach (Protocol 1) as this protocol recommends starting all three strands of a cluster investigation (investigation of the health effects, investigation of the environmental exposures and communicating with the concerned community) from the outset, so that the three areas develop alongside each other rather than in stepwise sequence as is often the case with other protocols. Ten existing cluster investigation protocols are annexed to the report.

Preliminary Evaluation of a Cluster - Summary of Information Collected by Cluster Protocols

<u>Informant Information</u>
Name address, telephone number and background of informant (media, relative, friend, other)
Occupation of informant
How the informant learnt about the cluster
Is the informant willing to be contacted further?
Has the informant contact anyone else about the cluster (health agencies, GP, employer representative etc)

<u>General Information</u>
Setting of the suspected cluster (neighbourhood, workplace, school, other)
Time period of concern
Geographic boundaries of cluster
Types of birth defect
Number of cases
Usual number of cases seen

<u>Case Information</u>
Names of case(s)
Date of delivery
Gestational age
Sex
Ethnicity
Addresses of cases at diagnosis/birth
Current address and how long has the mother lived there
Diagnosis (birth defects of concern)
Hospital of birth/where diagnosis was made
Dates of diagnosis
Mother's age at delivery
Occupational history of parents
    Type of industry
    Job
    Year job began and ended
Other medical conditions (parents)
Family history
Other possible exposures (parental)

Contact details (method for contact or individual to contact)
If deceased: date and place of death, home address at time of death
Name and address of General Practitioner

Exposure Information
Details of environmental issues if any:
Type of exposure
Address where exposure occurred
Date exposure began
Date exposure ended
Details of any changes in exposure

Details of other clinical, media, public officials involved
Any other information

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Cluster Investigation Protocols

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Environmental Risk Factors

Direct link to this page was: http://www.eurocat-network.eu/clustersandtrends/clusteradvisoryservice/environmentalriskfactors

This webpage directed the reader to EUROCAT's Review of Environmental Risk Factors for Congenital Anomalies. Currently accessible at http://www.eurocat-network.eu/preventionandriskfactors/primaryprevention

Completed Cluster Investigations

Direct link to this page was: http://www.eurocat-network.eu/clustersandtrends/clusteradvisoryservice/completedclusterinvestigations

Cluster Investigations Published in Scientific Journals

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Cluster Reports Available on Worldwide Web

Childhood cancer incidence: health consultation: a review and analysis of cancer registry data, 1979-1995 for Dover Township (Ocean County) New Jersey
http://www.state.nj.us/health/eoh/hhazweb/cansumm.pdf

Freshkills landfill site, child health problems, infertility and miscarriage, Richmond County, New York
http://www.atsdr.cdc.gov/hac/pha/pha.asp?docid=195&pg=0

Public Health Assessment: US Marine Corps Camp Lejeune Onslow County, North Carolina
http://www.atsdr.cdc.gov/hac/pha/pha.asp?docid=1082&pg=0

Public Health Assessment: National Zinc Company Bartlesville, Washington County, Oklahoma (birth defects)
http://www.atsdr.cdc.gov/hac/pha/pha.asp?docid=701&pg=0

Health Consultation: Evaluation of potential exposures from the Fallon JP-8 Fuel Pipeline. Fallon, Churchill County, Nevada
http://www.atsdr.cdc.gov/HAC/PHA/HCPHA.asp?State='NV'

Childhood cancer, Willmington, Massachusetts, USA
http://www.mass.gov/eohhs/gov/departments/dph/programs/environmental-health/investigations/wilmington/fact-sheet-on-the-wilmington-childhood-cancer.html

Churchill County (Fallon) Childhood Leukaemia
http://www.cdc.gov/nceh/clusters/fallon/genetictesting.htm

Identified disease clusters in USA
http://clusteralliance.org/clusters/

Acute lymphocytic leukaemia in Whatcom County, Washington, USA

https://www.co.whatcom.wa.us/health/pdf/leukemia_survey.PDF

Local Regional Investigations of the California Birth Defects Monitoring Programme

Monitoring for Birth Defects Following the Cantara Loop Spill (1992)
http://www.cdph.ca.gov/programs/CBDMP/Documents/MO-CBDMP-CantaraLoop.pdf

Neural Tube Defects in Kern County: Buttonwillow Area Cluster Investigation, Summary and Full Report (1993)
http://www.cdph.ca.gov/programs/CBDMP/Documents/MO-CBDMP-ButtonWillow.pdf

Birth Defects in Lompoc (1996)
http://www.cdph.ca.gov/programs/CBDMP/Documents/MO-CBDMP--Lompoc.pdf

Birth Defects in McFarland (1996)
http://www.cdph.ca.gov/programs/mcah/Documents/MO-BirthDefectsInMcFarland.pdf

Birth Defects in Bayview/Hunter's Point (1997)
http://www.cdph.ca.gov/programs/CBDMP/Documents/MO-CBDMP-BayViewHuntersPoint.pdf

Analysis of a cluster of adverse pregnancy outcomes around BKK landfill in Walnut, California (1994)
http://www.ehib.org/paper.jsp?paper_key=WALNUT_PREG_1994

Pregnancy outcomes in Santa Clara County 1980-1985 (1988)
http://www.ehib.org/paper.jsp?paper_key=SANTA_CLARA_PREG_1988

Water exposure and pregnancy outcomes (analysis of Fairchild Camera and Instrument Company solvent waste, San Jose, California) (1988)
http://www.ehib.org/paper.jsp?paper_key=WATER_PREG_1988

Protocol 1

Drijver M, Melse JM (1992), "Disease Clusters and Environmental Contamination I: A Guide for Public Health Services" (in Dutch), T Soc Gezondheidsz, Vol 70, pp 565-570. See also Local Environmental Health Concerns under Proceedings of Working Group meeting February 2003. Drijver M, Woudenberg F (1999), "Cluster Managmenet and the Role of Concerned Communities and the Media", European Journal of Epidemiology, Vol 15, pp 863-869.

<table>
<tr><th>Health Track</th><th>Environment Track</th><th>Communication Track</th></tr>
<tr><td colspan="3">Step 1: Orientation</td></tr>
<tr><td>General information about the expected frequency of disease, potential risk factors</td><td>General information about local exposure possibilities (site visit)</td><td>Preparation of visit to person who has contacted the health agency</td></tr>
<tr><td colspan="2">Gather background information about biological plausibility of a relation between exposure and disease (literature review)</td><td></td></tr>
<tr><td colspan="3">Step 2: Qualification</td></tr>
<tr><td>Ask concerned persons to list the number of health events together with basic data such as address, years of residence, age, sex, years of diagnosis or death, type of diseases, occupation, smoking habits etc.</td><td>Ask local residents for information on possible routes of exposure to an environmental pollutant</td><td rowspan="3">Personal communication with concerned person in their own environment:
Demonstrate genuine interest and concern
Enables an impression of the social context (how severe is level of worry)
Allows formation of an impression of the neighbourhood and socio-demographic characteristics (especially presence and age of children)
Allows exchange of information with local residents
Allows provision of general oral and written information on the disease of concern and its causes including the difficulties of proving causal relationships between disease and environment.
If media are already involved, ensure contact is made and arrangements made about information which will be provided (must provide information to community first)</td></tr>
<tr><td colspan="2">First assessment of cluster: combine health data with population data (or crude count of number of houses and people in neighbourhood) and compare with national or regional expected frequency or occurrence of disease. Additional medical information from general practitioners with patients in neighbourhood may be helpful to consider if cases constitute an aetiological entity.

