Congénitales Anomalies

Santé publique France

July 2026
SURVEILLANCE DATA

Epidemiological Surveillance of Congenital Anomalies in France using Population-Based Registries: Data for 2019–2021

Abstract

Epidemiological Surveillance of Congenital Anomalies in France using Population-Based Registries: Data for 2019–2021

Context and Objective

Congenital anomalies contribute to the global burden of non-communicable diseases due to their impact on perinatal and infant mortality, as well as on the care and quality of life of affected children. In France, surveillance of congenital anomalies currently relies on data collected by seven population-based registries. This report provides a summary of congenital anomalies surveillance in the geographical areas covered by five of these registries for the period 2019–2021. Its objective is to estimate the overall prevalence of reported anomalies and prevalence by groups of congenital anomalies, distinguishing cases diagnosed with one or more genetic disorders from those without identified genetic disorders. For each group, data are presented by pregnancy outcome, timing of anomaly diagnosis (prenatal or postnatal), and maternal age.

Materials and Methods

The data analyzed in this report come from five population-based registries that submitted pseudonymized data to the European Network of Population-Based Registries for the Epidemiological Surveillance of Congenital Anomalies (EUROCAT) for the period 2019–2021. These registries cover parts of mainland France (Paris, Auvergne, Brittany) and the French overseas departments and regions, specifically Guadeloupe and Martinique (in the West Indies), as well as Réunion Island. Together, they cover 16.4% of annual births in France. Each registry identifies and validates diagnoses of cases of congenital anomalies occurring during pregnancy or up to the first year of life by cross-referencing multiple data sources to ensure comprehensive data collection. EUROCAT ensures data harmonization at the European level, including continuous quality control of inclusion criteria and anomaly coding. Prevalence estimates (total, for live births, and terminations of pregnancy for fetal anomalies [TOPFA]) are expressed per 10,000 births, with 95% confidence intervals.

Results

During 2019-2021 in the geographical areas covered by the five participating registries, the overall prevalence of fetuses, newborns, and children with congenital anomalies was 352.5 per 10,000 total births. This prevalence varied by registry, ranging from 255.3/10,000 in the West Indies to 397.4/10,000 in Brittany. Cardiac anomalies were the most frequently observed anomalies (95.2/10,000), followed by genetic disorders (78.8/10,000) and limb (70.3/10,000) anomalies. Among fetuses, newborns, and children with multiple anomalies, abdominal wall defects had the highest proportion of cases with at least one genetic disorder (42.1%), followed by ear, face, and neck anomalies (30.4%), and ocular anomalies, oro-facial clefts, and central nervous system anomalies (23.5%). The overall prenatal diagnosis rate, among all types of anomalies, was 60.0% (95% CI [49.9–68.8]), exceeding 75% for fetuses with abdominal wall defects, kidney and urinary system anomalies, as well as genetic disorders and central nervous system anomalies. The most severe anomalies leading to TOPFA primarily involved genetic disorders (54.5/10,000) and central nervous system (23.8/10,000) and cardiac (15.7/10,000) anomalies. The risk of a fetus, newborn, or infant having a congenital anomaly with at least one genetic disorder was nearly eight times higher in mothers aged 40 years and older compared to those aged 24 years and younger. Without any genetic disorder identified, this maternal age-related difference was not observed, and the overall prevalence of congenital anomalies was slightly higher among younger mothers.

Discussion

Surveillance of congenital anomalies in France currently relies on population-based registries producing standardized data. This first national report provides an updated overview of key prevalence data, prenatal diagnosis, and pregnancy outcomes in the geographical areas covered by the five participating registries during 2019-2021. This information is essential for guiding public health policies for screening, prevention, and improving the care of children with congenital anomalies. In the short term, congenital anomalies surveillance in France will be strengthened by integrating data from the Rhône-Alpes and Nouvelle-Aquitaine registries. In addition, national coverage is planned for certain anomalies, complementing registry data through the development of algorithms to identify congenital anomalies in the National Health Data System for non-covered areas. These algorithms are needed as recent demographic changes, such as increasing maternal and paternal age, increasing rates of risk factors such as preconception obesity and gestational diabetes, and environmental exposures may influence the frequency of certain anomalies.

KEYWORDS: congenital anomalies, perinatal health, epidemiological surveillance, prevalence, pregnancy outcome, prenatal diagnosis, screening, medical termination of pregnancy.

Key Findings

- In the areas covered by the five French registries during 2019–2021, 1 in 28 total births (3.5%) was diagnosed with at least one major congenital anomaly.
- The most common groups of congenital anomalies were cardiac anomalies, genetic disorders (chromosomal and others), and limb anomalies (reduction defects, polydactyly, and others).
- Nearly 60% of congenital anomalies were diagnosed prenatally. Abdominal wall, renal, genetic, central nervous system, and complex cardiac anomalies were prenatally diagnosed in over 75% of cases.
- Among cases with congenital anomalies, 74.4% were live births, 24.1% resulted in medical termination of pregnancy (TOPFA), and 1.5% were stillbirths (≥ 22 weeks of gestation). The prevalence of TOPFA was highest among cases with genetic disorders (54.5 per 10,000 total births), central nervous system anomalies (23.8 per 10,000 total births), and cardiac anomalies (15.7 per 10,000 total births).
- Having a pregnancy affected by at least one genetic disorder was eight times higher in mothers aged 40 years and older compared to those 24 years and younger.

Suggested citation: El Rafei-Julia R, Chabaneix Thomas J, Bruneau L, Nathalie Lelong N, Monier I, Omarjee A, *et al.* Epidemiological surveillance of congenital anomalies in France in areas covered by a registry: data 2019-2021. Saint-Maurice: Santé publique France, 2026. 51 p. www.santepubliquefrance.fr

ISSN : 2534-6539 / ISBN-NET : 978-2-37986-091-1 / PRODUCED BY THE COMMUNICATION DIRECTORATE, SANTE PUBLIQUE FRANCE / LEGAL DEPOSIT: JULY 2026

Coordination of Congenital Anomalies Surveillance at Santé publique France

Perinatal, Early Childhood and Mental Health Unit, Directorate of Non-Communicable Diseases and Trauma, the Santé publique France: Rym El Rafei-Julia (epidemiologist); Daniel Bejarano-Quisoboni (health economist); Nolwenn Regnault (Head of the UPEPS Unit until September 30, 2025)

The French Congenital Anomalies Registries (responsible parties and/or coordination and affiliated structures)

West indies – REMALAN	Martinique University Hospital
Ianis Cousin	Registry Manager
Corinne Plavonil	Martinique Coordinator
Minerve Vatin	Guadeloupe Coordinator
Auvergne – CEMC	Clermont Ferrand University Hospital
Isabelle Perthus	Registry Manager
Brittany – REMABREIZH	Rennes University Hospital
Florence Rouget	Registry Manager
Emmanuelle Nicolas	Midwife Coordinator
Nouvelle Aquitaine – ATENA	Bordeaux University Hospital
Julie Chabaneix-Thomas	Registry Manager
Anne-Cecile Huby	Project Manager
Paris – REMAPAR	INSERM, OPPaLE team
Isabelle Monier	Registry Manager
Nathalie Lelong	Registry Co-Manager
Réunion island – REMACOR	CHU La Réunion
Léa Bruneau	Registry Co-Manager
Asma Omarjee	Registry Co-Manager
Jonathan Hoareau	Coordinator
Rhône-Alpes – REMERA	Lyon Civil Hospices
Emmanuelle Amar	Registry Manager
Ludivine De Brosses	Coordinator

Authors

Rym El Rafei-Julia[1], Julie Chabaneix (Thomas)[2], Léa Bruneau[3,4], Nathalie Lelong[5], Isabelle Monier[5], Asma Omarjee[3], Isabelle Perthus[6], Corinne Plavonil[7], Emmanuelle Amar[8], Ianis Cousin[7], Jonathan Hoareau[3], Anne-Cécile Huby[2], Emmanuelle Nicolas[9], Catherine Ryan[7], Minerve Vatin[7], Julie Boudet-Berquier[1], Daniel Bejarano-Quisoboni[1], Florence Rouget[10], Nolwenn Regnault[1]

1. Santé publique France, Directorate of Non-Communicable Diseases and Trauma
2. ATENA Registry, Medical and Surgical Unit for Congenital Cardiac Pathologies of the Fetus, Child, and Adult, Constitutive Reference Center M3C, Bordeaux University Hospital, Liryc IHU, Inserm 1045, University of Bordeaux, Pessac, France
3. La Réunion Congenital Malformations Registry (REMACOR), Public Health Department, Public Health Division, La Réunion University Hospital, Saint-Pierre, La Réunion, France
4. Clinical Investigation Center (CIC) 14-10, Inserm, Public Health Department, Public Health Division, La Réunion University Hospital, Saint-Pierre, La Réunion, France
5. Université Paris Cité and Université Sorbonne Paris Nord, Inserm, Inrae, Center for Research in Epidemiology and Statistics, Obstetrical, Perinatal and Pediatric Life course Epidemiology Research Team (OPPaLE), F-75004 Paris, France
6. Auvergne Congenital Malformations Study Center, Medical Genetics Department, Reference Center for "Developmental Anomalies and Malformative Syndromes", Clermont-Ferrand University Hospital, F-63003 Clermont-Ferrand, France
7. Antilles Registry, Prenatal Diagnosis Unit, Prenatal Diagnosis Center, Mother and Child Center, Martinique University Hospital
8. Rhône-Alpes Congenital Malformations Registry (Remera), Lyon Civil Hospices, Lyon, France
9. Brittany Congenital Anomalies Registry, Pediatrics Department, Rennes University Hospital, F-35000 Rennes, France
10. Brittany Congenital Anomalies Registry, Pediatrics Department, Rennes University Hospital, Univ Rennes, Inserm, School of Advanced Studies in Public Health (EHESP), Irset (Institute for Research in Health, Environment, and Work) – UMR S 1085, F-35000 Rennes, France

Acknowledgments

We would like to express our deepest gratitude to all those who contributed to the completion of this work.

We extend our thanks to the families for their trust, the healthcare institutions and professionals for their commitment to the care and surveillance of children with congenital anomalies, and the funding organizations supporting the registries.

We also express our gratitude to EUROCAT for their expertise in data analysis, with the invaluable support of (in alphabetical order) Hannah Johnson, Joan Morris, and Annie Perraud.

Finally, we thank the members of the Scientific Expert Committee for their recommendations and valuable contributions to the selection and interpretation of the data presented in this report (in alphabetical order): Jean-Luc Alessandri, Antony Atallah, Tiphaine Raia Barjat, Nathanael Beeker, Alexandra Benachi, Claire Beneteau, Nansi Boghossian, Jennifer Broughan, Ferdinand Dhombres, Charlotte Dubucs Gautier, Patrick Edery, Ester Garne, Kathryn Johnson, Elsa Kermorvant, Emmanuelle Lesieur, Benoît Marin, Wendy Nembhard, Sophie Patrier-Sallebert, Claire Philippat, Paul Romitti, and Marie-Hélène Saint Frison.

Learn more about congenital anomalies surveillance in France

Santé publique France	https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-de-la-mere-et-de-l-enfant/anomalies-et-malformations-congenitales
West Indies Registry	https://remalan.com/
Auvergne Registry	https://www.chu-clermontferrand.fr/liste-services/genetique-medicale/registre-cemc
Brittany Registry	https://www.chu-rennes.fr/remabreizh.html
Nouvelle Aquitaine Registry	https://registre-atena.fr/
Parisian Registry	https://cress-umr1153.fr/fr/project/registre-des-malformations-congenitales-de-paris-remapar/
La Réunion Island Registry	https://remacor.re/
Rhône-Alpes Registry	https://www.remera.fr/

List of Acronyms

ANSES	French Agency for Food, Environmental, and Occupational Health & Safety
BPA	British Paediatric Association
CAKUT	Congenital Anomalies of Kidney and Urinary Tract
CMA	Chromosomal Microarray Analysis
CNEOF	French National Conference on Obstetric and Fetal Ultrasound
CNS	Central Nervous System
CPDPN	Multidisciplinary Prenatal Diagnosis Centers
DPN	Prenatal Diagnosis
NIPT	Non-invasive Prenatal Testing
EUROCAT	European Network of Population-Based Registries for the Epidemiological Surveillance of Congenital Anomalies
FISH	Fluorescence In Situ Hybridization
GA	Gestational Age
HAS	The French Health Authority
ICD-10	International Classification of Diseases, 10th revision
MCO	Medicine, Surgery, Obstetrics, and Dentistry
NCARDRS	National Congenital Anomaly and Rare Disease Registration Service
NTD	Neural Tube Defect
PMSI	Medicalization Program for Information Systems
SNDS	French National Health Data System
TOPFA	Termination of Pregnancy for Fetal Anomalies
WHO	World Health Organization

Glossary

Major Congenital Anomalies	Major congenital anomalies are defined as structural anomalies and genetic disorders that can adversely affect the health and development of the fetus and child, regardless of their etiology or the timing of their occurrence.
Minor Congenital Anomalies	Minor congenital anomalies are those that do not pose significant health problems and generally have limited social or cosmetic consequences for the affected individual.
Cases (fetuses, newborns, and children) with at least one major congenital anomaly	A case includes a live birth, termination of pregnancy for fetal anomaly (TOPFA, regardless of gestational age), or a stillbirth after 22 weeks of gestation, with at least one major congenital anomaly.

