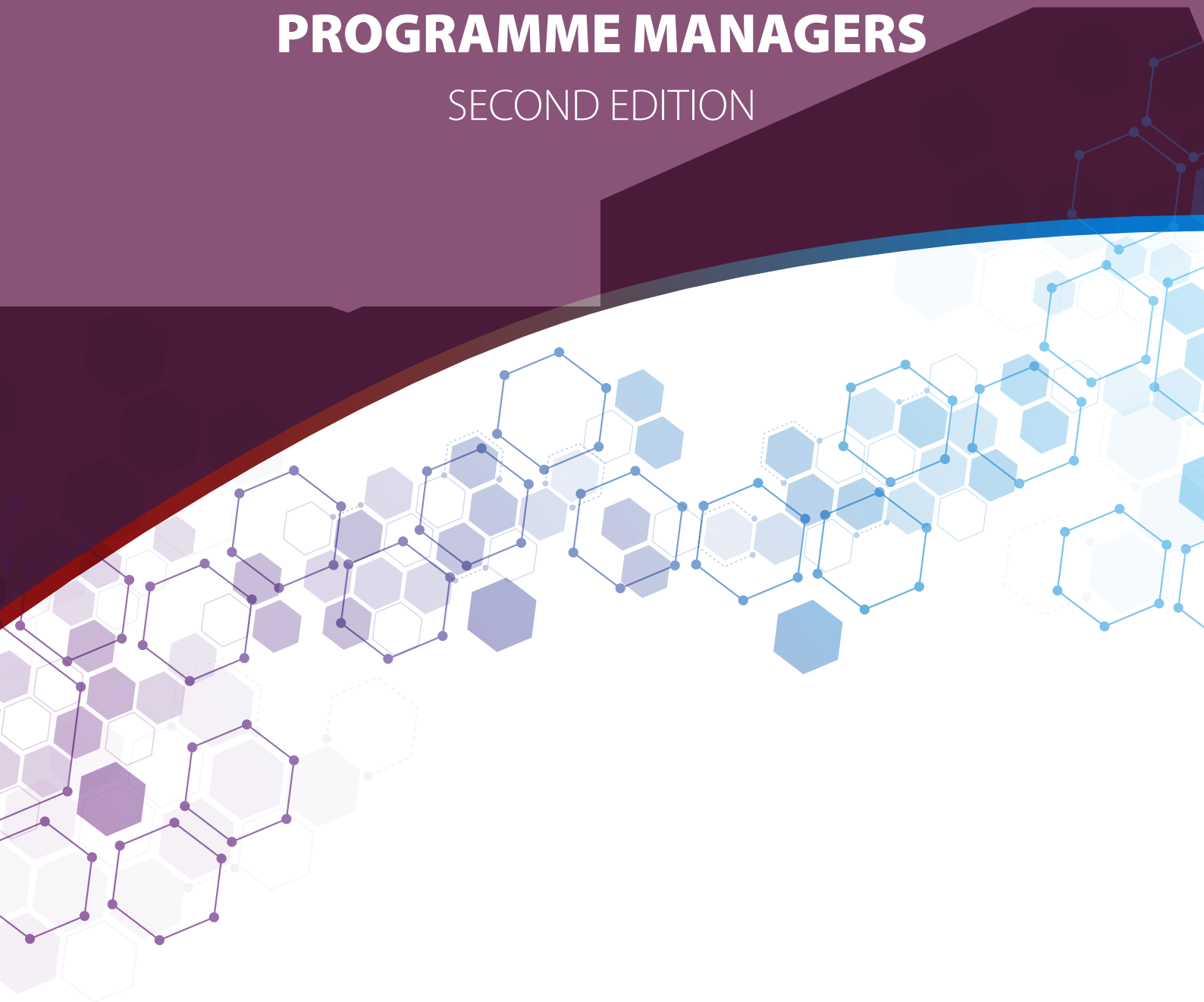
# BIRTH DEFECTS SURVEILLANCE

## A MANUAL FOR PROGRAMME MANAGERS

SECOND EDITION



World Health Organization

CDC

International Clearinghouse for Birth Defects Surveillance and Research

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# Contents

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## Abbreviations

| | |
|---|---|
| **AFP** | alpha fetoprotein |
| **ASD** | atrial septal defect |
| **cCMV** | congenital cytomegalovirus |
| **CDC** | United States Centers for Disease Control and Prevention |
| **CHARGE** | **c**oloboma, **h**eart defects, choanal **a**tresia, growth **r**etardation, **g**enital abnormalities, **e**ar abnormalities |
| **CHD** | congenital heart defect |
| **CLIA** | chemiluminescence immunoassay |
| **CMV** | cytomegalovirus |
| **CNS** | central nervous system |
| **CRI** | congenital rubella infection |
| **CRS** | congenital rubella syndrome |
| **CSF** | cerebrospinal fluid |
| **CT** | computed tomography |
| **CVS** | chorionic villus sampling |
| **CZS** | congenital Zika syndrome |
| **DORV** | double outlet right ventricle |
| **DQI** | data quality indicator |
| **d-TGA** | D(dextro)-transposition of the great arteries |
| **ECLAMC** | Latin American Collaborative Study of Congenital Malformations |
| **EIA** | enzyme immunoassay |
| **ELISA** | enzyme-linked immunosorbent assay |
| **ETOP** | elective terminations of pregnancy |
| **ETOPFA** | elective termination of pregnancy for fetal anomaly |
| **EUROCAT** | European Network of Population-Based Registries for the Epidemiological Surveillance of Congenital Anomalies |
| **HC** | head circumference |
| **HLHS** | hypoplastic left heart syndrome |
| **IAA** | interrupted aortic arch |

| | |
|---|---|
| **ICBDSR** | International Clearinghouse for Birth Defects Surveillance and Research |
| **ICD-9** | *International Statistical Classification of Diseases and Related Health Problems, Ninth revision* |
| **ICD-10** | *International Statistical Classification of Diseases and Related Health Problems, Tenth revision* |
| **Ig(G/M)** | immunoglobulin G/immunoglobulin M |
| **LMIC** | low- and middle-income country |
| **MCA** | multiple congenital anomalies |
| **MRI** | magnetic resonance imaging |
| **MURCS** | **mu**llerian, **r**enal, **c**ervicothoracic, **s**omite association |
| **NAATs** | nucleic acid amplification tests |
| **NBDPN** | National Birth Defects Prevention Network |
| **NCBDDD** | National Center on Birth Defects and Developmental Disabilities |
| **NOS** | not otherwise specified |
| **NTD** | neural tube defect |
| **OAV(S)** | **o**culo-**a**uriculo-**v**ertebral (**s**pectrum) |
| **OEIS** | **o**mphalocele, **e**xstrophy of the cloaca, **i**mperforate anus, **s**pinal defects |
| **PRNT** | plaque reduction neutralization test |
| **RCPCH** | Royal College of Paediatrics and Child Health |
| **RENAC** | National Network of Congenital Anomalies of Argentina |
| **RPR** | rapid plasma regain |
| **RT-PCR** | reverse transcriptase polymerase chain reaction |
| **SOP** | standard operating procedure |
| **TAR** | thrombocytopenia absent radius |
| **TEF (also TOF)** | tracheo-oesophageal fistula |
| **TEV** | talipes equinovarus |
| **TPHA** | Treponema pallidum hemagglutination assay |
| **TPPA** | Treponema pallidum particle agglutination assay |
| **USA** | United States of America |
| **VACTERL** | **v**ertebral, **a**nus, **c**ardiac, **t**rachea, o**e**sophagus, **r**enal, **l**imb |
| **VDRL** | Venereal Disease Research Laboratory |
| **WHO** | World Health Organization |
| **ZIKV** | Zika virus |

## Objectives of the manual

Congenital anomalies, also known as birth defects, are structural or functional abnormalities, including metabolic disorders, which are present at birth. Congenital anomalies are a diverse group of disorders of prenatal origin, which can be caused by single-gene defects, chromosomal disorders, multifactorial inheritance, environmental teratogens or micronutrient malnutrition.

This manual is intended to serve as a tool for the development, implementation and ongoing improvement of a congenital anomalies surveillance programme, particularly for countries with limited resources. The focus of the manual is on population-based and hospital-based surveillance programmes. Some countries might not find it feasible to begin with the development of a population-based programme. Therefore, the manual covers the methodology needed for the development of both population-based and hospital-based surveillance programmes. Further, although many births in predominantly low- and middle-income countries (LMICs) occur outside of hospitals, some countries with limited resources might choose to start with a hospital-based surveillance programme and expand it later into one that is population-based. Any country wishing to expand its current hospital-based programme into a population-based programme, or to begin the initial development of a population-based system, should find this manual helpful in reaching its goal.

This manual provides selected examples of congenital anomalies (see Appendix A). These anomalies are severe enough that many would probably be captured during the first few days following birth. While a number of the anomalies listed are external and easily identified by physical exam, others are internal and typically require more advanced diagnostic evaluations such as imaging. However, because of their severity and frequency, all these selected conditions have significant public health impact, and for some there is a potential for primary prevention. Nevertheless, these are just suggestions; countries might choose to monitor a subset of these conditions or add other congenital anomalies to meet their needs. In particular, this manual will help the reader to:

- describe the purpose and importance of public health surveillance of congenital anomalies;
- describe the use of logic models for planning and evaluation of a surveillance programme;
- understand how to present data to policy-makers;
- identify an initial list of congenital anomalies to consider for monitoring;
- describe the tools needed to ascertain and code identified cases;
- describe the processes for managing and analysing data; and
- understand how to calculate the prevalence of congenital anomalies.

Surveillance of congenital anomalies should be ongoing and should involve a systematic review of birth outcomes to determine the presence of congenital anomalies. If countries have the capacity to collect information on known risk factors associated with congenital anomalies – such as maternal exposures (e.g. use of medications during the first trimester) – these could be included in a surveillance programme. Alternatively, a pregnancy registry or a case–control study might be implemented to allow for the collection of exposure data during pregnancy.

This manual is intended to facilitate the collection of essential information for the purpose of assessing and tracking the burden of congenital anomalies. It must be noted that the manual does not present specific information on how to collect risk factor information or how to manage a neonate born with congenital anomalies.

# 1. Surveillance of congenital anomalies

## Introduction

Congenital anomalies are defined as abnormalities of body structure or function that are present at birth and are of prenatal origin *(1)*. Synonymous terms that are often used are "birth defects", "congenital abnormalities" and "congenital malformations", although the latter has a more specific meaning. For the purposes of this manual, the term "congenital anomalies" will be used throughout.

According to WHO, in 2010 an estimated 270 000 deaths globally were attributable to congenital anomalies during the first 28 days of life, with neural tube defects (NTDs) being one of the most serious and most common of these anomalies. In an effort to decrease the number of congenital anomalies worldwide, the Sixty-third World Health Assembly adopted a *Birth defects* resolution. Among other objectives, this resolution encourages countries to build in-country capacity related to the prevention of congenital anomalies and raising awareness about their effects *(2)*. Through the development of a population-based surveillance programme that accurately captures congenital anomalies, countries can better understand the burden of these conditions, become more aware of the risks involved, refer identified infants to services in a timely manner, and use prevalence estimates to evaluate any current prevention or clinical management programmes. Countries can also use the information gathered to inform stakeholders and policy-makers about the importance of investing in programmes aimed at reducing the occurrence of congenital anomalies, and to help them plan for appropriate services.

## The purpose of congenital anomalies surveillance

Public health surveillance is defined as the ongoing systematic collection, analysis and interpretation of health data for public health purposes, and the timely dissemination of public health information for assessment and public health response to reduce morbidity and mortality *(3, 4)*. Surveillance allows for the planning, implementation and evaluation of health strategies, and the integration of data into the decision-making process to help prevent adverse health conditions.

The ultimate purpose of a surveillance programme is to prevent adverse health conditions and their complications. Surveillance data, once collected, are critical for determination of whether a programme is having any effect, evaluation of whether new strategies are necessary, as well as detection of problem areas and intended populations that require more intensive intervention and follow-up.

The objectives of a surveillance programme for congenital anomalies are to:

- monitor trends in the prevalence of different types of congenital anomalies among a defined population;
- detect clusters of congenital anomalies (outbreaks);
- refer affected infants to appropriate services in a timely manner;
- disseminate findings and interpretations to appropriate partner organizations and government agencies, in a timely fashion;
- provide a basis for epidemiologic research (including risk factors) and prevention programmes; and
- allow evaluation of prevention programmes.

Surveillance of congenital anomalies has been used for one or more of the following purposes:

- measuring the burden of congenital anomalies and identifying high-risk populations;
- identifying disparities in prevalence and outcomes by factors such as race or ethnicity, maternal age, socioeconomic level or geographic region;
- assessing the effects of prenatal screening and diagnosis and other changes in diagnostic technologies on birth prevalence;

- describing short-term and long-term outcomes of children with congenital anomalies and providing information relevant to long-term management of individuals who are affected by serious congenital anomalies;
- informing public health and health-care policies and programmes and planning for needed services among the affected population(s);
- guiding the planning, implementation and evaluation of programmes to help prevent congenital anomalies *(4)* and minimizing complications and adverse outcomes among those affected by congenital anomalies; and
- assessing any additional risk(s) and the nature of adverse outcomes (including congenital anomalies) for fetuses and infants exposed to medicines during pregnancy, to improve management and to inform national and global public health policies *(5)*.

## Types of surveillance programmes

Surveillance programmes might be population based or hospital/facility based and take an active or passive case ascertainment approach, or a hybrid of the two. More information about types of programmes and case ascertainment can be found in Chapter 3.

Population-based congenital anomalies surveillance programmes capture birth outcomes with congenital anomalies that occur among a population that is resident in a defined geographical area. Hospital- or facility-based congenital anomalies surveillance programmes capture birth outcomes with congenital anomalies that occur in selected facilities. Sentinel congenital anomalies surveillance programmes are generally set up in one or a few facilities/hospitals to obtain rapid estimates of the occurrence of an adverse birth outcome.

## Congenital anomalies: definitions

Congenital anomalies comprise a wide range of abnormalities of body structure or function that are present at birth and are of prenatal origin. For efficiency and practicality, the focus is commonly on major structural anomalies. These are defined as structural changes that have significant medical, social or cosmetic consequences for the affected individual, and typically require medical intervention. Examples include cleft lip and spina bifida. Major structural anomalies are the conditions that account for most of the deaths, morbidity and disability related to congenital anomalies (see Box 1.1 for a list of selected external and internal major congenital anomalies). In contrast, minor congenital anomalies, although more prevalent among the population, are structural changes that pose no significant health problem in the neonatal period and tend to have limited social or cosmetic consequences for the affected individual. Examples include single palmar crease and clinodactyly. Major anomalies are sometimes associated with minor anomalies, which might be objective (e.g. preauricular tags) or more subjective (e.g. low-set ears). Box 1.2 presents selected external minor congenital anomalies frequently captured by different surveillance systems, but only when associated with any of the major anomalies under surveillance. For a more detailed listing of minor anomalies, please refer to Appendix B. Often, surveillance systems will collect information on specific syndromes that are multiple anomalies pathogenetically related due to a single cause – for example, genetic or environmental causes that are known to cause birth defects. Certain syndromes caused by infectious diseases are of special interest in many LMICs. For a detailed listing of selected syndromes of infectious origin that are of public health significance, please refer to Appendix B.

When establishing a new birth defects surveillance programme, the initial anomalies that are included can be limited to structural anomalies that are readily identifiable and easily recognized on physical examination at birth or shortly after birth. The list might vary, depending on the capacity and resources of the health-care system and surveillance programme, but typically includes major external congenital anomalies. Examples include orofacial clefts, NTDs and limb deficiencies. In contrast, detecting the vast majority of internal structural anomalies (e.g. congenital heart defects, intestinal malrotation and unilateral kidney agenesis) requires imaging techniques or other specialized procedures that might not be available consistently. In some cases, internal anomalies have external manifestations that allow the observer to suspect a particular diagnosis, as is the case with the urethral

| Box 1.1. Selected major congenital anomalies | |
|---|---|
| **External** | **Internal** |
| Neural tube defects | Congenital heart defects |
| Anencephaly | Hypoplastic left heart syndrome |
| Craniorachischisis | Common truncus |
| Iniencephaly | Interrupted aortic arch |
| Encephalocele | Transposition of great arteries |
| Spina bifida | Tetralogy of Fallot |
| Microcephaly | Pulmonary valve atresia |
| Microtia/Anotia | Tricuspid valve atresia |
| Orofacial clefts | Esophageal atresia/tracheoesophageal fistula |
| Cleft lip only | Large intestinal atresia/stenosis |
| Cleft palate only | Anorectal atresia/stenosis |
| Cleft lip and palate | Renal agenesis/hypoplasia |
| Exomphalos (omphalocele) | |
| Gastroschisis | |
| Hypospadias | |
| Reduction defects of upper and lower limbs | |
| Talipes equinovarus/club foot | |
| **Chromosomal** | |
| Trisomy 21 (Down syndrome) | |

| Box 1.2. Selected external minor congenital anomalies | |
|---|---|
| Absent nails | Lop ear |
| Accessory tragus | Micrognathia |
| Anterior anus (ectopic anus) | Natal teeth |
| Auricular tag or pit | Overlapping digits |
| Bifid uvula or cleft uvula | Plagiocephaly |
| Branchial tag or pit | Polydactyly type B tag, involves hand and foot |
| Camptodactyly | Preauricular appendage, tag or lobule |
| Cup ear | Redundant neck folds |
| Cutis aplasia (if large, this is a major anomaly) | Rocker-bottom feet |
| Ear lobe crease | Single crease, fifth finger |
| Ear lobe notch | Single transverse palmar crease |
| Ear pit or tag | Single umbilical artery |
| Extra nipples (supernumerary nipples) | Small penis (unless documented as micropenis) |
| Facial asymmetry | Syndactyly involving second and third toes |
| Hydrocele | Tongue-tie (ankyloglossia) |
| Hypoplastic fingernails | Umbilical hernia |
| Hypoplastic toenails | Undescended testicle |
| Iris coloboma | Webbed neck (pterygium colli) |

obstruction sequence. Similar to collecting information on internal defects, collecting information on syndromes often requires gathering data from multiple sources such as laboratory, imaging or genetic testing. Therefore, collecting surveillance data on internal defects and syndromes is typically not recommended when first starting a surveillance programme.

Classification by developmental mechanism or clinical presentation is important in surveillance because the same congenital anomaly might have different etiologies. Furthermore, the distinction might be important both clinically and in etiological studies. Please refer to Appendix C for more information about the causes of congenital anomalies and their classification according to developmental mechanism and clinical presentation.

## 2. Planning activities and tools

Many steps are required before conducting surveillance and collecting data. A logic model can be developed to help plan how a programme will be funded and staffed, identify activities, and specify short- and long-term outputs of the surveillance. The planning process would include identifying the existing rules and regulations pertaining to privacy and confidentiality issues surrounding data collection and reporting, and having a protocol in place that addresses handling of privacy and confidentiality.

### Logic models

One approach that can be helpful when planning, implementing and evaluating a congenital anomalies surveillance programme is the use of logic models. A logic model is a graphic representation of how the surveillance programme will work. Logic models can identify what activities are needed, the order in which they would occur, and how the outcomes are going to be achieved. Most often, logic models will include the following components:

- *Resources*: What resources currently exist? What resources will be required to build or expand a surveillance programme?
- *Activities*: What activities are required for the surveillance programme to function? Keep in mind that there might be more than one intended audience.
- *Outputs*: What are the expected outputs that will result from the activities?
- *Expectations*: What are the short-term, intermediate and long-term expectations (or outcomes) for each programme area?

Logic models can have any shape (i.e. round, linear, columnar or a combination of these), and have any level of detail (i.e. simple, moderate or complex). It is probably best to begin by placing all relevant information into a table format (see Table 2.1) and then developing a logic model based on that information (see Fig. 2.1).

Creating a logic model has benefits. It can help define goals and objectives, as well as foster agreement among stakeholders about roles and responsibilities related to different activities. It can also help to identify gaps or barriers and build connections between activities and results. Please refer to Appendix D for another example of a logic model.

### Partners and funding

The engagement of a wide variety of partners is essential for the development, implementation and maintenance of a surveillance programme. Key partners, funders and stakeholders can be identified and involved during the initial planning stages of the development of a surveillance programme. This can help to ensure that a surveillance programme is implemented and sustained for the long term. Determining what roles and responsibilities are needed can also help identify what kinds of partners would be invited to participate in the initiative.

Examples of possible areas for partner engagement are the development of goals and objectives for the surveillance programme, the development of policy measures and shepherding of measures through appropriate channels, and the identification of funding support for training hospital personnel.

The following are examples of potential partners for consideration when developing or implementing a surveillance programme:

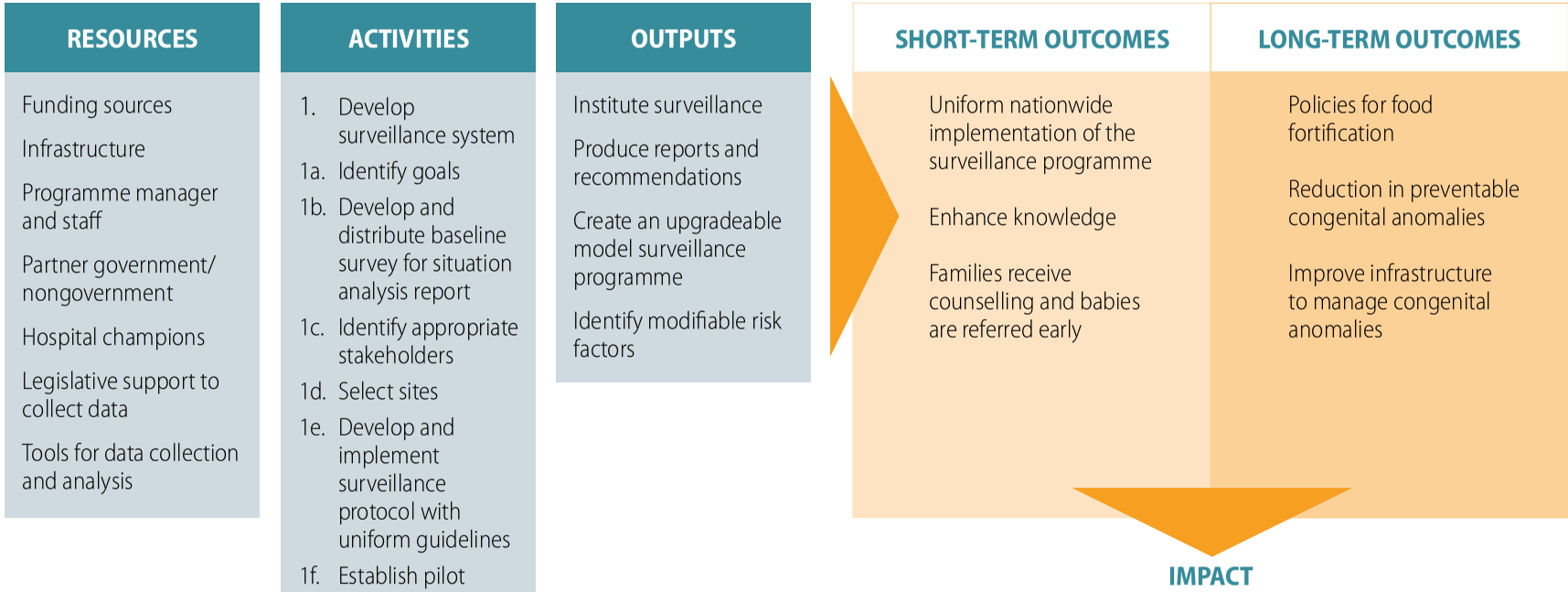
- ministry of health and other government agencies
- environment ministries, toxicology departments, poison control centres and children's environmental health units
- organizations and agencies that regulate hospitals, birthing centres and labour and delivery units
- medical and nursing professional associations

**Table 2.1. Sample information to include in a logic model**

| Resources | Activities | Outputs | Short- and long-term outcomes | Impact |
|---|---|---|---|---|
| Funding sources | 1. Develop surveillance system | Institute surveillance system | Uniform nationwide implementation of the surveillance programme | Improved quality of life for affected individuals |
| Infrastructure | 1a. Identify goals | Produce reports and recommendations | Enhance knowledge | Reduction in mortality in children aged less than 5 years |
| Programme manager and staff | 1b. Develop and distribute baseline survey for situation analysis report | Create an upgradeable model surveillance programme | Develop policies | Reduction in the prevalence of preventable congenital anomalies |
| Partner government/ nongovernment | 1c. Identify appropriate stakeholders | Identify modifiable risk factors | Improve need-based infrastructure to manage congenital anomalies | |
| Hospital champions | 1d. Select sites | | | |
| Legislative support to collect data | 1e. Develop and implement surveillance protocol with uniform guidelines | | | |
| Tools for data collection and analysis | 1f. Establish pilot for surveillance of congenital anomalies<br>1g. Assess data quality and utility<br>2. Engage partners<br>2a. Create task force<br>2b. Advocate<br>3. Evaluate and monitor | | | |

*Source:* adapted from: India team, Regional Workshop on Birth Defects Surveillance; Colombo, Sri Lanka, April 2012.

**Fig. 2.1. Logic model for surveillance of congenital anomalies**




*Source*: adapted from: India team, Regional Workshop on Birth Defects Surveillance; Colombo, Sri Lanka, April 2012.

- health-care providers
- health insurance companies
- universities
- community-based organizations that have an interest in congenital anomalies
- advocacy and community groups
- parent and family support groups for those with children affected by congenital anomalies
- privacy protection and legal ethics offices
- security, data access and information management offices
- researchers
- policy professionals
- media
- religious leaders

Appendix E can help in the development of a list of partners and determination of how partners can best participate and collaborate with the surveillance programme.

## Legislation

### *Mandatory reporting*

How a country defines mandatory reporting, who creates the mandate, and whether or not it is enforced will vary by country. In the United States of America (USA), mandatory reporting for a surveillance programme means that facilities are required to report all cases of congenital anomalies and fetal deaths to the surveillance programme within a determined time frame, and in a standardized format. Structured and reliable data provide a justification for countries to invest in sustainable programmes for prevention of congenital anomalies, and can help in the development of public policy for adequate distribution of resources for infants born with a congenital anomaly. Furthermore, regular reporting in a standardized format can greatly facilitate analyses of prevalence and trends for the congenital anomalies being monitored.

### *Voluntary reporting*

As countries vary in how they define mandatory reporting, so too can they vary in how they define voluntary reporting. Generally, in voluntary reporting, hospital/facility staff members are encouraged by the ministry of health of the country to keep a log and report all cases of congenital anomalies and fetal deaths to the surveillance programme; however, hospitals can choose whether or not to comply. The ministry of health can request that hospitals report cases in a uniform manner, but each hospital can decide whether, how and when they will report the information.

## Privacy and confidentiality issues

Each country has different laws, regulations and protocols for how to protect patient data. It is important to understand the laws or regulations related to the collection, use, dissemination and protection of personal information. Laws can be reviewed, and policies for collection, management and use of data can be implemented prior to initiating a congenital anomalies surveillance programme. Ideally, the authority to operate a surveillance programme will be made explicit by law and its regulations. It is important to have regulations in place to protect the public, as well as the providers and surveillance staff who report the information. During the preparation of the protocol for a congenital anomalies surveillance programme, it is important to specify the purpose of surveillance, the types of data that will be collected and why these are necessary, how they will be collected (paper based, electronically or both), who will have access to the data, how the data will be used, where the data will be stored and secured, and for how long the law requires the data to be archived. Also, it is important to educate hospital personnel on the purpose of the surveillance programme, and how patient privacy and confidentiality will be protected. Lastly, it is essential that surveillance programme personnel sign confidentiality agreements prior to beginning work in the programme.

### *Privacy*

In the matter of personal health information, privacy is an individual's right to control the acquisition, use and disclosure of their identifiable health information. To avoid using personal information, and to protect a family's privacy, each fetus or neonate with a congenital anomaly should be assigned a unique identifier.

### *Confidentiality*

In terms of patient data, confidentiality refers to an individual's right to have their personal, identifiable medical information kept secure. Confidential information must be kept secure according to the regulations in each country, and out of sight of unauthorized people. It is important to note that confidential information can be made available only to specific health-care providers and to specific personnel overseeing the surveillance programme. When sharing the data with others in the country (e.g. hospital managers and policy-makers), all reports are aggregated and do not have any potential patient identifiers (e.g. name or address). If possible, confidentiality agreements are signed on a regular basis, to ensure that personnel are reminded of the importance of this practice.

### *Security*

When dealing with patient information, security refers to the technological and administrative safeguards and practices designed to protect data systems against unwarranted disclosure, modification or destruction. All individuals have the right to have personal, identifiable medical information kept secure. Security, in this context, refers specifically to how personal information is stored, who has access to this information, and with whom this information can be shared.

### *Informed consent*

The processes and requirements related to informed consent vary by country. Because of the public health importance of evaluating and tracking the occurrence of congenital anomalies, most countries do not require informed consent prior to reporting a congenital anomaly diagnosis to a surveillance programme. If the country has a law that requires a consent form, then information might be shared only once this form has been signed. If the law does not require a consent form, parents can be told orally that the non-identifiable information will be shared.

## Data dissemination

One important aspect of the implementation process for a congenital anomalies surveillance programme, other than the collection and analysis of the surveillance data, is to plan in advance the way the information generated will be disseminated. Part of this advance planning involves identification of the processes by which documents (e.g. statistical reports and annual reports) are tailored to the different potential audiences who will be receiving information about the surveillance findings. Potential audiences can include partners, stakeholders, health-care providers and the public. Use of the surveillance data includes:

- identifying trends of congenital anomalies
- planning, implementing and evaluating evidence-informed interventions
- motivating action in the community
- informing policy-makers and government officials
- informing clinical and public health practitioners, nongovernmental organizations and the public
- identifying and referring children with special needs to applicable services

With this information, strategies for improving health outcomes among an intended population can be developed, infrastructure barriers can be identified and remediated, and efforts can be made to gain the support of local and regional partners.

The primary users of surveillance information are usually public health professionals and health-care providers. The information directed primarily to those individuals includes the analysis and interpretation of surveillance results, along with recommendations that stem from the surveillance data. It is important that participating providers and institutions be informed of the situation in their participating facilities or hospitals, as well as

in areas of the health system using the information, so as to assess progress in this type of programme. If possible, a committee might be established, with the participation of technical experts and stakeholders, to facilitate discussion of issues related to security and confidentiality, statistical analyses, presentation and sharing of data, and evaluation of the feasibility and merit of collaborative projects. If data are analysed and presented effectively, decision-makers at all levels will be better able to visualize and understand the implications of the information.

A protocol for communication and dissemination of information can be developed to address the needs of a variety of audiences. This protocol can address questions such as:

- What message is most relevant for a particular audience?
- Is there a timeline for when data will be disseminated?
- What will determine whether the information that was disseminated was useful and whether the objectives were reached?
- Which format and avenue need to be used to reach this audience?

There are different avenues for data dissemination: paper based or electronic, or a combination of the two. By using technology, news releases, letters, brochures, reports and scientific articles can be made available in web format or disseminated using social media outlets. Some examples of ways that data are disseminated can be found in several references *(6–11)*.

## Communicating with parents

It is important to remember that abstractors – those individuals who will be extracting information from hospital logs or medical records for the identification and classification of congenital anomalies – should not give information to parents about a diagnosis or services as these are usually done by a health-care provider. The topic on communicating with parents is included in this manual as a reminder to all programme staff that every identified "case" means that family members might have to cope with the death or disability of a child. Certified health-care providers – those doctors, nurses and midwives who have direct patient care responsibilities and are working as part of the surveillance programme – will benefit from receiving training on how to communicate sensitive information appropriately. Grieving parents might not fully comprehend a complicated diagnosis; therefore, it could be helpful to provide parents with written information about the diagnosis, along with details of available organizations, support groups, bereavement services and genetic counselling services. Please refer to Appendix F for suggestions on how health-care providers can communicate to families information about a diagnosis of a congenital anomaly.

# 3. Approaches to surveillance

This chapter describes some of the different methodological approaches used in the surveillance of congenital anomalies.

## Population coverage

Once the purposes of surveillance have been established, the next steps are to define the population under surveillance and identify the area of coverage. The programme might be population based or facility or hospital based (see Fig. 3.1). The coverage (geographical area) for a population-based surveillance programme can be a city, a region or an entire country. A population-based programme has a defined source population (typically defined by maternal residence), and all identified congenital anomalies occurring within that source population are ascertained and included, regardless of delivery site.

In contrast, the source population for a hospital-based programme typically cannot be defined accurately. The coverage for a hospital-based surveillance programme is usually at least a few hospitals or clinics in one geographic region. However, there generally are no distinct catchment areas for specific hospitals and thus no defined denominator of the entire source population from which all cases are ascertained. Hospital-based programmes work best when they capture most of the population of interest in a geographic region.

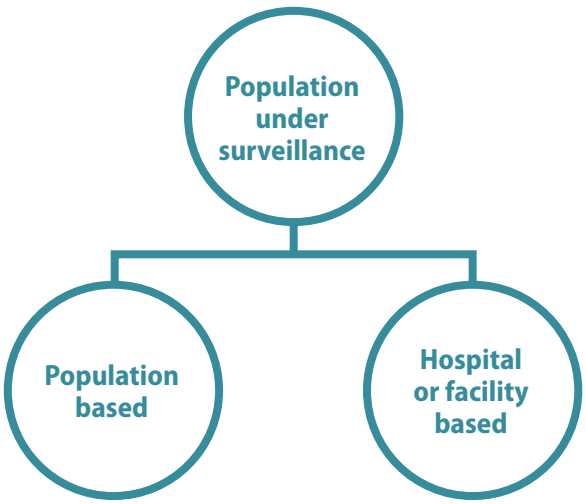
Owing to lack of resources or other restrictions, some countries might not find it feasible to start a surveillance programme as a population-based programme and might therefore choose to begin with the development of a facility-based or hospital-based programme. However, it is critical to understand the limitations of a hospital-based programme, and to interpret any findings from such a system within those limitations.

### *Population-based surveillance programmes*

Population-based congenital anomalies surveillance programmes collect data from an entire source population (fetuses or neonates with a congenital anomaly and the total number of births) born to resident mothers living in a defined catchment area (geographical area), within a defined time period.

Thus, the denominator used to calculate prevalence in a population-based programme consists of births to resident mothers. The corresponding numerator consists of fetuses or neonates with congenital anomalies born to resident mothers. Because of this definition, *all* births are collected in a population-based programme, including not only births occurring in hospitals or maternity hospitals, but also those occurring at home.

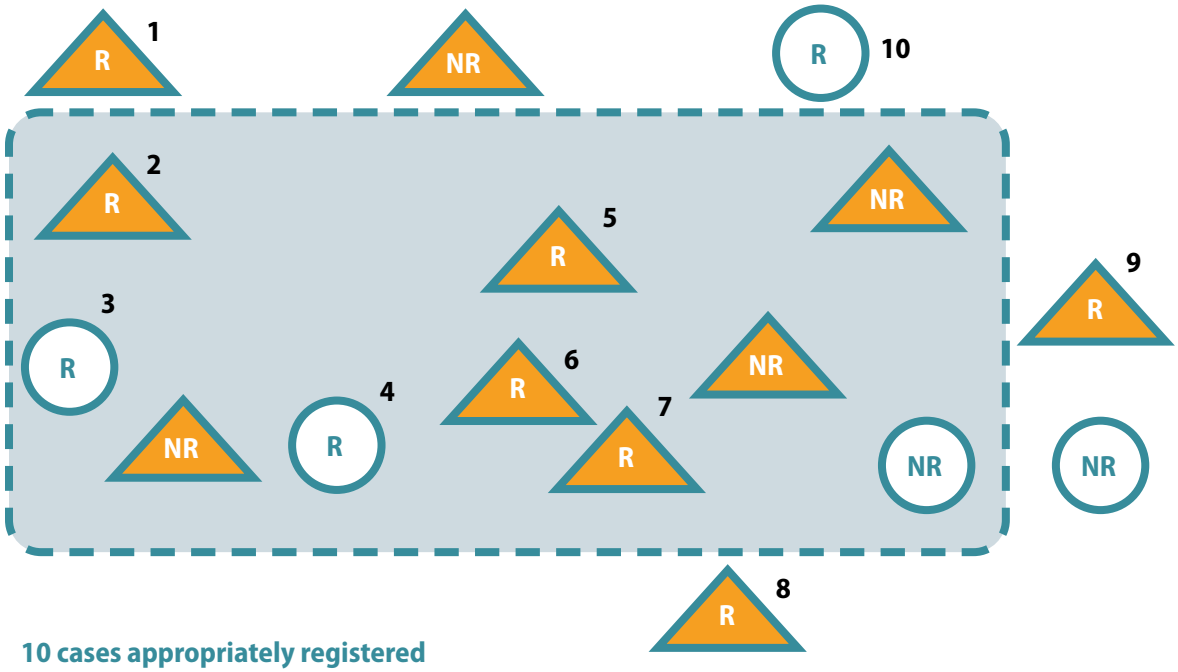
**Fig. 3.1. Population coverage in surveillance programmes**



Most congenital anomalies surveillance programmes use the mother's primary residence at the time of delivery or pregnancy termination to define the source population among which the cases occur. For example, residence can be defined as the mother's primary address during the three months prior to pregnancy and the first trimester of pregnancy. However, the crucial issue is that the definition of resident status used for cases (the numerator) must be the same as that used for all births (the denominator). Fig. 3.2 illustrates an example of a population-based programme. All fetuses or neonates identified with a congenital anomaly born to mothers residing *within* the catchment area (dashed area) are included in the programme (labels 2 through 7 in Fig. 3.2). Similarly, a fetus or neonate with a congenital anomaly that is born outside of the defined catchment area (including one that is born at home while the mother is visiting a family member living outside of the catchment area, for example) would still be included if the mother is herself a resident of the catchment area (labels 1, 8, 9 and 10 in Fig. 3.2). Fetuses or neonates identified with congenital anomalies and born to *non-resident mothers* are not included. Data sources include all health facilities within the catchment area where births occur, vital records (e.g. birth and death registries), referral treatment centres for individuals with congenital anomalies (up to the defined age period for inclusion), administrative databases, and any health-care facility that identifies a fetus or neonate with a congenital anomaly.

The steps for calculating prevalence, and information on how to define the denominator, are described later on in this chapter.

**Fig. 3.2. Catchment area for a population-based surveillance programme**




**R** = fetus or neonate with congenital anomaly whose mother is a resident.
**NR** = fetus or neonate with congenital anomaly whose mother is a non-resident.

### *Hospital-based surveillance programmes*

Hospital-based congenital anomalies surveillance programmes capture all pregnancy outcomes with congenital anomalies that occur in selected hospitals in a defined geographic area (e.g. a state, province or county).

The denominator used to estimate prevalence in a hospital-based programme consists of births occurring in the participating hospitals. The numerator (cases) typically consists of affected live births and stillbirths occurring in these hospitals. Fetuses or neonates with congenital anomalies that are delivered at home are not included, even if they are identified and captured in participating hospitals (because they are not part of the denominator).

Because the inclusion in a hospital-based programme depends on where the birth occurred rather than on the residence at birth, the source population of cases is difficult to establish. This becomes an issue in the surveillance of congenital anomalies when referral patterns skew the likelihood that an affected fetus or neonate is delivered at a hospital in the system. Thus, a major concern in hospital-based programmes is referral bias of cases – that is, the selective delivery of affected pregnancies in hospitals participating in the hospital-based programme. This referral bias can also vary over time, either because referral patterns change or because hospitals are added or removed from the surveillance programme. This, in turn, adds to the problem of using these hospital-based data longitudinally for monitoring.

Such hospital-based programmes typically collect data on live births and stillbirths. Because neonates are discharged from maternity hospitals within days following birth, hospital-based programmes typically capture only those congenital anomalies that are evident during the hospital stay, unless those readmitted to the hospital for surgery or other procedures are captured. Note that fetuses or neonates diagnosed after delivery in a hospital participating in a hospital-based programme are not included for the purposes of surveillance *unless* they were also delivered at a participating site in a hospital-based programme.

For illustration, Fig. 3.3 presents an example of participating and non-participating hospitals in a hospital-based surveillance programme. All fetuses or neonates with congenital anomalies born to mothers in participating hospitals, regardless of maternal residency, are included in the programme (labels 1 through 4 in Fig. 3.3). Fetuses or neonates with congenital anomalies born to resident mothers *but born outside of a participating hospital or at home* are not included. Fetuses or neonates with congenital anomalies born to *non-resident mothers* are included if they are born in a participating hospital.

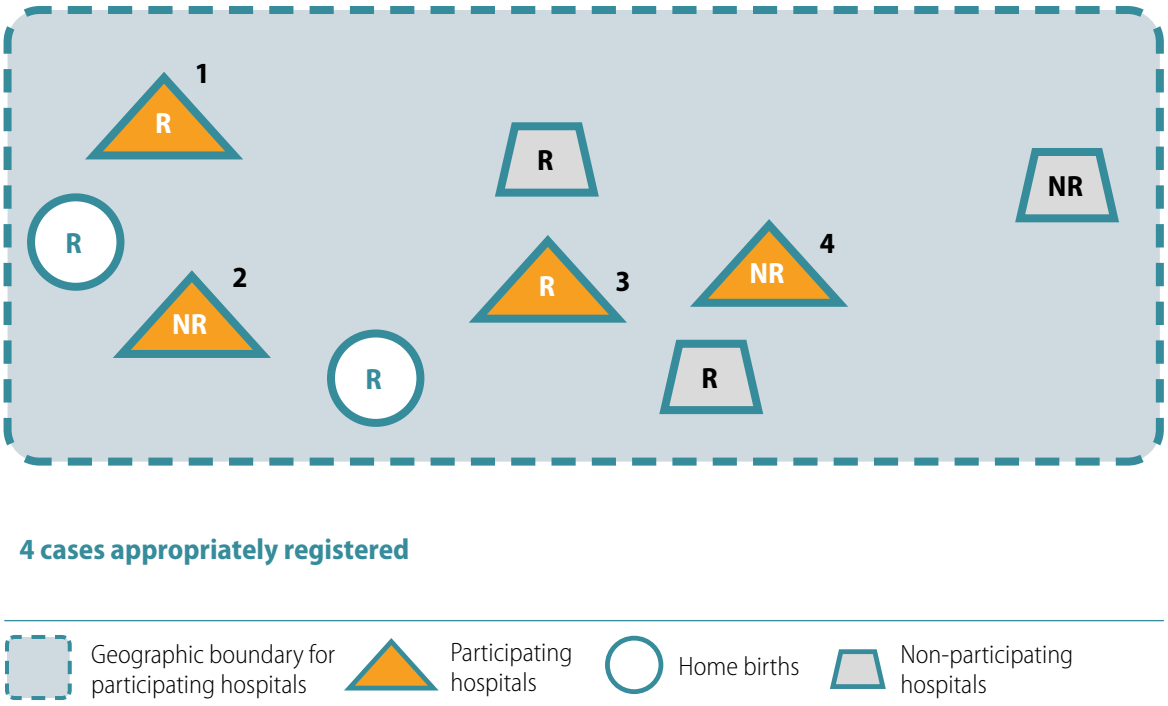
Ascertainment of fetuses or neonates identified with congenital anomalies in participating hospitals can vary. While some are primary hospitals, others might be specialized centres for certain conditions, or for prenatal diagnosis and care, and serve as referral hospitals for patients outside the catchment area. As discussed, such hospitals would disproportionately serve fetuses or neonates with congenital anomalies, thus introducing bias in the calculation of their birth prevalence.

The magnitude of bias might change over time, with fluctuations in referral patterns and the proportion of births occurring outside the hospital setting. This could lead to changes in rates that have nothing to do with the underlying prevalence but are the result of referral patterns. Also, the bias will depend on how many hospitals or facilities are included – all, half or only a small percentage.

Estimates of birth outcomes with congenital anomalies in hospital-based surveillance programmes represent only those births at reporting hospitals in which data are collected. The prevalence estimates could therefore be biased, particularly if the hospital births are a minority of all births, if they receive a high proportion of difficult or complicated pregnancies, and/or if they are not representative of the population of interest. Bias limits the representativeness and usefulness of the data for surveillance. However, if nearly all hospitals in a country participate in the surveillance programme and nearly all births occur in hospitals, the surveillance programme might approximate a population-based surveillance programme.

Finally, a subset of facility-based or hospital-based surveillance known as *sentinel surveillance* is generally set up in key sites to obtain rapid estimates of the occurrence of a birth outcome. Because congenital anomalies are relatively rare events, sentinel surveillance programmes might not be very effective for capturing them.

**Fig. 3.3. Catchment area for a hospital-based surveillance programme**




**R** = fetus or neonate with a congenital anomaly whose mother is a resident; included if the fetus or neonate is identified at a participating hospital.
**NR** = fetus or neonate with a congenital anomaly whose mother is a non-resident; included if the fetus or neonate is identified at a participating hospital.

Although population-based and hospital-based surveillance programmes have clear differences, there are some characteristics that are common to both. These include:

- participating clinicians can be motivated "champions" – leaders who are committed to the programme;
- data collected are useful for documenting that a problem might exist;
- data collected are useful for alerting health and government officials to the need for investing further in evaluating possible causes and promoting prevention strategies;
- affected children can be referred to services; and
- high-quality case data – including data on potential risk factors – can be generated.

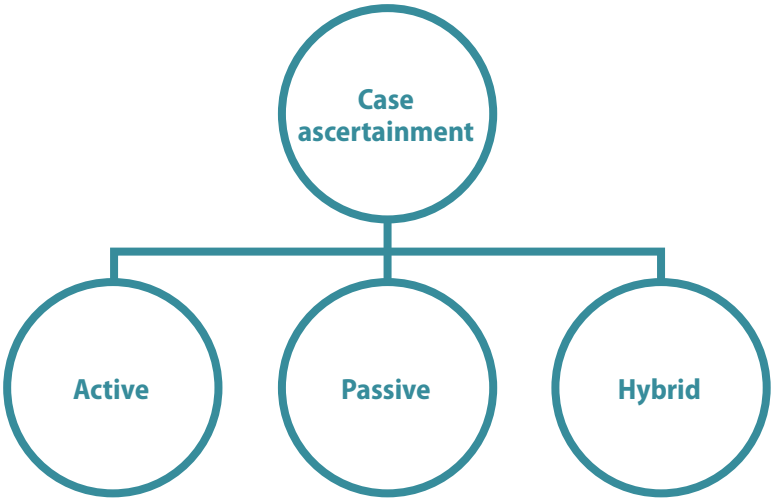
## Case ascertainment

Once the type of population coverage has been decided, the next step is to determine how cases will be ascertained. This can be done by taking active, passive or hybrid approaches (see Fig. 3.4).

### *Active case ascertainment*

With active case ascertainment, the surveillance personnel typically are hired and trained to conduct data abstraction (i.e. to be abstractors). Abstractors regularly visit, or have electronic access to, participating institutions (e.g. hospitals and clinics), and actively review multiple data sources (e.g. logbooks and medical, discharge and deaths records) to identify cases. Therefore, visiting all areas of the hospital where a potential fetus or neonate with a congenital anomaly can be identified could be important (e.g. labour and delivery unit; neonatal intensive care unit). For those fetuses or neonates identified in the logbooks as having a congenital anomaly, abstractors usually request maternal and infant medical records to abstract relevant information onto a reporting form (see Appendix G). It is noted that

**Fig. 3.4. Case ascertainment**




for this process to work well, medical records need to contain relevant information in a format that can be identified and abstracted easily by the abstractors, who usually have limited medical background.

Although this type of case ascertainment requires considerable resources and personnel, active case ascertainment tends to improve case detection and case reporting, and improves data quality because more extensive clinical details are collected.

To improve case ascertainment, the surveillance programme can link administrative databases (e.g. vital records, discharge data and insurance databases) with the surveillance programme database to identify potential additional cases that were not ascertained from the more common sources. The identified cases will require verification by personnel going to the maternity hospitals and reviewing the medical records.

### *Passive case ascertainment*

With passive case ascertainment, hospital personnel who identify a fetus or neonate with a congenital anomaly or anomalies report this information directly to the surveillance registry. Also, cases might be ascertained by linking administrative databases (e.g. vital records, discharge data and insurance databases) to the surveillance programme database. With passive case ascertainment, the information that is reported to the surveillance registry is typically not verified by direct abstraction of the medical record.

This type of case ascertainment is less expensive because fewer resources and personnel are required. However, the burden of reporting falls on hospitals or clinics, which might require time and effort of hospital staff who are already busy. This could result in a less than optimal reporting rate, less complete documentation or less timely reporting, or a combination thereof. It also usually yields less complete detail on each case and underestimates the number of congenital anomalies that occur. In addition, because reported information is not validated, it could also overestimate certain congenital anomalies.

### *Hybrid case ascertainment*

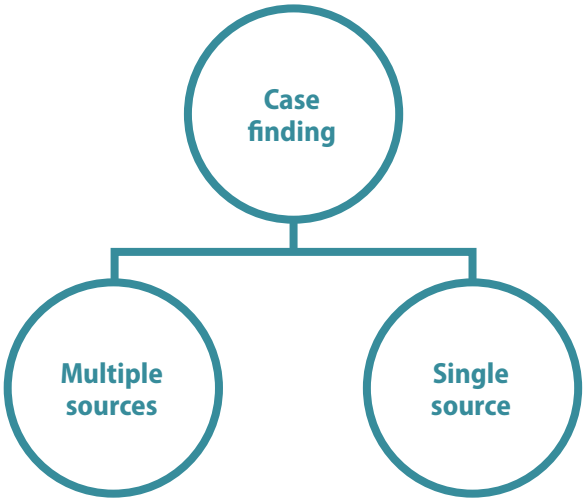
Hybrid case ascertainment refers to a combination of passive case ascertainment of most types of congenital anomalies, with active case ascertainment of specific congenital anomalies, or for a percentage of all reported congenital anomalies as a quality control tool. For example, a surveillance programme can conduct active ascertainment of NTDs to gather more detailed case information in a more timely manner, but carry out passive ascertainment of all other congenital anomalies under surveillance. Similarly, a programme can use passive reporting with active follow-up verification of certain congenital anomalies.

Regardless of the method selected for case ascertainment (active or passive), each participating hospital can identify a "champion" who is committed to the programme. This could help to ensure more complete participation of the different hospital units and services participating in the surveillance programme. Also, the role of this leader could be to train other personnel (such as doctors, nurses and technicians) on how to identify cases, record the information and oversee the information flow, so as to maintain an ongoing and active quality control on the quantity and completeness of information. The role of a leader, or champion, can be important to a programme's success.

## Case finding

Congenital anomalies surveillance programmes can decide the sources from which cases will be identified (see Fig. 3.5).

**Fig. 3.5. Case finding**




### *Data sources*

Using multiple sources might improve the completeness of case ascertainment by identifying cases that are not available from only one individual source. Additionally, it might improve the quality of the data, as having multiple sources might increase the amount and level of information available for a given case. For example, a diagnosis might not be possible in the delivery unit but might be established by specialists in the paediatric unit and further confirmed by laboratory tests. While the use of multiple data sources is more time consuming and delays the process of gathering information, it can improve overall case ascertainment and data quality. Using a single source for case ascertainment does not allow for ascertainment of the majority of fetuses or neonates with a congenital anomaly in most settings. For example, Fig. 3.6 depicts a marked under-ascertainment of NTDs in Puerto Rico when cases were ascertained from vital records alone, compared with case ascertainment from multiple sources (e.g. logbooks in the delivery room, neonatal care units, paediatric units) used by the Birth Defects Surveillance Programme.

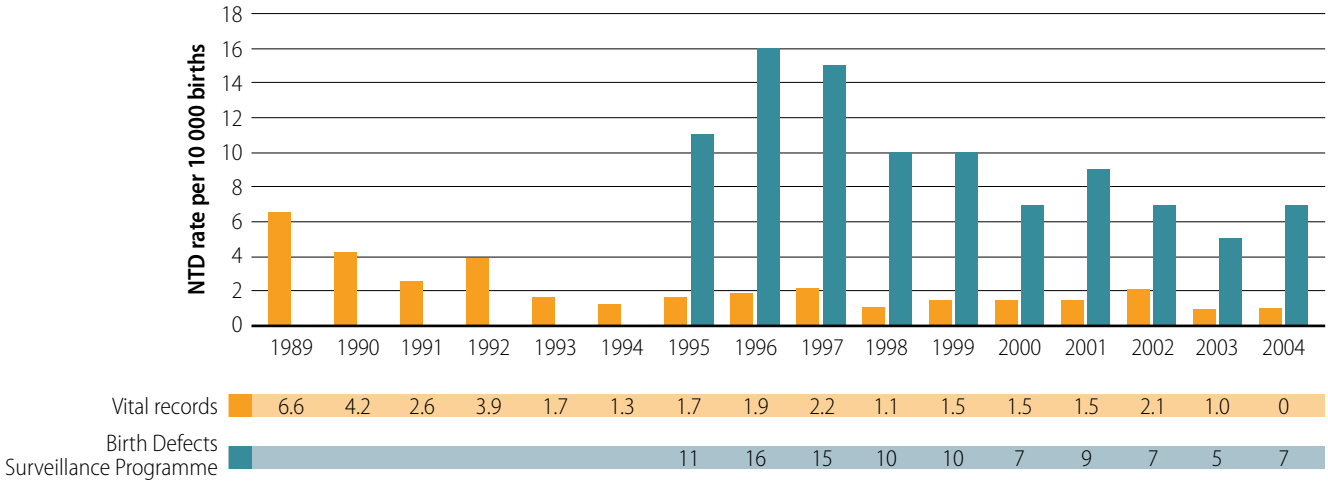
## Case inclusion

Each surveillance programme decides which congenital anomalies to include. A programme might choose to include all major congenital anomalies, while another programme might decide to include selected congenital anomalies, according to the needs of the country (see Fig. 3.7). As will be discussed in Chapter 4, one consideration is to start with a small number of easily recognizable congenital anomalies and then expand to include additional anomalies, as a programme gains experience and resources.

## Description formats for congenital anomalies

On the abstraction form, information about congenital anomalies is ideally captured using either a verbatim description or a checkbox, although sometimes both might be used (Fig. 3.8). From a quality standpoint,

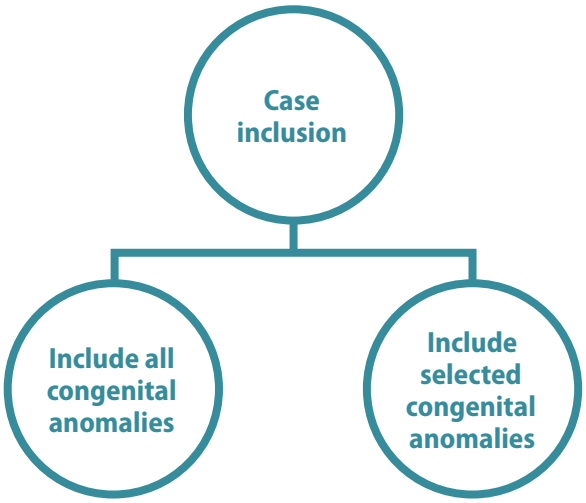
**Fig. 3.6. Prevalence of neural tube defects by case ascertainment sources, Puerto Rico Birth Defects Surveillance Programme**




NTD: neural tube defects

*Source*: Birth Defects Surveillance Programme Puerto Rico Department of Health, and Auxiliary Secretariat for Planning and Development, San Juan, Puerto Rico.

**Fig. 3.7. Case inclusion**




checkboxes alone are typically insufficient to achieve high data quality, both in initial data abstraction and in case review. However, if a country has the resources to collect data electronically, a checkbox could be useful as a first step, if there is a drop-down menu with more options to categorize the congenital anomaly. Nevertheless, having a field for verbatim descriptions allows details to be collected, and the additional information might help clarify the diagnosis and classification, be used to plan the child's health-care management, and help assess the accuracy and completeness of the information and coding during case review and ongoing quality assessment. Examples of verbatim and checkbox formats are presented in Fig. 3.9.

When coding the example case in Fig. 3.9, if the information available is limited to one of the checked boxes, the *International Statistical Classification of Diseases and Related Health Problems*, 10th revision (ICD-10) *(12)* code would be Q36.99 (cleft lip). However, if the verbatim description is available, it is possible to give a more specific code: Q36.9 (cleft lip, unilateral).

**Fig. 3.8. Description formats**

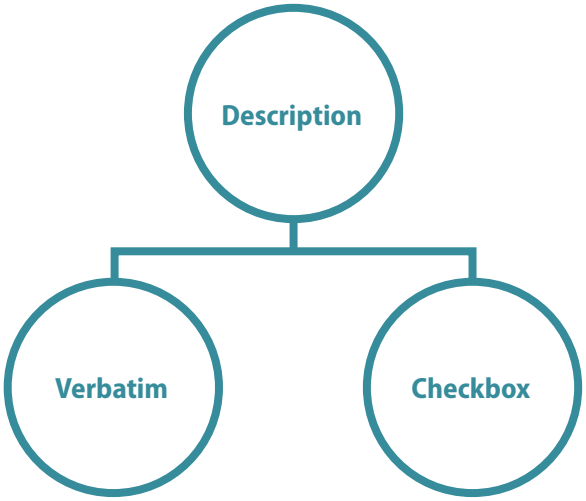



**Fig. 3.9. Examples of verbatim description and checkbox formats for documenting congenital anomalies**

**Verbatim description format**

| Selected congenital anomaly | Description/comments/details |
|---|---|
| 1. Cleft lip | Infant born with unilateral, left cleft lip; palate is intact. Infant also has microcephaly and clenched hands. |

**Checkbox format**

| Neural tube defects: |
|---|
| ☐ Anencephaly<br>☐ Encephalocele<br>☐ Spina bifida |
| **Orofacial clefts:** |
| ☒ Cleft lip<br>☐ Cleft palate<br>☐ Cleft lip and palate<br>☒ Other |

## Age of inclusion

Countries that have congenital anomalies surveillance programmes have different criteria for age of inclusion. Some include information about fetuses or neonates with a congenital anomaly ascertained only during the early neonatal period (see Table 3.1), while others include those ascertained up to 1 year of age and beyond (see Fig. 3.10).

The Western Australian Birth Defects Registry includes cases diagnosed up to 6 years of age. Fig. 3.11, derived from Bower et al. (2010) *(13)*, indicates the cumulative percentage of cases with major external and internal

**Table 3.1. Periods of infancy**

| Time period | Days |
|---|---|
| Neonatal | 0–27 |
| Early neonatal | 0–6 |
| Late neonatal | 7–27 |
| Post neonatal | 28–364 |

**Fig. 3.10. Age of inclusion in a congenital anomalies surveillance programme**

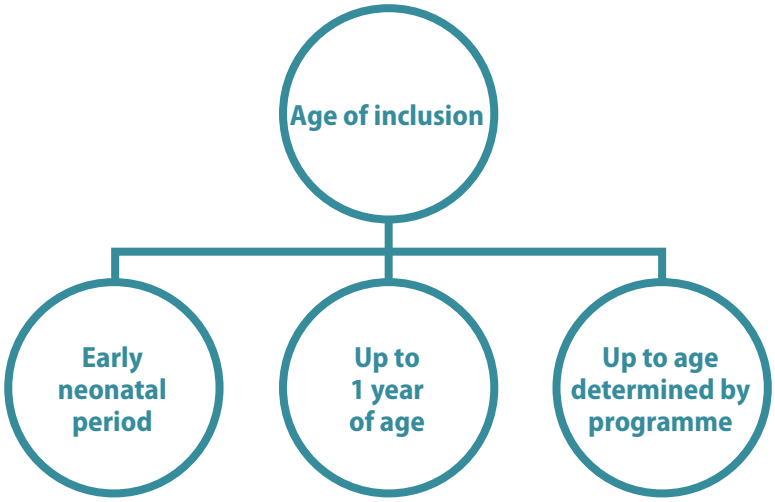
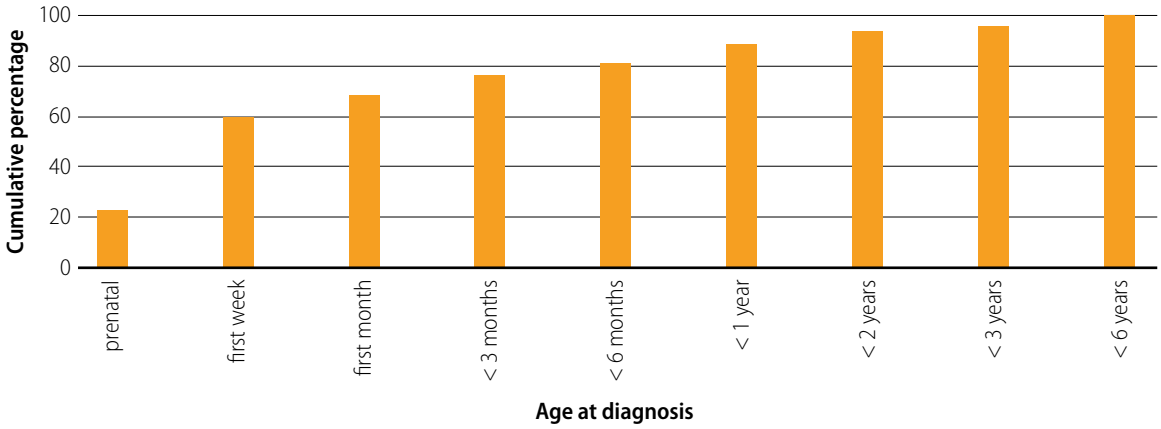



**Fig. 3.11. Cumulative percentage of cases of major congenital anomalies by age at first diagnosis**




*Source*: Bower et al., 2010 *(13)*. Reproduced with permission from the publisher.

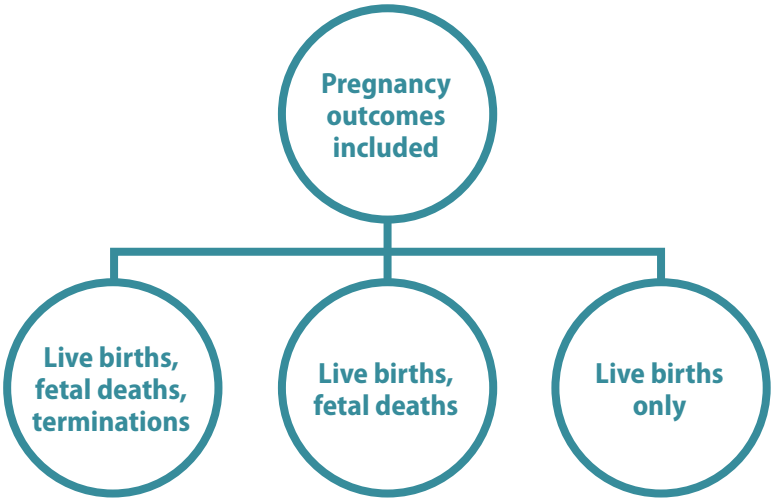
congenital anomalies by age at first diagnosis. The authors examined the age at diagnosis for all congenital anomalies reported to the Birth Defects Registry from 2000 to 2001. Nearly 60% of all major congenital anomalies were diagnosed during the first week of life, nearly 70% by the first month, nearly 90% by the first year, and nearly 100% by the sixth year.

Age at diagnosis is a critical component of case definition. Typically, the higher the cut-off age, the greater the reported frequency of conditions, especially for conditions involving internal organs that might not be evident at birth. For example, whereas external anomalies such as NTDs and gastroschisis are evident at birth, some internal anomalies such as heart defects might not be identified until days, or even weeks or months, after delivery. In addition, certain anomalies might require postnatal confirmation.

## Inclusion of pregnancy outcomes

Surveillance programmes aim to ascertain congenital anomalies among all pregnancy outcomes – live births, fetal deaths and terminations of pregnancy – if possible (see Fig. 3.12). Some countries have the ability and resources to ascertain all or most of these outcomes when they occur relatively late in pregnancy, but it is extremely difficult to systematically ascertain those occurring prior to 28 weeks' gestation and, in particular, those in which the pregnancy is terminated. For these reasons, if prenatal ascertainment of congenital anomalies is not an available option in a given catchment area, it would be more feasible initially to limit the ascertainment to live births and to fetal deaths occurring at 28 weeks' gestation or older, or alternatively, with a birth weight of at least 1000 g (if gestational age is not available). However, in many countries and settings, ascertainment among live births alone is a significant limitation that can lead to unreliable rates and trends, particularly for conditions with a high rate of loss prior to 28 weeks' gestation (e.g. anencephaly). If a country has the capacity to ascertain cases prior to 28 weeks' gestation, doing so can help provide a more accurate estimate of the prevalence of a condition such as anencephaly. Programmes interested in more detailed information on inclusion of prenatal diagnosis in congenital anomaly surveillance can find some useful and practical suggestions and tips in the guidelines developed by the National Birth Defects Prevention Network (NBDPN) in the USA *(14)*.

**Fig. 3.12. Inclusion of pregnancy outcomes**



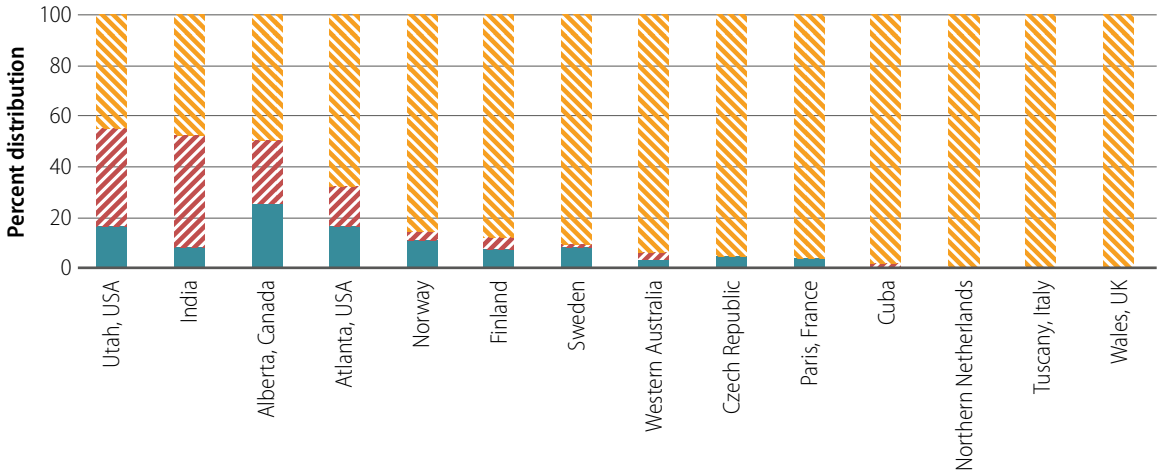

Figs. 3.13 and 3.14 show how inclusion of the different types of pregnancy outcomes has improved case ascertainment for anencephaly and spina bifida in 14 countries. It is important to note that programmes that include terminations of pregnancy find the terminations based on monitoring prenatal diagnosis. For example, the majority of fetuses with anencephaly are ascertained through fetal deaths or terminations. Fig. 3.13 indicates that in Wales, Tuscany (in Italy) and Northern Netherlands, for example, 100% of fetuses with anencephaly are ascertained through pregnancy terminations, while in Utah (in the USA), 50% are ascertained through terminations, 40% through fetal deaths and 10% as live births. Similarly, as Fig. 3.14 indicates, a much greater proportion of fetuses with spina bifida in Wales, Tuscany and Northern Netherlands are ascertained through pregnancy terminations, as compared to the other countries, regions or states represented.

## Coding system

Most countries use the ICD-10 coding system *(12)* to classify congenital anomalies (please refer to Chapter 6 for more information on coding). While countries can develop their own local coding system, WHO recommends the use of ICD-10 for international reporting and comparisons.

The following sections describe case inclusion and exclusion criteria, procedures for data collection and components of a protocol for data collection.

## Fig. 3.13. Distribution of pregnancy outcomes among ascertained anencephaly cases, 2007–2009



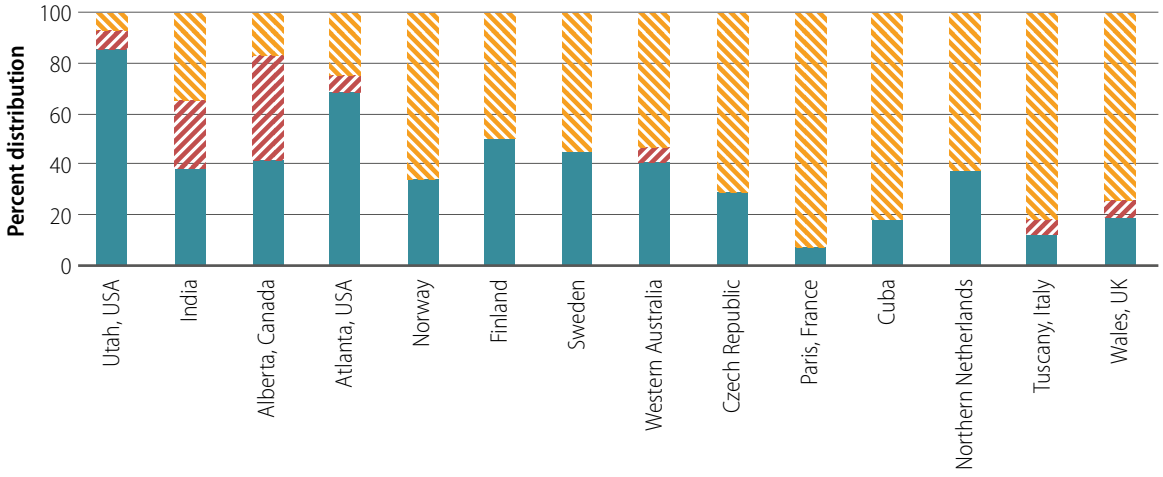

| | Utah, USA | India | Alberta, Canada | Atlanta, USA | Norway | Finland | Sweden | Western Australia | Czech Republic | Paris, France | Cuba | Northern Netherlands | Tuscany, Italy | Wales, UK |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ETOPFA | 45% | 48% | 50% | 68% | 86% | 88% | 91% | 94% | 96% | 97% | 99% | 100% | 100% | 100% |
| Fetal death | 39% | 45% | 25% | 16% | 4% | 5% | 1% | 3% | 0% | 0% | 1% | 0% | 0% | 0% |
| Live births | 16% | 7% | 25% | 16% | 10% | 7% | 7% | 3% | 4% | 3% | 0% | 0% | 0% | 0% |

ETOPFA = elective termination of pregnancy for fetal anomaly

*Note*: All surveillance programmes are population based except for that in India.

*Source:* International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR).

## Fig. 3.14. Distribution of pregnancy outcomes among ascertained spina bifida cases, 2007–2009




| | Utah, USA | India | Alberta, Canada | Atlanta, USA | Norway | Finland | Sweden | Western Australia | Czech Republic | Paris, France | Cuba | Northern Netherlands | Tuscany, Italy | Wales, UK |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ETOPFA | 7% | 35% | 17% | 25% | 66% | 50% | 55% | 53% | 72% | 93% | 82% | 63% | 82% | 75% |
| Fetal death | 7% | 27% | 41% | 6% | 0% | 0% | 0% | 6% | 0% | 0% | 0% | 0% | 6% | 7% |
| Live births | 86% | 38% | 41% | 69% | 34% | 50% | 45% | 41% | 28% | 7% | 18% | 38% | 12% | 19% |

ETOPFA = elective termination of pregnancy for fetal anomaly

*Note*: All surveillance programmes are population based except for that in India.

*Source:* International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR).

### *Potential inclusion/exclusion criteria*

To standardize the inclusion criteria for a case (fetus or neonate with a congenital anomaly) in a congenital anomalies surveillance programme, it is essential to characterize the criteria related to the diagnoses. Some examples of these criteria include the age at which the anomaly is diagnosed (discussed previously), the type of pregnancy outcome (discussed previously), the gestational age at delivery and birth weight, and maternal residence. More information about the latter two criteria follows.

#### Gestational age at delivery and birth weight

Gestational age at delivery and birth weight are important components of the case definition, because the frequency of some congenital anomalies varies depending on these factors. For example, preterm and low-birth-weight babies have a higher frequency of patent ductus arteriosus and undescended testes than term infants, and these conditions are considered physiologically normal among preterm infants if they resolve within a short time frame without intervention. Please refer to the Glossary of Terms at the end of this document for definitions of birth weight and gestational age.

#### Maternal residence

The mother's primary residence at the time of delivery or pregnancy termination is used by most congenital anomalies surveillance programmes to define the source population in which the cases occur. For example, residence can be defined as the mother's primary address during the three months prior to pregnancy and the first trimester of pregnancy. This is important because residence and place at delivery might be different, particularly in areas with strong referral patterns. It is essential to focus on residence rather than place at delivery, in order to correctly identify the appropriate denominator (the population of births from which the cases derive) and numerator. Correct denominators and numerators are prerequisites for accurate monitoring of the prevalence of a congenital anomaly and monitoring of changes over time.

## Examples of inclusion criteria for population-based surveillance

- Live births and fetal deaths (stillbirths):
  - delivered with at least one of the selected major congenital anomalies (see Appendix A);
  - delivered to a mother who resides within a catchment area;
  - delivered at an age of 28 weeks' gestation or more, or, alternatively, a birth weight of at least 1000 g when gestational age is not available, or with a gestational age defined by the programme. WHO recommends using an age of 28 weeks' gestation or more, or birth weight of at least 1000 g when gestational age is not available. However, each country can use its own standards, which will allow it to link with vital statistics data.
- The congenital anomaly might be diagnosed prenatally (and confirmed at birth), at birth, during the neonatal hospitalization period, or up to an age limit predetermined for case ascertainment.
- If follow-up of the infants is available in the country, then the surveillance programme could consider capturing infants within a defined time period, to include the follow-up period (e.g. up to 1 year after birth).
- If the site has the capacity to capture terminations of pregnancy, the programme can include those fetuses with at least one of the selected major congenital anomalies at any gestational age, for the subset of congenital anomalies for which a prenatal diagnosis is considered definitive (e.g. anencephaly). Each country will have different provisions to capture termination of pregnancies, but in many settings this is done by including prenatal diagnostic centres as potential case-finding sources.
- Programmes that are interested in more detailed information on inclusion of prenatal diagnosis in congenital anomalies surveillance can find some useful and practical suggestions and tips in the guidelines developed by the NBDPN in the USA *(14)*.

## Examples of inclusion criteria for hospital-based surveillance

- Live births and fetal deaths (stillbirths):
  - delivered with at least one of the selected major congenital anomalies (see Appendix A);
  - delivered at a participating hospital; and
  - delivered with an age of 28 weeks' gestation or more, or, alternatively, a birth weight of at least 1000 g if gestational age is not available. The gestational age can be determined by each country, depending on its capacity to identify congenital anomalies occurring earlier than 28 weeks' gestation.
- The congenital anomaly might be diagnosed prenatally (and confirmed at birth), at birth or during the neonatal hospitalization period. The usual hospitalization period after delivery varies among countries, but could be defined as up to seven days after birth.
- If the programme has the capacity to capture terminations of pregnancies, it can consider including those fetuses with at least one of the selected major congenital anomalies at any gestational age for the subset of congenital anomalies for which a prenatal diagnosis is considered definitive (e.g. anencephaly). Each country will have different provisions to capture termination of pregnancies, but in many settings this is done by including prenatal diagnostic centres as potential case-finding sources.
- Programmes that are interested in more detailed information on inclusion of prenatal diagnosis in congenital anomalies surveillance can find some useful and practical suggestions and tips in the guidelines developed by the NBDPN in the USA *(14)*.

## Examples of exclusion criteria for both population- and hospital-based surveillance

- All neonates that do not have one of the selected major congenital anomalies listed in the initial inclusion list (see Appendix A).
- All neonates – with or without congenital anomalies – of less than 28 weeks' gestational age or with a birth weight of less than 1000 g, if gestational age is not available (or who are less than the gestational age or weight defined by the programme).
- All live births and fetal deaths with congenital anomalies identified outside of the participating hospital (hospital based) or outside of the ascertainment area (population based).
- Maternal residence status is not met (the three months prior to pregnancy and the first trimester of pregnancy occurred outside the catchment area).

Table 3.2 gives examples of criteria used by different countries to define congenital anomalies.

**Table 3.2. Examples of criteria used by select countries to define congenital anomalies**

| Programme | Coverage | Age at diagnosis | Fetal death criteria |
|---|---|---|---|
| Australia: VBDR | Population based, statewide | ≤ 18 years | 20 weeks or 400 g |
| Costa Rica: CREC | Population based, national | ≤ 1 year | 22 weeks or 500 g |
| Finland | Population based, national | ≤ 1 year | 22 weeks or 500 g |
| Japan | Hospital based, national | ≤ 7 days | 22 weeks |
| Spain | Hospital based, national | ≤ 3 days | 24 weeks or 500 g |
| USA – California | Population based, regional | 1 year | 20 weeks |
| USA – Utah | Population based, regional | 2 years | 20 weeks |

VBDR = Victorian Birth Defects Register

CREC= Costa Rican Birth Defects Register Center

After a programme has defined the inclusion and exclusion criteria, a standardized data collection process can be developed. This would include identifying the core ascertainment variables to be included in the surveillance programme and the development of a protocol for standardized data collection procedures.