Sequentiality of the time relationship between the exposure and the health effect.</td></tr>
<tr><td>Number of cases is higher than expected</td><td>Biologically plausible and logical temporal relationship with an environmental agent.</td></tr>
</table>

<table>
<tr><th colspan="3">Step 3: Quantification</th></tr>
<tr><td>More extended and controlled epidemiological investigation:

Frequency of occurrence of disease compared with adequate reference data (age standardised) OR advanced form of cluster analysis.</td><td>Further investigation of routes and amount of exposure:

Environmental risk assessment essential to decide if accepted exposure limits are exceeded (generally using water, air, soil or crops is sufficient).

Environmental intervention (“first clean up the mess”) may be more important than proving a causal relation</td><td>Conclusions and following investigations must be shared with the community.</td></tr>
<tr><td colspan="2">If an increased risk is found that cannot be explained by artefact (eg. reporting bias) and an elevated exposure is determined, proceed to case control study</td><td></td></tr>
<tr><th colspan="3">Extended Epidemiological Study</th></tr>
<tr><td colspan="2">If an investigation is carried out, it is probably that it will only find a causal association if:

1. minimal 5 patients with homogeneous disease
2. relative risk at least 10
3. sufficient publicity to minimise exposure suspicion bias
4. minimal publicity to minimise exposure suspicion bias (preferably study is carried out in another population then the concerned one).</td><td>Inform the communication about the progress of the study. Preferably have regular meetings at intervals (allows researchers to inform community and community to participate in deciding about basic assumptions).

As soon as a conclusion is reached and the concerned community is informed, should then inform the media (design pro-active media strategy together with community members).</td></tr>
<tr><td colspan="3">Recommendations:

• Take worries about exposure to local environmental factors seriously
• Pay attention at an early stage to risk communication and public participation
• Perform a systematic and transparent exposure assessment
• Consider exposure reducing measures in case of any nuisance or undesirable exposure
• Pay attention to any possible somatic consequences of stress
• Follow a stepwise approach to environment-related diseases clusters
• Take into account coincidence as an explanation of detected disease clusters
• Be critical when conducting descriptive epidemiological studies
• Explain under which conditions a further epidemiological study would be advisable
• Involve communication specialists in epidemiological studies</td></tr>
</table>

Protocol 2

CDC MMWR (1990), "Guidelines for Investigating clusters of Health Events"

Definition of a Cluster: An unusual aggregation, real or perceived, of health events that are grouped together in time or space and that are reported to a health agency.		
Cluster investigation likely to be fruitful if: Cluster has a definable health outcome either new or rare, a potential exposure or agent is suspected along with a connection between the exposure and health event, the situation is highly unusual and statistical testing confirms the investigators impression and the short term public health impact is immediate and self-evident.		
Stage	**Action**	**Outcome**
Stage 1 Initial contact and response	Gather identifying information on caller, gather initial data on potential cluster, obtain identifying information on persons affects, discuss initial impressions with the caller, request further information and plan further telephone follow-up, assure that s/he will receive a written response, maintain a log of initial contacts, notify health agency's public health office (or equivalent)	**Criteria to continue to Stage 2:** If single and rare disease entity, plausible exposure or plausible clustering.
Stage 2a Preliminary evaluation	Geographical area and time period, which cases are included in the analysis, appropriate reference population, calculate rates and asses significance (chi^2, Poisson regression) or clustering statistics (see Appendix)	If preliminary evaluation suggests an excess proceed to Stage 2b
Stage 2b Case evaluation	Verify the diagnosis: contact responsible physicians/health event registry, obtain copies of relevant records (eg. pathology), and obtain histological evaluation.	If cases verified and excess confirmed proceed to Stage 2c
Stage 2c Occurrence evaluation	Define appropriate geographic (community) boundaries, ascertain all potential cases within space time boundary, identify appropriate database for numerator and denominator data, in depth review of literature, assess likelihood that an event-exposure relationship may be established, assess community perceptions, reactions and needs, complete investigation.	**Criteria to continue to feasibility study:** If an excess is confirmed and epidemiological and biological plausibility is high proceed to major feasibility study. If excess is confirmed but no relationship to exposure is apparent, terminate the investigation and inform persons concerned. If excess not confirmed terminate investigation and report findings to the caller. **If no further follow-up:** Inform concerned persons.

Stage 3 Feasibility study	Examines the potential for relating the cluster to some exposure: review detailed literature search, consider appropriate study design (including costs and outcomes of alternatives), determine what data should be collected, delineate the logistics of data collection and processing, determine the plan of analysis, assess the current social and political ambience, assess the resource implications and requirements of both the study and the alternatives.	**If aetiologic investigation warranted proceed to stage 4:** Decision to proceed will be related to allocation of resources. If feasibility study suggests little gain, summarise the results of process and report back to concerned parties.
Stage 4	Aetiological investigation	

Risk Communication

Investigators of clusters should understand the ways in which individuals respond to stressful situations and react to uncertainties. Investigators should be able to recognise the source of community suspicions and demands. A perceived problem must be resolved responsibly and sympathetically even if no underlying cluster or health problem exists.

Once the investigator has estimated the degree of risk to the community this information should be given to the community – including putting the risk into perspective. Understand the divergence between scientific estimates and community perceptions of risk based on psychological factors such as voluntariness, equity etc. Public health agencies should also be aware of media imperatives.

Additional Information

Skills and knowledge required - understanding of risk perception; functions of media; awareness of legal ramifications.

Scientific skills - how to apply epidemiological or statistical approach and know its limitations; familiar with concept of statistical power; able to conduct environmental sampling; collect, analyse and interpret biological monitoring samples; psychological factors (risk communication etc.).

Organisational requirements – locus of responsibility and control; a process for involving concerned groups and individuals; a set of operating procedures; dedicated resources.

Appendix and Section 4 deal with statistical and epidemiological techniques for investigating clusters.