Data sources: Groups defined according to the EUROCAT classification

Tables, Figures, and Appendices

Tables

Figures

Appendices

Table of Contents

Preface

Ferdinand Dhombres (Chair) and Paul Romitti (Vice-Chair) of the Scientific Expert Committee on Congenital Anomalies

Congenital anomalies represent a major public health challenge. They affect approximately 3% of births in Europe, with a lasting impact on the health and quality of life of children and their families. Furthermore, they are one of the leading causes of neonatal morbidity and mortality.

With this report, Santé publique France (SPF) consolidates, for the first time at the national level, estimates of the prevalence of selected congenital anomaly groups. These data were submitted by five population-based registries (West indies, Auvergne, Brittany, Réunion Island, and Paris) for the period 2019–2021. Future reports are expected to include two additional registries (Rhône-Alpes and Nouvelle-Aquitaine).

Although the registry data cover only a proportion of births, they provide reliable and standardized prevalence estimates of congenital anomalies in the covered regions, enabling comparisons with data from other registries across Europe. These data, which are essential for monitoring population health, contribute to the early detection of signals that may indicate environmental, toxic, or drug exposures, as well as correlations with social and territorial inequalities.

This initial report is part of an ongoing program led by SPF to expand the surveillance of congenital anomalies to all regions of France. This effort involves both the consolidation and deployment of the two previously mentioned registries and the use of additional data sources. The French National Health Data System (SNDS) is a resource under consideration to supplement registry data for uncovered areas, enable rapid analyses, and provide sufficient sample sizes for more detailed studies. Data from Multidisciplinary Prenatal Diagnosis Centers (CPDPN) may also be incorporated into future reports.

The ambition to integrate national data sources for monitoring congenital anomalies will require designing data processing algorithms and standardized indicators, aligning data with French registries, while maintaining strict requirements for quality control and data protection.

As Chair and Vice-Chair of the Scientific Expert Committee on Congenital Anomalies, it is an honor for us, on behalf of the committee, to introduce this report. The committee is tasked with advising SPF on congenital anomaly surveillance, with the ambition of extending coverage nationally, in order to produce reliable indicators for estimating the prevalence of congenital anomalies and interpreting their variations.

This document is the result of the rigorous work of the registry teams and SPF, as well as the commitment of numerous clinicians, epidemiologists, midwives, geneticists, biostatisticians, and health information system professionals. We extend our gratitude to all of them.

BACKGROUND AND OBJECTIVES

Congenital anomalies are structural malformations affecting one or more organs, occurring during pregnancy, mostly in the first trimester (embryogenesis). In Europe, nearly 3% of fetuses, newborns, and children have one or more congenital anomalies among all pregnancy outcomes combined (1,2). Among them, approximately 22% result in a medical termination of pregnancy for fetal anomaly (TOPFA) or fetal death. Although relatively rare on an individual level, these anomalies are a major cause of perinatal and neonatal mortality. Their potential for life long sequelae can impact the quality of life of affected children and their families, while also generating significant costs for the healthcare and social care systems (3,4).

In France, epidemiological surveillance of congenital anomalies relies on data collected by population-based registries. Initially established following the thalidomide health crisis, its primary aim was to detect clusters of cases and identify potential teratogenic agents—whether environmental or drug-related. Today, these registries play a central role in public health monitoring, the evaluation of perinatal health policies, and the advancement of research in the field of congenital anomalies.

This first surveillance report aims to describe the prevalence of congenital anomalies, both overall and by group, using data submitted by French congenital anomaly registries to the European Network of Population-Based Registries for the Epidemiological Surveillance of Congenital Anomalies (EUROCAT) (5) for the period 2019–2021. For each group of anomalies, additional analysis of prevalence was conducted according to pregnancy outcome (live birth, fetal death, or TOPFA), timing of diagnosis (prenatal or postnatal), and maternal age.

More detailed analyses are provided for specific groups of anomalies or selected anomalies due to their frequency, potential impact on viability, or quality of life: cardiac anomalies, central nervous system (CNS) anomalies, and hypospadias. The analysis also includes cases diagnosed with at least one genetic disorder, such as aneuploidies, chromosomal micro-rearrangements, or monogenic syndromes.

INTRODUCTION: EPIDEMIOLOGICAL SURVEILLANCE OF CONGENITAL ANOMALIES IN FRANCE AND EUROPE

Geographical Coverage

In France, epidemiological surveillance of congenital anomalies has historically relied on population-based registries and is evolving towards a multi-source system. It currently draws on data from seven population-based registries, which are considered the gold standard for descriptive epidemiology in the geographical areas they cover. This is due to the quality of their data collection, medical validation of cases, and standardization of data according to the criteria of EUROCAT (5). In the future, this system may be supplemented by the use of medico-administrative data from the SNDS to expand national coverage for certain congenital anomalies in areas not covered by a registry (6). This type of data source holds considerable importance to strengthen the geographical coverage of congenital anomalies surveillance. However, certain methodological limitations remain to be evaluated, particularly concerning the identification of cases and access to specific clinical variables.

The geographical location, covered population, and historical establishment of the registries contributing to congenital anomalies surveillance in France vary across regions (Figure 1, Table 1). Coverage is projected to increase from 16.4% to nearly 23.6% of births by 2026, following the implementation of the Nouvelle-Aquitaine registry.

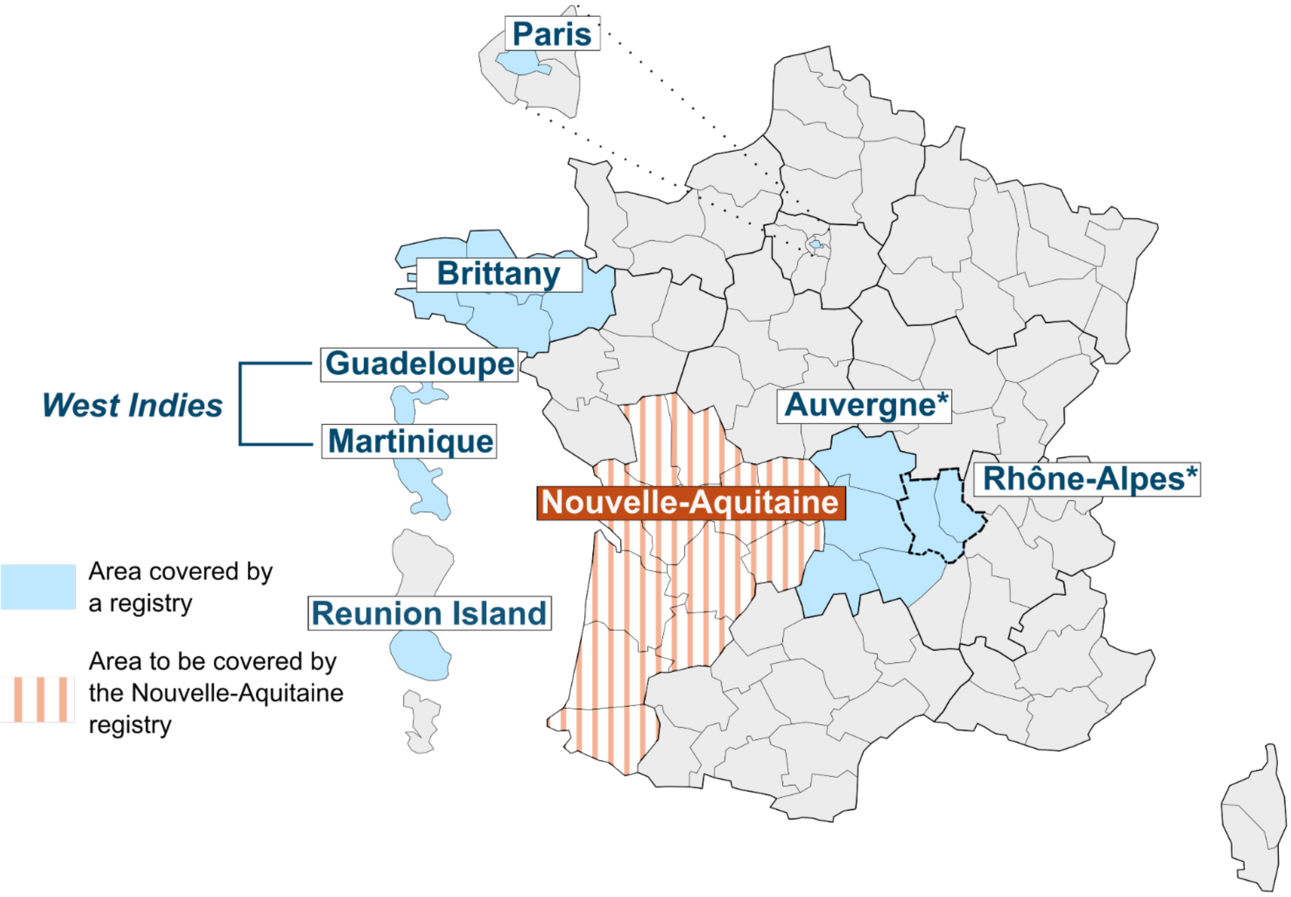


Figure 1. Geographical coverage of the seven French congenital anomaly registries participating in national and European surveillance (status in 2025)

* The Auvergne-Rhône-Alpes region is covered by two registries: in Auvergne, the four departments of Allier, Cantal, Haute-Loire, and Puy-de-Dôme; and in Rhône-Alpes, the two departments of Rhône and Loire.

Table 1. Characteristics of the French congenital anomaly registries contributing to national and European surveillance (France, 2019–2021)

French Registry	Year of Establishment	Average Number of Total Births[#] (2019-2021)
West Indies[¤]	2009	8264
Auvergne	1983	12099
Brittany	2011	31740
Reunion Island	2001	13360
Nouvelle Aquitaine*	2022	53392
Paris	1981	23700
Rhône-Alpes^	1973	54621

[#] Total births include live births and fetal deaths (≥22 weeks of gestation).

[¤] West Indies include Guadeloupe and Martinique, but the islands of Saint-Martin and Saint-Barthélemy are not included in the registry.

* Estimate of the total annual number of births that would have been covered during 2019-2021 if the registry had been operational during that period.

^ The Rhône-Alpes registry initially covered the departments of Rhône, Loire, Isère, and Savoie. Since 2012, Savoie has been replaced by Ain. Since 2023, only Rhône and Loire have been included in the registry.

Case Definition

The registries ensure continuous and comprehensive recording of congenital anomaly cases occurring within their geographical area, from the time of diagnosis during pregnancy up to the child's first birthday. Each recorded case undergoes a rigorous validation process based on the review of available medical data to ensure the quality and reliability of the collected information. A case is defined as any congenital anomaly diagnosed in a live-born child, a stillborn fetus from 22 weeks of gestation, or in the context of a medical termination of pregnancy, regardless of gestational age (GA).

To achieve comprehensive coverage, the registries employ a multi-source strategy, engaging all public and private facilities involved in the diagnosis or management of fetuses, newborns, or children with congenital anomalies. These sources include multidisciplinary prenatal diagnosis centers (CPDPN), maternity wards, pediatrics, genetics, imaging, surgery, pediatric cardiology, and fetopathology departments, as well as health certificates. Hospitalization data from the Medicalization Program for Information Systems (PMSI) are also utilized. Cross-referencing these sources maximizes case identification and ensures data quality.

Most registries include cases where the mother resides in the covered territory, regardless of the place of delivery, to avoid bias related to inter-regional mobility. However, the registries in the West Indies, Réunion Island, and Paris only record births where the mother both resides and gives birth within the covered geographical area.

Inclusions cover all cases diagnosed during the first year of life to account for late diagnoses. Surveillance data are therefore only available beginning two years after the year of birth. The Parisian registry only includes cases diagnosed or suspected before discharge from the maternity ward or neonatal hospitalization.