## Core ascertainment variables

The first step in determining what core variables will be included in a surveillance programme is to define the goals and objectives of the congenital anomalies surveillance programme. Countries that already have a surveillance programme in place that includes the identification of populations at risk might consider including demographic variables such as maternal age, race and ethnicity, consanguinity, and other factors relevant to the local setting.

To facilitate data collection, countries can evaluate and summarize the availability of existing data sources (e.g. vital registries, and logbooks in hospital units) to determine what information regarding congenital anomalies is already being collected. Also, establishing the percentage of all births that are documented in vital registries, and determining whether the documentation includes only live births or both live births and fetal deaths, can be very useful.

After the list of core variables has been determined, these variables can then be incorporated into the methodology for case ascertainment. Table 3.3 lists core variables to be considered for inclusion in a congenital anomalies surveillance programme. Please refer to Appendix H for a list of core variables for consideration, and their definitions.

The following optional variables can be included if the surveillance programme in the country has the information available. See Appendix I for a list of optional variables and definitions for each.

- Report
  - source of information
- Father
  - occupation or work
  - family health history, environmental health history/form or occupational health form
- Mother
  - environmental health history/form or occupational health form
  - demographic information
    - civil or marital status
    - occupation or work at time of conception
    - years and months residing in country
    - country identification number
    - weight (before pregnancy)
    - education (years or highest level)
    - religion (if applicable)
    - socioeconomic status
  - obstetric history
    - chronic diseases
    - date of last menstrual period
    - prenatal care, when it started, measure of adequacy
    - prenatal tests
    - family health history
    - medications or vaccines taken during pregnancy
    - any traditional medications commonly used
- Infant
  - type of delivery

## Table 3.3. Potential core ascertainment variables

| Report | Father | Mother | Infant |
|---|---|---|---|
| • Case identification code<br>• Date of report<br>• Reporting hospital<br>• City, province, state or territory<br>• Name of person completing report | **Identification information**<br>• Name: Given name, family name<br>• Date of birth or age<br>• Race and ethnicity (if applicable) | **Identification information**<br>• Name: Given name, family name (including maiden name if appropriate)<br>• Date of birth or age<br>• Race and ethnicity (if applicable)<br>• Address during the three months prior to pregnancy and the first trimester of pregnancy<br>• Current address<br>• Telephone number<br>**Obstetric history**<br>Total number of:<br>• Live births<br>• Stillbirths (fetal deaths)<br>• Spontaneous abortions<br>• Terminations of pregnancy | **Identification information**<br>• Name: Given name, family name<br>• Date of birth<br>• Sex<br>• Date of diagnosis<br>• Birth outcome<br>**Birth measurements**<br>• Gestational age (weeks)<br>• Weight (g)<br>• Length (cm)<br>• Head circumference (cm)<br>**Birth information**<br>• Pregnancy outcome<br>• Birth order, if multiple birth<br>• Date of diagnosis<br>• Date of death<br>• Parental consanguinity[a]<br>**Congenital anomaly/ anomalies present:**<br>• Type<br>• Description:<br>– detailed description of congenital anomaly<br>– drawings or illustrations of congenital anomaly<br>• Code<br>• Diagnostic technique(s) (e.g. radiographs)<br>• Photographs<br>*Note:* if an infant has more than one anomaly, any major congenital anomaly/ anomalies are recorded first, followed by any other anomalies.<br>**Autopsy results**<br>• Description |

a Consanguinity has long been recognized as a significant factor in the occurrence of autosomal recessive diseases. However, its effect in the determination of single major congenital anomalies remains controversial. Even though some studies have shown variable degrees of association between consanguinity and non-syndromic neural tube defects, hydrocephalus and oral clefts, the majority are based on small numbers of individuals. In addition, differences in methodological approaches hinder comparisons between the different studies. The situation appears to be different for congenital heart defects, for which significant increases among the offspring of consanguineous couples have been identified in several multinational studies *(15–21)*.

## Data collection methods and tools

Data gathering involves the use of appropriate recording forms. The data will provide the opportunity to measure the programme objectives, collect numbers of cases and help to determine trends. Once a decision is made regarding the data variables to be collected, an abstraction form (see Appendix G) can be created.

### *Paper-based data collection*

For many years, data for congenital anomalies surveillance have been collected and processed using either a predetermined list (checkbox) format or the recording of verbatim descriptions on paper. These data collection methods are still used widely for vital registration and various surveillance and research purposes. Paper-based data collection can be cost-effective, but the process can require more time from data collection to analysis. It is also more prone to errors than electronic data collection because the data are first collected on paper and then transcribed into an electronic format for analysis *(22–24)*. Nevertheless, well-structured, paper-based forms are often still used in low-resource settings for collecting data on congenital anomalies.

### *Electronic data collection*

An alternative to paper-based data collection is electronic data collection. Gradually, data collection methods have evolved from manual, paper-based formats to electronic formats. Improving electronic surveillance programmes can be a long and costly process that requires regular updating of a system's hardware and software to maintain a high level of security and data quality. The availability of electronic data collection will depend on the resources of each country.

The ideal collection tool allows data to be collected, transmitted securely to a data management centre for storage and analysis, and retrieved, processed or analysed when necessary. In the last few decades, the evolution of technology has significantly improved the options for potential electronic data collection tools.

Internet advances have allowed web-based reporting to progress gradually into real-time reporting *(25)*. The more recently introduced use of laptops, tablets and smartphones provides additional options for data collection. Because of the variability in access to, use of and resources for electronic systems, each country will need to determine which method best fits its needs.

### *Data collection using smartphones or tablets*

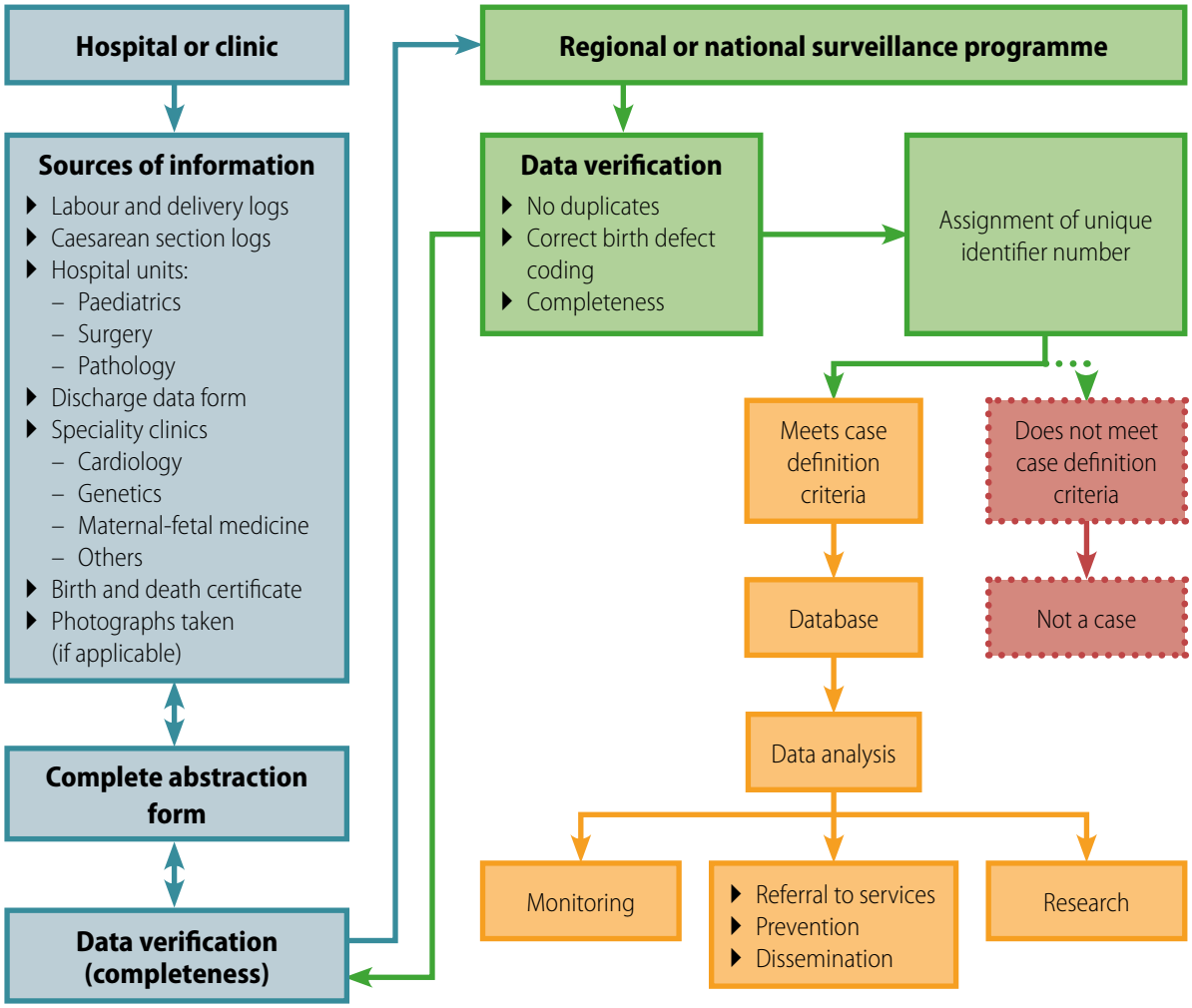
With the growing availability of smartphones and tablets in countries whose populations are predominantly middle- and low-income, the use of this technology as part of a congenital anomaly surveillance programme might improve the accuracy of data collection and reduce the time required for – and cost of – data transmission and retrieval.

Users of smartphones and tablets can capture and transmit pictures, and might have access to databases of clinical information, including photographs to assist with differential diagnosis. Furthermore, the use of these mobile devices can be a novel, simple, efficient and instructive approach to the collection of data. The larger-sized tablets can also facilitate data entry. The use of these technologies could offer great potential for encouraging motivated personnel to contribute data to central databases using their mobile devices; however, such devices can easily be lost or stolen, so it is essential that they are programmed to encrypt all data, to ensure the privacy and security of information collected by the system.

## Data management and protocols

Data management is essential to ensuring the integrity and confidentiality of surveillance data. Data management will not be possible unless all participating personnel are trained in the protocol for data collection. This ensures the proper use of all tools and a standardized method for data collection. This can be achieved by creating and maintaining an organized system for smooth data flow that ensures the regular availability of data but that also has high levels of security to preserve confidentiality. Fig. 3.15 is an example of how data collected at the hospital or clinic level progress through a surveillance programme.

**Fig. 3.15. Example flow chart for data management**




The protocol for data collection and management includes procedures for:

- identification and registration of congenital anomalies by health-care professionals in each participating hospital unit;
- training of personnel responsible for coding congenital anomalies according to the ICD-10 *(12)* coding system;
- taking photographs of fetuses or neonates with congenital anomalies, if appropriate for the setting (see Appendix J);
- verifying the information at the participating hospital site; and
- sending information to the regional or national-level surveillance programme.

Cases of congenital anomalies are usually identified as they occur in the participating delivery settings in a catchment area. Hospital personnel who identify a fetus or neonate with a congenital anomaly/anomalies usually record this information in a logbook, based on established standardized procedures.

Identification of cases is based on specific criteria, and diagnosis at birth is made by an experienced health-care provider. If an experienced health-care provider is not available at the site, photographs of the fetus or neonate with a congenital anomaly can be taken and kept in the medical record for later verification of the diagnosis by an

experienced health-care provider or specialist, or a panel of experts, working as part of the congenital anomalies surveillance programme *(26)*. A member of the hospital staff, or a specially trained individual, usually takes at least three pictures – one frontal photograph of the fetus or neonate, one showing the back, and one or more pictures of the affected part(s) of the body. It is important, if possible, to place a tape measure next to the affected area or areas when taking the photograph, to document the size of the affected area, and ensure that some form of identification number is included in the photograph in order for it to be correctly linked to a particular case. For more suggestions on taking photographs of the fetus or neonate with a congenital anomaly, please refer to Appendix J.

The frequency of reporting data to the regional or national registry (e.g. weekly or monthly reporting) can be defined in the surveillance protocol and will depend on the availability of surveillance personnel and the individual circumstances of the participating unit.

A protocol is developed for the regional or national level, for personnel working in the surveillance programme. The protocol includes procedures for:

- data verification;
- criteria to include cases in the database;
- analysing data;
- reporting and sharing data;
- protecting the patient's and family's private information;
- maintaining confidentiality (please refer to Chapter 2 for more information on privacy and confidentiality); and
- case referral and management – clinical and surgical, if applicable.

Data management personnel are responsible for reviewing information sent from the participating hospitals, assessing the completeness of data forms, whether each item has been completed, and whether the verbatim and coded diagnoses have been included. In situations in which information appears incorrect or incomplete, personnel overseeing the verification of data can return the form to the site and ask for it to be re-reviewed or completed, or both. Cases submitted to the surveillance programme are then to be reviewed by a clinician, to verify the congenital anomaly and its coding prior to the case being entered into the database.

## Data collection and management

Accurate data collection and management, including storage and analysis, are key components of any programme conducting congenital anomalies surveillance, and different instruments and methods of data gathering can be used for this purpose. Well-designed data systems improve data management, permit statistical analyses and data sharing among different surveillance programmes, and support linking of congenital anomalies data with other available information for surveillance, research and prevention purposes.

### *Data collection*

It is important that the collection and analysis of data for the surveillance of congenital anomalies is done in a systematic way by trained surveillance personnel. It is also important that data are accurate and of high quality before analysis is performed. If done well, data analysis will provide accurate, timely and complete information on the occurrence of congenital anomalies.

### *Data quality*

There are three main attributes to data quality: completeness, accuracy and timeliness.

*Completeness* refers to the extent to which data are all-inclusive and comprehensive. For example, all cases at a given source in a specific time frame have been identified, and all required data have been abstracted. Hospital audits and linkage of cases to vital records or to specialized diagnostic centres can help evaluate the completeness of case ascertainment.

*Accuracy* refers to the extent to which data are exact, correct and valid. Approaches to help ensure data accuracy include: re-abstraction of information, validity audits (e.g. identification of missed diagnoses or coding issues), clinical reviews (e.g. verification of codes, tests and procedures) and verification of data entry (e.g. customized programmes for range checks, automated fields, rejection of data that are known to be inaccurate, routinely running data queries to identify duplicate entries, and identifying problems with variables).

*Timeliness* refers to the extent to which data are collected and analysed in a timely manner. It is measured by time that elapses between the date of diagnosis and date of abstraction; the date of abstraction and the date information is sent to the office; and the date of arrival in the office and the date entered in the system.

Data collection procedures should be carried out properly and systematically. Protocols usually include reviews of the information in the data sources, to verify that data are being recorded in a standardized way. Also, if feasible, having a process whereby a sample of the medical records can be reviewed will ensure that information in the abstraction forms reflects the information on the medical record.

Poor-quality data can lead to erroneous conclusions about the occurrence of a congenital anomaly among a population and could have a substantial effect on the decision-making process of public health authorities.

The following are examples of factors that could affect data quality:

- missing values (e.g. empty data fields in the abstraction form);
- duplicate entry of cases;
- errors in the diagnosis, description or coding of congenital anomalies; and
- bias related to lack or excess of representation, or if data include only very severe cases:
  - if data include only cases from urban settings,
  - if data include only private sector data sources, and
  - if data include cases from outside of the catchment area.

Programmes interested in more detailed information on data management can find suggestions in the guidelines developed by the NBDPN in the USA *(14)*.

## *Data analysis and interpretation*

### Prevalence

In surveillance of congenital anomalies, the term "incidence" is not commonly used to describe their occurrence. "Prevalence" refers to *all* new cases of congenital anomalies. Because spontaneous abortions cannot be counted accurately, the suggested measure of occurrence of congenital anomalies is "live birth prevalence", "birth prevalence" or "total prevalence".

In a population-based surveillance programme, the prevalence of congenital anomalies is calculated by aggregating the number of unduplicated existing cases (i.e. live births and fetal deaths or terminations) as the numerator, and the total number of live births among the source population as the denominator, for a specific catchment area and time period. For hospital-based surveillance, the prevalence of congenital anomalies is calculated by aggregating the number of unduplicated hospital cases as the numerator, and the total number of hospital live births as the denominator for a specific hospital. Hospital-based prevalence can include one or more hospitals.

*Note*: It is important to remember that hospital-based prevalence estimates can be biased, in that they give the prevalence of a condition only for the participating hospital. Prevalence estimates based on hospital data are not true estimates of the prevalence of a condition among a population.

When measuring the prevalence of congenital anomalies, it is important to note what is being counted in the numerator and in the denominator.

Usually, the prevalence of congenital anomalies is calculated and presented as prevalence per 10 000 live births. This prevalence can be calculated for all congenital anomalies, for a specific individual anomaly, or for groups of anomalies. The following expression is used to calculate the birth prevalence of congenital anomalies, with the assumption that both live births and fetal deaths are being captured:

Birth prevalence = $a/b \times 10\,000$

*a*: Number of live births and fetal deaths (stillbirths) with a specific congenital anomaly (e.g. spina bifida) counted among the source population in a given year.

*b*: Number of live births and fetal deaths (stillbirths) (during the same year).

1. Live birth prevalence of congenital anomalies $= \frac{\text{live birth cases}}{\text{total live births}} \times 10\,000$

2. Birth prevalence of congenital anomalies $= \frac{\text{live birth cases + fetal death (stillbirths) cases}}{\text{total live births + fetal deaths (stillbirths)}} \times 10\,000$

3. Total prevalence of congenital anomalies $= \frac{\text{live birth cases + fetal death (stillbirths) cases + ETOPFA cases}}{\text{total live births + total fetal deaths (stillbirths) + total ETOPFA}} \times 10\,000$

ETOPFA = elective termination of pregnancy for fetal anomaly

The numerator includes live births and known fetal deaths (stillbirths) with congenital anomalies, and pregnancy terminations with congenital anomalies (if these data are available), or all. The denominator comprises only live births and fetal deaths (stillbirths) (if these data are available) because it is practically impossible to assess the total number of pregnancy losses. Because the number of pregnancy losses is relatively small compared with the number of live births, its exclusion has little effect on the prevalence estimate. Spontaneous abortions (also called miscarriages) are not included in the numerator or in the denominator because it is practically impossible to assess the total number of spontaneous abortions.

Case counts and crude prevalence are common measures of burden that are often presented with respect to time, geographic area, demographic characteristics or various combinations (e.g. age-by-race-by-sex). When variations in prevalence are identified, they are described and analysed. Many factors could affect the prevalence of a health event: population changes due to migration, improved diagnostic procedures, enhanced reporting techniques, and changes in the surveillance system or methods. It is important to consider these factors when interpreting the results.

Description of changes over time is an important way of detecting trends. A comparison of the number of case reports collected during a particular time period might help identify differences in the number of cases for a current time period compared with time periods in previous years. These differences can help to determine seasonal patterns. The number of cases can vary by geographic location, and analysis by place can help identify where an increase in cases is occurring. In the case of rare congenital anomalies, the size of the geographic unit to be considered is important in order to provide stable estimates. The analysis of demographic characteristics provides information on the characteristics of those individuals with particular congenital anomalies. The most frequently used demographic variables for analysis are age, sex, and race and ethnicity.

### Interpretation

Table 3.4 presents an example of calculating the prevalence of congenital anomalies that highlights the importance of knowing the denominator. Knowing only the number of cases (numerator data) without

having information about the denominator can result in a misinterpretation of the true burden of a congenital anomaly.

**Table 3.4. Example of calculating prevalence and the importance of the denominator**

| | Numerator: total number of cases of congenital anomalies per year | Denominator | Prevalence | Cases per 10 000 live births |
|---|---|---|---|---|
| Country (example A) | 100 | 100 000 (total live births per year in region or total catchment area) | 0.001 | 10 per 10 000 |
| Country (example B) | 100 | 10 000 (total live births per year in eight hospitals of the total catchment area) | 0.01 | 100 per 10 000 |
| Country (example C) | 100 | 1000 (total live births per year in one referral hospital of the total catchment area) | 0.1 | 1000 per 10 000 |

*Example A*

A country decides to start a congenital anomalies surveillance programme in one region where the total number of live births per year is estimated to be 100 000. The surveillance programme will be population based and will include all fetuses or neonates identified with congenital anomalies in the region. After one year, the programme identifies 100 fetuses or neonates with congenital anomalies. The prevalence of congenital anomalies for that region will be 0.001 (10 cases per 10 000 live births).

*Example B*

A country decides to start a congenital anomalies surveillance programme in all maternity hospitals in one region, and eight hospitals will participate. Only fetuses or neonates with congenital anomalies born in one of the eight participating hospitals will be counted. The total number of births per year in the eight hospitals is estimated to be 10 000. After one year, the programme identifies 100 fetuses or neonates with congenital anomalies. The prevalence of congenital anomalies for those hospitals will be 0.01 (100 cases per 10 000 live births).

*Example C*

A country decides to start a congenital anomalies surveillance programme in a referral hospital in one region. This hospital is where prenatally identified fetuses with congenital anomalies are usually referred for delivery. The hospital typically has 1000 births per year. After one year, the hospital identifies 100 fetuses or neonates with congenital anomalies. The prevalence of congenital anomalies for that particular hospital is 0.1 (1000 cases per 10 000 live births).

Without knowing the denominator for each example, the prevalence estimate could be misinterpreted. The prevalence estimate for Example C might indicate that this country has a high prevalence of congenital anomalies, when in reality the estimate resulted from a small denominator and the site is a referral hospital. The prevalence estimates for Examples B and C represent the prevalence for eight hospitals and one referral hospital, respectively. These would not be considered true prevalence estimates. The prevalence estimate for Example A is based on the total number of live births for a population and thus it yields the most accurate prevalence estimate.

# 4. Diagnosing congenital anomalies

## Lists of selected external and internal congenital anomalies to consider for monitoring

For surveillance programmes just starting out, the following are suggested as an initial list of external congenital anomalies to consider for monitoring. They were chosen because they are relatively easy to identify at birth, have significant public health impact, and, for some congenital anomalies, there is the potential for primary prevention.

- Congenital malformations of the nervous system
  - Anencephaly
  - Craniorachischisis
  - Iniencephaly
  - Encephalocele
  - Spina bifida
  - Microcephaly
- Congenital malformations of the eye, ear, face and neck
  - Microtia/Anotia
- Cleft lip and cleft palate
  - Cleft palate alone
  - Cleft lip alone
  - Cleft palate with cleft lip
- Congenital malformations of the genital organs
  - Hypospadias
- Congenital malformations and deformations of the musculoskeletal system
  - Talipes equinovarus
  - Reduction defects of upper and lower limbs (longitudinal, transverse, and intercalary)
  - Exomphalos (omphalocele)
  - Gastroschisis

Some countries have more diagnostic resources or more developed programmes than others. For these countries, including selected internal congenital anomalies might be of interest. The following is a list of internal congenital anomalies that are commonly collected by most major congenital anomaly surveillance programmes. Considerations for selection of these anomalies included the public health significance and opportunities for prevention and intervention.

- Congenital malformations of the circulatory system
  - Common truncus (truncus arteriosus)
  - Hypoplastic left heart syndrome
  - Interrupted aortic arch
  - Pulmonary valve atresia
  - Tetralogy of Fallot
  - Transposition of the great arteries
  - Tricuspid valve atresia and stenosis
- Congenital malformations of the urinary system
  - Renal agenesis/hypoplasia
- Congenital malformations of the digestive system
  - Esophageal agenesis/hypoplasia
  - Large intestinal atresia/stenosis
  - Rectal atresia/stenosis
- Chromosomal abnormalities
  - Trisomy 21 (Down syndrome)

As participating facilities or hospitals and surveillance programme personnel gain experience during the development process, additional congenital anomalies such as the internal anomalies listed above (or others) can be added in a stepwise fashion, starting with those that are of special interest or concern to the country or region, and eventually could include all of the major congenital anomalies listed in Chapter XVII of the ICD-10: "Congenital malformations, deformations and chromosomal anomalies (Q00–Q99)". However, high-quality data on a smaller number of congenital anomalies will be more useful for public health than poor-quality data on all congenital anomalies.

The list of congenital anomalies included in this manual is not exhaustive. Programmes interested in more detailed information on the inclusion of additional defects or in prenatal diagnosis in congenital anomalies surveillance programmes can find some useful and practical suggestions and tips in the guidelines developed by the NBDPN in the USA.

The decision on selecting which defects to include in a surveillance programme should be evaluated based on available resources. If the fetus or neonate has at least one eligible congenital anomaly, this and any other observable major and minor congenital anomalies are described in detail and included on the abstraction form (see Appendix G).

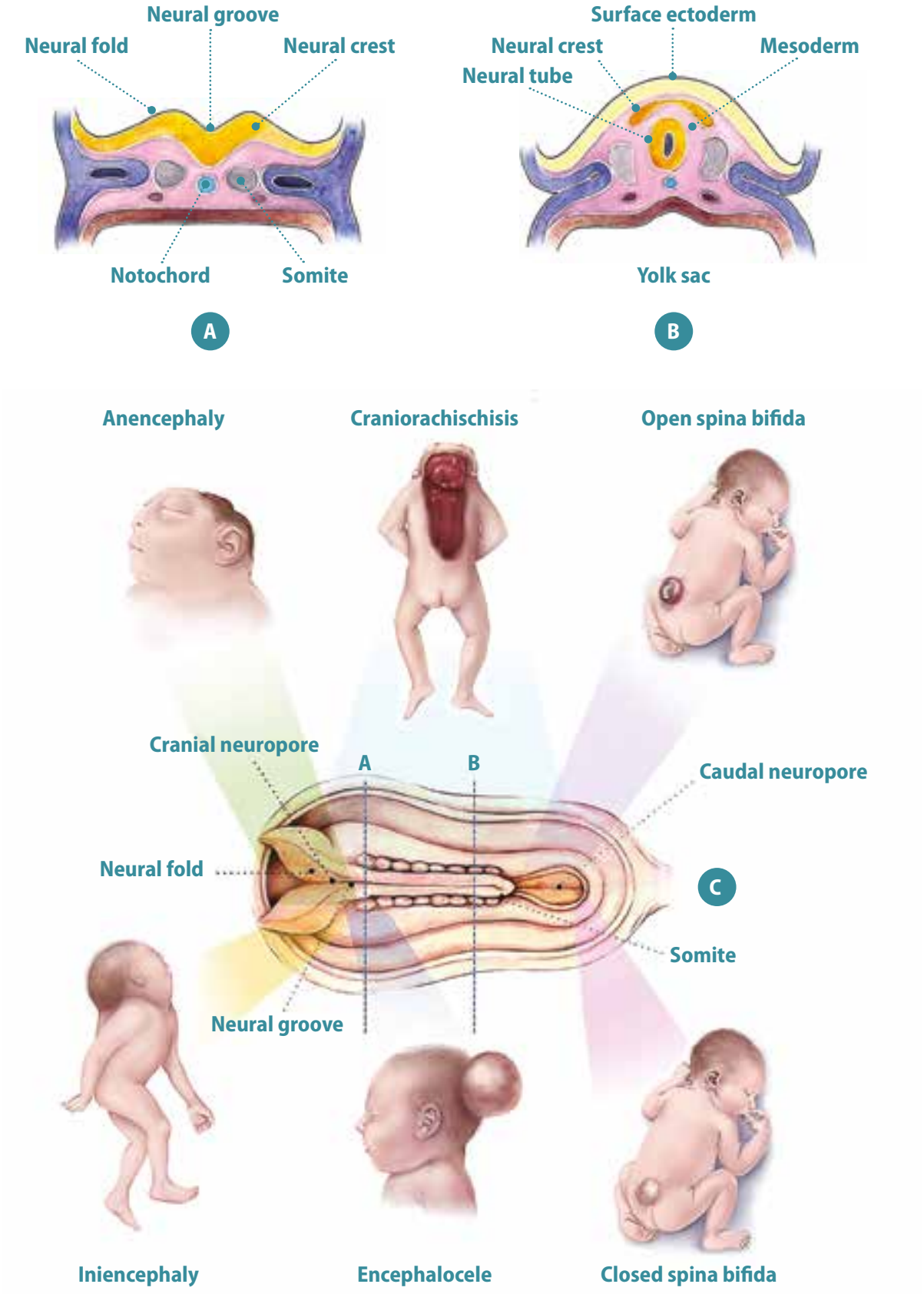
When coding the congenital anomalies, it is important to be as specific as possible and to avoid using codes that are nonspecific or too general. Please refer to Chapter 6 for more information about coding.

## Congenital anomalies of the nervous system: Neural tube defects

Neural tube defects (NTDs) affect the brain and spinal cord and are among the most common of the congenital anomalies (see Fig. 4.1). *Panel A* shows a cross section of the rostral end of the embryo at approximately three weeks after conception, showing the neural groove in the process of closing, overlying the notochord. The neural folds are the rising margins of the neural tube, topped by the neural crest, and demarcate the neural groove centrally. *Panel B* shows a cross section of the middle portion of the embryo after the neural tube has closed. The neural tube – which will ultimately develop into the spinal cord – is now covered by surface ectoderm (later, the skin). The intervening mesoderm will form the bony spine. The notochord is regressing. *Panel C* shows the developmental and clinical features of the main types of NTDs. The diagram in the centre is a dorsal view of a developing embryo, showing a neural tube that is closed in the centre but still open at the cranial and caudal ends. The dotted lines marked A and B refer to the cross sections shown in *panels A and B*. Shaded bars point to the region of the neural tube relevant to each defect.

The most prevalent types of NTDs are anencephaly, encephalocele and spina bifida. In anencephaly, the absence of the brain and calvaria can be total or partial. Craniorachischisis is characterized by anencephaly accompanied by a contiguous bony defect of the spine and exposure of neural tissue. In open spina bifida, a bony defect of the posterior vertebral arches (in this case, the lower thoracic vertebrae) is accompanied by herniation of neural tissue and meninges and is not covered by skin. In iniencephaly, dysraphia in the occipital region is accompanied by severe retroflexion of the neck and trunk. In encephalocele, the brain and meninges herniate through a defect in the calvaria. In closed spina bifida, unlike open spina bifida, the bony defect of the posterior vertebral arches (in this case, the lumbar vertebrae), the herniated meninges and neural tissue are covered by skin.

**Fig. 4.1. Neural tube defects**




*Source*: adapted from: Botto et al. (1999) *(27)*. Reproduced with permission from the publisher.

Anencephaly is a condition characterized by a total (holo) or partial (mero) absence of the brain with absence of the cranial vault (calvarium) and covering skin. Anencephaly is an NTD that results from a failure of the anterior (rostral) portion of the embryonic neural tube (anterior neuropore) to close properly. Many affected fetuses are either stillborn or die shortly after birth. In locations where prenatal diagnosis is prevalent and termination of pregnancy is permitted, fetuses with anencephaly might be missed if surveillance does not include this outcome. The calvarial defect extends through the foramen magnum in infants with holoanencephaly (Fig. 4.2, *panel a* – total absence), which is more common than meroanencephaly (Fig. 4.2, *panel b* – partial absence) in which the foramen magnum is not involved.

## Relevant ICD-10 codes

Q00.0 Anencephaly

## Diagnosis

***Prenatal.*** Anencephaly is readily diagnosed. However, anencephaly could be confused with craniorachischisis, acrania or amniotic band syndrome. For this reason, a prenatal diagnosis of anencephaly should always be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** The newborn examination confirms the diagnosis and will distinguish anencephaly from the other rare anomalies that might involve the brain and cranium. In anencephaly, the eyes are normally formed but tend to bulge as a result of the absent frontal portion of the cranial vault. The cerebellum, brain stem and spinal cord are intact.

## Clinical and epidemiologic notes

Distinguishing anencephaly from the other abnormalities of the brain and spinal cord is important because these conditions have different causes and associated anomalies. With careful examination, the diagnosis of anencephaly is straightforward. Rare conditions that might be misdiagnosed as anencephaly include acrania, acephaly, and atypical "anencephaly" in amniotic band spectrum.

Acrania is a term that refers to acalvaria, or absence of the neurocranium (calvarial bones, dura mater and associated muscles), and is thought to be unrelated to NTDs. However, in some countries, the term acrania is used synonymously with the term anencephaly, so it is important to review clinical findings to ensure appropriate classification. Acephaly – absence of the head – is part of a pattern seen in acardiac twins. In the amniotic band spectrum and limb-body wall spectrum, the skull and brain might be affected in a way that resembles an unusual form of "anencephaly". However, there are often other findings (facial schisis, limb and ventral wall anomalies, bands) that make the diagnosis straightforward and allow the differentiation from typical anencephaly.

Anencephaly is a fatal condition with rare survival past the first few days of birth and is often an isolated (approximately 70–80%), non-syndromic anomaly. For this reason, it is crucial to report all findings and obtain good clinical photographs for the expert reviewer. Anencephaly is reported to occur more commonly in females.

Non-genetic risk factors include pregestational diabetes, folate insufficiency/deficiency, obesity, and hyperthermia (e.g. fever) in early pregnancy. Adequate periconceptional use of folic acid (as a supplement or through fortification) can prevent most cases of anencephaly.

The birth prevalence of anencephaly varies widely, between 0.8 to 16 per 10 000 births. Median prevalence, when stratified by country income level, decreases with increasing income categories. Prevalence is also higher among areas without mandated folic acid fortification of foods.

## Inclusions

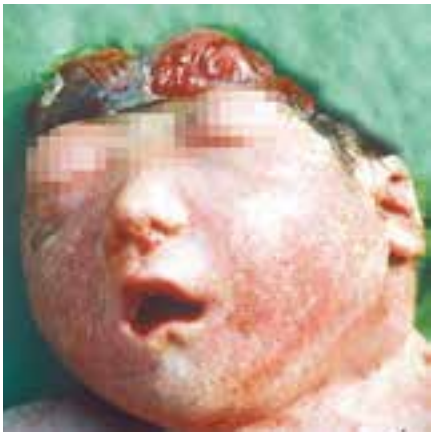
Q00.0 Anencephaly

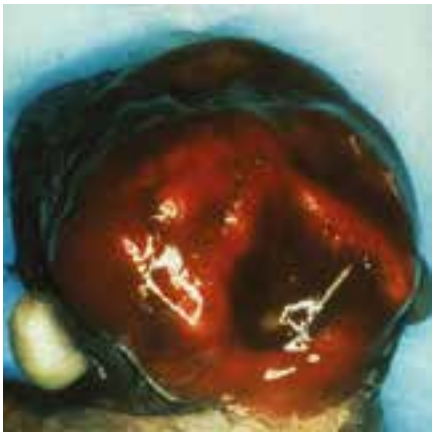
Note that holoanencephaly and meroanencephaly are coded the same and are counted together.

**Fig. 4.2. Types of anencephaly**

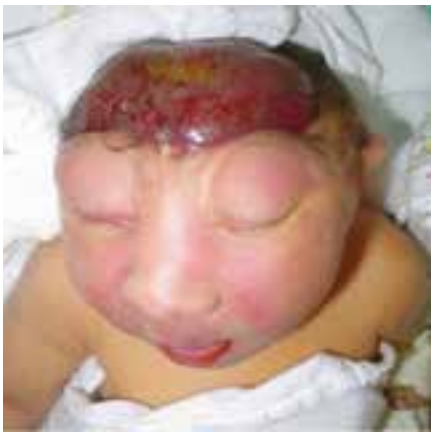
Anencephaly (Q00.0)

a Holoanencephaly (total)





b Meroanencephaly (partial)



*Photograph sources:* Latin American Collaborative Study of Congenital Malformations (ECLAMC); CDC–Beijing Medical University collaborative project.

## Exclusions

Acrania, acephaly: These have the same code as anencephaly (Q00.0) but must be excluded from prevalence counts of anencephaly.

Q00.1 Craniorachischisis
Q00.2 Iniencephaly
Q00.20 Iniencephaly, open
Q00.21 Iniencephaly, closed

## Checklist for high-quality reporting

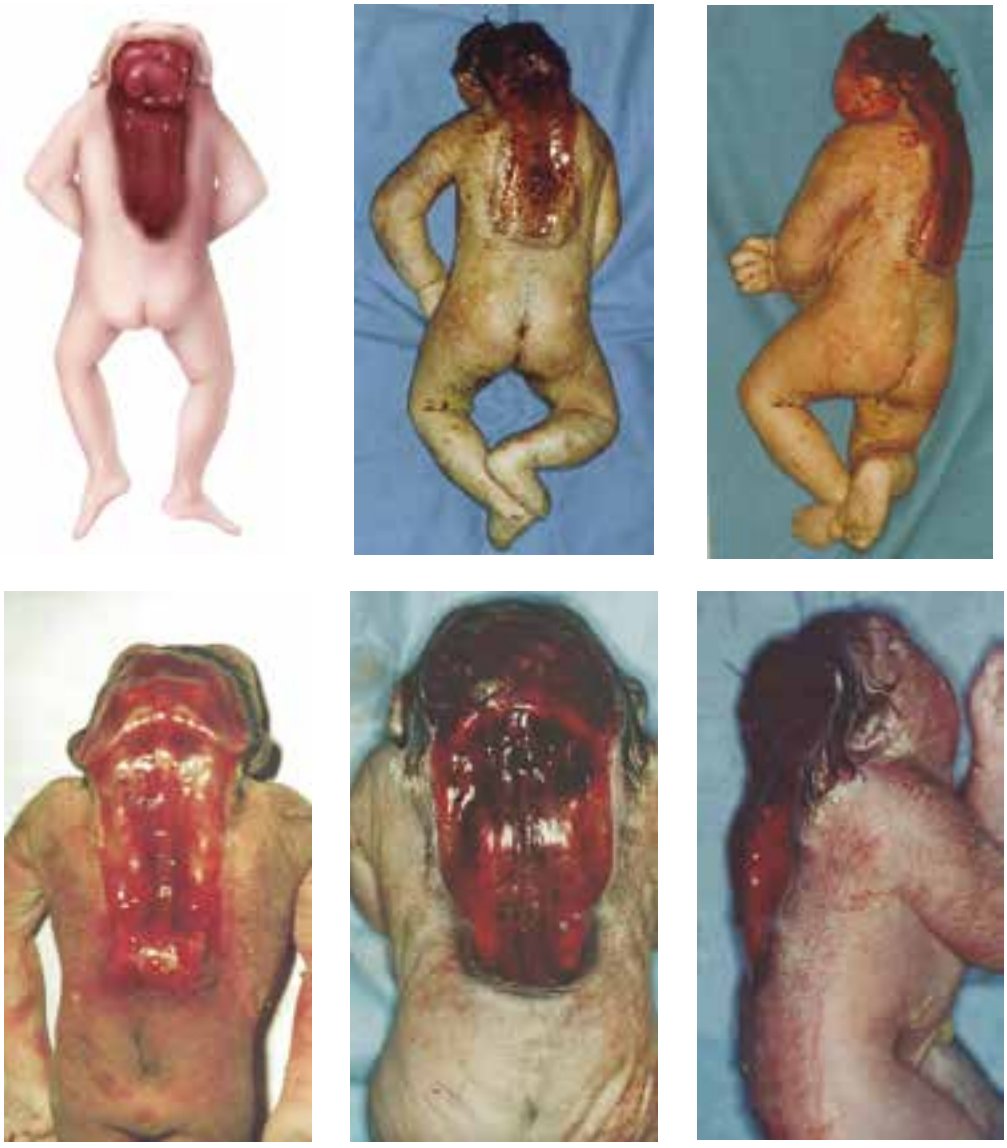
| Anencephaly – Documentation Checklist |
|---|
| ☐ **Describe defect in detail:**<br>▸ Extent – whether holoanencephaly or meroanencephaly.<br>▸ Cervical spine – document no contiguous defects.<br>▸ Whether a non-contiguous spina bifida is present (location).<br>▸ Whether evidence of amniotic bands is present. |
| ☐ **Take and report photographs:** *Show clearly* the missing cranium; can be crucial for review. |
| ☐ **Describe evaluations to find or rule out related and associated anomalies:**<br>▸ Eyes protruding but normally developed (do not include as an associated anomaly).<br>▸ Head circumference will be small – do not code as microcephaly. |
| ☐ **Report whether autopsy (pathology) findings are available and if so, report the results.** |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | ▸ Review sample for documentation of key descriptor (absence of calvarium and brain, not covered by skin; complete or incomplete).<br>▸ Take and attach photographs – essential for review and correct classification.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations. |
| **Coding** | ▸ Code as Q00.0.<br>▸ Avoid coding acrania and acephaly (extremely rare; the latter only in some monozygotic twin pregnancies).<br>▸ Track and minimize cases coded with generic ICD-10 RCPCH code Q00.<br>▸ Track and review unusual codes such as Q00.1 (incomplete anencephaly, hemianencephaly, hemicephaly).<br>▸ Code non-contiguous spina bifida separately (Q05.6–Q05.8). |
| **Clinical classification** | ▸ Track proportion of anomalies and syndromes occurring with anencephaly (approximately < 30% combined is expected). Do not include findings that are a direct consequence of the condition (such as prominent eyes, talipes, etc.).<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence – prevalence varies by country/region, country income level and race/ethnicity. A birth prevalence (including stillbirths and pregnancy terminations) < 6 per 10 000 births in a country without widespread and proven folic acid fortification strongly suggests under-ascertainment. |

Craniorachischisis is a very serious NTD characterized by the combination of anencephaly (absence of the brain and cranial vault, without skin covering) with a contiguous bony defect of the spine (also without meninges covering the neural tissue – rachischisis) (see Fig. 4.3). Spine involvement can be limited to the cervical spine where it might be difficult to clinically differentiate from holoanencephaly. Rarely, the open defect can extend to the thoracic or even lumbosacral spine (craniorachischisis totalis). Craniorachischisis results from failed closure of the anterior neuropore, but the mechanism leading to failure of closure of the contiguous spine is not well understood. In some infants, there is accompanying retroflexion of the spine, which results in a body habitus resembling another rare NTD, iniencephaly (see Fig. 4.5). Because of the early lethality of this condition, many affected fetuses are either stillborn or result in a termination of pregnancy (if prenatally diagnosed and pregnancy terminations are permitted).

**Fig. 4.3. Craniorachischisis**



*Photograph source:* CDC–Beijing Medical University collaborative project.

**Fig. 4.4. Craniorachischisis with spinal retroflexion**

*Photograph source:* CDC-Beijing Medical University collaborative project.

## Relevant ICD-10 codes

Q00.1 Craniorachischisis

## Diagnosis

***Prenatal.*** Craniorachischisis is readily diagnosed using ultrasound. However, it can be confused with other defects involving the brain – anencephaly, acrania or amniotic band syndrome. For this reason, a prenatal diagnosis of craniorachischisis should always be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** Careful examination of the fetus or newborn can confirm the diagnosis of craniorachischisis and distinguish it from the other rare anomalies that involve the brain, cranium and spine. In craniorachischisis, the eyes are usually normally formed but tend to bulge as a result of the absent frontal portion of the cranial vault, and the neck might appear to be shortened and is sometimes retroflexed. The craniorachischisis lesion is always open and the spinal lesion is always continuous with the anencephaly.

## Clinical and epidemiologic notes

Distinguishing craniorachischisis from other abnormalities of the brain and spinal cord is important because these conditions have different causes and associated anomalies. With careful examination, the diagnosis of craniorachischisis is straightforward. Craniorachischisis is a uniformly fatal condition and is often isolated and non-syndromic. However, the co-occurrence of cleft lip and palate, omphalocele, limb defects, cyclopia or trisomy 18 has been reported in some cases, but no robust population-based studies have been conducted to understand the proportion of isolated cases or associated anomalies. For this reason, it is very important to report all physical findings and obtain good clinical photographs for the expert reviewer. Craniorachischisis is reported to occur more commonly in females.

Craniorachischisis is a rare defect and is most prevalent in countries with an overall high prevalence of NTDs. Because of the rarity of craniorachischisis, studies of non-genetic risk factors are challenging. Presumably the non-genetic risk factors should be similar to that of other NTDs, including pregestational diabetes, obesity, and hyperthermia (e.g. fever) in early pregnancy, and folic acid insufficiency/deficiency. Adequate periconceptional use of folic acid (as a supplement or through fortification) might also prevent craniorachischisis.

Few reports on NTD prevalence specifically mention craniorachischisis. The reported prevalence varies widely, with estimates ranging between 0.1 to 10.7 per 10 000 live births. Craniorachischisis is counted when calculating total NTD prevalence.

## Inclusions

Q00.1 Craniorachischisis

## Exclusions

Q00.0 Anencephaly, acrania, acephaly
Q00.2 Iniencephaly
Q00.20 Iniencephaly, open
Q00.21 Iniencephaly, closed

## Checklist for high-quality reporting

**Craniorachischisis – Documentation Checklist**

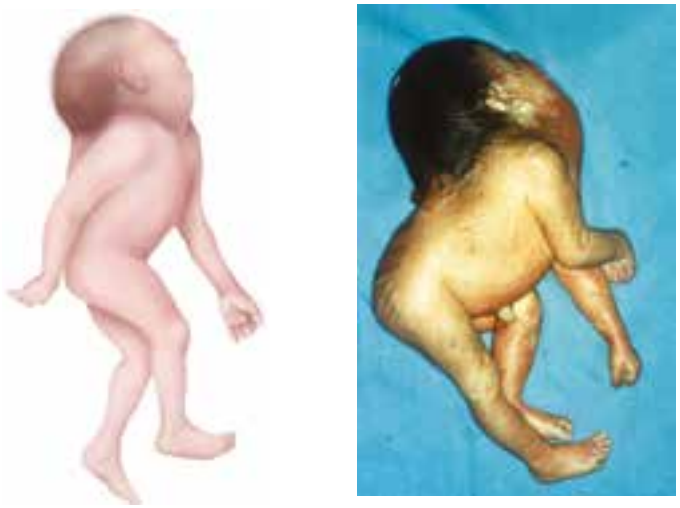
- ☐ **Describe in detail:**
  - Defect – overall presentation.
  - Extent of spinal involvement (cervical spine or lower) – especially comment on and document the fact that the head involvement (anencephaly) and the spine defect are contiguous, without intervening normal appearing spine.
  - Retroflexion of neck and spine – this is more typical of iniencephaly, so important to note.
  - If amniotic bands are present – disruptions by amniotic bands could possibly mimic severe atypical NTDs.
  - If the spinal lesion and the anencephaly are separated by intact skin, the case would be considered a multiple NTD and not craniorachischisis.
- ☐ **Take and report photographs:** *Show clearly* the missing cranium and spine; can be crucial for review.
- ☐ **Describe evaluations to find or rule out related and associated anomalies:**
  - Orbits – usually protruding but normally developed (do not include as an associated anomaly).
  - Head circumference will be small – do not code as microcephaly.
  - Spina bifida (mention but do not code contiguous defects).
  - Other anomalies or chromosomal abnormality.
  - Iniencephaly (do not code).
- ☐ **Report whether autopsy (pathology) findings are available and if so, report the results.**

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | ▸ Review sample for documentation of key descriptor (absence of skull and brain, not covered by skin; spinal defect).<br>▸ Take and attach photographs – essential for review and correct classification.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations. |
| **Coding** | ▸ Code as Q00.1 (if anencephaly and open spina bifida are contiguous).<br>▸ Do not code the contiguous spina bifida as a separate defect. Only code if spina bifida is not contiguous with craniorachischisis. |
| **Clinical classification** | ▸ Track proportion of anomalies and syndromes occurring with craniorachischisis. Do not include findings that are a direct consequence of the condition (such as prominent eyes, talipes, etc.).<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence – prevalence varies by country/region, country income level and race/ethnicity. |

Iniencephaly is a rare and complex NTD involving the occiput and inion, resulting in extreme retroflexion of the head, variably combined with occipital encephalocele or rachischisis of the cervical or thoracic spine. The cranium is typically closed and skin covered, and an occipital encephalocele can be present. The face appears as upward looking; the neck, because of spine anomalies, is very short and might appear to be missing (see Fig 4.5). The occipital bone is abnormal leading to an enlarged foramen magnum with fusion of the cervical and thoracic vertebrae. The internal spine abnormalities result in the skin of the face being directly connected to the chest skin and the skin of the scalp continuous with the skin of the back. Many affected fetuses end in a miscarriage or are stillborn.

**Fig. 4.5. Iniencephaly**



*Photograph source:* CDC-Beijing Medical University collaborative project.

## Relevant ICD-10 codes

Q00.2 Iniencephaly

## Diagnosis

***Prenatal.*** Iniencephaly might be difficult to diagnose precisely by ultrasound in the prenatal period, as it can be confused with other defects involving the brain and spine – encephalocele or craniorachischisis, as well as teratomas, goiter, lymphangioma and some syndromes. For this reason, a prenatal diagnosis of iniencephaly should always be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** Careful examination of the fetus or newborn can confirm the diagnosis of iniencephaly and distinguish it from the other rare anomalies that involve the brain, cranium and spine. In iniencephaly, the cranial vault is always closed and the neck might appear shortened or not present.

## Clinical and epidemiologic notes

Distinguishing iniencephaly from other abnormalities of the brain and spinal cord is important because these conditions have different causes and associated anomalies. With careful examination and radiograph confirmation, the diagnosis of iniencephaly is usually straightforward; however, the presence of an accompanying encephalocele or spina bifida might be confusing in some instances. The majority (84%) of affected infants have additional anomalies: micrognathia, cleft lip and palate, cardiovascular disorders, diaphragmatic hernias, and gastrointestinal malformations have been reported. Chromosomal conditions associated with iniencephaly include trisomy 13 and 18, and monosomy X. However, no population-based studies have been conducted to understand the proportion of isolated versus syndromic cases or the associated anomalies. It is crucial to report all physical findings and obtain good clinical photographs for the expert reviewer. Iniencephaly is reported to occur more commonly in females. Iniencephaly is a uniformly fatal condition.

Observational studies of non-genetic risk factors for iniencephaly are challenging given its very low prevalence. Presumably, since iniencephaly is an NTD, the non-genetic risk factors should be similar to other NTDs – pregestational diabetes, obesity, and hyperthermia (e.g. fever) in early pregnancy, and folic acid insufficiency/deficiency. Adequate periconceptional use of folic acid (as a supplement or through fortification) might also prevent iniencephaly.

Few reports on NTD prevalence specifically mention iniencephaly. The prevalence of iniencephaly is reported to vary widely between 0.1 to 10 per 10 000 births. Iniencephaly is counted when calculating total NTD prevalence.

## Inclusions

Q00.2 Iniencephaly

## Exclusions

Q00.0 Anencephaly, acrania, acephaly
Q00.1 Craniorachischisis

## Checklist for high-quality reporting

**Iniencephaly – Documentation Checklist**

- ☐ **Describe in detail:**
  - Defect description – note in particular whether cranium is skin covered, head retroflexed.
  - Presence or absence of occipital encephalocele.
  - Presence or absence of spina bifida (open or closed).
  - Report other anomalies.
- ☐ **Take and report photographs:** *Show clearly* the lateral view of the cranium and spine; can be crucial for review.
- ☐ **Describe evaluations to find or rule out related and associated anomalies:**
  - Head circumference might be large – do not code as hydrocephaly.
  - Spina bifida (code as non-contiguous defect).
  - Encephalocele (code although contiguous defect).
  - Include radiographs (or report) of the spine if performed.
- ☐ **Report whether autopsy (pathology) findings are available and if so, report the results.**

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | ▸ Review sample for documentation of key descriptor (intact cranium, head retroflexed).<br>▸ Take and attach photographs – essential for review and correct classification.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations. |
| **Coding** | ▸ Code as Q00.2.<br>▸ Code spina bifida (e.g. open, lumbar) if separate defect from iniencephaly.<br>▸ Code encephalocele (occipital) to better describe type of iniencephaly, but not counted in analyses of encephaloceles. |
| **Clinical classification** | ▸ Track proportion of anomalies or syndromes occurring with iniencephaly.<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence – prevalence varies by country/region, country income level and race/ethnicity. |

Encephalocele is an NTD characterized by a pedunculated or sessile cystic, skin-covered lesion protruding through a defect in the cranium (skull bone). Encephaloceles can contain herniated meninges and brain tissue (encephalocele or meningoencephalocele) or only meninges (cranial meningocele), and can vary in location and size (see Fig. 4.6). The most common type of encephalocele is occipital (approximately 74%), followed by parietal (13%) encephalocele.

Encephalocele is more likely to occur with other unrelated structural anomalies or syndromes than either anencephaly or spina bifida.

**Fig. 4.6. Encephalocele**


*Photograph sources:* CDC–Beijing Medical University collaborative project; Dr Jaime Frias.

## Relevant ICD-10 codes

Q01.0 Frontal encephalocele
Q01.1 Nasofrontal encephalocele
Q01.2 Occipital encephalocele
Q01.80 Parietal encephalocele
Q01.81 Orbital encephalocele
Q01.82 Nasal encephalocele
Q01.83 Nasopharyngeal encephalocele
Q01.9 Encephalocele, unspecified

## Diagnosis

***Prenatal.*** Encephalocele can be diagnosed prenatally using ultrasound, and might co-occur with a number of brain abnormalities such as Dandy-Walker malformation or a Chiari malformation. Encephaloceles might be confused with the amniotic band spectrum of anomalies. For this reason, a prenatal diagnosis of encephalocele should always be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** The newborn examination, x-ray and computed tomography (CT) or magnetic resonance imaging (MRI) confirm the diagnosis and distinguish it from the other anomalies that might involve the brain and cranium.

## Clinical and epidemiologic notes

Distinguishing encephalocele from the other abnormalities of the brain and cranium is important because this condition has different causes and associated anomalies. The diagnosis of an encephalocele requires a careful examination with radiographs (to evaluate the intracranial connection) and imaging (MRI, CT scan to determine the content of the cephalocele).

Approximately 20% of infants diagnosed with an encephalocele will have at least one additional unrelated major birth defect. Encephaloceles are also known to occur in over 30 syndromes, which include both single-gene disorders (e.g. Meckel–Gruber syndrome) and chromosomal anomalies (e.g. trisomies 13 and 18). For this reason, it is crucial to report all findings and obtain good clinical photographs for the expert reviewer.

In the amniotic band spectrum, the skull and brain might resemble an "encephalocele". However, the occurrence of other findings (facial schisis, limb and ventral wall anomalies, strands of amniotic sac tissue) points towards the diagnosis of an amniotic band disruption and allows the differentiation from encephalocele.

As with other NTDs, non-genetic risk factors might include pregestational diabetes, obesity, and hyperthermia (e.g. fever) in early pregnancy, and folic acid insufficiency/deficiency. Adequate preconceptional use of folic acid (as a supplement or through fortification) might prevent some cases of encephalocele.

The reported birth prevalence of encephalocele varies widely worldwide, with a range between 0.1 to 26.5 per 10 000 births. The location of the encephalocele also varies geographically. Most frequently, encephaloceles are located in the occipital area, except in South-East Asia, where anterior location (frontal or nasofrontal) is most common.

## Inclusions

Q01.0 Frontal encephalocele
Q01.1 Nasofrontal encephalocele
Q01.2 Occipital encephalocele
Q01.80 Parietal encephalocele
Q01.81 Orbital encephalocele
Q01.82 Nasal encephalocele
Q01.83 Nasopharyngeal encephalocele
Q01.9 Encephalocele, unspecified

## Exclusions

Q79.8 Amniotic band syndrome

## Checklist for high-quality reporting

| Encephalocele – Documentation Checklist |
|---|
| ☐ **Describe in detail:**<br>▸ Defect location – occipital, frontal, nasal, parietal, etc.<br>▸ Extent – size and whether brain is present in the sac.<br>▸ Skin covering – is the norm with encephalocele (but could be ruptured).<br>▸ Other anomalies – internal and external anomalies, including polydactyly, renal anomalies, etc.<br>▸ Cephalohematoma or caput succedaneum (benign scalp swelling) – can be confused with encephalocele.<br>▸ Amniotic bands or limb-body wall anomalies – check if present and describe. |
| ☐ **Take and report photographs:** *Show clearly* the cranial lesion; can be crucial for review. |
| ☐ **Describe evaluations to find or rule out related and associated anomalies:**<br>▸ Head circumference might be small – do not code as microcephaly.<br>▸ Hydrocephalus might be present – do not code as hydrocephalus.<br>▸ Genetic or chromosomal testing performed, where available.<br>▸ Specialty consultations and surgical reports. |
| ☐ **Report whether autopsy (pathology) findings are available and if so, report the results.** |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | ▸ Review sample for documentation of key descriptor (location of lesion and size, skin covered or not).<br>▸ Take and attach photographs – essential for review and correct classification.<br>▸ Report results from specialty consultations, imaging and surgery.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations. |
| **Coding** | ▸ Code as Q01.xx for specific location of encephalocele, if documented.<br>▸ Code a non-contiguous spina bifida separately (Q05.6–Q05.8).<br>▸ Code Dandy-Walker anomaly or other brain anomalies.<br>▸ Code non-central nervous system (CNS) malformations. |
| **Clinical classification** | ▸ Track proportion of anomalies and syndromes occurring with encephalocele (~20–30% is expected). Cases with findings related or secondary to encephalocele (such as hydrocephalus in occipital encephalocele, absent corpus callosum, dorsal cysts, and Dandy-Walker anomaly) are classified as isolated.<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence – prevalence varies by country/region, country income level and race/ethnicity.<br>▸ Compare prevalence by sub-types: Expect occipital > parietal, frontal, nasal > nasopharyngeal. |

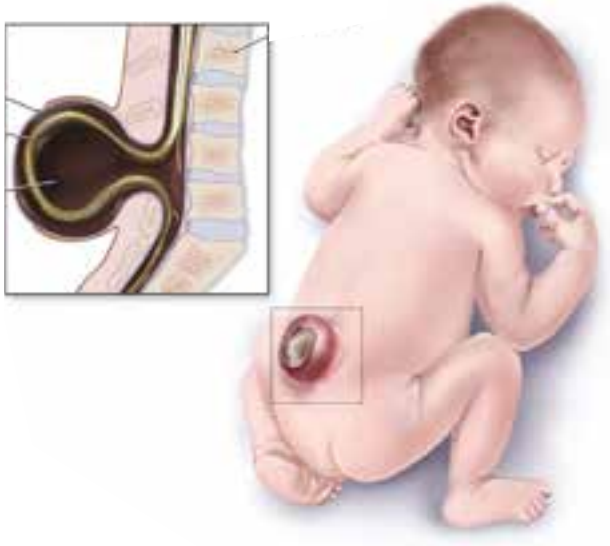
Spina bifida is a general term used to describe an NTD of the spine in which part of the meninges (Fig 4.7, *panel a:* meningocele) or spinal cord (Fig. 4.7, *panel c:* myelocele or myeloschisis) or both (Fig. 4.7, *panel b:* myelomeningocele) protrudes through an opening in the vertebral column. Spina bifida is the most common type of NTD. Hydrocephalus is a common complication, especially among children with open meningomyeloceles.

Specific types of spina bifida include:

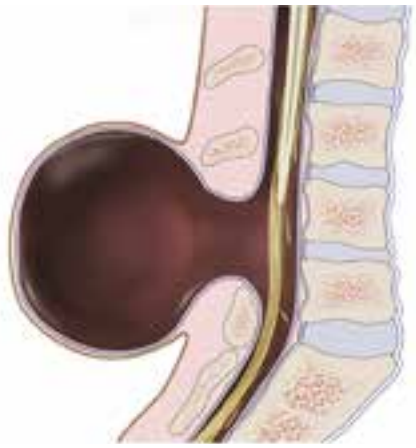
- Meningocele: Characterized by herniation of the meninges through a spinal defect, forming a cyst filled with cerebrospinal fluid. This lesion does not contain spinal cord, but might have some nerve elements.
- Meningomyelocele (myelomeningocele): Characterized by a protrusion of the meninges and the spinal cord through an opening in the vertebral column.
- Myelocele (myeloschisis, rachischisis): Characterized by a splayed vertebral column and plaque-like spinal cord without membrane or skin covering.

**Fig. 4.7. Spina bifida**

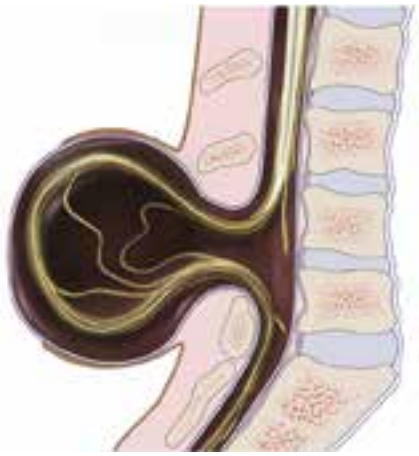
Spina Bifida (Open Defect)



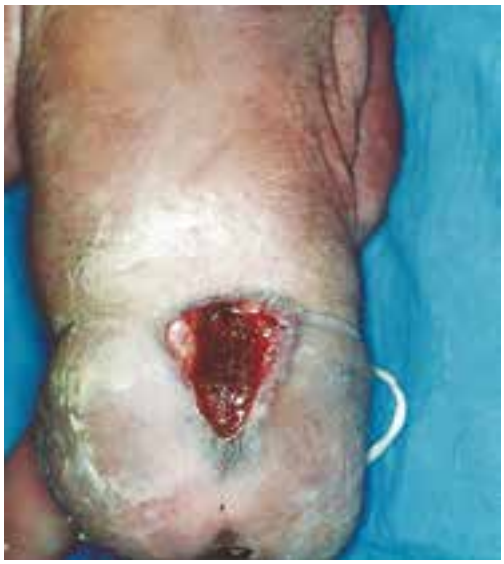
a. Meningocele (Q05)



b. Myelomeningocele (Q05)



c. Myelocele or myeloschisis (Q05)



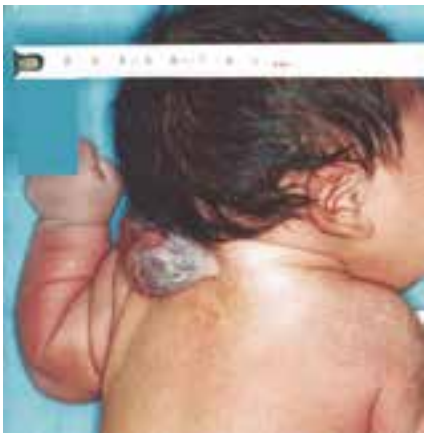
*Photograph source:* CDC–Beijing Medical University collaborative project.

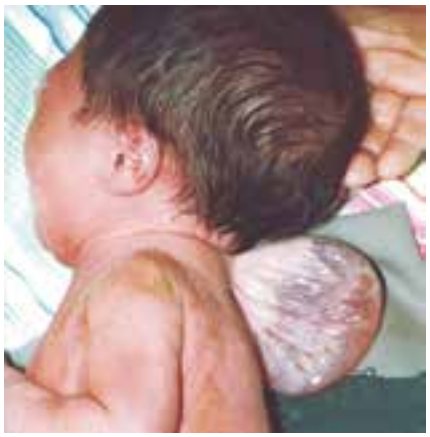
Spina bifida can occur at any level of the spinal cord, including cervical (Fig.4.8), thoracic (Fig.4.9), lumbar (Fig.4.10), and sacral (Fig.4.11).

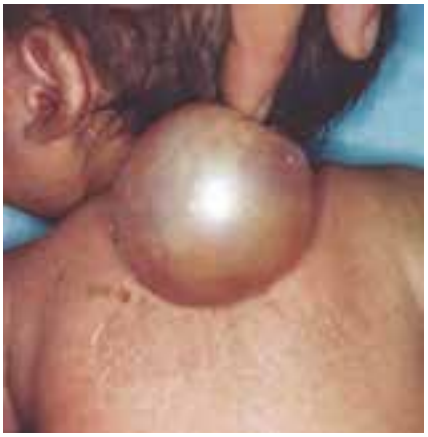
## Spina bifida lesion levels

### *Cervical spina bifida*

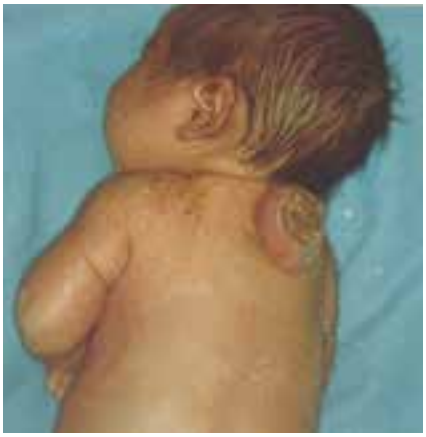
**Fig. 4.8. Cervical spina bifida**







Cervical spina bifida with hydrocephalus (Q05.0)



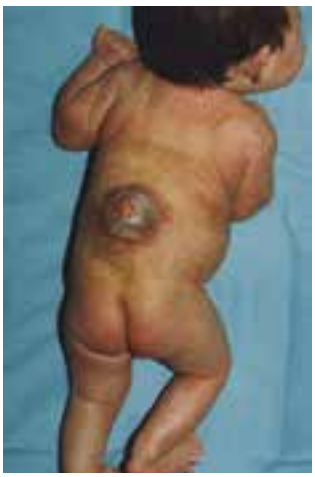
Cervical spina bifida without hydrocephalus (Q05.5)

*Photograph source:* CDC–Beijing Medical University collaborative project.

### *Thoracic spina bifida*

**Fig. 4.9. Thoracic spina bifida**

Thoracic spina bifida with hydrocephalus (Q05.1)

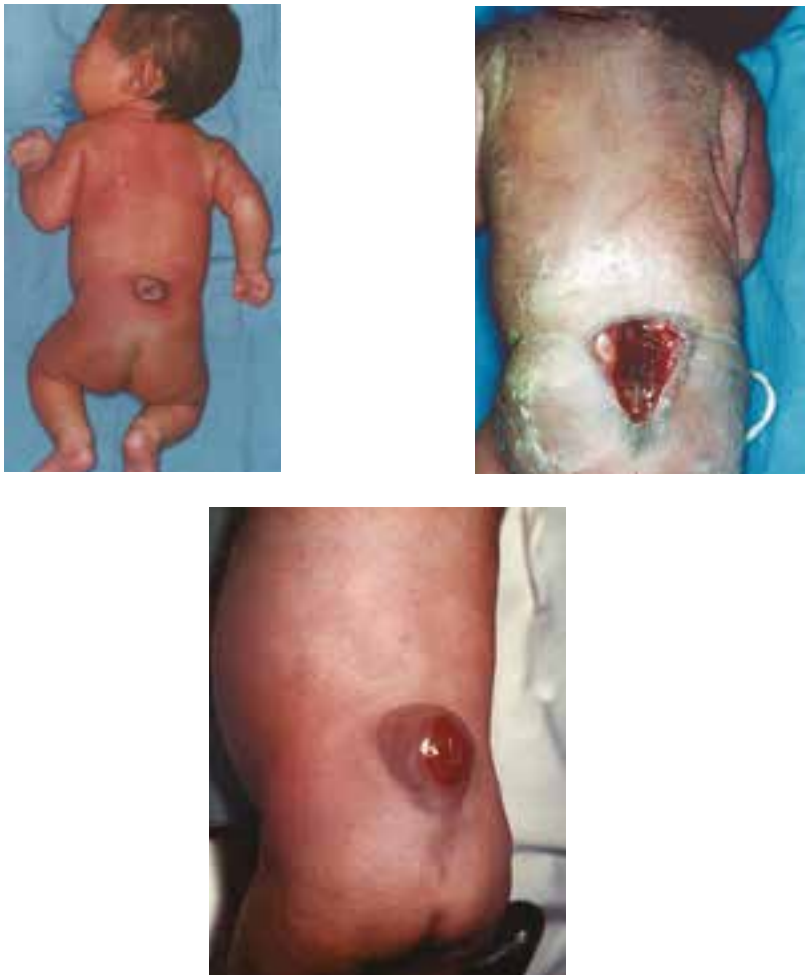


Thoracic spina bifida without hydrocephalus (Q05.6)

*Photograph source:* CDC–Beijing Medical University collaborative project.

*Lumbar spina bifida*

**Fig. 4.10. Lumbar spina bifida**



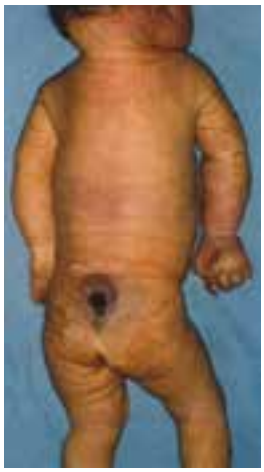
Lumbar spina bifida with hydrocephalus (Q05.2)

Lumbar spina bifida without hydrocephalus (Q05.7)

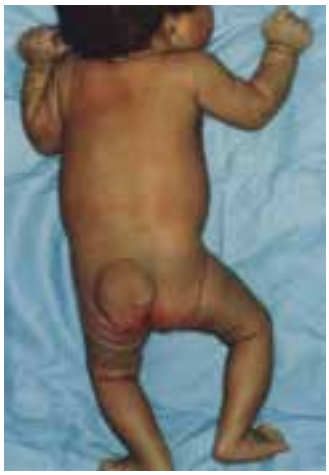
*Photograph sources*: CDC–Beijing Medical University collaborative project; Idalina Montes, MD, and Rafael Longo, MD, FACS, Puerto Rico.

### *Sacral spina bifida*

**Fig. 4.11. Sacral spina bifida**



Sacral spina bifida with hydrocephalus (Q05.3)



Sacral spina bifida without hydrocephalus (Q05.8)

*Photograph source:* CDC–Beijing Medical University collaborative project.

The lumbar spine is the most common location for spina bifida, followed by sacral, thoracic and cervical. Spina bifida lesions are designated as "open" if they are membrane covered and "closed" if covered by normal-appearing skin. Myelomeningocele is the most common type of spina bifida, constituting about 90% of all cases. Myelomeningoceles (which are usually open) can be clinically severe and disabling, and can cause a sequence of related findings (e.g. Chiari II malformation, hydrocephalus, hip dislocation, talipes, lower limb paralysis, and loss of sphincter control including neurogenic bladder). For infants with myelomeningocele, nerve function is intact above the lesion; therefore, lower lesions have greater preservation of neurologic function.

Infants that have meningoceles (containing only meninges and cerebral spinal fluid typically with normal structure and location of the spinal cord and nerves) experience considerably less clinical impact.

Lipomeningoceles, or lypomeningomyeloceles, are made up of a midline mass of fatty tissue (lipoma) with various amounts of tissue attached to the lower end of the spinal cord (the filum terminale). Often lipomeningo(myelo)celes are covered with a hemangioma, a patch of hair, or skin that can appear normal or have pigmentary changes. Many programmes do not classify

lipomeningo(myelo)celes as an NTD. Therefore, it is critically important when developing a case definition for spina bifida to determine whether lipomeningo(myelo)celes will be included or not, and then apply the case definition consistently. If a programme chooses to include lipomeningo(myelo)celes, the most common ICD-10 Royal College of Paediatrics and Child Health (RCPCH) code used is Q05.4 – "Spina bifida unspecified". Other terminal defects – such as myelocystocele (which might present as a sacral mass), or occult spinal dysraphisms such as split spinal cord malformation, tethered cord syndrome, or spinal lipomas, among others – are also not classified as NTDs and are coded as Q06.8 – "Other specified congenital malformations of spinal cord". Spina bifida occulta is a defect in the posterior vertebral arches without neural involvement, most commonly at the lumbosacral junction, and is also not classified as an NTD. The RCPCH code for this defect is Q76.0 –"Spina bifida occulta".

## Relevant ICD-10 codes

Q05.0 Cervical spina bifida with hydrocephalus
Q05.1 Thoracic spina bifida with hydrocephalus
Q05.2 Lumbar spina bifida with hydrocephalus (includes lumbosacral spina bifida with hydrocephalus)
Q05.3 Sacral spina bifida with hydrocephalus
Q05.4 Unspecified spina bifida with hydrocephalus
Q05.5 Cervical spina bifida without hydrocephalus
Q05.6 Thoracic spina bifida without hydrocephalus
Q05.7 Lumbar spina bifida without hydrocephalus (includes lumbosacral spina bifida without hydrocephalus)
Q05.8 Sacral spina bifida with hydrocephalus
Q05.9 Spina bifida, unspecified

## Diagnosis

***Prenatal.*** Spina bifida might be diagnosed prenatally using ultrasound. However, if the entire spine is difficult to image, distinguishing whether the lesion is open or closed is challenging. Results of maternal serum screening for alpha fetoprotein (AFP), if available, might help to determine if the lesion is open or closed, as AFP seeps out of the open lesion into the amniotic fluid and subsequently into the mother's blood. Spina bifida is sometimes confused with sacrococcygeal teratoma, isolated scoliosis/kyphosis or amniotic band syndrome. Therefore, a prenatal diagnosis of spina bifida should be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** The newborn examination usually confirms the diagnosis. Neurologic impairment will vary by spina bifida type, level of lesion and severity. Imaging (when available) can provide additional information to characterize the location, extent and content of the lesion, as well as the presence or absence of frequently co-occurring brain findings (e.g. hydrocephalus, Chiari II malformation).

## Clinical and epidemiologic notes

Distinguishing spina bifida from the other abnormalities of the spine is important because these conditions have different causes and associated anomalies. With careful examination, the diagnosis of spina bifida is straightforward, but imaging (when available) is very helpful. The extent of the spinal dysraphism has been shown to extend above the visible lesion and the highest level per x-ray should be coded. Conditions that might be misdiagnosed as spina bifida either prenatally or postnatally include sacrococcygeal teratoma, isolated scoliosis/kyphosis and amniotic band syndrome.

Spina bifida is often an isolated, non-syndromic anomaly. For this reason, it is crucial to report all findings and obtain good clinical photographs for the expert reviewer. However, spina bifida can occur with genetic syndromes (e.g. trisomy 18) and is occasionally a manifestation of single-gene disorders such as Waardenburg syndrome.

Non-genetic risk factors include pregestational diabetes, obesity, seizure medications (i.e. valproic acid, carbamazepine), hyperthermia (e.g. fever) in early pregnancy, and folic acid insufficiency/deficiency. Adequate periconceptional use of folic acid (as a supplement or through fortification) can prevent most cases of spina bifida.

The birth prevalence of spina bifida varies widely, between 0.6 to 38.9 per 10 000 births. Prevalence is higher among women of Hispanic ancestry compared to non-Hispanic white and non-Hispanic black women. Lower-income countries and countries without mandated folic acid fortification of staple foods have a higher prevalence of spina bifida.