Protocol 3

Texas Birth Defects Monitoring Division (1999), "Birth Defect Cluster Investigation Protocol", (for full protocol contact peter.langlois@tdh.state.tx.us)

Stage	Action	Outcome
Stage 1 Initial contact and response	Collect initial data on the cluster (type of defect, number of cases, geographical area, time period, usual number of cases), information on each case (name, birth defect, date of delivery, mothers age at delivery, mothers race, mothers address at delivery), any ideas on what caused the cluster, discuss initial impressions, clarify what caller wants, what they want register to do. Get identifying details from caller, ask how they learned of the cluster, give them your name and phone number.	**Criteria to continue to Stage 2:** 2 or more cases of the same BD or multiple birth defects that may be related to an exposure reported in the literature to be a possible teratogen, or there is inadequate information to judge the above criteria, or the informant insists on further evaluation. NB document outcome.
Stage 2 Preliminary evaluation	Determine the case definition (geographic area, time period, birth defect diagnosis). Determine the number of live births in the area and time period specified. Find an appropriate reference rate (use published data if possible). Calculate expected cases, do O/E and assess statistical significance.	**Criteria to continue to Stage 3:** If there is an excess of cases (O/E.1) AND the excess is statistically significant at 5% OR the informant insists on further evaluation (or other circumstances make it seem appropriate). If no further investigations write to the informant giving full details.
Stage 3 Case finding and verification	Identify sources to help ascertain other cases (vital records, CA registries etc.), for each case ascertain name, diagnosis, date of delivery, gestational age, mothers age/place of residence at delivery, mothers race. Verify defects by referral to CA registry or by contacting physician caring for the child, tabulate all verified cases, if necessary form a team to work on cluster. If a specific exposure has been mentioned; review literature for epidemiological and biological plausibility, assess the likelihood that an event-exposure relationship may be established (help from Toxicology and Environmental Epidemiology divisions), determine availability of exposure data in the area of interest. Evaluate the need for environmental monitoring data and gather and analyse data if necessary. Assess community perceptions/ reactions/needs. Re-evaluate the cluster: confirm case definition, re-do O/E (crude and adjusted if necessary eg. for maternal age).	Write a report **Criteria to continue to Stage 4:** The birth defects are the same or the same type, AND there is an excess of cases (O/E>1) which is statistically significant, AND at least 3 cases exist with a biologically plausible exposure in common OR at least 5 cases and an observed rate 10x greater than expected OR other circumstances warrant. **If no further follow-up:** Write to the informant indicating findings, continue to monitor occurrence of that CA in the area, disseminate report to appropriate officials (medical directors, health dept etc.)

Feasibility Study	Consider the appropriate study design with attendant costs and expected outcomes including: geographical area and time period of concern, case finding, appropriateness of using previously identified cases, confirmation of diagnoses, selection of controls. Determine appropriate plan of analysis. Determine methods for environmental exposure measures if needed, delineate the logistics of data collection and processing, consult with experts and advisory committee, assess resource implications, write report summarising feasibility study.	Proceed if Aetiologic investigation warranted. If not write to informant, copy to official/ appropriate parties.
Stage 4 Aetiologic investigation	Protocol develop using feasibility study as a guide.	

Protocol 4

California Birth Defects Monitoring Programme (1999), "Investigating Clusters of Birth Defects: Guidelines for a Systematic Approach",
(http://www.cbdmp.org/pdf/investbdclusters.pdf)

Definition of a Cluster More than the expected number of birth defects cases in a population group for a defined geographical area and a specific period. Characteristics of clusters of birth defects: large excess of the same defect (characteristic pattern of defects), biologically plausible exposure (previous studies suggest risk, timing is in sensitive period, pathway exists for pregnancy exposure).		
Cluster investigation likely to be fruitful if: A biologically plausible exposure among many of the cases, regardless of the rate or an excess of more than 10 times the expected rate.		
Stage	**Action**	**Outcome**
Stage 1 Initial report evaluation	Details of person reporting, birth defects of concern and how it came to reporters notice, CA details: population group, setting, time period, any idea about common cause: characteristics mothers have in common (age rate worksite neighbourhood etc.), with whom concerns have been discussed, whom to contact for more information, index case information for each case (name, address now/at birth, date and hospital of birth, other hospitals of treatment, diagnosis, parental history medical occupational, other family history, other exposure.	**Criteria to contine to stage 2:** At least 3 cases exist with the same or developmentally related birth defects, there is sufficient information to verify the index cases and establish the time period, geographic area and/or population group AND no other immediate explanation is evident.
Stage 2 Index case and exposure verification	Visit hospital of birth and review records (using standard procedures), medical records reviewed by specialists to note relevant information on exposures. Environmental health and infectious disease specialists help verify alleged exposures. Review index case and exposure information exclude case if: residence outside geographic boundaries, initial diagnosis ruled out, malformation is part of underlying condition (eg. Down Syndrome), condition cannot be systematically diagnosed (heart murmur), physical findings do not meet specific diagnostic criteria established by geneticist or specialist.	**Criteria to continue to Stage 3:** At least 3 cases with the same or developmentally related defect, case verification supports evidence of a cluster.

Stage 3 Complete case ascertainment	Revise case definition/broaden diagnostic criteria (eg. if Down Syndrome may then include all trisomies). Examine same sources plus birth, death and foetal death records for additional information. Review by epidemiologists, paediatricians and/or geneticist to confirm compliance with case definition. Calculate observed rate in the population and compare with expected rate for a similar population (if available user prior year rates). Plot cases on a map to look at geographical clustering, look at seasonal or other temporal patterns. Is the apparent increase meaningful? Are there known epidemiological patterns which may provide clues for analysis? Are certain agents suspected of contributing to the defects? What is the vulnerable period in embryological development of this defect?	**Criteria to continue to Stage 4:** Birth defects are the same or developmentally related AND there are at least 3 cases and a biologically plausible exposure OR 5 cases and an observed rate of more than 10 times the expected rate.
Stage 4	Investigation is assigned to a team of epidemiologists who design a study based on current scientific knowledge about the birth defect in question and the alleged exposure.	
Risk communication Community response: answer questions, discuss how and when investigation will proceed, provide realistic explanations about possible outcomes, communicate investigation status regularly, share findings openly, participate in community meetings, work with local health dept, work with media. Also periodic written and verbal updates to person reporting the cluster, public health office and community affected, plus final report by phone and in writing.		

Protocol 5

Washington State Department of Health (2001), "Guidelines for Investigating Clusters of Chronic Disease and Adverse Birth Outcomes"

Cluster investigation likely to be fruitful if: The disease is extremely rare AND the frequency of the disease has suddenly increased		
Stage	**Action**	**Outcome**
Stage 1	Collect initial information and provide education and information to the informant: complete 'new cluster' page (Department of Health intranet): type of illness, number of cases, ages of people affected, time period, location, is there a suspected exposure, have others been contacted about the cluster, organisational affiliation of the caller. Contact local health jurisdiction and others (industry etc), check database for previous cluster of same illness (might be included with this one).	**Criteria to continue to stage 2:** At least 3 cases exist with the same or developmentally related birth defects or a specific exposure of concern (including a potential route of exposure) has been alleged. Once the decision is made then note made in cluster database, contact appropriate officials (Department of Health, health and safety etc.), provide feedback to the caller.
Stage 2 Preliminary assessment	Assess the magnitude of the reported cluster: team from Department of Health assigned to the investigation based on skills, availability etc, local health jurisdiction invited to participate (or take the lead if occupational exposure). Develop case definition, literature review on epidemiology of disease, background rates, common risk factors, confirm cases using readily available data if possible (otherwise assume all real cases), review literature on exposure of concern, calculate preliminary O/E (define geographic and time periods, determine reference population available using pre-existing data).	**Criteria to continue to stage 3:** Disease is of known aetiology and exposure to the causal agent may exist OR the reported exposure has previously been associated with the reported condition, OR the disease is of unknown aetiology and unusual exposures exist in his case, OR the disease is extremely rare.