Through an agreement between Santé publique France and EUROCAT, and following individual agreements with each registry, data from French registries are transmitted annually to Santé publique France to fulfill its surveillance and analysis missions.

Governance

As part of its mission to monitor the health status of the population—particularly to support decision-making—Santé publique France coordinates the surveillance of congenital anomalies. This effort relies on a network of stakeholders, including healthcare professionals, healthcare facilities, and population-based registries (7,8). This coordination is managed by the Perinatal, Early Childhood, and Mental Health Unit within the Directorate of Non-Communicable Diseases and Trauma. Its responsibilities include analyzing temporal trends for major groups of congenital anomalies using comprehensive data collected by the registries. If unusual clusters of cases are reported in a specific area or during a given time period, the Regional Health Agency may request Santé publique France to conduct epidemiological investigations. These efforts are supported by a scientific expert committee, established in 2023, comprising 21 French and international experts (9).

In parallel with the coordination led by Santé publique France, a national collective of congenital anomaly registries, named REMAFRANCE, was established in 2023. This collective brings together the seven population-based registries in mainland France and overseas territories, which collaborate regularly through monthly meetings, joint projects, and the sharing of best practices. REMAFRANCE aims to enhance the consistency and effectiveness of surveillance at the national level by promoting the harmonization of data collection, coding, and analysis methods, as well as the pooling of expertise. It serves as a platform for scientific and technical coordination among registries, facilitating the development of multicenter research projects and dialogue with institutions. A national collaboration agreement, currently being finalized, will formalize the collective's operations and strengthen its governance. This initiative is part of a broader effort to better structure the registries' contributions to surveillance, health monitoring, and perinatal research, building on the work led at the European level by EUROCAT.

Box 1. EUROCAT

EUROCAT (10) was established in 1979 and includes data from 43 population-based registries located in 21 European countries, currently covering nearly 1.5 million births annually. The network's missions are multifaceted and primarily aim, through the analysis of data collected by the registries, to describe temporal trends at the European level. One mission is to facilitate the identification of teratogenic exposures and assess the impact of primary prevention and prenatal screening policies. Another mission, building on decades of expertise, is to ensure continuous quality control of the inclusion criteria for congenital anomaly cases and their coding. EUROCAT updates a list of minor anomalies to be excluded, establishes coding rules to harmonize the classification of congenital anomalies, defines subgroups of congenital anomalies, and provides algorithms for classifying multiple congenital anomalies (EUROCAT Guide 1.5). Registries participating in EUROCAT submit pseudonymized data annually, which are compiled, processed, and published in an annual surveillance report (11) on EUROCAT website (12,13).

MATERIALS AND METHODS

Study Population and Period

The data presented in this report come from the five registries that submitted pseudonymized data to EUROCAT for the period 2019–2021: the West indies, Auvergne, Brittany, Paris, and Réunion Island. A three-year period (2019-2021) was selected to provide recent, pooled data while ensuring a sufficient number of cases for robust statistical analysis. This time period also accounts for the mandatory two-year delay required for data validation and transmission to EUROCAT, where the data undergo quality control prior to use.

Data Collection

Congenital anomalies

In this report, a case refers to a fetus, newborn, or child with at least one "major" congenital anomaly. According to EUROCAT definition, an anomaly is considered major if it involves a structural change present at birth, of congenital origin, non-functional, and likely to have medical, social, or cosmetic consequences (14). All anomalies observed in a single case are validated by the registry through the consolidation of information from various clinical sources. Up to eight anomalies can be recorded for a single case in EUROCAT, with the option to add free-text details if needed. Each anomaly is coded according to the International Classification of Diseases, 10th Revision (ICD-10), supplemented by a one-digit extension proposed by the British Paediatric Association (BPA). Additional free-text descriptions are also provided to ensure optimal detail. "Minor" anomalies are also reported to EUROCAT, but only when associated with at least one major anomaly. The term "minor" refers to anomalies with no significant health impact and generally limited social or cosmetic consequences. (14).

The groups of structural congenital anomalies and genetic disorders presented in this report are defined by the EUROCAT network based on shared etiologic mechanisms or clinical characteristics. These groups include:

- Central nervous system (CNS) anomalies
- Ocular anomalies
- Ear, face, and neck anomalies
- Cardiac anomalies
- Respiratory anomalies
- Oro-facial clefts
- Gastrointestinal anomalies
- Abdominal wall defects
- Congenital Anomalies of Kidney and Urinary Tract (CAKUT)
- Genital anomalies
- Limb anomalies
- Genetic disorders

The detailed list of anomalies included in each of these groups corresponds to the standardized EUROCAT network classification provided in Appendices 1 and 2 (15).

Other variables collected

In addition to collecting data on congenital anomalies, registries also gather a range of supplementary variables for each case (15). The analyses presented in this report are based on the following information:

- Pregnancy outcome (live birth, fetal death ≥22 weeks of gestation and/or 500 grams, or TOPFA regardless of the term and weight)
- Maternal age (≤24 years, 25–29 years, 30–34 years, 35–39 years, ≥40 years)
- Timing of diagnosis (prenatal or postnatal; in cases of multiple anomalies, a case is considered prenatally diagnosed if at least one major congenital anomaly was identified prenatally)

Statistical Analysis

Prevalence calculation

In the context of congenital anomalies surveillance, prevalence is used rather than incidence (16). Incidence refers to the number of new cases occurring in a population over a given time period. However, this approach is not applicable here because many anomalies go undiagnosed when a pregnancy ends in spontaneous miscarriage during the first trimester (i.e., early miscarriages). The prevalence of congenital anomalies is therefore estimated at birth, based on the number of cases identified among total births, defined as all live births or fetal deaths ≥22 weeks of gestation or weighing more than 500 grams. Prevalence estimates are expressed per 10,000 total births.

When calculating the overall prevalence of congenital anomalies, each affected child was counted only once, even if they have multiple anomalies from different groups (i.e., one case). However, for prevalence by anomaly group, the same fetus, newborn, or child may have been counted in multiple groups if they had multiple anomalies. In this case, the measure refers to the number of anomalies, not the number of cases.

All prevalence estimates presented in this report are accompanied by their 95% confidence intervals and were calculated for a specific time period and geographical area.

- **Prevalence of cases with congenital anomalies per 10,000 total births:**

$$= \frac{(\text{Number of live births}) + (\text{Number of TOPFA}) + (\text{Number of fetal deaths})\ \text{with congenital anomalies}}{(\text{Number of live births}) + (\text{Number of fetal deaths} \geq 22\ \text{GA})}$$

- **Prevalence of cases with congenital anomalies per 10,000 live births:**

$$= \frac{\text{Number of live births with congenital anomalies}}{\text{Number of live births}}$$

- **Prevalence of cases with severe congenital anomalies leading to TOPFA per 10,000 total births:**

$$= \frac{\text{Number of TOPFA}}{(\text{Number of live births}) + (\text{Number of fetal dealths} \geq 22\ \text{GA})}$$

Estimation of Confidence Intervals:
The lower and upper bounds of the confidence intervals accompanying the prevalence estimates were estimated assuming a Poisson distribution. They were calculated using the following formulas:

Lower bound of confidence interval at 95% = $\frac{(\frac{1,96}{2}-\sqrt{\text{Number of cases}+0.02})^2}{\text{Number of total births}} \text{ x } 10\,000$

Upper bound of confidence interval at 95% = $\frac{(\frac{1,96}{2}+\sqrt{\text{Number of cases}+0.96})^2}{\text{Number of total births}} \text{ x } 10\,000$

Sources used for the denominator:
The total number of births (live births and fetal deaths) was estimated from two sources: (i) data from the National Institute of Statistics and Economic Studies (INSEE), which provide the annual number of live births by geographical area covered by a registry and (ii) data from the PMSI, which are used to estimate the number of fetal deaths ≥22 weeks of GA (17). Since 2008, this source has officially replaced INSEE data for recording fetal deaths. This change follows a legislative amendment in 2008, allowing a stillbirth certificate to be issued based on a medical birth certificate, without gestational or weight criteria (22 weeks or 500 grams). This modification has led to an artificial increase in the number of fetal deaths reported by INSEE from 2008-forward, due to the inclusion of spontaneous miscarriages occurring before 22 weeks of GA according to the definition of the World Health Organization (WHO).

Calculation of Proportions of Congenital Anomaly Groups

To calculate the proportion of congenital anomaly groups diagnosed prenatally, postnatally, or at an unspecified time, we used generalized structural equation models (GSEM) applied to aggregated data from the five registries. This type of model accounts for the exclusivity of categories (a single case can only be diagnosed at one time) and adjusts estimates for inter-registry variability, which may arise from differences in medical practices or sociodemographic characteristics of the covered populations. It is reasonable to assume that a fetus, newborn, or child recorded in one registry is more comparable to other cases within the same registry than to those from different regions. Using these models, therefore, yields more robust estimates by considering the hierarchical structure of the data (18). All numerical data underlying the figures presented in this report are detailed in a supplementary technical document “Data Sheet_Congenital Anomalies Report_2019-2021”.

RESULTS

I. Prevalence of Cases with Congenital Anomalies

During 2019-2021, 9,429 fetuses, newborns, and infants under one year of age with at least one major congenital anomaly were recorded in the areas covered by the registries of the West Indies, Auvergne, Brittany, Paris, and Réunion Island. With 267,488 total births registered in these regions, this corresponds to a prevalence of 352.5 cases per 10,000 total births (95% CI [345.4–359.7]), or approximately 3.5% (Figure 2; Data Table 1 in "Data Sheet_Congenital Anomalies Report_2019-2021").

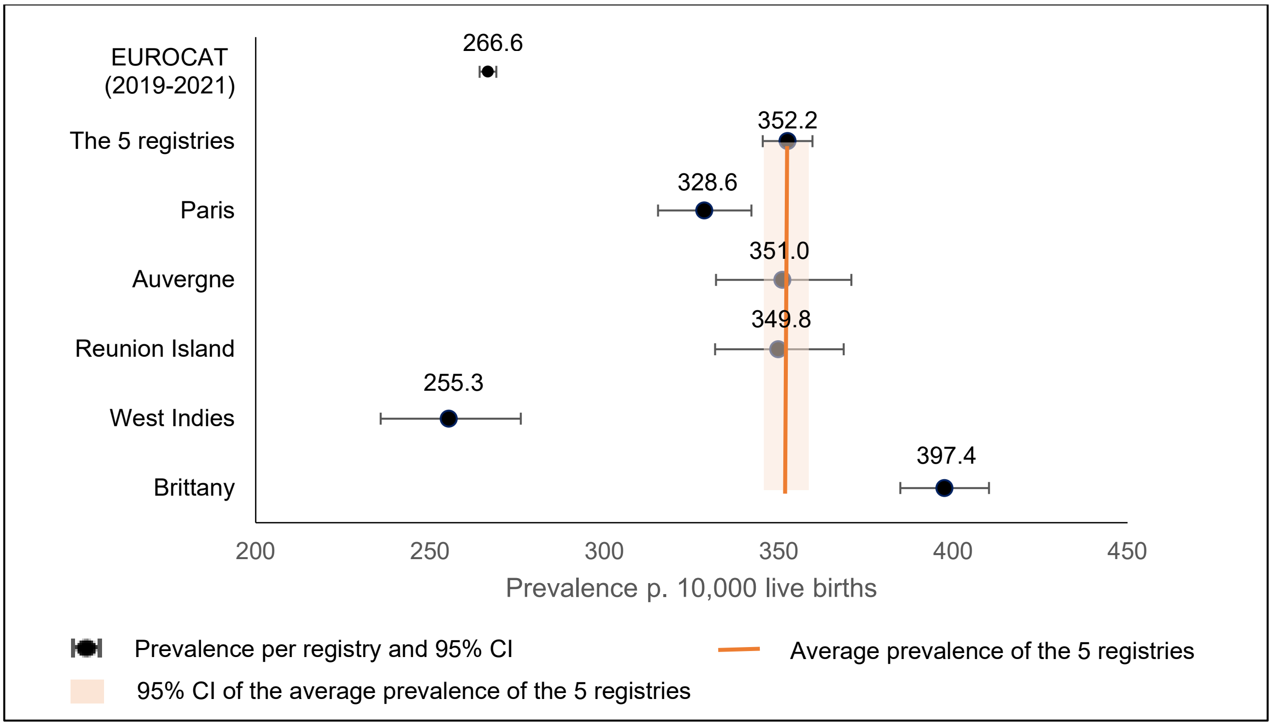


Figure 2. Prevalence of cases with congenital anomalies among total births, overall and by registry, 2019–2021

The black dots indicate the registry-specific prevalences, accompanied by their 95% confidence intervals (horizontal bars). The orange line represents the overall aggregated prevalence for all registries, with its 95% CI (orange box).