## Inclusions

Q05.0 Cervical spina bifida with hydrocephalus
Q05.1 Thoracic spina bifida with hydrocephalus
Q05.2 Lumbar spina bifida with hydrocephalus (includes lumbosacral spina bifida with hydrocephalus)
Q05.3 Sacral spina bifida with hydrocephalus
Q05.4 Unspecified spina bifida with hydrocephalus
Q05.5 Cervical spina bifida without hydrocephalus
Q05.6 Thoracic spina bifida without hydrocephalus
Q05.7 Lumbar spina bifida without hydrocephalus (includes lumbosacral spina bifida without hydrocephalus)
Q05.8 Sacral spina bifida with hydrocephalus
Q05.9 Spina bifida, unspecified

## Exclusions

D48 Neoplasm of uncertain behavior (sacrococcygeal teratoma)
Q06.8 Other specified congenital malformations of spinal cord
Q07 Other congenital malformations of nervous system
Q76.0 Spina bifida occulta

## Checklist for high-quality reporting

**Spina Bifida – Documentation Checklist**

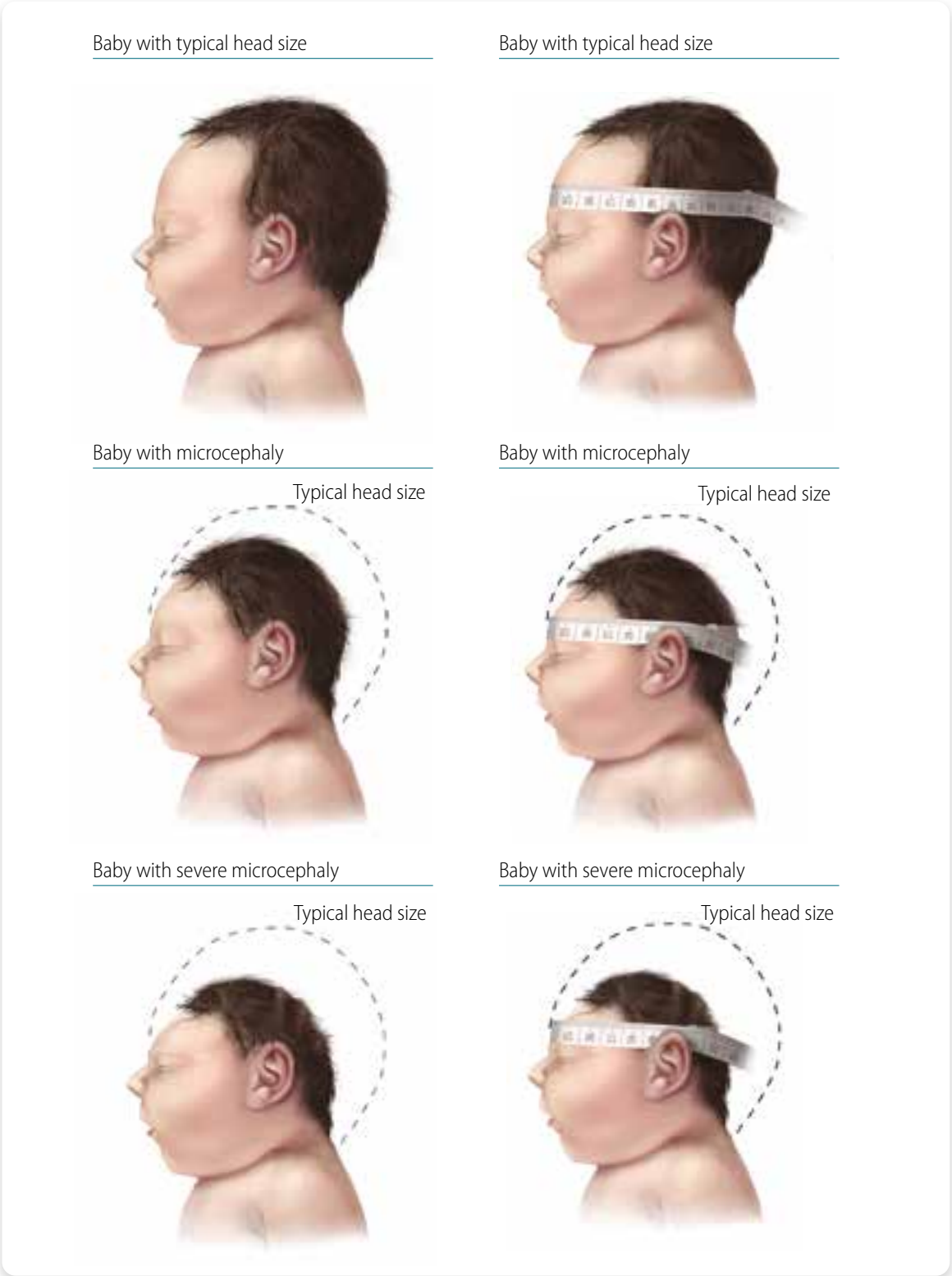
- ☐ **Describe defect in detail:**
  - Location – specify level (e.g. cervical, thoracic, thoracolumbar, lumbar, lumbosacral, sacral etc.).
  - Size of lesion.
  - Covering – covered by skin or not covered by skin.
  - Content – only meninges (meningocele) or also spinal cord (myelomeningocele – spinal cord visible).
  - Anomalies – document sequence defects (hydrocephalus, talipes) and other anomalies.
- ☐ **Take and report photographs:** *Show clearly* the level of spina bifida (back and side if possible); can be crucial for review.
- ☐ **Describe evaluations to find or rule out related and associated anomalies:**
  - Sequence – hydrocephalus, talipes, other.
  - Other unrelated anomalies – describe procedures to assess other anomalies.
  - Genetic or chromosomal conditions.
  - Specialty consultations, imaging and surgery.
- ☐ **Report whether autopsy (pathology) findings are available and if so, report the results.**

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical description for documentation of key descriptors:<br>▸ Open (not skin covered but often membrane covered) versus closed (skin covered) spina bifida – important for neurological disability.<br>▸ Lesion level and size – cervical, thoracic, lumbar, sacral, etc., and extent of lesion.<br>▸ Attach photographs, consultation reports; essential for review and correct classification.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations. |
| **Coding** | ▸ Code as Q05.X for specific type, if documented.<br>▸ Track and minimize cases coded with generic ICD-10 RCPCH code Q05. |
| **Clinical classification** | ▸ Track ratio of spina bifida with hydrocephalus/spina bifida without hydrocephalus:<br>– Because hydrocephalus is common in lumbar spina bifida, low ratios suggest underreporting of hydrocephalus.<br>▸ Track frequency of congenital anomalies occurring with spina bifida. Do not include findings that are a direct consequence of the condition (such as talipes).<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence: Prevalence varies by country/region, country income level and race/ethnicity. A birth prevalence (including stillbirths and pregnancy terminations) < 6 per 10 000 births in a country without widespread and proven folic acid fortification of staple foods strongly suggests under-ascertainment. |

Microcephaly (microcephalus) describes a cranial vault that is smaller than normal for the infant's sex and gestational age at birth (congenital). The size of the cranial vault is an indicator of the size of the underlying brain. Microcephaly can be diagnosed prenatally but is more often diagnosed after delivery. Fig. 4.12 shows newborns with normal head size, microcephaly, and severe microcephaly, and the correct position of a tape to measure the head circumference.

**Fig. 4.12. Microcephaly**



## Relevant ICD-10 codes

Q02 Microcephaly

## Diagnosis

***Prenatal.*** Transabdominal ultrasound between 18 and 37 weeks' gestation might identify a small head size, with serial ultrasounds showing poor growth over time. Measurement of the fetal head circumference (HC) and biparietal diameter should be made on the axial image through the thalami at the level of the cavum septi pellucidi.

***Postnatal.*** At delivery, a measurement of the occipito-frontal circumference or HC that is three standard deviations below the mean for the age- and sex-appropriate distribution curves is diagnostic of severe microcephaly. See the link below on how best to measure HC at birth.

***Report if using a different definition or cut-off point*** (e.g. two standard deviations below the mean).

Cranial ultrasound, CT or MRI scans can confirm the diagnosis of an underlying brain abnormality.

## Clinical and epidemiologic notes

*Timing of measurement*. Although head moulding and/or swelling can occur during the birthing process, HC measurements should be obtained within the first 24 hours of life. Standards for HC are based on early measurements (i.e. INTERGROWTH-21st measurements were obtained before 12 hours of life and WHO measurements were obtained before 24 hours of life). Therefore, postponing HC measurements until after 24 hours of life to allow for birth process changes to subside results in not having appropriate comparison standards.

*Calculating the percentile of HC*. The INTERGROWTH-21st project provides data on HC based on a multicenter, multi-ethnic and population-based project. The online tool (http://intergrowth21.ndog.ox.ac.uk) can be used to enter data to calculate the percentile of the HC or to compare to standards based on the infant's sex and gestational age *(28)*.

*Causes*. Microcephaly is occasionally a normal trait in a family, so measuring parents' HC if possible is reasonable. Many genetic syndromes are associated with microcephaly (> 1000 matches in www.OMIM.org) *(29)*. Teratogenic conditions that can cause microcephaly include congenital rubella (P35.0), congenital cytomegalovirus (cCMV) (P35.1), congenital Zika (P35.4) and congenital toxoplasmosis (P37.1) infections. Detailed imaging and expert consultations (e.g. paediatric geneticist, paediatric neurologist) can help identify underlying causes of microcephaly.

## Inclusions

Q02 Microcephaly

## Exclusions

Small brain – without confirmation of HC measurement demonstrating microcephaly.

Microcephaly associated with anencephaly or encephalocele.

Acquired microcephaly; for example, secondary to a birth or delivery complication, postnatal insult or trauma, neonatal meningitis, and birth asphyxia.

## Checklist for high-quality reporting

| Microcephaly – Documentation Checklist |
|---|
| ☐ **Describe in detail:**<br>▸ Measure and document HC in newborn.<br>▸ Establish and use a standardized approach (e.g. follow standard rules for taking HC measurement within 24 hours after birth).<br>▸ Document the HC percentile or standard deviation, by gestational age and sex [use the recommended references for HC provided by INTERGROWTH-21st (*28*) or WHO].<br>▸ Distinguish microcephaly from craniosynostosis. |
| ☐ **Take and report photographs:** *Show full face and body photographs, if allowed*; can be crucial for review. |
| ☐ **Describe evaluations to find or rule out related and associated anomalies:**<br>▸ Report neurologic status and signs (e.g. tone, seizures, irritability).<br>▸ Report whether laboratory examinations (e.g. serology to identify infections) or specialty consultations (e.g. genetics) were done, and results. |
| ☐ **Report whether autopsy (pathology) findings are available and if so, report the results**. |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | ▸ Review sample for documentation of key descriptor (HC measurement).<br>▸ Take and attach photographs – essential for review and correct classification.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations. |
| **Coding** | ▸ Code as Q02. |
| **Clinical classification** | ▸ Track proportion of anomalies and syndromes occurring with microcephaly.<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence: Prevalence varies by country/region, country income level and race/ethnicity. |

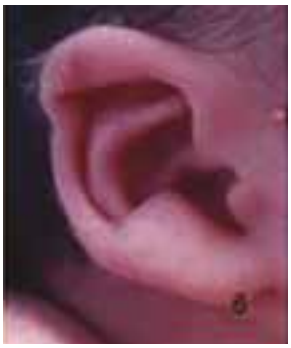
**Fig. 4.13. Main types of microtia, including anotia**

**Normal infant ear**

**Microtia I**

- Ear is small
- Ear canal may be narrowed
- Structures and ear shape are otherwise normal

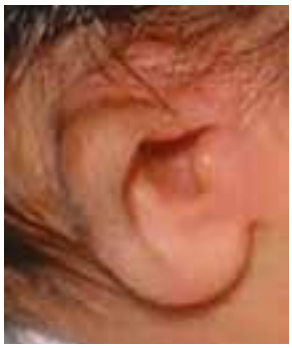
**Microtia I**
**Q17.21**



**Microtia II**

- Ear is small
- Some components are missing
- Shape is markedly abnormal
- Ear is still recognizable

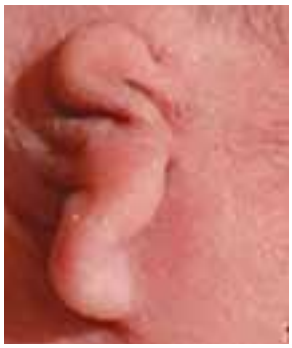
**Microtia II**
**Q17.22**



**Microtia III**

- Ear consists of a vertical mass of soft tissue and cartilage
- Typically associated with atresia of the external canal

**Microtia III**
**Q17.23**



**Microtia IV or Anotia**

- Most extreme and rarest form
- All external ear structures are absent

**Microtia IV or Anotia**
**Q16.0**

*Photograph source:* http://en.atlasedamc.org

Microtia/anotia is a congenital malformation of the ear in which the external ear (auricle) is either underdeveloped and abnormally shaped (microtia) or absent (anotia). The external ear canal might be atretic (absent). The spectrum of severity in microtia ranges from a measurably small external ear (defined as longitudinal ear length more than two standard deviations below the mean, or approximately 3.3 cm in the term newborn) with minimal structural abnormality, to an ear that consists of few rudimentary structures and an absent or blind-ending external ear canal.

Based on morphology, microtia/anotia has been categorized *(29)* in the following four categories (see Fig. 4.13):

1. **First degree (type I)**, in which the external ear is small and the ear canal might be narrowed, but the structures and ear shape are otherwise normal (*first-degree microtia is typically excluded in surveillance programmes* because it does not have major health consequences).
2. **Second degree (type II)**, in which the ear is small, some components are missing so that the shape is markedly abnormal (resembling a hook, an S, or a question mark) but the ear is still recognizable.
3. **Third degree (type III)**, in which the external ear consists of a vertical mass of soft tissue with no resemblance to a normal auricle, typically associated with atresia of the external canal.
4. **Fourth degree or anotia (type IV)**, the most extreme and rarest form, in which all external ear structures are absent.

Microtia is usually unilateral (in which case it occurs more often on the right side). If bilateral, the severity can vary between the left and right sides.

## Relevant ICD-10 codes

Q16.0 Congenital absence of (external ear) auricle (anotia, also known as fourth-degree microtia)
Q17.2 Microtia

Note that an additional digit could be added to specify the degree of microtia:
Q17.21 First degree (excluded in most programmes)
Q17.22 Second degree
Q17.23 Third degree

## Diagnosis

***Prenatal.*** Microtia/anotia is easy to miss prenatally. Delineating the position and shape of the ear might require three-dimensional ultrasound. Even if prenatal ultrasonography suggests microtia/anotia, the diagnosis should always be confirmed postnatally. When such confirmation is not possible – due, for example, to termination of pregnancy or unexamined fetal death – the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** Microtia/anotia can be easily recognized and classified based on the newborn physical examination. However, detection of middle and inner ear abnormalities, commonly associated with the more severe degrees of microtia, will require advanced imaging (CT or MRI scan), surgery or autopsy. Because microtia (second degree and above) is associated with hearing loss, *hearing should be evaluated* as soon as possible, ideally in the newborn period, so that appropriate management can be put in place.

## Clinical and epidemiologic notes

Microtia/anotia is an isolated finding in 60–80% of infants. For this reason, it is crucial to report all findings and obtain good clinical photographs for expert review. Of note, microtia/anotia can occur in conjunction with other anomalies and syndromes, especially those involving the mandible and face. Such conditions include the oculo-auriculo-vertebral spectrum (OAVS) and Goldenhar "syndrome" (Q87.04), as well as genetic syndromes, such as Treacher-Collins syndrome (Q87.0A) and trisomy 18 (Q91.0), or teratogenic, such as retinoic acid embryopathy.

Non-genetic risk factors for microtia/anotia include maternal pregestational diabetes, and maternal use of isotretinoin (Accutane®), thalidomide or mofetil (CellCept®), taken periconceptionally or early in pregnancy.

The reported prevalence of microtia/anotia varies between 1 in 3000 to 1 in 20 000 births. The prevalence might vary by country and race/ethnicity but this is likely dependent on what forms of microtia are included in studies. Prevalence is reported to be higher in males than females.

## Inclusions

Q16.0 Congenital absence of (external ear) auricle (anotia or also known as fourth-degree microtia)
Q17.2 Microtia
Q17.22 Microtia, second degree
Q17.23 Microtia, third degree

## Exclusions

Small ear (microtia first degree) with normal auricle, including lop or cup ear

Imperforate auditory meatus with a normal auricle, dysplastic or low-set ears

The following conditions in the absence of microtia/anotia (but code if microtia/anotia is present):

Q16.1 Congenital absence, atresia and stricture of auditory canal (external)
Q16.2 Absence of eustachian tube
Q16.3 Congenital malformation of ear ossicles
Q16.4 Other congenital malformations of middle ear
Q16.5 Congenital malformation of inner ear
Q16.9 Congenital malformation of ear causing impairment of hearing, unspecified
Q17.21 Microtia, first degree
H 90 Hearing loss

## Checklist for high-quality reporting

**Microtia/Anotia – Documentation Checklist**

- ☐ **Describe in detail:**
  - Defect (unilateral, bilateral).
  - Severity (absent structures, shape, compare to degrees second–third–fourth).
  - Presence/absence of ear canal, presence of ear tags.
- ☐ **Take and report photographs:** *Show clearly* the side and front; can be crucial for review.
- ☐ **Describe evaluations to find or rule out related and associated anomalies:**
  - Exclude microtia type I: Small ear with normal components or with minor anomalies of individual structures is a minor anomaly, not to be included in public health surveillance.
  - Check for preauricular tag or pits (describe; code as Q17.0).
  - Downslanting palpebral fissures, small jaw, eyelid coloboma – suggests selected syndromes.
  - Cervical vertebral anomalies suggests OAVS (check for radiographs).
  - Hearing evaluation.
  - Genetic or chromosomal testing.
  - Specialty consultations and surgical reports.
- ☐ **Report whether autopsy (pathology) findings are available and if so, report the results.**

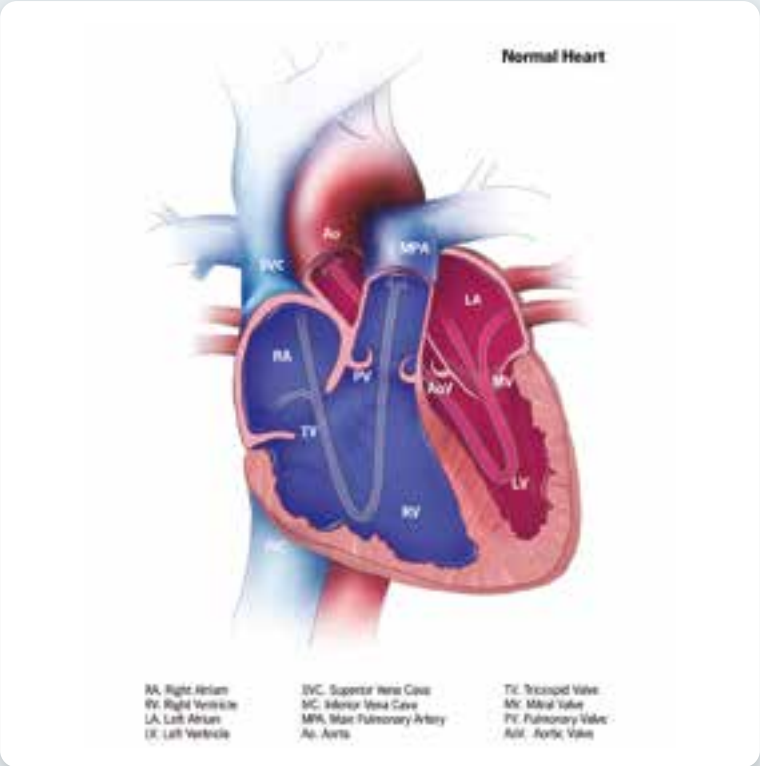
## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors; severity (degrees second to fourth), laterality, presence of ear canal, preauricular tags or pits, lower lid coloboma, downslanting palpebral fissures:<br>▸ Take and attach photographs – essential for review and correct classification. If photo is unavailable, try to draw the malformation.<br>▸ Report results from specialty consultations, imaging and surgery.<br>▸ Note whether hearing test was completed and if so, the results.<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Coding** | ▸ Code as Q17.X for specific type, if documented:<br>– Track and minimize cases coded with Q17.2, if possible.<br>▸ Code preauricular tag or pits if identified (Q17.0).<br>▸ Code cervical vertebral anomalies if identified. |
| **Clinical classification** | ▸ Track proportion of anomalies and syndromes occurring with microtia/anotia.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations. |
| **Prevalence** | ▸ Monitor prevalence: Prevalence varies by country/region, country income level and race/ethnicity. |

## Congenital heart defects: Prenatal diagnosis and postnatal confirmation

### *Overview*

**Fig. 4.14. Normal heart**




Congenital heart defects/diseases (CHDs), and especially critical CHDs (the most severe CHDs that present with critical illness early in life), require early and accurate diagnosis for optimal care. Whereas newborn screening of critical CHDs via pulse oximetry is relatively straightforward and requires comparatively simple instrumentation, a precise diagnosis requires substantial clinical expertise and technologic means – ideally in the form of a paediatric cardiologist aided by imaging such as an echocardiogram. Because of the emphasis on early detection, evaluation of the fetal heart is increasingly a critical component of prenatal imaging. Current guidelines recommend specific cardiac views as part of the anatomic survey in obstetric sonograms. Findings indicating a possible CHD can be followed by more specialized imaging such as fetal echocardiography, to confirm and to better define the anomaly. The following sections briefly introduce some approaches to prenatal diagnosis and postnatal confirmation.

- ***Obstetric sonogram.*** Many obstetric guidelines for fetal ultrasound imaging include the *four-chamber* view (which focuses on the atria and ventricles) as well as *outflow tracts* views. The inclusion of these views improves the detection rate for many clinically severe CHDs such as d-transposition of the great arteries, which was often missed when only the four-chamber view was systematically performed.
- ***Fetal echocardiogram.*** The next step for an accurate and complete diagnosis is a fetal echocardiogram. This specialized imaging, typically supervised and read by a paediatric cardiologist, is often done when the obstetric sonogram detects a potential CHD, or in situations where the risk for CHDs in the fetus is higher, such as concerns about a syndrome or extracardiac anomalies, a known teratogenic exposure (e.g. retinoic acid), select maternal chronic illnesses (e.g. diabetes or uncontrolled phenylketonuria), or strong family history of CHDs. The fetal echocardiogram makes use of multiple views as well as color Doppler imaging to systematically scan the heart, segment by segment, to characterize the anatomy, rhythm and function of the fetal heart.

### *Prenatal detection*

In high-risk pregnancies or when sonogram findings are suggestive of a CHD, obstetric sonograms followed by fetal echocardiogram might diagnose more than 80% of significant CHDs, especially critical CHDs.

- Detection rates for significant CHDs have improved over time but vary significantly by type of CHD. The conditions that are more easily diagnosed are critical CHDs that directly affect the ventricles – either the left ventricle (e.g. hypoplastic left heart syndrome or critical aortic stenosis) or the right ventricle (e.g. tricuspid atresia or pulmonary atresia with intact ventricular septum). Conditions that might be missed – if, for example, the outflow tract view is not included or is inadequate in an obstetric sonogram – are those that primarily involve the outflow tracts but impact the ventricles subtly, if at all (e.g. simple d-transposition of the great arteries).
- Detection of CHDs also likely depends on the operator (knowledge, skill and technique), the imaging equipment, time allotted for obstetric scan, gestational age, maternal body habitus and fetal lie. Additionally, there are system-level factors that might influence access to and use of prenatal services, including socioeconomic status, insurance status, education and location (e.g. rural versus urban).

### *Postnatal confirmation of prenatal diagnoses*

These considerations can provide some guidance to surveillance systems that collect data on prenatal diagnosis. In general, prenatal diagnoses should be confirmed postnatally, typically by echocardiogram. This approach is expected to provide the most accurate and complete diagnosis, establish prevalence and allow for longitudinal outcome studies. If a prenatal diagnosis is not followed by postnatal confirmation (e.g. because of termination of pregnancy, loss of follow-up, early neonatal death, comfort care without imaging, etc.), then a reasonable approach for a programme is as follows:

- Develop an *explicit* and *transparent* process to determine whether a case is confirmed or probable. The parameters might vary depending on the type of CHD and the local context (e.g. experience, training of the operator, correlation between pre- and postnatal diagnoses in other cases, etc.).
- Have a field in the database associated with each diagnosis that specifies whether the diagnosis was a prenatal diagnosis only versus confirmed after birth. This allows for a flexible and easy parsing of cases for different types of analyses and comparisons (internally as well as with other programmes).

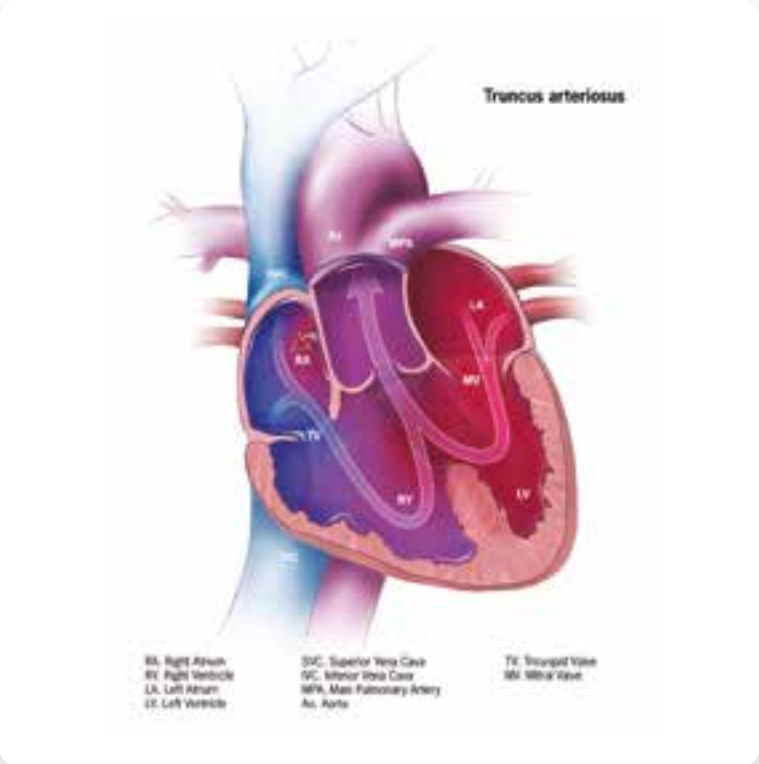
### Postnatal screening and diagnoses

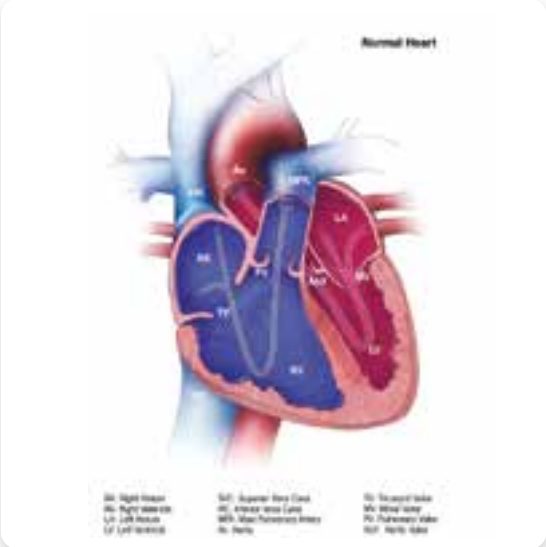
In hospitals where there is a neonatologist or a paediatrician it would be possible to suspect CHD based on clinical signs and confirm with expert consultation and imaging. Newborn screening for critical CHDs using pulse oximetry provides a non-invasive and relatively simple way to screen for severe cardiac disease very early in life, before clinical deterioration becomes obvious and before the infant is discharged home. Screening detects low oxygen saturation but does not provide a specific diagnosis (the infant might have a CHD or other serious disease such as pneumonia or sepsis). Expert consultation and imaging (typically an echocardiogram) can quickly provide a firm and specific diagnosis, and this information can be used to guide targeted management and care for better outcomes.

Common truncus or common arterial trunk is a structural heart defect characterized anatomically by having a single common arterial trunk, rather than a separate aorta and main pulmonary artery (see Fig. 4.15). This common trunk carries blood from the heart to the body, lungs and the heart itself – that is, the common trunk gives rise to the systemic, pulmonary and coronary circulation. A ventricular septal defect is present. Other terms for the condition are (persistent) truncus arteriosus.

The anatomy of common truncus varies, especially in the origin of the pulmonary arteries from the common truncus. Such variations are the basis of the two main classifications: the Edwards classification (types I–IV, of which types I–III are properly common truncus) and the van Praagh classification (A1–A4).

**Fig. 4.15. Common truncus**



## Relevant ICD-10 codes

Q20.0 Common arterial trunk

## Diagnosis

***Prenatal.*** Common truncus can be diagnosed prenatally by fetal echocardiography, although in some cases it might be difficult to conclusively distinguish from other conditions (e.g. pulmonary atresia with ventricular septal defect or aortic atresia with ventricular septal defect). Common truncus can be missed prenatally if the outflow tract is not fully examined. Prenatal diagnoses should be confirmed postnatally, typically by echocardiography.

***Postnatal.*** The clinical findings after birth depend on the volume of pulmonary blood flow and the status of the truncal valve (e.g. degree of valvar insufficiency). If the valve is severely insufficient, the infant might present early with heart failure, which can be characterized by fast breathing, fast heart rate, poor feeding and excessive sweating. Otherwise, the physiologically high pulmonary vascular resistance at birth will delay this presentation and lead to a degree of cyanosis, usually mild, at the outset.

Newborn screening for critical CHD via pulse oximetry can detect common truncus if a sufficient degree of hypoxia is present at the time of screening.

## Clinical and epidemiologic notes

As noted, the clinical presentation in the newborn period might include a combination of cyanosis and heart failure.

Common truncus is included among the conotruncal heart anomalies, together with tetralogy of Fallot, interrupted aortic arch type B, and d-transposition of the great arteries. Common truncus can occur in association with genetic conditions – especially deletion 22q11 – and can be familial.

Among modifiable risk factors, maternal pregestational diabetes is common and well established. The birth prevalence of common truncus is approximately is 0.5 to 1 in 10 000 births.

## Inclusions

Q20.0 Common truncus

## Exclusions

Pulmonary atresia with ventricular septal defect (common truncus type IV in the Edwards classification)

## Checklist for high-quality reporting

**Common Truncus – Documentation Checklist**

- ☐ **Describe in detail the clinical and echocardiographic findings:**
  - Anatomy – specify intracardiac anomalies, including the presence and type of ventricular septal defects, the origins of the pulmonary arteries, and the morphology of the truncal valve.
  - Procedure – specify whether the cardiac findings are from a prenatal or postnatal echocardiogram, or from other investigations (e.g. catheterization, MRI), surgery or autopsy.
  - Additional cardiac findings – specify any additional findings in addition to the basic anatomy of truncus (see above).
- ☐ **Look for and document extracardiac birth defects:** Common truncus can occur with genetic syndromes such as deletion 22q11, in which many external (e.g. cleft palate) as well as internal anomalies have been described.
- ☐ **Report whether specialty consultation(s) have been done:** In particular, report whether the diagnosis was done by a paediatric cardiologist, and whether the patient was seen by a geneticist.
- ☐ **Report genetic testing (e.g. chromosomal studies, genomic microarray, genomic sequencing):** Report whether this was done and if so, the results.

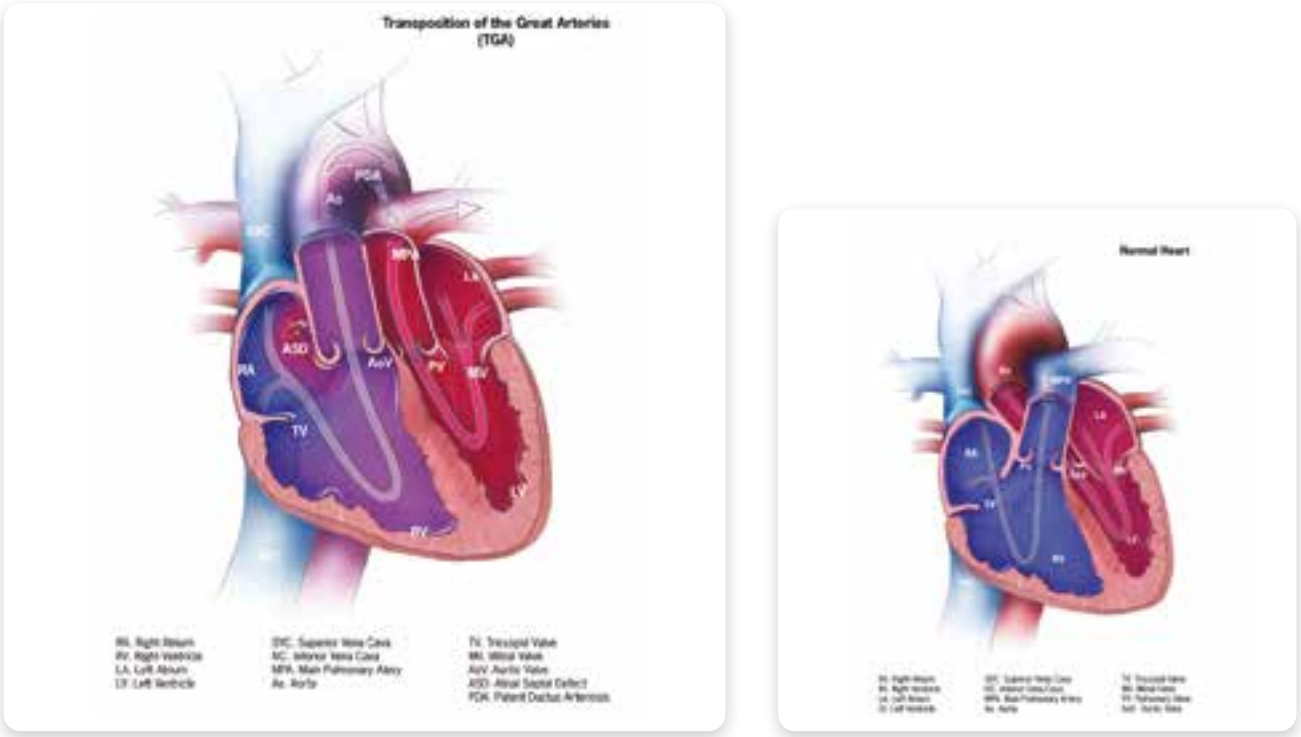
## Suggested data quality indicators

| Category | Suggested Practices and Quality indicators |
|---|---|
| **Description and documentation** | Review sample of clinical descriptions for documentation of key elements:<br>▸ Anatomy: Presence of ventricular septal defect, origin of the pulmonary arteries, common valve, additional findings.<br>▸ How cardiac findings were detected (e.g. echocardiography).<br>▸ Who made the diagnosis (e.g. paediatrician, paediatric cardiologist).<br>▸ Specialists who evaluated the child, in particular, a paediatric cardiologist and geneticist.<br>▸ Key evaluations done, especially genetic testing. |
| **Coding** | ▸ Coding is straightforward (Q20.0, common truncus/common arterial trunk). A ventricular septal defect is nearly always present so programmes need to have a rule about whether or not to code the septal defect (many programmes do not code septal defects separately in this setting). |
| **Clinical classification** | ▸ Track proportion of congenital anomalies and syndromes occurring with common truncus: If < 10%, consider under-ascertainment of these co-occurring conditions, especially deletion 22q11. |
| **Prevalence** | ▸ Monitor prevalence: If low (< 0.3 per 10 000 births) suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units. |

d(dextro)-transposition of the great arteries (d-TGA) is a structural heart anomaly characterized clinically by cyanosis (usually) and anatomically by an abnormal origin of the great arteries, such that the aorta exits from the right ventricle (instead of the left) and the pulmonary artery exits from the left ventricle (instead of the right) (see Fig. 4.16).

d-TGA can occur with or without a ventricular septal defect. These two forms are sometimes called "incomplete" and "complete" d-TGA, respectively, though these terms are infrequently used and are not particularly useful.

**Fig. 4.16. Transposition of great arteries**




## Relevant ICD-10 codes

Q20.3 Transposition of great arteries

Note:

- Transposed great arteries can also occur as part of complex heart anomalies such as heterotaxy. Because of this heterogeneity, it is recommended that public health surveillance track separately the simple forms of d-TGA. These can be defined as those with at most a ventricular septal defect and limited valvar involvement, and excludes those cases that, for example, are part of heterotaxy or single ventricle phenotype (Q20.4).
- Transposed great arteries can occur with double outlet right ventricle (DORV). These cases are often classified, grouped and tracked with DORV rather than with d-TGA.
- l(levo) transposition of the great arteries (l-TGA, Q20.5) is a different condition, epidemiologically, anatomically and developmentally, and it is not recommended to be included with d-TGA.

## Diagnosis

***Prenatal.*** d-TGA can be suspected prenatally on a second trimester obstetric anatomic scan – with the outflow tract view being especially important – but can be missed. Prenatally diagnosed or suspected cases should be confirmed postnatally.

***Postnatal.*** Infants with d-TGA present in a variety of ways, depending on the presence or absence of a ventricular septal defect and other intracardiac anomalies. With an intact ventricular septum, infants present early after birth with cyanosis. With a large ventricular septal defect, the cyanosis might not be as apparent, and infants can present (sometimes later) with heart failure because of pulmonary over-circulation.

Newborn screening via pulse oximetry, which is based on the non-invasive detection of low blood oxygen saturation, can detect many cases of d-TGA even before overt signs and symptoms. Echocardiography can provide a firm, specific diagnosis, though other imaging techniques have a role in some cases.

## Clinical and epidemiologic notes

As noted, infants present typically early after birth with cyanosis but occasionally – depending on presence and size of the ventricular septal defect and the level of pulmonary vascular resistance – also with congestive heart failure. Rapid clinical deterioration is expected as the ductus arteriosus closes.

d-TGA is considered one of the conotruncal heart defects, like tetralogy of Fallot and interrupted aortic arch type B. However, compared to tetralogy of Fallot, d-TGA is more likely an isolated heart anomaly and less likely to be associated with single-gene conditions or genomic imbalances (e.g. deletion 22q11). Extracardiac anomalies are found in ~10% of cases.

Maternal pregestational diabetes is a well-established modifiable risk factor for d-TGA.

d-TGA occurs with a frequency of approximately 1 in 3000 to 4000 births, and is more common in males.

## Inclusions

Q20.3 Transposition of great arteries

Note:

- Q20.3 has also been used for cases of l-TGA, as there is not a specific code for it unless it occurs as part of corrected transposition of the great vessels (Q20.5). For public health surveillance, l-TGA should not be coded with Q20.3 in order to track d-TGA appropriately.
- d-TGA with ventricular septal defect is best coded with the d-TGA code and with the appropriate ventricular septal defect code.

## Exclusions

Q20.2 Double outlet right ventricle
Q20.5 I(levo)-transposition of the great arteries

## Checklist for high-quality reporting

**d-Transposition of Great Arteries – Documentation Checklist**

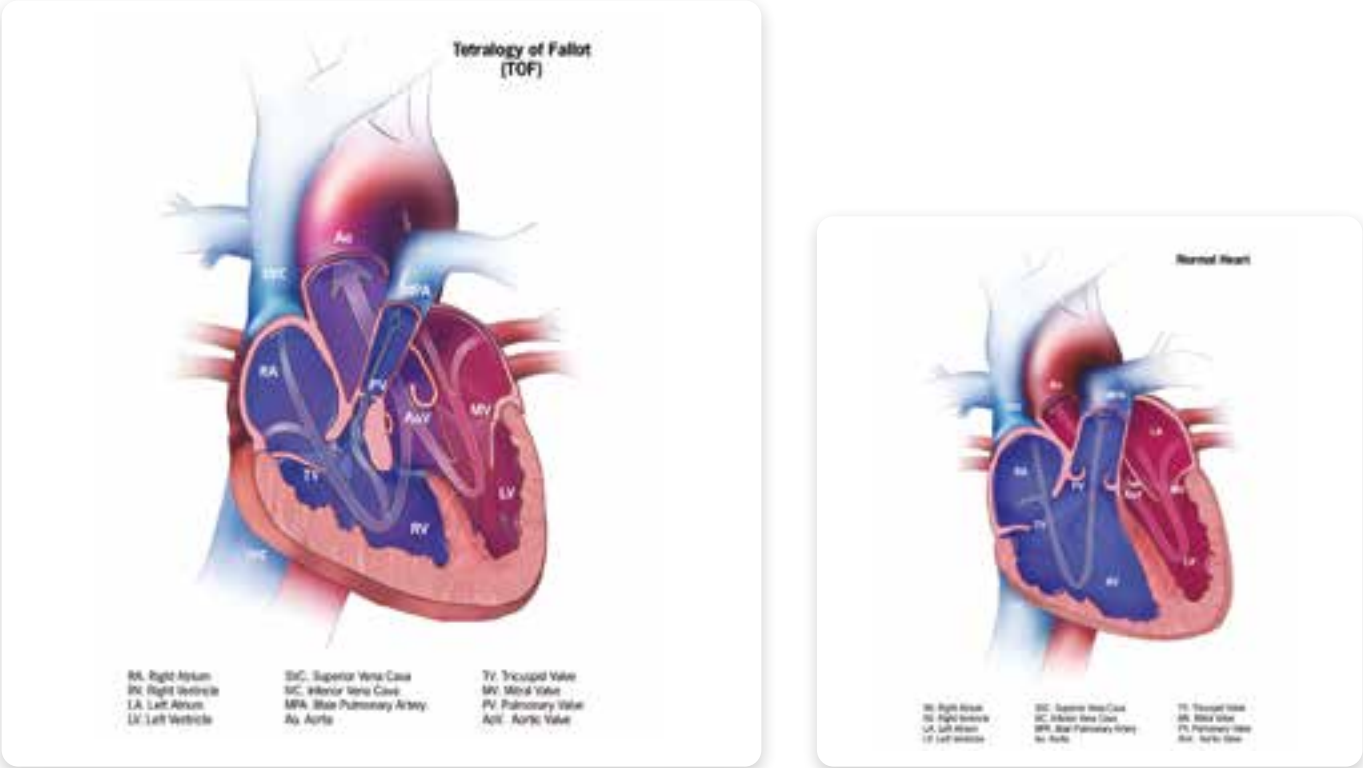
- ☐ **Describe in detail the clinical and echocardiographic findings:**
  - Anatomy – specify intracardiac anomalies, including the presence and type of valvar involvement, of ventricular septal defects, and whether there is evidence of DORV, single ventricle (double inlet left ventricle) or heterotaxy (the latter would make the case not part of simple d-TGA).
  - Procedure – specify whether the cardiac findings are from a prenatal or postnatal echocardiogram, or from other investigations (e.g. catheterization, MRI), surgery or autopsy.
  - Additional cardiac findings – specify any additional findings, including atrial septal defect, atrial isomerism, etc.
- ☐ **Look for and document extracardiac birth defects:** These are not as common as in other conotruncal defects, but can occur.
- ☐ **Report whether specialty consultation(s) were done:** Report whether the diagnosis was made by a paediatric cardiologist, and whether the patient was seen by a geneticist.
- ☐ **Report any genetic testing and results (e.g. chromosomal studies, genomic microarray, genomic sequencing).**

## Suggested data quality indicators

| Category | Suggested Practices and Quality indicators |
|---|---|
| **Description and documentation** | Review sample of clinical descriptions for documentation of key elements:<br>▸ Anatomy – presence of ventricular septal defect, other intracardiac and extracardiac anomalies.<br>▸ How cardiac findings were detected (e.g. echocardiography).<br>▸ Who made the diagnosis (e.g. paediatrician, paediatric cardiologist).<br>▸ Specialists who evaluated the child – in particular, a paediatric cardiologist and geneticist.<br>▸ Key evaluations done, especially genetic testing. |
| **Coding** | ▸ Track and evaluate cases of d-TGA with and without ventricular septal defect: A very low proportion of cases with ventricular septal defect might indicate that this commonly associated intracardiac anomaly is being underreported or not documented and coded correctly. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies and syndromes occurring with d-TGA: If < 5%, consider under-ascertainment of these co-occurring conditions. |
| **Prevalence** | ▸ Monitor prevalence: If very low (< 1 per 10 000 births) it suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units. |

Tetralogy of Fallot is a structural heart anomaly that comprises a *spectrum* of disease, from severe to mild, with a common anatomic finding of right ventricular outflow tract obstruction – due to pulmonic and subpulmonic stenosis or atresia, or an absent pulmonary valve – associated with a malpositioned aorta that overrides a ventricular septal defect (see Fig. 4.17). The functional consequence is shunting/mixing of poorly oxygenated blood from the right ventricle to the aorta and thus to the systemic circulation. Depending on the degree of the shunting, which is a function of the severity of outflow tract obstruction, the child might become cyanotic, either constantly or intermittently. This form of CHD requires surgical treatment.

**Fig. 4.17. Tetralogy of Fallot**




## Relevant ICD-10 codes

Q21.3 Tetralogy of Fallot
Q21.82 Pentalogy of Fallot (do not use, see below)
Q22.0 Pulmonary valve atresia with Q21.0 (ventricular septal defect)

Note:

- Pulmonary valve atresia with ventricular septal defect is nearly always a form of tetralogy of Fallot (a very severe form), and for this reason it is grouped with classic tetralogy of Fallot.
- Pentalogy of Fallot – which comprises tetralogy of Fallot plus atrial septal defect – is an old term seldom used now. If tetralogy of Fallot occurs with an atrial septal defect, code separately the two defects; this approach also allows the atrial septal defect to be coded using a more specific code.

## Diagnosis

***Prenatal.*** Tetralogy of Fallot can be suspected prenatally on a second trimester obstetric anatomic scan, using a combination of four-chamber and outflow tract views, and confirmed with fetal echocardiography. Detection rates are improving but diagnosis can be challenging. Postnatal confirmation is necessary for a firm diagnosis, especially to distinguish between tetralogy of Fallot with pulmonary stenosis versus with pulmonary atresia.

***Postnatal.*** Echocardiography has largely superseded other imaging techniques. Newborn screening via pulse oximetry – which is based on the non-invasive detection of peripheral blood hypoxygenation – is effective in detecting tetralogy of Fallot as long as the condition causes the level of blood oxygenation (oxygen saturation) to go below the cut-off for newborn screening testing. For this reason, some cases of tetralogy of Fallot, especially milder cases, might be missed at newborn screening or on clinical examination before discharge from the nursery.

## Clinical and epidemiologic notes

Because tetralogy of Fallot includes a spectrum of disease (depending on the severity of right ventricular obstruction), the clinical presentation and age at presentation can vary considerably, from an asymptomatic murmur in a newborn with normal or near normal oxygenation ("pink tets") to early-onset severe cyanosis.

In some cases, there might be diagnostic uncertainty about whether the diagnosis is tetralogy of Fallot (Q21.3) or DORV (Q20.2). In this situation, the best approach is to record the primary data (e.g. reports of echocardiograms and consultations) and involve an expert clinical reviewer for final disposition.

Approximately half of cases of tetralogy of Fallot have a genetic basis, most commonly deletion 22q11 (approximately 15–20%). Tetralogy of Fallot can be found in other chromosomal conditions (e.g. the common trisomies) as well as in more than 100 single-gene conditions. Maternal pregestational diabetes is a modifiable risk factor for tetralogy of Fallot and other conotruncal conditions (e.g. truncus arteriosus).

Tetralogy of Fallot is the most common cyanotic CHD, with a frequency of approximately 1 in 2500 births.

## Inclusions

Q21.3 Tetralogy of Fallot
Q22.0 Pulmonary valve atresia with Q21.0 (ventricular septal defect)

## Exclusions

Q20.2 Double outlet right ventricle

## Checklist for high-quality reporting

**Tetralogy of Fallot – Documentation Checklist**

- ☐ **Describe in detail the clinical and echocardiographic findings:**
  - Anatomy – specify the type of right ventricular outflow tract obstruction (severity of stenosis, or presence of atresia) and the presence and type of ventricular septal defect (e.g. "subaortic", "perimembranous").
  - Procedure – specify whether the cardiac findings are from a prenatal or postnatal echocardiogram, or from other investigations (e.g. catheterization, MRI), surgery or autopsy.
  - Additional cardiac findings – specify any additional findings, including atrial septal defect, pulmonary collaterals, etc.
- ☐ **Look for and document extracardiac birth defects:** In deletion 22q11, the heart anomaly can be associated with several internal and external anomalies, including cleft palate, spina bifida, vertebral anomalies or other defects.
- ☐ **Report whether specialty consultation(s) were done:** Report whether the diagnosis was made by a paediatric cardiologist, and whether the patient was seen by a geneticist.
- ☐ **Report any genetic testing and results (e.g. chromosomal studies, genomic microarray, genomic sequencing).**

## Suggested data quality indicators

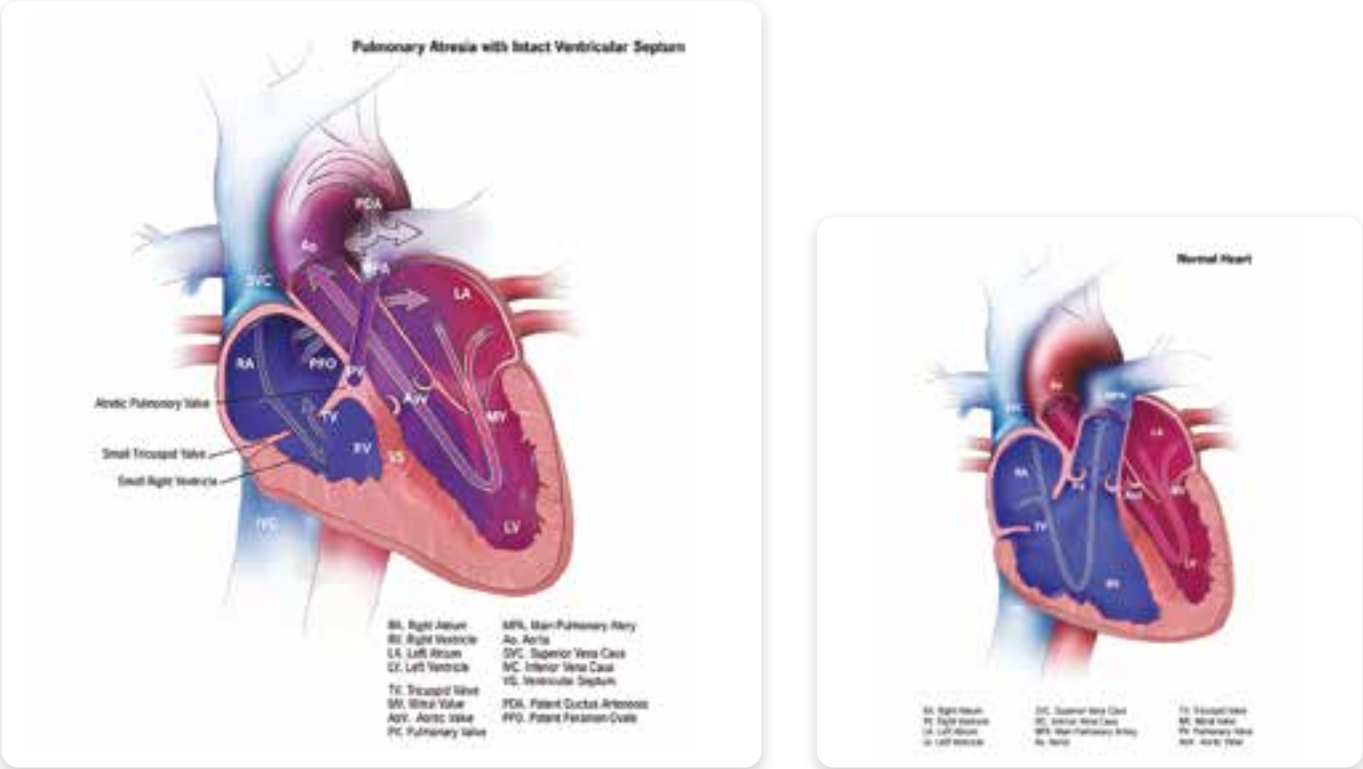
| Category | Suggested Practices and Quality indicators |
|---|---|
| **Description and documentation** | Review a sample of clinical descriptions for documentation of key elements:<br>▸ Anatomy.<br>▸ How cardiac findings were detected (e.g. echocardiography).<br>▸ Who made the diagnosis (e.g. paediatrician, paediatric cardiologist).<br>▸ Specialists who evaluated the child, in particular, a paediatric cardiologist or geneticist.<br>▸ Key evaluations done, especially genetic testing. |
| **Coding** | ▸ Track and evaluate cases of pulmonic stenosis (Q22.1) with ventricular septal defect (Q21.0) and review for inclusion with tetralogy of Fallot. Track and recode cases with pentalogy of Fallot (Q21.82, recode as tetralogy of Fallot, and code separately the specific type of atrial septal defect). |
| **Clinical classification** | ▸ Track the proportion of congenital anomalies and syndromes occurring with tetralogy of Fallot: If < 10%, then under-ascertainment of these co-occurring conditions is likely. |
| **Prevalence** | ▸ Monitor prevalence: A low prevalence (< 2 per 10 000 births) suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units. |

Pulmonary valve atresia is a structural heart anomaly characterized clinically by cyanosis and anatomically by an imperforate pulmonary valve that blocks the flow of blood through the right ventricular outflow tract completely. The imperforate pulmonary valve can look like a membrane, or – because it failed to form altogether – the atresia takes the form of a muscular atretic segment.

Two main forms must be distinguished, based on whether or not a ventricular septal defect is present. These two forms differ in presentation, epidemiology and risk factors.

- In most cases, pulmonary valve atresia with a ventricular septal defect is considered as a conotruncal defect – specifically the more severe end of the spectrum of tetralogy of Fallot.
- Pulmonary atresia with intact ventricular septum is a different entity (see Fig. 4.18) unrelated to conotruncal heart defects.

**Fig. 4.18. Pulmonary valve atresia**




## Relevant ICD-10 codes

Q22.0 Pulmonary valve atresia
(Q21.0 Ventricular septal defect)

## Diagnosis

***Prenatal.*** Pulmonary valve atresia can be suspected prenatally on a second trimester obstetric anatomic scan, using a combination of four-chamber and outflow tract views, and further characterized by fetal echocardiography. Because of diagnostic challenges, however, postnatal confirmation is necessary for a firm diagnosis.

***Postnatal.*** Infants with pulmonary atresia (with or without ventricular septal defect) typically present early in the neonatal period with cyanosis and hypoxemia that worsens as the ductus closes. Echocardiography is the key diagnostic procedure, although other imaging techniques, including catheterization, might be necessary to better guide management and care.

## Clinical and epidemiologic notes

Infants with pulmonary atresia with intact ventricular septum typically present with cyanosis; massive cardiomegaly might also occur.

Pulmonary atresia *with* ventricular septal defect can be associated with deletion 22q11, unlike the form with an intact ventricular septum.

The overall birth prevalence of pulmonary atresia is estimated to be approximately 1 in 7500 births. The birth prevalence of pulmonary atresia with intact ventricular septum is approximately 1 in 15 000 live births (more frequent among stillbirths).

## Inclusions

Q22.0 Pulmonary valve atresia (without ventricular septal defect)
Q22.0 Pulmonary valve atresia with Q21.0 (ventricular septal defect)

## Exclusions

Q22.1 Congenital pulmonary valve stenosis

Note:

- Some surveillance programmes group together pulmonary valve stenosis (Q22.1) and atresia (Q22.0). **This is not recommended.** Whereas severe pulmonary stenosis might present similarly to pulmonary atresia, mild forms of pulmonary stenosis are much more common, such that lumping stenosis with atresia generates a heterogeneous group of cardiac defects in which the severe forms cannot be accurately assessed and tracked.
- Pulmonary atresia with ventricular septal defect is in most cases a conotruncal defect and should be grouped with tetralogy of Fallot and *not* with pulmonary atresia with intact ventricular septum.

## Checklist for high-quality reporting

**Pulmonary Atresia – Documentation Checklist**

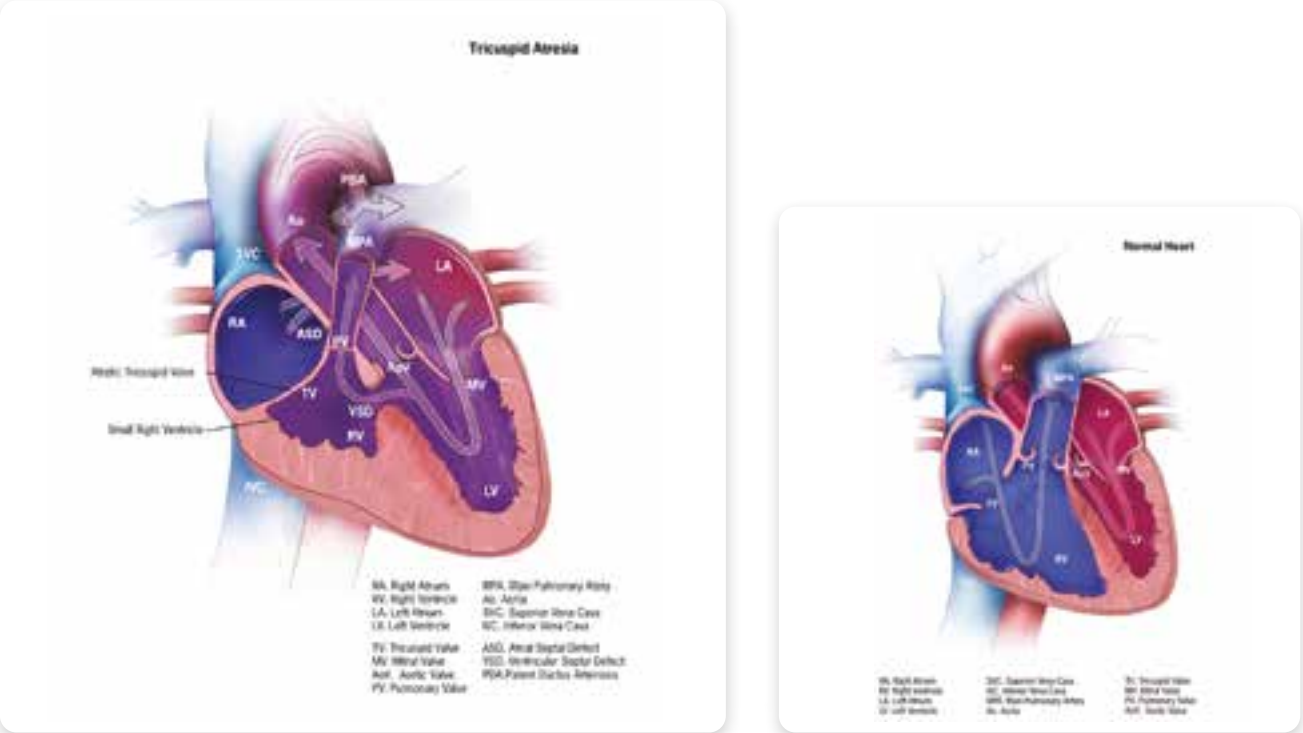
- ☐ **Describe in detail the clinical and echocardiographic findings:**
  - Specify intracardiac anatomy, including the presence of valve atresia, the involvement of the tricuspid valve, and whether the right ventricle is underdeveloped.
  - Specify whether the ventricular septum is intact or whether a ventricular septal defect is present (if so, note whether a specific type of ventricular septal defect is described in the notes).
  - Specify whether the cardiac findings are from a prenatal or postnatal echocardiogram, or from other investigations (e.g. catheterization, MRI), surgery or autopsy.
  - Document any additional cardiovascular finding, including atrial septal defect, pulmonary collaterals, etc.
- ☐ **Look for and document extracardiac birth defects:** In deletion 22q11, the heart anomaly can be associated with several internal and external anomalies, including cleft palate, spina bifida, vertebral anomalies or other defects.
- ☐ **Report whether specialty consultation(s) were done:** Report whether the diagnosis was made by a paediatric cardiologist, and whether the patient was seen by a geneticist.
- ☐ **Report any genetic testing and results (e.g. chromosomal studies, genomic microarray, genomic sequencing).**

## Suggested data quality indicators

| Category | Suggested Practices and Quality indicators |
|---|---|
| **Description and documentation** | Review sample of clinical descriptions for documentation of key elements:<br>▸ Anatomy.<br>▸ How cardiac findings were detected (e.g. echocardiography).<br>▸ Who made the diagnosis (e.g. paediatrician, paediatric cardiologist).<br>▸ Specialists who evaluated the child, in particular, a paediatric cardiologist or geneticist.<br>▸ Key evaluations done, especially genetic testing. |
| **Coding** | ▸ Track and evaluate cases of pulmonic atresia (Q22.0) with ventricular septal defect (Q21.0). A very low proportion of such cases compared to pulmonary atresia without a ventricular septal defect suggests that ventricular septal defects are either missed or not coded. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies and syndromes occurring with pulmonary atresia. The expectation is that the proportion is higher for pulmonary atresia with ventricular septal defect compared to pulmonary atresia without ventricular septal defect. |
| **Prevalence** | ▸ Monitor separately the prevalence of pulmonary atresia with and without ventricular septal defect.<br>▸ If larger monitoring groups are necessary, consider grouping pulmonary atresia with ventricular septal defect with tetralogy of Fallot (part of the same spectrum).<br>▸ Monitor prevalence: If low (< 1 per 10 000 births) it suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units. |

Tricuspid valve atresia is a structural heart defect characterized anatomically by a complete agenesis (failure of formation) of the tricuspid valve, leading to absence of direct communication and blood flow from the right atrium to the right ventricle. Having an atrial septal defect (ASD) (Fig. 4.19) is crucial for survival. Blood mixing causes significant cyanosis.

**Fig. 4.19. Tricuspid valve atresia**




## Relevant ICD-10 codes

Q22.4 Tricuspid valve atresia (this code includes both atresia and stenosis)

## Diagnosis

***Prenatal.*** Tricuspid valve atresia can be readily suspected prenatally on a second trimester obstetric anatomic scan based on the absence of the tricuspid valve and the discrepancy in size of the ventricles (left ventricle > right ventricle). A suspected case should be confirmed postnatally.

***Postnatal.*** The common clinical presentation in the newborn is cyanosis. Echocardiography has largely superseded other imaging techniques, although these have a role (e.g. catheterization to assess right ventricular pressures and resistance).

Newborn screening via pulse oximetry – which is based on the detection of low blood oxygen saturation – is expected to detect most cases of hypoxia due to tricuspid atresia.

## Clinical and epidemiologic notes

Survival of the newborn depends on the presence of an ASD to allow the exit of blood from the right atrium to the left atrium (see Fig. 4.19), and an open ductus arteriosus to allow blood to reach the lungs to be oxygenated. Infants with only a small ASD or with a closing ductus will present early with severe symptoms.

Tricuspid atresia can co-occur with complex cardiovascular anomalies; for example, with heterotaxy, DORV or malposed great arteries. When the ventricular septum is intact, severe pulmonary valve stenosis or atresia might also be present, together with underdevelopment of the right ventricle.

Tricuspid atresia has been diagnosed in infants with deletion 22q11 (5–10%), common trisomies and other rarer genetic conditions.

Tricuspid atresia is one of the more common cyanotic CHDs, with a frequency of approximately 1 in 10 000 to 15 000 births. Tricuspid atresia is more common in males.

## Inclusions

Q22.4 Tricuspid valve atresia (this code also include stenosis; see note below)

Notes:

- Although clinically severe tricuspid stenosis can resemble tricuspid atresia, most cases of tricuspid stenosis are mild. Tricuspid stenosis and tricuspid atresia should be kept separate in public health surveillance of prevalence and outcomes.
- **Unfortunately, ICD-9 (International Classification of Diseases, Ninth Revision), ICD-10 and RCPCH coding systems use the same code for tricuspid atresia and stenosis.** An option for differentiating the two conditions includes adding an additional digit to the ICD-10 core.

## Exclusions

A programme must be clear about what is included when collecting data on tricuspid atresia and then apply the codes consistently.

## Checklist for high-quality reporting

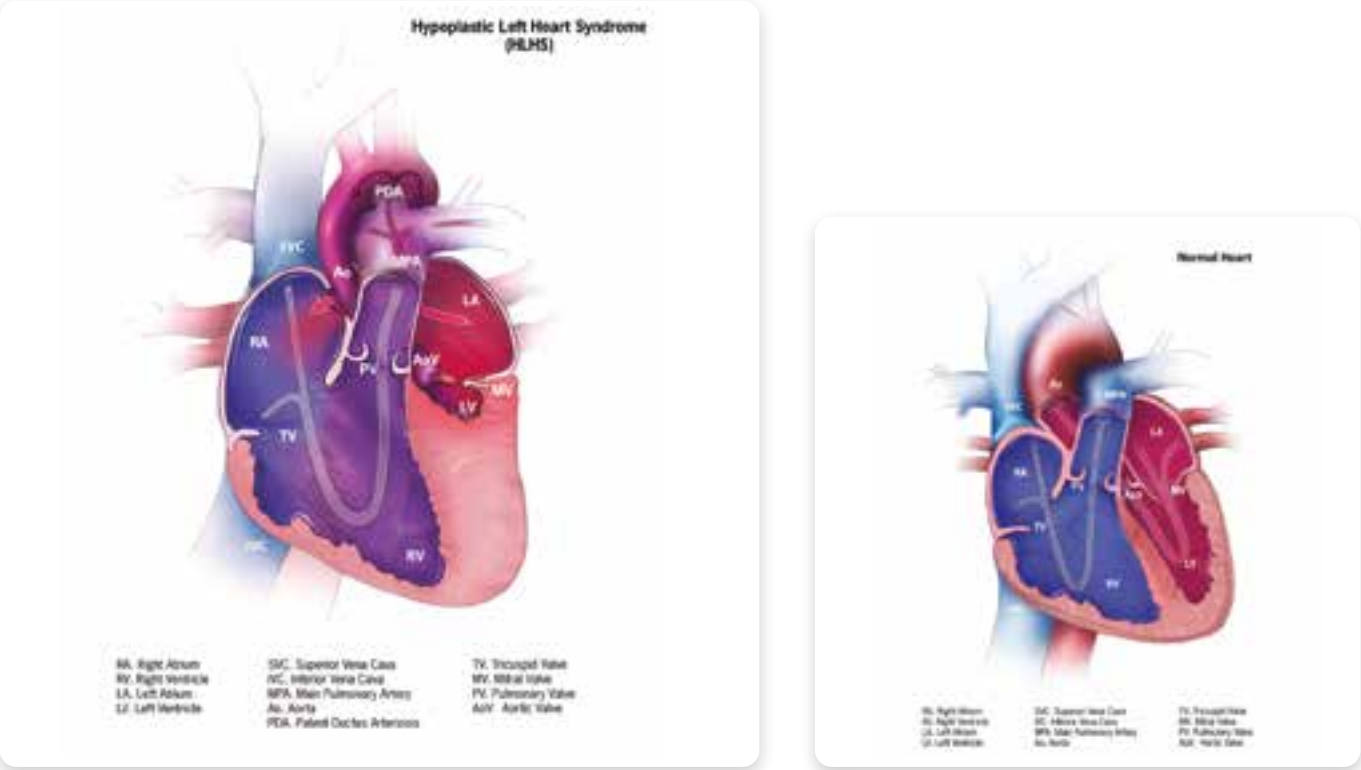
| Tricuspid Atresia – Documentation Checklist |
|---|
| ☐ **Describe in detail the clinical and echocardiographic findings:**<br>▸ Anatomy – specify intracardiac anomalies, including the presence of ventricular septal defects, abnormally small right ventricle, pulmonary valve stenosis or atresia, transposition or malposition of the great arteries.<br>▸ Procedure – specify whether the cardiac findings are from a prenatal or postnatal echocardiogram, or from other investigations (e.g. catheterization, MRI), surgery or autopsy. |
| ☐ **Look for and document extracardiac birth defects and genetic conditions, such as deletion 22q11.** |
| ☐ **Report whether specialty consultation(s) was done:** Report on whether the diagnosis was made by a paediatric cardiologist, and whether the patient was seen by a geneticist. |
| ☐ **Report any genetic testing and results (e.g. chromosomal studies, genomic microarray, genomic sequencing).** |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical descriptions for documentation of key elements:<br>▸ Anatomy: Note also ventricular septal defect, pulmonary valve anomalies, additional findings.<br>▸ How cardiac findings were detected (e.g. echocardiography).<br>▸ Who made the diagnosis (e.g. paediatrician, paediatric cardiologist).<br>▸ Specialists who evaluated the child, in particular, a paediatric cardiologist or geneticist.<br>▸ Key evaluations done, especially genetic testing. |
| **Coding** | ▸ Coding is straightforward (Q22.4) but the code includes stenosis. The programme should determine whether coding stenosis will be separate from coding atresia (e.g. by using an additional digit). The presence of ventricular septal defect is important clinically and should be noted and coded. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies and syndromes occurring with tricuspid atresia: if < 5%, consider under-ascertainment of these co-occurring conditions, especially deletion 22q11. |
| **Prevalence** | ▸ Monitor prevalence: If low (< 0.4 per 10 000 births) it suggests under-ascertainment; if much higher than 1 per 10 000 it suggests inclusion of cases of stenosis.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units. |

Hypoplastic left heart "syndrome" (HLHS) is a structural heart anomaly characterized clinically by variable degrees of heart failure in the newborn and anatomically by an underdeveloped left side of the heart, especially the left ventricle and aorta (see Fig. 4.20). Key findings in HLHS include a small left ventricle; a small, narrowed or atretic mitral valve or aortic valve; and an underdeveloped ascending aorta. For these reasons, the heart is unable to sustain systemic circulation, especially after the ductus arteriosus closes.

**Fig. 4.20. Hypoplastic left heart syndrome**




## Relevant ICD-10 codes

Q23.4 Hypoplastic left heart syndrome

## Diagnosis

***Prenatal.*** HLHS can be suspected and diagnosed prenatally. The basic four-chamber view of the heart – which is included in the standard second trimester obstetric ultrasound scan – can readily identify conditions that dramatically affect the ventricles, including HLHS. Prenatal confirmation is reliable if done by a paediatric cardiologist with a sufficiently detailed prenatal echocardiographic exam. However, prenatal diagnoses should be confirmed postnatally; for example, by echocardiography.

***Postnatal.*** Echocardiography has largely superseded other imaging techniques. Newborn screening via pulse oximetry – which is based on the non-invasive detection of low peripheral oxygen saturation – is effective in detecting HLHS as long as the condition decreases the blood oxygen saturation below the cut-off for newborn screening testing. Note that HLHS, especially in the presence of a widely open ductus arteriosus, might be missed in the early newborn period and could become clinically obvious only after the ductus closes, which might happen after discharge from the nursery or birthing centre.

## Clinical and epidemiologic notes

In HLHS, the clinical norm is early-onset heart failure (cardiogenic shock). The timing of heart failure varies. An ASD and a patent ductus arteriosus can allow some circulation of oxygenated blood to the body for a period of time (usually not more than a few days in the case of a patent ductus arteriosus). When the ductus closes, the clinical status of the newborn quickly deteriorates. Some infants develop signs and symptoms of congestive heart failure and shock (systemic hypoperfusion) very early, whereas

others might have a "normal" physical exam in the first day of life, and then rapidly decompensate later. The timing of symptoms depends on the evolution of pulmonary vascular resistance, the closure of the ductus arteriosus, and the size of the ASD.

Because blood hypoxygenation is often present before clinical signs and symptoms appear, newborn screening via pulse oximetry is critically important for early detection, and can prompt treatment. Other cases can be suspected because of absence of pulses.

Though more than 75% of all HLHS cases are isolated, HLHS can be associated with genetic conditions. Familial forms are increasingly recognized. When including all left-sided lesions, the frequency of left-sided heart anomalies is as high as 10–12% in some families in which a child was born with HLHS. For this reason, echocardiographic screening of family members is suggested.

Some genetic syndromes associated with HLHS include Turner syndrome (Q96), Kabuki syndrome, Noonan syndrome (Q87.14), Holt-Oram syndrome (Q87.20), and the common trisomies.

Birth prevalence of HLHS is approximately 1 in 4000 births. HLHS is slightly more common in males.

Notes:

- Left-sided obstructive defects such as aortic stenosis/atresia and mitral stenosis/atresia might occur together but do not necessarily qualify as a diagnosis of HLHS. **The latter diagnosis should be made by a paediatric cardiologist when possible.**
- **Despite its name, HLHS is not a true "syndrome"** but simply a structural heart anomaly that, like other birth defects, can be isolated (most of the time), associated with other birth defects, or part of a syndrome (i.e. due to a known cause, genetic or teratogenic).

## Inclusions

Q23.4 Hypoplastic left heart syndrome

## Exclusions

Individual left-sided obstructive defects (e.g. aortic atresia, mitral stenosis) that do not qualify as HLHS.

## Checklist for high-quality reporting

**Hypoplastic Left Heart Syndrome (HLHS) – Documentation Checklist**

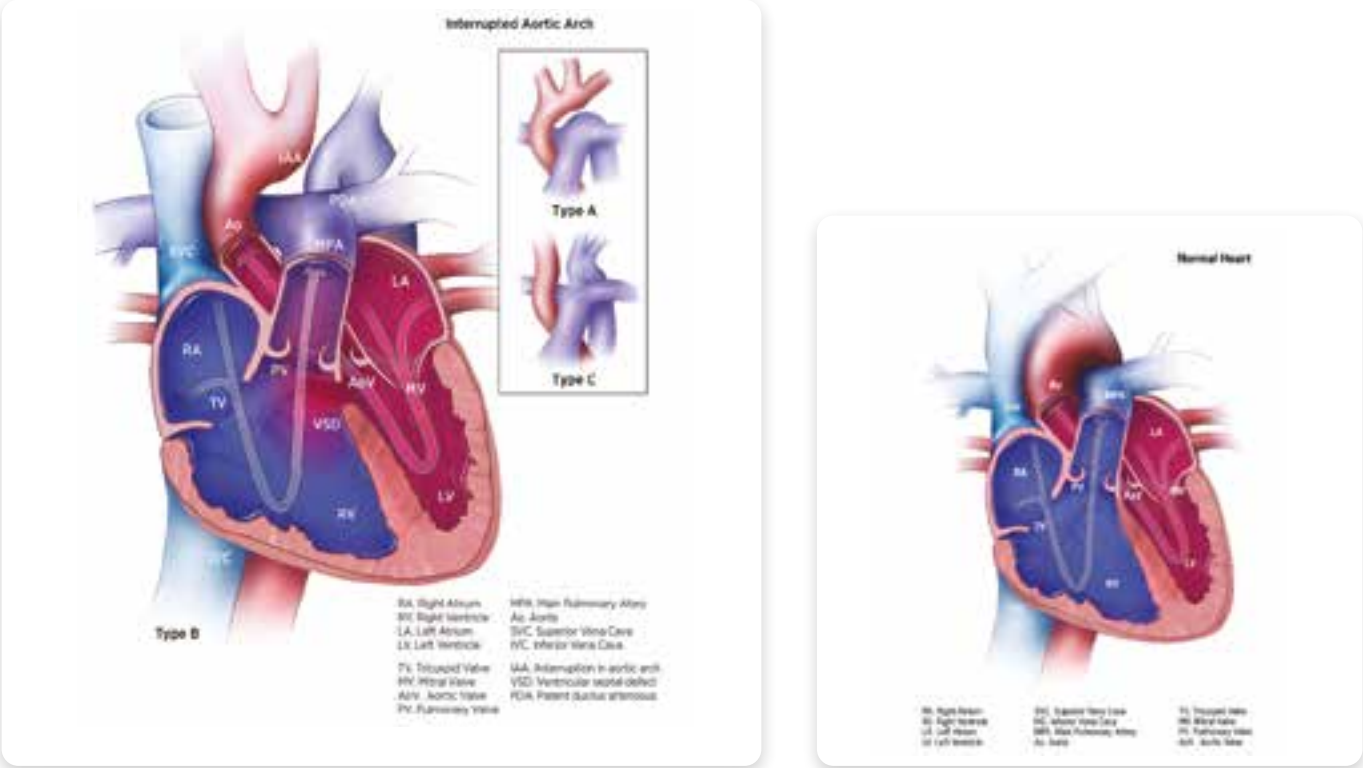
- ☐ **Describe in detail the clinical and echocardiographic findings:**
  - Anatomy – specify the elements of HLHS present in the child; for example, mitral stenosis or atresia, hypoplastic left ventricle, stenosis or atresia of the aortic valve, hypoplastic aorta, interrupted aortic arch, endocardial fibroelastosis, etc.
  - Procedure – specify whether the cardiac findings are from a prenatal or postnatal echocardiogram, or from other investigations (e.g. catheterization, MRI), surgery or autopsy.
  - Additional cardiac findings – specify any additional findings, including ASD, patent ductus arteriosus, etc.
- ☐ **Look for and document extracardiac birth defects, major or minor (minor anomalies can suggest Turner syndrome).**
- ☐ **Report whether specialty consultation(s) was done:** Report whether the diagnosis was made by a paediatric cardiologist, and whether the patient was seen by a geneticist.
- ☐ **Report any genetic testing and results (e.g. chromosomal studies, genomic microarray, genomic sequencing).**

## Suggested data quality indicators

| Category | Suggested Practices and Quality indicators |
|---|---|
| **Description and documentation** | Review sample of clinical descriptions for documentation of key elements:<br>▸ Anatomy – presence and severity of left-sided anomalies (mitral and aortic valves, left ventricle, left ventricular endocardium, aorta and aortic arch).<br>▸ How cardiac findings were detected (e.g. echocardiography).<br>▸ Who made the diagnosis (e.g. paediatrician, paediatric cardiologist).<br>▸ Specialists who evaluated the child, in particular, a paediatric cardiologist or geneticist.<br>▸ Key evaluations done, especially genetic testing. |
| **Coding** | ▸ Track and evaluate cases with multiple left-sided anomalies to assess whether cases should be re-coded as HLHS. Left-sided anomalies include mitral valve stenosis or atresia (Q23.2), aortic valve stenosis or atresia (Q23.0), atresia of the aorta (Q25.2), etc. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies and syndromes occurring with HLHS: If < 5%, under-ascertainment of these co-occurring conditions is likely. |
| **Prevalence** | ▸ Monitor prevalence: If low (< 1 per 10 000 births), it suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units. |

Interrupted aortic arch (IAA) is a structural heart defect characterized anatomically by a discontinuity (interruption) along the aortic arch. Depending on the site of discontinuity, IAA is classified into three types (see Fig. 4.21). Type B is the most common (50–70%), type A is less common (30–45%) and type C is rare.