Stage 3	Verify initial assessment: may expand team membership to include DOH and local health jurisdiction personnel. Cluster team develops a plan for verification of illness and exposure, refine the geographic area and time period of interest, obtain information on all reported cases to verify diagnosis, time of onset and exposure profile, if necessary refine the case definition. Active Case Finding: review additional medical records/databases, determine whether there is an excess using standard analytical methods (O/E, comparison of rates ATSDR Cluster 3.1 or MMWR describes tests), assess exposure (review of data- not environmental sampling at this stage), review literature on other risk factors.	**Criteria to continue to stage 4:** At least 5 cases of the disease, AND an O/E> (number of cases/100) AND the investigation is likely to have a public health impact AND 1) for diseases of known or suspected aetiology: plausible exposure and route of exposure (esp. that latency period is plausible); 2) for diseases of unknown aetiology: unique exposure, plausible route of exposure, weight of evidence from scientific literature should not render the association unlikely. **If no further follow up:** Note in cluster database, email a synopsis to staff involved, notify other parties who have been consulted, provide feedback to caller.
Feasibility study	First check if investigation team needs to be expanded. Then as for CDC guidelines.	Proceed if the team decides If not then summarise findings, send written reports to initial informant and other concerned parties.
Stage 4	Aetiologic investigation: standard epidemiological study	Share results of the investigations, make public health recommendations

Protocol 6

California Department of Health Sciences Environmental Toxicology Branch, "Investigating Non-Infectious Disease Clusters", available on request from Environmental Health Investigations Branch, 1515 Clay Street, Suite 1700, Oakland, CA 94612, Tel: +1 (510) 6224500, Fax: +1 (510) 6224545.

Definition of a cluster: 'A mini epidemic of some condition so rare that even a handful of cases begs an explanation'.		
Stage	**Action**	**Outcome**
Stage 1 Complaint evaluation	Take initial report (standard form appendix c- caller information, place of clusters, statement of problem, type of illness time period, geographical boundaries, callers occupation, case information). NB should be trained personnel, may be able to resolve concerns at this stage. Form initial case definition, collect basic information and evaluate complaint (appendix d has form for collecting information by mail).	**Criteria to continue to Stage 2:** Unusual numbers of rare conditions, presence of biologically plausible exposures or intense community concern (CH7 gives statistics for determining if an excess)
Stage 2 Verifying index case and exposure	First determine who should do case verification, identify records that can be used (hospital, physician, population registries, monitoring data, etc) NB ensure confidentiality, then review records and verify cases	**Criteria to continue to Stage 3:** Two courses of action: 1. case reports not verified: update informant by phone call and letter 2. case reports verified consult with relevant health services dept. eg. BDMP, document investigation and outcome and keep copy of written report.
Stage 3 Full case ascertainment	Establish a case finding team (epidemiology, environmental health, public health), revise case definition (health outcome, time period, geographical area and/or population), develop strategy for case finding, determine exact data to be collected (name date of birth, race, sex, age at diagnosis, diagnosis and source of diagnosis, family history, occupation of parent, employment history, known exposure at work, length of residence at address, past history of residence, other relevant exposures). Then count and summarise cases	**Criteria to continue to Stage 4:** Is there an excess and is it worrisome, if an excess is present is it statistically worthy of further study, is the exposure hypothesis biologically plausible, is the community concerned, are cases increasing over time or continuing in most recent years, are cases more concentrated around suspected environmental sources or in suspected occupational groups 1. End the investigation: (no excess found), inform the community of the investigation findings 2. targeted surveillance, if there is an excess but it is of low significance or biological plausibility 3. special study: if excess is worrisome and both biologically and statistically worthy of further study.

Risk Communication
Basic principles:

- Listen to and acknowledge community concerns
- Be honest in admitting when you don't know the answers
- Be consistent ad reliable in following up
- Involve community members in the process wherever possible
- Provide continuous opportunities for communication between the Department and the community (meeting times, training opportunities, newsletters, speaking engagements).

Also advises taking an inventory of already available resources (community organisations/advisory committees/media relations etc.), analysing the history and development of the area's industrial base vis-à-vis community demographics, identifying community concerns via direct contact with the concerned community, planning convening and following up after meetings and working with the press and media.

Additional information
Ch6: sources of population and health data, Ch7 data analysis and interpretation Ch8 role of local and state health departments (specific to the US system) Ch9 developing a team Ch 10 developing partnerships with the medical community

Protocol 7

Arrundale J, Bain M, Botting B, Brewster D, Cartwright R, Chalmers J, Coggan D, Elliott P, Jackson I, McKinney T, McNally R, Miles DPB, Quinn MJ, Sharp L, Staines A, Stiller C, Wilkinson P (1997), "Handbook and Guide to the Investigation of Clusters of Diseases". Leukaemia Research Fund, 43 Great Ormond Street, London, WC1N 3JJ.

Definition of cluster:
A cluster is an aggregation of cases in terms of disease group, time and space where the number of cases is statistically greater than one would expect when the natural history of the disease and chance fluctuations are taken into account. The majority of clusters are post hoc.

Stage	Action	Outcome
First contact	Log all information about cases, (name, date of birth, diagnosis and origin of diagnosis, address of cases, details of information source)	**Criteria to continue:** If 3 or more of the cases can be verified continue. If only 1 or 2 are verified suspend the investigation and organise follow up surveillance over a pre-specified time period (see Ch 7).
Case confirmation and ascertainment	Ascertain further cases- determine diagnosis and age span of interest, time span in question, geographical area in question.	If data are not available for making the estimate of expected numbers, consider conducting a further study or abandoning the enquiry (depends on feasibility, cost, and justification in terms of the benefits).
Computation of expectation	Give careful consideration to the quality of data available for comparison (to derive 'expected') since if data is deficient will end up with excess of observed cases.	**Criteria to continue:** If no excess, or O>E P>0.1, or O>E 0.05<p<0.1 then either abandon or set up surveillance. Ch 7 gives outline of 'negative' report (risk communication). If statistically significant excess write preliminary report and consult.