Differences in prevalence were observed among registries. The lowest prevalence was in the West Indies, with 255.3 cases (95% CI: 235.8–276.0) per 10,000 total births. The highest prevalence was in Brittany, with 397.4 cases (95% CI: 384.8–410.3) per 10,000 total births. These differences persisted even when excluding cases diagnosed with at least one genetic disorder (data not shown).

Interpretation of results:

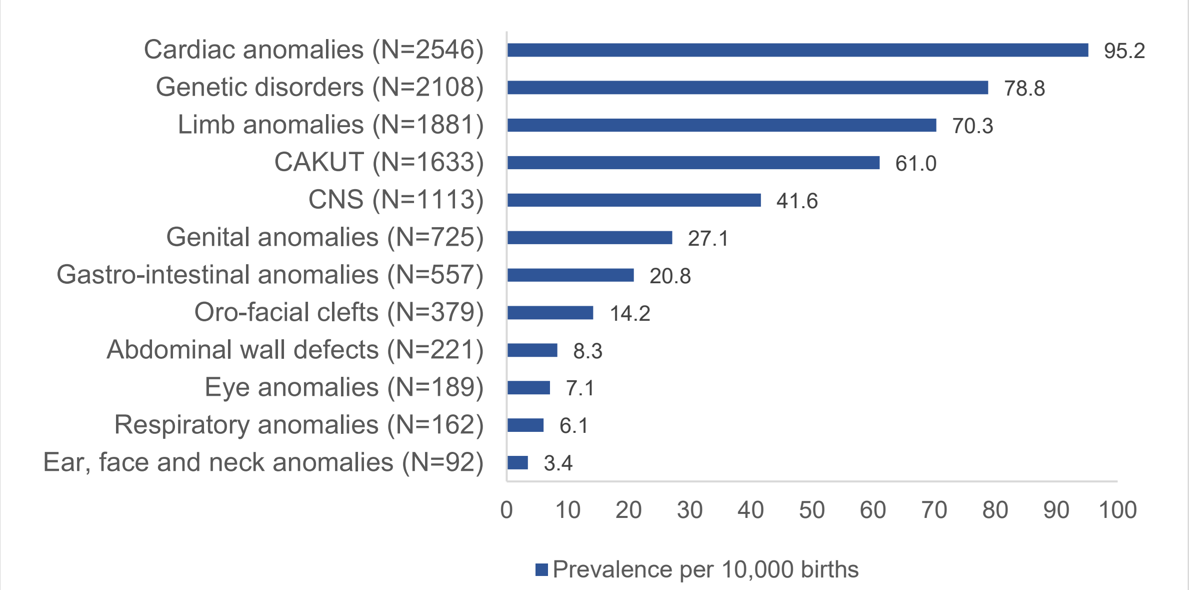
Differences in prevalence observed among the French registries can be attributed to methodological differences. Unlike the other registries, the Paris registry does not include cases diagnosed up to one year of age. Additionally, the registry in the West Indies was not comprehensive until 2022 for polydactyly and certain non-severe cardiac anomalies, including ventricular septal defects and atrial septal defects. These differences can also be explained by sociodemographic factors and/or population characteristics specific to each region. For example, Brittany has historically reported a very high prevalence of congenital hip dislocation (19), which may influence more systematic screening practices in this region.

An analysis was conducted to determine whether the differences in prevalence among registries could be explained by the absence in Paris of cases diagnosed after hospital discharge (the only major methodological difference between registries). By including these cases, estimated at 251 additional cases for 2019–2021 based on the mean postnatal diagnosis proportions from the other registries, the prevalence in the Parisian registry would increase from 328.6 to 363.9 per 10,000 total births. Maternal age standardization was then applied to account for differences in age structure among the registry populations. After adjusting the Paris registry data for case recording duration and standardizing by maternal age, the standardized prevalences per 10,000 total births were as follows: 355.3 in Auvergne, 249.0 in the West Indies, 350.4 in Réunion Island, 387.2 in Brittany, and 355.8 in Paris. The results show fairly similar prevalences among Auvergne, Réunion, and Paris, with a less pronounced gap for Brittany compared to the other registries (see the methodological note included in the "Data Sheet_Congenital Anomalies Report_2019-2021").

In Europe, the overall prevalence of congenital anomalies was 276,2 per 10,000 total births for 2019-2021 (95% CI: 274.2–278.3) (13) and varies considerably among registries (20). These differences can be explained by variations in healthcare system organization, prenatal screening policies, demographic characteristics of populations, as well as disparities in data access and case registration methods used by the registries.

II. Prevalence of Cases with Congenital Anomalies by Anomaly Group and Presence or Absence of One or More Genetic Disorders

The most common groups of congenital anomalies were cardiac anomalies (95.2 cases per 10,000 total births; 95% CI [91.5–99.0]), genetic disorders (78.8 [75.5–82.2]), limb anomalies (including reduction defects—transverse, longitudinal, or intercalary—polydactyly, syndactyly, clubfoot, and hip dislocation) (70.3 [67.2–73.6]), and CAKUT (61.0 [58.1–64.1]) (Figure 3; Data Table 2 in "Data Sheet_Congenital Anomalies Report_2019-2021"). The least frequent anomalies were ear, face, and neck, respiratory, and eye (prevalence < 10 cases per 10,000 total births).



Sources: Registries of Auvergne, Brittany, Paris, Reunion Island, West Indies 2019-2021

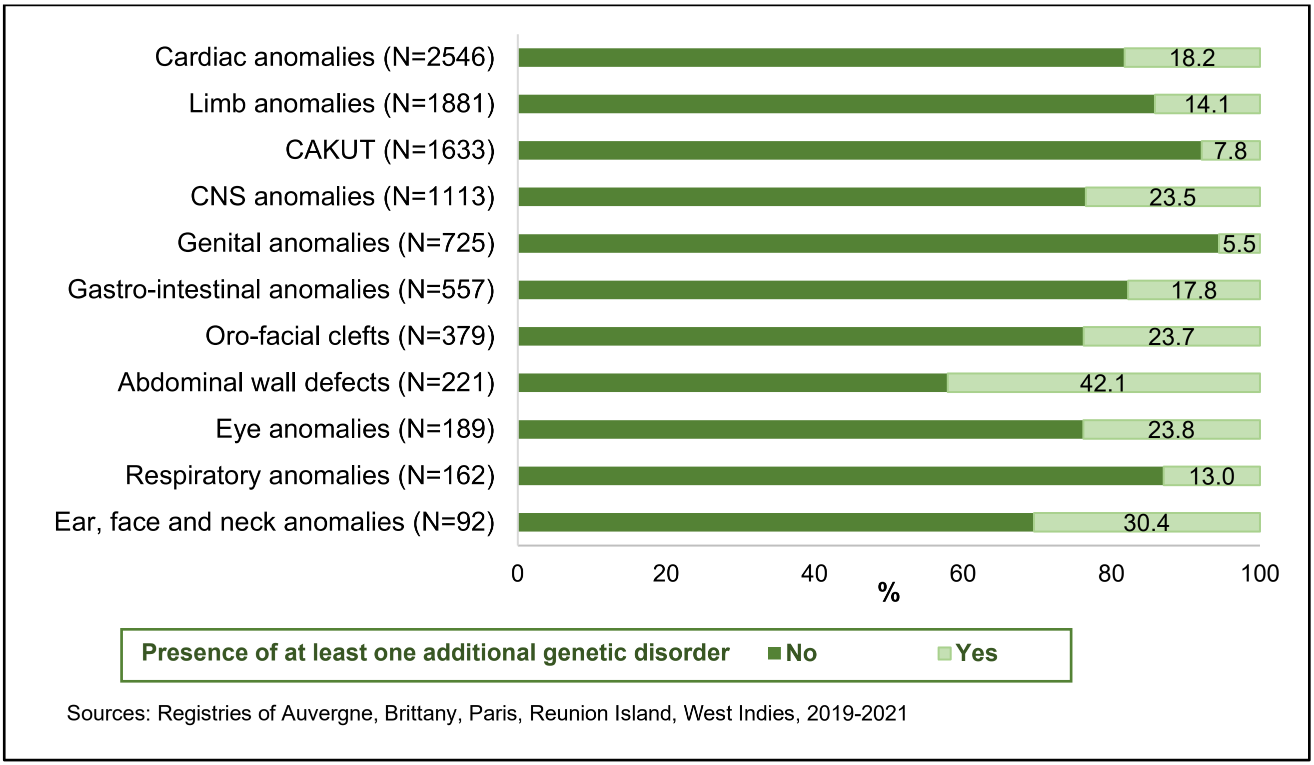
Note: A single fetus, newborn, or child affected by multiple groups of anomalies may be counted in several corresponding bars of the graph. For example, a fetus with a cardiac anomaly, limb anomaly, and genetic disorder would be represented in the respective three bars.

Figure 3. Prevalence of cases with congenital anomalies among total births, by anomaly group, 2019-2021

Interpretation of results:

These results confirm the trends observed in other European registries for the same study period (2019–2021) regarding the ranking of the most common congenital anomalies; however, observed prevalences in France are slightly higher for cardiac anomalies (95.2 vs. 79.4 cases per 10,000 total births) and genetic disorders (78.8 vs. 65.2 cases per 10,000 total births). Differences between French and EUROCAT data are more pronounced for limb anomalies (70.3 vs. 38.5 cases per 10,000 total births) and CAKUT (61.0 vs. 36.6 cases per 10,000 total births). These differences may be attributed to differences in prenatal screening practices among countries. In contrast, rare anomalies—such as those of the ear, face, neck, eye, and respiratory system—remain the least frequent and comparable, with a prevalence of fewer than 10 cases per 10,000 total births in all studied regions.

For cases with multiple anomalies, the groups of congenital anomalies most frequently diagnosed in the presence of at least one genetic disorder were: abdominal wall defects (42.1%, 95% CI [35.8–48.6]), ear, face, and neck anomalies (30.4%, 95% CI [22.2–40.2]), as well as eye (23.8%, 95% CI [18.4–30.3]), oro-facial clefts (23.7%, 95% CI [19.8–28.3]), and CNS (23.5%, 95% CI [21.1–26.0]) anomalies (Figure 4; Data Table 3 in "Data Sheet_Congenital Anomalies Report_2019-2021").



Sources: Registries of Auvergne, Brittany, Paris, Reunion Island, West Indies, 2019-2021

Note: A single fetus, newborn, or child affected by multiple groups of anomalies may be counted in several corresponding bars of the graph.

Figure 4. Distribution of cases with congenital anomalies among total births by anomaly group and presence or absence of at least one genetic disorder in each group, 2019–2021

Interpretation of results:

These results are consistent with those from other European registries for the same period (13), although the French registries show slightly higher proportions for: abdominal wall defects 42.1% (vs. 30.6%) and ear, face, and neck 30.4% (vs. 21.8%); eye 23.8% (vs. 12.3%); oro-facial clefts 23.7% (vs. 14.8%); and CNS 23.5% (vs. 17.2%) anomalies.

III. Proportion of Congenital Anomaly Groups by Timing of Diagnosis

Box 2. Expert Commentary: Asma Omarjee, Gynecologist-Obstetrician, REMACOR Registry, Réunion Island

Prenatal screening for congenital anomalies relies on three systematic ultrasound scans, one per trimester of pregnancy. The first-trimester ultrasound is also part of the combined screening for trisomy 21, the most common viable chromosomal anomaly, which justifies its systematic screening. Depending on the estimated risk, a non-invasive prenatal test (NIPT) using circulating cell-free fetal DNA or an invasive procedure (amniocentesis or chorionic villus sampling) may be offered to confirm the diagnosis.

Pregnancy monitoring includes two additional ultrasound scans: one in the second trimester (20–25 weeks) to detect fetal anomalies and assess morphological growth, and another in the third trimester (30–35 weeks) to monitor fetal well-being, position, and growth, allowing for the detection of late-onset anomalies or perinatal complications. Fetal ultrasound is thus a major screening tool, integrated into a structured system governed by the French National Conference on Obstetric and Fetal Ultrasound (CNEOF).