**Fig. 4.21. Interrupted aortic arch**




- Type A: The discontinuity is distal to the left subclavian artery (approximately in the same region as coarctation of the aorta).
- **Type B (the most common form): The discontinuity is more proximal, between the left carotid and subclavian.**
- Type C: The discontinuity is more proximal still, between the brachiocephalic artery and the common carotid artery.

## Relevant ICD-10 codes

Q25.21 Interruption of aortic arch (preferred)
Q25.2 Atresia of aorta
Q25.4 Other congenital malformations of aorta (heterogeneous; might include interrupted aortic arch)

## Diagnosis

***Prenatal.*** IAA is easily missed on the obstetric anomaly scan, though it might be suspected based on discrepancy between the left and right ventricular sizes. Prenatally diagnosed cases should be confirmed postnatally.

***Postnatal.*** Infants can present clinically in the early neonatal period, when the ductus closes, with signs and symptoms of congestive heart failure and systemic hypoperfusion (cardiogenic shock). Newborn screening via pulse oximetry can lead to earlier diagnosis.

## Clinical and epidemiologic notes

As noted, an early presentation is heart failure and cardiogenic shock, with rapid clinical deterioration as the ductus closes. Because of right-to-left shunting at the ductus arteriosus, infants might initially show differential oxygen saturation or cyanosis. In type A, the difference in saturation is between the upper and lower limbs, with the lower limbs having lower saturation; in type B, there is a difference in saturation between the left and right arms, with the left arm having lower saturation.

Ventricular septal defect and other intracardiac defects are often present.

The three types of IAA differ in their association with genetic risk factors. For example, deletion 22q11 occurs in 50% or more of cases of type B IAA, and is rare in the other types. Other syndromes that can occur with IAA include CHARGE syndrome (Q30.01).

Environmental risk factors include use of the medication isotretinoin (specifically for type B IAA) and maternal pregestational diabetes.

Birth prevalence of IAA, all types, is approximately 1 in 15 000 births (approximately 0.7 per 10 000 births).

## Inclusions

Q25.21 Interruption of aortic arch

## Exclusions

Q25.43 Congenital aneurysm of aorta
Q25.44 Congenital dilation of aorta
Q25.45 Double aortic arch
Q25.46 Tortuous aortic arch
Q25.47 Right aortic arch
Q25.48 Anomalous origin of subclavian artery

## Checklist for high-quality reporting

**Interrupted Aortic Arch (IAA) – Documentation Checklist**

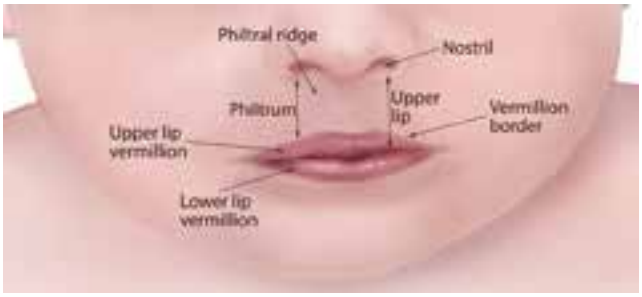
- ☐ **Describe in detail the clinical and echocardiographic findings:**
  - Anatomy – specify site of discontinuity, type of IAA as noted in echocardiographic report, and intracardiac anomalies, including the presence of ventricular septal defects.
  - Procedure – specify whether the cardiac findings are from a prenatal or postnatal echocardiogram, or from other investigations (e.g. catheterization, MRI), surgery or autopsy.
- ☐ **Look for and document extracardiac birth defects:** IAA can occur with genetic syndromes such as deletion 22q11, which is associated with many external and internal anomalies.
- ☐ **Report whether specialty consultation(s) was done:** Report whether the diagnosis was made by a paediatric cardiologist, and whether the patient was seen by a geneticist.
- ☐ **Report any genetic testing and results (e.g. chromosomal studies, genomic microarray, genomic sequencing).**

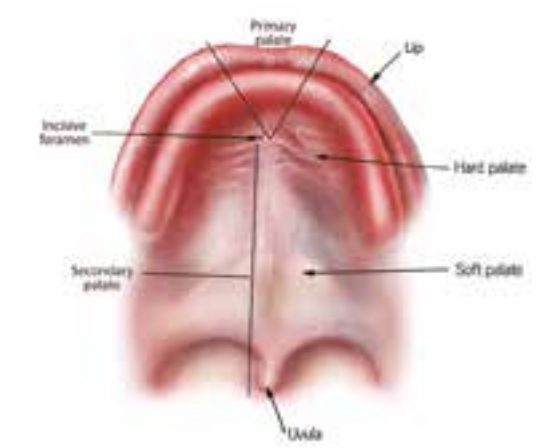
## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical descriptions for documentation of key elements:<br>▸ Anatomy: Note site of interruption and type (A, B or C), presence of ventricular septal defect, and other aortic or intracardiac anomalies.<br>▸ How cardiac findings were detected (e.g. echocardiography).<br>▸ Who made the diagnosis (e.g. paediatrician, paediatric cardiologist).<br>▸ Specialists who evaluated the child, in particular, a paediatric cardiologist or geneticist.<br>▸ Key evaluations done, especially genetic testing. |
| **Coding** | ▸ Code as Q25.21; track and minimize codes Q25.1 (atresia of the aorta) and Q25.4 (other congenital anomalies of the aorta) so that cases of IAA are not dispersed across different codes. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies and syndromes occurring with IAA: If considerably < 50% for type B, or < 25% overall, consider under-ascertainment of co-occurring conditions, especially deletion 22q11. |
| **Prevalence** | ▸ Monitor prevalence: If low (< 0.3 per 10 000 births) it suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units. |

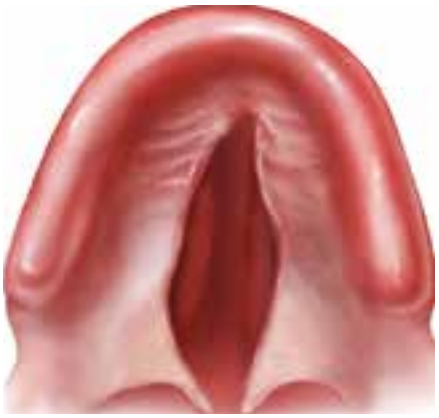
## Orofacial clefts

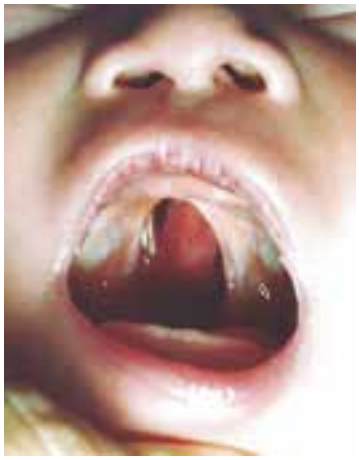
**Fig. 4.22. Cleft palate, including hard and soft palate**




Cleft palate, including hard and soft palate (Q35.5)





*Photograph source:* CDC–Beijing Medical University collaborative project.

Cleft lip with or without cleft palate, and cleft palate alone, are collectively referred to as orofacial clefts. Descriptions for each of these conditions follow. To aid understanding of the individual conditions, the structure of a normal palate and the anatomy of a normal lip is shown above. Clefts should be coded using a single ICD code. For example, no infant should have a cleft only code plus a cleft lip code, but instead should have a single code for cleft lip and palate.

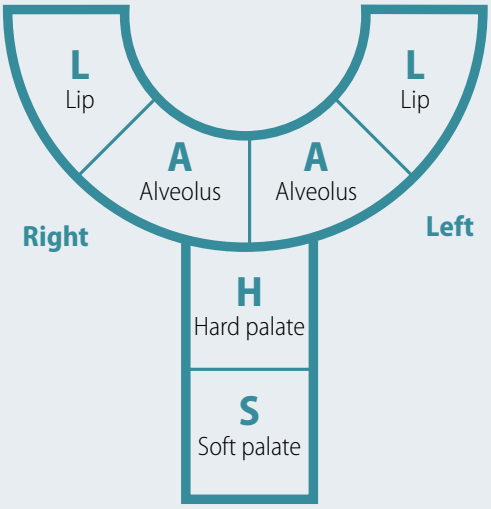
Some programmes might find it useful to provide more detail for certain conditions to aid in final diagnoses and for referral purposes. For orofacial clefts, many programmes use the LAHSAL system. LAHSAL is a simple method for describing and classifying oral clefts. One advantage of this system is that LAHSAL is often used by plastic surgeons to evaluate treatment outcomes.

LAHSAL (see Fig. 4.23) is an acronym for a sequence of descriptors:

Lip, right – Alveolus, right – Hard palate – Soft palate – Alveolus, left – Lip, left

The letters are read from the patient's right to left.
Upper-case letters represent complete clefts: L
Lower-case letters represent incomplete clefts: l
No cleft is represented with a dot: .
An asterisk represents a microform cleft: *

**Fig. 4.23. LAHSAL**




https://www.researchgate.net/publication/260290042_Labio_yo_paladar_hendido_una_revision/figures?lo=1

Cleft palate (also called palatoschisis) is characterized by a fissure in the secondary palate (posterior to the incisive foramen) and can involve the soft palate only or both the hard palate and the soft palate. The cleft can be narrow (V-shaped) or wider (U-shaped). The lip is intact. Laterality of cleft palate is difficult to ascertain and some believe it does not exist.

Cleft palate only (a term often used to refer to cleft palate with intact lip) is more often associated with additional birth defects and syndromes, so a careful physical examination with appropriate internal organ assessment is strongly recommended.

## Relevant ICD-10 codes

Q35.1 Cleft hard palate
Q35.3 Cleft soft palate
Q35.5 Cleft hard palate with cleft soft palate
Q35.59 Complete cleft palate
Q35.9 Cleft palate, unspecified
Q35 Cleft palate: Avoid using this generic code if more specific information is available

## Related ICD-10 code

Q87.0 Robin sequence or defect, with core components including retro-micrognathia, posterior displacement of the tongue (glossoptosis) and respiratory obstruction. Cleft palate is a common though not required component of the Robin sequence. Whereas ICD-10 lists Robin sequence as an exclusion from the Q35 series, because it is such a common condition, the Q87.0 code is suggested.

Notes:

- Q35 is the generic code for cleft palate. However, avoid using this code if more specific information is available.
- A simple alternative approach to classification and coding is the LAHSAL method, used often by plastic surgeons to assess for treatment outcomes (see Fig. 4.23). In surveillance it is best used in addition to, rather than instead of, the ICD codes.

## Diagnosis

***Prenatal.*** Cleft palate alone can be suspected prenatally, but it can easily be missed or misdiagnosed. Cases identified or suspected prenatally should be confirmed postnatally before inclusion in the surveillance programme.

***Postnatal.*** Cleft palate can be missed at the external newborn examination if the palate is not systematically and carefully examined. This requires visualization of the entire length of the palate. When examining the palate, check for the presence of lower lip pits, which are a diagnostically useful sign of a specific autosomal dominant condition, and for signs of Pierre Robin sequence (microretrognathia, glossoptosis, respiratory obstruction). Clinically, a cleft palate might manifest with nasal regurgitation of feeds or difficulty feeding.

## Clinical and epidemiologic notes

Photographs can be very helpful in uncertain or difficult cases, as they allow expert review, but good-quality images of a cleft palate might be difficult to obtain. Additional useful imaging techniques include CT and MRI.

Be sure to note "lip pits" in the lower lip pits in the context of orofacial clefts (including cleft palate alone), which is indicative of the autosomal dominant condition van der Woude syndrome, and is the most common syndrome associated with otherwise apparently isolated clefts.

All orofacial clefts (cleft lip, cleft palate, and cleft lip with cleft palate) have similar non-genetic risk factors. Non-genetic risk factors for cleft palate include maternal smoking, drinking alcohol, use of some medications (selected seizure medications such as barbiturates, valproate and topiramate), obesity and high fever. Some suggested additional risk factors include pregestational diabetes, substances that are folic acid antagonists, and systemic steroids.

Cleft palate occurs with a birth prevalence of approximately 6 per 10 000 births (or ~1 in 1500 births), but with a very wide variation in different studies and populations. Outside of methodologic factors, the main factor in variability appears to be ethnicity, with higher prevalence in people of Northern European, Native American/First People, and Asian ancestry.

## Inclusions

Q35 and subgroups except for Q35.7 (bifid uvula): Cleft palate (excluding bifid uvula and submucous cleft palate)

## Exclusions

Q37 Cleft palate with cleft lip
Q35.7 Bifid (cleft) uvula
Q38.5 Absence of uvula

Submucous cleft palate: This defect is not a considered a major anomaly and should not be included in prevalence counts of cleft palate. Submucous cleft palate does not have a specific code.

## Checklist for high-quality reporting

| Cleft Palate – Documentation Checklist |
|---|
| ☐ **Describe in detail, including:**<br>▸ Extension (cleft palate) – hard palate, soft palate.<br>▸ Lower lip – pits present or absent (when present, van der Woude syndrome should be strongly suspected).<br>☐ **Describe procedures to assess further additional malformations, and if present, describe these.**<br>☐ **Take and report photographs:** Very useful; can be crucial for review<br>☐ **Report whether specialty consultation(s) done, and if so, report the results:** Plastic surgery and genetics consultation reports are useful. |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical description for documentation of key descriptors:<br>▸ Description of extension (partial, complete cleft) – indicates systematic observation and reporting.<br>▸ Documentation of lip pits (if present or absent) or any other minor anomaly.<br>▸ Description of cleft as U-shaped or V-shaped (can be useful in suspecting some syndromes).<br>▸ Drawings, photographs and consultation reports. |
| **Coding** | ▸ Code as Q35.X for specific type, if documented.<br>▸ Monitor and minimize the number of cases coded with generic Q35 code.<br>▸ Monitor and minimize the number of cases coded as unspecified (Q35.9).<br>▸ Monitor and recode cases with separate codes for cleft lip and for cleft palate (Q35 + Q36/Q37).<br>▸ For programmes that choose to add the LAHSAL classification system, the example demonstrates how cleft palate would be classified.<br>▸ Example: Complete (hard and soft) cleft palate (with intact lip) would be coded as [. . HS . .]. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies occurring with orofacial clefts, which should be higher in cleft palate compared to cleft lip and palate (and cleft lip).<br>▸ More severe anatomy (complete cleft) has greater clinical impact and complex outcomes. |
| **Prevalence** | ▸ Monitor prevalence: Prevalence varies considerably, but if very low (< 1.5 per 10 000), it strongly suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units.<br>▸ Compare prevalence of subtypes: Expectation is cleft lip and palate > cleft palate > cleft lip. |

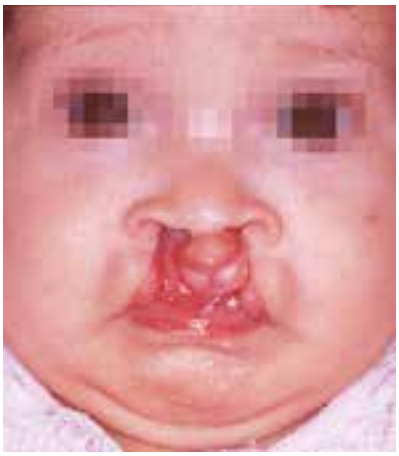
Cleft lip is characterized by a partial or complete fissure of the upper lip. It can be unilateral (Fig. 4.24, *panels a, b*) or bilateral (Fig. 4.24, *panel c*). In bilateral cleft lip, a median remnant of the philtrum is always present. The cleft lip can extend through the gum, but not beyond the incisive foramen. If the cleft extends further backwards into the secondary palate it becomes a different entity – a cleft lip with cleft palate.

**Fig. 4.24. Cleft lip**

Unilateral (Q36.9)

Unilateral (Q36.9)

Bilateral (Q36.0)



*Photograph sources*: (b) Dr Jaime Frías (EE. UU.); (c) Dr Pedro Santiago and Dr Miguel Yanez (EE. UU.).

Rarer conditions that could be confused with typical cleft lip are median cleft lip (Q31.1) and atypical or Tessier type craniofacial clefts. Median cleft lip can be distinguished from bilateral cleft lip because in medial cleft lip there is no tissue below the philtrum (see below for more information on median cleft lip). In bilateral cleft lip (*panel c*) a midline remnant of tissue is always present. Atypical or Tessier type craniofacial clefts are a group of defects that involve clefts of the cranial and/or facial skeleton. Unlike cleft lip where the cleft extends up towards the nose, the 14 various Tessier's clefts extend through radiating axes of facial and cranial bones, including towards the eye or nasolacrimal canal (oro-orbital or Tessier 5 cleft), or even more laterally towards the ear (oro-auricular or Tessier 7 cleft). Both median and Tessier type clefts are much rarer than typical cleft lip.

## Relevant ICD-10 codes

| | |
|---|---|
| Q36.0 | Cleft lip, bilateral |
| Q36.9 or Q36.90 | Cleft lip, specified as unilateral |
| Q36.99 | Cleft lip, unspecified |

Note:

- Q36 is the generic ICD-10 code for cleft lip. However, avoid using this general code if more specific information is available.

## Diagnosis

***Prenatal.*** Cleft lip can be suspected prenatally, but it can easily be missed or misdiagnosed. Cases identified or suspected prenatally should be confirmed postnatally before inclusion in the surveillance programme.

***Postnatal.*** Cleft lip is easily recognized on physical examination after delivery. The palate should be checked carefully to exclude the presence of cleft lip with cleft palate.

## Clinical and epidemiologic notes

Older terms for cleft lip, no longer in use and best avoided, include cheiloschisis, congenital fissure of lip, harelip (pejorative), and labium leporinum (pejorative).

Unilateral cleft lip is much more common than bilateral cleft lip. Left-sided cleft lip is more common than right-sided cleft lip.

Photographs can be very helpful in uncertain or difficult cases, as they allow expert review.

Microform cleft lip resembles a typical cleft lip that has healed prenatally, leaving what appears to be a scar where a cleft lip typically occurs (see Fig. 4.25). Microform cleft lip is not a major congenital anomaly and is typically excluded by most programmes.

In median cleft lip, there is no remnant of tissue (philtrum) in the area below the nasal septum. Median cleft lip is part of a condition called absent premaxilla and is often an external finding in holoprosencephaly, a severe brain malformation.

Absent premaxilla and holoprosencephaly are associated with genetic syndromes, including trisomy 13.

In addition to median cleft lip and Tessier type cleft, other atypical clefts occur, albeit rarely. Other atypical clefts include incomplete median cleft lip (which occurs in oro-facio-digital syndromes and hydrolethalus syndrome) and clefts that can be seen with amniotic band or limb-body wall spectrum anomalies (a disruptive event rather than a primary malformation).

Note any "lip pits" in the lower lip (see Fig. 4.26). This finding in the context of cleft lip (and also cleft lip and palate) is indicative of an autosomal dominant condition called van der Woude syndrome.

**Fig. 4.25. Microform ("healed" cleft lip)**

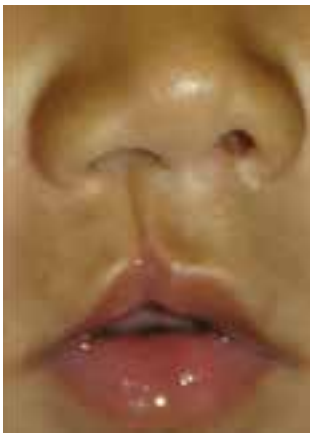
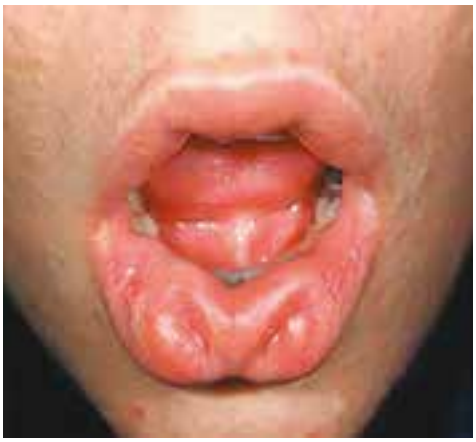


**Fig. 4.26. Lip pits**



*Photograph source*: permission from the library of Dr Travis Tollefson.

All orofacial clefts (cleft lip, cleft palate, and cleft lip with cleft palate) have similar non-genetic risk factors. Non-genetic risk factors for cleft lip include maternal smoking, drinking alcohol (especially binge drinking), obesity, fever, some medications (selected seizure medications), and pregestational diabetes. Folic acid or multivitamin supplement use has been associated with a moderately reduced risk of cleft lip (with or without cleft palate).

Cleft lip occurs with a birth prevalence of approximately 3.5 per 10 000 births (or approximately 1 in 3000 births). Prevalence has been reported as higher in some Asian groups and possibly lower in people of African ancestry.

## Inclusions

| | |
|---|---|
| Q36 | Cleft lip: Avoid using this non-specific code in favour of more specific codes |
| Q36.0 | Cleft lip, bilateral |
| Q36.9 or Q36.90 | Cleft lip, specified as unilateral |
| Q36.99 | Cleft lip, unspecified |

## Exclusions

| | |
|---|---|
| Q36.1 | Median cleft lip<br>Median cleft lip is different etiologically and epidemiologically; it should be excluded and assessed separately from typical cleft lip. |
| Q37–Q37.9 | Cleft palate with cleft lip<br>Cleft palate with cleft lip is included in a separate group of orofacial clefts. |

Microform cleft lip (or pseudocleft) is not a major malformation and is not included with cleft lip. There is no associated ICD-10 code for microform cleft lip.

Craniofacial clefts (Tessier type clefts) are different etiologically and epidemiologically. These rare defects should be excluded and assessed separately from cleft lip. Tessier clefts do not have a separate code and are best coded as Q75.8: "Other specified congenital malformations of skull and face bones".

## Checklist for high-quality reporting

**Cleft Lip – Documentation Checklist**

- ☐ **Describe in detail, including:**
  - Laterality – right, left or bilateral.
  - Lower lip – pits present or absent (when present, van der Woude syndrome should be suspected).
  - Extension of the cleft lip – minimum, partial or total involvement of the gum extending at most through the alveolus to the incisive foramen (not beyond).
- ☐ **Describe procedures to assess further additional malformations, and if present, describe these.**
- ☐ **Take and report photographs:** Very useful; can be crucial for review.
- ☐ **Report whether specialty consultation(s) done, and if so, report the results.**

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical description for documentation of key descriptors: Laterality, extension (in lip or palate), lip pits, premaxilla.<br>▸ Excellence in documentation includes drawings, photographs and consultation reports.<br>▸ Consistently specifying laterality (unilateral versus bilateral) indicates systematic observation and reporting. |
| **Coding** | ▸ Code as Q36.X for specif type, if documented.<br>▸ Track and minimize cases coded with generic Q36 codes.<br>▸ Track and minimize cases of cleft lip with laterality unspecified (Q36.99).<br>▸ Median cleft lip is rare, but no reported cases suggests potential miscoding as typical cleft lip.<br>▸ Typical cleft lip code (e.g. Q36.90) in child with holoprosencephaly or trisomy 13 should be reviewed for possible miscoding. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies occurring with orofacial clefts, which should be lower in cleft lip than cleft palate.<br>▸ Consider using severity of anatomic involvement (bilateral) as factor in clinical outcome assessment. |
| **Prevalence** | ▸ Monitor prevalence: Varies by geography and ethnicity, but if very low (< 2 per 10 000 births) it suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units.<br>▸ Compare prevalence of subtypes: Expectation is cleft lip and palate > cleft palate > cleft lip. |

**Fig. 4.27. Cleft palate with cleft lip**

Cleft palate with unilateral cleft lip (Q37.10)

Cleft palate with bilateral cleft lip (Q37.4)

*Photograph source*: Dr Pedro Santiago and Dr Miguel Yáñez (EE. UU.).

Cleft palate with cleft lip is characterized as a cleft of the upper lip extending through the hard palate (primary and secondary palate) and might also extend through the soft palate (*left panel*).

Other conditions that can be confused with – and that need to be differentiated from – typical cleft palate with cleft lip are the atypical or Tessier type clefts and the amniotic band spectrum. Atypical or Tessier type craniofacial clefts are a group of defects that involve clefts of the cranial and/or facial skeleton. Unlike a typical orofacial cleft where the cleft extends up towards the nose, the 14 various Tessier clefts extend through radiating axes of facial and cranial bones, including towards the eye or nasolacrimal canal (oro-orbital or Tessier 5 cleft), or even more laterally towards the ear (oro-auricular or Tessier 7 cleft). Tessier type clefts are substantially rarer than cleft palate with cleft lip. Amniotic band spectrum can cause facial disruptions that involve both the lip and palate, and often include atypical skull and brain lesions (e.g. atypical encephaloceles).

## Relevant ICD-10 codes (see quick reference table on the right for the most common forms)

Q37.0 Cleft hard palate with bilateral cleft lip
Q37.10 Cleft hard palate with cleft lip, specified as unilateral
Q37.19 Cleft hard palate with cleft lip, unspecified
Q37.2 Cleft soft palate with bilateral cleft lip
Q37.3 Cleft soft palate with unilateral cleft lip
Q37.4 Cleft hard palate and soft palate with bilateral cleft lip
Q37.5 Cleft hard palate and soft palate with unilateral cleft lip
Q37.59 Cleft hard palate and soft palate with cleft lip, unspecified
Q37.8 Unspecified cleft palate with bilateral cleft lip
Q37.9 Unspecified cleft palate with unilateral cleft lip
Q37.99 Cleft palate with cleft lip, unspecified

| | Cleft Palate | | |
|---|---|---|---|
| **Cleft lip** | **Hard** | **Hard and soft** | **Unspecified** |
| **Bilateral** | Q37.0 | Q37.4 | Q37.8 |
| **Unilateral** | Q37.10 | Q37.5 | Q37.9 |
| **Unspecified** | Q37.19 | Q37.59 | Q37.99 |

Notes:

- Q37 is the generic code for cleft palate with cleft lip. However, avoid using this code if more specific information is available.
- A simple alternative approach to classification and coding is the LAHSAL method, used often by plastic surgeons to assess for treatment outcomes (see Fig. 4.23). In surveillance, it is probably best used in addition to, rather than instead of, the ICD codes.

## Diagnosis

***Prenatal.*** Cleft palate with cleft lip can be suspected prenatally, but it is easily missed or misdiagnosed. Cases identified or suspected prenatally should be confirmed postnatally before inclusion in the surveillance programme.

***Postnatal.*** Cleft palate with cleft lip is easily recognized on physical examination after delivery, provided the palate is also checked carefully.

## Clinical and epidemiologic notes

Though used mostly for cleft lip, older terms, no longer in use and best avoided, include cheiloschisis, harelip (pejorative) and labium leporinum (pejorative).

Photographs can be very helpful in uncertain or difficult cases (like differentiating between atypical clefts such as Tessier type craniofacial clefts or amniotic bands), as they allow expert review.

Photographs can also help reviewers detect "lip pits" in the lower lip. This finding in the context of cleft lip (and also cleft palate with cleft lip) is indicative of an autosomal dominant condition called van der Woude syndrome.

All orofacial clefts (cleft lip, cleft palate, and cleft palate with cleft lip) have similar non-genetic risk factors. Non-genetic risk factors for cleft palate with cleft lip include maternal smoking, drinking alcohol (especially binge drinking), obesity, fever, some medications (selected seizure medications), and diabetes. Folic acid or multivitamin supplement use has been associated with a moderately reduced risk of cleft lip (with or without cleft palate).

Cleft palate with cleft lip occurs with a birth prevalence of approximately 6 per 10 000 births (or approximately 1 in 1500 births). Prevalence has been reported as higher with Asian ancestry and possibly lower in people of African ancestry.

## Inclusions

Q37–Q37.9 Cleft palate with cleft lip

## Exclusions

Q36 and subgroups These include all types of cleft lip alone, including median cleft lip

Craniofacial clefts (Tessier type clefts) are different etiologically and epidemiologically. These rare defects should be excluded and assessed separately from cleft palate with cleft lip. Tessier clefts do not have a separate code and are best coded as Q75.8: "Other specified congenital malformations of skull and face bones".

Amniotic band spectrum is coded as Q79.80 (congenital constriction bands). Be sure to note all affected parts of the body.

## Checklist for high-quality reporting

**Cleft Palate with Cleft Lip – Documentation Checklist**

- ☐ **Describe in detail, including:**
  - Laterality – right, left or bilateral.
  - Extension (cleft palate) – hard palate, soft palate.
  - Lower lip – pits present or absent (when present, van der Woude syndrome should be strongly suspected).
- ☐ **Describe procedures to assess further additional malformations, and if present, describe these.**
- ☐ **Take and report photographs:** Very useful; can be crucial for review.
- ☐ **Report whether specialty consultation(s) done, and if so, report the results.** Plastic surgery consultation reports are often useful.

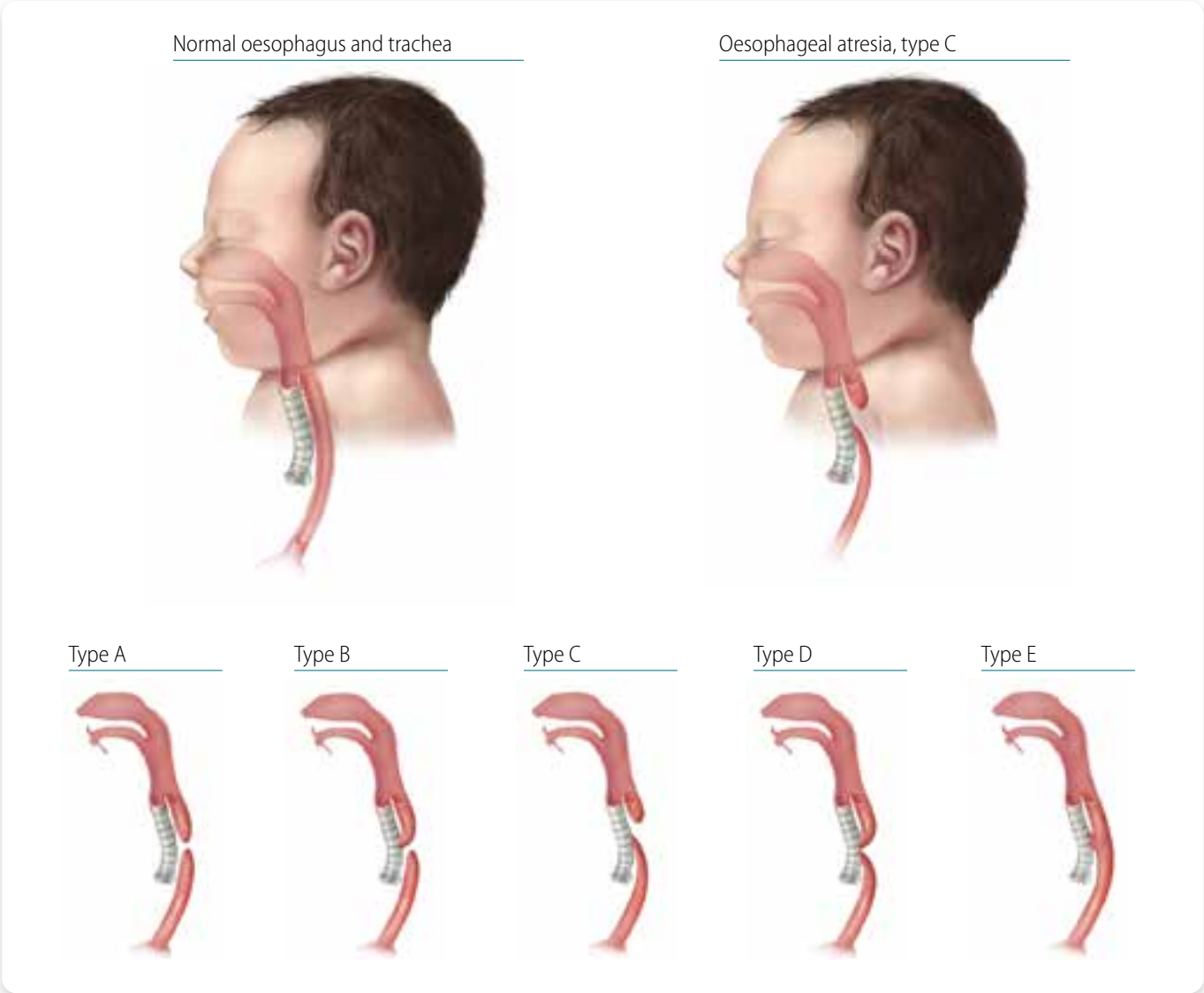
## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical description for documentation of key descriptors: Laterality, extension (in lip or palate), lip pits.<br>▸ Excellence in documentation includes drawings, photographs and consultation reports.<br>▸ Consistently specifying laterality (unilateral versus bilateral) indicates systematic observation and reporting. |
| **Coding** | ▸ Code as Q37.X for specific type, if documented.<br>▸ Track and minimize cases coded with generic Q37 and Q37.99 codes.<br>▸ Track and minimize cases with unspecified laterality (Q37.19).<br>▸ For programmes that choose to add the LAHSAL classification system, the example below demonstrates how cleft palate with cleft lip would be classified.<br>Example: The findings illustrated in the photograph (left-sided cleft palate with cleft lip) would be coded as **[. . H S A L]** – indicating no cleft on the right side (. .), a cleft of hard and soft palate with cleft lip and alveolus on the left.<br>  |
| **Clinical classification** | ▸ Track proportion of congenital anomalies occurring with orofacial clefts, which should be lower in cleft palate and cleft lip than in cleft palate alone.<br>▸ Consider using severity of anatomic involvement (bilateral) as factor in clinical outcome assessment. |
| **Prevalence** | ▸ Monitor prevalence: Varies by geography and ethnicity, but if very low (< 2 to 3 per 10 000 births), it suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units.<br>▸ Compare prevalence of sub-types: Expectation is cleft lip and palate > cleft palate > cleft lip. |

# OESOPHAGEAL ATRESIA/TRACHEO-OESOPHAGEAL FISTULA (Q39.0–Q39.2)

Oesophageal (esophageal) atresia is a congenital malformation characterized by the oesophagus ending in a blind pouch that does not connect to the stomach (see Fig. 4.28). Tracheo-oesophageal fistula (TEF or TOF) consists of a communication between the oesophagus and the trachea that is not normally present. Although it might occur alone, TEF is commonly associated with oesophageal atresia.

**Fig. 4.28. Oesophageal atresia/tracheo-oesophageal fistula**




The anatomical types of oesophageal atresia are:

- Type A: Oesophageal atresia *without* TEF
- Type B: Oesophageal atresia with *proximal* TEF
- **Type C: Oesophageal atresia with *distal* TEF**
- Type D: Oesophageal atresia with proximal and distal TEF
- **Type E:** TEF ***without*** oesophageal atresia.

Types A–D are typically recognized oesophageal atresia, with type C being by far the most common. Type E is a fistula without atresia and is variably ascertained by surveillance programmes.

## Relevant ICD-10 codes

Q39.0 Atresia of oesophagus without fistula
Q39.1 Atresia of oesophagus with trachea-oesophageal fistula
Q39.2 Congenital trachea-oesophageal fistula without atresia

## Diagnosis

***Prenatal.*** Oesophageal atresia is rarely diagnosed prenatally but can be suspected if the stomach or stomach bubble cannot be visualized or if there is polyhydramnios (however, such excessive amniotic fluid has many causes). A prenatal diagnosis should always be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** At birth, signs of oesophageal atresia include vomiting immediately after feeding, excessive drooling or mucus, and, if TEF is present, respiratory distress. Oesophageal atresia can be diagnosed radiographically when a feeding tube cannot pass from the pharynx into the stomach and, if there is no TEF, by an absence of air in the stomach.

TEF can be diagnosed by CT or MRI scan, surgery or autopsy. Because of the variability in symptoms, the diagnosis of TEF without oesophageal atresia might be delayed for weeks, months or even years.

## Clinical and epidemiologic notes

Oesophageal atresia is frequently (55%) associated with additional birth defects (particularly cardiac, anorectal, skeletal/vertebral, and urogenital). Oesophageal atresia can occur in association with other structural anomalies, anomaly complexes (e.g. OAVS – Q87.04, VATER/VACTERL association – Q87.26) or genetic syndromes (e.g. trisomy 18 – Q91, trisomy 21 – Q90, CHARGE syndrome – Q30.01, Feingold syndrome – Q87.8, several others).

The birth prevalence of oesophageal atresia is approximately 1 per 3000 to 5000 births. No non-genetic risk factors have been consistently associated with oesophageal atresia with or without TEF. Advanced paternal age and assisted reproductive technologies have been associated with oesophageal atresia, but these associations require further study.

## Inclusions

Oesophageal atresia with or without trachea-oesophageal fistula
Q39.0 Atresia of oesophagus without fistula
Q39.1 Atresia of oesophagus with trachea-oesophageal fistula
Q39.2 Congenital trachea-oesophageal fistula without atresia

## Exclusions (if occurring in the absence of oesophageal atresia or trachea-oesophageal fistula)

J39.8 Stenosis/stricture of trachea
Q32.1 Congenital malformations of trachea and bronchus (including absent/agenesis/atresia of trachea)
Q32.2 Congenital bronchomalacia
Q39.3 Congenital stenosis and stricture of oesophagus
Q39.4 Congenital oesophageal web

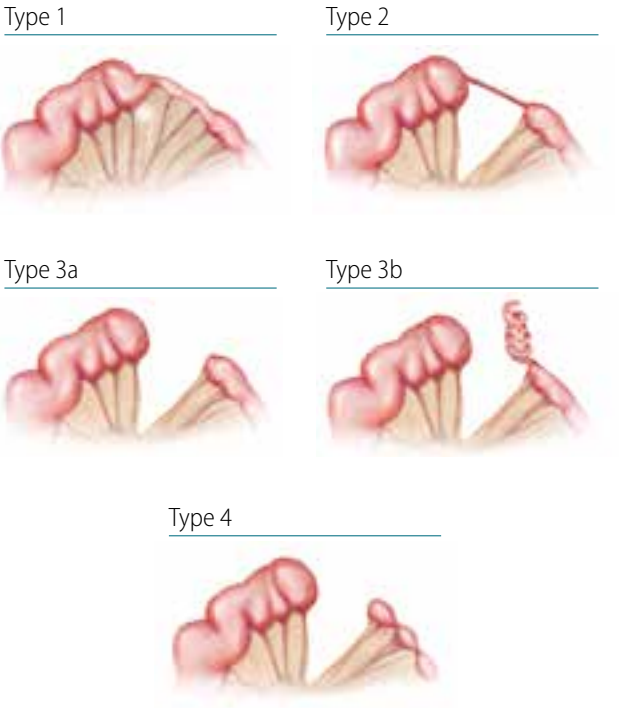
## Checklist for high-quality reporting of oesophageal atresia with or without TEF

| Oesophageal Atresia with or without TEF – Documentation Checklist |
|---|
| ☐ **Describe in detail:**<br>▸ Defect – anatomical type of oesophageal atresia with or without TEF (types A–E).<br>☐ **Describe evaluations to rule out additional malformations/associations/syndromes:**<br>▸ Especially OAVS, VATER/VACTERL, trisomies 18 and 21, CHARGE, Feingold, etc.<br>▸ Genetic or chromosomal testing performed.<br>▸ Specialty consultations and surgical reports.<br>☐ **Take and report photographs:** Show clearly oesophageal atresia and if present, TEF type; can be crucial for review.<br>☐ **Report whether autopsy (pathology) findings are available and if so, report the results.** |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical description for documentation of key descriptors:<br>▸ Description of oesophageal atresia, and if present, type of TEF.<br>▸ Documentation that includes drawings, photographs and consultation notes. |
| **Coding** | ▸ Code as Q39.X for specific type, if documented.<br>▸ Track and minimize cases coded without type of oesophageal atresia. |
| **Clinical classification** | ▸ Track type of oesophageal atresia with and without TEF.<br>▸ Check if an evaluation has been done. Track frequency of associated birth defects and syndromes, particularly those associated with a chromosome anomaly that are not rare with oesophageal atresia – check if karyotype has been done; check if clinical genetic consultation has been done. |
| **Prevalence** | ▸ Monitor prevalence: Prevalence might vary by country/region. |

**Fig. 4.29. Main types of large intestinal atresia**




Large intestinal atresia or stenosis – also known as colonic atresia – is characterized by the complete (atresia) or partial obstruction of the opening (lumen) within the colon. The large intestine includes the ascending, transverse and descending portions of the colon and the sigmoid region.

Four types have been recognized (see Fig. 4.29). In type 1, the lumen is occluded by internal tissue (mucosal web) with intact mesentery. In type 2, the atretic segment is a fibrous cord, and connects the two ends of the large intestine. In type 3, the atretic segment occurs with a V-shaped mesenteric gap defect (in type 3b, there is an "apple peel" appearance of a portion of the gut). In type 4, the atresia involves two or more regions of the colon, with an appearance described as a string of sausages (approximately one third of all large intestinal atresias are type 4).

Congenital stenosis of the large intestine occurs less frequently than atresia and should be distinguished from acquired stenosis. Though extremely rare, total absence of the colon might occur.

## Relevant ICD-10 codes

Q42 Congenital absence, atresia and stenosis of large intestine
(Note: Q42 is the generic ICD-10 code for atresia and stenosis of the large intestine. Avoid using this general code if more specific information is available.)
Q42.8 Congenital absence, atresia and stenosis of large intestine
Q42.9 Congenital absence, atresia and stenosis of large intestine, part unspecified

## Diagnosis

***Prenatal.*** These conditions are challenging to diagnose by prenatal ultrasound. If large intestinal atresia or stenosis is suspected, it should be confirmed postnatally.

***Postnatal.*** Large intestinal atresia or stenosis should be suspected in the newborn infant who fails to pass meconium or stool, has abdominal distention and/or bilious vomiting. Symptoms of atresia might be delayed in the newborn but will usually appear within the first few days of life. Diagnosis is confirmed through direct imaging of the bowel by x-ray, barium enema, surgery or autopsy. Depending on the degree of obstruction, partial colonic stenosis might be diagnosed later, even weeks after delivery.

## Clinical and epidemiologic notes

Compared to small intestinal atresia and anorectal atresia, large intestinal atresia is rare. Its prevalence is estimated to be approximately 1 in 20 000 births, and it represents less than 10% of all intestinal atresias.

Non-genetic risk factors include maternal varicella infection and possibly prenatal exposure to vasoconstrictive compounds, such as cocaine.

## Inclusions

Q42.8 Large intestinal atresia or stenosis
Q42.8 Sigmoid atresia or stenosis
Q42.8 Agenesis of the recto-sigmoid portion of the colon
Q42.90 Colonic atresia or stenosis

## Exclusions

Q41 Congenital absence, atresia and stenosis of small intestine
Q41.0 Congenital absence, atresia and stenosis of duodenum
Q41.1 Congenital absence, atresia and stenosis of jejunum
Q41.2 Congenital absence, atresia and stenosis of ileum
Q41.8 Congenital absence, atresia and stenosis of other specified parts of small intestine
Q41.9 Congenital absence, atresia and stenosis of small intestine, part unspecified
Q43.1 Hirschsprung's disease
Q79.3 Gastroschisis with intestinal atresia

Apple peel intestinal atresia
Acquired colonic stenosis
Microcolon

## Checklist for high-quality reporting

**Large Intestinal Atresia/Stenosis – Documentation Checklist**

- ☐ **Describe the anatomy in detail, using a combination of clinical, imaging, and surgical reports; specifically include information on the following elements:**
  - Atresia/stenosis location in large intestine.
  - Single versus multiple atresias.
  - Vesicoenteric fistula present.
  - Jejunal atresia – found in 10–20% of cases.
- ☐ **Describe procedures to assess further additional malformations:**
  - Most involve the gastrointestinal system (e.g. malrotation, aganglionosis, volvulus).
  - Craniofacial or ocular anomalies.
- ☐ **Copy and attach key imaging.**
- ☐ **Report findings of surgery or autopsy.**
- ☐ **Report whether specialty consultation(s) done, and if so, report the results.**

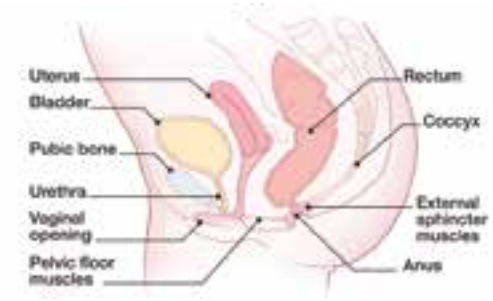
## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical description for documentation of key descriptors:<br>▸ Describe atresia/stenosis level.<br>▸ Describe the presence or absence of a fistula. |
| **Coding** | ▸ Code as Q42.X for specific type, if documented.<br>▸ Track and minimize cases coded with generic Q42. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies occurring with large intestinal atresia/stenosis.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations.<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence overall: Prevalence might vary by sex (male > female). |

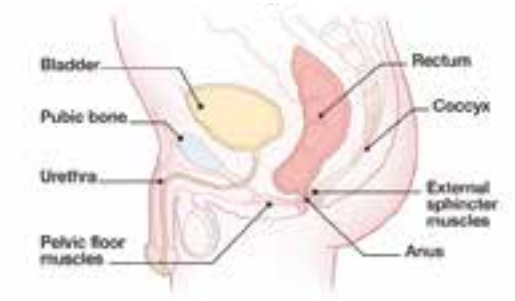
Anorectal anomalies include a wide spectrum of anomalies in which the atresia or stenosis involves the anus alone or an additional segment of the rectum. Imperforate anus is a term that properly reflects the outward appearance in the physical examination of a child, but internally the anomaly can be much more complex, involving the rectum, and is often associated with fistulas (e.g. Fig. 4.30, *panel C* – rectovaginal fistula in a girl, *panel F* – rectovesical fistula in a boy).

**Fig. 4.30. Anorectal atresia/stenosis**

A. Normal anatomy female




D. Normal anatomy male




B. Anal opening missing or closed off

E. Anal opening missing or closed off

C. Rectum connects to vagina

F. High rectum connects into bladder

Anorectal anomalies have been classified in different ways. A simple and practical approach classifies them as "low" or "high" lesions, depending on whether or not the rectum has descended into the sphincter complex (e.g. compare *panel E* – low lesion – with *panel F* – high lesion). Low and high lesions tend to vary by clinical presentations (e.g. presence or not of a dimple in the area of the anus), frequency of associated malformations (greater in high lesions), and surgical complexity.

## Relevant ICD-10 codes

Q42.0 Congenital absence, atresia and stenosis of rectum with fistula
Q42.1 Congenital absence, atresia and stenosis of rectum without fistula
Q42.2 Congenital absence, atresia and stenosis of anus with fistula
Q42.3 Congenital absence, atresia and stenosis of anus without fistula

| | Fistula present | Fistula absent |
|---|---|---|
| **Anorectal anomaly (High)** | Q42.0 | Q42.1 |
| **Anal anomaly (Low)** | Q42.2 | Q42.3 |

## Diagnosis

***Prenatal.*** Anorectal anomalies might be difficult to diagnose prenatally by ultrasonography and might be missed if isolated. If an anal dimple is demonstrated or the bowel is dilated on ultrasound, this suggests an anorectal anomaly. For this reason, a prenatal diagnosis of anorectal anomalies should always be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** Anal atresia or stenosis is usually easily recognized at birth by visual inspection during the newborn physical examination. If missed at birth, rectal atresia or stenosis might be suspected in the first 24 hours when the newborn develops abdominal distension; does not pass meconium or stool; or, when a fistula is present, if meconium is passed through the urethra or vagina. The diagnosis of rectal atresia or stenosis is confirmed through direct imaging of the bowel by radiography, barium enema, surgery or autopsy. As discussed, the external examination does not predict the level of the lesion.

## Clinical and epidemiologic notes

Because only one third of anorectal anomalies are isolated, infants must be evaluated for the presence of additional anomalies. These include structural anomalies of the urinary tract, of the vertebrae or sacrum with tethered cord (the association of anorectal atresia with sacral defect and presacral mass forms the Currarino triad, often an autosomal dominant condition), and in females, with anomalies of the vagina and uterus (e.g. bicornuate uterus or uterus didelphys). In general, associated anomalies are more prevalent with higher rectal pouches.

Anorectal atresia is also part of some non-syndromic multiple congenital anomaly patterns, including caudal regression (Q89.80), exstrophy of the cloaca (Q64.10), OEIS (Q79.52; **o**mphalocele, cloacal **e**xstrophy, **i**mperforate anus, **s**pinal defects) and the VATER or VACTERL association (**v**ertebral, **a**nus, **c**ardiac, **t**rachea, o**e**sophagus, **r**enal, **l**imb; Q87.26). Anorectal atresia is also seen in more than 100 genetic syndromes, including Townes-Brocks syndrome (autosomal dominant, SALL1 gene), cat-eye syndrome (tetrasomy 22q11), Opitz G-BBB syndrome (X-linked, MID1 gene), among many others.

Suggested non-genetic risk factors for anorectal atresia include thalidomide exposure and maternal pregestational diabetes.

Anorectal atresias as a group affect approximately 1 in 1000 to 5000 births, more commonly in males than females. Rectal atresia alone is very rare. Low-level lesions are more common than high-level lesions.

## Inclusions

Rectal atresia or stenosis with or without fistula
Anal atresia or stenosis with or without fistula
Q42.0 Congenital absence, atresia and stenosis of rectum with fistula
Q42.1 Congenital absence, atresia and stenosis of rectum without fistula
Q42.2 Congenital absence, atresia and stenosis of anus with fistula
Q42.3 Congenital absence, atresia and stenosis of anus without fistula
Q42.3 Imperforate anus

## Exclusions

Q43.5 Ectopic anus (e.g. anteriorly displaced anus)
Q43.7 Persistent cloaca

Notes:
Several complex conditions have anorectal malformations as obligate (e.g. cloacal exstrophy) or frequently occurring (e.g. sirenomelia) components. Because they are so different clinically and epidemiologically from the simple or isolated forms of anorectal atresia, it is recommended that cases with these conditions be coded with the specific malformation complex code (e.g. cloacal exstrophy) in addition to the code for anorectal atresia (if present). This approach will help clarify whether there is a pattern such as OEIS (see Clinical and epidemiologic notes).

Q64.10 Bladder exstrophy
Q64.12 Cloacal exstrophy
Q43.7 Cloacal malformation including persistent cloaca
Q76.49 Sacral agenesis
Q87.2 Sirenomelia

## Checklist for high-quality reporting

| Anorectal Atresia – Documentation Checklist |
|---|
| ☐ **Describe in detail, including:**<br>▸ Atresia limited to anus versus including rectum.<br>▸ Level of atresia – high or low.<br>▸ Fistula – absent or present.<br>▸ Fistula type – involving which structures. |
| ☐ **Describe procedures to assess further additional malformations (e.g. spine radiographs, echocardiogram) and if one or more is present, describe these.** |
| ☐ **Take and store photographs of anomaly and infant.** |
| ☐ **Find and store key diagnostic imaging.** |
| ☐ **Report findings of surgery or autopsy.** |
| ☐ **Report whether specialty consultation(s) done, and if so, report the results.** |

## Suggested data quality indicators

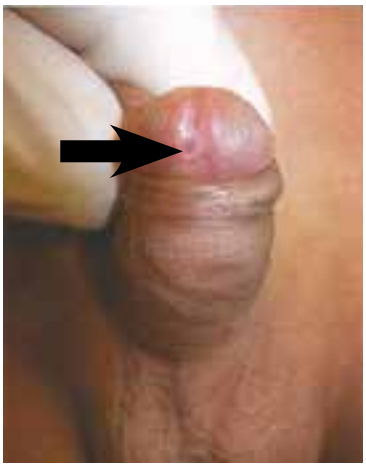
| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical description for documentation of key descriptors:<br>▸ Describe whether or not the rectum has descended into the sphincter complex (a trait that helps distinguish high from low lesions, see Fig. 4.30).<br>▸ Describe whether an anal dimple is present or not (more typical of low lesions).<br>▸ Describe the presence or absence of a fistula.<br>▸ Track surgical complexity. |
| **Coding** | ▸ Track and minimize cases coded with generic Q42. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies occurring with anorectal atresia. The expectation is that it will be greater in high lesions.<br>▸ Track any associated anomalies and/or syndromes.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations.<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence overall and by high/low and fistula: Prevalence might vary by sex (male > female). |

Hypospadias is characterized by an abnormal (ventral) placement of the external urethral meatus in male infants. Normal placement of the urethral meatus is on the tip of the penis, whereas in hypospadias the meatus is ventrally and proximally displaced (on the underside of the penis). Hypospadias is classified by severity (see Fig. 4.31), depending on the location of the meatus: first-degree hypospadias includes the more distal forms, glanular and coronal; second-degree hypospadias includes subcoronal and penile shaft hypospadias; and third-degree – the most severe – includes scrotal and perineal hypospadias.

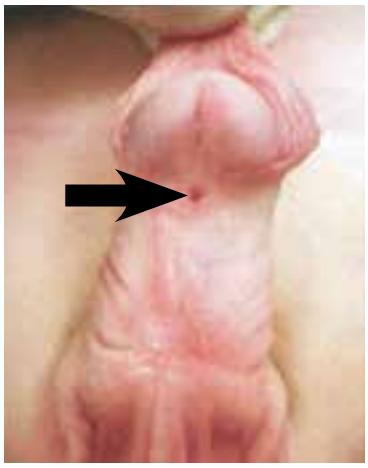
The shortening of the ventral side of the penis found in hypospadias can result in a curvature of the penis, known as chordee. Chordee is common in severe cases of hypospadias, but it can also occur independently. Chordee by itself is considered a minor anomaly.

**Fig. 4.31. Hypospadias**

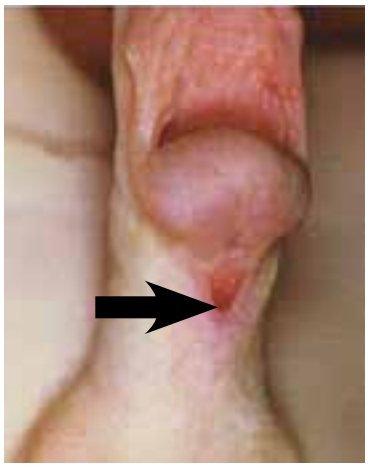
1. Q54.0 Glanular



2. Q54.1 Subcoronal

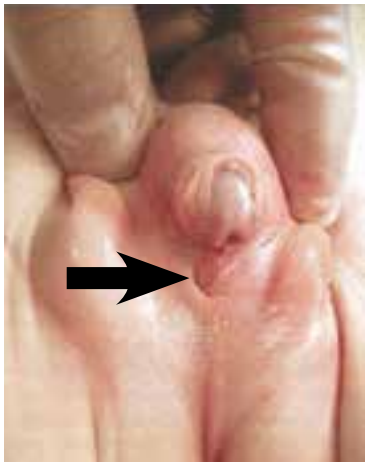


3. Q54.1 Penile



4. Q54.2 Scrotal

5. Q54.3 Perineal



*Photograph source*: 1, 2, 4, 5: Nelson Textbook of Pediatrics (http://www.slideshare.net/wadoodaref/congenital-anomalies-videosession-v3-11680674).

## Relevant ICD-10 codes

Q54.0 Hypospadias, balanic (coronal, glanular)
Q54.1 Hypospadias, penile (includes subcoronal and midshaft)
Q54.2 Hypospadias, penoscrotal
Q54.3 Hypospadias, perineal
Q54.8 Hypospadias, other
Q54.9 Hypospadias, unspecified

## Diagnosis

***Prenatal.*** Hypospadias is difficult to diagnose prenatally by ultrasonography, and might be confused with micropenis, penile cyst, chordee or ambiguous genitalia. For this reason, a prenatal diagnosis of hypospadias should always be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** A careful, systematic examination of the male newborn should allow a firm diagnosis of hypospadias. Note that the milder forms such as balanic (glanular) hypospadias are easily missed at delivery and might be discovered during circumcision. The surgical report might provide definitive detail of the urethral placement and whether chordee are present.

## Clinical and epidemiologic notes

The diagnosis of hypospadias might be missed, especially with the less severe forms. Observing the flow of urine can aid in the diagnosis and in establishing the degree/severity of the condition. Identifying severity is important because of the different disease associations and the clinical impact. The most severe forms of hypospadias (e.g. scrotal hypospadias) are more often associated with syndromes compared to the milder forms (e.g. balanic [glanular]) of hypospadias.

Hypospadias is often an isolated (> 80%), non-syndromic anomaly. However, the proportion of isolated defects decreases with increasing severity (penile and scrotal) of hypospadias. For this reason, it is crucial to report all findings. Obtaining good clinical photographs is important for the expert reviewer but is not easy to do. Documenting the severity using drawing might help in selected cases.

Suggested non-genetic risk factors for hypospadias include advanced maternal age (> 35 years) and environmental exposure to certain chemicals (endocrine disruptors).

The birth prevalence of hypospadias varies widely, between 2 and 39 per 10 000 births.

## Inclusions

Q54.0 Hypospadias, balanic (coronal, glanular)
Q54.1 Hypospadias, penile (includes subcoronal and midshaft)
Q54.2 Hypospadias, penoscrotal
Q54.3 Hypospadias, perineal
Q54.8 Hypospadias, other
Q54.9 Hypospadias, unspecified

## Exclusions

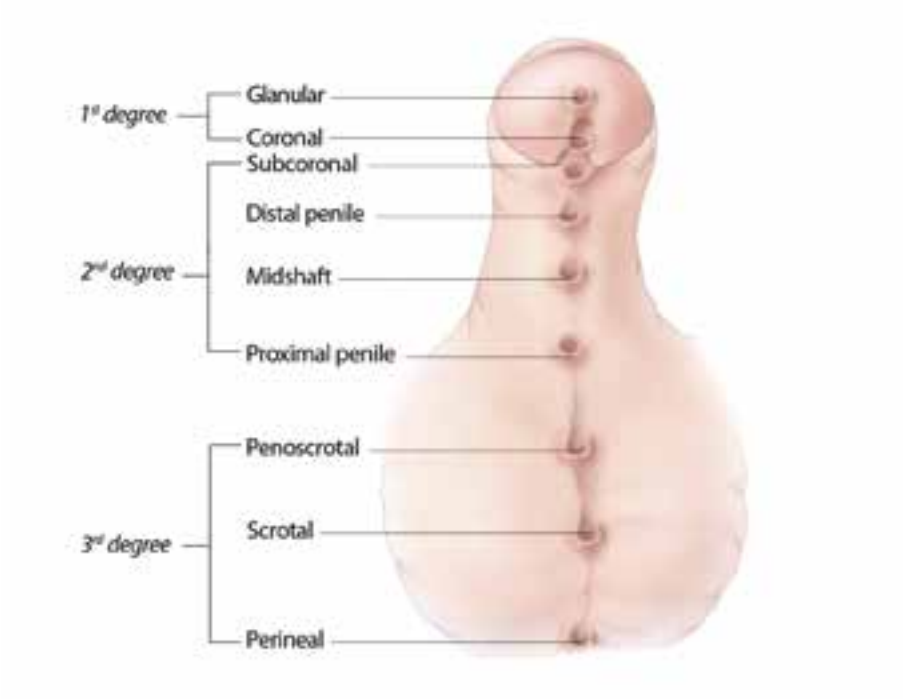
Q54.4 Chordee (a minor anomaly if isolated)

## Checklist for high-quality reporting

**Hypospadias – Documentation Checklist**

- ☐ **Describe in detail:**
  - Location of urethral meatus – glanular, coronal, subcoronal, shaft, scrotal, perineal.
  - Testes present or absent (if not palpable, consider diagnoses of virilization in females, such as in cases of congenital adrenal hyperplasia).
  - Presence of chordee.
- ☐ **Include photographs:** *Show clearly* the location of the urethra or use drawing; can be crucial for review.
- ☐ **Describe evaluations to find or rule out related and associated anomalies:**
  - Report undescended testis (unilateral Q53.1, bilateral Q53.2).
  - Chordee – do not report cases of isolated chordee if no hypospadias.
  - Surgical reports – can be very helpful to identify type.
  - Other anomalies of urinary tract (renal) or genitalia.
  - Report if specialty consultations were done and if so, report the results.
  - Genetic/chromosomal/biochemical testing if syndrome suspected.
- ☐ **Report whether autopsy (pathology) findings are available and if so, report the results.**

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors – location of urethral meatus:<br>▸ Use figure or photographs to document the specific location of the meatus. |
| **Coding** | ▸ Code penile urethral location specifically as Q54.X.<br>▸ Track and minimize the use of Q54.9. |
| **Clinical classification** | ▸ Track any congenital anomalies and/or syndromes occurring with hypospadias (expect ~20% of cases).<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations.<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence overall and by degree: Prevalence might vary by country/region, country income level and race/ethnicity. |
| **Key illustration** |  <br>Note: Illustration indicates all possible locations for the malformation, but typically a case will only have an opening in one location. |

Renal agenesis is a complete absence of one (unilateral) or both (bilateral) kidneys. If bilateral, renal agenesis is a lethal condition: the fetus will be stillborn or die shortly after delivery. In utero, bilateral renal agenesis leads to oligohydramnios (too little amniotic fluid), which causes Potter sequence (syndrome) – abnormal facies, talipes (clubfoot) and other contractures, and pulmonary hypoplasia. In renal aplasia, the kidney has failed to develop beyond its most primitive form. In practice, renal agenesis and renal aplasia might be indistinguishable.

Renal hypoplasia is a congenitally small kidney (< 50% of expected weight) without dysplasia, which can be bilateral or unilateral. Renal hypoplasia might be associated with hydronephrosis but is not usually associated with abnormal ureters or other urinary tract findings.

Renal agenesis must be distinguished from renal multicystic dysplasia (Q61.40 and Q61.41) – considered a specific developmental anomaly – and from polycystic renal disease (Q61.1, Q61.2, Q61.3, a single-gene disorder with infantile and later-onset forms). These have different etiologies and ICD codes.

**Fig. 4.32. Renal agenesis/hypoplasia**

## Relevant ICD-10 codes

Q60.0 Unilateral renal agenesis
Q60.1 Bilateral renal agenesis
Q60.2 Unspecified renal agenesis
Q60.3 Renal hypoplasia, unilateral
Q60.4 Renal hypoplasia, bilateral
Q60.5 Renal hypoplasia, unspecified
Q60.6 Potter sequence with renal agenesis

## Diagnosis

***Prenatal.*** Bilateral renal agenesis or severe hypoplasia should be suspected prenatally in a pregnancy with severe oligohydramnios (urine from fetal kidneys accounts for most of the amniotic fluid from 14 weeks' gestations onward). Fetal kidneys might be small or absent, and the bladder might not be visualized (empty). In contrast, multicystic/polycystic kidneys tend to be large and "bright" on fetal ultrasound. Of note, in some cases, large dysplastic kidneys can reduce and disappear by the time of birth, and in others a kidney might be absent on one side and dysplastic on the contralateral side, suggesting that some cases of agenesis might have started as dysplasia.

***Postnatal.*** At delivery, bilateral renal *agenesis* should be considered in an infant with features of Potter sequence (Q60.6), which include respiratory distress (due to pulmonary hypoplasia), characteristic facial traits (wide-set eyes, flat face, low-set large ears, small chin, loose or excessive skin), and joint contractures (talipes and others). Bilateral renal *hypoplasia* might or might not be recognized after delivery, depending on the severity and degree of residual kidney function. Renal agenesis or hypoplasia is conclusively diagnosed only through direct assessment by abdominal ultrasound, CT or MRI scan, surgery or autopsy.

Unilateral renal agenesis or hypoplasia can be clinically silent at delivery if the contralateral kidney is not impaired, such that the diagnosis might occur months or years after birth, if at all. Some unilateral cases are diagnosed only as incidental findings during evaluation for other conditions, or in screening of family members of a patient with bilateral renal agenesis.

## Clinical and epidemiologic notes

At least half of cases of bilateral renal agenesis are estimated to be associated with other structural anomalies (e.g. urogenital, cardiac, skeletal, CNS) or syndromes (chromosomal or genetic). The non-syndromic multiple anomaly patterns include the VATER/VACTERL association (**v**ertebral, **a**nus, **c**ardiac, **t**rachea, o**e**sophagus, **r**enal, **l**imb (radial agenesis); Q87.26), MURCS (**mu**llerian, **r**enal **c**ervicothoracic, **s**omite) association (Q51.8), sirenomelia (Q87.24), and caudal dysplasia "syndrome" (also seen in maternal pregestational diabetes). Renal agenesis is seen in hundreds of genetic conditions (Mendelian and chromosomal), including common trisomies, deletion 22q11, Melnick-Fraser syndrome, Fraser cryptophthalmos syndrome and branchio-oto-renal syndrome.

Bilateral renal agenesis occurs in 1 in 4000 births and is more common in stillbirths and in males. Unilateral renal agenesis is more common on the left side, is associated with an absent ureter on the same side, and at times with renal hypoplasia in the contralateral kidney. The frequency of unilateral agenesis is estimated as 1 in 3000 births but it is likely underdiagnosed. Non-genetic risk factors include maternal pregestational diabetes.

## Inclusions

Q60.0 Unilateral renal agenesis
Q60.1 Bilateral renal agenesis
Q60.3 Renal hypoplasia, unilateral
Q60.4 Renal hypoplasia, bilateral
Unilateral renal agenesis with contralateral renal hypoplasia

Renal agenesis is a defect reported as part of VATER or VACTERL association (**v**ertebral, **a**nus, **c**ardiac, **t**rachea, o**e**sophagus, **r**enal, **l**imb (radial agenesis)).

## Exclusions

| | |
|---|---|
| Q61.1, Q61.19 | Autosomal recessive, polycystic kidney, infantile type |
| Q61.11-Q61.3 | Multicystic dysplastic kidney, multicystic renal dysplasia |

## Checklist for high-quality reporting

| Renal Agenesis/Hypoplasia – Documentation Checklist |
|---|
| ☐ **Describe in detail**, including:<br>▸ Unilateral (specify side) versus bilateral.<br>▸ Agenesis and/or hypoplasia (unilateral renal agenesis with contralateral renal hypoplasia).<br>☐ **Take and report photographs of any external defects:** *Especially show clearly* the location of the urethra; can be crucial for review.<br>☐ **Describe evaluations to find or rule out related and associated anomalies:**<br>▸ Other anomalies of urinary tract (renal) or genital organs.<br>▸ Other unrelated anomalies (such as VATER, VACTERL).<br>▸ Report if specialty consultations were done and if so, report the results.<br>▸ Genetic or chromosomal testing if syndrome suspected.<br>☐ **Report whether autopsy (pathology) findings are available and if so, report the results.** |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | ▸ Review sample for documentation of key descriptors: Side of renal agenesis and/or hypoplasia.<br>▸ Take and attach photographs: Essential for review and correct classification.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations. |
| **Coding** | ▸ Code renal agenesis and/or hypoplasia specifically Q60.x.<br>▸ Track unilateral, bilateral agenesis with/without hypoplasia. |
| **Clinical classification** | ▸ Track any congenital anomalies and/or syndromes occurring with renal agenesis/hypoplasia.<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence overall and by sex.<br>▸ Monitor prevalence by specific subtype (unilateral, bilateral). |

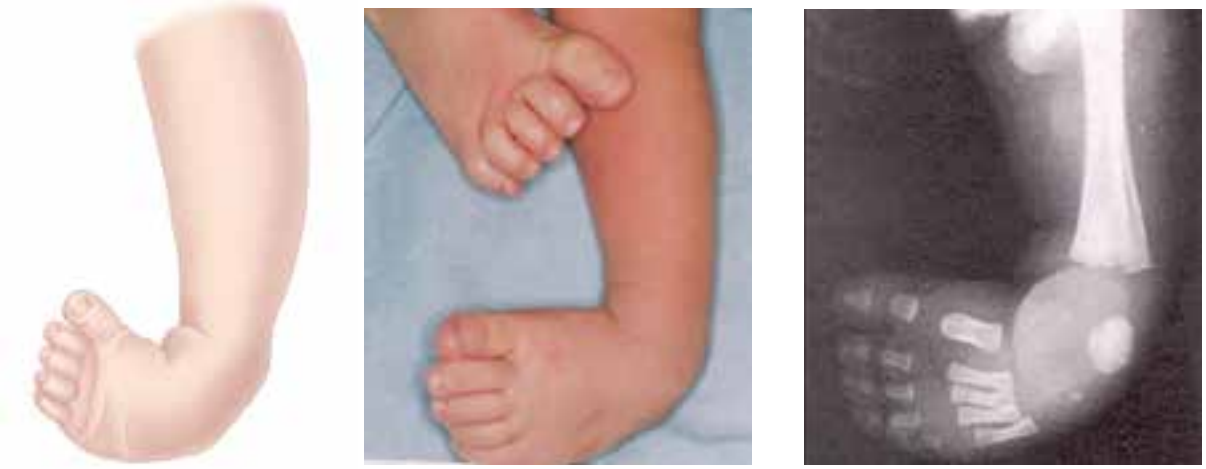
Talipes equinovarus (TEV) is a specific and common type of what is sometimes called "clubfoot", a term that encompasses a range of anomalies of the ankle or foot present at birth (see Fig. 4.33). TEV can be defined as fixation of the foot (forefoot and hindfoot) in plantar flexion (equinus), deviation toward the midline (varus) and upward rotation so the foot rests on its outer side (supinatus). In other words, the foot points downward and inward and is rotated outward axially as shown in Fig. 4.34.

TEV has a wide spectrum of severity. In milder cases it is "positional", meaning that it can be gently manipulated into a normal position and typically does not require orthopaedic or surgical interventions, and is excluded from birth defects surveillance. In more severe cases it can be "rigid" or "fixed", in that it cannot be manipulated into a normal position and requires orthopaedic or surgical treatment, and is considered a major birth defect.

The most common congenital deformity of feet is TEV; however, there are other forms of clubfoot, specifically talipes calcaneovalgus (in which the ankle joint is dorsiflexed and the forefoot deviated outwards), and talipes calcaneovarus (in which the ankle joint is dorsiflexed and the forefoot deviated inwards).

**Fig. 4.33. Talipes equinovarus**

Talipes equinovarus (Q66.0)



*Photograph and x-ray source*: Dr Idalina Montes and Dr Rafael Longo (Puerto Rico).

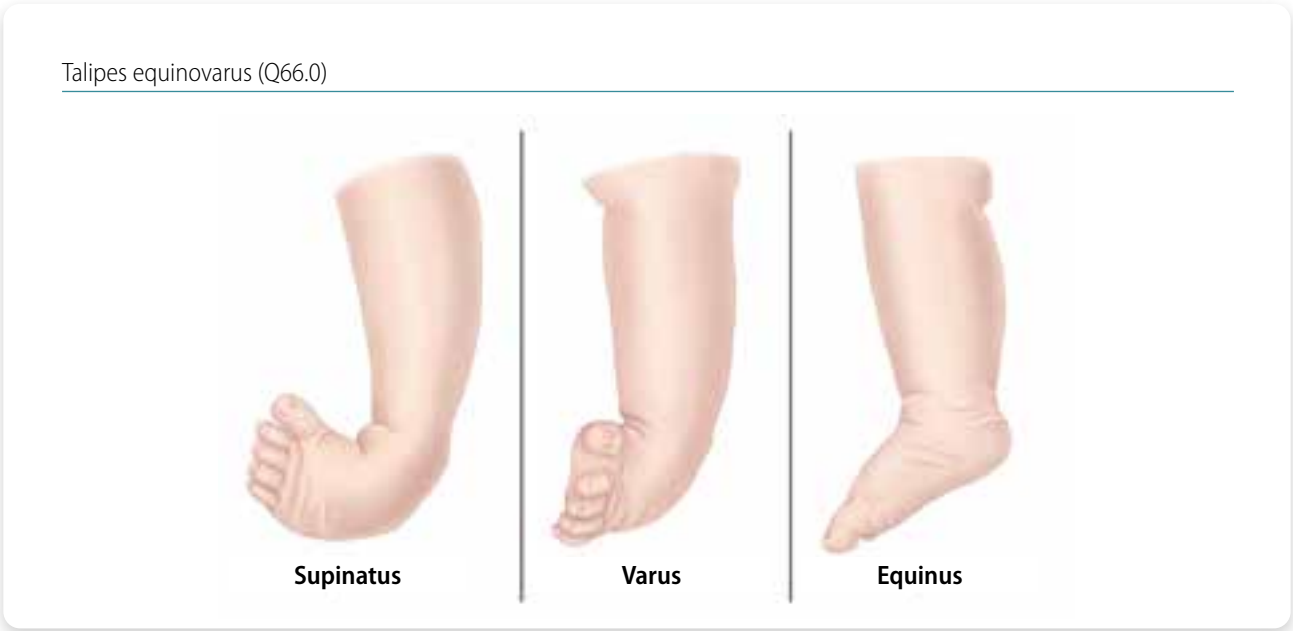
## Relevant ICD-10 codes

Q66.0 Talipes equinovarus
Q66.8 Other congenital deformities of feet, clubfoot NOS (not otherwise specified)
Q66.1 Talipes calcaneovarus
Q66.4 Talipes calcaneovalgus

Note:

- Q66 Congenital deformities of feet: Avoid using this general code if more specific information is available.
- Q66.8 Other congenital deformities of feet; Clubfoot NOS (not otherwise specified): Minimize the use of this code if possible; describe the anomaly so a more specific code (e.g. Q66.0) can be used.

**Fig. 4.34. Foot positions**




## Diagnosis

***Prenatal.*** TEV can be identified or suspected on prenatal ultrasound. However, it should not be included in birth defects surveillance data without postnatal confirmation. The primary utility of prenatal diagnosis of TEV is in its indication for additional evaluations for the genetic conditions and structural anomalies that are commonly associated with TEV.

***Postnatal.*** TEV is readily diagnosed in the newborn examination. Cases should be followed and evaluated sequentially to assess the degree of severity and whether treatment other than manipulation is necessary. Sometimes other birth defects of the foot or leg might mimic clubfoot. For example, a deficiency of the tibial bone in the leg might look like a talipes. Imaging studies (typically, radiographs) might provide supplemental information to aid in diagnosis.

## Clinical and epidemiologic notes

TEV is bilateral in about 60% of cases, and when unilateral, TEV is slightly more common on the right side. Especially in the severe forms (fixed or rigid TEV), the calf muscles on the affected side are hypotrophic (smaller).

In about half of all cases, TEV occurs alone, or with other related musculoskeletal abnormalities such as torticollis, developmental dysplasia of the hip, and anomalies of multiple joints (e.g. arthrogryposis). TEV can occur with other birth defects, especially those affecting the brain and spine (e.g. spina bifida), through a mechanism thought to involve a deficit of innervation of the limb segments across joints that in turn leads to decreased movement in utero. Multiple deformations that include TEV can occur with genetic conditions that affect the formation of bones and joints (e.g. campomelic dysplasia, Larsen syndrome). More frequently, TEV can occur in chromosomal anomalies such as triploidy, deletion 4p-, and trisomies (though in trisomy 18, the type of clubfoot is calcaneovalgus, with dorsiflexion rather than plantar flexion of the foot).

Non-genetic risk factors reported to be associated with an increased risk for TEV include maternal smoking and early amniocentesis. In addition, the risk for TEV appears to be multifactorial, in that the recurrence risk for first-degree relatives is 3–6%, and the concordance in monozygotic twins is much higher than in dizygotic twins (30% versus approximately 3%).

The reported birth prevalence is 10–15 per 10 000 births, with moderate variability. Such variability is likely due in part to methodology (ascertainment, inclusion criteria), though ethnicity appears to play a role, with higher reported rates in certain groups (e.g. Maori, Polynesians, Australian Aborigines).

## Inclusions

Congenital talipes equinovarus (including congenital, idiopathic, and neurogenic)

Talipes not otherwise specified, clubfoot not otherwise specified (minimize this group)

Q66.0 Talipes equinovarus
Q66.1 Talipes calcaneovarus
Q66.4 Talipes calcaneovalgus
Q66.8 Other congenital deformities of feet, Clubfoot NOS (not otherwise specified)

## Exclusions

Clubfoot, positional (exclude; positional talipes is not considered a major defect)

Other presentations of congenital deformities of the foot (e.g. metatarsus varus or valgus, rocker-bottom foot, pes planus, pes cavus, etc.)

## Checklist for high-quality reporting

**Talipes Equinovarus – Documentation Checklist**

- ☐ **Describe in detail, including:**
  - Laterality – right, left or bilateral.
  - Mobility of foot – rigid (contracted) versus flexible (flexible is the same as positional, and is excluded in most systems).
  - The typical features of talipes equinovarus (plantar flexion, varus deformity, upward rotation).
  - Related findings if present (medial creases, hypotrophic calf).
- ☐ **Describe other deformations if present** (e.g. knees, fingers, elbows) especially if rigid (e.g. in arthrogryposis).
- ☐ **Describe procedures to assess further additional malformations; if one or more is present, describe these.**
- ☐ **Take and report photographs** of the anomaly and the entire infant; useful for review but not sufficient as confirmation.
- ☐ **Specialty consultations:** Report which were done (including genetics and orthopaedics) and results.
- ☐ **Note that the following:**
  - Flexible/positional talipes equinovarus or other presentations of deformities of the foot are excluded from surveillance tracking because of variability, frequency and minor health impact.
  - Talipes associated with neuromuscular sequences and syndromes are included in surveillance tracking; note that programmes should code the associated clubfoot but should consider whether or not these cases are included in prevalence estimates of talipes.
  - Other presentations of deformities of the foot.