Results are unlikely to be due to chance if:

1. the disease in question has consistently been reported to cluster
2. the numbers of excess cases are large (>10) or the probability of excess is very low (<0.001)
3. follow up or surveillance shows the results are consistently high over a later time period, or the same phenomenon has been seen in several places over that time span
4. the hypothesis of occurrence are testable in other areas

Further investigation	Consider the original data (cases, comparison data and census) for veracity and any possible sources of bias. Consider the disease in question and its current known associations, causes and biological bases.	1. Do nothing (write report explaining reasons for line of action) 2. Further descriptive/ecologically based statistical analysis on available data or further readily available data 3. Specific surveillance scheme in original neighbourhood or in wider area (particularly with an equivocal cluster with a small excess of cases or marginally non-significant excess, or occurrence is unexpected, little is known of the aetiology of the condition or there is great local concern).
Stage 4	Set up associated epidemiological studies-investigate the specific environmental issues either from the original report or from other sources (disease registers, analytical studies, environmental investigation).	

Additional information

Ch3: Sources, availability and quality of data in the UK, Ch4: Basic area methods in cluster investigation (statistical tests for calculating an excess incl. SMR, Poisson probability tests). Ch6 Management of an a priori cluster (e.g. from routine surveillance).

Risk Communication

Investigator should have knowledge of the community, experience in dealing with the public, sensitive to needs of public e.g. consultant in public health medicine. Need a written log of events, log and follow up all telephone calls with a letter. Essential to have an open relationship about progress and activities of investigators. Ch 7 covers putting the results into context and how to proceed.

Report writing on a negative investigation

Should explain the thought processes which indicate how far it was possible to get and why. Should contain the calculation of the expected number of cases and the probabilities with respect to the observed events with full explanations.

A typical report to the health authority or the lay public would contain:

Executive summary and recommendations

1. Introduction and background- the events leading to the enquiry
2. The Parameters- decisions about cases and supposed cases (duly anonymised), how the areas and time spans were chosen and why, the source of population and general disease data.
3. The analysis-see ch4 on stats methods
4. Conclusion- why the investigation could go no further and what the results mean
5. Detailed recommendations
6. Glossary of technical terms

Protocol 8

Fiore BJ, Hanrahan LP and Anderson HA (1990), "Public Health Response to Reports of Clusters", American Journal of Epidemiology, Vol 132, Suppl 1.

Stage	Action	Outcome
Stage 1 Circumscribe the cluster	Key elements requested include: disease outcome or diagnosis, vital status of the cases, number of cases, age race and sex, space or geographic location (including addresses of cases), time period, population affected and at risk, suspected cause.	**Criteria to continue to stage 2:** Case specificity (e.g. single Vs multiple diagnoses), age of cases, latency and exposure (for cancer clusters), political pressure or informant insistence.
Stage 2 Case ascertainment	Using routine data sources e.g. death certificates, medical records, hospital discharge survey data, birth certificates (for congenital anomalies).	
Stage 3 Characterise the exposed population	Identify an appropriate reference population (age, race and sex) and associated disease rates.	
Stage 4 Analysis	Standardised mortality ratios, Poisson regression and relative risk ratios.	
Stage 5 Examine potential exposure	Using existing environmental monitoring data or by carrying out environmental testing.	
Stage 6 Assess biological plausibility	By consultation with physicians and toxicologists and literature review.	
Stage 7 Decide to proceed	In consultation with staff epidemiologists and physicians	**Further investigation and (if appropriate) reduction of the putative exposure if:** 1. disease rate is high and there is documented exposure and biological plausibility 2. high disease rate, no determined exposure but biological plausibility that disease may be linked to another exposure 3. no high disease rate, significant environmental exposure and biological plausibility that such exposure may cause a disease excess in the future and 4. high disease rate and documented exposure but no biological plausibility that the disease could be a result of the exposure.
Stage 8 Report results	Further epidemiological study or investigation closed. Report writing and provision of report to the initial informant. A Public meeting may be held to present the study report.	

Protocol 9

Fleming LE, Ducatman AM, Shalat SL (1992), "Disease Clusters in Occupational medicine: A Protocol for their Investigation in the Workplace", American Journal of Industrial Medicine, Vol 22, pp 33-47.

Definition of a cluster: An apparent numerator excess of a certain disease in a retrospectively defined population over a fixed time period and/or space		
Cluster investigation fruitful if: Pursue single disease outbreaks, not unrelated conditions		
Stage	**Action**	**Outcome**
Stage 1 Observation of index cases	Definition of the disease endpoint (case definition criteria include histopathology, lab, and/or symptomology, and appropriate latency assumptions). Ascertainment and verification of cases by consistently applying the case definition, and scrutiny of the workforce to identify any additional cases	**Criteria to continue further:** 2/3 cases of a very rare disease or a common disease but in an unusual population, or for common or chronic diseases if a clear epidemiological excess, public pressure or availability of resources. Otherwise continue surveillance.
Stage 2	Work history of index and discovered cases (job location, known toxic exposure, length of time exposed, total dose, peak exposures, personal risk factors, possible confounders). Industrial hygiene survey (basic demographic factors of the workforce, assessment of plant, historic processes or procedures.	Formation of hypotheses of possible shared exposures.
Stage 3 Establish unexposed comparison/ control groups	Carry out initial study: for acute disease clusters a cross sectional or nested case control study, if chronic a proportionate mortality ratio study or mortality odds ratio study. Gather information on exposed and comparison populations concerning competing risks and potential confounders. Examine the data with and without the index cases, a true cluster aetiologic agent should continue to cause a cluster even in the absence of the index cases. May have to expand the time period to gain more cases, any change in time periods must be explicit and must be aware of Texas sharpshooter.	**Criteria to continue to Stage 4:** Statistically significant excess. If no statistical excess can still leave open mechanisms for further case finding, but cease active investigation. If there is a statistically significant excess of a disease with no previously attributable cause then proceed to further studies.
Stage 4	Review the aetiologic hypothesis and criteria for case and exposure definitions. Follow up studies in comparable populations using Standardised Mortality Ratio studies to establish whether the original cluster was due to chance.	

Additional Information Personnel needed to perform a cluster investigation, necessity for outside consultants.
Risk communication Before starting the investigation should ensure the affected populations should understand the statistical likelihood of any disease occurring, the likelihood that any cluster will be due to chance, the limits of statistical and epidemiological analysis in the context of small population events and the prediction that the end point of the investigation will be at best the generation of a hypothesis not certainties. Early recognition of outcome expectation from the different participants is important. Continue open communication of progress at regular intervals.