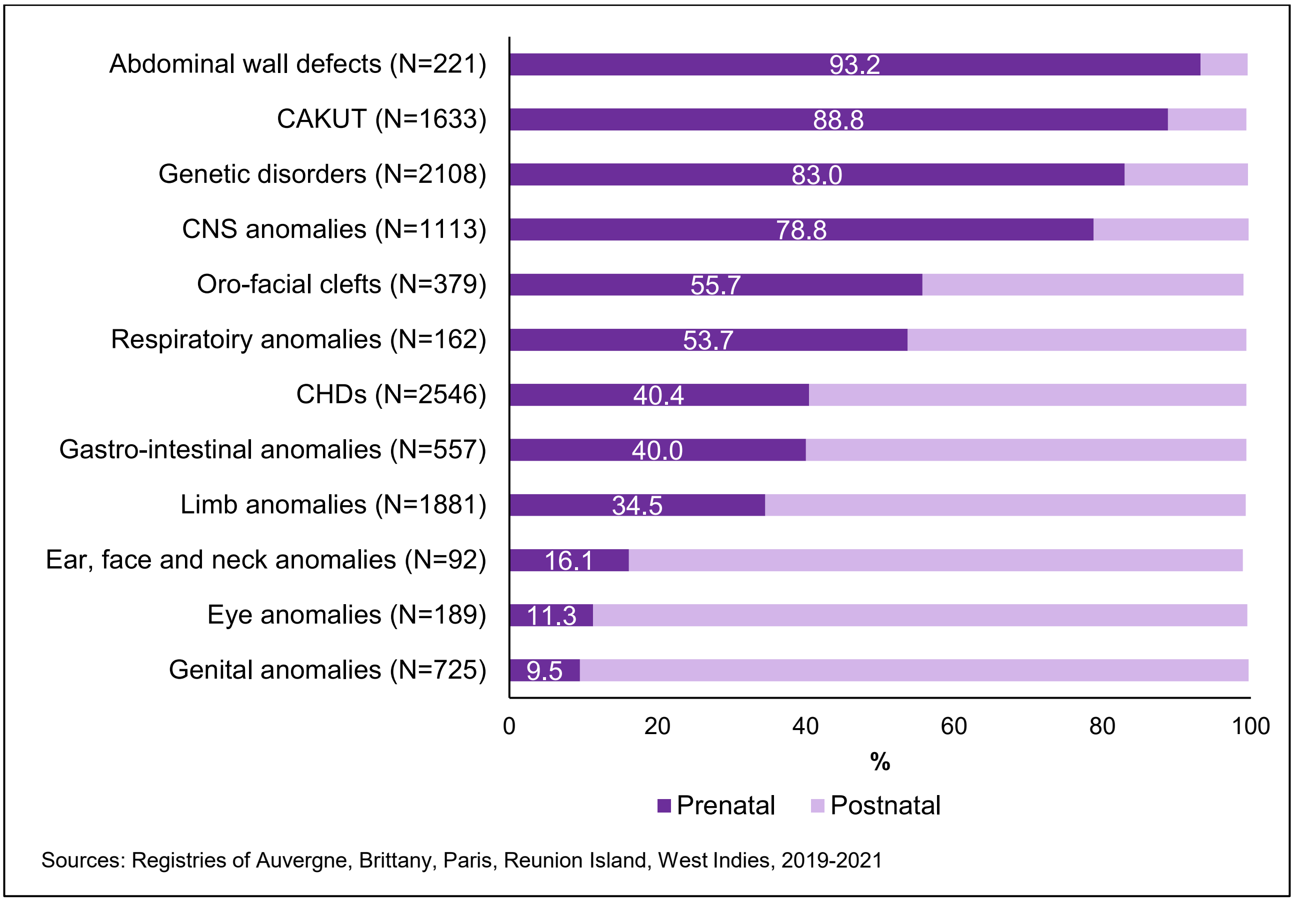
When anomalies are suspected or confirmed, management is handled by the CPDPN. These centers bring together specialists in ultrasound, genetics, obstetrics, and pediatrics to coordinate medical follow-up, multidisciplinary discussions, and parental counseling. The CPDPN also oversees decisions regarding medical termination of pregnancy, always in consultation with the family and in compliance with French law. This structured approach ensures early and reliable detection of anomalies, accurate diagnosis, and appropriate medical and ethical support throughout pregnancy.

During 2019-2021, nearly 60% of recorded congenital anomalies were identified before birth. Detection rates varied depending on the type of anomaly: more visible anomalies, such as abdominal wall defects or CNS, were more easily detected, whereas anomalies affecting less accessible structures, such as the ears, eyes, or genital organs, are more likely to be undetected during prenatal screening.

Since 2022, strengthened CNEOF guidelines, including new mandatory ultrasound items, along with the increasing use of genomic sequencing in prenatal care, suggest potential improvements in the detection of congenital anomalies. The next step will be to assess the impact of these advancements on the prevalence of diagnosed anomalies and on medical and parental decision-making.

Among the 9,429 fetuses, newborns, and infants with at least one congenital anomaly, nearly 60% (95% CI [49.9–68.8]) were diagnosed prenatally. This rate decreases to nearly 51% when excluding cases with multiple anomalies in the presence of at least one genetic disorder (data not shown).

Some anomalies have particularly high prenatal diagnosis rates (>75%), including abdominal wall defects, CAKUT, genetic disorders, and CNS anomalies (Figure 5; Data Table 4 in “Data Sheet_Congenital Anomalies Report_2019-2021”).



Sources: Registries of Auvergne, Brittany, Paris, Reunion Island, West Indies, 2019-2021

Note: A single fetus, newborn, or child affected by multiple groups of anomalies may be counted in several corresponding bars of the graph.

Figure 5. Distribution of cases with congenital anomalies among total births, by anomaly group and timing of diagnosis (prenatal or postnatal), 2019–2021

Conversely, groups of congenital anomalies predominantly diagnosed after birth are those whose detection relies more on clinical examination than prenatal ultrasound. These include genital, eye, and ear, face, and neck anomalies, as well as certain non-severe cardiac anomalies (Appendix 3) (see the chapter on cardiac anomalies, Table 2).

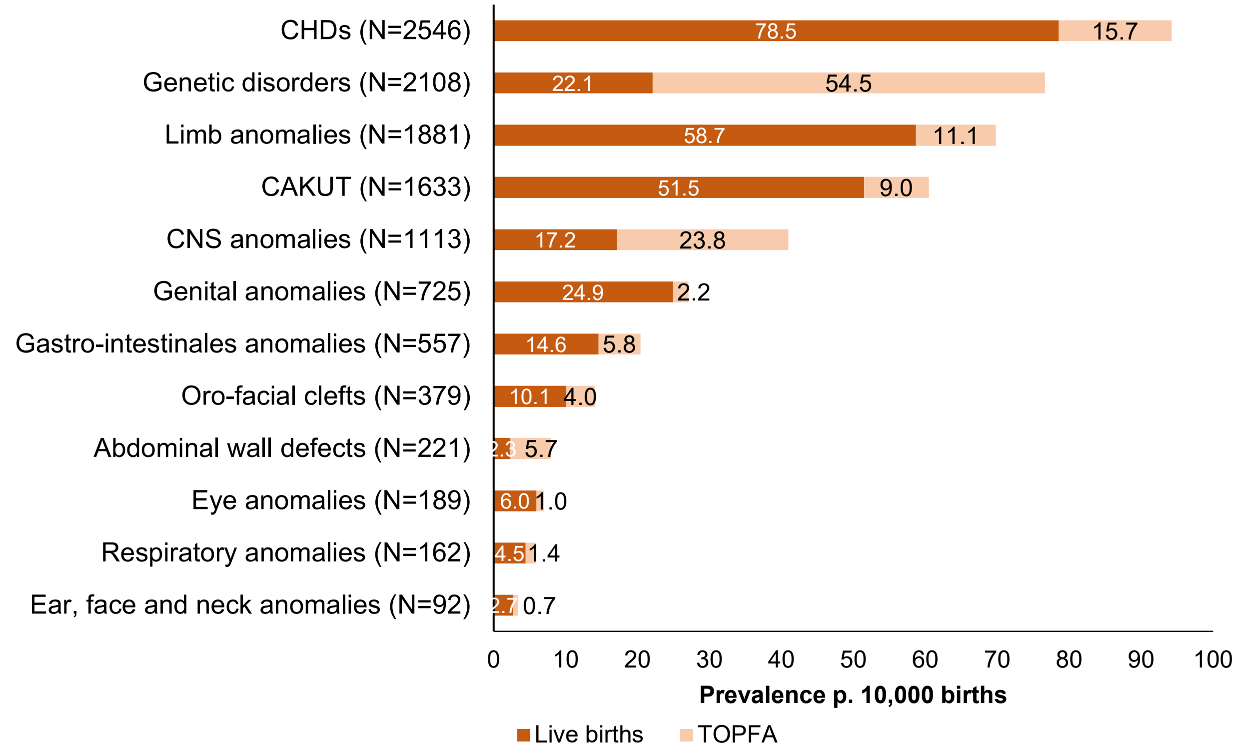
Interpretation of results:

In France, public health policies regarding prenatal diagnosis enable early detection for several groups of congenital anomalies. The highest prenatal diagnosis rates by anomaly group, according to data from French registries, were comparable to those reported by the National Congenital Anomaly and Rare Disease Registration Service (NCARDRS) in England for abdominal wall defects and CAKUT. However, rates were slightly higher in France for genetic disorders (83% vs. 70%) and lower for CNS anomalies (78.8% vs. 89.9%) (21).

IV. Pregnancy Outcomes

Among all recorded cases, 74.4% resulted in live births, 24.1% underwent TOPFA, regardless of GA, and 1.5% resulted in spontaneous intrauterine fetal deaths at or after 22 weeks of gestation (data not shown).

The most frequent groups of congenital anomalies among live births were cardiac (78.5 per 10,000 live births; 95% CI [75.2–82.0]), limb (58.6 [55.8–61.6]), and CAKUT (51.5 [48.8–54.3]) (Figure 6; Data Table 5 in “Data Sheet_Congenital Anomalies Report_2019-2021”).



Sources: registries of Auvergne, Brittany, Paris, Reunion Island, West Indies 2019-2021

Note (1) A single fetus, newborn, or child affected by multiple groups of anomalies may be counted in several corresponding bars of the graph.
Note (2) Fetal deaths were excluded from this analysis due to their low prevalence.

Figure 6. Prevalence of congenital anomaly cases by pregnancy outcome (live births and TOPFA), by congenital anomaly group, 2019-2021

The most severe anomalies leading to TOPFA primarily included genetic disorders (54.5 [51.8–57.4] cases per 10,000 total births), followed by CNS anomalies (23.8 [22.0–25.7]) and CHDs (15.7 [14.2–17.3]). When excluding cases with multiple anomalies including one or more genetic disorders, CNS anomalies had the highest TOPFA prevalence, with 16.7 cases per 10,000 total births (95% CI [15.3–18.5]) (data not shown).

