British Isles Network of Congenital Anomaly Registers

BINOCAR Standard Operating Procedure for Clusters

Instructions for the Registration and Surveillance of Congenital Anomalies in England and Wales

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Introduction

One of the objectives of congenital anomaly registration is to detect, and to respond to the detection of, potential clusters and/or teratogenic exposures within their defined population.

Most registers belonging to the BINOCAR have had the experience that clusters of congenital anomalies detected in their routine surveillance or by others (health services or the 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 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.

Currently, statistical monitoring is conducted by both BINOCAR and the EUROCAT Cluster Advisory Service to detect changes in time within each register. Statistical methods have been chosen which are relatively straightforward for public health bodies to understand and communicate.

All registries able to meet the annual February data transmission deadline to EUROCAT participate in cluster detection monitoring by BINOCAR and EUROCAT.

What is a Cluster?

There are many different definitions of a cluster. EUROCAT has adopted the following definition of a cluster:

'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 definition of space employed in this 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.

Classification of Cluster Types

We consider four situations where different investigative strategies apply:

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

Stages of Investigation

A preliminary evaluation to provide a quick rough estimate of the likelihood that an important excess of cases has occurred by identifying:

i. How many cases are in the cluster?
   - Taking into account appropriate geographical and time boundaries and the types of anomalies to be included

ii. How many cases would be expected, on average?
   - Ideally by applying an appropriate reference rate.

1. **Case evaluation** to verify diagnosis.

2. **Occurrence evaluation** to ensure all relevant cases have been recorded.

Clusters identified locally should be investigated in the same way as those identified by central monitoring (see below – guidelines for the preliminary investigation of clusters), and reported to BINOCAR.

Following preliminary investigations, plausible clusters not resulting from data quality errors can be reported to BINOCAR and, if appropriate, to EUROCAT for communication to all local registries for further investigation (i.e. are similar clusters occurring elsewhere?). In this way, the situation across the UK and Europe may be monitored for early detection of possible new teratogens.

Support with the investigation of clusters can be accessed through BINOCAR and through EUROCAT. The link below will take you to the EUROCAT website where you can access the statistical monitoring protocols and publications

http://www.eurocat-network.eu/clustersandtrends/statisticalmonitoring

Statistical Monitoring

Statistical monitoring is essentially a screening method to scrutinise data regularly and systematically to detect any previously unrecognised increases in frequency of congenital anomalies which may be associated with exposure to teratogenic drugs or environmental chemical pollutants. An annual Statistical Monitoring Report is published detailing the cluster and trends detected by statistical monitoring conducted at EUROCAT Central Registry and the methodology used. The annual report also includes the results of the preliminary investigations into the identified clusters and trends carried out by local registries. It is the responsibility of the local registries to report any concerns to local public health authorities.

Guidelines for the preliminary investigation of clusters

Each year, clusters are divided into “new” clusters, “continuing” clusters and “old” clusters. New clusters are those which have not been detected previously. Continuing clusters are those which were detected the previous year but have continued in time. These are particularly important to investigate. Old clusters are those which were detected and investigated the previous year, but have not continued.

BINOCAR and EUROCAT alert registers to new and continuing clusters. Registers must make sure that they look at the full 5-year timeline for the congenital anomaly subgroup of interest, as this shows the time distribution of all cases.

Register staff have access to detailed guidelines on conducting preliminary investigation of clusters, including a template for recording and presenting findings (Appendix A) and the EUROCAT protocol which can be downloaded using the link below.

http://www.eurocat-network.eu/clustersandtrends/statisticalmonitoring

The investigations include:

• **Case verification**
Confirmed and accurate diagnoses; identification of duplicates; confirmed cases by residence.
• **Diagnostic dimension**
Heterogeneous diagnoses; isolated anomalies or part of syndrome; family histories; associated clusters
• **Space dimension**
Geographically close residents; single hospital/ NHS trust; other UK clusters (ask BINOCAR)
• **Time dimension**
Is this cluster art of trend? If so investigate as trend not cluster; start and end; create timeline of cases; check by data of conception as well as date of birth
• **Diagnostic & reporting factors**
Changes in diagnosis, training, personnel, reporting methods; does registry have comparatively low rate prior to cluster (comparison with other registries via BINOCAR)
• **Aetiological factors**
Which factors have been investigated?
• **Local context**
Was there a prior awareness of cluster? Are there any local environmental concerns

If the investigation of clusters identifies data errors (e.g. incorrect diagnoses, incorrect dates of birth) these errors should be corrected and updated data included in the next data transmission to EUROCAT. A record of these errors should be included in the local cluster reports sent to BINOCAR and EUROCAT.

If during the preliminary investigation, or subsequently, the appearance of a cluster is 'explained' or found to be artefact, then that explanation should be documented in the report and it should be made clear whether there will be a following period of close surveillance or a return to statistical monitoring.

If the cluster is to be investigated further then there should be clear documentation of that investigation, including a record of health authorities notified. Both BINOCAR and EUROCAT should be informed so that other registries can be alert to the occurrence of similar clusters.

Appendix A

Reporting the results of investigations

The following template has been designed to assist registers with initial investigations into clusters.

Methods and results of case verification
Dimensions Diagnostic dimension: Spatial dimension: Time dimension:
Methods and results of any investigations as to whether changes in diagnostic or reporting practices might have contributed to the cluster.
Aetiological factors examined and result. Please include the following information: • **Which factors have been investigated?** • **Which of these factors are recorded within the registry database (please list variables)?** • **Which of these factors are NOT recorded within the registry database (please list variables)?** **Do any of these appear to explain the cluster?**
Local context
Conclusion: **Do you consider the cluster 'explained' by your preliminary investigation? Yes/No.** **If yes, give a summary of your explanation.** **If no,** **-Does the cluster require a further period of surveillance before a decision is made to investigate further? Why?** **OR** **-Is there going to be further aetiological/other investigation? Please give details.**
Which public health authorities have been or will be notified about this cluster? Please give details.

Has your registry used the EDMP statistical monitoring function in the last year to look for clusters or trends in more recent data, or for different anomaly subgroups, or any other purpose? Yes/No.

If yes, please give details.

If no, can you please tell us why you do not use the EDMP statistical monitoring program.

N.B. A summary of local monitoring will be included in the next Annual Statistical Monitoring Report.

In last year's statistical monitoring which used 2008-2012 data we detected a new cluster in subgroup **A**. We would be interested to know what the Public Health Authority response was to this.

*Please note time period