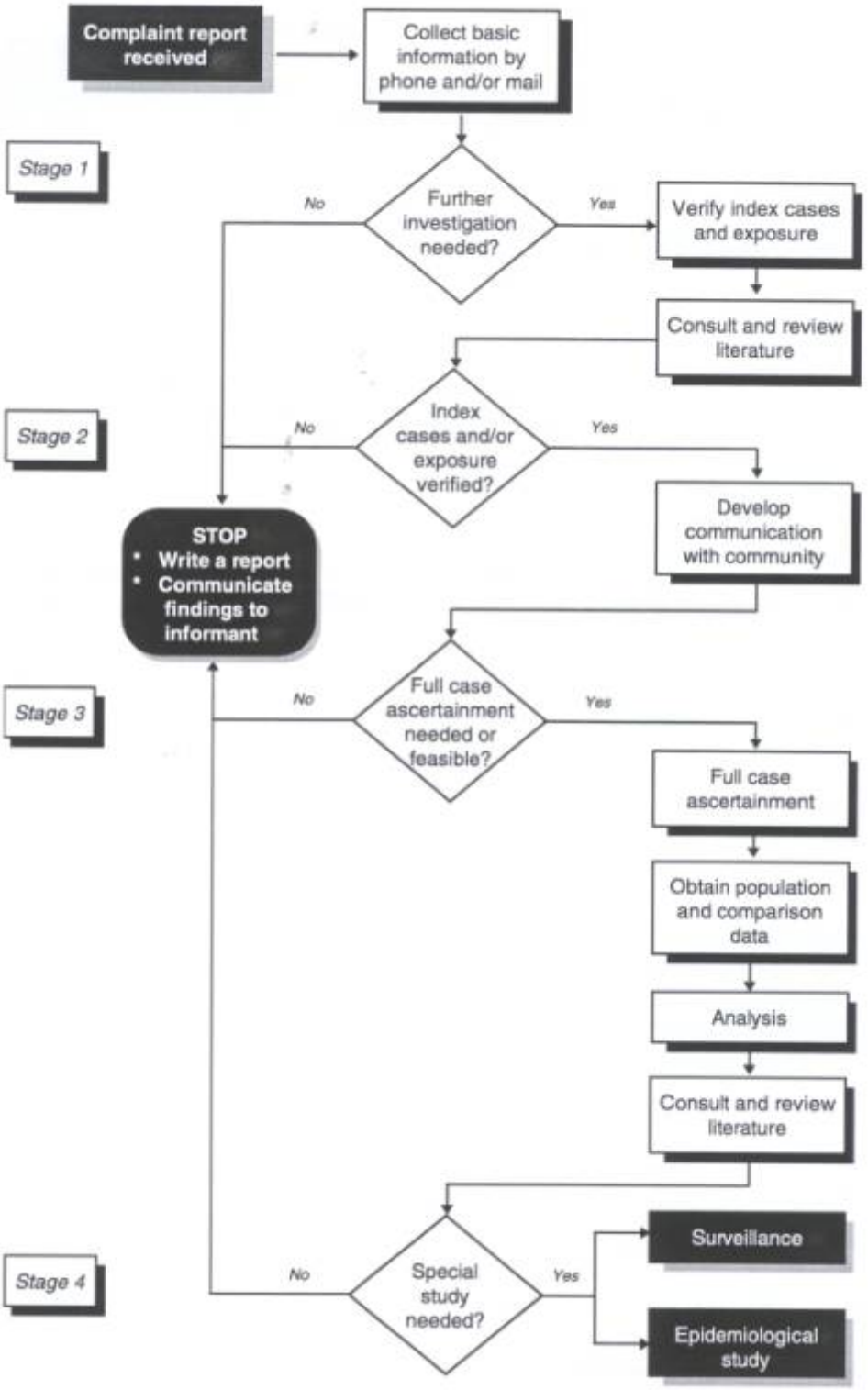
Protocol 10

New Zealand Ministry of Health (1997), "Investigating Clusters of Non-communicable Disease" (http://www.moh.govt.nz/moh.nsf/Files/cluster/$file/cluster.pdf)

Definition of a cluster: An aggregation of some relatively uncommon disease or event: definable health event, usually at least 2 cases, perceived closeness of cases within a time period and/or area defined by the informant, a potential exposure is suspected, the situation is generally unusual or unexpected, the informant or community requests some explanation of the health event		
Cluster likely to be fruitful if: At least 5 cases, a high relative risk (>20), a unique and detectable class of agents has been responsible for the disease in the past, the pathophysiological mechanism for the disease is well understood, the agent persists in the environment and can be measured there, the agents persist or leave measurable response in the individual, exposure is heterogeneous in the community, accurate self exposure is possible by questionnaire or can be obtained from records, a multi-community study with both exposed and unexposed is feasible, the cluster is an un-investigated endemic (e.g. cluster is a stable persistent problem).		
Stage (Fig 1)	**Action**	**Outcome**
Stage 1 Preliminary evaluation	Record the initial report (standard form - asks background details of informant, nature of problem, basic information about index case)	Tell the informant what will be done and how long it will take.
	Form initial case definition based on: specific disease, location, time, background of cases, specific exposures.	Follow up with the informant (e.g. may stop here with just explanation etc), then consult and review information- let the informant know the outcome of the decision. **Criteria to continue to stage 2:** Unusually high number of cases, biologically plausible exposure, and intense community concern. If decide not to continue: write a report, obtain appropriate peer review, and communicate results to the public.
Stage 2 Verification of index case and exposure reports	Establish who should do the verification, review the literature, identify the records that can be used for verification, review the appropriate records and verify case and exposure.	May then end up with no apparent cluster, explained apparent cluster, unexplained apparent cluster. **Criteria to continue to stage 3:** Type of disease and exposure, size of apparent cluster, biological plausibility.

Stage 3 Full case ascertainment	Establish a case finding team, revise the case definition (define health events, time period, and geographical location) develop and implement case finding strategy (NB ethics), count and analyse case data.	**Criteria to continue to stage 4:** Increased need for further study if there is excess cases and: excess is of concern, warrants further study, exposure biologically plausible, sudden increase in cases in a recent period or cases been increasing over time, cases more concentrated around suspected environmental hazards or in suspected occupational groups. **If no further follow up:** Write a report with summary and conclusion, obtain appropriate peer review, and communicate results to public
Stage 4 Surveillance/epidemiological study: surveillance more suitable if excess is of low statistical significance or the exposure has weak biological plausibility. Epidemiological study if there is an excess of cases and there is a biologically plausible connection between the case and some environmental exposure		
Additional information in protocol Standardised cluster report form and data abstraction form		
Risk communication Responding to the community's fears and concerns aroused by a cluster is integral to a cluster investigation. Goal of risk communication is to establish trust and credibility. Successful risk communication involves the mutual understanding and resolution of any conflict between the public's expectation of a cluster investigation and the science of carrying out the analysis within the limits of available knowledge. The public perception of risk is more based on the trust and credibility attributed to the source of information than to the scientific data about risk. Scientific reports can create confusion, dissatisfaction and a demand for continuing investigation. Reports of cluster investigations should contain clear unambiguous messages, use plain language, avoid jargon and reflect the perspective, technical capacity and concerns of the public. Principles of risk communication cited (from Sandman, 1991).		