Interpretation of results:

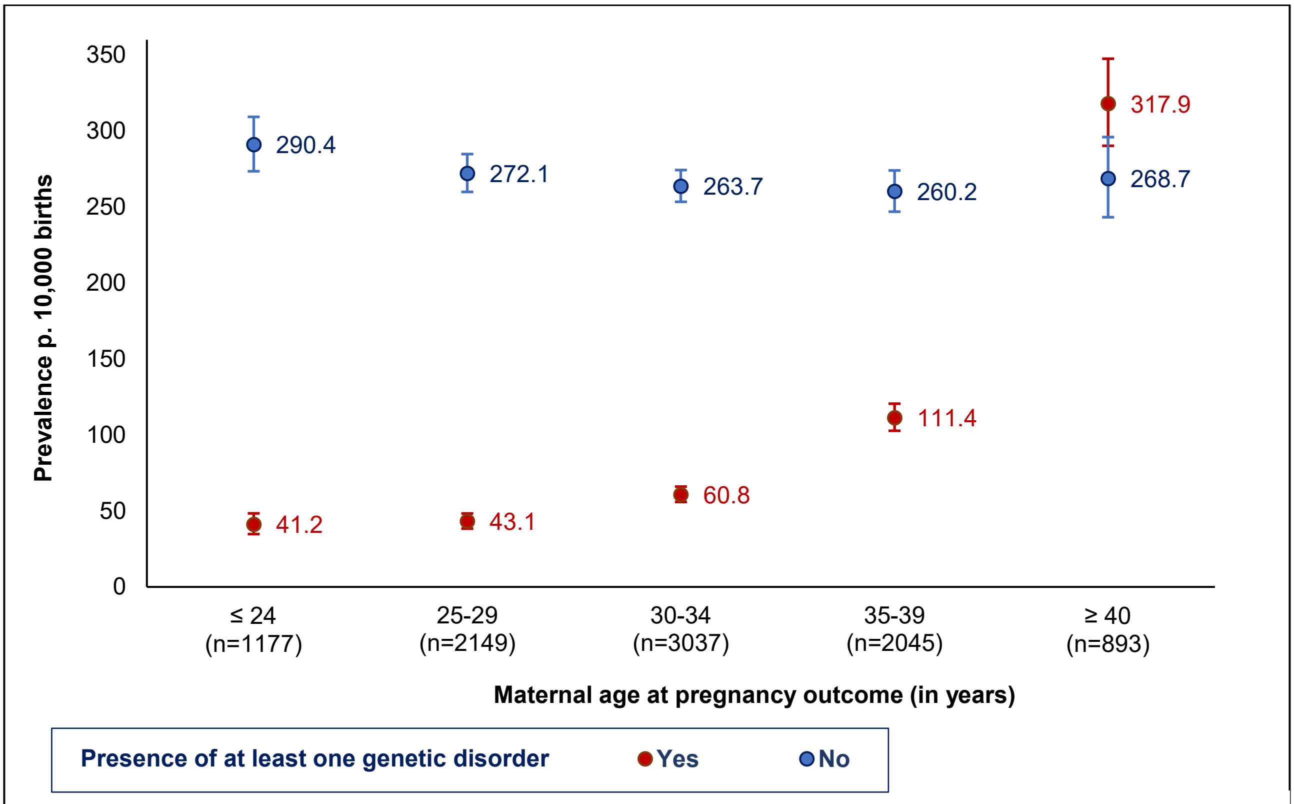
Pregnancy outcomes recorded by French registries are comparable to those reported by EUROCAT for the same period, with 78.7% live or stillbirths and 21.3% TOPFA. Among live births, prevalence for each group of anomalies tended to be comparable to those observed by EUROCAT for the same period (13), except for higher prevalences of cardiac anomalies (78.5 vs. 69.1), limb anomalies (58.6 vs. 34.0), and CAKUT (51.5 vs. 31.6) (per 10,000 live births for French registry data vs. per 10,000 live or stillbirths for EUROCAT data).

Regarding TOPFA, the observed trends were also consistent with those reported by EUROCAT for the same period. Genetic disorders remain the leading reason for TOPFA, followed by CNS and cardiac anomalies. Prevalence estimates reported by French registries for these three groups (54.5, 23.8, and 15.7 per 10,000 births, respectively) were higher than those reported by EUROCAT (33.1, 14.9, and 10.4 per 10,000 total births, respectively) (13).

Finally, excluding cases with multiple anomalies including one or more genetic disorders (data not shown), showed that the French registry and EUROCAT prevalence estimates were similar. In particular, CNS anomalies remained the group most frequently leading to TOPFA (14.5 per 10,000 total births in the French registries, compared to 12.1 per 10,000 total births for EUROCAT).
Differences in public health policies, screening practices, and regulations concerning TOPFA may partly explain the variations observed across Europe. In France, TOPFA is possible up to term when the fetus is affected by a particularly severe condition, as confirmed by a CPDPN (22). In some European countries, TOPFA is not permitted or is no longer possible after a certain GA.

V. Prevalence of Congenital Anomaly Groups by Maternal Age

The prevalence of fetuses, newborns, and children with congenital anomalies that included at least one genetic disorder increased significantly with maternal age (Figure 7; Data Table 6 in "Data Sheet_Congenital Anomalies Report_2019-2021"). Among mothers aged 40 years and older, prevalence reached 317.9 cases per 10,000 total births, which is nearly eight times higher than that for mothers aged 24 years or younger (41.2 cases per 10,000 total births).



Sources: Registries of Auvergne, Brittany, Paris, Reunion Island, West Indies, 2019-2021

Figure 7. Prevalence of congenital anomaly cases by presence or absence of a genetic disorder among total births and maternal age, 2019–2021

In the absence of a genetic anomaly, this age-related trend disappears, and a slightly higher prevalence is observed in the group of mothers aged 24 years and younger.

Interpretation of results:

The notable increase in the prevalence of genetic disorders with advancing maternal age is consistent with the literature. Among mothers aged 40 years and older, this marked increase is primarily explained by a higher occurrence of chromosomal anomalies, particularly aneuploidies such as trisomy 21. The link between advanced maternal age and increased risk of chromosomal anomalies is well established in the literature (15, 18, 19) and is attributed to the progressive decline in oocyte quality and ovarian reserve with age (20–22).

At the other end of the maternal age spectrum, mothers aged 24 years and younger also exhibited an increased risk for certain congenital anomalies, even without the presence of genetic disorders, particularly abdominal wall defects. This association has been specifically observed for gastroschisis, whose prevalence is significantly higher in this age group compared to older mothers aged 40 years and older. These findings align with the literature, including data from the National Birth Defects Prevention Network in the United States, which identified similar findings based on analysis from 13 surveillance programs (23).

Indicators for Selected Congenital Anomalies

Cardiac Anomalies

Box 3. Expert Commentary: Dr Julie Chabaneix (Pediatric Cardiologist, Coordinator of the ATENA Registry, Nouvelle-Aquitaine, Bordeaux University Hospital)

Among congenital anomalies, cardiac anomalies hold a distinct position due to their high frequency and impact on morbidity and mortality. They remain the leading cause of neonatal mortality from congenital anomalies in developed countries. However, major advancements in prenatal screening, cardiac surgery, and resuscitation over recent decades have dramatically improved their prognosis; nearly 85% of affected children now reach adulthood. The challenge has shifted beyond survival to reducing the risk of long-term sequelae, particularly neurodevelopmental issues, which may arise even in the absence of concomitant genetic disorder. In this context, prenatal screening plays a central role, both in organizing optimal neonatal care and in supporting families facing potentially severe diagnoses that may lead to TOPFA.

EUROCAT classification identifies a specific subgroup of "severe" cardiac anomalies, corresponding to cardiac conditions associated with major vital or hemodynamic consequences that require specialized management, often surgical, from the neonatal period (see Appendix 3). Beyond this subgroup, EUROCAT does not provide a classification for other heart defects, which encompass highly heterogeneous clinical situations—ranging from truly non-severe (or simple) anomalies to complex heart conditions not classified as severe (e.g., certain heterotaxies or less specific codes).

In this report, to enhance the clarity of results and the interpretation of prenatal diagnosis and pregnancy outcome indicators, we chose to define a specific group of non-severe cardiac anomalies. This group is limited to anomalies traditionally considered non-severe in cardiology practice: ventricular septal defects, atrial septal defects, patent ductus arteriosus, and valvular pulmonary stenosis. This methodological choice aims to avoid biases associated with a non-exclusive anomaly approach and to enable a more relevant analysis of prenatal diagnosis rates and TOPFA for these truly non-severe forms. Additionally, within both severe and non-severe cardiac anomalies, we further distinguished isolated cases, defined as those without a concomitant extracardiac anomaly or genetic disorder.

During 2019–2021, cardiac anomalies were the most common group of congenital anomalies in France. A total of 2,546 cases with at least one cardiac anomaly were recorded in the five registries, corresponding to a prevalence of 95.2 per 10,000 total births (Table 2; Data Table 7 in “Data Sheet_Congenital Anomalies Report_2019-2021”). Among these cases, 464 had at least one cardiac anomaly in the presence of at least one identified genetic disorder, representing a prevalence of 17.3 per 10,000 total births and a proportion of 18.2%.

Table 2. Frequencies, prevalences, and rates of prenatal diagnosis and TOPFA in cases with cardiac anomalies, by group of cardiac anomalies, 2019-2021

Group of Cardiac Anomalies	N	Prevalence per 10,000 total births	Prenatal diagnosis (%)	N TOPFA	% TOPFA
All cardiac anomalies	2546	95.2	31.6	420	16.5
Cardiac anomalies in the presence of at least one genetic disorder	464	17.3	40.4	243	52.4
Total severe cardiac anomalies[1]	706	26.4	78.5	256	36.3
Isolated severe cardiac anomalies[2]	412	15.4	73.9	83	20.2
Total non-severe cardiac anomalies[3]	1540	57.6	20.0	93	8.9
Isolated non-severe cardiac anomalies[4]	1196	44.7	12.7	2	0.2

[1] Includes cases defined as severe cardiac anomalies by EUROCAT (15)

[2] Includes cases defined as severe cardiac anomalies by EUROCAT, as well as isolated cardiac anomalies classified by the algorithm developed by EUROCAT among cases with multiple anomalies (15)

[3] Includes cases with ventricular septal defect, atrial septal defect, pulmonary valve stenosis, or patent ductus arteriosus in term infants, without an associated severe cardiac anomaly (as defined by EUROCAT), for cases with multiple cardiac anomalies

[4] Includes cases as defined above, as well as isolated cardiac anomalies classified by the algorithm developed by EUROCAT among cases with multiple anomalies (15)

When looking into severe cardiac anomaly cases, 706 included at least one severe cardiac anomaly, according to the EUROCAT definition (Appendix 3), corresponding to a prevalence of 26.4 per 10,000 total births. Among these cases, 412 were not diagnosed in the presence of an extracardiac anomaly or one or more genetic disorders, comprising the subgroup of isolated severe cardiac anomalies.

Furthermore, 1540 cases presented with at least one non-severe cardiac anomaly (ventricular septal defect, atrial septal defect, pulmonary valve stenosis, patent ductus arteriosus), with a prevalence of 57.6 per 10,000 births. Among these, 1196 cases were not diagnosed in the presence of an extracardiac anomaly, a severe cardiac anomaly (as defined by EUROCAT), or a genetic disorder, defining the group of isolated non-severe cardiac anomalies. The prevalence of this group was 44.7 per 10,000 total births.

The prenatal diagnosis rate varied significantly between subgroups: 78.5% for severe cardiac anomalies, 20.0% for non-severe forms, and 12.7% for isolated non-severe cardiac anomalies. Regardless of severity, 40.4% of cardiac anomalies with one or more genetic disorders were diagnosed prenatally.

TOPFA was performed in 52.4% of cardiac anomalies with one or more genetic disorders, 36.3% of severe CHDs, and 2.0% of isolated severe cardiac anomalies. For non-severe cardiac anomalies, the rate of TOPFA (8.9%) decreased markedly after excluding cases diagnosed with at least one severe cardiac anomaly and/or at least one genetic disorder (0.2%). Additional cardiac anomalies data are available in “Data Sheet_Congenital Anomalies Report_2019-2021, Data Table 8”.

Interpretation of results:

These results confirm the major epidemiological burden of cardiac anomalies within the landscape of congenital anomalies, characterized by high prevalence, considerable heterogeneity of forms, and a substantial impact on care pathways and parental decisions.

The prevalence observed in this report (95.2 per 10,000 total births) was higher than that reported by EUROCAT (84.2 per 10,000 total births). This difference may be explained by variations in the completeness of data collection, access to prenatal and postnatal diagnosis, as well as methodological differences between registries, as previously discussed. It highlights the importance of cautious interpretation of international comparisons and the need to contextualize results according to healthcare and surveillance systems.

The prenatal diagnosis rate for severe cardiac anomalies (74.7%) reflects the performance of prenatal screening in France. It aligns with previous studies showing a steady improvement in the antenatal detection of severe forms over the past two decades (24,25). This performance is based on the structured organization of care networks, specialized training for professionals, the use of reference centers, and coordination provided by CPDPN. However, this effectiveness remains unevenly distributed across the country, as evidenced by the interregional disparities regularly observed and documented in European and national literature (26,27).

The impact of prenatal screening is no longer limited to improving survival rates. For certain cardiac anomalies, such as transposition of the great arteries, a reduction in neonatal mortality has been demonstrated since the late 1990s (28). In a context where the most severe forms are now predominantly identified prenatally and where neonatal and surgical care have significantly advanced, the challenge of screening also concerns supporting families, anticipating care pathways, and aiding decision-making.

The high rates of TOPFA observed for severe cardiac anomalies, as well as those diagnosed in the presence of a genetic disorder or polymalformative syndrome, are consistent with international data. These data report TOPFA rates often exceeding 50% and reaching up to 85%, particularly for cases involving cardiac anomalies with at least one genetic disorder or extracardiac anomaly, illustrating the major influence of prenatal screening on TOPFA decisions in these contexts (29–32) .