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample of clinical description for documentation of key descriptors:<br>▸ Description of deformations – equinus, varus, supination.<br>▸ Description of whether the deformation is positional (flexible) or rigid (fixed).<br>▸ Description of related findings (present or absent), on the foot/lower leg (e.g. medial crease, calf hypotrophy), and of other deformations involving other joints.<br>▸ Documentation of whether it is left, right or bilateral.<br>▸ Drawings, photographs and consultation reports. |
| **Coding** | ▸ Code as Q66.X for specific type, if documented.<br>▸ Monitor and minimize the use of generic code for clubfoot; use Q66.0.<br>▸ Consider adding a sixth digit to identify positional versus rigid talipes equivarus. |
| **Clinical classification** | ▸ Track proportion of congenital anomalies and syndromes occurring with clubfoot; a proportion substantially < 30–40% suggests under-ascertainment of clinically important conditions. |
| **Prevalence** | ▸ Monitor prevalence: Prevalence varies moderately, especially by ethnicity, but if very low (< 5 per 10 000 births) it strongly suggests under-ascertainment.<br>▸ Compare prevalence among the smallest site/time units: Statistically significant dissimilar results suggest a possible methodological problem in one or more site/time units.<br>▸ Compare prevalence by ethnicity and compare with expectation. |

## Congenital anomalies and deformations of the musculoskeletal system: Limb reduction defects/limb deficiencies

Limb reduction defects, or limb deficiencies, are major structural anomalies characterized by the absence or severe hypoplasia of any limb or part of a limb. Severe hypoplasia can be defined as hypoplasia (small size) with an abnormal shape. This definition helps to distinguish these limb deficiencies from those seen in many skeletal dysplasias (e.g. achondroplasia), where the hypoplasia can be significant but occurs with relatively normal limb shape.

Milder cases of hypoplasia with normal shape are also excluded from this definition of limb deficiency. The main reason is that such presentation does not require treatment and can be considered a minor anomaly. Examples include brachydactyly without severe hypoplasia or absent bones of hand or feet (Q74.80); or clinodactyly, defined as absence/marked hypoplasia of middle phalange of the fifth finger (Q68.10).

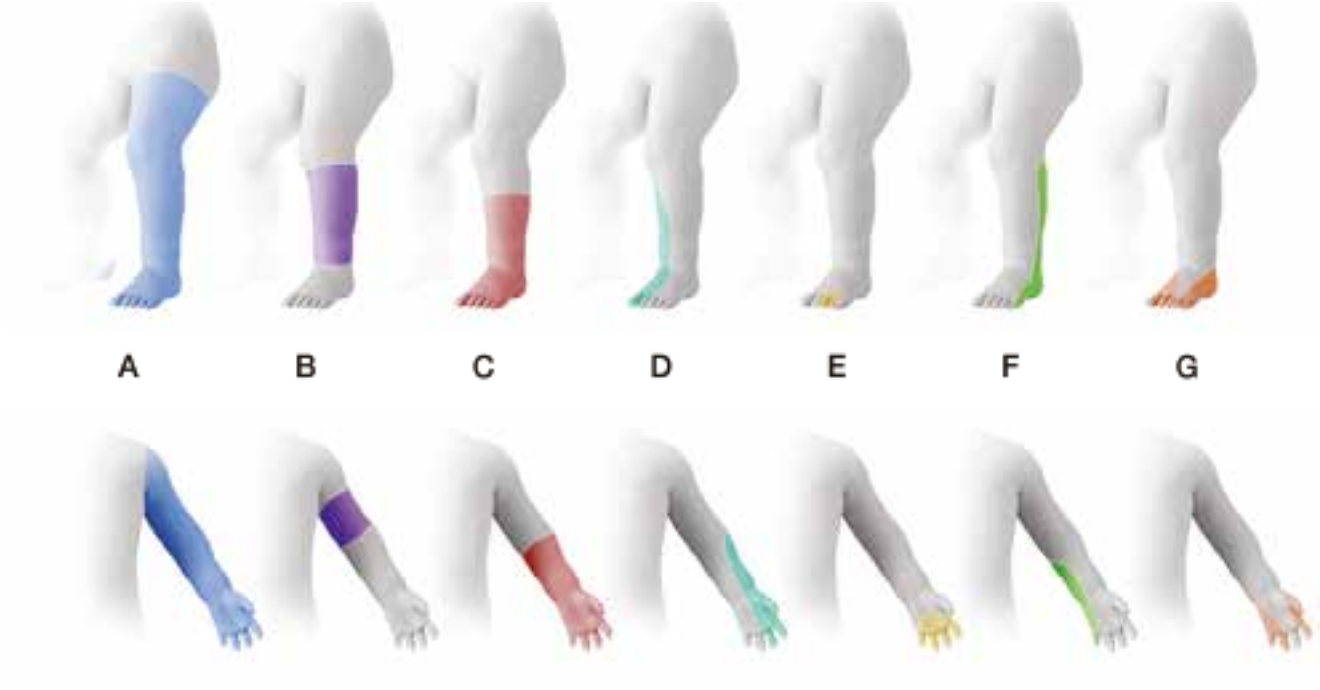
Other conditions that are not included in this definition are severe syndactyly (Q70) with partial absence of digits, and sirenomelia (Q87.24), a severe sequence with fusion of lower limbs and visceral anomalies.

The standard nomenclature recognizes two basic types of limb deficiencies – longitudinal and transverse – each comprising additional subtypes. Longitudinal deficiencies occur along the long axis of the limb, and include preaxial deficiencies (radial and tibial side), postaxial deficiencies (ulnar and fibular side), and axial deficiencies (central). In contrast, transverse deficiencies occur across, rather than along, the long axis of the limb, and are distinguished into terminal (more frequent, when the terminal part of the limb is completely missing), and intercalary (when the terminal part of the limb is present, even if abnormal, but the more proximal parts are absent). Classifying limb deficiencies in the specific subtypes is important both clinically and for the purposes of public health surveillance, as the different types tend to differ in their pathogenesis, etiology and associations with other congenital anomalies and syndromes (see Table 4.1 and Fig. 4.35).

**Table 4.1. Types of limb deficiencies by axis and segment involved**

| Axis of the limb | Segment | Involvement |
|---|---|---|
| **Complete absence** | All segments | Amelia |
| **Transverse** | Terminal | Absence of terminal part of limb (at any level) |
| | Intercalary | Absence or hypoplasia of part of limb with normal or nearly normal terminal part, including:<br>• typical and atypical intercalary defects<br>• femoral hypoplasia |
| **Longitudinal** | Preaxial | Radial, tibial, first (with or without second) digits or toes involved |
| | Axial | Hand/foot involved only: Third (with or without second and fourth) ray involved. Include typical split hand/foot and split hand/foot monodactyly type |
| | Postaxial | Fifth (with or without fourth) digits or toes involved |
| **Mixed** | | Any other combination of two or more subtypes. For example, femoral-fibula-ulnar complex |

**Fig. 4.35. Types of limb deficiencies by axis and segment involved**




Absent or hypoplastic structures are shaded. A: complete absence of limb (amelia); (B) intercalary defect; (C) terminal transverse defect; (D) longitudinal defect, preaxial; (E) longitudinal defect, central; (F) longitudinal defect, postaxial; (G) longitudinal, pre- and postaxial.

*Source*: adapted from Gold et al., 2011 ***(31)***.

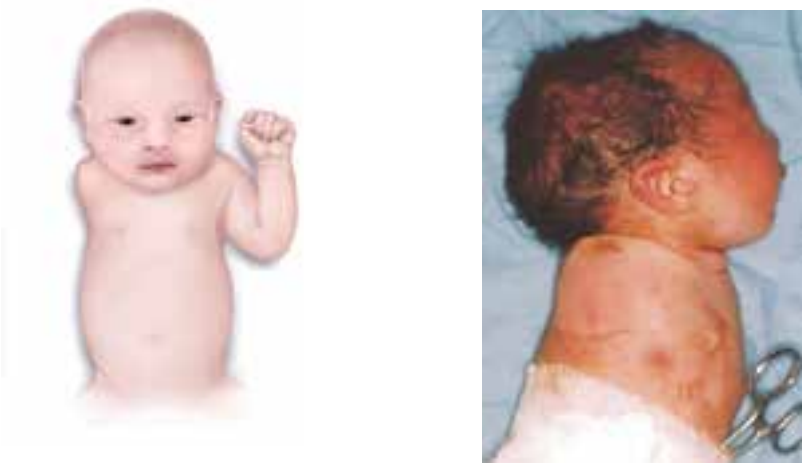
Notes:

- Some of the terms previously used for limb deficiencies should no longer be used because they are either imprecise (ectrodactyly, meromelia, micromelia, hemimelia), or are considered pejorative ("lobster claw", "seal limb").
- Overall, the reported prevalence of limb deficiency is approximately 5.0–7.0 per 10 000 births. Transverse terminal defects are the most frequent (around 50%), followed by longitudinal preaxial, longitudinal postaxial, transverse intercalary, and longitudinal axial.
- Limb deficiencies affect upper limbs only in 65% of the cases, followed by lower limbs only, and then both upper and lower limbs. Most cases are unilateral (80%).
- Limb deficiencies are more commonly isolated (50%), but can occur with other birth defects (40%). Syndromes are relatively less common (10%) and are more frequently associated with longitudinal preaxial limb deficiencies.

Amelia is a congenital anomaly characterized by the complete absence of one or more limbs (see Fig. 4.36).

**Fig. 4.36. Amelia**

Amelia of the upper limb (Q71.0)



Amelia of the lower limb (Q72.0)

*Photograph source:* CDC–Beijing Medical University collaborative project.

## Relevant ICD-10 codes

Q71.0 Congenital complete absence of upper limb(s); amelia of upper limb
Q72.0 Congenital complete absence of lower limb(s); amelia of lower limb
Q73.0 Congenital absence of unspecified limb(s); amelia NOS

Note:
Avoid using the generic Q71, Q72 or Q73 code for amelia. These generic codes include other limb deficiencies. Q73.0 is used for amelia when the limb (upper or lower) is not specified. The use of the code Q73.0 should be minimized.

## Diagnosis

***Prenatal.*** Amelia can be diagnosed or strongly suspected prenatally. However, it might be missed. The distinction from other limb deficiencies is difficult and error-prone in prenatal diagnosis. For this reason, a prenatal diagnosis should always be confirmed postnatally.

When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** The newborn examination confirms the diagnosis of amelia and distinguishes it from other limb deficiencies (e.g. terminal transverse defects) and sirenomelia. Imaging (radiographs) might provide further diagnostic information in cases that are less clear.

## Clinical and epidemiologic notes

Distinguishing amelia from other limb deficiencies is important because these conditions have different causes and associated anomalies. With careful clinical and radiological examination, the diagnosis of amelia is usually straightforward. Radiology is strongly recommended to confirm the absence of the proximal segment of the humerus or femur. In typical amelia, there is no bony limb structure.

In most cases of amelia, only one limb is absent, with each side being affected with approximately equal frequency. Upper limb amelia occurs slightly more often than lower limb amelia.

Amelia is often associated with other anomalies. The most frequent congenital anomalies seen with amelia are other types of musculoskeletal defects, as well as intestinal, renal and genital defects; oral clefts; cardiac septal defects; and anencephaly. Syndromes are uncommon in amelia, but do occur, including Roberts syndrome and thalidomide embryopathy.

Complex conditions potentially confused with amelia are sirenomelia and limb-body wall spectrum. Sirenomelia cases should not be included as amelia. In sirenomelia there is complete or partial fusion of lower limbs, variably associated with sacral defects, anal atresia, abnormal external genitalia and absence of kidneys.

Cases with limb-body wall complex defects should not be included as amelia. Limb-body wall spectrum defects include transverse terminal limb deficiencies, abdominal wall disruption, atypical exencephaly/encephalocele, atypical facial clefts, and at times, amniotic bands.

Amelia is very rare. The overall total prevalence of amelia ranges from 0.4 to 2.4 per 100 000 births. The prevalence of amelia among stillbirths is at least 30 times higher than that among live births.

## Inclusions

Q71.0 Congenital complete absence of upper limb(s); amelia of upper limb
Q72.0 Congenital complete absence of lower limb(s); amelia of lower limb
Q73.0 Congenital absence of unspecified limb(s)

## Exclusions

Q71.1 Congenital absence of upper arm and forearm with hand present
Phocomelia of upper limb
Q71.2 Congenital absence of both forearm and hand
Q71.3 Congenital absence of hand and finger(s)
Q71.30 Congenital absence of finger(s)
Q72.1 Congenital absence of thigh and lower leg with foot present
Phocomelia of lower limb
Q72.2 Congenital absence of both lower leg and foot
Q72.3 Congenital absence of foot and toe(s)
Q72.4 Longitudinal reduction defect of femur
Proximal femoral focal deficiency
Q72.30 Congenital absence or hypoplasia of toe(s) with remainder of foot intact
Q87.24 Sirenomelia
Q87.25 Thrombocytopenia absent radius syndrome
Q89.81 Limb-body wall complex

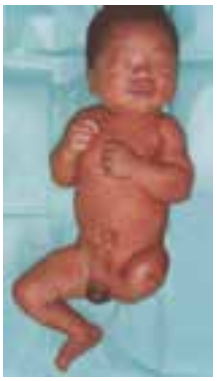
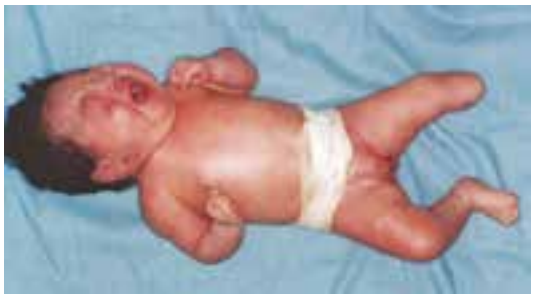
## Related codes

Q86.82 Congenital malformations due to thalidomide

## Checklist for high-quality reporting

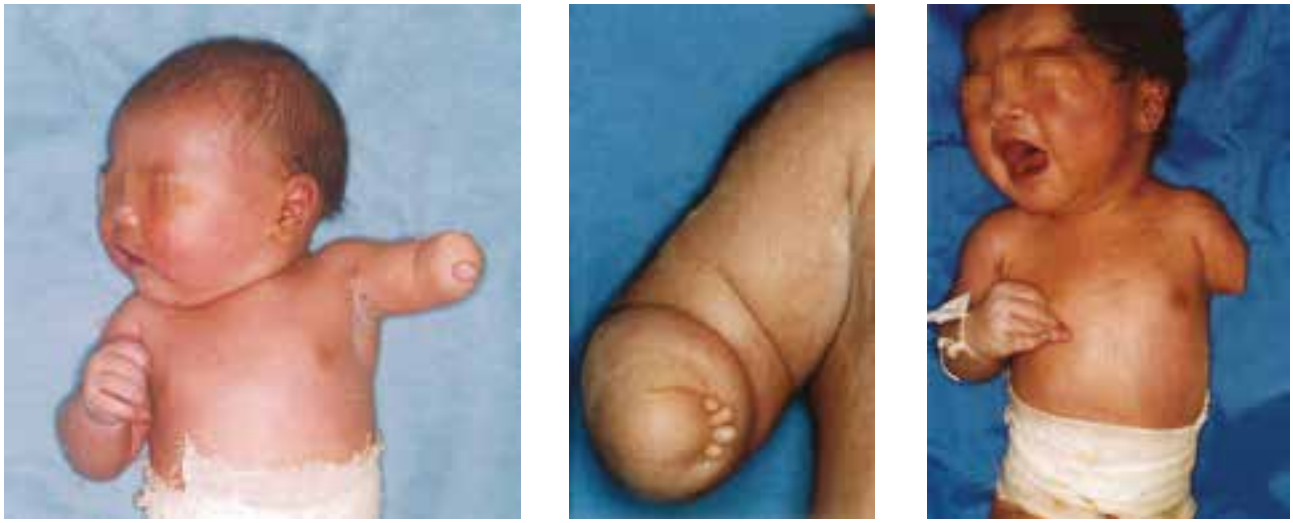
| Amelia – Documentation Checklist |
|---|
| ☐ **Describe in detail** (avoid using only the term "amelia"), including:<br>▸ Limb(s) involved.<br>▸ The segment(s) involved for each affected limb – confirm that all segments of the limb are absent.<br>▸ Laterality – right, left, bilateral. |
| ☐ **Use Fig. 4.35 to distinguish amelia from other limb deficiencies.** |
| ☐ **Describe procedures to assess further additional malformations** and, if one or more is present, describe these. |
| ☐ **Distinguish from transverse terminal defects, sirenomelia, and limb-body wall complex.** |
| ☐ **Take and report photographs:** Very useful; often crucial for review. |
| ☐ **Take and report radiographs:** Crucial for review and classification. |
| ☐ **Report whether specialty consultation(s) done, and if so, report the results.** |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors:<br>▸ Take and attach radiographs and photographs – essential for review and correct classification.<br>▸ Specify which limbs are involved and laterality. |
| **Coding** | ▸ Track and minimize cases coded with generic ICD-10 RCPCH codes: Q71, Q72, Q73 and Q73.0. |
| **Clinical classification** | ▸ Associated anomalies are frequent in amelia: Check if a full evaluation has been done. |
| **Prevalence** | ▸ Prevalence is low (< 2.5 per 100 000 births). A higher prevalence suggests misclassification with transverse terminal defects. |
| **Key visuals** | Distinguishing amelia from transverse limb deficiencies and sirenomelia (side-by-side comparison):<br>  <br>Amelia of the right lower limb (Q72.0)<br>*Photograph source*: CDC–Beijing Medical University collaborative project.<br>  <br>Transverse terminal defect of left limb, with missing foot and partial absence of leg<br>*Photograph source*: CDC–Beijing Medical University collaborative project.<br>  <br>Sirenomelia sequence (Q87.24)<br>*Photograph source*: Latin American Collaborative Study of Congenital Malformations (ECLAMC).<br>  <br>Limb-body wall complex: Very severe lethal defects involving abdominal wall, limb, and often craniofacial structures. Note the partial absence of the left lower limb as a component of the complex in this photograph. Limb-body wall complex is excluded in prevalence counts of amelia.<br>*Photograph source*: CDC–Beijing Medical University collaborative project. |

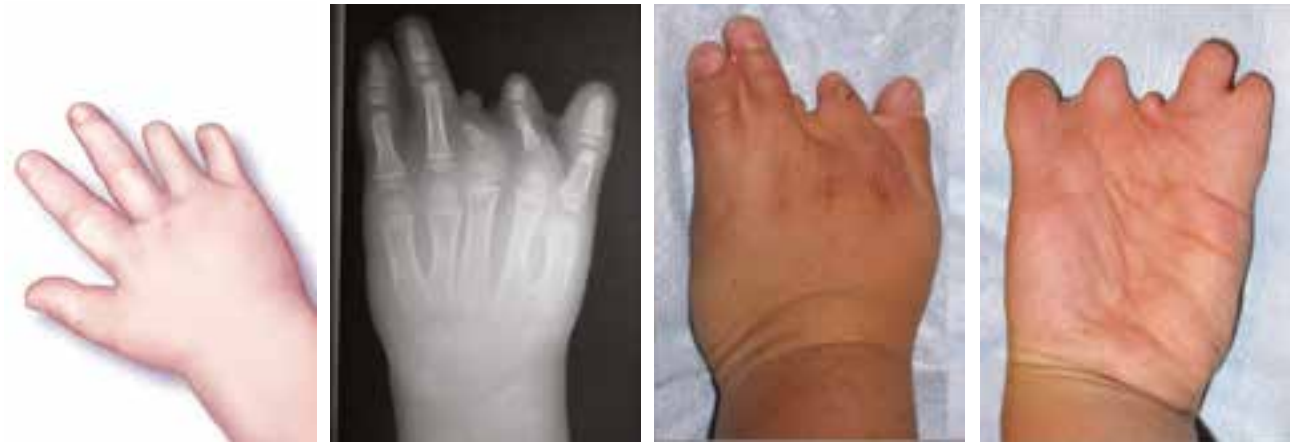
## Fig. 4.37. Transverse terminal

Congenital absence of both forearm and hand (Q71.2)



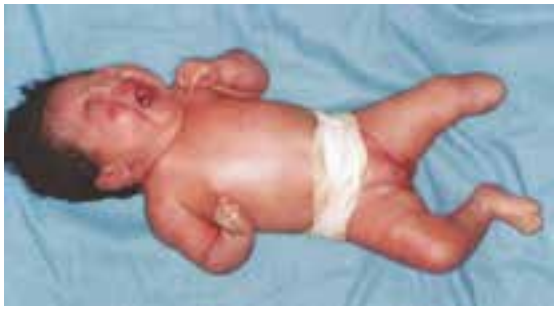
*Photograph source*: CDC–Beijing Medical University collaborative project.

Congenital absence of finger(s) (remainder of hand intact) (Q71.30)



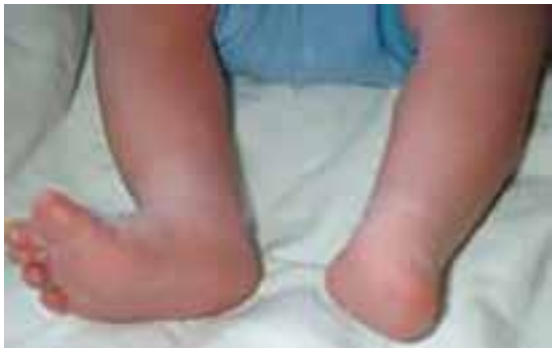
*Photograph and x-ray source*: Dr E. Gene Deune, Johns Hopkins Department of Orthopedic Surgery, Division of Hand Surgery.

Congenital absence of both lower leg and foot (Q72.2)



*Photograph source*: CDC–Beijing Medical University collaborative project.

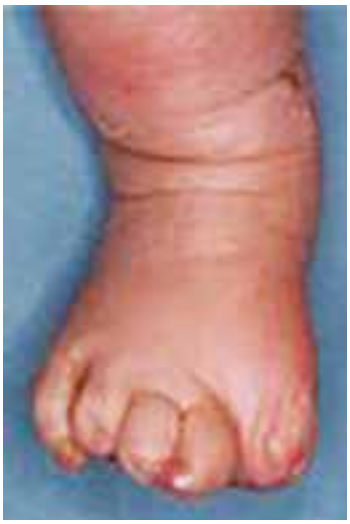
Congenital absence of foot and toes (Q72.3)



*Photograph source*: ECLAMC.

**Fig. 4.37. Transverse terminal** (continued)

Congenital absence or hypoplasia of toe(s) with remainder of foot intact (Q72.30)



*Photograph source*: CDC–Beijing Medical University collaborative project.

Constriction ring (Q84.81)

*Photograph source*: ECLAMC.

Terminal transverse limb deficiency is a congenital anomaly that appears as an "amputation" of an arm, leg or digit/toe. The limb is missing the terminal (distal) segment(s), with preservation of all the segment(s) proximal to the missing segment. For example, if fingers are missing, the remainder of the hand, forearm and arm are all still present (small nubbins may be present terminally; see clinical description below). Radiographs are strongly recommended and can be essential to confirm the condition and characterize the bony anatomy.

## Relevant ICD-10 codes

Q71.2 Congenital absence of both forearm and hand
Q71.3 Congenital absence of hand and finger(s)
Q71.30 Congenital absence of finger(s)
Q72.2 Congenital absence of both lower leg and foot
Q72.3 Congenital absence of foot and toe(s)
Q72.30 Congenital absence or hypoplasia of toe(s) with remainder of foot intact

Note:
Avoid using the generic Q71, Q72 or Q73 to code transverse terminal limb deficiencies. These generic codes include other limb deficiencies.

## Diagnosis

***Prenatal.*** Terminal transverse limb deficiencies might be diagnosed or strongly suspected prenatally. However, they can be missed or misdiagnosed as one of the other limb deficiencies. For these reasons, a prenatal diagnosis should always be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** The newborn examination confirms the diagnosis of terminal transverse limb deficiency and distinguishes it from other limb deficiencies. It is important to underline the importance of a detailed examination and documentation, including imaging (photographs and radiographs).

## Clinical and epidemiologic notes

Distinguishing terminal transverse defects from other limb deficiencies is important because these conditions have different causes and associated anomalies. With careful clinical and radiological examination, transverse terminal limb deficiencies can be reliably diagnosed.

Terminal transverse deficiency represents a wide spectrum of limb abnormalities, with partial amputation of the distal limb. The terminal partial amputation can involve digits, toes, forearm, arm, leg or thigh. Transverse deficiencies are the most common limb deficiencies, most often caused by the early amnion rupture disruption sequence, also referred to as amniotic bands. The damage from an amniotic band can range from constriction of a limb to hypoplasia of digits with syndactyly, rudimentary digits, and absence of the limb distally from the site of the in-utero amputation. Amniotic bands can also cause disruptions at other sites, such as the face and body wall. Typically, the transverse deficiencies are not symmetric.

In cases involving the hand, there can be small soft tissue "nubbins" arranged in a pattern suggesting rudimentary digits. Most cases of terminal transverse deficiency occur sporadically and as an isolated abnormality involving a single limb in an otherwise healthy individual.

The risk of transverse terminal limb deficiencies increases with the use of misoprostol in failed abortions. Chorionic villus sampling (CVS) at 9 weeks or earlier has been associated with transverse terminal limb deficiencies. Among genetic syndromes, consider Adams–Oliver syndrome if the terminal transverse limb defect is associated with aplasia cutis congenita and/or CHD.

From an epidemiologic perspective, transverse terminal limb deficiencies are the most frequent type of limb deficiency, with a birth prevalence of approximately 2.5 per 10 000 births.

## Inclusions

Q71.2 Congenital absence of both forearm and hand
Q71.3 Congenital absence of hand and finger(s)
Q71.30 Congenital absence of finger(s)
Q72.2 Congenital absence of both lower leg and foot
Q72.3 Congenital absence of foot and toe(s)
Q72.30 Congenital absence or hypoplasia of toe(s) with remainder of foot intact

## Related codes

Q79.80 Amniotic band
Q84.81 Constriction ring
Q89.81 Limb-body wall complex

## Exclusions

Q71.0 Congenital complete absence of upper limb(s); amelia of upper limb
Q71.1 Congenital absence of upper arm and forearm with hand present
Phocomelia of upper limb
Q71.6 Congenital cleft hand
Q72.0 Congenital complete absence of lower limb(s); amelia of lower limb
Q72.1 Congenital absence of thigh and lower leg with foot present
Phocomelia of lower limb
Q72.4 Longitudinal reduction defect of femur
Proximal femoral focal deficiency
Q72.7 Split foot
Q73.0 Congenital absence of unspecified limb(s)

## Checklist for high-quality reporting

**Transverse Terminal Defects – Documentation Checklist**

- ☐ **Describe in detail**, including:
  - Limbs involved.
  - Note each segment involved for each limb affected – describe what is deficient or absent; indicate involvement of digits, toes, forearm, arm, leg, thigh.
  - Laterality – right, left, bilateral.
  - Report whether or not soft tissue nubbins are present.
  - Report whether or not amniotic bands and/or ring constrictions are present.
  - Document specialty consultations (e.g. genetics, orthopaedics).
- ☐ **Use Fig. 4.35 to distinguish transverse terminal defects from other subtypes of limb deficiencies.**
- ☐ **Describe procedures to assess further additional malformations; if one or more is present, describe these.**
- ☐ **Describe procedures to assess syndromes.**
- ☐ **Distinguish from other limb deficiencies** (e.g. amelia or axial defects).
- ☐ **Take and report photographs:** Very useful; can be crucial for review.
- ☐ **Take and report radiographs:** Crucial for review and classification, at times even more so than photographs.
- ☐ **Report whether specialty consultation(s) done, and if so, report the results.**

## Suggested data quality indicators

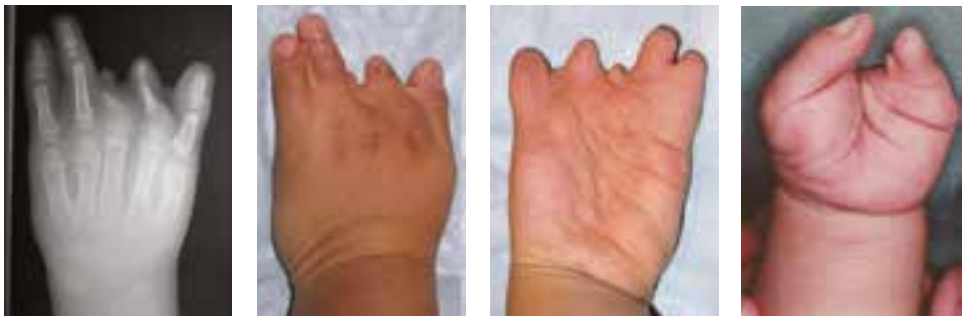
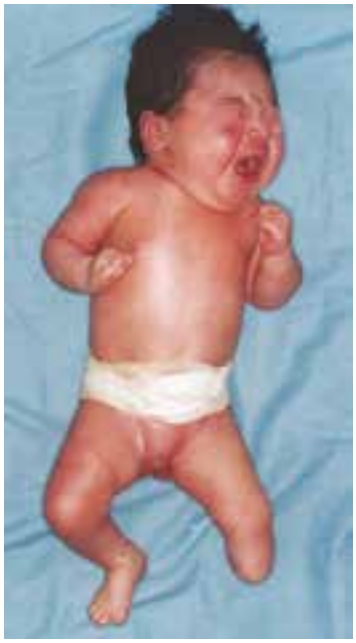
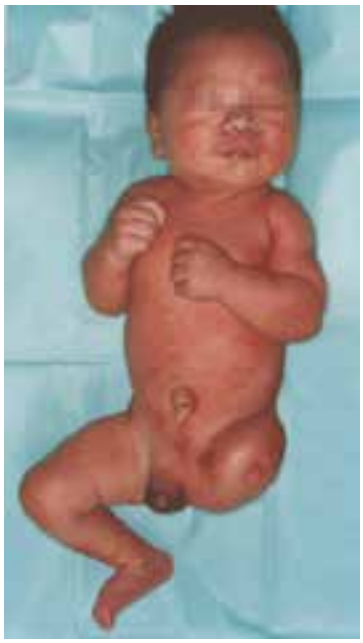
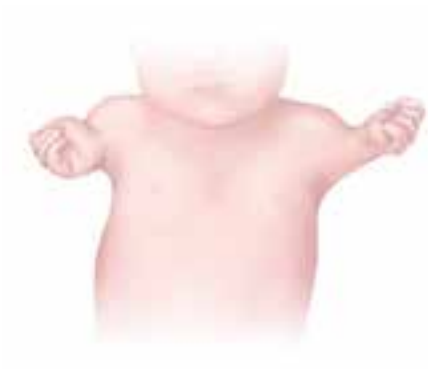
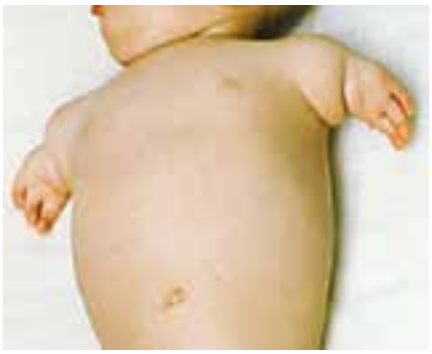
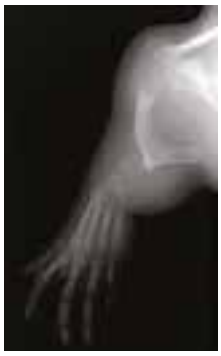
| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors:<br>▸ Take and attach radiographs and photographs – essential for review and correct classification.<br>▸ Specify which limbs are involved and laterality.<br>▸ Specify affected segments (fingers, toes).<br>▸ Specify affected bones. |
| **Coding** | ▸ Track and minimize cases coded with generic ICD-10 RCPCH codes: Q71, Q72, Q73. |
| **Clinical classification** | ▸ Syndromes are not frequent in transverse terminal defects. A high proportion of syndromes suggests misclassification with other limb deficiencies. |
| **Prevalence** | ▸ Prevalence is around 2.5 per 10 000 births. A significantly lower prevalence suggests under-ascertainment or misclassification with other limb deficiencies. |
| **Key visuals** | Distinguishing transverse terminal defects from longitudinal axial defects and amelia (side-by-side comparison):<br>  <br>Transverse terminal defect: absence of fingers (Q71.30)<br>*Photograph source:* Dr E. Gene Deune, Johns Hopkins Department of Orthopedic Surgery, Division of Hand Surgery<br>Longitudinal axial defect: cleft hand (Q71.6)<br>*Photograph source:* CDC-Beijing Medical University collaborative project<br>  <br>*Photograph source:* CDC-Beijing Medical University collaborative project<br>Congenital absence of both lower leg and foot (Q72.2)<br>  <br>*Photograph source:* CDC-Beijing Medical University collaborative project<br>Amelia of the right lower limb (Q72.0) |

**Fig. 4.38. Transverse intercalary**

Congenital absence of upper arm and forearm with hand present (Q71.1)





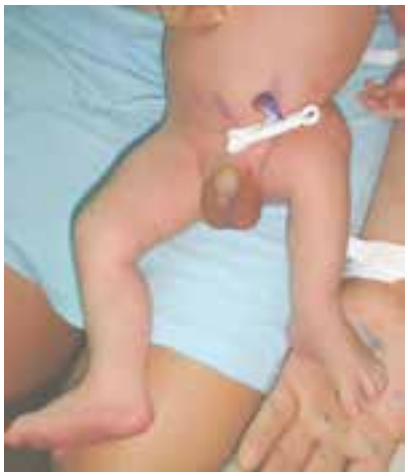


*Photograph source*: Dr Jaime Frias (EE. UU.).

Congenital absence of thigh and lower leg with foot present (Q72.1)

*Photograph source*: ECLAMC.

Longitudinal reduction defect of femur (Q72.4)



*Photograph source*: ECLAMC.

Transverse intercalary limb deficiencies are characterized by the absence of proximal or middle segments of a limb with all or part of the distal segment present. Radiographs are strongly recommended to confirm the condition and characterize the bony anatomy.

## Relevant ICD-10 codes

Q71.1 Congenital absence of upper arm and forearm with hand present
Phocomelia of upper limb
Q72.1 Congenital absence of thigh and lower leg with foot present
Phocomelia of lower limb
Q72.4 Longitudinal reduction defect of femur
Proximal femoral focal deficiency

Note:
Avoid using the generic Q71, Q72 or Q73 codes for intercalary limb deficiencies. These generic codes include other limb deficiencies.

## Diagnosis

***Prenatal.*** Transverse intercalary limb deficiency can be suspected prenatally, but is easily missed or misdiagnosed. Cases identified or suspected prenatally should be confirmed postnatally before inclusion in the surveillance programme. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** The newborn examination confirms the diagnosis of intercalary limb deficiency and distinguishes it from other limb deficiencies (such as amelia). A careful clinical examination and documentation, aided by imaging (photos and radiographs), are essential for an accurate and complete diagnosis.

## Clinical and epidemiologic notes

Typical intercalary deficiencies present with absence of all limb bones proximal to a normal or malformed hand or foot which attaches directly to the trunk. Atypical intercalary deficiencies present with absence of humerus or femur, or both radius-ulna (tibia-fibula) with normal or malformed hand or foot. Distinguishing intercalary defects from other limb reduction defects is important because these conditions have different causes and disease associations. With careful clinical and radiological examination, the diagnosis of intercalary limb deficiencies is possible.

Note that the English translation for the term "phocomelia" is considered pejorative and should not be used. Translation from Latin to English alludes to the shape of the limb resembling that of a flipper on a seal.

About half of transverse intercalary limb deficiency cases are isolated. Most of the remaining cases have multiple congenital anomalies. A small proportion of cases are syndromic. Syndromes with intercalary limb deficiencies include Roberts syndrome; in its most severe form, thrombocytopenia absent radius (TAR) syndrome can have intercalary limb deficiencies.

A teratogen that can cause intercalary limb deficiencies is thalidomide. Maternal pregestational diabetes has been associated with femoral hypoplasia-unusual facies syndrome (now more commonly called femoral-facial syndrome). This condition is characterized by unilateral or bilateral deficiency of femurs, with variable deficiencies of other long bones.

The prevalence of intercalary limb deficiencies is around 0.45 per 10 000 births.

## Inclusions

Q71.1 Congenital absence of upper arm and forearm with hand present
Phocomelia of upper limb
Q72.1 Congenital absence of thigh and lower leg with foot present
Phocomelia of lower limb
Q72.4 Longitudinal reduction defect of femur
Proximal femoral focal deficiency

## Related codes

Q87.25 Thrombocytopenia absent radius syndrome
Q86.82 Congenital malformations due to thalidomide

## Exclusions

Q71.0 Congenital complete absence of upper limb(s); amelia of upper limb
Q71.2 Congenital absence of both forearm and hand
Q71.3 Congenital absence of hand and finger(s)
Q71.30 Congenital absence of finger(s)
Q72.0 Congenital complete absence of lower limb(s); amelia of lower limb
Q72.2 Congenital absence of both lower leg and foot
Q72.3 Congenital absence of foot and toe(s)
Q72.30 Congenital absence or hypoplasia of toe(s) with remainder of foot intact
Q73.0 Congenital absence of unspecified limb(s)

## Checklist for high-quality reporting

**Intercalary Defects – Documentation Checklist**

- ☐ **Describe in detail**, including:
  - Limbs involved.
  - Note each segment involved for each limb affected – describe what is deficient or absent. Indicate involvement of forearm, arm, leg, thigh. Indicate bones involved.
  - Laterality right, left, bilateral.
  - Avoid using solely a "diagnostic term" (e.g. phocomelia).
  - Document specialty consultations (e.g. genetics, orthopaedics).
- ☐ **Use Fig. 4.35 to distinguish transverse intercalary defects from other subtypes of limb deficiencies.**
- ☐ **Describe procedures to assess further additional malformations; if one or more is present, describe these.**
- ☐ **Describe procedures to assess syndromes.**
- ☐ **Distinguish from other limb deficiencies** (e.g. transverse terminal deficiencies).
- ☐ **Take and report photographs:** Very useful; can be crucial for review.
- ☐ **Take and report radiographs:** Crucial for review and classification, at times even more so than photographs.
- ☐ **Report whether specialty consultation(s) done, and if so, report the results.**

## Suggested data quality indicators

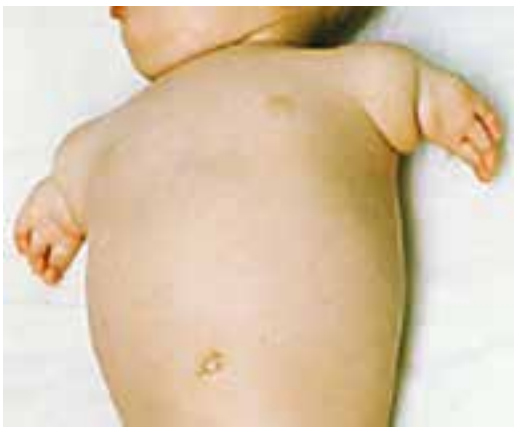
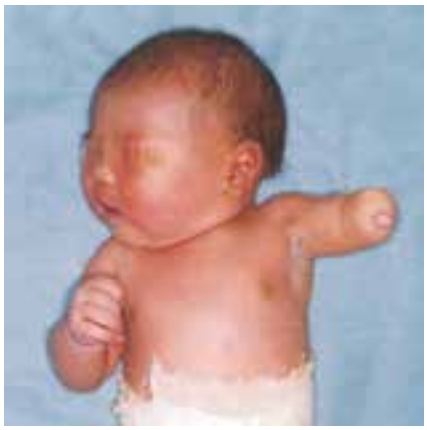
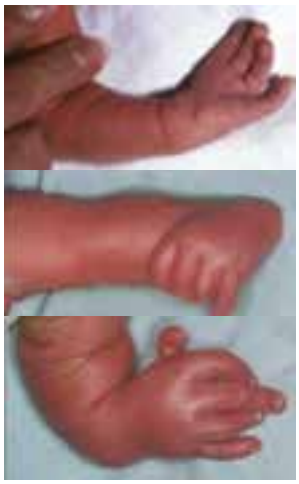
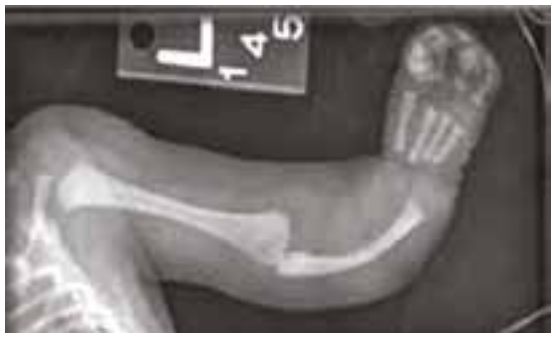
| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors:<br>▸ Take and attach radiographs and photographs – essential for review and correct classification.<br>▸ Specify which limbs are involved and laterality.<br>▸ Specify affected segments.<br>▸ Specify affected bones. |
| **Coding** | Use the specific code. Track and minimize cases coded with generic ICD-10 RCPCH codes: Q71, Q72, Q73. |
| **Clinical classification** | Syndromes are not frequent in intercalary defects. A high proportion of syndromes suggests misclassification with other limb deficiencies. |
| **Prevalence** | Prevalence is around 0.45 per 10 000 births. A higher prevalence suggests misclassification with other limb deficiencies. |
| **Key visuals** | Distinguishing intercalary defects from transverse terminal defects (side-by-side comparison):<br>  <br>Typical transverse intercalary defect: Absence of upper arm and forearm with hand present (Q71.1)<br>*Photograph source*: Dr Jaime Frias (EE. UU.).<br>  <br>Transverse terminal defect: Absence of both forearm and hand (Q71.2)<br>*Photograph source*: CDC–Beijing Medical University collaborative project. |

**Fig. 4.39. Longitudinal preaxial**

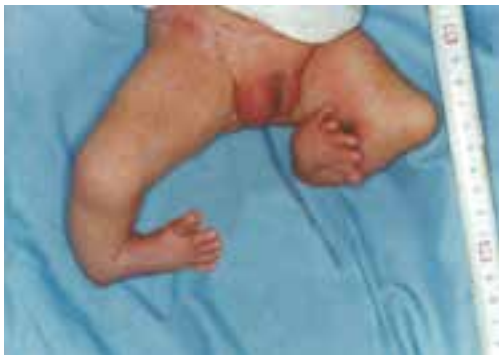
Absence/hypoplasia of thumb (Q71.31)



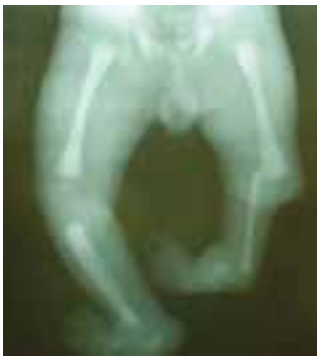
Longitudinal reduction defect of radius (Q71.4)



Hypoplasia of first toe with other digits present (Q72.31)



Longitudinal reduction defect of tibia (Q72.5)



*Photograph source:* ECLAMC.

Preaxial limb deficiency is characterized by the absence or hypoplasia of the "preaxial" segments (those on the side of the thumb or big toe side) of the upper or lower limb (see Fig. 4.39). Preaxial limb deficiencies include:

- hypoplasia/absence of the thumb (sometimes of the second finger)
- hypoplasia/absence of the radius
- hypoplasia/absence of the big toe (sometimes of the second toe)
- hypoplasia/absence of the tibia.

Radiographs are strongly recommended to confirm the diagnosis and characterize the bone anatomy.

## Relevant ICD-10 codes

Q71.31 Absence or hypoplasia of thumb (other digits intact)
Q71.4 Longitudinal reduction defect of radius
Clubhand (congenital)
Radial clubhand
Absence of radius
Q72.31 Absence or hypoplasia of first toe with other digits present
Q72.5 Longitudinal reduction defect of tibia
Absence of tibia

Note:
Avoid using the generic Q71, Q72 or Q73 codes for longitudinal preaxial limb deficiencies. These generic codes include other limb deficiencies.

## Diagnosis

***Prenatal.*** Longitudinal preaxial limb deficiencies might be diagnosed or strongly suspected prenatally. However, they can be missed. Moreover, the distinction from other limb deficiencies might be difficult and error-prone. For this reason, a prenatal diagnosis should always be confirmed postnatally.

When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** The newborn examination can identify a longitudinal preaxial limb deficiency and distinguish it from other limb deficiencies (e.g. longitudinal postaxial defects). An accurate and complete diagnosis requires a detailed physical examination aided by radiography to characterize completely the bony anatomy.

## Clinical and epidemiologic notes

Radial deficiency is often associated with hypoplasia or aplasia of the thumb and a bowing of the ulna (so-called radial club hand, angulated to the radial side of the wrist). Isolated thumb hypoplasia or triphalangeal thumb is the mildest manifestation of a preaxial deficiency.

Radial deficiencies are commonly associated with other anomalies such as in the VATER/VACTERL association, as well as several genetic syndromes. Some possible genetic diagnoses include trisomy 18, Fanconi anaemia, Holt-Oram syndrome and TAR syndrome. Of note, several genetic conditions with radial deficiency present also haematologic abnormalities (Diamond-Blackfan anaemia, Fanconi anaemia, TAR syndrome), some of which can be suspected with simple blood tests (although normal findings do not exclude the diagnosis).

Thalidomide and valproate are known teratogens associated with longitudinal preaxial defects (as well as other types of limb deficiency). Longitudinal preaxial defects of the lower limb include absence or hypoplasia of the first toe with or without hypoplasia or absence of the tibia. Tibial deficiencies are less common than radial deficiencies. They are often associated with equinovarus deformities, and there might be fibular hypoplasia/aplasia. Tibial deficiencies occur most often as an isolated, unilateral malformation with the fibula present.

Absence of the tibia and preaxial polydactyly of the first toe is more common among infants of diabetic mothers. Absence of the tibia is also part of the spectrum of skeletal effects produced by exposure to thalidomide. The affected child would usually have other skeletal and visceral anomalies.

Prevalence of preaxial limb deficiencies is around 0.75 per 10 000 births. It is the second most prevalent limb deficiency subtype, after transverse terminal defects.

## Inclusions

Q71.3 Absence or hypoplasia of thumb
Q71.4 Longitudinal reduction defect of radius
Q72.31 Absence or hypoplasia of first toe with other digits present
Q72.5 Longitudinal reduction defect of tibia

## Related codes

| | |
|---|---|
| Q87.20 | Holt-Oram syndrome |
| Q87.25 | Thrombocytopenia absent radius syndrome |
| Q87.26 | VACTERL association |
| Q86.82 | Congenital malformations due to thalidomide |
| Q91.0–Q91.2 | Trisomy 18 |
| D61.0 | Fanconi anaemia with absent radius |

## Exclusions

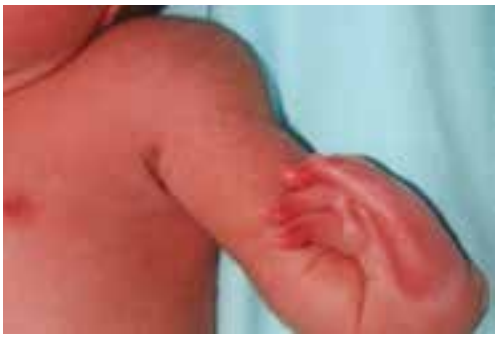
Q71.5 Longitudinal reduction defect of ulna
Q72.6 Longitudinal reduction defect of fibula
Q71.6 Congenital cleft hand
Q72.7 Split foot

## Checklist for high-quality reporting

**Longitudinal Preaxial Defects – Documentation Checklist**

- ☐ **Describe in detail**, including:
  - Limbs involved.
  - Note each segment involved for each limb affected – describe what is deficient or absent. Indicate involvement of radius, tibia, first–second finger, first–second toe, fibula, and others.
  - Laterality – right, left, bilateral.
  - Document specialty consultations (e.g. genetics, orthopaedics).
- ☐ **Use Fig. 4.35 to distinguish longitudinal preaxial defects from other subtypes of limb deficiencies.**
- ☐ **Describe procedures to assess further additional malformations and, if one or more is present, describe these.**
- ☐ **Describe procedures to assess syndromes.**
- ☐ **Distinguish from other longitudinal limb deficiencies** (e.g. longitudinal postaxial).
- ☐ **Take and report photographs:** Very useful; can be crucial for review.
- ☐ **Take and report radiographs:** Crucial for review and classification, at times even more so than photographs.
- ☐ **Report whether specialty consultation(s) done, and if so, report the results.**

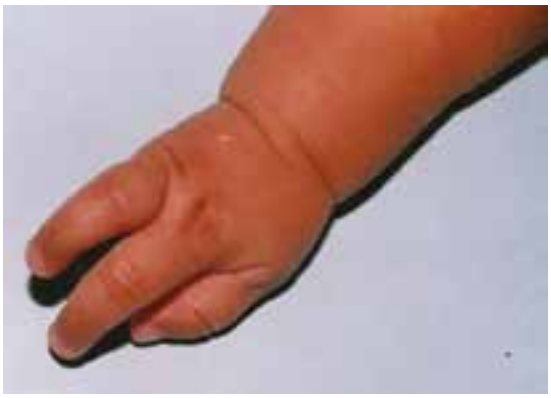
## Suggested data quality indicators

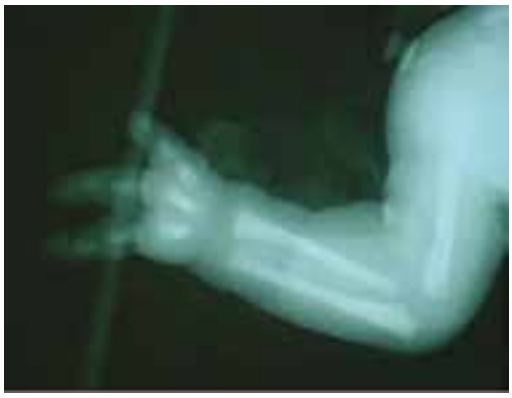
| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors:<br>▸ Take and attach radiographs and photographs – essential for review and correct classification.<br>▸ Specify which limbs are involved and laterality.<br>▸ Specify affected segments (hand, forearm, foot, leg).<br>▸ Specify affected bones.<br>▸ Specify if blood tests were performed. |
| **Coding** | ▸ Use the specific code. Track and minimize cases coded with generic ICD-10 RCPCH codes: Q71, Q72, Q73. |
| **Clinical classification** | ▸ Syndromes are frequent in longitudinal preaxial defects. A low proportion of syndromes suggests misclassification with other limb deficiencies. |
| **Prevalence** | ▸ Prevalence is around 0.75 per 10 000 births. A higher prevalence suggests misclassification with other limb deficiencies. |
| **Key visuals** | Distinguishing longitudinal preaxial defects from longitudinal postaxial defects (side-by-side comparison):<br>  <br>Longitudinal preaxial: Absence of thumb (Q71.31)<br>*Photograph source*: ECLAMC.<br>  <br>Longitudinal postaxial: Congenital absence of fourth and fifth fingers (Q71.30)<br>*Photograph source*: ECLAMC. |

Postaxial limb deficiency is characterized by absence or hypoplasia of the fifth toe/finger (sometimes also including the fourth toe/finger) with or without absence/hypoplasia of the fibula or ulna (*see* Fig. 4.40). Radiographs are strongly recommended to confirm the findings and characterize the bony anomalies.

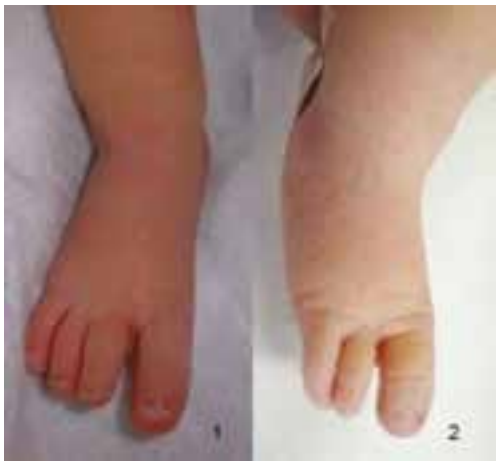
**Fig. 4.40. Longitudinal postaxial**

Congenital absence of fourth and fifth fingers (Q71.30)





Congenital absence or hypoplasia of toe(s) with remainder of foot intact (Q72.30)



*Photograph source:* ECLAMC.

## Relevant ICD-10 codes

Q71.5 Longitudinal reduction defect of ulna
Q72.6 Longitudinal reduction defect of fibula
Absence of fibula
Q71.30 Congenital absence of finger(s) with remainder of hand intact
Q72.30 Congenital absence or hypoplasia of toe(s) with remainder of foot intact

Note:
Avoid using the generic Q71, Q72 or Q73 codes for longitudinal postaxial limb deficiencies. These generic codes include other limb reduction defects.

When using Q71.30 – congenital absence of finger(s) with remainder of hand intact – or Q72.30 – congenital absence or hypoplasia of toe(s) with remainder of foot intact – be sure to denote which fingers and toes are affected to be able to differentiate from transverse terminal defects.

## Diagnosis

***Prenatal.*** Longitudinal postaxial limb deficiencies might be diagnosed or strongly suspected prenatally. However, they can be missed. The distinction from other limb deficiencies is difficult and error-prone. For this reason, a prenatal diagnosis should always be confirmed postnatally.

When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** The newborn examination can identify a longitudinal postaxial limb deficiency and distinguish it from other limb deficiencies (e.g. longitudinal postaxial defects). An accurate and complete diagnosis requires a detailed physical examination aided by radiography to characterize completely the bony anatomy.

## Clinical and epidemiologic notes

Absence or hypoplasia of the ulna typically affects only one arm. With complete absence of the ulna, there is often a marked flexion deformity of the elbow. The hand can be straight or angulated to the ulnar side of the wrist.

Ulnar deficiency is less common than radial deficiency. Ulnar hypoplasia is often associated with radioulnar synostosis (fusion of the radius and ulna), absence of the postaxial digits (fourth and fifth fingers) and fibular deficiency.

Some associations and syndromes described with postaxial defects include the following:

- femur-fibula-ulna complex, characterized by the unilateral absence or hypoplasia of the ulna, femur and fibula;
- ulnar-mammary syndrome (a genetic condition), characterized by deficiencies of the ulna, fibula and postaxial digits; hypogenitalism; and absence of one or both breasts/nipples; and
- Miller syndrome, in which facial differences are associated with postaxial deficiencies of the upper limb.

Distinguishing longitudinal postaxial defects from other limb reduction defects is important because these conditions have different causes and associated anomalies. With careful clinical and radiological examination, the diagnosis of longitudinal postaxial limb deficiencies is possible.

The reported prevalence of postaxial limb deficiencies is approximately 0.45 per 10 000 births.

## Inclusions

Q71.30 Congenital absence of finger(s)
Q71.5 Longitudinal reduction defect of ulna
Q72.30 Congenital absence or hypoplasia of toe(s) with remainder of foot intact
Q72.6 Longitudinal reduction defect of fibula

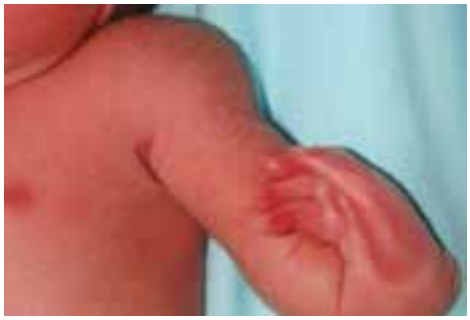
## Exclusions

Q71.31 Absence or hypoplasia of thumb
Q71.4 Longitudinal reduction defect of radius
Q71.6 Congenital cleft hand
Q72.31 Absence or hypoplasia of first toe with other digits present
Q72.5 Longitudinal reduction defect of tibia
Q72.7 Split foot

## Checklist for high-quality reporting

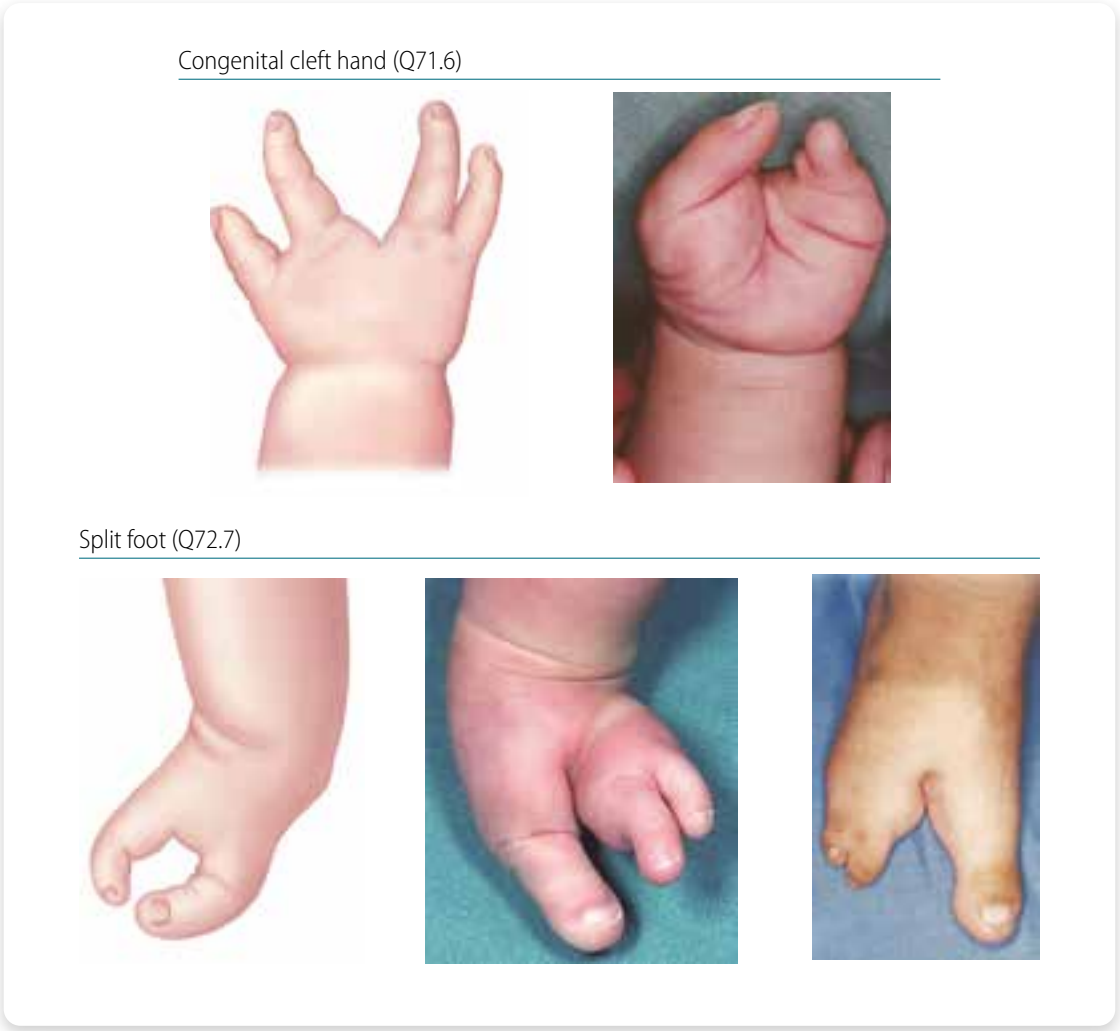
| Longitudinal Postaxial Defects – Documentation Checklist |
|---|
| ☐ **Describe in detail**, including:<br>▸ Limbs involved.<br>▸ Note each segment involved for each limb affected – describe what is deficient or absent. Indicate involvement of ulna, fibula, fourth–fifth finger, fourth–fifth toe, and others.<br>▸ Laterality – right, left, bilateral.<br>▸ Document specialty consultations (e.g. genetics, orthopaedics). |
| ☐ **Use Fig. 4.35 to distinguish longitudinal postaxial defects from other subtypes of limb deficiencies.** |
| ☐ **Describe procedures to assess further additional malformations and, if one or more is present, describe these.** |
| ☐ **Describe procedures to assess syndromes.** |
| ☐ **Distinguish from other longitudinal and transverse limb deficiencies** (e.g. longitudinal preaxial). |
| ☐ **Take and report photographs:** Very useful; can be crucial for review. |
| ☐ **Take and report radiographs:** Crucial for review and classification, at times even more than photographs. |
| ☐ **Report whether specialty consultation(s) done, and if so, report the results.** |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors:<br>▸ Take and attach radiographs and photographs – essential for review and correct classification.<br>▸ Specify which limbs are involved and laterality.<br>▸ Specify affected segments (hand, forearm, foot, leg).<br>▸ Specify affected bones. |
| **Coding** | Use the specific code. Track and minimize cases coded with generic ICD-10 RCPCH codes: Q71, Q72, Q73. |
| **Clinical classification** | Syndromes are not frequent in longitudinal postaxial defects. A high proportion of syndromes suggests misclassification with preaxial limb deficiencies. |
| **Prevalence** | Prevalence is around 0.45 per 10 000 births. A much higher or lower prevalence suggests misclassification with other limb deficiencies. |
| **Key visuals** | Distinguishing longitudinal postaxial defects from longitudinal preaxial defects (side-by-side comparison):<br>  <br>**Postaxial** defect: Absence of fourth and fifth finger(s) (Q71.30)<br>*Photograph source*: ECLAMC.<br>  <br>**Preaxial** defect: Absence of thumb (Q71.31)<br>*Photograph source*: ECLAMC. |

The longitudinal axial or split hand/split foot deficiency is characterized by a deficiency of the central digits/toes often involving the associated carpal/tarsal bones, leading to the typical external appearance that gave rise to the name split hand or split foot (see Fig. 4.41).

**Fig. 4.41. Split hand and foot**




*Photograph source:* CDC–Beijing Medical University collaborative project.

## Relevant ICD-10 codes

Q71.6 Congenital cleft hand
Q72.7 Split foot

Note:
Avoid using the generic Q71, Q72 or Q73 codes for split hand and split foot. These generic codes include other limb reduction defects.

## Diagnosis

***Prenatal.*** Split hand and split foot might be diagnosed or strongly suspected prenatally. However, they can be missed. Moreover, the distinction from other limb deficiencies is difficult and error-prone. For this reason, a prenatal diagnosis should always be confirmed postnatally.

When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** The newborn examination can identify the typical external appearance of this condition, although on occasion there is confusion with terminal transverse deficiencies involving the middle fingers. An accurate and complete diagnosis requires a detailed physical examination aided by radiography to characterize completely the bony anatomy of the axial (central) segments of the hands and feet.

## Clinical and epidemiologic notes

Note that older terms such as ectrodactyly and lobster claw hands have been used in the past but should be avoided, as these are either imprecise or pejorative.

Cases of split hand or split foot can occur with syndactyly and hypoplasia of some of the remaining digits. The most severe form of split hand or split foot is monodactyly, where the hand or foot only has a single digit.

This condition can involve only the hands, only the feet, or both the hands and feet. Hands are affected much more frequently than feet. Most cases are unilateral, with the right side more commonly affected.

Split hand and split foot might occur with deficiency of the adjacent long bones of the limbs.

Split hand/split foot is part of a large group of syndromes due to one of several single-gene conditions or genomic rearrangements, some of which involve other organ systems. Examples include the EEC syndromes (ectrodactyly, ectodermal dysplasia, cleft lip/palate), and the limb-mammary syndrome (split hand split foot, absence of breast tissue, cleft palate).

The prevalence of axial limb deficiencies is around 0.15 per 10 000 births.

## Inclusions

Q71.6 Congenital cleft hand
Q72.7 Split foot

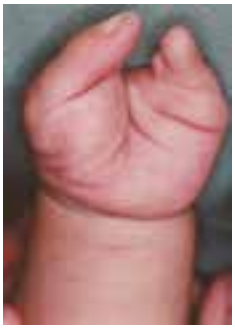
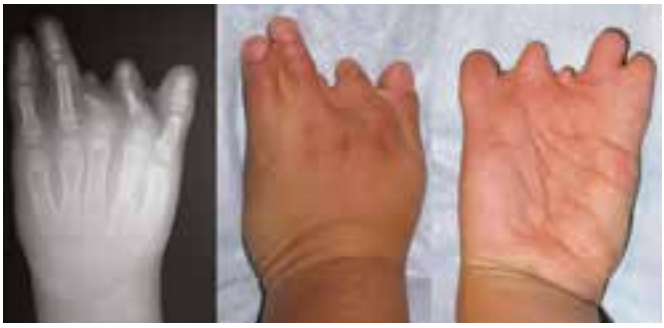
## Exclusions

Q68.10 Clinodactyly
Q70 Syndactyly
Q71.3 Congenital absence of hand and finger(s)
Q71.30 Congenital absence of finger(s)
Q71.31 Absence or hypoplasia of thumb (other digits intact)
Q72.3 Congenital absence of foot and toe(s)
Q72.30 Congenital absence or hypoplasia of toe(s) with remainder of foot intact
Q72.31 Absence or hypoplasia of first toe with other digits present
Q74.80 Brachydactyly

## Checklist for high-quality reporting

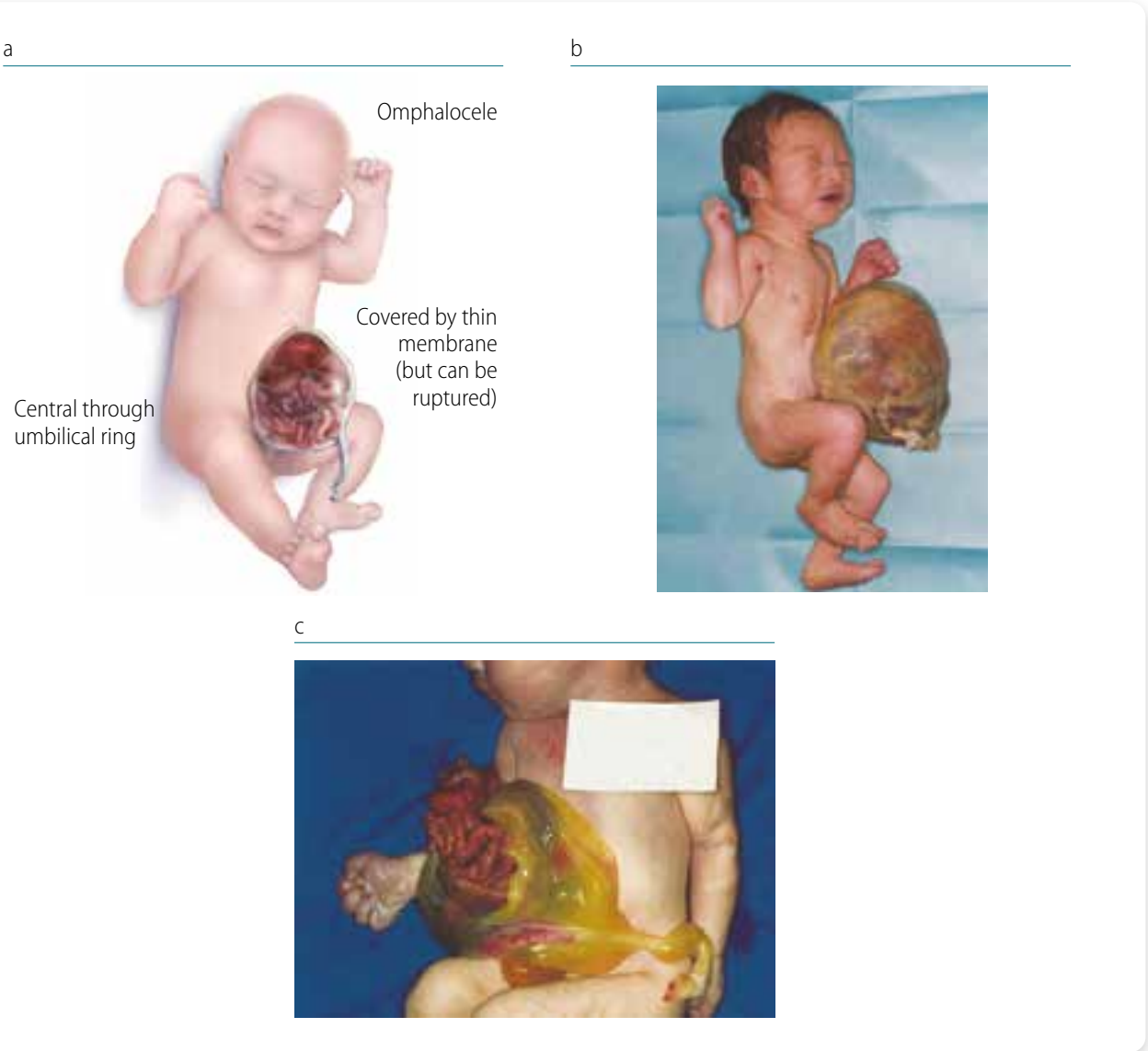
| Split Hand and Foot – Documentation Checklist |
|---|
| ☐ **Describe in detail**, including:<br>▸ Limbs involved.<br>▸ Note each segment involved for each limb affected – describe what is deficient or absent. Indicate involvement of digits and toes (third, with or without second and fourth).<br>▸ Laterality – right, left, bilateral.<br>▸ Document specialty consultations (e.g. genetics, orthopaedics). |
| ☐ **Use Fig. 4.35 to distinguish longitudinal axial defects from other subtypes of limb deficiencies.** |
| ☐ **Describe procedures to assess further additional malformations and, if one or more is present, describe these.** |
| ☐ **Describe procedures to assess syndromes.** |
| ☐ **Distinguish from other longitudinal and transverse limb deficiencies** (e.g. transverse terminal deficiencies of fingers or toes). |
| ☐ **Take and report photographs:** Very useful; can be crucial for review. |
| ☐ **Take and report radiographs:** Crucial for review and classification, at times even more so than photographs. |
| ☐ **Report whether specialty consultation(s) done, and if so, report the results.** |

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors:<br>▸ Take and attach radiographs and photographs – essential for review and correct classification.<br>▸ Specify which limbs are involved and laterality.<br>▸ Specify affected segments (fingers, toes).<br>▸ Specify affected bones. |
| **Coding** | ▸ Use the specific code for hand (Q71.6) or foot (Q72.7). Track and minimize cases coded with generic ICD-10 RCPCH codes: Q71, Q72, Q73. |
| **Clinical classification** | ▸ Syndromes are frequent in axial defects. A low proportion of syndromes suggests misclassification with other limb deficiencies. |
| **Prevalence** | ▸ Prevalence is around 0.15 per 10 000. A higher prevalence suggests misclassification with transverse terminal defects of fingers or toes. |
| **Key visuals** | Distinguishing longitudinal axial defects from transverse terminal defects of hand/foot (side-by-side comparison):<br>  <br>**Longitudinal axial** defect: Congenital cleft hand (Q71.6)<br>*Photograph source:* CDC-Beijing Medical University collaborative project<br>  <br>**Transverse terminal** defect: Congenital absence of fingers (Q71.30)<br>*Photograph source:* Dr E. Gene Deune, Johns Hopkins Department of Orthopedic Surgery, Division of Hand Surgery |

Omphalocele or exomphalos is a birth defect of the central portion of the anterior abdomen in which the herniated organs (intestines and sometimes other abdominal organs such as liver) are covered by a thin membrane (Fig. 4.42, *panels a, b*). At times, the membrane – which consists of the peritoneum and amnion – might be ruptured (*panel c*) or matted. The key finding in omphalocele is that the herniation occurs *centrally* – the organs herniate through an enlarged umbilical ring, with the umbilical cord inserting in the distal part of the membrane covering the defect (*panels a, b*). This presentation is in contrast to what is seen in gastroschisis, in which the abdominal defect is lateral to the umbilical cord and herniated organs are never covered by membrane.

**Fig. 4.42. Omphalocele (Exomphalos)**




*Photograph source:* CDC–Beijing Medical University collaborative project.

## Relevant ICD-10 codes

Q79.2 Omphalocele (exomphalos)

Note:
Avoid using the generic Q79 code for congenital malformations of the musculoskeletal system not elsewhere classified. This generic code includes other anomalies that must be distinguished from omphalocele.

## Diagnosis

***Prenatal.*** Omphalocele might be diagnosed prenatally and distinguished from gastroschisis, but it can be missed and the distinction from gastroschisis is difficult and error-prone. For this reason, a prenatal diagnosis should always be confirmed postnatally.

When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** Careful examination of the newborn can confirm the diagnosis of omphalocele and help distinguish omphalocele from gastroschisis as well as from several rarer similar phenotypes (e.g. limb-body wall defects). Typically the membrane covering an omphalocele is thin and translucent, but at times this membrane will rupture during or shortly after birth and the surface of the membrane might appear matted and covered by fibrous material as a result of prolonged exposure to amniotic fluid in utero.

## Clinical and epidemiologic notes

Distinguishing omphalocele from gastroschisis is important because these conditions have different causes, associated anomalies, approaches to treatments and outcomes.

On the mild end of the spectrum, omphalocele can be occasionally confused with umbilical hernia. To differentiate, an umbilical hernia is completely covered by skin, unlike an omphalocele which is covered by a thin translucent membrane. On the more severe end of the spectrum, omphalocele must be distinguished from rarer anomalies such as bladder exstrophy and cloacal exstrophy, as well as from the very rare limb-body wall defects and pentalogy of Cantrell. It is crucial to report all findings and obtain good clinical photographs for the expert reviewer.

Omphalocele is frequently (50% of cases or more) associated with additional birth defects (particularly cardiac, urogenital, brain, spina bifida), with certain complex anomaly patterns (pentalogy of Cantrell, OEIS), or with genetic syndromes (e.g. trisomies 13 and 18, Beckwith-Wiedemann syndrome, Donnai-Barrow syndrome). Omphalocele can occur with related anomalies that should also be identified and reported, such as intestinal malrotation and pulmonary hypoplasia.

Clinically, the size of the omphalocele correlates with the risk of associated anomalies and syndromes (the larger the omphalocele the higher the risk). Large omphaloceles require more complex surgeries, have a higher surgical risk, and are associated with higher mortality (e.g. due to respiratory insufficiency).

The birth prevalence of omphalocele is approximately 2–3 per 10 000 births (might be lower in Asian populations and higher in non-Hispanic black populations in the USA). Suggested non-genetic risk factors include folic acid insufficiency or deficiency, maternal obesity and pregestational diabetes, and possibly second-hand smoking and certain medications (e.g. methimazole).