Figure 1: Overview of the cluster investigation process



Local environmental health concerns

Marjon Drijver, MD, MSc
Health Council / Public Health Service, the Netherlands
PO Box 16052, 2500 BB The Hague, the Netherlands; e-mail: marjon.drijver@gr.nl

Introduction

Concerned citizens are increasingly contacting local authorities to ask whether seemingly unusually large numbers of similar health complaints or disorders in their neighbourhood ('disease clusters') may be related to exposure to local environmental factors (van Poll, 2001). The President of the Health Council of the Netherlands consequently instructed an *ad hoc* Health Council Committee to produce an advisory report on epidemiological research methods in response to public concerns about local environmental health issues and aspects of risk perception and risk communication[a].

The Committee detailed its task as follows (Health Council, 2001):

1 Compile and evaluate the possibilities and limitations of risk communication in situations of local environmental health concerns, with attention to the differences in risk perceptions of the parties involved.
2 Compile and evaluate the possibilities and limitations of a risk assessment in situations of suspected exposure to local environmental factors.
3 Compile and evaluate the possibilities and limitations of research into possible relations between local environmental factors and disease clusters, as observed by the public.

According to an estimate of the National Institute of Public Health and the Environment (RIVM), two to five percent of the total number of disability adjusted life years in the Dutch population is attributable to environmental pollution (RIVM, 2000). Besides air and noise pollution caused by traffic, factors in the indoor environment make the largest contribution, especially in the form of dampness, radon and passive smoking.

[a] This paper is based on the Executive Summary of the Advisory Report of the Health Council of the Netherlands 'Ongerustheid over lokale milieufactoren; risicocommunicatie, blootstellingsbeoordeling en clusteronderzoek' (www.gr.nl).

The relatively large impact of general risk factors, including demographic and socio-economic characteristics, as well as life style, makes it difficult to determine the direct effect of physical or chemical environmental factors on local differences in the occurrence of diseases or health complaints (Elliott95a). The health status of a neighbourhood or district may for instance depend significantly on the local age distribution.

In view of the natural variation in place and time, a concentration of certain disorders in a particular area may also be based on coincidence (Neutra, 1990). However, it is understandable that people note such a disease cluster and report it, especially if they are concerned about the quality of the local environment.

Concern about health effects of exposure to local environmental factors may lead people to experience, notice and report health problems, particularly non-specific health complaints, such as headaches, dizziness and tiredness. This is apparent from various studies on the prevalence of such health complaints attributed to environmental pollution, such as waste dumps, air pollution and electromagnetic fields (Neutra, 1991). Sensory observations, such as odour and noise nuisance may play a role in this (Ursin, 1997). It is striking that many complaint patterns display similarities, regardless of the differences in exposure to hazardous agents (Spurgeon, 1996, 1997). If a somatic cause cannot be found, the complaints are categorised as 'medically unexplained' (Barsky, 1999). Such physical complaints do not arise directly from the exposure but indirectly through uncertainty and concern. They occur often if residents experience a lack of control of the situation or if they have no trust in the authorities concerned (MacGregor, 1996). This process of chronic stress, symptom perception and attribution may be reinforced by authorities or health care workers playing down health problems or by the media magnifying them (Frost, 1997). The Committee believes that insight into and the recognition and acceptance of the effect of stress factors on health could prevent a (further) increase in medically unexplained complaints in stressful situations.

Risk perception and risk communication

When assessing the risks, experts place the emphasis on quantitative data, whereas citizens are much more likely to base their opinions on qualitative aspects, such as the nature and origin of the contamination to which they consider to be exposed, usually involuntarily (Blake, 1995). For example, when evaluating risks, members of the public take into account considerations such as the lack of familiarity with or lack of control over the pollution or its source. They also take into consideration the uncertainty about the possible health risks, the credibility of the source of the information and the level of trust in the executive or supervisory bodies.

The discrepancies between the public's opinion about the risk and that of the risk assessors or the authorities can create a great deal of tension. The government cannot therefore do with scientific explanations of the risks but must also pay particular attention to the risk perception of all parties involved.

In the case of local environmental health problems, the Committee believes early risk communication is extremely important, in the sense of an exchange of information and opinions between the authorities, the public and the other parties involved about the nature and extent of the risk. Proper risk communication can help ensure that those involved are able to form a considered opinion about any risks posed by local environmental factors and can help create greater understanding and trust between the parties. In this respect, the Committee believes the involvement of local residents is a precondition for an effective policy to address a local environmental health problem. If notified in good time about research results, for example, the media can play a positive role in this area too. The Committee believes that guidelines for risk communication and citizen participation may be useful in the approach to local environmental health problems, although hardly any research has been conducted into the efficacy of such guidelines. Risk communication and public participation are not only important in making a hazardous situation controllable. There must also be sufficient opportunity for an anticipatory policy on environmental health. This could lay the foundations for a better relationship based on trust between the authorities and the public, which could possibly prevent unjustified concerns arising.

Exposure assessment

The most suitable instrument for evaluating possible health effects of exposure to environmental factors is a risk assessment (Health Council, 1996). An important feature of risk assessment is the comparison between the degree of exposure and health-based recommended exposure limits.

In the case of local environmental health problems, estimating external exposure by determining the concentrations in water, air, soil or crops will generally suffice. The Committee believes that a determination of internal exposure (body burden) will only be necessary in exceptional cases and only if certain conditions are met. The possible advantages of this, such as reducing the uncertainty or concern about any effects on health have to be weighed against the disadvantages, such as difficulties with interpreting individual measurement results.

On the basis of an exposure and risk assessment it can be determined whether the exposure exceeds relevant health-based limits and whether measures or advice on behaviour are necessary to reduce the health risks.

The transparency of the entire process is important, as an exposure and risk assessment can be fairly complex. As far as possible, the perspective and knowledge of those concerned must be taken into account.

Cluster investigation

In the Netherlands questions from the public about disease clusters that are attributed to environmental exposures by those reporting them are often addressed to the Municipal Health Service. The Committee is in favour of the stepwise approach the Municipal Health Services take to disease clusters (Drijver, 1992). This approach is now widely supported and distinguishes between 3 phases (orientation, verification and quantification) and 3 tracks (the health, environmental and relationship track); see Appendix. In a survey among Municipal Health Services of how they dealt with suspected disease clusters in the years 1993 to 1997, it emerged that already in the (qualitative) verification phase the number of health problems in the potentially exposed population was found not to differ from what would be expected on the basis of global population characteristics (van Poll, 2001).

If the verification phase of a cluster study does support the suspicion that a disease cluster exists, it is advisable to use the data from existing health registries to investigate the degree to which the number of disease cases has increased. The Committee's preferred practice for adoption by the Municipal Health Service is the calculation of standardised morbidity ratios for the area concerned, rather than the use of advanced cluster analysis methods, the most of which are too complex for decentralised use.

Little significance can be attached to the results of statistical testing, performed after the cluster has been noticed (Elliott, 1995b). The reason for this is that testing afterwards does not meet the fundamental condition for the validity of a statistical test, as no real random sample has been taken. Moreover, the delineation in terms of place and time is only made afterwards.