The introduction in October 2023 of cardiac views during the first-trimester ultrasound, as part of the good practice guidelines from the CNEOF, represents a recent evolution in prenatal screening for cardiac anomalies. This approach aims to improve the early detection of certain severe forms, such as univentricular heart defects. Several studies have demonstrated the feasibility of this strategy in specialized settings, with good diagnostic performance for certain severe anomalies (33). However, its wider implementation requires a high level of technical expertise, adaptation of care pathways, and specific training for sonographers. Evaluating its real-world implementation, acceptability, and impact on medical decisions and pregnancy outcomes will be a major challenge in the coming years.

Genetic Disorders

Box 4. Expert Commentary: Isabelle Perthus (Geneticist, Head of the CEMC-Auvergne, Medical Genetics Department, Clermont-Ferrand University Hospital)

Genetic disorders include chromosomal number abnormalities (aneuploidies), chromosomal micro-rearrangements (microdeletions, microduplications, unbalanced translocations, etc.), and monogenic syndromes whose clinical presentation may include congenital anomalies. However, non-malformative genetic syndromes (e.g., cystic fibrosis, hemophilia, Fragile X syndrome, muscular dystrophies, metabolic syndromes, etc.) or chromosomal micro-rearrangements associated with isolated neurodevelopmental disorders are not recorded by the registries.

Within the framework of standardized surveillance conducted by registries following the methodology of EUROCAT (15), a congenital anomaly is considered "genetic" when, based on current knowledge, it is part of the clinical spectrum of the genetic disorders identified in the fetus or child. If this is not the case, information regarding the associated genetic diagnosis is recorded, but the congenital anomaly is not considered to be linked to a genetic disorder. This distinction is important for public health monitoring and during investigations into suspected case clusters, for example.

The diagnosis of a genetic disorder is based on cytogenetic analyses – karyotype, Chromosomal Microarray Analysis (CMA), Fluorescence In Situ Hybridization (FISH)), or molecular genetic analyses (targeted gene/panel analysis or pan-genomic analyses: exome or genome sequencing). These tests can be conducted prenatally or postnatally, depending on the clinical context and parents' wishes.

The request for prenatal cytogenetic or molecular diagnosis is based on the identification of a situation involving an increased risk of a genetic disorder, whether this risk is known before pregnancy (e.g., parent(s) carrying a genetic disorder, diagnosis in a previous child) or identified during screening examinations (first trimester organized screening, ultrasound markers, etc.). The conditions for accessing prenatal diagnosis are defined in the French Public Health Code (34,35).

Postnatally, a genetic diagnosis may be established sometime after the case (fetus or child) is included in the registry. This delay is related to the timing of access to genetic testing and the evolution of techniques, with facilitated access to genome sequencing for diagnostic purposes since 2020 (according to several pre-indications selected by the French National Authority for Health [HAS] under the France Genomic Medicine 2025 Plan). Parents are, of course, always free to refuse the offer of genetic testing. It is possible to update the registry database once the genetic results are known, without any time limit after inclusion.

During 2019-2021, the prevalence of genetic disorders was 78.8 per 10,000 total births (or 1 case per 127 births) (Table 3; Data Table 9 in "Data Sheet_Congenital Anomalies Report_2019-2021").

Table 3. Frequencies, prevalences, and prenatal diagnosis rates of cases with genetic disorders among total births, 2019–2021

Genetic Disorders	N	Prevalence per 10 000 total births	Prenatal diagnosis (%)
All genetic disorders	2108	78.8	83.0
Trisomies (13,18, 21)	1249^	46.7	93.9
Other (chromosomal micro-rearrangements and monogenic syndromes)	691	25.8	64.3

^ One case had two trisomies

More than one-half of these cases involved aneuploidies (46.7 per 10,000), primarily trisomy 21 (33 per 10,000), which is the leading cause of intellectual disability worldwide (Tables 3 and 4).

Table 4. Frequencies, prevalences, and prenatal diagnosis rates of cases with chromosomal number abnormalities (aneuploidies) among total births and pregnancy outcomes in cases of genetic disorders diagnosed prenatally, 2019–2021

				Pregnancy outcomes among cases diagnosed prenatally		
Chromosomal Aneuploidies	N	Prevalence per 10,000 total births	% PND	% LB	% TOPFA	% FD
Trisomy 13	107	4.0	93.5	7.0	90.0	3.0
Trisomy 18	260	9.7	95.8	7.7	87.5	4.8
Trisomy 21	883	33.0	92.3	14.1	83.8	2.1
Polyploïdies	42	1.6	91.6	0.0	97.2	2.8
Sex chromosome anomalies[1]	131	4.9	87.8	21.7	75.7	2.6

PND= Prenatal Diagnosis; FD= Fetal deaths; LB= Live Births; TOPFA= Termination of Pregnancy for Fetal anomaly

[1] Sex chromosome anomalies refer to numerical abnormalities of the sex chromosomes, including Monosomy X (Turner syndrome), 47, XXY (Klinefelter syndrome), and Triple X

Among live births (data not shown), 166 children were diagnosed with trisomy 21, corresponding to a prevalence of 6 per 10,000 live births (1 case per 1,587 live births). Prevalence estimates for trisomies 18 and 13, which generally manifest as severe polymalformative syndromes with early pregnancy loss, were 9.7 and 4.0 per 10,000 total births, respectively (Table 4; Data Table 10 in "Data Sheet_Congenital Anomalies Report_2019-2021"), with approximately 1 per 10,000 live birth for each trisomy (data not shown).

Polyploidies, which involve cells containing multiples of the haploid number of chromosomes (69 chromosomes in triploidy, 92 chromosomes in tetraploidy), most often result in early pregnancy loss. In cases where the pregnancy progresses, there is a polymalformative syndrome with severe growth restriction, almost always lethal in utero. The prevalence of cases recorded by the registries was 1.6 per 10,000 total births (exceptionally rare at birth, 1 child per 16,666 live births, with short-term lethality). Regarding sex chromosome anomalies, the prevalence of cases recorded by the registries is 4.9 per 10,000 total births (Table 4).

In over 80% of cases, genetic disorders were diagnosed prenatally. This prenatal diagnosis rate is particularly high, at 93.9%, for aneuploidies (Table 3). It is 64.3% for other disorders (chromosomal micro-rearrangements, monogenic syndromes) (Table 3).

Following a prenatal diagnosis of trisomy 21, nearly 84% of couples requested termination of pregnancy. In 14% of cases, parents chose to continue the pregnancy, and the children were born alive. In 2.1% of cases, spontaneous intrauterine death occurred. For trisomies 13 and 18, nearly 90% of couples requested termination of pregnancy. Polyploidies, corresponding to very severe and almost always in utero lethal clinical presentations, resulted in no live births after prenatal diagnosis (termination of pregnancy in 97.2% of cases, intrauterine death in 2.8%). Regarding sex chromosome anomalies: termination of pregnancy was performed in 75.7% of cases after a prenatal diagnosis. These diagnoses included severe Monosomy X cases with severe fetal phenotypes, often lethal in utero (severe early-onset hydrops fetalis, complex cardiac anomalies, etc.), or those where termination of pregnancy was due to a co-occurring diagnosis of another severe congenital anomaly with the sex chromosome anomaly (termination due to the congenital anomaly, not the sex chromosome anomaly) (Table 4).

Interpretation of results:

Data from EUROCAT for 2019–2021 showed an overall prevalence of genetic disorders of 65.2 per 10,000 total births (13). French registries reported a higher prevalence of 78.8 per 10,000 total births (more than one-half of which were aneuploidies). This difference may be partly explained by variability in public health policies and access to genetic diagnosis among countries.

For trisomy 21, the prevalence in France was also higher than the European average: 33 per 10,000 total births (compared to 26.3 in EUROCAT data for the same period) (13). However, when considering only live births, the prevalence is 6.3 per 10,000 (approximately 1 case per 1,587 live births), compared to 10.6 per 10,000 in Europe (including live births and fetal deaths). It is important to note that the prevalence of trisomy 21 at conception is similar among all populations worldwide (36). The prevalence at birth is estimated between 1 in 400 and 1 in 3,000 live births (37).

The prevalence of trisomy 21 at birth in a country depends on the maternal age structure of the population, public health policies regarding prenatal diagnosis and access to termination of pregnancy, as well as societal attitudes and public policies concerning the overall care of individuals with disabilities (healthcare, accessibility, inclusion, etc.).

The prenatal diagnosis rate for aneuploidies is particularly high (nearly 94% for trisomies 21, 18, and 13), linked to France’s organized first-trimester screening policy for trisomy 21, offered to all pregnant women. Screening for fetal aneuploidies (trisomies 21, 18, and 13) using cell-free fetal DNA analysis in maternal blood began in France in 2013. In 2017, the HAS published recommendations on the "Role of cell-free fetal DNA testing in screening for trisomy 21." The best practice recommendations and reimbursement decree were issued in December 2018, and authorization for laboratories to perform NIPT started in 2019. Screening using cell-free fetal DNA quickly expanded to include trisomies 13 and 18, and gradually other chromosomal anomalies, following informed consent from the pregnant woman. An increase in the number of prenatal diagnoses of trisomy 21 has been observed in France since 2017, with implementation of NIPT reducing the number of invasive procedures (38).

During 2019-2021, EUROCAT data showed prevalence of trisomies 18 and 13 at 7.31 and 2.78 per 10,000 total births, respectively. Higher prevalence was observed in France (9.7 per 10,000 for trisomy 18 and 4.0 per 10,000 for trisomy 13). Fetuses with trisomies 18 or 13 most often present with severe polymalformative syndromes, usually lethal in utero (about 95% of cases). Prenatal diagnosis is primarily based on invasive sampling due to ultrasound markers in the first trimester, but also in some instances through NIPT. Early prenatal diagnosis allows registries to record fetuses meeting their inclusion criteria (particularly terminations for aneuploidy in the first trimester), whereas their spontaneous progression would likely have led to miscarriage before 22 weeks of gestation. It is worth noting that European registries only include fetal deaths from 22 weeks of gestation. Thus, the increased performance of prenatal diagnosis in late first trimester may suggest an increase in the number of cases, although it mainly reflects earlier detection of situations that would otherwise not have been recorded.

Sex chromosome anomalies include numerical abnormalities such as Turner syndrome (Monosomy X), Klinefelter syndrome (47, XXY), and Triple X syndrome. Cases recorded by registries include severe early fetal forms of Monosomy X (with hygroma/anasarca and/or associated with certain cardiac or kidney anomalies) and cases incidentally discovered during karyotyping for positive first-trimester screening or ultrasound markers. However, diagnoses of sex chromosome anomalies (except for certain severe Monosomy X cases) are generally made later, often at puberty or in adulthood. Turner syndrome is estimated to affect 1 in 2,500 girls, and Klinefelter syndrome 1 in 600 boys (39,40). The prevalences of sex chromosome anomalies from registry data (4.9 per 10,000 total births) are therefore underestimated and tend to decrease due to the reduction in invasive procedures resulting from the increasing use of NIPT. In France, the decision was made not to systematically report results concerning gonosomal anomalies as part of NIPT, which further limits the incidental discovery of sex chromosome anomalies, often associated with a good prognosis.

Regarding chromosomal micro-rearrangements and monogenic syndromes, the prenatal diagnosis rate is lower (64.3%), primarily relying on ultrasound screening. Clinical presentations during the fetal period, often similar (presence of one or more malformations, growth restriction, etc.), lead to the recommendation of invasive sampling for genetic etiological assessment, once the warning signs are confirmed by reference ultrasound. If a risk is known before pregnancy (e.g., family history, parental balanced translocation, risk of transmitting a monogenic syndrome), cytogenetic or molecular prenatal diagnosis can be used as a first-line option at the couple’s request.

Central Nervous System Anomalies: Neural Tube Defects

Box 5. Expert Commentary: Isabelle Monier (Epidemiologist, Head of the Paris Registry, Cochin University Hospital, Paris) and Nathalie Lelong (Project Manager, Co-Head of the Paris Registry, Cochin University Hospital, Paris)

Neural tube defects (NTDs) include anencephaly, encephalocele, and spina bifida.

In Europe, the prevalence is estimated at approximately 11.4 per 10,000 total births and 2.7 per 10,000 live births and stillbirths (13). These anomalies are responsible for severe disabilities and deaths, leading to termination of pregnancy in about 80% of cases. The majority of these anomalies (>80%) are detected prenatally through ultrasound.

NTDs can occur even without a family history but are more likely in the presence of risk factors, such as a previous NTD or the use of certain antiepileptic medications.

Prevention of NTDs is possible through folic acid (vitamin B9) supplementation during the preconception period. In France, the HAS recommends taking 0.4 mg/day of folic acid starting 4 weeks before pregnancy and continuing through the first three months of pregnancy. For individuals with risk factors for NTDs, the recommended dosage is 5 mg/day.