## Inclusions

Q79.2 Omphalocele (exomphalos)

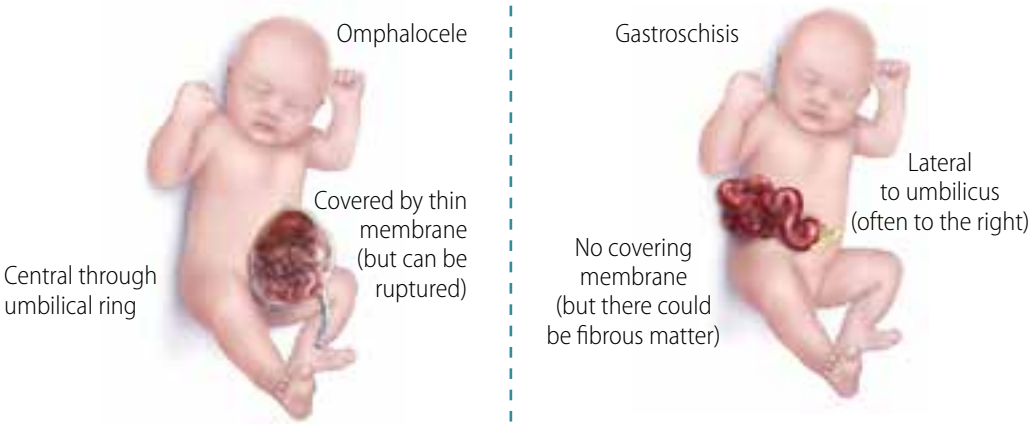
## Exclusions

Q79.3 Gastroschisis
Q79.8 Umbilical hernia
P02.69 Newborn affected by other conditions of umbilical cord

## Checklist for high-quality reporting of omphalocele

| Omphalocele – Documentation Checklist |
|---|
| ☐ **Describe in detail.** Avoid using just the term "omphalocele"; add further details:<br>▸ Cord insertion – describe if midline, over umbilicus.<br>▸ Covering membranes – yes/no, intact/ruptured.<br>▸ Size – measure/estimate (in cm).<br>▸ Extruded organs – small intestine, liver, spleen, etc.<br>▸ **Describe evaluations to rule out additional malformations/syndromes** – Especially trisomies 13 and 18, Beckwith-Wiedemann syndrome.<br>▸ **Take and report photographs** – show clearly umbilical cord/membrane; can be crucial for review. |
| ☐ **Report whether specialty consultation(s) were done** (including genetics, surgery), **and if so, report the results.** |

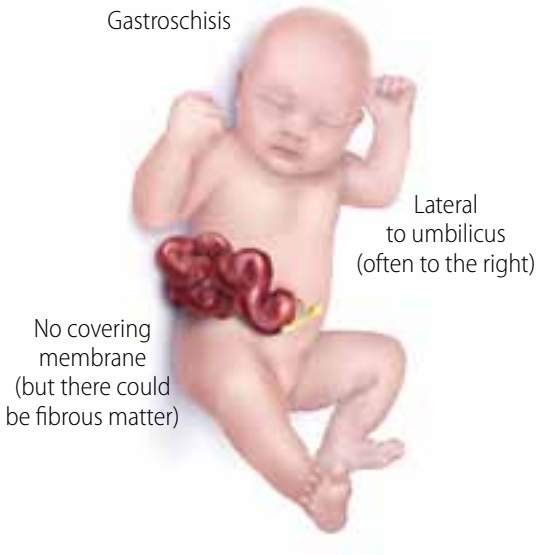
## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors:<br>▸ Description of umbilical cord, covering, size, herniated organs.<br>▸ Documentation that includes drawings, photographs and consultation notes. |
| **Coding** | ▸ Code as Q79.2.<br>▸ Track and minimize cases coded with generic ICD-10 RCPCH codes.<br>▸ Q79 is not acceptable for coding omphalocele as it includes other different conditions. |
| **Clinical classification** | ▸ Syndromes – particularly those associated with a chromosome anomaly – are common with omphalocele: Check if karyotype has been done; check if clinical genetic consultation has been done.<br>▸ Associated anomalies are frequent: Check if a full evaluation has been done. |
| **Prevalence** | ▸ Prevalence varies between 2.0 and 5.0 per 10 000 births.<br>▸ Low prevalence (< 2.0 per 10 000 births) suggests under-ascertainment; check by small areas and time.<br>▸ Higher prevalence (> 5.0 per 10 000 births) suggests misclassification with gastroschisis; check specific prevalence by maternal age and review all cases of abdominal defects. |
| **Key visuals** | Distinguishing omphalocele from gastroschisis (side-by-side comparison):<br>  <br> |

Gastroschisis is a birth defect of the anterior abdominal wall accompanied by herniation of the small intestine and part of the large intestine, and occasionally other abdominal organs. Two key findings in gastroschisis (Fig. 4.43, *panels a, b*) are *location* – the defect is lateral to the inserted umbilical cord (generally to the right) – and *covering* – there is an absence of a covering membrane, though the herniated organs might at times be covered by fibrous material due to in utero exposure to fluids. This presentation is in contrast to what is seen in omphalocele, in which the organs herniate centrally through a widened umbilical ring, and are covered by a thin, often translucent membrane (when intact).

**Fig. 4.43. Gastroschisis**

a




b

*Photograph source:* CDC–Beijing Medical University collaborative project.

## Relevant ICD-10 codes

Q79.3 Gastroschisis

Note:
Avoid using the generic Q79 code for congenital malformations of the musculoskeletal system not elsewhere classified. This generic code includes other anomalies such as omphalocele that must be distinguished from gastroschisis.

## Diagnosis

***Prenatal.*** Gastroschisis might be diagnosed or strongly suspected prenatally; however, it can be missed. Moreover, the distinction from omphalocele prenatally is difficult and error-prone. Also, in early pregnancy there is a normal physiologic hernia that might be confused with gastroschisis. For this reason, a prenatal diagnosis should always be confirmed postnatally. When this is not possible (e.g. termination of pregnancy or unexamined fetal death), the programme should have criteria in place to determine whether to accept or not accept a case based solely on prenatal data.

***Postnatal.*** Careful examination of the newborn can confirm the diagnosis of gastroschisis and distinguish it from omphalocele and some other rare anomalies that might involve the anterior abdominal wall (e.g. limb-body wall defects, pentalogy of Cantrell). Note that sometimes the organs herniated in gastroschisis might be covered by fibrous material, which is thought to result from prolonged exposure to amniotic fluid in utero.

## Clinical and epidemiologic notes

Distinguishing gastroschisis from omphalocele is important because these conditions have different risk factors, associated anomalies, approaches to treatments and outcomes.

With careful examination, the diagnosis of gastroschisis is usually straightforward. Rare conditions that might engender diagnostic confusion include limb-body wall defects and pentalogy of Cantrell. In these cases, several other anomalies are present. In limb-body wall defects, one can find atypical exencephaly/encephalocele, atypical facial clefts, and at times amniotic bands. Note that liver is usually extruded in limb-body wall defects, but rarely in gastroschisis. For this reason, it is crucial to report all findings and obtain good clinical photographs for the expert reviewer.

Gastroschisis is frequently (80% or more of cases) an isolated, non-syndromic anomaly. Syndromes are very rare. However, gastroschisis often co-occurs with related anomalies, most often of the gut. These include intestinal malrotation, small intestinal atresia, microcolon, and several others. Pulmonary hypoplasia might also occur. These related anomalies can affect survival and long-term function.

The birth prevalence of gastroschisis varies widely, as much as between 0.5 to 10 per 10 000 births. Prevalence is several-fold higher in young mothers (especially < 19 years of age, but also < 25 years, compared to women 25–29 years). The prevalence has been increasing in several countries for unclear reasons. In addition to young maternal age, other suggested non-genetic risk factors include low body mass index, genitourinary tract infections, smoking, illicit drug use, possibly some medications (e.g. aspirin, antidepressants), and some other factors (e.g. change in paternity). The protective role of folic acid has been suggested but not proven.

## Inclusions

Q79.3 Gastroschisis

## Exclusions

Q79.2 Omphalocele (exomphalos)
Q89.81 Limb-body wall complex

## Related codes

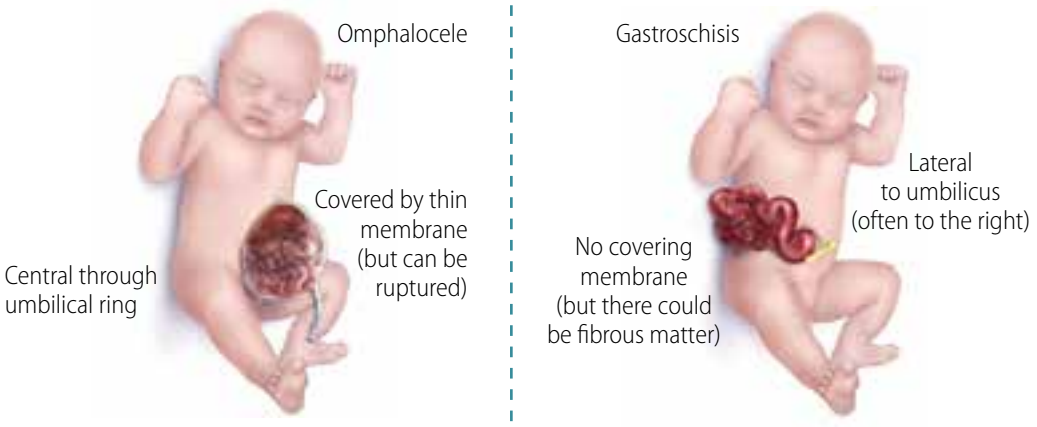
Q41 and sub-codes Intestinal atresia (e.g. Q41.2, atresia of the ileum)

## Checklist for high-quality reporting

**Gastroschisis – Documentation Checklist**

- ☐ **Describe in detail.** Avoid using only the term "gastroschisis" and specify the following details:
  - Side relative to the umbilical cord – right/left. If left, is there situs inversus? Describe the cord attachment – for example, it is attached on the left side and no attachment on the right side.
  - Covering membranes – yes/no.
  - Size – extension of the abdominal defect (in cm).
  - Extruded organs – also specify bowel segment involved.
- ☐ **Take and report photographs:** *Show clearly* the umbilical cord; can be crucial for review.
- ☐ **Describe evaluations to find or rule out related and associated anomalies:** If present, describe these anomalies.
- ☐ **Report whether specialty consultation(s) were done** (particularly surgery), **and if so, report the results.**

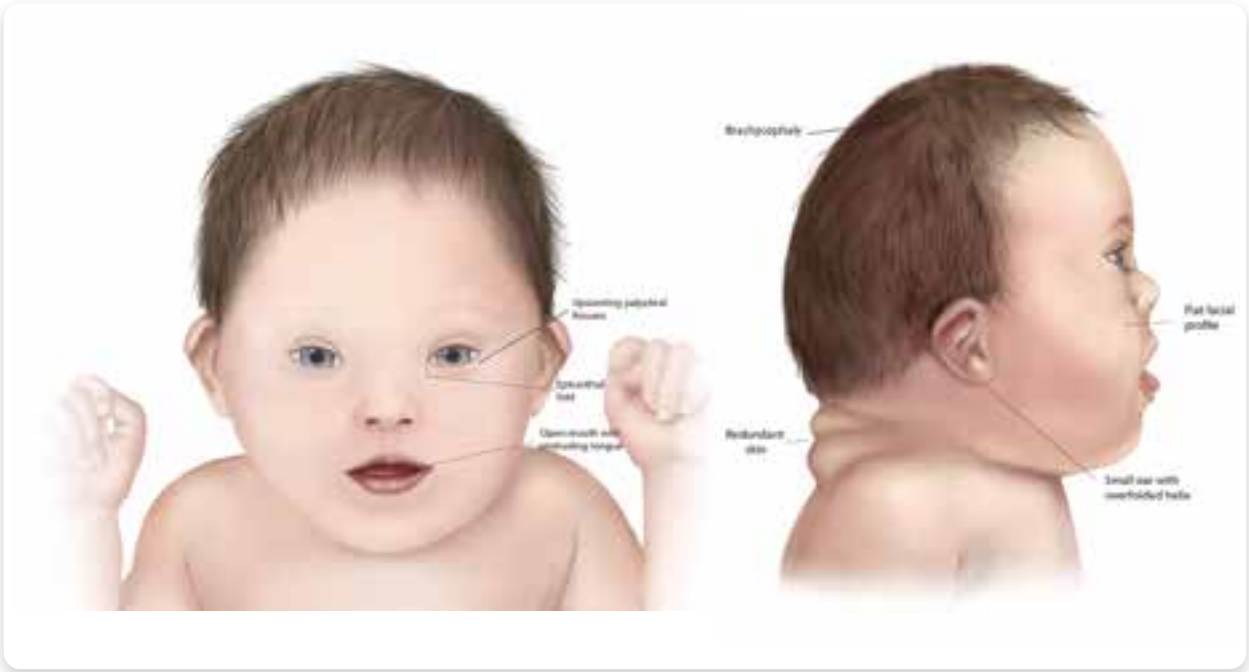
## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors:<br>▸ Position versus umbilical cord, covering, size, herniated organs.<br>▸ Documentation that includes drawings, photographs and consultation notes. |
| **Coding** | ▸ Code as Q79.3.<br>▸ Track and minimize cases coded with generic ICD-10 RCPCH codes.<br>▸ Q79 is not acceptable for gastroschisis as it includes other different conditions. |
| **Clinical classification** | ▸ Syndromes are very rare with gastroschisis: Syndromic "gastroschisis" could be a misclassified case of omphalocele, so recommend reviewing those records.<br>▸ Associated anomalies are < 15–20% of cases: A higher proportion suggests that some related conditions (intestinal atresia) are counted as associated, or that misclassification with omphalocele or limb-body wall defect has occurred. |
| **Prevalence** | ▸ Prevalence varies by maternal age and might vary by geography.<br>▸ Prevalence in mothers < 20 years old and 20–24 years old should be higher than prevalence in mothers > 24 years old. |
| **Key visuals** | Distinguishing omphalocele from gastroschisis (side-by-side comparison):<br>  <br> |

Trisomy 21, also known as Down syndrome, is a condition characterized by a distinctive pattern of minor and major anomalies associated with excess chromosome 21 material (see Fig. 4.44). About 95% of cases result from chromosomal non-disjunction, leading to each cell in the infant having three full copies of chromosome 21 (47,XX,+21 or 47,XY,+21) at conception. Rarer forms occur because of translocation, mosaicism or other chromosomal rearrangements/duplications. Translocation trisomy 21, accounting for about 2% of cases, is often familial, and commonly involves chromosomes 14 and 21. Mosaicism (concurrent presence of trisomy and normal cells) accounts for about 2% of cases. It results from post-zygotic non-disjunction or more rarely from trisomic rescue; that is, the loss in some cells of a chromosome 21 in a trisomic zygote. In the remaining 1% of cases, the extra chromosome 21 material originates from other rearrangements. The portion of chromosome 21 critical for the phenotype seems to be the 21q22 region.

Such classification is important for recurrence risk counselling, which varies by type of trisomy.

**Fig. 4.44. Down syndrome**



## Relevant ICD-10 codes

Q90.0 Trisomy 21, nonmosaicism (meiotic nondisjunction)
Q90.1 Trisomy 21, mosaicism (mitotic nondisjunction)
Q90.2 Trisomy 21, translocation
Q90.9 Down syndrome, unspecified

## Diagnosis

***Prenatal.*** Trisomy 21 (Down syndrome) can be diagnosed through direct analysis of fetal chromosomes obtained from amniocentesis, CVS or percutaneous umbilical blood sampling. Because the placenta might contain mosaic cell lines not present in the fetus, mosaic trisomy 21 diagnosed through CVS should always be confirmed by a postnatal specimen from the infant. Analysis of fetal DNA in maternal blood can detect extra chromosome 21 material with high sensitivity and specificity, though it is still considered a screening test rather than a diagnostic test.

***Postnatal.*** In most cases, Down syndrome can be strongly suspected or diagnosed clinically during the neonatal period by recognizing the typical physical traits. Clinical diagnosis should be confirmed by genetic testing (typically, karyotype from infant's blood or tissue). The physical traits with greatest discriminant diagnostic value (in descending order) include the following *(32)*:

- up-slanting palpebral fissures evaluated when the infant is crying
- flat nasal bridge
- decreased muscle tone (hypotonia)
- wider space between first and second toes ("sandal gap")
- nystagmus
- brachycephaly
- incurving of the fifth finger (clinodactyly)
- narrow palate
- overfolded helix of the ear (especially with a small ear)
- short-appearing neck with redundant skin on the back of the neck
- broad and short hands and feet
- single transverse crease in the palm of the hand.

## Clinical and epidemiologic notes

Major malformations associated with Down syndrome include some heart defects (in about 50%, most notably endocardial cushion defects), gastrointestinal atresias (duodenal or esophageal atresia), and vertebral abnormalities, among others.

Over time, infants with Down syndrome can present many other health and developmental issues, which need to be diagnosed, treated or prevented. These include hypothyroidism, diabetes, vision and hearing issues (e.g. cataracts) and intellectual disability of varying degree. Published clinical guidelines provide guidance for preventive and anticipatory health management.

Birth prevalence is approximately 1 in 1000 but varies depending on the maternal age profile of the population (the higher the age, the higher the frequency).

## Inclusions

Q90.0 Trisomy 21, nonmosaicism (meiotic nondisjunction)
Q90.1 Trisomy 21, mosaicism (mitotic nondisjunction)
Q90.2 Trisomy 21, translocation
Q90.9 Down syndrome, unspecified (clinical diagnosis only)

## Exclusions

Q92.9 Trisomy and partial trisomy of autosomes, unspecified
Q95.0 Balanced Robertsonian translocations involving chromosome 21

## Checklist for high-quality reporting

**Trisomy 21 (Down syndrome) – Documentation Checklist**

- ☐ **Describe in detail:**
  - Clinical signs that allowed the diagnosis.
  - Karyotype available – report results.
  - Karyotype not available – check clinical signs on which diagnosis was based.
  - In all cases, report:
    - Associated malformations.
- ☐ **Take and report photographs:** Show clearly the side and front view of the face; can be crucial for review.
- ☐ **Describe evaluations to find or rule out related and associated anomalies:**
  - **General** – hypotonia.
  - **Head and neck** – brachycephaly, large anterior fontanelle, short neck, excess nuchal skin, protruding tongue, narrow palate, flat nasal bridge, upslanting palpebral fissures, epicanthal folds, nystagmus, Brushfield spots on iris, small ears (< 3 cm), overfolded helix (ear).
  - **Chest** – absent breast buds.
  - **Extremities** – short broad hands, fifth finger clinodactyly, fifth finger single flexion crease, single palmar crease, wide gap between first and second toes.
- ☐ **Document specialty consultations (e.g. genetics, cardiology).**
- ☐ **Report whether autopsy (pathology) findings are available and if so, report the results.**

## Suggested data quality indicators

| Category | Suggested Practices and Quality Indicators |
|---|---|
| **Description and documentation** | ▸ Review sample for documentation of karyotype or chromosomal microarray and key descriptor.<br>▸ Take and attach photographs: Essential for review and correct classification.<br>▸ Report and track proportion of cases among live births, stillbirths and pregnancy terminations. |
| **Coding** | ▸ Code as Q90.X based on karyotype results or clinical diagnosis.<br>▸ Track and minimize cases coded as Q90.9 (unspecified, clinical diagnosis only). |
| **Clinical classification** | ▸ Track proportion of congenital anomalies occurring with Down syndrome.<br>▸ If the fetus was stillborn, or a pregnancy termination performed, check for a pathology report and physical description at delivery. |
| **Prevalence** | ▸ Monitor prevalence: Prevalence varies by country/region, country income level and race/ethnicity. |

## 5. Congenital infectious syndromes

This section presents common congenital infectious conditions during pregnancy that contribute to the burden of birth defects, stillbirths and neonatal deaths, namely, congenital rubella syndrome (CRS), congenital syphilis, congenital cytomegalovirus (cCMV) infection and congenital Zika syndrome (CZS). Vaccination, prompt detection and treatment, and other preventive strategies can reduce the number of adverse pregnancy outcomes (birth defects, miscarriages, stillbirths and neonatal deaths) resulting from congenital infections. Surveillance can assess the national and international burden of maternal infection and adverse outcomes, and formulate strategies to reduce transmission from the mother to the fetus.

This chapter includes information on each congenital infection, including background of the infectious agent, clinical manifestations in the mother and the infant, case definitions, laboratory and radiology needed for diagnosis, photographs, and the relevant ICD-10 codes that could be used for surveillance. The diagnostic methods for congenital infections, including laboratory and imaging, are subject to change and might vary by country. This manual provides general information about these methods, but is not intended to be a comprehensive resource for evaluation of at risk or affected individuals. Each section also includes a checklist of items that need to be done as part of the management of a suspected case with a congenital infectious syndrome.

When infection during pregnancy is clinically suspected, laboratory tests to detect congenital infection might include those for cytomegalovirus, herpes simplex virus, rubella, HIV, toxoplasmosis, syphilis, and Zika virus. Prospective mother-infant linked surveillance coupled with birth defects surveillance can provide a more complete picture of these infections and the outcomes associated with them *(33)*.

## Background

Rubella virus (RV) is a togavirus of the genus *Rubivirus*, transmitted through droplets shed from the respiratory secretions of infected persons. Teratogenic effects of infection during pregnancy can cause harm to the embryo and developing fetus. CRS is heavily underreported, as many countries lack the capacity to conduct surveillance for this condition. It is estimated that there are approximately 105 000 CRS cases worldwide each year. Countries with sustained high rates of immunization have greatly reduced or eliminated rubella and CRS.

## Main clinical manifestations in the mother

The incubation period of RV infection is 14 days (range, 12–23 days). Clinical symptoms include mild illness with low-grade fever (< 39 °C), headache, conjunctivitis and rhinitis. A characteristic feature is post-auricular, occipital and posterior cervical adenopathy (swelling of the lymph nodes), which precedes a red, maculopapular rash by 5–10 days. The rash occurs in 50–80% of rubella-infected persons, begins on the face and neck, and progresses to the lower parts of the body, lasting about three days. In 70% of women, joint pain (arthralgia) also occurs.

## Main clinical manifestations in the infant

If primary rubella infection occurs during pregnancy, the virus can infect the placenta and fetus, causing a constellation of specific malformations labelled CRS. The classic triad of clinical manifestations associated with CRS among surviving neonates are hearing impairment, congenital heart defects – in particular, branch pulmonary artery stenosis and patent ductus arteriosus – and eye anomalies such as cataract(s), pigmentary retinopathy (salt and pepper type), chorioretinitis or congenital glaucoma. Additional clinical signs include skin purpura (blueberry muffin skin lesions), splenomegaly (enlargement of the spleen), microcephaly (small head circumference), developmental delay, meningoencephalitis, low birth weight, radiolucent bone disease and jaundice within 24 hours after birth (Fig. 5.1). The periconception period and early pregnancy (8–10 weeks) are the most vulnerable time frames and pose the greatest risk of CRS, which is as high as 90%. CRS can result in fetal death. For infants with CRS, hearing impairment, eye symptoms and developmental delay might not be detected until later.

If maternal rubella infection is diagnosed beyond 18 weeks of gestation, the fetus might be infected but does not typically develop signs and symptoms of CRS. Infants with laboratory evidence of rubella and without any signs or symptoms of CRS are classified as having congenital rubella infection (CRI) only.

## Diagnosis

### *Laboratory:*

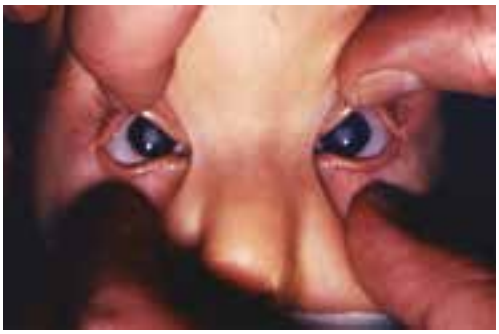
- Rubella immunoglobulin M (IgM) antibody detected (infants < 6 months old) in serum; or
- Sustained rubella immunoglobulin G (IgG) antibody level detected in serum; present on at least two occasions between 6 and 12 months of age (in the absence of having received rubella vaccine or being exposed to rubella); or
- Rubella virus detection (nucleic acid amplification tests [NAATs]* or rubella virus isolation) from a clinical sample. The optimal sample is a throat swab; however, nasal swabs, blood, urine or cerebrospinal fluid are also acceptable.

* Nucleic acid amplification tests (NAATs) include, but are not limited to, reverse transcriptase polymerase chain reaction (RT-PCR), real-time RT-PCR, quantitative RT-PCR, and next-generation sequencing.

### *Infants:*

In CRS and CRI cases, IgM might be negative at birth and a suspected infant should be tested again at 1 month of age. Although IgM might persist up to 12 months of age, in 50% of the cases, IgM is negative at 6 months of age, and should be complemented with IgG testing. The IgG testing should include serial testing to ensure sustained levels of IgG after 10 months (when maternal antibodies have waned) and before vaccination. Testing should also include virus detection (through NAATs or virus isolation) over several months for virus shedding until testing negative at two occasions at least one month apart. Infants with CRS or CRI have been demonstrated to shed virus up to 27 months after birth and might be the source of rubella outbreaks.

## Fig. 5.1. Clinical findings in the infant



Infant with typical cloudiness of the eye lenses; that is, ***cataracts***, in a case of CRS.

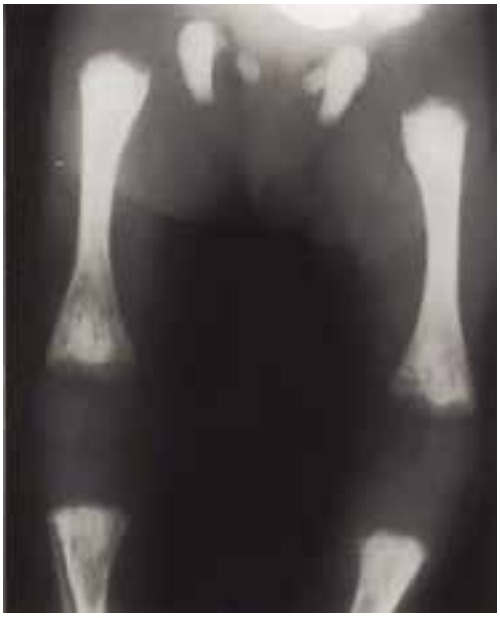
*Photograph source*: CDC public health image library/Dr Andre J. Lebrum

***Congenital glaucoma (and cataract)*** in a 7-month-old infant with CRS. The left eye displays a congenital cataract; the right eye is normal. The infant was operated on on day 3 of life to correct the congenital cataract.

*Photograph source*: CDC public health image library/Dr Andre J. Lebrum.

Infant with congenital rubella and ***"blueberry muffin" skin lesions***. Lesions are sites of extramedullary hematopoiesis and can be associated with several different congenital viral infections and hematologic diseases.

*Photograph source*: CDC public health image library/Dr Andre J. Lebrum.



***Radiolucent bone disease.*** X-ray of the lower limbs in a newborn with CRS. The ends of the long bones are ragged and streaky (like celery stalks) – changes due to active rubella infection.

*Photograph source*: Government of Canada web page (Public health/ Rubella).

***Pregnant women:***

Pregnant women exposed to rubella should undergo IgM testing of serum. If IgM for rubella is detected in a pregnant woman with no history of illness or contact with a rubella illness case, further laboratory investigation to rule out a false-positive test result is warranted.

In some countries, pregnant women are routinely screened for rubella IgG antibody. If IgG antibody is negative, vaccination is recommended after delivery because the vaccine contains live virus. Rubella vaccination during pregnancy should be avoided.

## Case definition

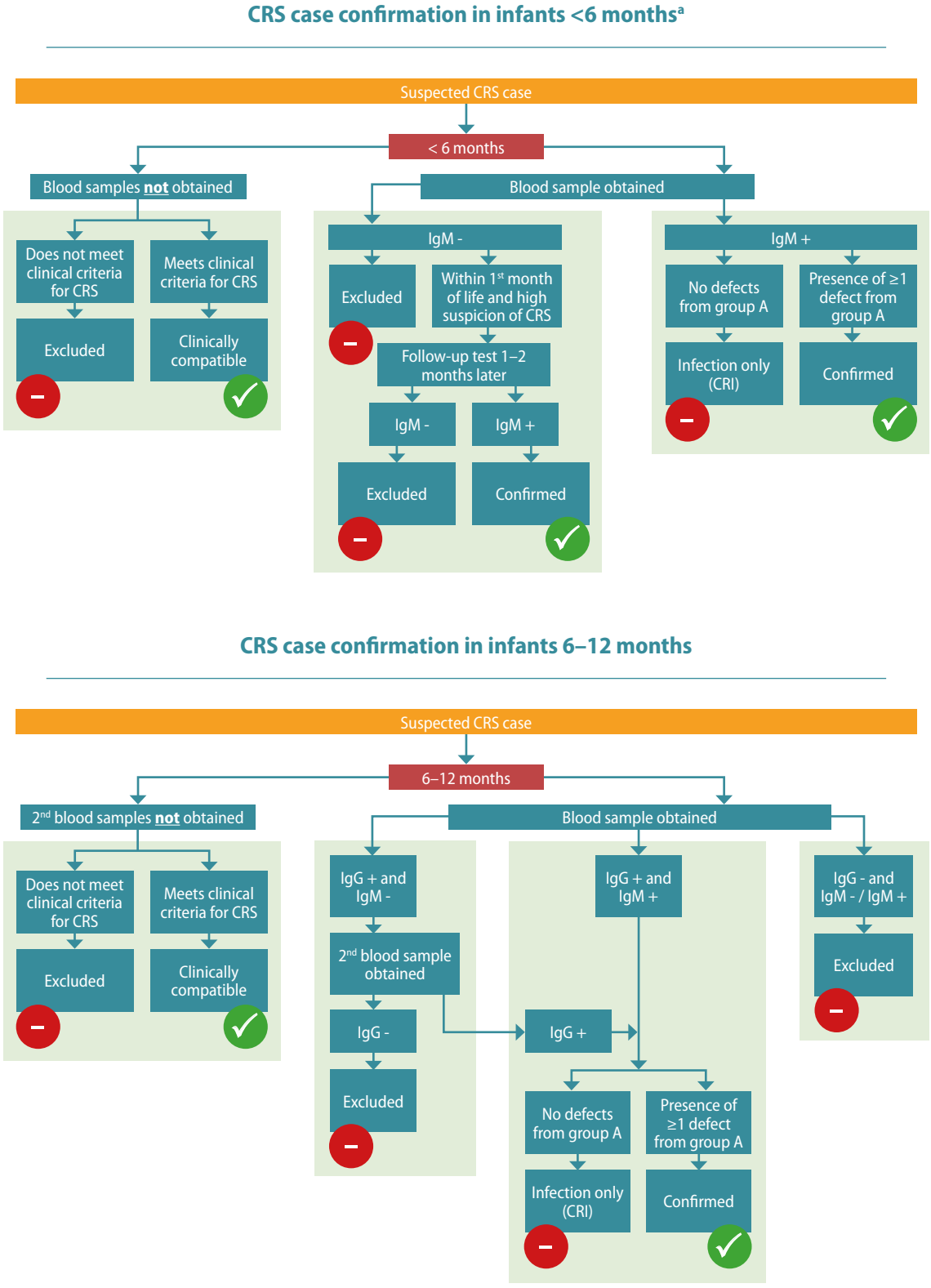
Clinical diagnosis alone is unreliable and should be verified with laboratory testing. Routine surveillance of CRS is focused on infants < 12 months of age (Table 5.1). The algorithm for CRS case confirmation in infants < 6 months and 6–12 months is presented in Fig. 5.2.

### Table 5.1. CRS case definition

| | |
|---|---|
| **Suspected CRS case** | Any infant < 12 months with suspicion of CRS. The following clinical manifestation should lead to suspicion of CRS:<br><br>(1) congenital heart disease; and/or (2) suspicion of hearing impairment; and/or (3) one or more of the following eye signs: (a) cataract;[a] or (b) congenital glaucoma;[b] or (c) pigmentary retinopathy (salt and pepper).<br><br>In addition, if the infant's mother has a history of suspected or confirmed rubella during pregnancy, a clinician should suspect CRS, even if the infant shows no signs of CRS. |
| **Clinically confirmed CRS case** | An infant of < 12 months in whom a qualified clinician detects:<br><br>At least two of the complications listed in group A or one in group A and one in group B:<br><br>**Group A:** Cataract(s), congenital glaucoma, congenital heart disease, hearing impairment, pigmentary retinopathy.<br><br>**Group B:** Purpura,[c] splenomegaly,[d] microcephaly, meningoencephalitis, radiolucent bone disease, jaundice that begins within 24 hours after birth. |
| **Laboratory-confirmed CRS case** | An infant who is a suspected case with one condition from group A (as above) and meets the laboratory criteria for CRS laboratory confirmation. |
| **CRI** | An infant who does not have group A clinical signs of CRS but who meets the laboratory criteria for CRS is classified as having congenital rubella CRI. |

[a] cataract, opaque or white lens; [b] congenital glaucoma, enlarged eyeball; [c] purpura, blueberry muffin skin lesions; [d] splenomegaly, enlarged spleen

## Fig. 5.2. CRS case confirmation




[a] Testing should also include virus detection (through NAAT or virus isolation) over several months for virus shedding until testing negative at two occasions at least one month apart.

## Relevant ICD-10 codes

P35.0 Congenital rubella syndrome (CRS)
Q02 Microcephaly
Q12.0 Congenital cataract
Q15.0 Congenital glaucoma
Q25.0 Patent ductus arteriosus
Q25.6 Stenosis of pulmonary artery

## Checklist

| Checklist |
|---|
| ☐ **Examine the neonate for:**<br>▸ Eye: Glaucoma, cataracts, chorioretinitis or pigmentary retinopathy (salt and pepper) and the sclera for jaundice<br>▸ Skin: Jaundice that begins within 24 hours after birth and purpura<br>▸ Abdomen: Splenomegaly<br>▸ Cardiac: Murmur<br>▸ Neurological system: Developmental delay, meningoencephalitis. |
| ☐ **Additional clinical examinations:**<br>▸ Skeletal radiograph: Radiolucent bone disease<br>▸ Hearing screening test: Hearing impairment (failed hearing screening must be followed with diagnostic testing to verify hearing loss)<br>▸ Echocardiography: CHD. |
| ☐ **Inquire about maternal medical health and pregnancy history to ascertain rubella infection and vaccination status. Lack of a history of known infection should not preclude suspicion of CRS.** |
| ☐ **Collect neonatal samples for laboratory testing (IgM and IgG).** |
| ☐ **Determine whether the case is suspected, clinically confirmed, laboratory-confirmed, CRI, or excluded.** |
| ☐ **Obtain photographs of any malformations noted.** |
| ☐ **Record diagnostic information and report.** |

## Background

Syphilis is caused by the bacterium *Treponema pallidum*. The infection is most commonly transmitted through sexual contact (vaginal, oral, or anal sex). Birth defects can occur in infants born to women who are infected with syphilis prior to or during pregnancy.

## Main clinical manifestations in the mother

In primary syphilis, a sore or multiple sores appear at the site where the bacterium entered the body – typically near the genitals, the rectum or the oral cavity. The sores are usually firm, round and painless. In secondary syphilis, fever, swollen lymph nodes and skin rash, and wart-like genital lesions (condyloma lata) can be seen. In the latent stage, there are no signs or symptoms. In tertiary syphilis, several medical problems affecting the heart, neurologic system and other organs can be seen. Individuals with the infection move from one stage to the next in the absence of treatment.

## Main clinical manifestations in the infant

Some infants with early congenital syphilis are asymptomatic at birth. Clinical manifestations of early congenital syphilis might include rhinitis ("snuffles"), hepatosplenomegaly, pustules on palms and soles, skin rash with desquamation, chorioretinitis and pigmentary chorioretinopathy (salt and pepper type), glaucoma, cataracts, interstitial keratitis, optic neuritis, periostitis and cortical demineralization of metaphysis and diaphysis areas of long bones, anaemia and thrombocytopenia (see Fig. 5.3). Some clinical signs consistent with congenital syphilis – such as hydrops and hepatosplenomegaly – might be detected by ultrasound during pregnancy. Infants who remain undiagnosed and untreated can progress to late congenital syphilis, resulting in numerous additional clinical manifestations, including, but not limited to: saddle nose due to destruction of cartilage, frontal bossing due to periostitis, tibial thickening (saber shins), joint swelling (clutton joints), perforation of hard palate, abnormal tooth development (Hutchinson's teeth, mulberry molars), interstitial keratitis, neurologic deafness and optic nerve atrophy.

## Diagnosis

### *Laboratory and radiography:*

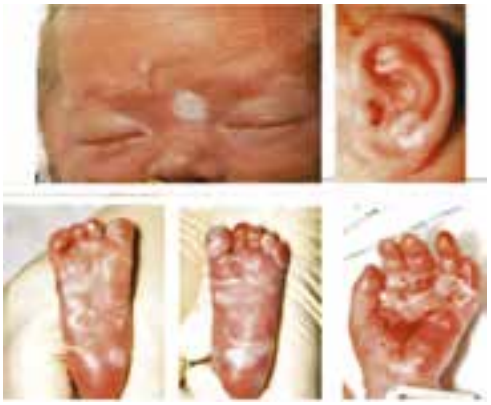
WHO recommends universal screening of pregnant women for syphilis. Diagnosis of congenital syphilis primarily relies on the diagnosis and treatment of the pregnant mother. Serum-based tests available for **maternal diagnosis** of syphilis include:

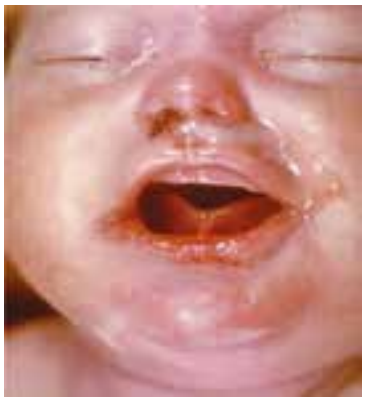
1. rapid or laboratory-based treponemal tests (e.g. *Treponema pallidum* particle agglutination assay [TPPA]; *Treponema pallidum* hemagglutination assay [TPHA]; enzyme immunoassay [EIA]; chemiluminescence immunoassay [CLIA]); and
2. non-treponemal tests (e.g. rapid plasma reagin [RPR] and venereal disease research laboratory [VDRL] tests).

Any of the following laboratory or radiography findings in the infant are consistent with a clinical **diagnosis of congenital syphilis**:

1. demonstration of *Treponema pallidum* by darkfield microscopy; fluorescent antibody detection; immunohistochemical staining; or NAATs in the umbilical cord, placenta, nasal discharge or skin lesion material or autopsy material of a neonate or stillborn infant;
2. cerebrospinal fluid (CSF) reactivity for VDRL test, and elevated CSF cell count or protein (without other possible cause);
3. reactive non-treponemal serology titre (RPR or VDRL) in an infant that is fourfold or more than that of the mother at birth;
4. reactive non-treponemal serology titre in an infant that is less than fourfold more than that of the mother but that remains reactive at least six months after delivery;
5. long bone radiographs suggestive of congenital syphilis (e.g. osteochondritis, diaphyseal osteomyelitis, periostitis).

**Fig. 5.3. Clinical findings in the infant**

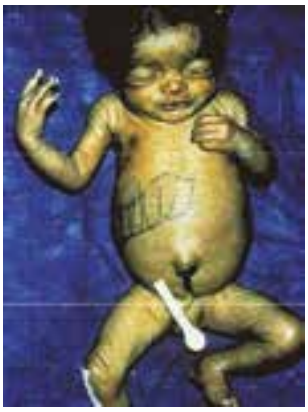




Typical desquamating and maculopapular skin lesions; punched out, pale, blistered lesions mainly on ears and nasal bridge, and desquamation of feet and palm.

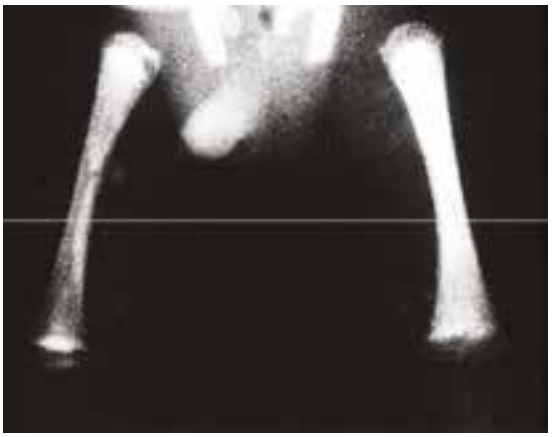
Rhinitis with mucopurulent nasal discharge.

*Photograph source*: Dr Ronald Ballard.



Hepatosplenomegaly and jaundice in an infant with congenital syphilis. Black markings on infant indicate liver margins.

*Photograph source*: Dr Ronald Ballard.



X-ray of bone abnormalities, syphilitic metaphysitis in an infant with diminished density in the ends of the shaft and destruction at the proximal end of the tibia (right).

*Photograph source*: Dr Ronald Ballard.

## Case definition

Some children with congenital syphilis are born without clinical manifestation and many are not diagnosed at the time of birth. These can progress to late manifestations if left undiagnosed and untreated. To improve the diagnosis and treatment of infants who are undiagnosed at birth – leading to the prevention of long-term sequelae – WHO endorses a surveillance definition of congenital syphilis composed of two parts. Infants can be classified as cases of congenital syphilis based upon the diagnosis and treatment status of their mothers, as well as based upon their own laboratory and clinical findings.

The global surveillance case definition† for congenital syphilis is given below:

| | |
|---|---|
| 1. | A live birth or fetal death (stillbirth) at > 20 weeks of gestation or > 500 g (including stillbirth) born to a woman with positive treponemal (TPPA, TPHA, EIA, IgM or rapid treponemal test) or non-treponemal (RPR, VDRL) syphilis serology and without adequate syphilis treatment. |
| 2. | A live birth, stillbirth or child aged < 2 years born to a woman with positive syphilis serology or with unknown serostatus, and with laboratory and/or radiographic and/or clinical evidence of syphilis infection (regardless of the timing or adequacy of maternal treatment). (See laboratory diagnosis above.) |

† Surveillance case definitions might vary by country and available resources.

## Relevant ICD-10 codes

A50.9 Congenital syphilis, unspecified
Q12.0 Congenital cataract
Q15.0 Congenital glaucoma

## Checklist

**Checklist**

- ☐ **Examine the neonate for:**
  - Face: Rhinitis (snuffles) with mucopurulent nasal discharge.
  - Skin: Jaundice, rash and desquamation, pustules on palms and soles.
  - Abdomen: Hepatosplenomegaly (enlarged liver and spleen).
  - Eye: Chorioretinitis and pigmentary chorioretinopathy (salt and pepper type), glaucoma, cataracts, interstitial keratitis, optic neuritis.
- ☐ **Additional clinical examinations:**
  - Radiographs: Osteochondritis, diaphyseal osteomyelitis, periostitis.
  - Hearing test: Hearing impairment (failed hearing screening must be followed with diagnostic testing to verify hearing loss).
- ☐ **Obtain maternal medical health and pregnancy history for syphilis diagnosis.**
- ☐ **Collect maternal and neonatal blood samples for laboratory testing (maternal titres RPR or VDRL, neonatal blood count and thrombocytopenia).**
- ☐ **As indicated, test CSF for reactivity for VDRL test, or elevated CSF cell count or protein.**
- ☐ **Use darkfield microscopy or fluorescent antibody detection to detect *Treponema pallidum* in relevant tissue samples.**
- ☐ **Obtain photographs of the congenital anomalies observed.**
- ☐ **Record and report.**

## Background

Cytomegalovirus (CMV) is a very common virus of the *Herpesviridae* family. Most people are infected at some point during their lifetime. CMV is transmitted through close person-to-person contact with infected secretions, including urine, saliva, blood transfusions, semen, cervical secretion and breast milk. Women caring for children (such as mothers and teachers) are at high risk as infected children can shed the virus in their urine and saliva for months and even years after infection. Congenital cytomegalovirus infection (cCMV) occurs when the virus crosses the placenta during pregnancy and infects the fetus. The highest risk of fetal infection is among mothers experiencing a primary infection during the first and second trimesters of pregnancy. Fetal transmission can also occur if a pre-existing infection is reactivated during pregnancy (i.e. non-primary infection) or if the mother is infected with a new strain of CMV; however, the risk of transmission is much lower. Higher rates of cCMV also occur in the offspring of women who are immunocompromised; for example, due to HIV infection. The prevalence of cCMV infection ranges from 0.2–0.7% of live births in high-income regions to 1–6% in low- and middle-income regions.

## Main clinical manifestations in the mother

CMV infection is very common and in most healthy people presents with mild flu-like symptoms or is asymptomatic (subclinical infection).

## Main clinical manifestations in the infant

Most infants with cCMV will not have signs or symptoms of cCMV disease at birth and will remain well. Infants born with symptoms – which might include growth restriction, ascites/hydrops, hepatosplenomegaly, jaundice, petechiae, hepatitis (raised transaminases or bilirubin), thrombocytopenia, anaemia, microcephaly, seizures, chorioretinitis and sensorineural hearing loss – are at the highest risk of poor neurodevelopmental outcomes. Rarely, infants with cCMV have severe microcephaly that is characterized by marked reduction in cranial vault height with overlapping sutures and redundant scalp with rugae or folds. This presentation is indistinguishable from congenital Zika syndrome by physical examination alone (see Fig. 5.4).

Long-term sequelae: While the majority of infants born with cCMV will not have any long-term sequelae, 10–20% will go on to have neurodevelopmental disabilities, including sensorineural hearing loss, epilepsy, cerebral palsy, visual impairment and learning difficulties. CMV is the most common infectious cause of sensorineural hearing loss and neurodevelopmental abnormalities in high-income settings, and is likely more common, but under-identified, in low-resource settings. cCMV is a known cause of stillbirth and neonatal death.

## Diagnosis

### *Laboratory: Maternal and fetal testing*

Routine CMV screening of pregnant women is not currently recommended. However, pre-pregnancy or early-pregnancy screening with CMV IgG might be used for women at high risk of infection. These results can also distinguish primary infection from reactivation/reinfection. Primary CMV infection is diagnosed based on the new appearance of CMV-specific IgG in a previously seronegative woman, or detection of CMV IgM antibody with low IgG avidity.

A diagnosis of fetal CMV infection can be made after 20–21 weeks of gestation, and at least six weeks from the time of maternal infection, by testing amniotic fluid for CMV using nucleic acid amplification tests (NAATs, which include, but are not limited to, reverse transcriptase polymerase chain reaction [RT-PCR], real-time RT-PCR, quantitative RT-PCR and next-generation sequencing).

### *Laboratory: Infant testing*

Where cCMV infection is suspected, or to differentiate from other congenital infections such as CZS, the diagnosis of cCMV in an infant must include NAATs of saliva, urine or both within the first three weeks of life.

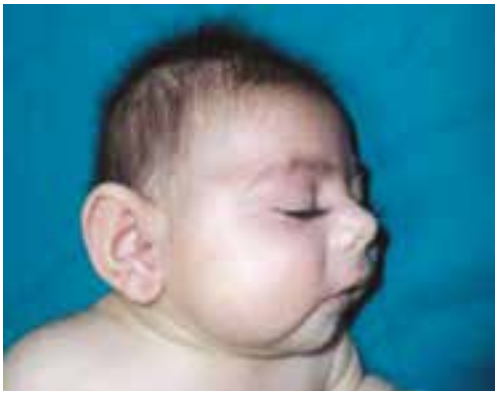
**Fig. 5.4. Clinical findings in the infant**

Petechial rash (blueberry muffin rash) and jaundice in infant with cCMV.

*Photograph source*: Jacob Johan.

Infant born with cCMV. Note severe microcephaly and lower limb spasticity similar to features of severe congenital Zika infection.

*Photograph source*: CDC Public Health Image Library.



Microcephaly in an infant with cCMV.

*Photograph source*: Işikay S, Yilmaz K. Congenital cytomegalovirus infection and finger anomaly. Case Reports. 2013;2013:bcr2013009486.

### *Imaging*

Cerebral imaging, where available, can reveal brain malformations, intracranial calcifications, neuronal migration abnormalities, cerebral atrophy, cerebellar abnormalities, ventricular dilatation, cysts and white matter abnormalities and microcephaly that are also common to other congenital infections, including CZS. The location of intracranial calcifications can help differentiate cCMV from other congenital infections. Although calcifications due to cCMV can be seen in the basal ganglia and brain parenchyma, concentrated calcifications in the periventricular regions are typical.

### *Case definition*

Where cCMV infection is suspected, or to differentiate from other congenital infections such as CZS, the diagnosis of cCMV in an infant must include NAATs of saliva, urine or both within the first three weeks of life. For the purposes of surveillance of cCMV infection as a cause of birth defects, the surveillance system should record the birth defects presenting in the child, which might include microcephaly, other brain malformations and functional deficits, including sensorineural hearing loss. Congenital contractures and a distinctive pigmentary retinopathy associated with CZS are features that clinically differentiate it from cCMV.

## Relevant ICD-10 codes

P35.1 Congenital cytomegalovirus infection (CMV)

## Checklist

**Checklist**

- ☐ **Examine the neonate for:**
  - Eye: Glaucoma, cataracts, pigmentary retinopathy, chorioretinitis, chorioretinal scars, optic nerve atrophy (and the sclera for jaundice). Later nystagmus, strabismus and cortical visual impairment.
  - Skin: Jaundice that begins 24 hours after birth and purpura.
  - Abdomen: Hepatosplenomegaly.
  - Neurological system: Microcephaly, seizures, hyper/hypotonia, poor suck.
- ☐ **Additional clinical examinations:**
  - Blood tests: Complete blood count, liver enzymes, bilirubin.
  - Imaging: Cranial ultrasound, followed by MRI and CT scan (might show ventricular calcifications).
  - Hearing screening test: Hearing impairment (failed hearing screening must be followed with diagnostic testing to verify hearing loss).
- ☐ **Obtain maternal medical health and pregnancy history to ascertain CMV exposure, such as HIV status (or other immune-compromising condition); caring for young children.**
- ☐ **Collect neonatal samples (urine, blood and/or saliva) for laboratory testing within three weeks of life.**
- ☐ **Obtain photographs of the malformations observed.**
- ☐ **Record diagnostic information and report.**

## Background

Zika virus (ZIKV) is a flavivirus (family Flaviviridae), an RNA virus primarily transmitted by *Aedes* mosquitoes. These mosquitoes generally bite during the day, with peak times in the morning and early evening. These mosquitoes also transmit dengue, chikungunya and yellow fever viruses. Transplacental (vertical) and sexual transmission of the virus have been documented, as well as transmission by blood transfusion. Although Zika virus has been detected in human milk, transmission through breastfeeding has not been definitively demonstrated.

## Main clinical manifestations in the mother

The risk of a pregnant woman acquiring a primary infection is the same as that of other adults. Symptoms of ZIKV infection are generally mild, non-specific and self-limited, lasting two to seven days. Symptoms vary and might include maculopapular rash, low-grade fever, conjunctivitis, muscle and joint pain, arthritis, malaise and headache. However, a large percentage of infections are asymptomatic.

The most concerning feature of ZIKV infection is maternal infection during pregnancy, which poses a risk of congenital ZIKV infection and resultant birth defects in the fetus. ZIKV infection should be suspected based upon symptoms and exposure (residence in or travel to an area with active ZIKV transmission) or sexual contact with a person who has been exposed, with confirmatory laboratory testing whenever possible.

## Main clinical manifestations in the infant

Congenital ZIKV infection can lead to a spectrum of birth defects. Severe manifestations can result in a recognized pattern of birth defects known as CZS. Although many of the components of this syndrome – such as cognitive, sensory and motor disabilities – are shared by other congenital infections, there are five features that are rarely seen with other congenital syndromes or are unique to congenital ZIKV infection (see Fig. 5.5):

1. severe microcephaly with partially collapsed skull and redundant scalp with rugae (extra skin folds);
2. thin cerebral cortices with subcortical calcifications;
3. macular scarring and focal pigmentary retinal mottling;
4. congenital contractures of major joints (arthrogryposis)[‡]; and
5. marked early hypertonia or spasticity and symptoms of extrapyramidal involvement[‡].

[‡] Noted in infants with structural brain anomalies only.

Since the publication of initial clinical descriptions, three additional features that appear to be unique to congenital infection with ZIKV compared with other established congenital infections include paralysis of the diaphragm, hypertensive hydrocephalus following severe microcephaly, and neurogenic bladder. The first two features appear to be low-prevalence findings. Neurogenic bladder appears to be a common finding among infants with CZS phenotype; however, numbers tested are small.

Other anomalies commonly reported with congenital ZIKV infection can be seen with congenital CMV but less so compared with other congenital infections, including cortical atrophy, corpus callosal agenesis/hypoplasia, cerebellar (or cerebellar vermis) hypoplasia, neuronal migration defects such as gyral anomalies or heterotopia, periventricular calcifications, hydrocephalus ex vacuo, glaucoma, and postnatal-onset microcephaly. Additional anomalies that are common to a number of congenital infections (including CZS) are microcephaly, hydrocephaly/ventriculomegaly/colpocephaly, calcifications of basal ganglia or unspecified regions, hearing loss, porencephaly, hydranencephaly, microphthalmia/anophthalmia, optic nerve hypoplasia, coloboma, and cataracts – these anomalies cannot reliably be used to differentiate among congenital infections.

Primary ZIKV infection during the first and early-second trimesters of pregnancy is more commonly reported in infants with adverse outcomes that are severe. Infection in the third trimester is associated with less severe defects of the brain and eyes. Milder cognitive effects such as learning disabilities have also been reported but are not yet linked to a specific trimester of exposure. Congenital ZIKV infection has been associated with other adverse birth outcomes, such as miscarriage, stillbirth and neonatal death, but studies are not conclusive.

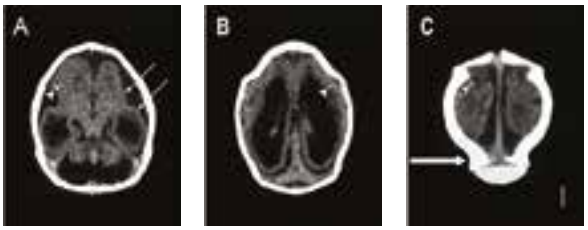
## Fig. 5.5. Clinical findings in the infant

Lateral views showing collapse of the cranium and extreme reduction in height of the cranial vault.

*Photograph source*: Moore et al., 2017 *(34)*; Ritter et al., 2017 *(35)*

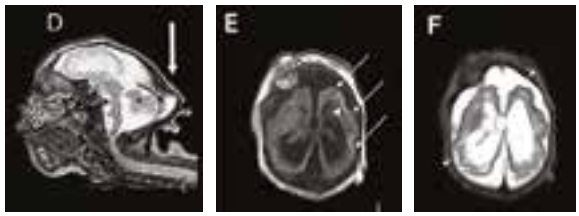
Posterior scalp view showing redundant scalp with folds (rugae).

*Photograph source:* Moore et al., 2017 *(34)*.




*Computed tomographic (CT) scan* in one infant with prenatal ZIKV exposure shows scattered punctate calcifications (*A, B and C*; white arrowheads), striking volume loss shown by enlarged extra-axial space and ventriculomegaly (*A, B and C*), poor gyral development with few and shallow sulci (*A*; long white arrows). The occipital "shelf" caused by skull collapse (*C*; white arrow).

*Photograph source:* Moore et al., 2017 *(34)*.

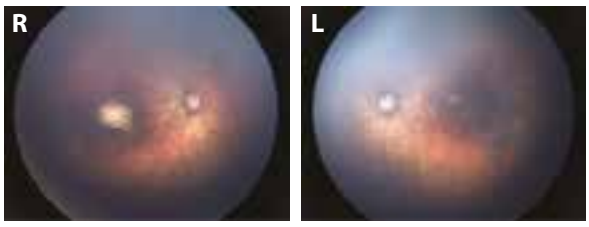



*Magnetic resonance imaging (MRI)* in infant with prenatal Zika exposure shows scattered punctate calcifications (*E*; white arrowheads), very low forehead and small cranial vault (*D*), striking volume loss shown by enlarged extra-axial space and ventriculomegaly (*D, E and F*), poor gyral development with few and shallow sulci (*E*; long white arrows), poor gyral development with irregular "beaded" cortex most consistent with polymicrogyria (*F*; white arrowheads), flattened pons and small cerebellum (*D*; black arrowhead and asterisk). The occipital "shelf" caused by skull collapse is seen in both infants (*D*; white arrowhead).

*Photograph source:* Moore et al., 2017 *(34)*.

*Left*: Newborn infant with bilateral contractures of the hips and knees, bilateral talipes calcaneovalgus, and anterior dislocation of the knees. *Right*: Newborn infant with bilateral contractures of the shoulders, elbows, wrists, hips, knees, and right talipes equinovarus. Hips are bilaterally dislocated in both infants.

*Photograph source:* Moore et al., 2017 *(34)*.




Fundus images of right and left eye: Optic nerve hypoplasia with the double-ring sign, gross pigmentary mottling, and chorioretinal scar in the macular region.

*Photograph source:* Moore et al., 2017 *(34)*.

## Diagnosis

The diagnosis of ZIKV infection is laboratory based. ZIKV RNA has been detected in blood, urine, saliva, CSF, semen and amniotic fluid, as well as tissue samples. WHO recommends testing blood and urine to diagnose ZIKV infection and, when collected for other diagnostic purposes, CSF.

### *Laboratory testing: Pregnant women*

Women who should be tested are those living in areas of ZIKV transmission or potentially exposed to someone with ZIKV infection, and who develop rash or other symptoms consistent with possible ZIKV infection during pregnancy. In areas with co-circulation of dengue and other flaviviruses, testing for multiple arboviral infections – most notably, dengue – might also be indicated. ZIKV infection during pregnancy is confirmed by NAATs* performed on blood and/or urine collected from women generally within seven days of symptom onset. Some reports indicate that NAAT results for pregnant women might remain positive longer. Specimens with positive NAAT results should have RNA re-extracted from the same specimen and be retested by NAATs for confirmation.

* Nucleic acid amplification tests (NAATs) include, but are not limited to, reverse transcriptase polymerase chain reaction (RT-PCR), real-time RT-PCR, quantitative RT-PCR, and next-generation sequencing.

ZIKV IgM antibody testing can be performed on serum from women collected at least seven days after symptom onset. Caution should be exercised in interpretation of ZIKV IgM test results in pregnancy for two major reasons: First, currently available IgM might give false-positive results because of nonspecific reactivity or cross-reactivity among antigens found on ZIKV as well as on dengue and other flaviviruses; second, ZIKV IgM can persist up to two years; therefore, presence of ZIKV IgM might reflect infection that occurred *prior* to pregnancy and that does not pose a threat to the developing fetus.

Plaque reduction neutralization tests (PRNTs) are quantitative assays that measure virus-specific neutralizing antibody titres for dengue, Zika, and other flaviviruses to which the patient might have been exposed. PRNTs can resolve false-positive IgM antibody results caused by nonspecific reactivity and, in certain cases, can help identify the infecting virus. In primary flavivirus infections, a neutralizing antibody titre that is at least fourfold higher than titres against other flaviviruses to which the person might have been exposed usually determines the specific infecting flavivirus. However, PRNT testing has been available in limited settings to date.

The majority of ZIKV infections are asymptomatic. Asymptomatic ZIKV infections during pregnancy can result in CZS and other adverse pregnancy outcomes. Testing asymptomatic pregnant women by NAATs is recommended for outbreak settings as the interpretation of serologic results can be challenging due to the increased risk of false-positive test results. There are no perfect tests for ZIKV. NAATs have a narrow window of identification of ZIKV RNA (< 7 days in blood and 14 days in urine), and currently available IgM assays have the limitations described above. Proper confirmation of positive test results in asymptomatic pregnant women is of particular importance. The WHO case definition for ZIKV infection is presented in Table 5.2.

**Table 5.2. WHO case definition for ZIKV infection for pregnant women and general population**

| | |
|---|---|
| **Suspected case** | A person presenting with rash and/or fever and at least one of the following signs or symptoms:<br>• arthralgia; or<br>• arthritis; or<br>• conjunctivitis (non-purulent/hyperemic). |
| **Probable case** | A suspected case with presence of IgM antibody against ZIKV[a] and an epidemiological link[b]. |
| **Confirmed case** | A person with laboratory confirmation of recent ZIKV infection:<br>• presence of ZIKV RNA or antigen in serum or other samples (e.g. saliva, tissues, urine, whole blood); or<br>• IgM antibody against ZIKV positive and PRNT90 for ZIKV with titre ≥20 and ZIKV PRNT90 titre ratio ≥4 compared to other flaviviruses *and* exclusion of other flaviviruses. |

[a] No evidence of other flavivirus infection.

[b] Sexual or bloodborne contact with a confirmed case or a history of residing in or travelling to an area with local transmission of ZIKV within two weeks prior to onset of symptoms.

### *Laboratory testing: Women and infants after delivery*

Suspected cases of CZS based on prenatal and postnatal detection of possible Zika-related birth defects should be investigated for evidence of ZIKV infection, including laboratory testing and clinical examination of liveborn infants, stillbirths and fetal deaths, although Zika-related birth defects are difficult to prenatally detect in early fetal losses. ZIKV RNA has been detected for extended periods of time in affected infants. Specimens collected from mothers and liveborn infants should be tested for ZIKV RNA (blood, urine) and IgM (serum). Tissue recovered from fetal deaths and stillbirths might also be tested for ZIKV RNA. Cord blood should not be used because positive results might reflect contamination with maternal blood and are not indicative of congenital infection. Because the possibility of the newborn having had a previous flavivirus infection is low, and IgM does not typically cross the placental barrier, detection of IgM antibodies against ZIKV in neonatal serum constitutes an important finding indicative of intrauterine infection. Molecular analysis (NAATs) and the detection of anti-ZIKV IgM antibodies by enzyme-linked immunosorbent assay (ELISA) can also be performed in a CSF sample obtained by medical indication for the diagnosis of the congenital syndrome, but is not exclusively used for diagnosing ZIKV infection. Positive test results indicate a confirmed or probable case of CZS; however, the sensitivity and specificity of infant testing has not been determined and negative test results do not definitively rule out CZS. Other factors to take note of include:

- NAATs should be performed on blood and/or urine collected from patients within seven days of symptom onset.
- IgM antibody testing should be performed on blood from patients at least seven days after symptom onset.
- If available, NAAT or IgM antibody testing can be performed on CSF.
- Whenever possible, paired serum specimens should be collected at least two to three weeks apart, ideally with the first serum specimen collected during the first five days of illness.
- Patients should be tested for infection with ZIKV in addition to dengue and other circulating flaviviruses if applicable, and chikungunya virus either sequentially or in parallel if specifically suspected based on symptoms or epidemiology.

### *Radiology*

Assessment for brain anomalies due to congenital ZIKV infection should be performed for all infants with known or suspected exposure. Initial investigation using head ultrasound can reveal decreased brain parenchyma associated with loss of cortical tissue, midline defects such as agenesis of the corpus callosum, increased fluid collection in the form of hydrocephalus ex vacuo and, less reliably, cortical malformations such as pachygyria and peripherally located calcifications between the cortical and subcortical layers. With microcephaly and a small anterior fontanelle, views of the periphery as well as the posterior fossa might be limited. Demonstration of calcifications is optimally obtained by CT scan and characterization of cortical malformations by MRI.

Prenatal imaging by ultrasound or MRI can detect Zika-related brain malformations; however, the sensitivity and specificity of prenatal ultrasound is not known. Microcephaly might not be detected prenatally until late-second or early-third trimesters. Prenatally diagnosed abnormalities should be confirmed by CT scan or MRI after birth. Case definitions for ZIKV infection are presented in Table 5.3.

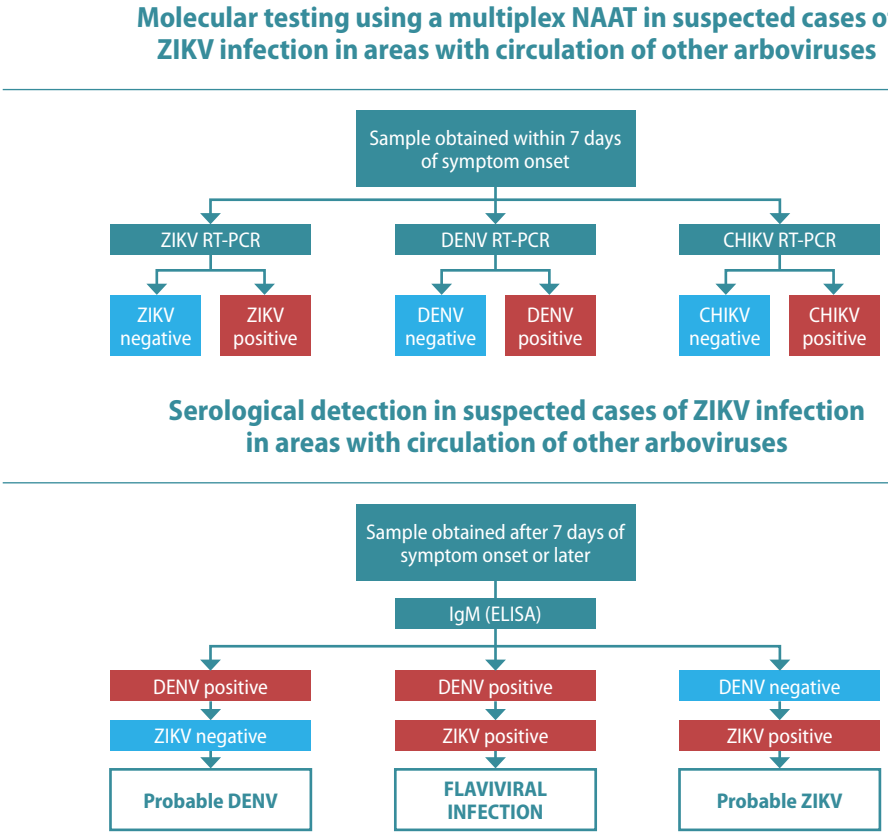
**Table 5.3. Case definition for ZIKV infection**

| | |
|---|---|
| **Suspected case of congenital syndrome associated with asymptomatic maternal ZIKV infection** | Liveborn infant, fetal death or stillbirth with microcephaly (head circumference [HC] < –2 standard deviations [SD]; measured before 24 hours of birth for liveborn infants, standardized for gestational age and sex according to WHO growth standards); *or*<br><br>any congenital malformation of the central nervous system;[a] *or*<br><br>manifestations such as severe microcephaly (HC ≤ –3 SD) with partially collapsed skull and congenital contractures of major joints; *and*<br><br>whose mother, during pregnancy, resided in or travelled to an area with known or suspected ZIKV circulation; *or* had unprotected sex with a partner who resided in or travelled to an area with known or suspected ZIKV circulation. |
| **Probable case of congenital syndrome associated with symptomatic maternal ZIKV infection** | Liveborn infant, fetal death or stillbirth that meets the criteria of suspected case of congenital syndrome associated with ZIKV; *and*<br><br>has specific intracranial morphological alterations diagnosed by any imaging method (such as intracranial calcifications, loss of cortical tissue, or corpus callosum anomalies)[b] and/or specific eye anomalies (such as macular scarring or focal pigmentary retinal mottling)[b], and excluding other known possible causes; *or*<br><br>whose mother had a rash during pregnancy. |
| **Confirmed case of congenital syndrome associated with ZIKV infection** | Liveborn infant, fetal death or stillbirth of any gestational age that meets the criteria for suspected case of congenital syndrome associated with ZIKV infection, *and*<br><br>has laboratory confirmation of ZIKV infection. |

[a] Excludes early brain malformations such as NTDs and holoprosencephaly.

[b] See main clinical manifestations in the infant (p. 162).

**Fig. 5.6. Testing in suspected cases of ZIKV infection**




CHIKV: chikungunya virus; DENV: dengue virus; ELISA: enzyme-linked immunosorbent assay; IgM: immunoglobulin M; neg: negative; pos: positive; RT-PCR: reverse transcriptase polymerase chain reaction; ZIKV: Zika virus

## Relevant ICD-10 codes

P35.8 Other congenital viral diseases
Q02 Microcephaly

## Checklist

**Checklist**

- ☐ **Examine the neonate for:**
  - Severe microcephaly with collapsed skull and redundant scalp.
  - Congenital contractures of major joints (arthrogryposis).
- ☐ **Hypertonia and spasticity.**
- ☐ **Macular scarring and focal pigmentary retinal mottling (paediatrician or ophthalmologist).**
- ☐ **Additional clinical examinations:**
  - Radiographs: Thin cerebral cortices with subcortical calcifications.
  - Hearing assessment: Screening by auditory brain stem response methodology with diagnostic testing to verify hearing loss.
- ☐ **Obtain maternal medical health and pregnancy history to ascertain ZIKV infection.**
- ☐ **Collect maternal and neonatal samples for diagnostic testing.**
- ☐ **Determine whether the case is suspected, probable or confirmed.**
- ☐ **Obtain photographs of the malformations observed.**
- ☐ **Record diagnostic information and report.**

# 6. Coding and diagnosis

## Coding of congenital anomalies

One of the essential aspects of a congenital anomalies surveillance programme is its ability to efficiently generate information. Central to this process is the proper and accurate coding of the recorded diagnostic information. Coding of diagnostic information using a disease classification system allows a surveillance programme to capture and classify cases with congenital anomalies in a standardized way. Entering coded information into an electronic system makes it easier to retrieve and analyse the data. It is important to understand and follow a standardized coding system, in order to accurately and consistently classify and code the various types of congenital anomalies.

The more precise the clinical description of congenital anomalies present in a fetus or neonate, the more accurate the classification and coding that can be achieved. For example, not knowing the lesion level of spina bifida (such as cervical, thoracic or lumbar) or whether hydrocephalus is present, or either of these conditions, would result in coding the congenital anomaly as "spina bifida, unspecified". It is important to obtain the best possible clinical description, carefully review and classify the congenital anomaly, and assign the right code(s) based on the description. To the extent possible, the database should preserve both the codes and the detailed clinical description.

Photographs of the external congenital anomalies present can supplement the clinical description and help to ensure that the proper code is assigned. Although it is relatively easy to take photographs, it requires some training to obtain the best photographs (e.g. timing, views). Please refer to Appendix J for suggestions on taking photographs of fetuses or neonates with congenital anomalies. Privacy issues also need to be considered and appropriate measures to ensure confidentiality should be in place. Because some photographs might identify the neonate, it is critical to maintain these securely as confidential surveillance documents. More information on privacy and confidentiality is included in Chapter 2.

## International Classification of Diseases

The ICD-10 is considered the international standard diagnostic classification system for all general epidemiological purposes, health data management purposes and clinical use, and is widely used in many countries as a classification system for diseases. Use of this standardized coding system will facilitate partnerships and collaborations with other programmes using the same coding system.

The ICD-10 is developed and maintained by WHO. The most recent version is available on the WHO website *(12)*. It is available in the six official languages of WHO (Arabic, Chinese, English, French, Russian and Spanish), as well as in 36 other languages. A list of contact points for the 42 language versions of ICD-10 can be found on the WHO website *(36)*.

On the WHO website, an ICD-10 interactive self-learning tool is available for training purposes *(37)*.

The ICD-10 has been used to classify diseases in health records and vital records, as a basis for the compilation of national mortality and morbidity statistics by WHO Member States.

The ICD-10 codes are listed in alpha-numeric order and are described in detail.

Classification of structural congenital anomalies is found in Chapter XVII:

"Congenital malformations, deformations and chromosomal abnormalities (Q00–Q99)"

This chapter contains the following blocks of codes:

- **Q00–Q07** Congenital malformations of the nervous system
- **Q10–Q18** Congenital malformations of eye, ear, face and neck
- **Q20–Q28** Congenital malformations of the circulatory system
- **Q30–Q34** Congenital malformations of the respiratory system
- **Q35–Q37** Cleft lip and cleft palate
- **Q38–Q45** Other congenital malformations of the digestive system
- **Q50–Q56** Congenital malformations of genital organs
- **Q60–Q64** Congenital malformations of the urinary system
- **Q65–Q79** Congenital malformations and deformations of the musculoskeletal system
- **Q80–Q89** Other congenital malformations
- **Q90–Q99** Chromosomal abnormalities, not elsewhere classified.

## ICD-10 modifications

The ICD-10 codes lack specificity for uniquely coding some congenital anomalies and most genetic syndromes. Therefore, some congenital anomalies surveillance programmes use their own local modification of the ICD-10 that contains additional codes for some specific congenital anomalies not found in the ICD-10, or add an extra digit, or both, to allow for more detailed coding of some defects and certainty of diagnosis.

The following is an example of how the RCPCH (formerly known as the British Paediatric Association) developed an adaptation of the ICD-10 by adding an extra digit to the ICD-10 codes to expand and allow for more detailed coding *(38)*. For example, in this adaptation, specific codes are added to differentiate parietal, orbital, nasal and nasopharyngeal encephaloceles, as follows:

- **Q01.8** Encephalocele of other sites (ICD-10 code)
- **Q01.80** Parietal encephalocele
- **Q01.81** Orbital encephalocele
- **Q01.82** Nasal encephalocele
- **Q01.83** Nasopharyngeal encephalocele

## Personnel responsible for diagnosing and coding

Depending on how a congenital anomalies surveillance programme is set up, the coding of congenital anomalies might take place in a hospital or clinic, or at the central registry, based on the clinical information provided. It is important to train the hospital or clinic staff responsible for diagnosing and coding congenital anomalies. If coding is done at the hospital or clinic, it is also important and recommended that someone who is knowledgeable about congenital anomalies (e.g. a neonatologist, paediatrician, clinical geneticist or dysmorphologist) reviews and confirms the diagnosis and assigns the proper codes. Codes for, or specific descriptions of, congenital anomalies are then submitted to the central registry, where final review and verification of all codes reported by participating sites occurs.

Not every site will have personnel who are knowledgeable about congenital anomalies. If no knowledgeable staff member is available, it is suggested that coding be done at the central registry level. Having a description of a congenital anomaly that is as complete and thorough as possible, and that includes photographs with the description, will increase the likelihood that the reviewer at the registry will be able to assign an accurate code. It is important to remember that a description that includes abbreviated words can easily be misunderstood or misinterpreted by the reviewer.

The reliability of coding can also be affected by the expertise of the personnel recording the information and the expertise of the surveillance staff reviewing the information.

## Effect of the certainty of diagnosis on coding

### *Prenatal and postnatal diagnosis*

The certainty of a diagnosis can vary for live births and fetal deaths (stillbirths), as well as when the diagnosis is prenatal only or postnatal. With pregnancy terminations, a prenatal diagnosis might not be verified for many reasons, including the method of termination, the condition of the specimen, or a lack of post-termination examination or autopsy. Programmes that are interested in more detailed information on inclusion of prenatal diagnosis in congenital anomaly surveillance can find some useful and practical suggestions and tips in the guidelines developed by the NBDPN in the USA *(14)*. Among liveborn neonates who die shortly after birth, the diagnosis could also cause difficulties if certain examinations (e.g. x-rays and karyotyping) or an autopsy are not done.

## Coding possible and confirmed diagnoses

When the diagnosis is uncertain (e.g. hydrocephalus suggested by prenatal ultrasound, but for which no postnatal confirmation is done), it is beneficial to distinguish possible diagnoses from confirmed diagnoses. This can be done by using a separate field on the congenital anomalies abstraction form to include this information (see Appendix G), or by adding an extra digit to the ICD-10 codes, which has been done by some surveillance programmes *(38)*.

## Coding multiple congenital anomalies

Approximately 75% of fetuses and neonates with a major congenital anomaly present as isolated anomalies, and the remaining 25% have more than one major anomaly *(39, 40)*.

More details about the types of congenital anomalies according to clinical presentation are presented in Appendix C.

When more than one congenital anomaly is present, a detailed description of each major anomaly is recorded. Congenital anomalies surveillance programmes vary in terms of the number of codes they record for a fetus or neonate, but allowing coding for at least 10 anomalies should be sufficient. Major anomalies are given priority over any minor anomalies for being captured within the minimum number of diagnoses recorded.

Certain syndromes can also be coded according to the ICD-10 classification *(12)*. When the ICD-10 code is not specific enough (e.g. codes listed in the group Q87 – "Other specified congenital malformation syndromes affecting multiple systems"), then using the classification developed by the RCPCH could be beneficial *(38)*. Regardless of which classification(s) is used, a thorough description of any observed anomaly is very important for accurate coding of congenital anomalies.

## Use of codes for surveillance, data analysis and presentation

The following information is intended primarily for the staff of the central registry. To record ICD-10 codes, the most specific code format (i.e. Q##.#) is used. For example, frontal encephalocele is coded as Q01.0. The three-character format or group code (i.e. Q##) is commonly used only for data analysis and presentation purposes, to group and report all types of any condition. For example, when analysing and reporting all types of (total) encephalocele, the three-character format (Q01) can be used. Diagnoses coded as possible would still be excluded.

Along with the ICD-10 codes, a list with exclusions of several anomalies is provided in the ICD-10 classification system. The term "exclusion" does not necessarily mean that the case is excluded from the registry. Rather, it means that the particular anomaly is not coded using the same code or codes. For example, because "spina bifida occulta" is considered a different anomaly from the other types of spina bifida and has a specific code (Q76.0), the Q05.# ICD-10 codes are not used. Another example is cleft palate with cleft lip: If a fetus or neonate has both a cleft palate and cleft lip, the anomaly is not coded with a cleft palate code (Q35.1–Q35.9), but instead with a code listed under cleft palate with cleft lip (Q37.0–Q37.9).

It is important to keep in mind that, while for surveillance purposes all major anomalies affecting a fetus or neonate can be coded, for data analysis and presentation, the criteria to include or exclude certain anomalies can determine which codes are used. For example, although a case might have both anencephaly (Q00.0) and lumbar spina bifida without hydrocephalus (Q05.7), for reporting purposes, the case might be analysed only with other cases of anencephaly. In addition, if an anomaly is secondary to another anomaly, such as talipes equinovarus with spina bifida, the case would be included in analyses of spina bifida (Q05.#) but not in analyses of talipes equinovarus (Q66.0 or Q66.8). However, when both anencephaly and spina bifida are present and are contiguous, this is the condition called craniorachischisis, for which there is a unique ICD-10 code (Q00.1); therefore, anencephaly and spina bifida are not coded separately in this case.

Examples of the assignment of codes based on clinical description are presented next.