If more health problems are found than were expected, it is worthwhile considering a study of the occurrence of the disorder in earlier periods or in other areas with a comparable level of exposure. The delineation in terms of place and time can then be chosen in advance, on the basis of the exposure, in order to avoid bias of the results. The Committee believes that any such supra-regional study, which may also use advanced techniques, should be conducted by or in co-operation with organisations with expertise in spatial statistics and cluster analysis.

Further epidemiological research

If a disease cluster has been shown to exist ánd if a proper exposure assessment makes it plausible that the local environmental exposure is or has been sufficiently high to cause health effects, further etiological epidemiological research may be considered. Research of this kind, in which health data and exposure data are collected at the individual level, is intended to determine a possible link between personal exposure to environmental pollution and particular health effects. As a rule, this is only worthwhile if the study will be conducted under strict conditions; especially the number of cases has to be sufficiently high (Neutra, 1990). If the conditions are not met, the disadvantages may outweigh the benefits, especially if the research is combined with blood and urine analysis. It is therefore essential to discuss beforehand with those concerned about the possibilities and limitations of the investigation, in order to avoid creating expectations that cannot be met.

Recommendations

The Committee has defined the following aspects as important elements in any pragmatic approach of local environmental health problems by public bodies:

- take worries about exposure to local environmental factors seriously
- pay attention at an early stage to risk communication and public participation
- perform a systematic and transparent exposure assessment
- consider exposure reducing measures in case of any nuisance or undesirable exposure
- pay attention to any possible somatic consequences of stress
- follow a stepwise approach to environment-related disease clusters
- take into account coincidence as an explanation of detected disease clusters
- be critical when conducting descriptive epidemiological studies
- explain under which conditions a further epidemiological study would be advisable
- involve communication specialists in epidemiological studies.

The Committee recommends that the government supports citizen groups and environmental organisations in the publication of a 'citizen's guide' to risk, risk communication and participation. Some guidelines were recently drafted in the Netherlands for resident participation in soil remediation operations and health issues relating to specific local environmental problems. The Committee also recommends that Municipal Health Services draw up more guidelines on dealing with concerns about the possible health effects of local environmental factors.

Another condition for a proper approach to local environmental health problems is adequate expertise and time for risk communication. The Committee believes more attention should be paid to communication and participation in environmental health, before questions and complaints arise.

With regard to the undeniable existence of knowledge gaps, the Committee believes that more detailed information is required about the effectiveness of guidelines in risk communication. The Committee also calls for more research into the degree to which and the way in which psychosocial factors affect the experience and reporting of health complaints, especially with regard to hazards that are believed to exist in the local environment.

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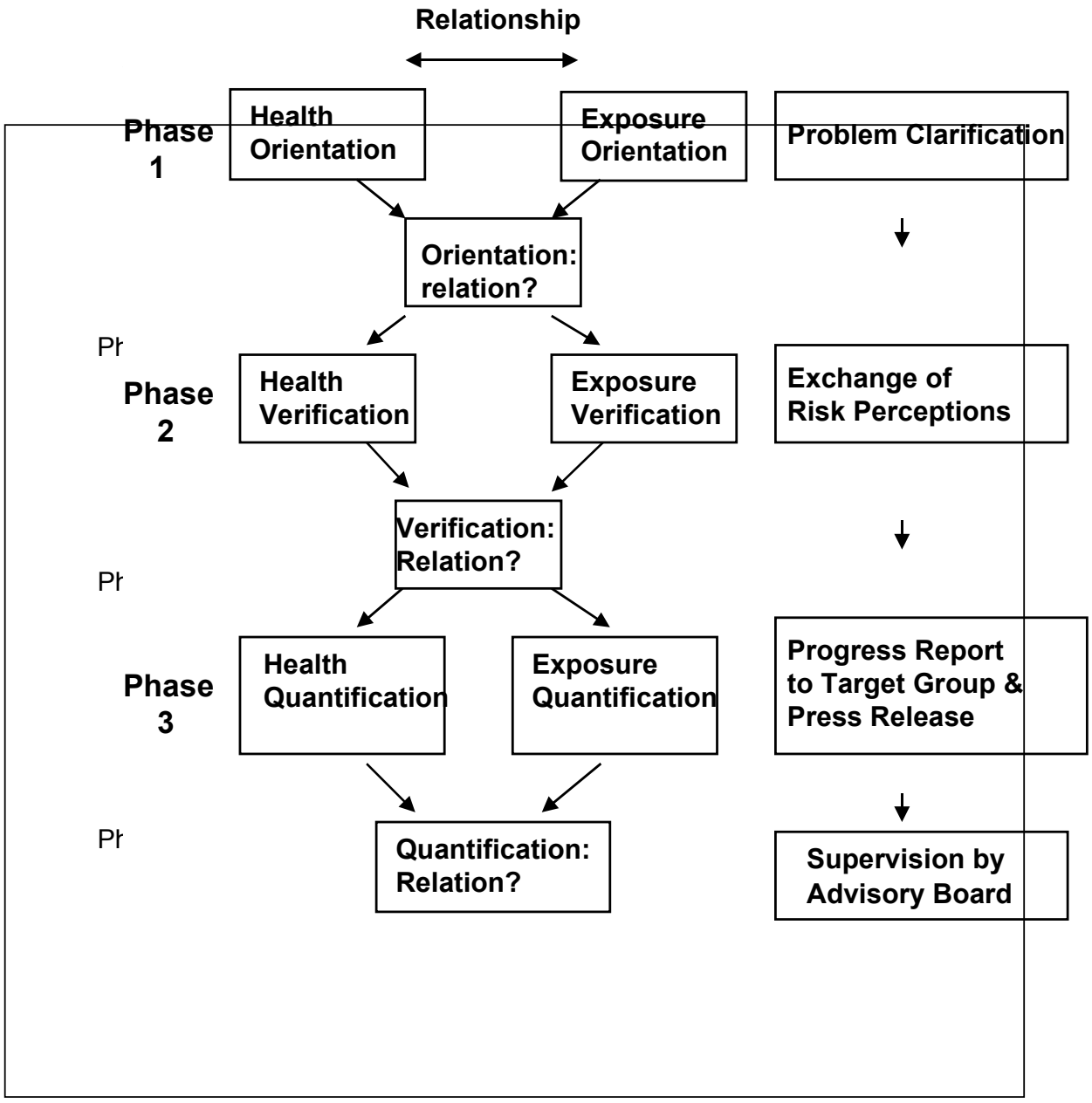
Health Track
Environmental Track
Communication Track
Relationship
Phase 1
Health Orientation
Exposure Orientation
Problem Clarification
Orientation: relation?
Phase 2
Health Verification
Exposure Verification
Exchange of Risk Perceptions
Verification: Relation?
Phase 3
Health Quantification
Exposure Quantification
Progress Report to Target Group & Press Release
Quantification: Relation?
Supervision by Advisory Board