***Example 1:***

The following diagnosis and clinical description are provided for a neonate:

"spina bifida with LS meningocele and massive hydrocephalus"

In this case, "LS" is used as an abbreviation of "lumbosacral". Although the description might suggest two anomalies (spina bifida and hydrocephalus), hydrocephalus is common among children with spina bifida and it is considered a consequence of spina bifida, the primary major congenital anomaly in this case. There are specific codes for "spina bifida with hydrocephalus" in the ICD-10. The suggested ICD-10 code to assign to this case is Q05.2 (lumbosacral spina bifida with hydrocephalus). This case would not be included in analyses of hydrocephalus as a primary anomaly.

***Example 2:***

The following diagnosis and clinical description are provided for a neonate:

"cleft lip and palate"

Because it is not specified whether the soft palate, hard palate, or both are affected, and no information is provided regarding the laterality (sidedness) of the cleft lip, the suggested ICD-10 code is Q37.9 (unspecified cleft palate with unilateral cleft lip).

Note: For cleft palate, it is uncommon to have the detailed description available (whether the soft or hard palate is affected), unless the description is provided as a result of a surgical repair.

***Example 3:***

The following diagnosis and clinical description are provided on a medical record:

"cleft lip NOS; spina bifida NOS; ear tags"

The abbreviation "NOS" means "not otherwise specified". The suggested ICD-10 code for cleft lip NOS is Q36.9 (cleft lip NOS) and for spina bifida NOS is Q05.9 (spina bifida, unspecified). Ear tags are considered minor anomalies; therefore, coding them is optional. If coded, the suggested ICD-10 code for ear tags is Q17.0 (preauricular appendage or tag). Although "NOS" is a valid code in the ICD-10, it is used only when there is no possibility of obtaining a better description for a specific congenital anomaly.

***Example 4:***

The following diagnosis and clinical description are provided for a neonate:

"amelia upper and lower limbs"

There are two ICD-10 codes to be assigned. One is for amelia of upper limbs: Q71.0 (congenital complete absence of the upper limb(s)); the other is for amelia of lower limbs: Q72.0 (congenital complete absence of

lower limb(s)). However, for reporting and analytical purposes, it is suggested to count them only once, using the ICD-10 code Q71.0.

***Example 5:***

The following diagnosis and clinical description are provided as part of an autopsy report:

"anencephaly infant with gross abnormalities; bilateral cleft lip; cleft palate"

The suggested ICD-10 code for anencephaly is Q00.0 (anencephaly). The "gross abnormalities" description is vague, and coding is optional. If coded, the suggested ICD-10 code is Q89.9 (congenital malformation, unspecified). Although the description might suggest two anomalies (cleft lip and cleft palate), there is a specific ICD-10 code to assign to cleft palate with bilateral cleft lip. Because the type of cleft palate is not specified, the suggested ICD-10 code is Q37.8 (unspecified cleft palate with bilateral cleft lip).

Note: Avoid using the Q89.9 ICD-10 code if possible because it does not provide any specificity and has very minimal value in congenital anomalies surveillance.

***Example 6:***

The following diagnosis and clinical description are provided for a neonate:

"myelomeningocele, T3–T4 open"

Since it is not mentioned or specified whether hydrocephalus is present or not, one can assume that the defect is "spina bifida without hydrocephalus" and code as Q05.6 (thoracic spina bifida without hydrocephalus). However, it is also possible to use the ICD-10 code Q05.9 (spina bifida, unspecified) but by using this code the specificity for lesion level would not be captured. It is recommended that the birth defect surveillance programme include information in its protocol on how to code spina bifida when hydrocephalus is not mentioned or described in medical records.

The ICD-10 *(12)* and references *(29, 41–43)* provide more information on coding and classification of congenital anomalies.

# 7. Primer on data quality in birth defects surveillance

## Why data quality matters

In public health, a crucial source of evidence for action is surveillance data – the tracking of key health indicators and using the information to prevent diseases and improve population health. In birth defects surveillance, the focus is on tracking the impact of birth defects in populations by monitoring the occurrence of birth defects (ideally throughout life, from fetus to adult) and their impact on health and daily living (ideally, encompassing mortality, morbidity, disability and quality of life). These data can help provide needed services, identify disparities and inequalities, detect trends, and assess the effect of interventions.

Public health surveillance is a worthy societal investment precisely because it provides such value to the community – an ongoing and sustained source of public health data on which interventions can be based. For such interventions to be correct, the data must be reliable: accurate, complete and timely; hence, the value of high-quality data. In fact, not only are high-quality data beneficial, but poor-quality data might at times be worse than having no data at all, since they can lead to misguided decisions strengthened by the illusion of doing the right thing based on evidence.

There is also a second reason to focus on quality data. Improving quality in a system can reduce its costs. With better surveillance systems, there are fewer errors to correct, fewer products to discard. Reducing cost is important everywhere but is especially crucial in areas of the world where resources are limited and stretched thin across many different health needs. For birth defects prevention and care, lower-resource areas are particularly relevant, as they encompass regions of large populations and high birth rates – regions such as Asia and Africa, where most births (and most birth defects) occur.

Evaluating and improving data quality in birth defects surveillance is a multi-step process. This primer will focus on a few basic ideas as starting points for discussion and action within birth defects programmes and networks. Specifically, areas covered include the value of and need for high-quality data, how quality improvements are possible everywhere, and simple tools that are available to ensure quality is embedded into the surveillance process.

## A surveillance scenario

Imagine that a surveillance programme has been created to monitor an indicator that is important to the community – e.g. the livebirth prevalence of NTDs (see Fig. 7.1). After a period of stable prevalence, suddenly the programme staff starts to see an apparent increase (arrow 1). How could this change be interpreted and what could be done about it? As time goes on, an apparent decline is then observed (arrow 2). How could this change be interpreted and what could be done now?

After a longer period of time, the prevalence seems to stabilize (arrow 3) and a new baseline continues. Why is there a new baseline? What has changed since the previous baseline? What does this mean?

Clearly, something is going on. Do these changes truly reflect what is happening in the population? Are these changes real? Or are these changes spurious – due to changes in how a surveillance programme is able to interact with the target population? And if they are due to surveillance activities, is it because of "noise" or errors in the surveillance process (e.g. incomplete or miscoded cases)?

Below are some critical questions and possible actions that the surveillance programme might take:

- Will an investigation be launched to find a new teratogen, if the decision is made that the increase at point 1 is real? However, if the increase is spurious, the investigation would be a waste of time and resources.
- Will the focus instead be on understanding whether processes of the surveillance system have changed – for example, a new referral hospital added, new staff hired but not trained, or loss of a data source, leading to changes in ascertainment and reporting?

- Will an assessment be performed to determine what local/regional/country-wide decisions have changed that could affect pregnant women and pregnancy outcomes, such as elective termination?
- Will nothing be done in the hopes that the issue will go away? (This is usually not a good strategy.)

Clearly, something should be done to understand both the biology of the condition under surveillance, as well as each methodological step of the surveillance programme. In addition, understanding the health-care context and the community will be important. For example, what policies or initiatives are in place or have changed that might affect the programme, and specifically, which part of the programme might they influence (e.g. ascertainment, reporting, clinical case review, coding)?

The relation between a true signal in the population and the signal detected by the surveillance programme can be visualized in a two-by-two table (see Fig. 7.2).

As shown in *panel a* of Fig. 7.2, the system aims to detect only true signals, without overcalling events (false positives) or missing events (false negatives). False positives and false negatives both have costs.

**Fig. 7.1. Interpreting changes in rates of an indicator in a birth defect surveillance system**

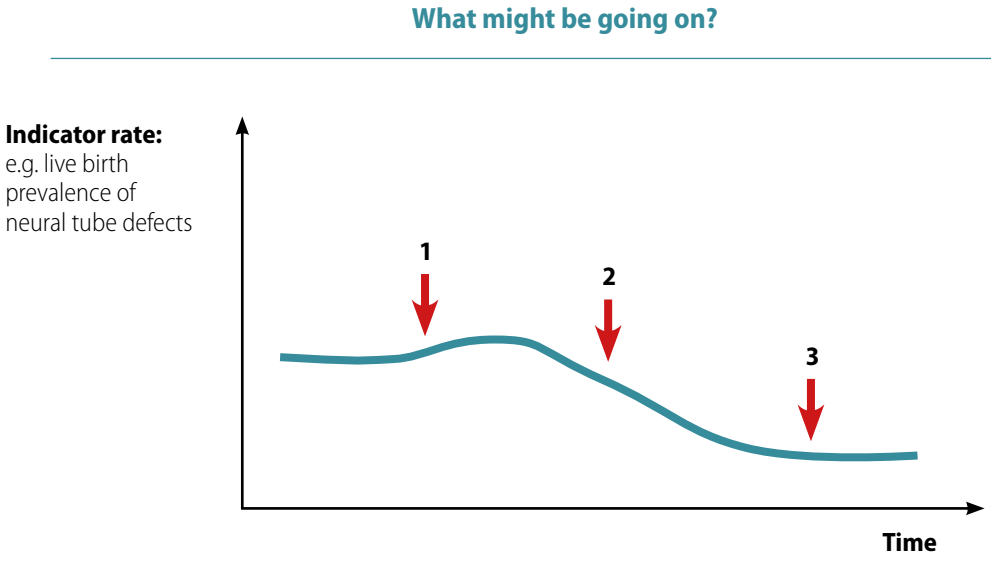
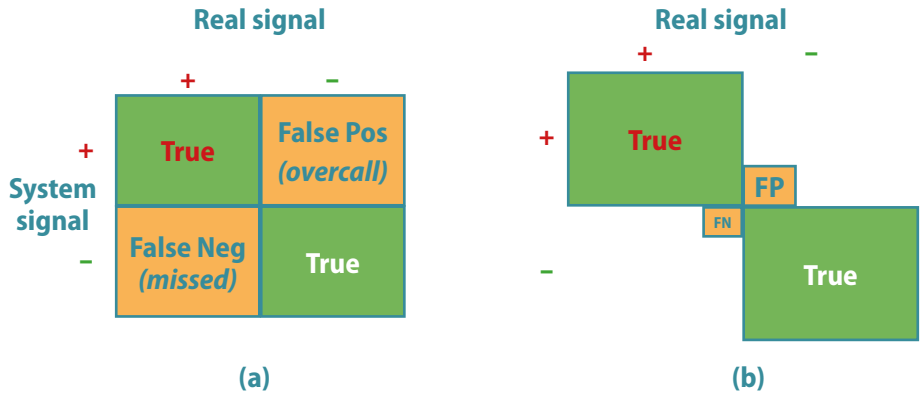



**Fig. 7.2. Real versus system-generated signals in a birth defect surveillance programme**




Cost of false positives (false pos; FP; overcalling): inappropriate (wasteful) alarms, cluster investigations, concerns.
Cost of false negatives (false neg; FN; undercalling): missed "epidemic", missed benefit of intervention.

Improving the quality of a surveillance programme aims at minimizing those errors that cause false negatives and false positives (smaller squares), and at boosting confidence that the system can reliably track events in the population (larger squares). For example, imagine that the surveillance system detects an apparent decrease in the occurrence of spina bifida in an area where primary prevention efforts are being pursued. Is this truly a reflection of the success of the primary prevention intervention? Or is the completeness or accuracy of case ascertainment being degraded because, for example, trained staff have left the birthing centres or pregnancy terminations have increased but have not been captured by the programme?

Data quality improvement is a process. Quality can always be improved. The key is to improve, stabilize those improvements and build on them.

## Data that are "fit for use"

A broad definition of high-quality data is data that are fit for use. Once operationalized, this apparently simple definition has profound implications for a surveillance programme.

"Fit for use" speaks to the need to understand in detail the goals ("use") of the programme and to assess the data and data systems created. The best programmes embed quality by design into the surveillance process. In practice, the programme should have explicit and detailed information about what it is seeking as the end product of surveillance, and then work back to design the data acquisition and processing that can support the programme's goals.

The first crucial step is ensuring that everyone – from the programme director to the front-line staff – is clear as to what information the programme wants to assess, track, and disseminate – and why. Even if such goals are flexible and might change with time, making them explicit and measurable is critical. As an example, for a programme that includes NTDs as an eligible condition, what type of data are "fit for use"?

Clearly, the data needed to adequately describe a child with spina bifida will vary to some extent depending on whether these data are for the surgeon, for the clinical follow-up programme, or for public health surveillance. For public health surveillance, the collected data will vary depending on the goals of the programme: is it tracking prevalence among live births (or some other birth outcome) or does it also include tracking linkage to services and health outcomes? For example, meaningful tracking of health outcomes to determine severity and potential complications will require details such as size, location, skin covering and associated findings/sequences such as hydrocephalus. Likewise, if a surveillance programme aims to also track risk factors, then details on exposures and supplement uses will be important.

Reflecting on "fit for use" also helps a programme develop not only explicit *data variables* and related quality parameters, but also to design *efficient data structures and databases*. Having clear and detailed goals for what a programme wants to track, report and communicate will help optimize the way the data are organized so that the information is not only easy to input but also extracted and analysed efficiently.

## SMART and SMARTER goals

When developing a programme's goals, it helps to consider the SMART framework *(44)*. While all elements are not necessarily relevant in all situations, the SMART framework can be used to help a surveillance team develop and critically examine the stated goals of their programme. For our purposes, the SMART acronym features the following attributes:

- **S**pecific – targets a specific outcome, indicator, or area for improvement
- **M**easurable – quantifies the indicator(s)
- **A**chievable – states what results can realistically be achieved with available resources
- **R**elevant – provides meaning and importance to the community
- **T**ime-related – specifies when the result(s) can be achieved.

Going through the exercise of setting specific and measurable goals not only clarifies to everyone in the programme what must be achieved, but begins to provide a basis for quality assessment and improvement. A few basic examples can illustrate this point.

***S****pecific*. A programme that sets out to "monitor all birth defects" does not have a specific goal – what are "all" birth defects? A more specific goal would be to monitor an explicit list of selected birth defects (e.g. spina bifida, omphalocele, gastroschisis, and so on – together with clear case definitions), among well-defined birth outcomes (e.g. all live births, all live births plus stillbirths plus pregnancy terminations, etc.) in a well-defined source population (e.g. births delivered in a hospital network, or from mothers living in a defined geographic area).

***M****easurable*. A measurable indicator of such a specific goal could be prevalence at birth, maternal age-specific prevalence at birth (important for conditions such as Down syndrome or gastroschisis), perinatal mortality, infant mortality, and so on – with each indicator having its explicit definition and the means to access the appropriate data on denominators.

***A****chievable*. Having achievable and realistic goals is extremely important. The goal can be a stretch but should be doable given available resources. For example, programmes that are starting or have limited resources would want to strongly consider focusing, at least in the initial stages, on a shortlist of birth defects that can be reliably ascertained and evaluated with simple means: typically, a shortlist of external birth defects, visible at birth, of significant clinical and public health impact. Likewise, the type of data to be collected for each case will need to be carefully calibrated so that they serve the specific goals of the programme. Such sets of conditions and variables have been developed by several organizations and networks (e.g. list from NBDPN, PreSurv database of the ICBDSR, and the list provided in Chapter 4 of this manual). These resources are good starting points that can be tailored to a programme's need.

Having achievable goals also serves as a reminder that a programme must have trained staff to do the work well. In birth defects surveillance, this means, for example, having both the epidemiologic and clinical capacity to identify, describe, code and classify relatively rare and sometimes complex conditions. In practice, a programme needs to think about appropriate training for front-line staff (e.g. nurses in the birthing centres) and having expert clinicians for case review and classification (e.g. at the central or coordinating programme office), in addition to data managers, analysts and epidemiologists.

***R****elevant*. Good goals are meaningful to the programme and to the community. This shared belief and commitment will drive a programme forward in good and bad times. A relevant goal is one that seems worthwhile, that is applicable to the community's social and cultural environment, and that is relevant for the times. For example, a relevant goal might be to conduct surveillance on clinically important birth defects with known modifiable risk factors (e.g. NTDs) and to link a birth defects surveillance programme with programmes that monitor and intervene in such risk factors (e.g. nutrition and fortification programmes, diabetes screening programmes, etc.). Programmes operating in settings with specific concerns or risk factors (e.g. high use of concerning medications) might include those concerns when deciding on their goals.

***T****ime-related*. Finally, a good goal is time-related or time-bound. Having a defined time horizon helps meet goals and keep track of progress. A good time-related goal is not too ambitious but also not too diffuse; for instance, having a goal of monitoring spina bifida in 10 years is too far in the future to be useful. One can have long-term goals, but in such cases, these need to be associated with shorter-term goals that can be used to track and assess progress.

Two additional points deserve emphasis. First, thinking carefully about data and data quality from the perspective of the end product – the goals of the surveillance programme – is not an academic exercise but a necessity. Time spent in this phase will save much time and effort later on. In the planning phase, the planners should realize that data are expensive – it takes time and resources to gather, check, store and analyse data, and such time and resources are limited. There should be no "recreational data collection" – *all data to be used should be collected;*

*all data collected should be used.* A simple exercise once a proposed list of data elements has been created is to develop a set of tables in which those variables will be used. If there is no use for certain data elements, or if a programme is unable to collect those data accurately, then an argument can be made for not including them in the surveillance system.

Second, a well-planned programme will be forward thinking and have an explicit plan for expansion. For example, a programme might begin operations focusing on a core set of conditions and data elements. Depending on resources and the success of operations, a programme can then develop and implement an expansion plan to add conditions and data elements.

In fact, a variant of the **SMART** acronym is **SMARTER** – goals are also to be ***E****valuated* and ***R****eviewed*. This extension speaks to the dynamic nature of goals. Everything can be improved, including goals. Regular evaluation and review is critical to ensuring the best use of a programme's resources for the benefit of the community.

With goals set in place and having developed a first list of data elements to serve those goals, a programme will need to implement broad strategies and good practices to start embedding quality into such data elements.

## General good data strategies and practices

Some simple practices in data definition and collection can prevent errors and improve the consistency and quality of surveillance. Crucially, these practices should be developed at the planning stage, before data are collected and should be incorporated into staff training.

- *Explicitly define all data elements.* Each data element (even apparently obvious ones such as sex, birth weight, residence) should be defined explicitly, including where they will be found and how they will be coded.
- *Explicitly give instructions for challenging data elements*. Real life is messy, so give instructions for data that are not in the chart (unknown data) or fields left blank on data forms (missing data). The goal is consistency (everybody sharing the same approach to similar issues) and efficiency (no guessing needed).
- *Store raw data rather than calculated variables.* For many key elements, raw data are best because they are easily preserved and data granularity can be preserved. For example, instead of recording body mass index, a programme should collect height and weight data. Body mass index can be calculated from height and weight, but not the converse. For some complex data, such as an echocardiogram, this is not feasible, so a report will suffice. However, a programme should strongly consider storing photographs or copies of radiographs to assist with centralized case review; for instance, in cases of limb deficiencies, complex phenotypes, or potential syndromes.
- *Do not categorize continuous variables.* Examples include birth weight, height, weight, gestational age and maternal age. Although in many cases these data will eventually be coded during data analysis, collecting the actual value is much more valuable in the long run (e.g. providing flexibility for new analyses), does not take additional work, and allows for better error checks.
- *If using categorical variables, code at data collection.* In some cases, coding at data collection is reasonable and might save time. Examples include gender (e.g. 1 = male, 2 = female, etc.) or race/ethnicity (if a fairly comprehensive list can be generated, with an option for "other – specify"). It is good practice to be consistent with coding, using similar codes for similar questions (e.g. 1 = no, 2 = yes, etc.). If using a data collection form (paper-based or electronic), it is good practice to show the code with the label (e.g. 1 = no, 2 = yes, etc.).
- *Minimize open-ended, free text in data entry fields.* Free text is difficult to analyse and requires expert review to transform into analysable data. However, the recommendation is to minimize free text – not to avoid it completely – because at times it is necessary and in fact critical to preserve the information content. Examples include verbatim description of the birth defect or phenotype, and comment sections of certain areas on the abstraction forms. Birth defects are complex conditions, and the data abstractor must have an opportunity to describe the complexity or uncertainty so that experts at the central/coordination level can review and resolve appropriately.

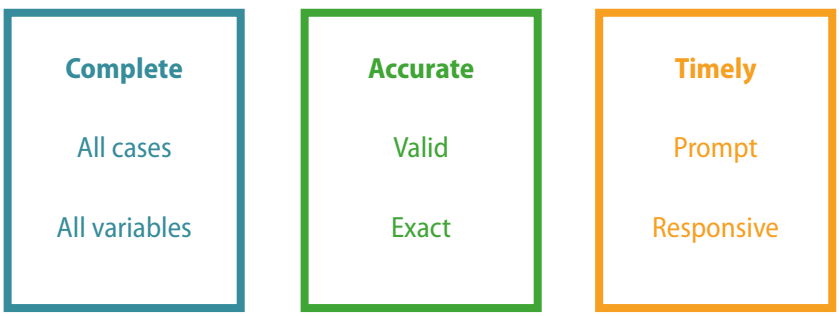
- *Include a thoughtful set of potential confounders.* In addition to basic descriptive data (e.g. demographics, birth defect description, etc.), consider including information that can be used to adjust, stratify and compare across groups, such as maternal age, smoking, prenatal care, etc. To make a rational and efficient choice (every piece of data has a cost), review the goals of the programme and the information that one wishes to analyse and report to ensure that these additional data can be collected, that the quality is "fit for use", and that the data will be used.
- *Develop standard operating procedure (SOP) manual for a programme.* All the processes of a surveillance programme should be incorporated into an SOP manual, including all issues discussed in this section. This manual should be clear and up to date. Developing and maintaining such a manual is a significant commitment, but if used well, it is crucially important for several reasons: First, it forces planners to map out in detail the programme's processes, and helps identify roadblocks and potential solutions. Second, such a manual is a key training resource that can provide clear instructions for new staff as well as for refresher training, thus ensuring consistent processes in a programme. Third, a SOP manual helps hold staff accountable since both the processes and the responsibilities are clearly described. Fourth, a detailed SOP manual provides transparency and increases trust at all levels of the programme and among stakeholders. Finally, and more broadly, a SOP manual becomes an aid in creating a visual/written and detailed process map (to be discussed later), as well as setting explicit standards for data, guidelines for processes and ongoing evaluation.
- *Nurture teams with training, feedback, communication and recognition.* The human element is critical in any public health surveillance process. The best programmes use teams to meet their goals, and the teams include representatives from all levels and processes of the programme, from front-line staff (e.g. nurse abstractors) to data managers to analysts to administrators. This approach fosters communication; shared understanding of goals, processes and issues; and provides a valuable resource to identify solutions to data quality problems. Front-line staff are especially critical, as they are responsible for collection of the primary data. Collecting high-quality primary data is crucial and will be the focus of a later section.

## Key characteristics of data quality in public health surveillance

Once a programme has defined its SMART goals, developed the associated data variables so that these are adequately structured and relevant to its goals, and planned its processes and documentation (e.g. a SOP manual), how does such a programme begin to assess data quality? Three basic characteristics of high-quality data in public health surveillance are **c**ompleteness, **a**ccuracy, and **t**imeliness – summarized as the acronym CAT (see Fig. 7.3).

Data are *complete* when all cases are included (no cases are missed), and all data variables for cases are entered. Assessing the first criterion – whether all cases are included – can be challenging and might require additional information, resources and investigation. However, it is a crucial issue, as it speaks directly to the sensitivity of the surveillance programme to detect true cases. The use of selected data quality indicators for ascertainment, for example, can be helpful to assess this component and will be discussed further below.

**Fig. 7.3. Key elements of data quality in public health surveillance**



Data are *accurate* when the information entered reflects the truth (e.g. a case of spina bifida is indeed a case of spina bifida as defined by a programme's operational procedure manual, or when coding and classification are correct). Training and evaluation, including the use of data quality indicators for description, coding and classification, can help assess and improve this component of data quality.

Data are *timely* when they are available and disseminated at the time the programme needs them. Timeliness is particularly important in public health surveillance because of the focus on ongoing tracking of health events. Timeliness might be defined differently by programmes and even within a programme. For example, a programme might designate spina bifida for rapid ascertainment at the time of folic acid fortification, or microcephaly at the time of a potential Zika epidemic. Regardless, timeliness must be defined at the outset so it can be assessed and tracked as a key quality indicator. In the context of quality assessment and improvement, timeliness is best assessed not only for the overall surveillance system – for example, time from case detection to data analysis and reporting – but also for the individual processes that make up the system. This approach helps identify areas of "waste" (e.g. data sitting for long time waiting for the next phase) and improvement.

Having qualitatively described some elements of data quality in surveillance, the next step is developing a quantitative system of measurement to track them. This means assessing the current status of data quality and whether it is improving, stable, or getting worse. Objective data are easier to measure and track, and often less prone to noise (because definitions are more reproducible) than subjective or difficult-to-measure data. For this reason, data quality indicators are a powerful tool for surveillance programmes. However, to better understand the function and role of data quality indicators, it is crucial to understand the processes of the specific surveillance system. *The reason is that the quality of data and information is a direct consequence of the quality of the processes that generate them.*

## Quality data come from quality processes

A key insight in quality assessment and quality improvement is that the *quality of any product* generated by a system is the consequence of the *quality of the processes* that make up that system. A high-quality product can come only when quality is embedded in the processes that make it.

In public health surveillance, the "product" is the information generated by the surveillance system. This product is generated by the processes of the system, including ascertainment, description, coding, classification, and so on. To have high-quality information, programme staff should understand these specific processes (what they do and who does what) and how they interact, and then embed tools to ensure quality, such as checklists and specific indicators.

This insight highlights a key concept. Quality assessment evaluates the end product (the completeness, accuracy and timeliness of the information) – *it can detect the problem, but does not fix it or provide information on how to fix it.* To fix the problem, the root cause of the issue, such as incomplete, inaccurate or delayed data, should be determined. To address the root cause(s), an understanding of the processes is needed. For this reason, the next step is to understand in detail the processes of the surveillance programme.

## Processes must be made visible

To fully understand the processes of a surveillance system, it is helpful to produce a *visual map* of the processes – a map that details the processes as they really are, not as someone thinks they are. For this reason, producing this map – in practice, as a set of flowcharts – requires fundamental knowledge by those who operate those processes. It is the job of both the programme director and key staff. Importantly, this should involve front-line workers (e.g. data abstractors and nurses who interact with the potentially affected child within the health-care system), as well as clinical reviewers, data managers, analysts and administrators. It is often surprising to see how much can be gleaned (and how assumptions might be wrong) just by assembling this team and going step by step through the details of the surveillance workflow.

Process mapping is an important, yet time-consuming step. The processes can be complex, but in order for the process mapping to be useful for identifying issues and improving quality, the details of the mapping should focus on where people actually perform a specific task; for example, a nurse examining a child in the nursery. The processes should include tasks and people. These steps in which people perform specific tasks can then be evaluated to see which can be leveraged efficiently, where small changes can lead to big gains in quality.

The details of process mapping go beyond the scope of this primer. However, to illustrate a basic process mapping, this primer presents some simplified conceptual process maps to show how certain processes can be improved with the aid of specific tools and quality indicators.

A simplified process map is hierarchical. In Fig. 7.4, a basic map shows how the system is made of processes – ascertain, review, analyse, report – linked into a causal chain. This conceptual view is helpful but only a start. It lacks the detail necessary for action. This detail is made visible when each major process (here, the review process) is expanded to identify its components (e.g. review clinically, code, classify) and then each of these is further expanded until one reaches *the level at which people do specific tasks* – for example, the expert clinician at the central level reviewing a set of potential cases. This level, sometimes referred to as the decision level, is where issues of data quality can be usefully identified and corrected.

Another example, still fairly simple and conceptual, is illustrated in Fig. 7.5 and is shown to highlight a few important points.

The example in Fig. 7.5 expands slightly on the tasks of different staff members. It is not yet a flowchart (the activities are not connected explicitly but they can easily be in a next step) and the details are incomplete (e.g. the tasks of abstractors must be specific to the level of detailing which sources they look at and in which areas of the hospital or laboratory). More formal process maps would document the paths of data (which can be complex) as they are processed by the system, and some, such as the "swim lane" map, would also specify who is assigned to each task.

However, even in such conceptual form, this visual illustration begins to help a programme team have a shared understanding of the processes and tasks involved, as a starting point to develop, criticize and build. For example, in the context of quality improvement, the team might decide to test the use of description checklists at the level of the local staff and central abstractors, and the use of data quality indicators at the central level.

Fig. 7.6 shows a simple mapping example for a birth defects surveillance programme called RENAC, a hospital-based surveillance programme of major structural congenital anomalies that operates in maternity hospitals

**Fig. 7.4. Basic map of key processes**

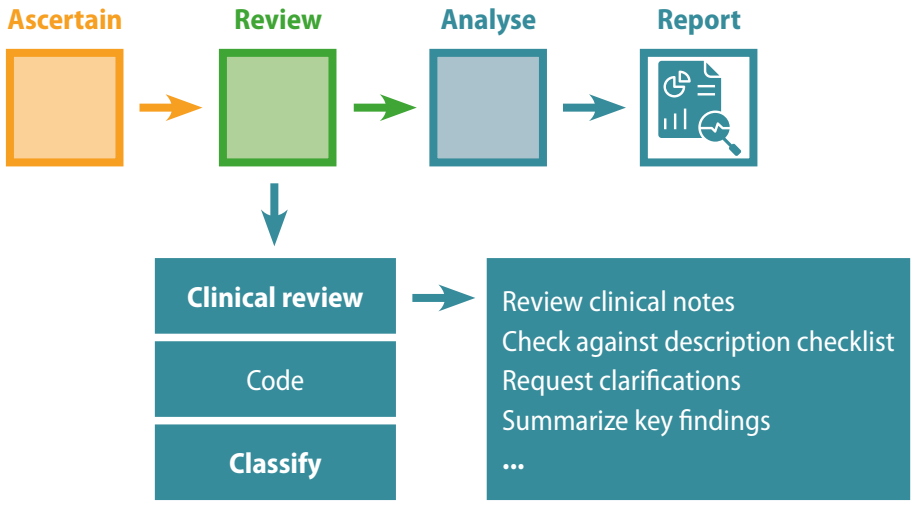


**Fig. 7.5. People and tasks – examples of key processes in birth defects surveillance**

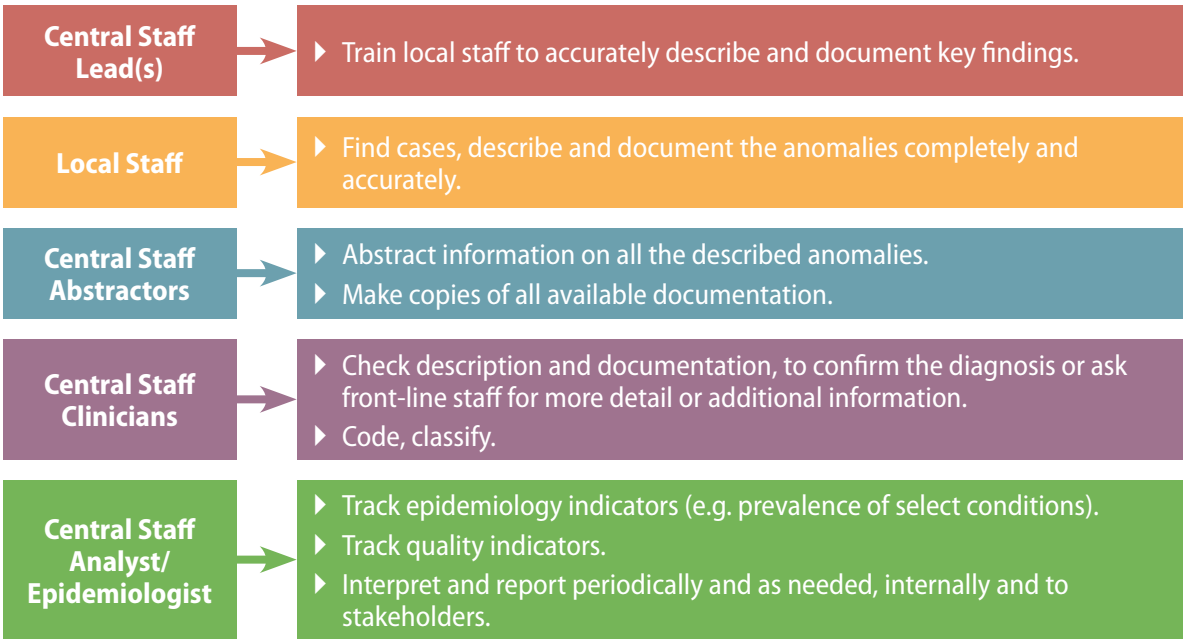
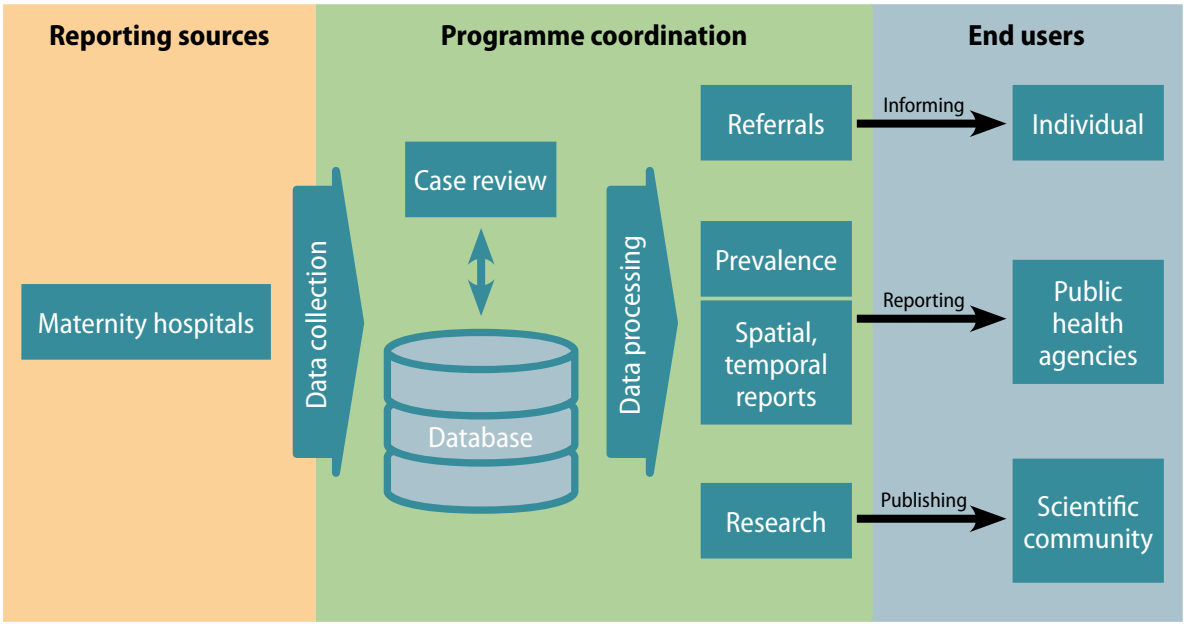



**Fig. 7.6. Example of high-level mapping of a hospital-based surveillance programme**




distributed in the 24 jurisdictions of Argentina. The programme includes live births and stillbirths with major structural congenital anomalies detected from birth until hospital discharge. Pregnancy terminations are not legally allowed in Argentina and are not included in the surveillance system.

In each maternity hospital, two RENAC champions, who are neonatalogists committed to the programme, are in charge of overseeing data collection. Each month, they send reports to the programme coordination team.

All cases are reviewed by the coordination team and submitted data are processed. Information is disseminated to end-users through reports, scientific publications and case referral.

As already noted, such a high-level map is helpful for a broad understanding of the system, and as a starting point for "deep dives" into the specific components. For example, the tasks in the maternity hospital and the interaction with the coordination team can be further expanded (Fig. 7.7a).

Local staff examine every newborn and stillbirth at the hospital, and if congenital anomalies are detected, a neonatologist from the maternity staff documents the findings in writing in a paper form.

Every month, the champions copy the information collected in the paper form into an Excel file. They then send the Excel file to the programme coordinator via a protected online forum. The reports include a verbatim description of the affected cases and a core set of variables.

The champions can send digital photographs of radiographs, clinical photographs or results of additional studies that can contribute to accuracy and completeness of the diagnosis. Sending the reports through the online forum allows timely review and discussion between the programme coordination team and the hospital champions. For example, the central staff can request clarification and the champions can ask for diagnostic support in complex cases, allowing for bidirectional interactions. Each case is then coded using the ICD-10 coding system with the RCPCH modification. This aspect is not clear from the previous illustration, so these steps can be expanded to provide further detail and specification on who is doing what (Fig. 7.7b).

These examples are simple illustrations of what needs to be a systematic and comprehensive approach to visualizing the processes in a surveillance system, so that they are clear, hierarchical, and eventually reach the "decision level" – the level at which specific staff do specific tasks. In doing so, the next steps in quality assessment and quality improvement become clear and shared among the entire team.

## Quality and "waste" in surveillance

It is well recognized that health care, in its current state, has a quality problem – and specifically, large amounts of "waste". Waste here is a technical term that addresses a significant problem in the production of a service through a series of linked processes. Waste is an activity that does not add value to the final product.

**Fig. 7.7a. Example of expanded tasks in maternity hospital and interaction with programme**

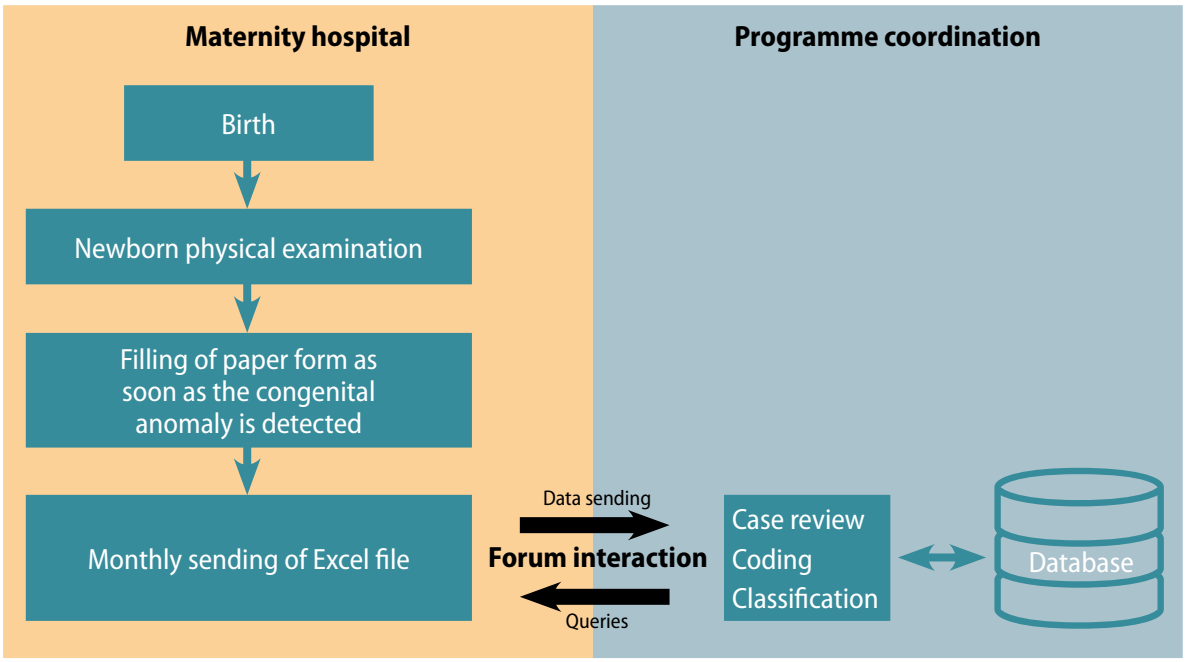
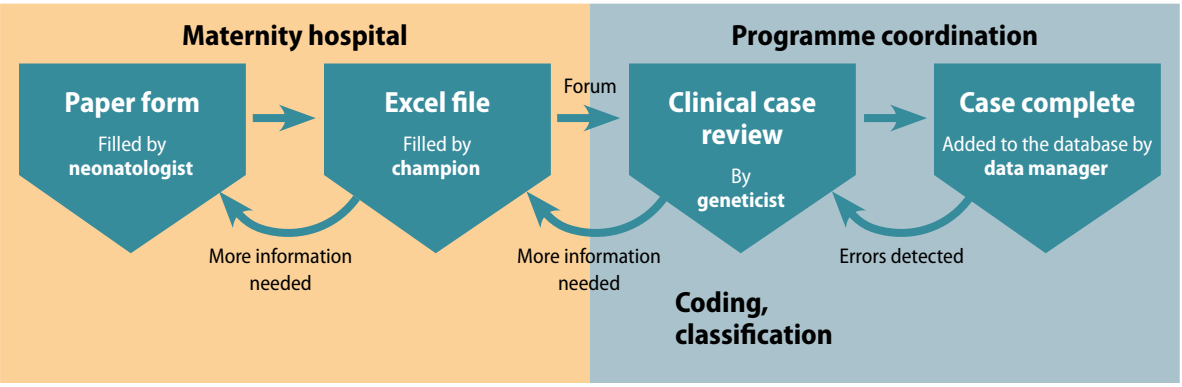


**Fig. 7.7b. Example of expanded tasks by staff in maternity hospital and interaction with programme**




The key insight here is that a crucial way to improve quality is to reduce waste. Waste is everywhere in health care – preventable errors are made every day, causing harm, and creating complications leading to hospitalizations and illnesses. In surveillance, waste is likely everywhere – data are stalled in one or more processes and delay timeliness, cases are missed because of inadequate physical examination or lack of good data sources (e.g. for stillbirths), cases are miscoded and misclassified leading to inaccurate reports and interpretation.

A programme team that wishes to improve quality should investigate such sources of waste and find ways to intervene. The first steps have already been made, leading to a clear visual map of the processes. The elements of data quality can then be tracked across some or all processes using measurable indicators for completeness, accuracy and timeliness.

The search for "waste" needs to start with an understanding of the common types that occur in health care and surveillance. The two most common types are quality waste and inefficiency waste.

Quality waste includes anything in the process that produces a flawed product, or any step in the process that does not add value to the final product. Another type of waste is inefficiency waste, which looks at two processes that generate the same product at different costs; the process that has the higher cost is comparatively inefficient. A major emphasis in industry and health care in recent decades has been not so much to decrease costs but to increase quality at a reasonable cost.

For a surveillance programme, the system is structured as a series of linked processes, aimed at producing a specific product. The product is a specific kind of information, but a product nonetheless. Like any other system, these processes have issues of efficiency, quality and potentially wasted resources. As shown in Fig. 7.8, cases in a birth defects surveillance programme might be missed, miscoded or misclassified.

Fixing the errors can be time and resource intensive, which might require the front-line staff to go back and re-abstract information, clinicians to re-review sets of cases with updated information, and so on. At times the errors might not be fixable; for example, if the primary records are flawed and there is no longer access to the infant, the case data might need to be discarded.

Some lessons can be gleaned so far:

a. Quality assessment is critical but not sufficient. Quality assessment relies on an inspection of the final product, and if a programme waits until the final product, it might be too late to fix the issues.
b. Quality assessment might identify the problem, but cannot solve it. In fact, in most cases, finding a flawed product does not even reveal the origin of the problem.

**Fig. 7.8. Quality waste in surveillance**


So, if quality assessment does not directly translate to better quality, what is the solution? The solution lies in first diagnosing the root causes of the quality problem and then treating it. To do so effectively requires a deep understanding of the processes in the production system. Such understanding comes from a careful and detailed process mapping developed by a team that involves all key staff, including the front-line staff and other personnel who have a fundamental knowledge of the system.

These strategies aim at finding the root causes of quality issues, which in turn helps to identify leverage points for improvement, where small changes can lead to significant increases in quality. For example, if the primary data on birth defects from the physical examination are inaccurate or incomplete, focused training of front-line staff together with systematic use of checklists can lead to large improvements in data quality.

To summarize, quality must not only be checked at the end, it must be built into – embedded into – each step of the process. There is ample justification for intentional and sustained efforts at assessing and improving data quality in public health surveillance. Surveillance generates data for action, and if the data are inaccurate, incomplete or untimely, the benefits of surveillance for public health are curtailed and limited resources are wasted. This primer briefly presents a broad overview of selected issues, such as defining data collected based on programme goals; developing SMART goals that provide meaningful operational guidance to the system; focusing on data quality attributes of completeness, accuracy and timeliness; and finally, mapping the key processes of the surveillance system. Programmes are encouraged to seek out available training and resources for quality improvements.

## Simple tools to improve data quality

Two simple tools that can benefit birth defects surveillance programmes are checklists and data quality indicators.

### *Using checklists*

Checklists have been used in high-reliability, high-complexity organizations and settings – for example, by pilots and surgeons. Checklists help users focus on key tasks, even simple tasks (for example, hand washing

in surgery). Checklists help avoid errors, improve data quality, and increase efficiency, especially in busy or charged environments where pressure and distractions can be significant.

In birth defects surveillance, checklists can be developed at various steps of the processes – ascertainment, clinical case review, analysis, and so on. A particularly important step is the collection of primary data on birth defects at the point of care. None of the other steps in surveillance can obviate the lack of high-quality primary data – especially a detailed description and appropriate documentation of the birth defect.

Training front-line staff and abstractors to use (and if necessary, tailor) a simple but complete checklist is an inexpensive and highly valuable tool for enhancing quality. It also speaks to the main theme of quality improvement, which is to embed quality in each step of the surveillance system and not wait until the end of the process.

A checklist should be simple and practical. An example of a checklist for gastroschisis is shown below that includes a few clearly stated items. Using checklists requires training to ensure that all terms and items are understood.

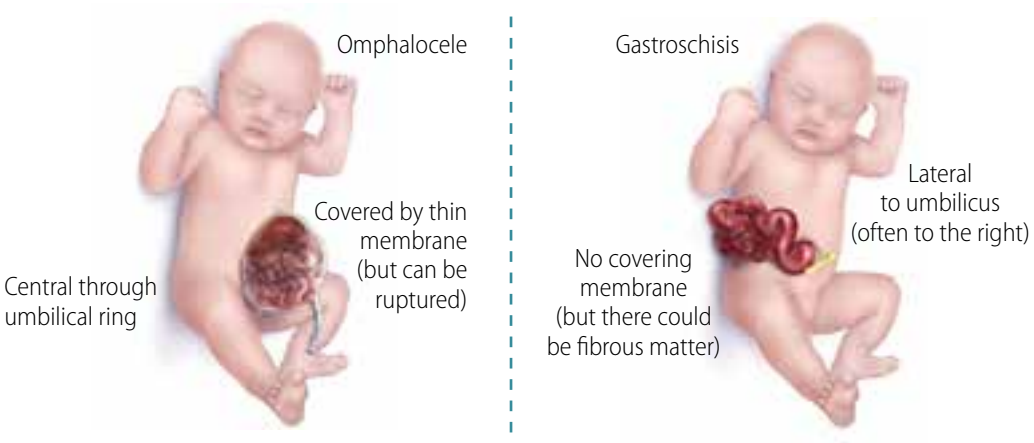
**Gastroschisis – Documentation Checklist**

- ☐ **Describe in detail.** Avoid using only the term "gastroschisis" and specify the following details:
  - **Side** relative to the umbilical cord – right/left.
  - **Covering membranes** – yes/no.
  - **Size** – extension of the abdominal defect (in cm).
  - **Extruded organs** – specify also bowel segment involved.
- ☐ **Take and report photographs:** Show clearly the umbilical cord, which can be crucial for review.
- ☐ **Describe evaluations to find or rule out related and associated anomalies.**
  - If present, describe these anomalies.
- ☐ **Report whether specialty consultation(s) were done** (particularly surgery), **and their results.**

Such a checklist can be improved by integrating visual aids, which can be especially useful for differentiating complex or potentially confusing defects. For instance, the following visual aid can help distinguish gastroschisis from omphalocele (see Fig. 7.9).

The checklists developed for high-quality description and documentation of selected birth defects are available in Chapter 4, where the conditions are fully described.

**Fig. 7.9. Visual aid for differentiating omphalocele and gastroschisis**



### *Using data quality indicators (DQI)*

A second set of tools for data quality is data quality indicators (DQI), which can be used to assess the quality of the "end product" of surveillance – the data. DQI can: (1) assist programmes to focus on areas needing improvement; (2) support data users in interpretation of findings; and (3) provide help in detection of variations (positive or negative) over time and among different sources or sites.

DQI for birth defects surveillance have been proposed by birth defects networks such as the European Network of Population-Based Registries for the Epidemiological Surveillance of Congenital Anomalies (EUROCAT) and the NBDPN. These are useful but tend to be more helpful for surveillance systems in high-resource areas or for specific uses within those networks. Because of the wider focus of the ICBDSR, which includes programmes operating in low-resource settings, a team of ICBDSR members developed a DQI tool that can be used more broadly.

These DQI include four domains that can be mapped to the main processes of a surveillance system: (1) description/documentation, (2) coding, (3) clinical classification and (4) analysis of prevalence (which reflects ascertainment). An example of DQI for gastroschisis is shown below.

| Category | Quality Indicators for Gastroschisis |
|---|---|
| **Description and documentation** | Review sample for documentation of key descriptors:<br>▸ Position with respect to umbilical cord, covering, size, herniated organs.<br>▸ Documentation that includes drawings, photographs and consultation notes. |
| **Coding** | ▸ Track and minimize cases coded with generic ICD-10 RCPCH codes.<br>▸ Q79 is not acceptable for gastroschisis, as it includes other different conditions. |
| **Clinical classification** | ▸ Syndromes are very rare with gastroschisis: Syndromic "gastroschisis" could be a misclassified case of omphalocele, so recommend reviewing those records.<br>▸ Associated anomalies are < 15–20% of cases: A higher proportion suggests that some related conditions (intestinal atresia) are counted as associated, or that misclassification with omphalocele or limb-body wall defect has occurred. |
| **Prevalence** | ▸ Prevalence varies by maternal age and might vary by geography.<br>▸ Prevalence in women < 20 years old and 20–24 years old should be higher than prevalence in women > 24 years old. |

Whereas these DQI can be assessed at the central or programme coordination level, some can be embedded within each step so that potential lapse in quality can be promptly detected and corrected.

DQI for selected birth defects, corresponding to the checklists described above, are also included in Chapter 4. Such sets of DQI can be embedded in easy-to-use tools. An example of an Excel-based tool is freely available for download at http://www.icbdsr.org/data-quality-indicators-tool/ and is further explained in Appendix K. Using this tool, a surveillance programme can input its own data and systematically apply the DQI on specific birth defects. Surveillance programmes can also incorporate these DQI into their data management system to facilitate routine checks.[59 60]

## Concluding remarks

This brief primer covers a basic framework for appreciating and understanding data quality in birth defects surveillance, together with a few strategies to start examining and addressing data quality issues. The road to quality is long, but often, significant successes can be achieved within the first few steps. The key is to continue along the road, as quality can always be improved. The reward is a birth defects surveillance programme that is effective and efficient in supporting public health goals of improved and healthy lives for all children.

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## Glossary of terms

**Abnormality or anomaly:** A deviation or departure from what is typical.

**Abstraction:** The act or process of extracting necessary information from hospital logs or medical records for the identification and classification of congenital anomalies in a case.

**Abstraction form or recording form:** A tool or instrument used in data collection.

**Acalvaria:** Absence of bones of the calvarium with normal skull base, normal facial bones and intact scalp.

**Acephaly:** A term that is inappropriately used occasionally to refer to anencephaly; its meaning – absence of the head – is more correctly applied to the description of acardiac twins.

**Amelia:** Congenital complete absence of an upper or lower limb.

**Amniocentesis:** A medical procedure used to remove a small amount of fluid from the sac that surrounds the fetus in the uterus; it is used most often to: (i) diagnose chromosomal or other genetic disorders early in the second trimester of pregnancy; and (ii) determine fetal lung maturity before birth.

**Amnion:** The inner of the two fetal membranes that form the amniotic sac, which surrounds the embryo or fetus.

**Amniotic band:** Strands of the amniotic sac tissue that entangle limbs or other parts of the fetus, causing disruption of the affected areas.

**Amniotic cavity or sac:** The fluid-filled cavity that surrounds the developing embryo or fetus.

**Anencephaly:** A neural tube defect characterized by partial or complete absence of the brain and skull *(14)*.

**Anomaly:** A deviation from the norm.

**Arnold–Chiari malformation:** A malformation of the brain consisting of downward displacement of the cerebellar tonsils through the foramen magnum.

**Arthrogryposis:** A multiple, nonprogressive congenital joint contracture in two or more body areas *(45)*.

**Ascertaining:** In birth defects surveillance, the process of identifying embryos, fetuses, neonates, infants and children who have a congenital anomaly, using existing sources and case definitions.

**Association:** In birth defects surveillance, a pattern of multiple anomalies that occur with a higher than random frequency, and that is not a sequence or a syndrome.

**Autopsy:** A postmortem examination to determine the cause of death.

**Birth defect:** *See* **Congenital anomaly**.

**Birth outcome:** A group of indicators that help measure the health and well-being of a neonate.

**Birth weight:** The first weight of the fetus or neonate obtained after birth; for live births, birth weight can be measured within the first hour of life before postnatal weight loss has occurred; actual weight is recorded to the degree of accuracy by which it is measured *(12)*.

- **Low birth weight:** Less than 2500 g, up to and including 2499 g.
- **Very low birth weight:** Less than 1500 g, up to and including 1499 g.
- **Extremely low birth weight:** Less than 1000 g, up to and including 999 g.

**Brachydactyly:** A shortening of the fingers and/or toes; at least 13 clinically and genetically distinct groups have been identified.

**British Paediatric Association (BPA)**: *See* **Royal College of Paediatrics and Child Health**.

**Burden of disease:** A time-based measure that combines years of life lost due to premature mortality and years of life lost due to time lived in states of less than full health.

**Capture:** When used in the context of surveillance, indicates that a case has been identified, abstracted and coded.

**Case:** In epidemiological terms, an individual who meets the criteria for inclusion in a surveillance programme. *Note*: Although this term is not commonly used in clinical settings when referring to a patient, it is a term that is widely used in epidemiology.

**Case definition:** The criteria used for inclusion of a case in a surveillance programme.

**Catchment area:** A defined population from which cases for surveillance are collected.

**Caudal dysgenesis:** A developmental anomaly characterized by abnormalities of the lumbar and sacral vertebrae, hypoplasia of the pelvis and lower extremities, and anal abnormalities.

**Central nervous system:** The part of the nervous system consisting of the brain and the spinal cord.

**Chorion:** The outer of the two fetal membranes that form the amniotic sac, which surrounds the embryo or fetus.

**Chorionic villus sampling (CVS):** A medical procedure done late in the first trimester of pregnancy that removes a small piece of placental tissue (chorionic villi) to detect chromosomal abnormalities and other genetic disorders in the fetus.

**Chromosomal abnormality:** The excess or absence (whether total or partial) of a chromosome, or structural changes in the chromosome that most commonly produce a set of intellectual and physical problems (congenital anomalies).

**Cleft lip:** A partial or complete fissure of the upper lip; it can be either unilateral or bilateral, and can be associated with a cleft of the gum.

**Cleft palate:** Fissure of the palate, which can affect the soft and hard palate, or only the soft palate.

**Cleft palate with cleft lip:** An association of a unilateral or bilateral cleft of the upper lip with a fissure of the secondary palate (the hard and soft palate posterior to the incisive foramen).

**Clubfoot, positional:** A normal foot that has been held in an abnormal position in utero and on examination of the neonate is found to be flexible and amenable to moving into a normal position.

**Clubfoot secondary to neuromuscular conditions:** Rigid clubfoot associated with spina bifida, arthrogryposis, myotonic dystrophy and other conditions.

**Clusters:** An unusual combination, whether real or apparent, of health events that are grouped in time or space, or both.

**Confidentiality:** An individual's right to have their personal, identifiable medical information kept secure.

**Congenital:** A condition that occurs during intrauterine life and that might be evident at birth or later in life; it might or might not be genetic.

**Congenital anomaly:** A structural or functional anomaly of organs, systems, or parts of the body that occurs during intrauterine life and is caused by genetic or environmental factors (e.g. exposure to toxic substances, micronutrient deficiencies or maternal diseases), or both.

**Consanguinity:** The relationship among people who descend from a common ancestor.

**Craniorachischisis:** Anencephaly with a contiguous spine defect without skin and meninges covering the neural tissue (rachischisis); it can be limited to the cervical region or affect the entire spine.

**Deformation:** The abnormal form, shape, or position of a part of the body caused by mechanical forces; these forces affect structures after their initial development.

**Disability:** A restriction or lack of ability (resulting from an impairment) to perform an activity in the manner or within the range considered normal for a human being *(12)*.

**Disruption:** A structural defect of an organ, part of an organ, or a larger region of the body, resulting from the extrinsic breakdown of, or an interference with, an originally normal developmental process.

**Dysplasia:** An abnormal organization of cells into tissue(s) and its morphologic results, which most often affect skin, brain, cartilage, or bone.

**Embryo:** The term given to the product of conception from implantation through the first eight weeks after conception (equivalent to 10 weeks of gestation computed from the day of the last menstrual period).

**Embryology:** The branch of biology and medicine concerned with the study of prenatal development.

**Encephalocele:** A pedunculated or sessile cystic lesion protruding through a defect in the skull; it can contain herniated meninges and brain tissue (encephalocele or meningoencephalocele) or only meninges (cranial meningocele); the vast majority of these defects are covered by skin.

**Epidemiology:** The study of the frequency and distribution of health events and their determinants among human populations, and the application of such research to the prevention and control of health problems.

**Exclusion criteria:** The specific factors or characteristics that define an individual and that are not considered as a case.

**External congenital anomaly:** A type of anomaly that can be identified by inspection during physical examination.

**Fetal death:** A fetus that is deceased at delivery; fetal death refers to death prior to the complete expulsion or extraction of a product of conception from its mother, irrespective of the duration of pregnancy; the death is indicated by the fact that, after such separation, the fetus does not breathe or show any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles *(12)*.

**Folic acid:** The synthetic form of vitamin B9 used in fortified foods and supplements; folic acid is more bioavailable than the natural form – folate – found in foods.

**Gastroschisis:** A congenital fissure of the anterior abdominal defect lateral to the umbilicus, accompanied by herniation of the small intestine and part of the large intestine, and occasionally other abdominal organs.

**Gestational age:** The time elapsed, measured in weeks, since conception. Because the exact date of conception is not always known, gestational age might also be defined as the time elapsed from the first day of the woman's last normal menstrual cycle. The duration of a normal pregnancy can range from 38 to 42 weeks. Gestational age is frequently a source of confusion when calculations are based on menstrual dates; for the purposes of calculation

of gestational age from the date of the first day of the last normal menstrual period and the date of delivery, it is borne in mind that the first day is day 0 and not day 1; days 0–6 therefore correspond to "completed week 0"; days 7–13 to "completed week 1"; and the 40th week of actual gestation is synonymous with "completed week 39"; where the date of the last normal menstrual period is not available, gestational age is based on the best clinical estimate; in order to avoid misunderstandings, tabulations are indicated in both weeks and days *(12)*.

- **Pre-term or premature:** Less than 37 completed weeks (less than 259 days) of gestation.
- **Term:** From 37 completed weeks to less than 42 completed weeks (259 to 293 days) of gestation.
- **Post-term:** Forty-two completed weeks or more (294 days or more) of gestation.

**Gum:** The mucosal tissue surrounding the maxilla and mandible.

**Health risk:** The likelihood of suffering ill-health, disease, or an adverse effect.

**Hemianencephaly:** *See* **Hemicephaly.**

**Hemicephaly:** A rarely used synonym for incomplete **anencephaly** or **meroanencephaly**.

**Histogenesis:** The differentiation of cells into the specialized tissues forming the various organs and parts of the body.

**Holoanencephaly:** A rarely used term to describe a type of anencephaly characterized by the bone defect extending through the foramen magnum, affecting the entire skull.

**Holoprosencephaly:** A malformation of the forebrain commonly associated with severe central cleft lip and premaxillary agenesis.

**Hospital-based surveillance programme:** A programme aimed at capturing all birth outcomes with congenital anomalies that occur in selected birthing hospitals. This approach can be useful in locations in which most births occur in hospital settings and a population-based surveillance programme is not feasible.

**Hypoplasia:** The underdevelopment or incomplete development of a tissue or organ.

**Hypospadias:** A common congenital defect of the male external genitalia in which the urethral meatus opens in the ventral side (underside) of the penis.

**Incidence:** The number of new cases of a disease among a given population and over a given time frame; not used when reporting congenital anomalies (*see* **Prevalence**).

**Inclusion criteria:** The specific factors or characteristics that define a case.

**Infancy period:** The time from birth to one year of age.

**Infant mortality:** A demographic indicator that shows the number of deaths among children in their first year of life out of every 1000 live births registered.

**Informed consent:** An agreement to participate in a study or procedure after receiving and understanding full disclosure of the risks and benefits of participation.

**Iniencephaly**: A rare and complex neural tube defect involving the occiput and inion, resulting in extreme retroflexion of the head, variably combined with occipital encephalocele or rachischisis of the cervical and thoracic spine; in iniencephaly, the cranium is always closed, which helps to differentiate iniencephaly from cases of anencephaly with spinal retroflexion.

**Inion:** The most prominent projecting point of the occipital bone at the base of the skull.

**Intercalary limb deficiency:** The complete or partial absence of proximal or middle segment(s) of a limb, with all or part of the distal segment present.

**Internal congenital anomaly:** An anomaly that requires imaging techniques, surgery, autopsy or other specialized procedures to detect.

**International Clearinghouse on Birth Defects Surveillance and Research (ICBDSR):** An international non-profit organization affiliated with WHO, whose mission is to bring together birth defects programmes from around the world, with the aim of conducting worldwide surveillance and research to prevent birth defects and to ameliorate their consequences.

***International Statistical Classification of Diseases and Related Health Problems*, 10th revision (ICD-10):** The standard diagnostic classification tool for epidemiology, health management and clinical purposes. It includes an analysis of the general health situation of population groups and monitoring of the incidence and prevalence of diseases and other health problems in relation to other variables, such as the characteristics and circumstances of the individuals affected, reimbursement, resource allocation, quality and guidelines *(12)*.

**Isolated anomaly:** A single anomaly; most (about 75% in the aggregate) congenital anomalies present as an isolated anomaly. Occasionally, an isolated major anomaly is associated with one or more minor anomalies.

**Limb deficiency:** An anomaly in limb development, characterized by the total or partial absence or different degrees of hypoplasia and abnormal shape of the skeletal structures of the limbs.

**Limb–body wall complex:** A complex anomaly involving lateral body wall defects, limb reduction defects, and occasionally neural tube defects, heart defects and other anomalies.

**Live birth:** The complete expulsion or extraction of a product of conception from a woman's body, irrespective of the duration of the pregnancy, which, after such separation, breathes or shows any other evidence of life such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles, whether or not the umbilical cord has been cut or the placenta is attached. Each product of such a birth is considered live born *(12)*.

**Logic model:** A visual element depicting how a programme operates, including the theories and assumptions underlying the programme; a logic model links outputs (both short- and long-term) with programme activities and the theoretical assumptions of the programme.

**Longitudinal limb deficiency:** The partial absence of a limb bone or segment extending parallel with the long axis of the limb and involving the preaxial, postaxial or central components.

**Major congenital anomaly:** A structural change that has significant medical, social or cosmetic consequences for the affected individual; this type of anomaly typically requires medical intervention.

**Malformation:** A structural defect of an organ, part of an organ, or a larger region of the body that arises during organogenesis (initial formation of a structure). For most organs, organogenesis takes place during the first eight weeks after fertilization; the resulting structure can be abnormally formed or incompletely formed, or might fail to form altogether. The term is occasionally used, incorrectly, as a synonym for birth defect.

**Meninges:** The membranes covering the brain and spinal cord.

**Meningocele:** A type of spina bifida characterized by herniation of the meninges through a spine defect, forming a cyst filled with cerebrospinal fluid. It does not contain the spinal cord, but can have some nerve elements.

**Meningomyelocele:** The most common type of spina bifida, constituting about 90% of all cases. It consists of a protrusion of the meninges and the spinal cord through an opening in the vertebral column, and most frequently is located in the lumbosacral area. It is also referred to as myelomeningocele.

**Meroanencephaly:** A rarely used term to describe a type of anencephaly characterized by the bone defect being limited to the anterior part of the skull.

**Microcephaly**: A disorder in which the head circumference is two or more standard deviations smaller than the average for sex and age, associated with microencephaly and, in some cases, with altered structure of the brain and neurodevelopmental problems. The presence of a head circumference less than two standard deviations below the mean for sex and age without evidence of structural abnormalities of the brain is not considered a major anomaly.

**Midline cleft of the upper and/or lower lip:** Vertical cleft in the centre of, more commonly, the upper lip; the prevalence is low and it is usually part of a syndrome.

**Minor congenital anomaly:** A structural change that poses no significant health problem and tends to have limited social or cosmetic consequences for the affected individual.

**Miscarriage:** A spontaneous loss for a clinical pregnancy before 20 completed weeks of gestational age (18 weeks after fertilization) or, if gestational age is unknown, the loss of an embryo or fetus of less than 400 g *(46)*.

**Monitor:** In birth defects surveillance, to watch, observe or check for the presence of congenital anomalies or diseases over a period of time.

**Morbidity:** The incidence or prevalence of a disease, or of all diseases in a population, in a given space and over time *(47)*. Morbidity is an important statistic in understanding the evolution, progress or regression of a disease, as well as the reasons for its appearance and potential solutions.

**Mortality rate:** A demographic indicator that shows the number of deaths within a population per each 1000 inhabitants during a given time frame (generally one year).

**Multifactorial:** Arising through the action of many factors; in genetics, arising as the result of the interaction of several genes, and usually non-genetic (environmental) factors.

**Mutation:** A permanent change in the DNA sequence of a gene.

**Myelocele or myeloschisis:** A type of spina bifida in which the open spinal cord, covered by a thin membrane, protrudes through a defect in the vertebral column.

**Neonatal death:** Deaths among liveborn infants during the first 28 completed days of life; neonatal deaths can be subdivided into early neonatal deaths, occurring within the first seven days of life, and late neonatal deaths, occurring after seven but before 28 completed days of life; the age at death during the first day of life (day 0) is recorded in units of completed minutes or hours of life; for the second (day 1), third (day 2) and through 27 completed days of life, the age at death is recorded in days *(12)*.

**Neonatal period:** The period that commences at birth and ends 28 completed days after birth.

**Neonate:** An infant in the first 28 days after birth.

**Neural tube:** The part of the embryo from which the brain and spinal cord develop.

**Neural tube closure:** Process by which the neural folds fuse to form the neural tube; it occurs within the first 28 days after conception.

**Neural tube defect:** A failure of the neural tube to close correctly.

**Oblique facial clefts:** The term given to orofacial clefts, which fall into four groups based on their position –

midline clefts, paramedian clefts, orbital clefts and lateral clefts.

**Oligohydramnios:** A diminished amount of amniotic fluid.

**Omphalocele:** A congenital defect of the anterior abdominal wall in which the herniated intestines and abdominal organs are usually covered by a membrane consisting of peritoneum and amnion. The abdominal contents are herniated through an enlarged umbilical ring and the umbilical cord is inserted in the distal part of the membrane covering the defect.

**Organogenesis:** The process through which the ectoderm, endoderm and mesoderm organize to develop the organs and systems of the body.

**Orofacial cleft:** The term used to refer to a cleft palate, a cleft lip or both.

**Pathogenesis:** The mechanisms or cellular events in the development of a pathologic condition or disease.

**Perinatal period:** The period that commences at 22 completed weeks (154 days) of gestation (the time when birth weight normally is 500 g) and ends seven completed days after birth *(12)*.

**Phocomelia:** An intercalary limb defect that refers to the congenital absence of an arm and forearm with the hand present, or the absence of a thigh and lower leg with the foot present.

**Policy-maker:** A person who determines or influences policies and practices.

**Polymorphism:** Variations in the DNA sequence of a gene or in the structure of a chromosome that have no adverse effects on the individual and are not due to new mutations. They occur with a frequency of at least 1% among the general population.

**Population-based surveillance programme:** A collection of data about a population residing in a defined geographical area.

**Preconception care:** Health care received before a woman becomes pregnant, with the purpose of helping reduce her risk for adverse pregnancy outcomes.

**Prenatal screening:** A systematic search for a specific condition among a large, asymptomatic subpopulation of pregnant women selected by personal or family history, or by demographic characteristics such as age and ethnicity; typically, it identifies at-risk groups for further diagnostic testing.

**Pregnancy outcome:** The result of conception and ensuing pregnancy, including live birth, stillbirth, spontaneous abortion and induced abortion.

**Prevalence:** A measure of the total number of existing cases of a condition, known as prevalent cases, for a given point in time or period, and among a given population, regardless of whether or not they are new cases; also an indicator of the magnitude of the occurrence of a disease or other health event in the population.

In birth defects epidemiology, the terms *live birth prevalence*, *birth prevalence* and *total prevalence* are used:

- **Live birth prevalence of congenital anomalies:** Measures the number of cases with congenital anomalies among live births and is defined as number of cases of live births with any congenital anomaly (numerator) among a defined cohort of live births (denominator). For example, the live birth prevalence of congenital anomalies in 2014 is computed as live births born with any congenital anomaly in 2014 divided by all live births born in 2014.
- **Birth prevalence of congenital anomalies:** Measures the number of cases with congenital anomalies among live births and fetal deaths (stillbirths), and is defined as number of cases of live births

and fetal deaths (stillbirths) with any congenital anomaly (numerator) among a defined cohort of live births plus fetal deaths (stillbirths) (denominator). For example, the birth prevalence of congenital anomalies in 2014 is computed as live births plus fetal deaths (stillbirths) with any congenital anomaly in 2014 divided by all live births plus fetal deaths (stillbirths) in 2014.

- **Total prevalence of congenital anomalies:** Measures the number of cases with congenital anomalies in live births, fetal deaths (stillbirths), plus elective terminations of pregnancy for fetal anomaly, and is defined as number of cases of live births, fetal deaths (stillbirths), elective terminations of pregnancy for fetal anomaly (numerator) among a defined cohort of live births, fetal deaths (stillbirths) and elective terminations (denominator). For example, the total birth prevalence of congenital anomalies in 2014 is computed as live births and fetal deaths (stillbirths) with any congenital anomaly plus elective terminations of pregnancy for fetal anomaly in 2014 (numerator) divided by all live births and fetal deaths (stillbirths) in 2014 plus all elective terminations of pregnancy for fetal anomaly occurring in 2014.

**Primary palate:** The front part, anterior to the incisor foramen, of the shelf separating the oral and nasal cavities, which is formed during early embryonic development.

**Privacy:** An individual's right to control the acquisition, use and disclosure of their identifiable health information.

**Pseudocleft:** A rare congenital anomaly that has the appearance of a cleft lip corrected in utero; it is also known as congenitally healed cleft lip.

**Public health:** The discipline responsible for protecting the health of a population; its purpose is to improve population health and to control and eradicate diseases.

**Public health surveillance:** The systematic, continuous, timely and reliable collection of relevant and necessary data regarding certain health conditions among a population; analysis and interpretation of the data must provide grounds for decision-making and be disseminated.

**Reproductive age:** The age at which a woman is biologically capable of becoming pregnant. WHO characterizes this as being 15 to 49 years of age.

**Risk factor:** A characteristic, attribute, circumstance or exposure that is detectable among individuals or groups and is associated with an increased likelihood of a disease, congenital anomaly or other health problem.

**Royal College of Paediatrics and Child Health:** Formerly known as the British Paediatric Association (BPA); developed an adaptation of the ICD-10 by adding an extra digit to the ICD-10 codes, to expand, and allow for more detailed, coding.

**Secondary palate:** The roof of the mouth posterior to the incisor foramen; the front, bony part is known as the hard palate, and the back part, consisting of muscular tissue and mucous membrane, as the soft palate.

**Security:** The technological and administrative safeguards and practices designed to protect data systems against unwarranted disclosure, modification or destruction.

**Sentinel surveillance programme:** A collection of data generally set up at one or a few sites, to obtain rapid estimates of the occurrence of a birth outcome.

**Sequence:** A pattern of multiple anomalies derived from a single known or presumed primary anomaly or mechanical factor. It represents a cascade of events that are consequences of a single primary malformation, disruption or deformation, and is considered an isolated anomaly, except when it is part of a syndrome.

**Single-gene defect:** A change (**mutation**) in the structure of a specific gene.

**Sirenomelia:** A lethal pattern of congenital anomaly, consisting of underdevelopment of the caudal pole of the body, characterized by fusion of the legs, absence of the sacrum, kidney agenesis, abnormal genitalia and imperforate anus.

**Spina bifida:** A general term used to describe a congenital defect of the spine caused by a failure of the posterior elements of the vertebrae to close, resulting in exposure of the meninges, with or without associated spinal cord herniation. It is most often located in the lumbar or sacral portion of the spine, and usually affects two or three vertebrae, although sometimes more vertebrae might be affected.

**Spina bifida occulta:** A relatively common anomaly that affects the spinous process and lamina of the posterior process, usually at the level of the fifth lumbar or the first sacral vertebra, and is covered by the skin. It is a relatively common anomaly that affects the spinous process and lamina of the posterior process, usually at the level of the fifth lumbar or first sacral vertebra, and is covered by skin. Spina bifida occulta is not considered a major congenital anomaly.

**Stakeholder:** An individual who is involved in or affected by a course of action.

**Stillbirth:** WHO defines stillbirth as third trimester fetal death (1000 g or more; 28 weeks or more) for international comparison purposes. However, in broader terms, a stillbirth is a fetal death after the gestational age of viability. The definition of viability is based on gestational age and/or weight, and is variable among countries.

**Submucous cleft:** A midline notch, covered by mucosa, in the bony segment of the secondary palate.

**Surveillance programme:** A public health programme that collects, monitors, analyses, interprets and disseminates data systematically in a timely manner, and that allows for planning, implementation and evaluation of health strategies.

**Syndrome:** A pattern of multiple anomalies thought to be pathogenetically related and not representing a sequence; it is due to a single cause – genetic or environmental – or to gene–environment interactions.

**Talipes equinovarus:** A deformity involving one or both feet, consisting of malalignment of the calcaneotalar–navicular complex.

**Transplacentally:** Passing through, or occurring across, the placenta.

**Transverse limb deficiency:** The complete or partial absence of distal structures of a limb in a transverse plane at the point where the deficiency begins, with proximal structures being essentially intact.

**Trend:** The general tendency in a set of data.

**Teratogen:** An agent capable of interrupting or altering the normal development of an embryo or fetus, often resulting in a congenital anomaly or embryonic or fetal death.

**United States Centers for Disease Control and Prevention (CDC):** A leading health protection agency, based in the United States of America, that collaborates with partners throughout the nation and the world to create expertise, information and tools that people and communities need to protect their health through health promotion, prevention of disease, injury and disability, and preparedness for new health threats.

**Urethral meatus:** The external opening of the urethra.

**Uvula, absence:** Congenital absence of the uvula is a minor anomaly occasionally seen as an isolated defect and, more frequently, in association with submucous cleft palate.

**Uvula, cleft:** A common minor anomaly in which the uvula is totally or partially bifurcated.

**Validation:** In surveillance, a process to evaluate surveillance data, using a quality control protocol that covers the integrity, consistency, uniformity and reliability of the data.

**Vital records:** Records of life events kept under governmental authority, including fetal death certificates, birth certificates, adoption records, legitimation, marriages, divorces and death certificates.

**World Health Organization (WHO):** The directing and coordinating authority for health within the United Nations system, responsible for providing leadership on global health matters, shaping the health research agenda, setting norms and standards, articulating evidence-based policy options, providing technical support to countries, and monitoring and assessing health trends.

# Appendix A

**Suggested initial list of congenital anomalies to consider for monitoring and relevant ICD-10 codes**

| Congenital anomaly | ICD-10 code *(12)* |
|---|---|
| **Congenital malformations of the nervous system** | |
| Anencephaly | Q00.0 |
| Craniorachischisis | Q00.1 |
| Iniencephaly | Q00.2 |
| Encephalocele | Q01.0–Q01.2, Q01.8, Q01.9 |
| Spina bifida | Q05.0–Q05.9 |
| **Cleft lip and cleft palate** | |
| Cleft palate | Q35, Q35.1, Q35.3, Q 35.5, Q35.59, Q35.9, Q87.0 |
| Cleft lip | Q36, Q36.0, Q36.9, Q36.90, Q36.99 |
| Cleft palate with cleft lip | Q37, Q37.0, Q37.1, Q37.2, Q37.3, Q37.4, Q37.5, Q37.8, Q37.9, Q37.99 |
| **Congenital malformations of genital organs** | |
| Hypospadias | Q54.0–Q54.4, Q54.8, Q54.9 |
| **Congenital malformations and deformations of the musculoskeletal system** | |
| Talipes equinovarus | Q66.0, Q66.1, Q66.4, Q66.8 |
| Reduction defects of upper limb | Q71.0–Q71.6, Q71.8, Q71.9 |
| Reduction defects of lower limb | Q72.0–Q72.9 |
| Reduction defects of unspecified limb | Q73.0, Q73.1, Q73.8 |
| **Abdominal wall defect** | |
| Exomphalos/omphalocele | Q79.2 |
| Gastroschisis | Q79.3 |

# Appendix B

## External minor congenital anomalies

| Congenital anomaly | ICD-10 *(12)* or RCPCH code *(37)* |
|---|---|
| **Eye** | |
| Congenital ectropion | Q10.1 |
| Congenital entropion | Q10.2 |
| Absence of eyelashes | Q10.3 |
| Dystopia canthorum | Q10.3 |
| Epicanthal folds | Q10.3 |
| Epicanthus inversus | Q10.3 |
| Fused eyelids | Q10.3 |
| Long palpebral fissure(s) | Q10.3 |
| Upward or downward slanting palpebral fissures | Q10.3 |
| Short palpebral fissures | Q10.3 |
| Long eyelashes | Q10.3 |
| Weakness of eyelids | Q10.3 |
| Stenosis or stricture of lacrimal duct | Q10.5 |
| Coloboma of iris | Q13.0 |
| Brushfield spots | Q13.2 |
| Iris freckles | Q13.2 |
| Blue sclera | Q13.5 |
| Exophthalmos | Q15.8 |
| Strabismus | Q15.8 |
| **Ear** | |
| Accessory tragus | Q17.0 |
| Auricular tag or pit | Q17.0 |
| Double ear lobule | Q17.0 |
| Ear pit or tag | Q17.0 |
| Preauricular appendage, tag or lobule | Q17.0 |
| Large ears | Q17.1 |
| Macrotia | Q17.1 |
| Absent tragus | Q17.3 |
| Asymmetric sized ears | Q17.3 |

| | |
|---|---|
| Crumpled ears | Q17.3 |
| Cup ear | Q17.3 |
| Ear lobe crease | Q17.3 |
| Ear lobe notch | Q17.3 |
| Lack of helical fold | Q17.3 |
| Lop ear | Q17.3 |
| Misshapen ears | Q17.3 |
| Pointed ear | Q17.3 |
| Primitive shape of ear | Q17.3 |
| Protruding ears | Q17.3 |
| Simple ear | Q17.3 |
| Small ears (excludes true microtia) | Q17.3 |
| Thickened or overfolded helix | Q17.3 |
| Low-set ears | Q17.4 |
| Misplaced ear | Q17.4 |
| Posteriorly rotated ears | Q17.4 |
| Bat ear | Q17.5 |
| Prominent ears | Q17.5 |
| Darwinian tubercle | Q17.8 |
| Narrow external auditory meatus | Q17.8 |
| **Face and neck** | |
| Branchial vestige | Q18.0 |
| Branchial tag or pit | Q18.0 |
| Fistula of auricle, congenital and fistula cervicoaural | Q18.1 |
| Pretragal (commonly referred to as preauricular) sinus and cyst<br>Q18.1 Redundant neck folds | Q18.3 |
| Webbed neck (pterygium colli) | Q18.3 |
| Macrostomia | Q18.4 |
| Microstomia | Q18.5 |
| Hypertrophy of lip, congenital or macrocheilia or large wide lips | Q18.6 |
| Short or long columella | Q18.8 |
| Angular lip pits | Q18.8 |
| Small lips | Q18.8 |
| Short neck | Q18.8 |

| | |
|---|---|
| Thin vermillion border | Q18.8 |
| Synophrys, confluent or medial flare eyebrows | Q18.80 |
| **Peripheral vascular system** | |
| Single umbilical artery | Q27.0 |
| **Nose** | |
| Notched or hypoplastic alae nasi | Q30.2 |
| Anteverted nares | Q30.8 |
| Flat or wide nasal bridge | Q30.8 |
| Small nares | Q30.8 |
| Smooth philtrum | Q30.8 |
| **Mouth** | |
| Cleft uvula | Q35.7 |
| Tongue tie | Q38.1 |
| Macroglossia | Q38.2 |
| Adhesion of tongue | Q38.3 |
| Bifid tongue | Q38.3 |
| Fissure of tongue | Q38.3 |
| Hypoglossia | Q38.3 |
| Hypoplasia of tongue | Q38.3 |
| Microglossia (hypoplasia of tongue) | Q38.3 |
| Ranula | Q38.4 |
| Absent uvula | Q38.5 |
| High arched palate | Q38.50 |
| Aberrant frenula | Q38.6 |
| Broad alveolar ridge | Q38.6 |
| Cleft gum (in the absence of cleft lip) | Q38.6 |
| Natal teeth | Q38.6 |
| **Anus and genitalia** | |
| Anterior anus (ectopic anus) | Q43.5 |
| Imperforate hymen | Q52.3 |
| Embryonal cyst of vagina | Q52.4 |
| Fusion of labia | Q52.5 |
| Fusion of vulva | Q52.5 |
| Prominent clitoris | Q52.6 or Q52.8 |

| | |
|---|---|
| Hypoplastic labia majora | Q52.8 |
| Hypoplastic labia minora | Q52.8 |
| Undescended testicle, unilateral | Q53.1 |
| Undescended testicle, bilateral | Q53.2 |
| Undescended testicle, unspecified | Q53.9 |
| Chordee (without hypospadias) | Q54.4 |
| Hypoplasia of testis and scrotum | Q55.1 |
| Shawl scrotum | Q55.2 |
| Retractile testis | Q55.20 |
| Bifid scrotum | Q55.21 |
| Absent or hooded foreskin of penis | Q55.6 |
| Curvature of penis lateral | Q55.6 |
| Phimosis | Q55.6 |
| Redundant foreskin | Q55.6 |
| Small penis (unless documented as micropenis) | Q55.6 |
| Hydrocele of testis | Q55.8 |
| Scrotalization of phallus | Q55.9 |
| **Foot** | |
| Metatarsus varus or metatarsus adductus | Q66.2 |
| Hallux varus | Q66.3 |
| Congenital pes planus | Q66.5 |
| Hallux valgus | Q66.6 |
| Metatarsus valgus | Q66.6 |
| Pes cavus | Q66.7 |
| Hammer toe, congenital | Q66.8 |
| Long toes | Q66.8 |
| Prominent calcaneus | Q66.8 |
| Prominent heel | Q66.8 |
| Short great toe | Q66.8 |
| Vertical talus | Q66.8 |
| Widely spaced first and second toes | Q66.8 |
| Recessed fourth and fifth toes | Q66.8 |
| Short fourth metatarsus | Q66.8 |
| Short or broad great toe | Q66.8 |

| | |
|---|---|
| Rocker-bottom feet | Q66.8 |
| Overlapping toe | Q66.8 |
| **Head, face, spine and chest** | |
| Facial asymmetry | Q67.0 |
| Compression facies | Q67.1 |
| Dolichocephaly | Q67.2 |
| Flat occiput | Q67.3 |
| Head asymmetry | Q67.3 |
| Plagiocephaly | Q67.3 |
| Squashed or bent nose, congenital | Q67.4 |
| Deviation of nasal septum | Q67.41 |
| Funnel chest | Q67.6 |
| Pectus excavatum | Q67.6 |
| Congenital pigeon chest | Q67.7 |
| Pectus carinatum | Q67.7 |
| Barrel chest | Q67.8 |
| Deformed chest | Q67.8 |
| Prominent sternum | Q67.8 |
| Shield-like chest | Q67.8 |
| **Other musculoskeletal (including limbs)** | |
| Congenital deformity of sternocleidomastoid muscle | Q68.0 |
| Contracture of sternocleidomastoid (muscle) | Q68.0 |
| Congenital torticollis | Q68.0 |
| Camptodactyly | Q68.1 |
| Congenital clubfinger | Q68.1 |
| Long fingers | Q68.1 |
| Overlapping digits, not otherwise specified | Q68.1 |
| Short fourth metacarpal | Q68.1 |
| Single crease fifth finger | Q68.1 |
| Tapered fingers | Q68.1 |
| Short fingers | Q68.1 |
| Clinodactyly | Q68.10 |
| Genu recurvatum | Q68.21 |
| Cubitus valgus | Q68.8 |

| | |
|---|---|
| Hyperextended joints, not otherwise specified | Q68.8 |
| Hyperextended knee | Q68.8 |
| Polydactyly type B of fingers (type B is, by definition, post axial and rudimentary (postminimi); type A is post axial, fully developed is a major anomaly – Q69.02A – and is not a minor anomaly) | Q69.02B |
| Polydactyly type B, not otherwise specified | Q69.02B |
| Polydactyly type B of toes | Q69.22B |
| Syndactyly (involving second and third toes) | Q70.3 |
| Genu valgum | Q74.1 |
| **Other anomalies of skull, face and spine** | |
| Scaphocephaly | Q75.0 |
| Trigonocephaly, other head deformations without synostosis | Q75.0 |
| Hypertelorism | Q75.2 |
| Macrocephaly (includes familial benign macrocephaly) | Q75.3 |
| Hypotelorism | Q75.8 |
| Maxillary hypoplasia or prominence | Q75.8 |
| Micrognathia | Q75.8 |
| Prognathia | Q75.8 |
| Frontal bossing | Q75.8 or Q75.80 |
| Large or small fontanelles | Q75.8 or Q75.80 |
| Metopic suture open to bregma | Q75.8 or Q75.80 |
| Narrow bifrontal diameter | Q75.8 or Q75.80 |
| Prominent occiput | Q75.8 or Q75.80 |
| Prominent or hypoplastic supraorbital ridges | Q75.8 or Q75.80 |
| Third fontanelle | Q75.8 or Q75.80 |
| Spina bifida occulta | Q76.0 |
| Congenital lordosis, postural | Q76.43 |
| **Abdomen** | |
| Diastasis recti | Q79.5 |
| Inguinal hernia | Q79.8 |
| Umbilical hernia | Q79.8 |
| **Skin, breast and other integument** | |
| Skin cyst | Q82.4 or Q84.4 |
| Angioma | Q82.5 |

| | |
|---|---|
| Benign skin neoplasm, pigmented naevus (ear and auditory canal) | Q82.5 |
| Benign skin neoplasm, pigmented naevus (eyelid) | Q82.5 |
| Benign skin neoplasm, pigmented naevus (face) | Q82.5 |
| Benign skin neoplasm, pigmented naevus (lip) | Q82.5 |
| Benign skin neoplasm, pigmented naevus (lower limb, hip) | Q82.5 |
| Benign skin neoplasm, pigmented naevus (other specified site) | Q82.5 |
| Benign skin neoplasm, pigmented naevus (scalp, neck) | Q82.5 |
| Benign skin neoplasm, pigmented naevus (trunk) | Q82.5 |
| Benign skin neoplasm, pigmented naevus (unspecified site) | Q82.5 |
| Benign skin neoplasm, pigmented naevus (upper limb, shoulder) | Q82.5 |
| Café-au-lait spot | Q82.5 |
| Hemangioma (other than face and neck) | Q82.5 |
| Lymphangioma | Q82.5 |
| Noncavernous, single, small hemangioma (4 cm diameter) | Q82.5 |
| Pigmented naevus, congenital non-neoplastic naevus | Q82.5 |
| Birthmark | Q82.50 |
| Naevus flammeus | Q82.51 |
| Port-wine stain | Q82.51 |
| Strawberry naevus | Q82.51 |
| Mongolian spot | Q82.52 |
| Cutis marmorata | Q82.8 or Q84.8 |
| Dimple, hand | Q82.8 or Q84.8 |
| Dimple, shoulder | Q82.8 or Q84.8 |
| Extra or absent hand or interphalangeal creases | Q82.8 or Q84.8 |
| Pilonidal or sacral dimple | Q82.8 or Q84.8 |
| Plantar furrow | Q82.8 or Q84.8 |
| Rectal fissure | Q82.8 or Q84.8 |
| Sole crease | Q82.8 or Q84.8 |
| Vaginal or hymenal tags | Q82.8 or Q84.8 |
| Single transverse palmar crease | Q82.80 |
| Anal tag | Q82.81 |
| Skin tag | Q82.81 |
| Unusual dermatoglyphics | Q82.84 |
| Absent nipple | Q83.2 |

| | |
|---|---|
| Extra nipples (supernumerary nipples) | Q83.3 |
| Supernumerary nipple | Q83.3 |
| Inverted nipples | Q83.8 |
| Small nipple (hypoplastic) | Q83.8 |
| Widely spaced nipples | Q83.8 |
| Monilethrix | Q84.1 |
| Pili annulati | Q84.1 |
| Pili torti | Q84.1 |
| Aberrant scalp hair patterning | Q84.1 or Q84.2 |
| Depigmentary hair changes | Q84.1 or Q84.2 |
| Hair upsweep | Q84.1 or Q84.2 |
| Low posterior hairline | Q84.1 or Q84.2 |
| Persistent lanugo | Q84.2 |
| Congenital hypertrichosis | Q84.20 |
| Absent nails (major if third phalanx is missing) | Q84.3 |
| Enlarged or hypertrophic nails | Q84.5 |
| Pachyonychia | Q84.5 |
| Congenital clubnail, koilonychia, malformation of nail, not otherwise specified | Q84.6 |
| Duplication of thumbnail | Q84.6 |
| Hyperconvex fingernails | Q84.6 |
| Hyperconvex toenails | Q84.6 |
| Hypoplastic fingernails | Q84.6 |
| Hypoplastic toenails | Q84.6 |
| Thickened toenails | Q84.6 |
| Aplasia cutis (major if large) | Q84.8 |

# Appendix C

## Causes of congenital anomalies and classification according to developmental mechanism and clinical presentation

### *Causes of congenital anomalies*

It has been estimated that about one quarter of all congenital anomalies might have a genetic cause *(45)*. However, more recent estimates suggest the proportion could be higher, as advances in cytogenetic and molecular techniques in the last two decades are allowing the identification of previously undetected chromosomal abnormalities, gene mutations and genetic polymorphisms. The two most common genetic causes of congenital anomalies are single-gene defects and chromosomal abnormalities.

Single-gene defects are caused by changes (mutations) in the structure of genes. These are responsible for slightly over 17% of congenital anomalies (*48*). Single-gene defects might be inherited from either one or both parents, or be caused by a sporadic (new) mutation. Single-gene mutations seem to be associated more often with multiple congenital anomalies that are syndromic, rather than with isolated malformations, though new research is increasingly uncovering single-gene defects that cause isolated anomalies, such as cleft lip with or without cleft palate and some types of congenital heart defects.

Abnormalities caused by chromosomal changes are identified in about 10% of children with congenital anomalies *(48)*, and might involve the autosomes or the sex chromosomes. Changes include numerical abnormalities such as having an extra chromosome (e.g. trisomies such as Down syndrome or trisomy 21, trisomy 13 and trisomy 18) or missing a chromosome (e.g monosomies such as monosomy X or Turner syndrome); and chromosomal structural abnormalities such as deletions (e.g. deletion of the proximal region in the long arm of chromosome 22 associated with the DiGeorge and velocardiofacial syndromes) and duplications (e.g. duplication of the short arm of chromosome 9). Chromosomal abnormalities are almost always associated with patterns of multiple congenital anomalies.

Identified environmental and maternal causes are responsible for an estimated 4–10% of congenital anomalies *(49)*. Examples include:

- maternal nutritional status
- exposure to chemicals, and possibly illicit drugs
- maternal infections (e.g. rubella)
- physical factors, such as ionizing radiation and hyperthermia *(49)*
- chronic maternal diseases (e.g. diabetes)
- exposure to known teratogenic prescription medicines (e.g. retinoic acid, valproic acid); for more information on medications, *see* fact sheet from the Organization of Teratology Information Specialists *(50)*.

For approximately 66% of congenital anomalies, the cause remains unknown *(49)*. This group includes those congenital anomalies that are believed to have environmental causes or to be multifactorial. Multifactorial means that multiple undefined gene variants interact with environmental factors to cause a specific anomaly.

Many potential gene–environment interactions have been tested in relation to different congenital anomalies. For example, mutations and polymorphisms of numerous genes – including *TGFA, TGFB3, CYP1A1, NAT1, NAT2* and *GSTT1* – have been studied to determine their level of association with an increased risk for oral clefts in the offspring of women who smoke cigarettes *(51)*. Another example of a gene–environment interaction involves prenatal exposure to phenytoin, a widely used anticonvulsant drug. Phenytoin is associated with structural congenital anomalies in 3–10% of infants exposed to this medication in utero. It has been shown that the presence of congenital anomalies in these infants correlates with reduced activity of epoxide hydrolase, a microsomal enzyme that normally detoxifies phenytoin metabolites *(52)*. When the enzyme epoxide hydrolase

is not working properly, some intermediate teratogenic metabolites do not get eliminated. This can result in a congenital anomaly in the developing fetus.

### *Congenital anomalies according to developmental mechanisms*

#### Malformation

Malformation is a structural defect of an organ, part of an organ, or larger region of the body that arises during organogenesis, that is, during the initial formation of a structure, as a result of an intrinsically abnormal developmental process. For most organs, organogenesis takes place during the first eight weeks after fertilization. The resulting structure might be abnormally formed or incompletely formed, or might fail to form altogether. Although the term malformation is occasionally used to refer to congenital anomalies, it is important to realize that congenital anomalies include more than malformations.

#### Disruption

Disruption is a structural defect of an organ, part of an organ, or larger region of the body, resulting from the extrinsic breakdown of, or an interference with, an originally normal developmental process. Examples of disruption defects include the amniotic band complex, some transverse limb deficiencies, and Moebius sequence (cranial nerve paralyses and limb and other abnormalities).

#### Dysplasia

Dysplasias refer to abnormalities of histogenesis or formation of tissues and most commonly affect skin, brain, cartilage or bone. Dysplasias might be localized (e.g. naevus) or generalized (e.g. achondroplasia and other chondrodysplasias, neurofibromatosis).

#### Deformation

Deformation is an abnormal form, shape or position of a part of the body, caused by mechanical forces. These forces affect structures after their initial development. Examples include intrauterine crowding as a result of twin pregnancies or uterine abnormalities, and oligohydramnios (diminished amniotic fluid) in bilateral renal agenesis leading to Potter sequence (i.e. distinctive facial findings, lung hypoplasia and some cases of clubfoot).

### *Congenital anomalies according to clinical presentation in a child*

#### Isolated

Most major congenital anomalies (about 75%) occur in isolation, meaning that there are no other unrelated major congenital anomalies present. Frequently, isolated major anomalies are associated with one or more minor anomalies.

#### Sequence

A sequence is a pattern of related anomalies that are known, or presumed, to derive from a single primary anomaly or mechanical factor. A sequence represents a cascade of events (anomalies) that are consequences of a single primary malformation, disruption or deformation. Examples include the Robin sequence (in which, because of micrognathia, there is posterior displacement of the tongue, which interferes with closure of the palatal shelves, leading to cleft palate) and clubfoot associated with spina bifida. A sequence is considered an *isolated* anomaly, except when it is part of a syndrome.

#### Multiple congenital anomaly

Multiple congenital anomaly is the occurrence of two or more major anomalies that are unrelated. This means that the major anomalies are presumed to be a random association, and do not constitute a sequence or a previously recognized syndrome. Most cases of multiple congenital anomalies fall into this category.

#### Association

An association is a pattern of multiple anomalies that occur with a higher than random frequency and that is not a sequence or a syndrome. Examples include the VACTERL association (**V**ertebral, **A**nal, **C**ardiac, **T**racheo–

oEsophageal fistula, Renal and Limb defects) and the MURCS association (MUllerian duct aplasia – Renal aplasia – Cervicothoracic Somite dysplasia). As knowledge and techniques advance, some of these entities might be recognized as syndromes. This was the case with the CHARGE association (Coloboma of the eye, Heart defects, Atresia of the choanae, Retardation of growth and/or development, Genital and/or urinary abnormalities, and Ear abnormalities and deafness) that was found in recent years to be caused by a mutation of the *CHD7* gene and is now considered to be a genetically determined syndrome *(53)*.

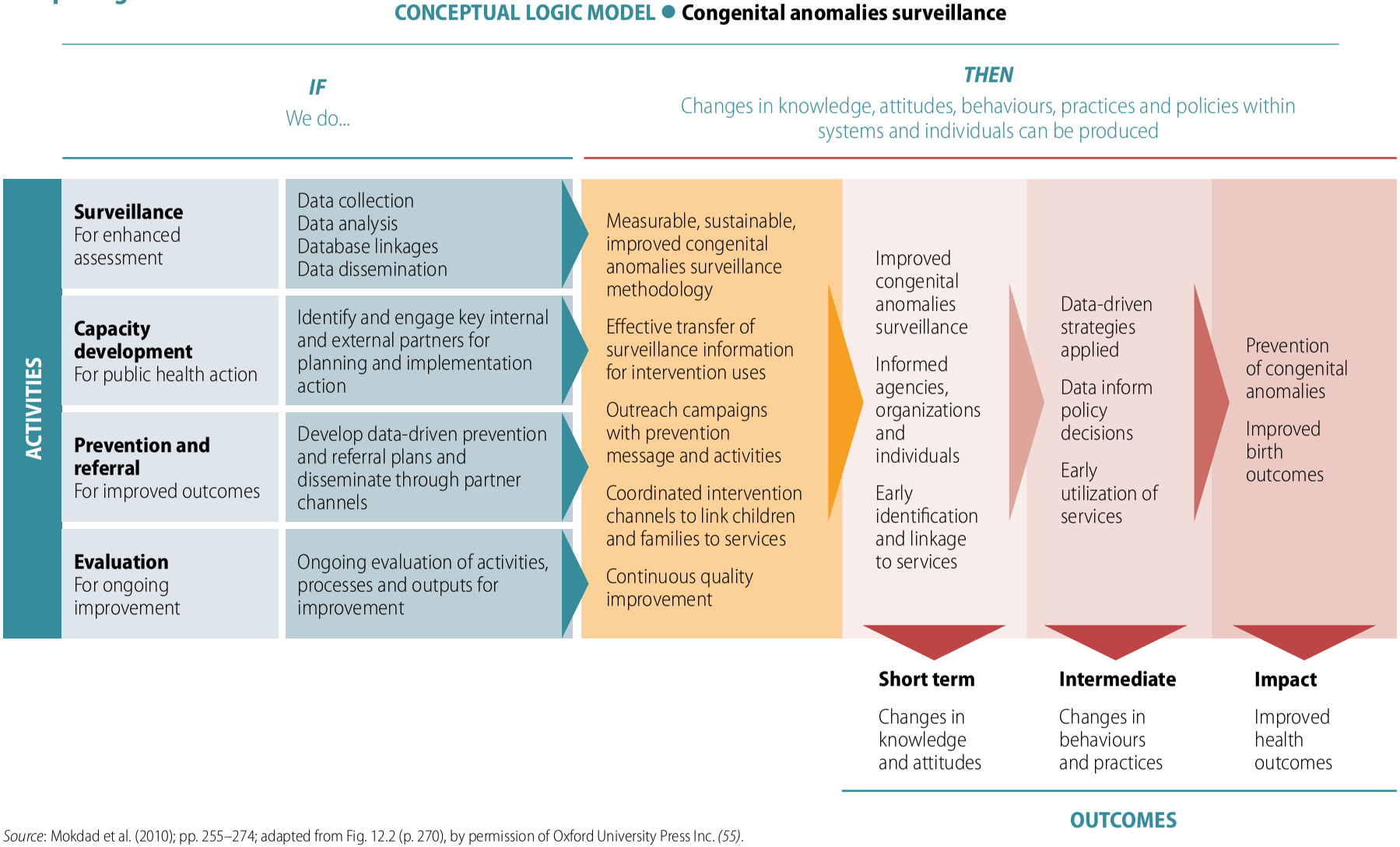
### Syndrome

A syndrome is a pattern of multiple anomalies thought to be pathogenetically related, but not representing a sequence. They are due to a single cause – genetic or environmental – or to gene–environment interactions. Examples include Down syndrome (trisomy 21, a chromosomal abnormality), deletion of the proximal region in the long arm of chromosome 22 (a genomic disorder due to microdeletion), achondroplasia (single-gene disorder) and congenital rubella syndrome (infectious cause). Despite advances in genetics, there are still clinically recognized syndromes for which the cause has not been identified.

For further information on case classification, please refer to Rasmussen et al. (2003) *(54)*.

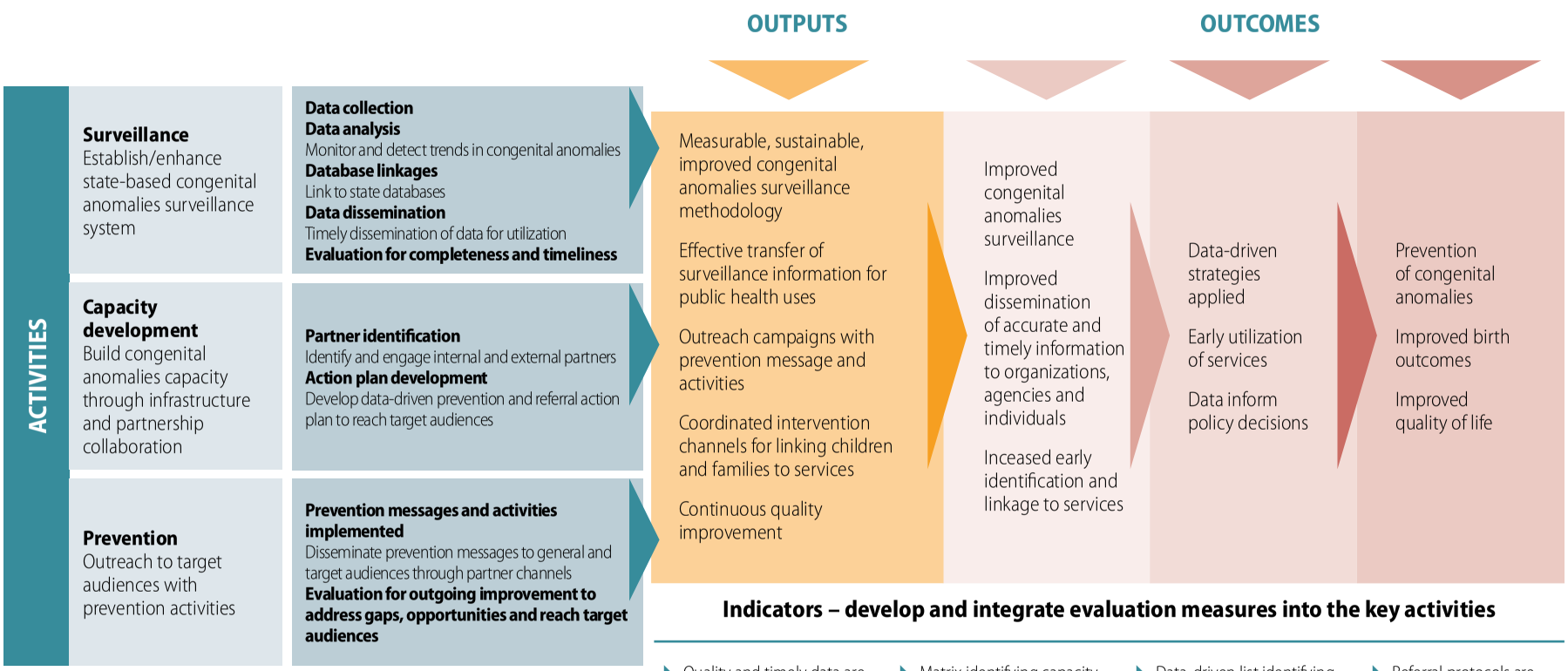
# Appendix D

## Sample logic model




*Source*: Mokdad et al. (2010); pp. 255–274; adapted from Fig. 12.2 (p. 270), by permission of Oxford University Press Inc. *(55)*.

## WORKING LOGIC MODEL ● Congenital anomalies logic model and process indicators




### Indicators – develop and integrate evaluation measures into the key activities

- Quality and timely data are produced and disseminated
- Quality assurance for completeness of data tested through ongoing improvement efforts using statistical methods
- Matrix identifying capacity-building objectives, strategies and partner list developed and approved
- Data-driven prevention and referral plans are developed through partnership engagement
- Ongoing partner meetings take place to exchange progress information and make mid-course modifications
- Data-driven list identifying at-risk populations is developed to guide prevention efforts
- Appropriate prevention partners are engaged and a plan to reach target audiences is developed
- Targeted audiences are reached using appropriate prevention/intervention strategies
- Referral protocols are tested for effectiveness and timeliness
- Baseline data are available to indicate changes in number of referrals and number of persons receiving early intervention and special education services
- Timely referral to service is evidenced

# Appendix E

## Worksheet for capacity development

| Examples of potential partners | Surveillance | Referral | Prevention | Examples of potential roles |
|---|---|---|---|---|
| Ministries of health | X | X | X | Set policies and regulations for health-care services and delivery. |
| Hospitals and, if applicable, hospital associations and clinics | X | X | | Serve as data sources; referral sources. |
| Regional and local health departments | X | X | X | Serve as data sources; conduits to audiences for referral and prevention activities. |
| Primary health centres and health-care providers | X | X | X | Serve as data sources and also as sources for prevention and outreach activities. |
| Community health workers/ community health volunteers | X | X | X | Serve as potential data sources because, in many countries, these individuals are present at the delivery; provide prevention information. |
| Congenital anomalies associations, foundations, and other nongovernmental organizations | X | | X | Provide advocacy for congenital anomalies infrastructure at national and local levels; serve as dissemination channels for prevention activities and messages; potential sources for outcome data; serve as possible data sources. |
| International organizations | X | X | X | Provide advocacy, technical assistance and expertise. |
| Medical schools/research agencies | X | | | Provide specialized laboratory services, such as chromosome analyses, or have clinics where individuals with congenital anomalies are seen; can help drive surveillance of congenital anomalies. |

# Appendix F

## Suggestions for delivering the news of a congenital anomaly diagnosis to a family

*Note*: It is important to remember that abstractors – those individuals who will be extracting information from hospital logs or medical records for the identification and classification of congenital anomalies – do not give information to parents about a diagnosis or services. **This is to be done by a health-care provider**. Please note the following:

- Parents are told about the diagnosis as soon as possible, even if it is suspected but not yet confirmed.
- The diagnosis is communicated in person, by a health-care professional with sufficient knowledge of the condition. Health-care providers should coordinate the message to ensure consistency in the information provided to the family.
- Begin the conversation with positive words and avoid using value judgments when starting the conversation, such as "I'm sorry" or "Unfortunately, I have bad news". Parents remember the exact words of the first contact with the health-care provider even after many years.
- The family is informed of the diagnosis, treatment and prognosis, in their preferred language. If possible, a professional medical interpreter is present at the time of disclosure.
- Discuss the diagnosis, treatment and prognosis in a private, comfortable setting, free from interruptions. The infant might be present in the room unless they are ill. Allow time for questions and make plans for a follow-up conversation. Stop, when possible, to assess for comprehension.
- Parents should be provided with accurate and up-to-date information. Information is normally given with a balanced perspective, including both positive aspects and challenges related to the congenital anomaly.
- Provide the information on diagnosis, treatment and prognosis in a sensitive and caring, yet confident and straightforward manner, using understandable, non-medical terms, and language that is clear and concise.
- Use sensitive language and avoid outdated or offensive terminology. In the neonatal setting, the infant is to be present, and to be referred to by name.
- Assess for knowledge of that specific congenital anomaly, including etiology. Because there might often be guilt or blame associated with congenital anomalies, often placed on the mother, it is important to discuss these issues with the parents.
- Informational resources can be provided, including contact information for local and national support groups, up-to-date printed information or fact sheets, and books. When appropriate, referrals to other specialists might also be helpful (e.g. medical geneticists, genetic counsellors, cardiologists, neonatologists).

*Source*: Suggestions modified from Sheets et al. (2011) *(56)*.

# Appendix G

## Sample abstraction form

**Birth Defects Surveillance Programme**

| | |
|---|---|
| Case record ID:<br>Date of report: (dd/mm/yyyy) | Name of health facility:<br>City:<br>Province/State/Territory: |

**FETUS / NEONATE**

Name, if available:

Date of birth: (dd/mm/yyyy) Date of diagnosis of congenital anomaly: (dd/mm/yyyy)

Sex:
○ male ○ female ○ ambiguous ○ missing/unknown

Outcome at birth:
○ live birth ○ stillbirth
○ elective termination of pregnancy with fetal anomaly

Gestational age: (completed weeks)

Best estimation: ultrasound: LMP: other:

Weight: (grams) Length: (cm)

Head circumference: (cm)

Multiple birth: ○ Yes ○ No If yes, specify:

Photographs taken: ○ Yes ○ No

Did neonate die? ○ Yes ○ No

If yes, specify date of death: (dd/mm/yyyy)

Cause of death:

Autopsy: ○ Yes ○ No If yes, specify details on back of this sheet.

**PARENTS**

Father's given name(s):

Father's family name(s):

Father's date of birth: (dd/mm/yyyy) Father's age: (completed years)

Race/ethnicity:

Mother's given name(s):

Mother's family name(s) (including maiden name):

Mother's date of birth: (dd/mm/yyyy) Mother's age: (completed years)

Race/ethnicity:

Primary address during 1st trimester of pregnancy:

Town/city: Province:

Current address (If different from above):

Town/city: Province:

Telephone number:

Total number of previous: live births: stillbirths:

spontaneous abortions: terminations of pregnancy:

Are parents of fetus/neonate related? ○ Yes ○ No

If yes, specify: ○ first cousins ○ second cousins ○ aunt – nephew ○ uncle – niece ○ other (specify):

| Congenital anomaly present | Full description of congenital anomaly (use back of form if needed) | ICD-10 code | C or P* |
|---|---|---|---|
| 1. | | | ○ C ○ P |
| 2. | | | ○ C ○ P |
| 3. | | | ○ C ○ P |
| 4. | | | ○ C ○ P |
| 5. | | | ○ C ○ P |
| 6. | | | ○ C ○ P |
| 7. | | | ○ C ○ P |
| 8. | | | ○ C ○ P |
| 9. | | | ○ C ○ P |
| 10. | | | ○ C ○ P |

Diagnostic tests performed, pending results, notes and comments:

* C = Confirmed diagnosis
P = Possible diagnosis

Name of professional completing the form: Contact information:
○ physician ○ nurse ○ other (specify):

Additional information for autopsy:

Additional information for congenital anomaly:

# Appendix H

## Potential core variables

The abstraction form can be modified according to the needs of each country. The explanation and instructions that follow can be reviewed accordingly.

The instructions for the abstraction form will help personnel participating in the congenital anomaly surveillance system to clarify doubts about how to fill in the form. Please review the variable column (third column) and the explanation column (fourth column) before completing the form.

Column 1: Variable number; useful when designing the database

Column 2: Different variable categories

Column 3: Variable name

Column 4: Instructions for completing the abstraction form for each particular variable.

| Variable number | Category | Variable name | Instructions |
|---|---|---|---|
| | **Report** | | |
| 1 | | Case record identification | Each case has a unique identification number. Each country can decide how to create the code; for example, the year and month the infant was born can be part of the unique identification. |
| 2 | | Date of report | Indicate the date when surveillance staff complete the form; report the day, month and year. |
| 3 | | Name of health facility | Indicate the name of the hospital where the fetus or neonate with a congenital anomaly was identified. |
| 4 | | City, province, state or territory | Indicate the city, province, state or territory where the delivery took place. |
| | **Father** | | |
| 5 | Identification information and demographic information | Name(s) | Indicate the father's given name(s) and family name(s), depending on what is commonly used in the country. |
| 6 | | Father's date of birth, or age if date of birth is not available | Indicate the father's date of birth. If known, please follow the same system as used in the date of report: day, month and year. If only the year is available, use year; if only age is available, use age. |
| 7 | | Race and ethnicity | Indicate the father's race and ethnicity, if applicable. |

| | | | |
|---|---|---|---|
| | **Mother** | | |
| 8 | Identification information and demographic information | Name(s) | Indicate the mother's given name(s) and family name(s), depending on what is commonly used in the country. Make sure to include her maiden name. |
| 9 | | Mother's date of birth, or age if date of birth is not available | Indicate the mother's date of birth. If known, please follow the same system as used in the date of report: day, month and year. If only the year is available, use year; if only age is available, use age. |
| 10 | | Race and ethnicity | Indicate the mother's race and ethnicity, if applicable. |
| 11 | | Primary address during pregnancy | Indicate the primary address for the mother during pregnancy. |
| 12 | | Current address | Indicate the maternal residence at the time of delivery, such as department and municipality. Use available country coding. |
| 13 | | Telephone number | Indicate the telephone number where the mother can be contacted. |
| | Obstetric history | | |
| 14 | | Total number of pregnancies | Indicate the total number of previous pregnancies: live births, stillbirths (fetal deaths), spontaneous abortions, and terminations of pregnancy. |
| | **Fetus/neonate** | | |
| 15 | Identification information and demographic information | Name, if available | Indicate the fetus's or neonate's given name and family name(s), depending on what is commonly used in the country. |
| 16 | | Date of birth | Indicate the fetus's or neonate's date of birth. If known, please follow the same system as used in the date of report: day, month and year. |
| 17 | | Sex | Indicate the sex of the fetus or neonate, if it is known. In case of ambiguous genitalia, indicate as "ambiguous"; if sex cannot be determined during the autopsy, please indicate as "unknown". |

| | | | |
|---|---|---|---|
| 18 | | Date of diagnosis | Indicate date of diagnosis of congenital anomaly/anomalies; write the date as indicated: day, month and year. |
| 19 | | Outcome at birth | Indicate whether pregnancy resulted in a live birth, fetal death, spontaneous abortion, or termination of pregnancy. |
| | **Birth measurements** | | |
| 20 | | Gestational age | Write the gestational age in weeks; estimate the number of weeks based on the first day of the last normal menstrual period or on a sonogram done during the first trimester, if the information is available. |
| 21 | | Weight | Register the fetus's or neonate's weight in grams. If the fetus or neonate was stillborn, document the weight (use grams if grams are used in the country). |
| 22 | | Length | Register the length in centimetres and use a comma to separate decimals. |
| 23 | | Head circumference | Register the head circumference in centimetres and use a comma to separate decimals. |
| 24 | | Multiple birth (birth order) | Indicate if the birth was multiple and, if yes, the birth order of the fetus or neonate with a congenital anomaly. Complete a form for each fetus or neonate if more than one has a congenital anomaly. Complete only one form if the babies are conjoined twins. |
| 25 | | Photographs taken | If possible, take at least three photographs: (i) the whole fetus or neonate; (ii) the fetus's or neonate's front and back; and (iii) the congenital anomaly/anomalies. Refer to Appendix J for information on taking photographs. |
| 26 | | Parental consanguinity | Indicate any biological relationship between the parents. |
| 27 | | If the neonate was born alive and died, include date of death | Write the date as indicated: day, month and year. |

| | | | |
|---|---|---|---|
| 28 | | Autopsy results | Indicate if an autopsy was performed and if the autopsy findings add to the diagnosis of the congenital anomaly. This information can go on the back of the form. |
| 29 | | Congenital anomaly/ anomalies present | Write the name(s) of the anomaly/ anomalies; list all congenital anomalies present. |
| 30 | | Describe in detail each congenital anomaly | Provide a full description for each congenital anomaly identified. |
| 31 | | Code | Code the congenital anomaly according to the *International classification of disease and related health problems*, 10th revision *(12)*. |
| 32 | | C or P | Indicate whether the diagnosis is confirmed (C) or possible (P) and whether more tests are needed. |
| 33 | | Diagnostic tests performed or pending; notes and comments | Indicate what tests were performed or are needed. Include any other relevant comments. |
| | **Hospital information** | | |
| 34 | | Name and profession of individual completing the form | Identify the name and the profession of the individual completing the form. |
| 35 | | Contact information | Indicate a name and telephone number if more information is needed to complete the form. |

# Appendix I

## Potential optional variables

| Variable number | Category | Variable name | Explanation and instructions |
|---|---|---|---|
| 1 | **Report** | Source of information | Indicate the different data sources inside the hospital where a fetus or neonate with a congenital anomaly is identified (e.g. delivery room or surgery). |
| | **Father** | | |
| 2 | | Occupation/ work | Code according to the 1988 *International standard classification of occupations*; *see* www.ilo.org/public/english/bureau/stat/isco/index.htm. |
| 3 | | Family health history | Indicate if there is someone in the father's family with a congenital anomaly/ anomalies, including the father himself. |
| | **Mother** | | |
| 4 | Demographic information | Civil/marital status | Indicate if the mother is married, single, separated, living with someone but not married, or a widow. |
| 5 | | Occupation/ work at conception | Code according to the 1988 *International standard classification of occupations*; *see* www.ilo.org/public/english/bureau/stat/isco/index.htm. |
| 6 | | Country identification number | This corresponds to any legal document that identifies the mother in each country; use if available in the country. |
| 7 | | Weight (before pregnancy) | Indicate the mother's weight before the pregnancy in kilograms or pounds, according to what the country uses. |
| 8 | | Education (years or highest level) | Indicate the highest level of education achieved by the mother. Refer to the *International standard classification of education* for 1997 for information; *see* http://www.unesco.org/education/information/ nfsunesco/doc/isced_1997.htm. |
| 9 | | Religion | Indicate the religious affiliation of the mother, if applicable. |
| 10 | | Socioeconomic status | Indicate the socioeconomic status of the mother. |

| | | | |
|---|---|---|---|
| | Obstetric history | | |
| 11 | Health | Chronic diseases | Indicate any illness the mother has (e.g. diabetes, epilepsy or infections). |
| | | Date of last menstrual period | Indicate the first day of the last normal menstrual period. Follow the system: day, month and year. |
| 12 | | Prenatal tests | Indicate if the mother received prenatal care services and at which month of pregnancy she started receiving the services. |
| 13 | | Family health history | Indicate if any of the following tests were performed: maternal serum alpha-fetoprotein, amniocentesis, chorionic villus sampling, sonogram or fetal echocardiogram. |
| 14 | | | Indicate if there is someone in the mother's family with a congenital anomaly/anomalies, including the mother herself. |
| | **Infant** | | |
| 15 | Birth information | Type of delivery | Indicate if the delivery was vaginal or by caesarean section; also indicate whether birth was induced. |

# Appendix J

## Suggestions for taking photographs of a fetus or neonate with a congenital anomaly

### *If parental consent is required for taking the photograph*

- Ensure the consent form is signed before taking the photograph.
  - *Note*: If parents do not consent to a photograph, the fetus or neonate can still be included in the surveillance programme.

### *Prior to taking the photograph*

- Have a clean, simple, non-patterned light or dark blue background (no blankets or other things in the bassinet or on the examination table).
- If there are objects on the examination table that affect the photograph, remove them before taking the photograph.

### *When taking the photograph*

- Take a view of the entire fetus or neonate, plus several focused views of the congenital anomaly/anomalies.
- Take a separate view of the face, if possible.
- Take a front or back view, or both, plus a side view, depending on the congenital anomaly.
- Avoid taking photographs at an angle; i.e. take all photographs holding the camera at 90° to the fetus or neonate.
- Use no personal identification; instead use coded identification.
- If more than one photograph is taken, make sure that all photographs can be identified with a code for that particular fetus or neonate.
- Assign identifiers to the photograph files, using a unique code and adding an extra number to indicate the number of photographs taken of the same fetus or neonate (e.g. 0001_1; 0001_2, etc.).
- Place a label next to, but not touching, the fetus or neonate, if needed. Similarly, place a ruler or measuring tape next to, but not touching, the fetus or neonate, to help estimate size.
- Ensure that there is adequate lighting and no shadows in the photograph. Use a flash if needed.
- Consider the cost of photograph storage.

**When a digital camera is used**

- Use high resolution, at least 300 ppi (pixels per inch).
- Review photographs quickly while on site.
- Save the image in jpeg (jpg) format; make sure each photograph is transferred to a computer file or other secure storage before deleting it from the camera.

Tablets or smartphones can also be used to take photographs.

# Appendix K

## Data Quality Indicator (DQI) Excel-based Tool

This DQI tool is freely available for download at http://www.icbdsr.org/data-quality-indicators-tool/. The tool is an Excel file, where a programme can enter its surveillance data and the DQI are automatically calculated. This tool is especially useful for programmes in low-resource settings (e.g. hospital-based with short follow-up, typically until discharge from birth hospital).

The DQI tool focuses on four key surveillance processes: (1) ascertainment, (2) description, (3) coding and (4) classification. A total of 40 quality indicators covering key surveillance processes are included in the Excel tool.

### *(1) Ascertainment DQI*

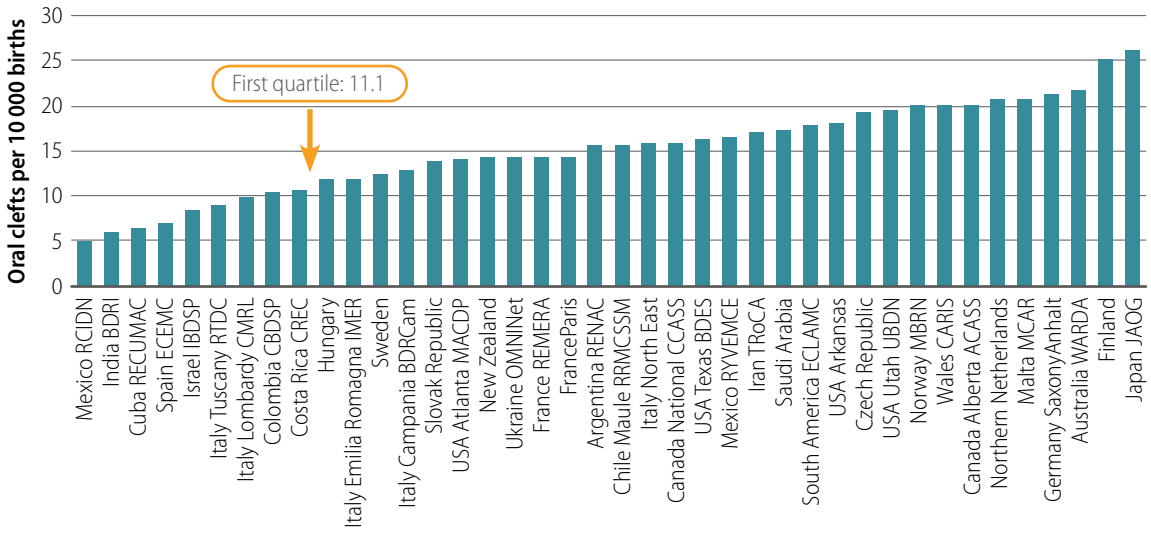
There are two types of ascertainment DQI: threshold values and expected ordering of birth prevalence.

#### Threshold values:

- These values compare the observed prevalence of specific birth defects with a "threshold prevalence", below which under-ascertainment is likely.
- The thresholds are based on the 2003–2012 annual ICBDSR reports for oral clefts, neural tube defects, abdominal wall defects, hypospadias, limb deficiencies and microtia/anotia.
- For the distribution of prevalence in ICBDSR programmes, the first quartile is arbitrarily defined as the threshold value.

In the following bar chart, the ICBDSR programmes are ordered by prevalence of oral clefts. The threshold value is the 1st quartile or 25th percentile.

**Prevalence of oral clefts per 10 000 births**




#### Expected ordering of birth prevalence:

Based on the published literature, it is expected that some subtypes are more frequent than others. For example:

- Cleft lip and palate > cleft palate > cleft lip
- Spina bifida > anencephaly > encephalocele
- Ratio of spina bifida/anencephaly = 1.00–1.33 (acceptable range)
- Gastroschisis > omphalocele

- Gastroschisis among mothers under 20 years old > 20 years old and above
- Transverse limb defects > preaxial defects > postaxial defects
- Upper limb reduction defects > lower limb reduction defects
- Postaxial polydactyly > preaxial polydactyly
- Down syndrome among mothers 35 years and older > under 35 years old.

### *(2) Description DQI*

Description DQI indicate how accurate and complete the description and documentation of birth defects are by the local staff using pre-established criteria. For example, some components of accurate and complete description are:

- Oral clefts: Laterality and extension
- Spina bifida: Level of lesion and skin coverage
- Encephalocele: Site (i.e. occipital, temporal, frontal, etc.)
- Abdominal wall defects: Localization, relation to umbilical cord, membrane covered
- Hypospadias: Degree specified (first, third; if programme includes first degree, assess separately)
- Limb reduction defects: Site (limb and segment) and type (preaxial, postaxial, etc.)
- Feet deformities: Rotation and position
- Congenital heart defects: Type
- Microtia: Degree (second, third, fourth – anotia)

### *(3) Coding DQI*

The coding DQI evaluate if there are errors in the coding process. Some examples include:

- Medial cleft lip miscoded as a typical cleft
- Cleft lip and palate coded using two codes (Q35 & Q36)
- Hypospadias coded as ambiguous genitalia (as the only diagnosis)
- Gastroschisis coded as a ruptured omphalocele.

### *(4) Classification DQI*

Classification DQI evaluate the distribution as isolated, multiples (multiple congenital anomalies [MCA]), and syndromes, for those birth defects whose typical distribution is well known from the literature. For example:

- Percentage syndromic and MCA cases in **cleft palate** > in **cleft lip with or without cleft palate**
- Percentage syndromic and MCA cases in **encephalocele** > in **spina bifida**
- **Omphalocele:** Percentage of MCA and syndromic cases > isolated
- **Gastroschisis:** Percentage isolated > 80%
- **Hypospadias:** Percentage isolated > 80%

These DQI of ascertainment, coding, classification can be proportions, sentinel or ratios.

- *Proportion-based DQI*: Expressed as percentage. The numerator is the number of cases with an accurate description of a birth defect, and the denominator is the total number of cases with that birth defect. For example, the proportion of cleft lip cases with laterality specified.
- *Sentinel DQI*: A sentinel indicator identifies the occurrence of events that are intrinsically (always) undesirable, and that should trigger further analysis and investigation. These undesirable events likely reflect a deficiency in data quality (for example, very low prevalence of a birth defect might be due to under-ascertainment). Sentinel indicators were marked as "achieved" or "not achieved".
- *Ratio DQI*: Quotient between two prevalences. For example, the ratio of spina bifida/anencephaly.

The DQI tool includes the following birth defects:

- Oral clefts
- Neural tube defects
- Omphalocele
- Gastroschisis
- Hypospadias
- Limb deficiencies
- Talipes equinovarus
- Critical congenital heart defects
- Microtia/anotia
- Polydactyly
- Down syndrome

The DQI for oral clefts included in the Excel tool are shown below.

*Note:* In the rightmost column of this and the following tables, the codes refer to the number of cases with that code. For example, "Q35.x + Q36.x + Q37.x" means "number of cases coded Q 35.x + number of cases coded Q36.x + etc."

| Birth Defect | Data Quality Indicator (DQI) | Surveillance Process Assessed | DQI Type | General Definition | Operational Definition by ICD-10 RCPCH codes (1) |
|---|---|---|---|---|---|
| Oral clefts | Minimum prevalence | Ascertainment | Sentinel | Prevalence of oral clefts > 11.1 per 10 000 births | (Q35.x + Q36.x + Q37.x)*10 000/Total number of births > 11.1 |
| Oral clefts | Prevalence by type | Ascertainment | Sentinel | Prevalence of cleft lip and palate > prevalence of cleft palate > prevalence of cleft lip | Q37.x*10 000/Total number of births > Q35.x*10 000/Total number of births > Q36.x*10 000/Total number of births |
| Cleft lip | Laterality | Description | Proportion | Proportion of cases with specified laterality of the cleft lip | (Q36.0 + Q36.1 + Q36.90)*100/ Q36.x |
| Cleft lip | Coding of median cleft | Coding | Sentinel | At least one reported case of median cleft lip. Median cleft lip is rare, but no reported cases suggests potential miscoding as typical cleft lip | Q36.1 > 0 |
| Cleft palate | Anatomic extension of cleft | Description | Proportion | Proportion (%) of cases with cleft palate, with specified extension (hard and/or soft palate) | (Q35.1 + Q35.3 + Q35.5 + Q35.7)*100/ Q35.x |

The first column lists selected birth defects. The second column describes the data quality indicator. The third column is for the process being evaluated (ascertainment, description, coding, classification). For oral clefts, the table includes DQI for the ascertainment, description and coding processes. In the fourth column, the type of DQI is specified: sentinel or proportion of ratio. In the fifth column, there is a general definition of the DQI. In the last column, the DQI is defined operationally, using ICD-10 codes.

The first indicator is for total oral clefts. It shows a minimum prevalence indicator, evaluating the ascertainment process. The type is sentinel, because the result can be "achieved" or "not achieved." The definition is a threshold; that is, achieving this indicator means that prevalence of total oral clefts for a programme should be higher than 11.1 per 10 000 births. If prevalence is below that threshold, under-ascertainment is possible.

The third indicator shown focuses on cleft lip. It is a description DQI since it evaluates the proportion of cleft lip cases with specified laterality. The type is proportion, and it is expressed as a percentage.

The next example shows DQI for neural tube defects (NTD).

| Birth Defect | Data Quality Indicator (DQI) | Specific Surveillance Process Assessed | DQI Type | General Definition | Operational Definition Based on ICD-10 RCPCH codes (1) |
|---|---|---|---|---|---|
| Neural tube defects | Minimum prevalence | Ascertainment | Sentinel | Prevalence of neural tube defects > 5.7 per 10 000 births | (Q00.x + Q01.x + Q05.x)*10 000/Total number of births > 5.7 |
| Neural tube defects | Prevalence by type | Ascertainment | Sentinel | Prevalence of spina bifida > prevalence of anencephaly > prevalence of encephalocele | Q05.x*10 000/Total number of births > Q00.x*10 000/Total number of births > Q01.x*10 000/Total number of births |
| Spina bifida | Skin coverage | Description | Proportion | Proportion (%) of spina bifida cases with skin coverage specified (open or closed) | (Q05.x1 + Q05.x2) *100 / Q05.x |
| Spina bifida | Level | Description | Proportion | Proportion (%) of spina bifida cases with specified level | (Q05.0x + Q05.1x + Q05.2x + Q05.3x + Q05.5x + Q05.6x + Q05.7x + Q05.8x)*100 / Q05.x |
| Spina bifida and anencephaly | Prevalence ratio spina bifida/ anencephaly | Ascertainment | Ratio | Ratio of spina bifida/ anencephaly should between 1.00 and 1.33 | 1.33 > Q05.x / Q00.x > 1.0 |

There are three ascertainment indicators and two description indicators. The ascertainment indicators include a minimum prevalence of NTD of 5.7 per 10 000 births. The prevalence of spina bifida should be highest, followed by the prevalence of anencephaly, and then prevalence of encephalocele.

The last row shows the prevalence ratio spina bifida/anencephaly indicator, which is an ascertainment indicator to evaluate under-ascertainment of anencephaly. Also, the indicators for spina bifida evaluate how accurate the description is regarding level and skin coverage.

### *Using the Excel DQI tool*

The Excel DQI tool allows the systematic evaluation of the quality of data obtained through surveillance of birth defects. It is available for download at http://www.icbdsr.org/data-quality-indicators-tool/.

The Excel DQI tool has four worksheets:

1. Frequently asked questions
2. Input dashboard
3. DQI report
4. DQI definitions.

The first tab of the Excel DQI tool contains **frequently asked questions** about the tool and its use.

### *Input Dashboard*

The second tab contains the worksheet for inputting data. This is the only tab where the user is asked to enter information.

The user has to enter the total number of cases, classified by clinical presentation (isolated, multiple, syndromes); the number of births by maternal age groups; and the number of cases by specified descriptions for selected conditions.

Table 1 allows the user to enter the number of cases and clinical classification (isolated, multiple, syndromes) of selected birth defects. These data are used to generate the ascertainment DQI and the classification DQI.

Table 2 allows the user to enter the number of births and Down syndrome cases by maternal age groups. These data are used to compute prevalence for the ascertainment DQI.

Table 3 allows the user to enter number of cases of selected birth defects with description specified; for example, oral cleft cases by laterality. These data are used to calculate description and coding DQI.

The following image shows "Table 1. Clinical classification and prevalence of selected birth defects."

**Table 1. Clinical classification and prevalence of selected birth defects. This table is used to generate the ascertainment DQI and the classification DQI**

| Birth defect (ICD-10 RCPCH) | Total cases | Clinical classification | | | | | | Prevalence per 10,000 |
|---|---|---|---|---|---|---|---|---|
| | | Isolated | | Multiple congenital anomalies | | Syndromes | | |
| | | n | % | n | % | n | % | |
| Congenital heart defects (Q20-Q26) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Critical congenital heart defects (*) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Neural tube defects (Q00, Q01, Q05) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Anencephaly (Q00) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Spina bifida (Q05) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Encephalocele (Q01) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Oral clefts (Q35-Q37) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Cleft lip only (Q36) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Cleft lip and palate (Q37) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Cleft palate only (Q35) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Hypospadias (Q54.0-Q54.3, Q54.8, Q54.9) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| First degree hypospadias (Q54.0) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Second degree hypospadias (Q54.1) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Third degree hypospadias (Q54.2-Q54.3) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Limb deficiencies (Q71-Q73) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Upper limb (Q71) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Lower limb (Q72) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Transverse (Q71.2-Q71.30) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Preaxial (Q71.31, Q72.5) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Postaxial (Q71.3; Q72.9) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Talipes (Q66) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Equinovarus (Q66.0) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Calcaneovalgus (Q66.4) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Microtia/anotia (Q16; Q17.2x) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Polydactyly (Q69) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Preaxial (Q69.00;Q69.1;Q69.20) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Postaxial (Q69.02; Q69.21) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Ventral Abdominal wall defects (Q79.2, Q79.3) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Omphalocele (Q79.2) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Gastroschisis (Q79.3) | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Maternal age < 20 y.o. | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Maternal age > 19 y.o. | | | #¡DIV/0! | | #¡DIV/0! | | #¡DIV/0! | #¡DIV/0! |
| Down sindrome (Q90) | | NA | NA | NA | NA | | #¡DIV/0! | #¡DIV/0! |
| Maternal age < 35 y.o. | | NA | NA | NA | NA | | #¡DIV/0! | #¡DIV/0! |
| Maternal age > 34 y.o. | | NA | NA | NA | NA | | #¡DIV/0! | #¡DIV/0! |

This table has two types of cells. The green cells are for entering data. The grey cells (with the division by zero error: #¡DIV/0!) will automatically calculate the results once data are entered in the green cells from this table as well as from Table 2.

The following is "Table 2. Number of births and Down syndrome cases by maternal age" of the input dashboard.

Table 2. Number of births and Down syndrome cases by maternal age.

| Maternal age | Number of births | Livebirths with Down syndrome | Down syndrome ETOP before 16 weeks | Down syndrome ETOP at 16 weeks or more | Down syndrome ETOP that would have ended as livebirths | Observed live births prevalence adjusted | Expected prevalence | Expected number of cases |
|---|---|---|---|---|---|---|---|---|
| <20 | | | | | | #¡DIV/0! | 5.70 | 0 |
| 20-24 | | | | | | #¡DIV/0! | 7.15 | 0 |
| 25-29 | | | | | | #¡DIV/0! | 9.11 | 0 |
| 30-34 | | | | | | #¡DIV/0! | 14.99 | 0 |
| 35-39 | | | | | | #¡DIV/0! | 45.07 | 0 |
| 40-44 | | | | | | #¡DIV/0! | 156.33 | 0 |
| 45+ | | | | | | #¡DIV/0! | 519.80 | 0 |
| Total | 0 | 0 | | | | #¡DIV/0! | #¡DIV/0! | 0 |

For each maternal age group, the table computes and compares the observed number of cases with Down syndrome (live births plus elective terminations of pregnancy [ETOP]), adjusted for spontaneous fetal losses that would have occurred if the pregnancy had been allowed to continue against the expected number of cases, based on the best available published data (the expected number is thought to depend exclusively on maternal age).

If the user does not have ETOP information, the user can leave the cells of the ETOP columns empty. This information is used to evaluate the DQI observed/expected ratio of Down syndrome. The result of this DQI will be shown in the DQI Report Worksheet of the tool.

Once the user inputs data in Table 1 and Table 2, the cells show the results for clinical classification and prevalence per 10 000 (see image).

**Table 1. Clinical classification and prevalence of selected birth defects. This table is used to generate the ascertainment DQI and the classification DQI**

| Birth defect (ICD-10 BCPCH) | Total cases | Clinical classification | | | | | | Prevalence per 10,000 |
|---|---|---|---|---|---|---|---|---|
| | | Isolated | | Multiple congenital anomalies | | Syndromes | | |
| | | n | % | n | % | n | % | |
| Congenital heart defects (Q20-Q26) | 1475 | 932 | 63.19 | 274 | 18.58 | 269 | 18.24 | 48.29 |
| Critical congenital heart defects (*) | 353 | 256 | 72.52 | 66 | 18.70 | 31 | 8.78 | 11.56 |
| Neural tube defects (Q00, Q01, Q05) | 270 | 221 | 81.85 | 42 | 15.56 | 7 | 2.59 | 8.84 |
| Anencephaly (Q00) | 57 | 51 | 89.47 | 6 | 10.53 | 0 | 0.00 | 1.87 |
| Spina bifida (Q05) | 175 | 147 | 84.00 | 22 | 12.57 | 6 | 3.43 | 5.73 |
| Encephalocele (Q01) | 39 | 23 | 58.97 | 15 | 38.46 | 1 | 2.56 | 1.28 |
| Oral clefts (Q35-Q37) | 502 | 351 | 69.92 | 124 | 24.70 | 27 | 5.38 | 16.43 |
| Cleft lip only (Q36) | 63 | 49 | 77.78 | 14 | 22.22 | 0 | 0.00 | 2.06 |
| Cleft lip and palate (Q37) | 341 | 252 | 73.90 | 70 | 20.53 | 19 | 5.57 | 11.16 |
| Cleft palate only (Q35) | 99 | 51 | 51.52 | 40 | 40.40 | 8 | 8.08 | 3.24 |
| Hypospadias (Q54.0-Q54.3, Q54.8, Q54.9) | 81 | 68 | 83.95 | 7 | 8.64 | 6 | 7.41 | 2.65 |
| First degree hypospadias (Q54.0) | 42 | 38 | 90.48 | 2 | 4.76 | 2 | 4.76 | 1.38 |
| Second degree hypospadias (Q54.1) | 7 | 5 | 71.43 | 0 | 0.00 | 2 | 28.57 | 0.23 |
| Third degree hypospadias (Q54.2-Q54.3) | 17 | 14 | 82.35 | 3 | 17.65 | 0 | 0.00 | 0.56 |
| Limb deficiencies (Q71-Q73) | 153 | 81 | 52.94 | 63 | 41.18 | 9 | 5.88 | 5.01 |
| Upper limb (Q71) | 109 | 56 | 51.38 | 47 | 43.12 | 6 | 5.50 | 3.57 |
| Lower limb (Q72) | 57 | 26 | 45.61 | 27 | 47.37 | 4 | 7.02 | 1.87 |
| Transverse (Q71.2-Q71.30) | 42 | 28 | 66.67 | 12 | 28.57 | 2 | 4.76 | 1.38 |
| Preaxial (Q71.31, Q72.5) | 19 | 3 | 15.79 | 15 | 78.95 | 1 | 5.26 | 0.62 |
| Postaxial (Q71.5; Q72.9) | 10 | 5 | 50.00 | 4 | 40.00 | 1 | 10.00 | 0.33 |
| Talipes (Q66) | 378 | 243 | 64.29 | 107 | 28.31 | 28 | 7.41 | 12.38 |
| Equinovarus (Q66.0) | 180 | 136 | 75.56 | 37 | 20.56 | 7 | 3.89 | 5.89 |
| Calcaneovalgus (Q66.4) | 16 | 12 | 75.00 | 4 | 25.00 | 0 | 0.00 | 0.52 |
| Microtia/anotia (Q16; Q17.2x) | 122 | 78 | 63.93 | 41 | 33.61 | 3 | 2.46 | 3.99 |
| Polydactyly (Q69) | 239 | 176 | 73.64 | 47 | 19.67 | 16 | 6.69 | 7.82 |
| Preaxial (Q69.00;Q69.1;Q69.20) | 46 | 36 | 78.26 | 6 | 13.04 | 4 | 8.70 | 1.51 |
| Postaxial (Q69.02; Q69.22) | 148 | 117 | 79.05 | 25 | 15.54 | 8 | 5.41 | 4.85 |
| Ventral Abdominal wall defects (Q79.2, Q79.3, | 315 | 259 | 82.22 | 42 | 13.33 | 14 | 4.44 | 10.31 |
| Omphalocele (Q79.2) | 66 | 29 | 43.94 | 24 | 36.36 | 13 | 19.70 | 2.16 |
| Gastroschisis (Q79.3) | 239 | 228 | 95.40 | 11 | 4.60 | 0 | 0 | 7.82 |
| Maternal age < 20 y.o. | 113 | 109 | 96.46 | 4 | 3.54 | 0 | 0 | 26.87 |
| Maternal age > 19 y.o. | 126 | 119 | 94.44 | 7 | 5.56 | 0 | 0 | 4.78 |
| Down sindrome (Q90) | 548 | NA | NA | NA | NA | 548 | 100 | 17.94 |
| Maternal age < 35 y.o. | 253 | NA | NA | NA | NA | 253 | 100 | 10.00 |
| Maternal age > 34 y.o. | 295 | NA | NA | NA | NA | 295 | 100 | 96.11 |

The following is "Table 3. Number of cases with description specified" in the input Dashboard. The data are used to compute the description DQI and the coding DQI, shown in the DQI Report Worksheet.

| | |
|---|---|
| **Oral clefts** | |
| Number of cases with laterality specified (Q36.0 + Q36.1 + Q36.90) | |
| Number of cases with median cleft lip (Q36.1) | |
| Number of cases with cleft palate, with specified extension - hard and/or soft palate (Q35.1+Q35.3+Q35.5+Q35.7) | |
| Number of cases with cleft lip and palate coded under the heading Q37 | |
| **NTD** | |
| Number of spina bifida cases with skin coverage specified - open or closed (Q05.x1+Q05.x2) | |
| Number of spina bifida cases with specified level (Q05.0x + Q05.1x + Q05.2x + Q05.3x + Q05.5x + Q05.6x + Q05.7x + Q05.8x) | |
| Number of encephalocele cases with a specified localization - occipital, temporal, frontal, etc (Q01.0 + Q01.1 + Q01.2 + Q01.8 + Q01.80 + Q01.81 +Q01.82 + Q01.89) | |
| **Hypospadias** | |
| Number of cases coded with ambiguous genitalia if hypospadias is the only diagnosis (Q54.x & Q56.4) | |

| | |
|---|---|
| **Limb deficiencies** | |
| Number of cases with limb deficiencies type and localization specified (Q71.0-Q71.6 + Q72.0-72.7) | |
| **Talipes** | |
| Number of of cases with rotation and position specified (Q66.0-Q66.7) | |
| **Congenital heart defects** | |
| Number of cases with specified congenital heart defects (Q20.0-Q20.6 + Q21.0-Q21.8 + Q22.0-Q22.6 + Q23.0-Q23.4 + Q24.0-Q24.6 + Q25.0-Q25.7) | |
| **Microtia/anotia** | |
| Number of cases with microtia with specified degree (Q16.0 + Q17.22 + Q17.23)* | |
| **Polydactyly** | |
| axial and post-axial) and localization (hand, feet, laterality) specified (Q69.0x-Q69.2x) | |
| **Down syndrome** | |
| Cases with congenital heart defects (Q20.x-Q25.x) | |

For example, oral clefts description DQI focus on laterality and extension (hard and/or soft palate). For NTDs description DQI, an accurate description should include details on skin coverage and lesion level of spina bifida, as well as localization of encephalocele.

### *DQI Report Worksheet*

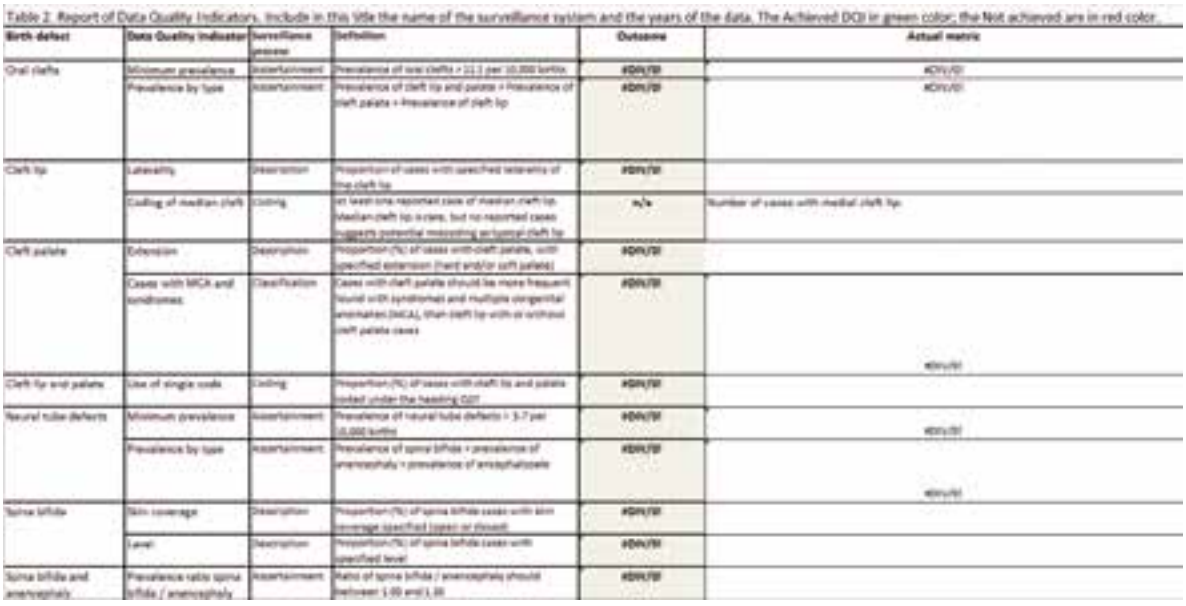
The third tab in the Excel tool is the DQI Report Worksheet, which has two tables: Table 1 "Summary of Data Quality Indicators, by process" and Table 2 "Report of Data Quality Indicators".

Table 1 is a summary with the total number of indicators by process, and the proportion marked as achieved.

| Process | Indicators marked as "Achieved" | Total number of indicators | Proportion of "achieved" indicators |
|---|---|---|---|
| Ascertainment | 0 | 18 | 0.00% |
| Description | 0 | 13 | 0.00% |
| Coding | 0 | 3 | 0.00% |
| Classification | 0 | 6 | 0.00% |

Description indicators are defined as "achieved" when the proportion of cases with a good description is greater than 80%.

Table 2 "Report of Data Quality Indicators" is the main table of the DQI Report Worksheet. This table shows the DQI results for each specific anomaly. The following image presents Table 2 before data are entered.



The table includes information on the birth defect, DQI, surveillance process evaluated, and indicator definition. Once the user completes the Input Dashboard worksheet, then the "blank" and error (#DIV/0!) cells will show the outcome for each DQI.

To illustrate the use of the Excel DQI tool, data from the National Network of Congenital Anomalies of Argentina (RENAC) are presented (see table on p. 234). The outcome column shows the results for each indicator. The achieved indicators are marked in green. The indicators that were not achieved are marked in red. For proportion indicators, "not achieved" are those with a result lower than 80%. The last column shows the actual data used for each DQI. This is useful to know for how much the DQI was not reached.

| Birth Defect | Data Quality Indicator | Surveillance Process | Definition | Outcome | Actual Metric |
|---|---|---|---|---|---|
| Oral clefts | Minimum prevalence | Ascertainment | Prevalence of oral clefts > 11.1 per 10 000 births | **Achieved** | Prevalence of oral clefts (per 10 000): 16.43 |
| | Prevalence by type | Ascertainment | Prevalence of cleft lip and palate > Prevalence of cleft palate > Prevalence of cleft lip | **Achieved** | Prevalence of cleft lip and palate (per 10 000): 11.16<br>Prevalence of cleft palate (per 10 000): 3.24<br>Prevalence of cleft lip (per 10 000): 2.06 |
| Cleft lip | Laterality | Description | Proportion of cases with specified laterality of the cleft lip | **92.06** | |
| | Coding of median cleft | Coding | At least one reported case of median cleft lip. Median cleft lip is rare, but no reported cases suggests potential miscoding as typical cleft lip | **Achieved** | Number of cases with medial cleft lip: 4 |
| Cleft palate | Extension | Description | Proportion (%) of cases with cleft palate, with specified extension (hard and/or soft palate) | **71.72** | |
| | Cases with multiple congenital anomalies (MCA) and syndromes | Classification | Cases with cleft palate should be more frequently found with syndromes and MCA than cleft lip with or without cleft palate cases | **Achieved** | Proportion (%) of cases with cleft palate found with syndromes and multiple congenital anomalies: 48.48<br>Proportion (%) of cases with cleft lip with or without cleft palate found with syndromes and multiple congenital anomalies: 26.1 |
| Cleft lip and palate | Use of single code | Coding | Proportion (%) of cases with cleft lip and palate coded under the heading Q37 | **100** | |

### *DQI Definitions Worksheet*

The fourth tab presents the Definitions Worksheet that includes the type of indicator (sentinel, proportion or ratios) and the operational definition with the codes and operations used to compute the DQI.

| Birth Defect | Data Quality Indicator | Surveillance Process | Type | Definition | ICD-10 RCPCH codes involved (1) |
|---|---|---|---|---|---|
| Oral clefts | Minimum prevalence | Ascertainment | Sentinel | Prevalence of oral clefts > 11.1 per 10 000 births | (Q35.x + Q36.x + Q37.x)*10 000/Total number of births > 11.1 |
| | Prevalence by type | Ascertainment | Sentinel | Prevalence of cleft lip and palate > Prevalence of cleft palate > Prevalence of cleft lip | Q37.x*10 000/Total number of births > Q35.x*10 000/ Total number of births > Q36.x*10 000/Total number of births |
| Cleft lip | Laterality | Description | Proportion | Proportion of cases with specified laterality of cleft lip | (Q36.0 + Q36.1 + Q36.90)*100 / Q36.x |
| | Coding of median cleft | Coding | Sentinel | At least one reported case of median cleft lip. Median cleft lip is rare, but no reported cases suggests potential miscoding as typical cleft lip | Q36.1 > 0 |
| Cleft palate | Extension | Description | Proportion | Proportion (%) of cases with cleft palate, with specified extension (hard and/or soft palate) | (Q35.1 + Q35.3 + Q35.5 + Q35.7)*100 / Q35.x |
| | Cases with multiple congenital anomalies (MCA) and syndromes | Classification | Sentinel | Cases with cleft palate should be more frequently found with syndromes and MCA than cleft lip with or without cleft palate cases | Proportion of syndromes and MCA (Q35.x) > Proportion of syndromes and MCA (Q36.x–Q37.x) |
| Cleft lip and palate | Use of single code | Coding | Sentinel | Proportion (%) of cases with cleft lip and palate coded under the heading Q37 | There should not be any cases with separate codes for cleft lip and for cleft palate (Q35 + Q36/ Q37) |

### *Interpretation of the results*

The basic goal of DQI is to make explicit and visible the metrics of data quality. This is a starting point: Programme staff and data users can use these metrics to continuously track "what is going on?" Asking "what is going on?" is the fundamental question of quality assessment that needs to be answered before quality improvement can start.

In general, DQI should be interpreted as **indicators that show where further investigation is needed:**

- Data quality is often but not always the driver: The variation in certain DQI **might in part reflect true variation over time or by geography. In interpreting DQI, ideally use specific reference or population data**.
  - Example: Hypospadias prevalence in Latin America is likely lower than in Europe *(57, 58)*

- **DQI make the data more visible and are helpful to:**
  - document and track the quality of the programme
  - target and support quality improvement efforts
  - compare different sites or data sources within a programme
  - interpret variation between programmes
  - enhance the information from the programme data when reporting to public and stakeholders.

The DQI should be interpreted **in the context of the programme methodology**.

- Example: Congenital heart defects (CHD)
  - If a programme only ascertains cases diagnosed up to discharge from the birthing hospital, then a fraction (considerable for some heart defects) would be missed, and the associated prevalence would be spuriously low.
  - Also, if a paediatric cardiologist is not available for diagnosis/case review/coding, then this lack of clinical input could be reflected in the CHD-related DQI.

DQI findings can suggest and support practical actions to improve data quality.

For example, a programme might develop:

- **regular, timely, constructive feedback** to hospitals and providers
- **meetings** with staff at local hospitals to **discuss, learn, train**
- **tools such as checklists** to promote the systematic description of all key features of the specific case or anomaly.

After the interventions, use the DQI to **track the impact** of these quality improvement interventions. Finally, quality control and quality improvement are different but complementary.

**For more information, please contact:**

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