Based on data from five congenital anomaly registries in France for 2019–2021, the prevalence of NTDs was estimated at 13.7 per 10,000 total births and 1.3 per 10,000 live births (Table 5; Data Table 11 in “Data Sheet_Congenital Anomalies Report_2019-2021”).

Table 5. Frequencies, prevalences, and prenatal diagnosis rates of NTD cases without genetic disorders among total and live births, and frequencies and distribution of TOPFA among prenatally diagnosed NTDs without genetic disorders, 2019–2021

	Total Births	Total Prevalence	Live Births	Prevalence LB	PND	TOPFA among cases diagnosed prenatally
	N	Per 10,000 total births	N	Per 10,000 live births	N (%)	N (%)
NTD (total)	366	13.7	34	1.3	352 (96.2)	321 (91.2)
Without the presence of genetic disorders	334	12.5	34	1.3	323 (96.7)	292 (90.4)
Spina bifida (total)	166	6.2	27	1.0	157 (94.6)	133 (84.7)
Without the presence of genetic disorders	152	5.7	27	1.0	145 (95.4)	121 (83.4)
Anencephaly (total)	155	5.8	<5	0.1	154 (99.3)	151 (98.1)
Without the presence of genetic disorders	145	5.4	<5	0.1	144 (99.3)	141 (97.9)
Encephalocele/ meningocele (total)	45	1.7	5	0.2	40 (89.7)	36 (90.0)
Without the presence of genetic disorders	37	1.4	5	0.2	33 (93.1)	29 (87.8)

PND= Prenatal Diagnosis; LB= Live Births; TOPFA= Termination of Pregnancy for Fetal anomaly

NTDs are rarely diagnosed in the presence of one or more genetic disorder. The majority of NTDs (>95%) are detected prenatally, and TOPFA is performed in approximately 90% of cases. The prevalences of spina bifida and anencephaly are roughly similar, at around 6 per 10,000 total births, whereas the prevalence of live births with these conditions is low (<1.5 per 10,000 live births). Encephalocele and meningocele are less common, with estimated prevalences of 1.7 per 10,000 total births and 0.2 per 10,000 live births (Table 5).

Interpretation of results:

Cases of NTDs rarely present with concomitant genetic disorders and are predominantly diagnosed prenatally. Among these, anencephaly is a lethal anomaly; encephalocele has a variable prognosis depending on its size and location; and spina bifida results in disability, with severity depending on the extent and location of the lesion. The prevalence of NTDs among live births is low (less than 2 per 10,000) due to their severe nature, which explains the high proportion of TOPFA. Prevention of NTDs is possible through daily maternal intake of 0.4 mg of folic acid, started in the preconception period and continued throughout the first trimester of pregnancy (41). However, results from the 2021 French National Perinatal Survey indicate that less than one-third of women report taking folic acid before pregnancy (42). Although this represents an increase compared to 2010 (14.8% in 2010 vs. 28.3% in 2021), it remains insufficient (42). Similarly, data from health examination surveys—such as the National Nutrition and Health Survey (ENNS) (2006) and the Study on Health, Environment, Biomonitoring, Physical Activity, and Nutrition (Esteban) (2014–2016), conducted by Santé publique France—show an increased occurrence of serum folate deficiency (< 3.0 ng/ml) among women of childbearing age, with a prevalence that nearly doubled over a decade (increasing from 7.2% to 13.4%) (43,44).

This insufficient pre-pregnancy supplementation results in no reduction in NTDs in France and, more broadly, across Europe (45). For the period 2019-2021, the prevalence of NTDs in France was 13.7 per 10,000 total births versus 11.4 per 10,000 total births in Europe. In October 2024, the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) recommended the systematic fortification of flour with folic acid to address this issue (46).

The self-reported data on folic acid intake from women's interviews (42), along with the findings from Santé publique France's studies on serum folate deficiency (43,44), clearly show that this recommended prevention is not sufficiently implemented (47). Additionally, the WHO recommendations for food fortification, endorsed by ANSES in France, are not being applied (48).

Genital Anomalies: Hypospadias

Box 6. Expert Commentary: Florence Rouget (Pediatric Epidemiologist, Head of the Brittany Registry, Rennes University Hospital)

Hypospadias is a variation in male genital development characterized by an ectopic opening of the urethral meatus (urinary outlet), which, instead of being located at the tip of the glans, is displaced on the ventral side of the penis. It may or may not be associated with ventral curvature of the penis (chordee) and an incomplete ventral foreskin, resembling a "sapper's apron." The severity and functional impact of hypospadias vary depending on the location of the meatus (glanular, penile, or perineoscrotal), with distal forms generally being less severe and more often isolated than proximal forms. Surgical management may be recommended, typically between 6 and 18 months of age, according to American guidelines.

French registries follow EUROCAT's inclusion guidelines and record all forms of hypospadias, including glanular types. Hypospadias affects approximately 22 out of 10,000 total births in Europe (13). However, considerable geographical disparities in hypospadias exist worldwide (49,50), with the highest prevalences observed in North America and Northern Europe (50).

Epidemiological trends for hypospadias have evolved over time. Several studies reported an increase in prevalence between the 1960s and 1990s (51). However, data from EUROCAT registries show no clear trend during 1980-2000 (52), overall stability during 2001-2010 (49), and a recent decline during 2013–2022 (2). In France, several studies have been conducted by Santé publique France on the temporal evolution of the surgical management rate of hypospadias, among other things (57,58). The first, in 2004, assessed trends in surgeries for cryptorchidism and hypospadias among children under 7 years of age, showing stable intervention rates during 1998-2001. A second study, published in 2011 and covering the period 1998–2008, updated these data and revealed an average annual increase of 1.2% (95% CI: [0.6%; 1.8%]), not significant, in metropolitan France.

The etiology of hypospadias is multifactorial, involving both genetic and environmental factors (53,54). Among environmental factors, fetal exposure to endocrine-disrupting chemicals is strongly suspected (55,56).

During 2019-2021, the five French registries recorded 593 cases of hypospadias, corresponding to a prevalence of 22.2 per 10,000 total births (Table 6; Data Table 12 in “Data Sheet_Congenital Anomalies Report_2019-2021”).

Table 6. Frequencies, prevalences, and prenatal diagnosis rates of hypospadias cases (total, isolated, or with other anomalies) among total births, 2019–2021

		Total Prevalence	**Prenatal diagnosis**	**Postnatal diagnosis**
	N (%)	Per 10,000 total births	N (%)	N (%)
Hypospadias				
Total	593	22.1	57 (7.9)	535 (91.9)
Isolated	511 (86.2)	19.1	35 (4.8)	475 (95.0)
Non-isolated	82 (13.8)	3.1	22 (26.2)	60 (73.8)

The majority of recorded cases were isolated, with a prevalence of 19.1 per 10,000 total births. Diagnosis was made postnatally in 92% of cases (95% for isolated hypospadias and 74% for non-isolated cases).

Interpretation of results:

The overall prevalence of hypospadias observed from the five French registries during 2019-2021 (22.2 per 10,000 total births) is similar to the average prevalence reported by EUROCAT for the same period (21.2 per 10,000 total births, 95% CI [20.7–21.8]). Caution is needed when comparing data from sources outside EUROCAT, as some surveillance programs do not include glanular forms, considered minor, unlike EUROCAT data.

Most hypospadias cases are diagnosed after birth (92%). These are often distal, less severe forms that are not visible on prenatal ultrasound and are identified during the pediatric examination in the maternity ward, later confirmed by a pediatric surgeon in the months following birth. Cases detected prenatally are usually the most severe, rarer forms, or those associated with other malformations, genetic syndromes, or dysgonosomal abnormalities.

DISCUSSION

This report is based on data collected for the period, 2019-2021, by five French registries, providing an overview of the prevalence of congenital anomalies in France. It presents overall prevalence and prevalence estimates by groups of anomalies, specifically distinguishing cases diagnosed with one or more genetic disorders from those without additional identified genetic disorders. Prevalence estimates are also shown by pregnancy outcomes, timing of diagnosis, and certain maternal factors, including maternal age.

The results show an overall prevalence of congenital anomalies comparable to that reported by EUROCAT for the same period, with variations among the French registries. The most frequently reported anomalies, excluding genetic disorders, are cardiac anomalies, limb anomalies, and CAKUT, which is consistent with European data.

Genetic disorders are also among the most frequent. They are often concurrent with other anomalies, particularly cardiac, limb, and CNS anomalies, highlighting their central role in the severity of complex malformative conditions. Identifying a genetic etiology not only clarifies the severity of fetal pathology, particularly the neurodevelopmental prognosis, but also supports couples in making decisions regarding the outcome of the pregnancy: welcoming the child with anticipatory medical and social care or termination of pregnancy. Additionally, it provides essential genetic counseling, clarifying the risk of recurrence for future pregnancies and for relatives.

The report also shows strong prenatal screening performance for certain groups: over 75% of cases are detected in utero for genetic disorders, abdominal wall defects, CAKUT, and CNS anomalies. Prenatal diagnosis allows, depending on each situation, for tailored pregnancy monitoring, improved management, and preparation for the child's birth. It can also, if necessary, confirm the particular severity of a pathology (validation by a CPDPN), allowing access to a request for TOPFA made by the pregnant woman (which is legally permitted in France until the end of pregnancy). This early diagnosis promotes coordinated care or, if necessary, a decision for TOPFA. Conversely, some anomalies remain predominantly diagnosed after birth, such as non-severe cardiac anomalies or isolated hypospadias. The rate of TOPFA is proportional to the severity of the malformative and/or neurodevelopmental prognosis. The anomalies most frequently leading to TOPFA are CNS, severe cardiac, and genetic disorders. In France, TOPFA is governed by specific legislation allowing termination without GA limits when a particularly severe pathology is diagnosed or suspected (22).

Analysis by maternal age highlights two groups at increased risk. In mothers aged 40 years and older, there is an eightfold higher prevalence of congenital anomalies diagnosed with one or more genetic disorders (i.e., aneuploidy) compared to other maternal age groups. Excluding genetic disorders, in mothers aged 24 years or younger, there is a slightly higher prevalence of congenital anomalies compared to other maternal age groups, particularly gastroschisis, an abdominal wall defect (data not shown).

Regarding analyses by type of anomaly, cardiac anomalies were the most frequent (2,546 cases, prevalence of 95.2 per 10,000 total births), with 18.2% of cases diagnosed with one or more genetic disorders. Nearly 30% of these were severe (706 cases), more than one-half of which were isolated (412 cases). Prenatal diagnosis reached 78.5% for severe cardiac anomalies and 40.4% for those diagnosed with one or more genetic disorders. The rate of TOPFA was 52.4% for cardiac anomalies diagnosed with one or more genetic disorders, 36.3% for severe cardiac anomalies, but only 0.2% for non-severe, isolated cardiac anomalies.

For genetic disorders, the prevalence was 78.8 per 10,000 total births. Aneuploidies, the most common (46.7 per 10,000), were primarily trisomy 21 (33 per 10,000 total births, resulting in 166 live births). Trisomies 18 and 13 were less frequent (9.7 and 4.0 per 10,000, respectively), with only 7% resulting in live births. Prenatal diagnosis, performed in over 80% of cases (up to 92% for aneuploidies), led to TOPFA in the majority of cases: 83.8% for trisomy 21, nearly 90% for trisomies 13 and 18, and 97.2% for polyploidies, which are always lethal. For sex chromosome anomalies (4.9 per 10,000 total births), 75.7% of prenatally diagnosed cases resulted in TOPFA, often due to co-occurring severe malformations.

Regarding CNS anomalies, NTDs were the most frequent, with a prevalence of 13.7 per 10,000 total births. They were rarely diagnosed with genetic disorders but were detected prenatally in over 95% of cases by ultrasound, leading to TOPFA in approximately 90% of cases. For all CNS anomalies, the prevalence of live births remained low, except for severe microcephaly (data not shown).

Finally, among genital anomalies, hypospadias was the most common, with 593 cases recorded (prevalence of 22.2 per 10,000 total births). Most cases were isolated (prevalence of 19.1 per 10,000), and diagnosis was primarily postnatal (92%).

Strengths and limitations of registry data

The main strength of the epidemiological data presented in this report lies in their origin: they come from population-based registries, considered the gold standard for monitoring congenital anomalies. Firstly, these registries ensure comprehensive and high-quality data collection by cross-referencing multiple sources of information. They enable standardized data collection (type of anomalies, the presence or absence with genetic disorders, as well as pregnancy outcomes, including live births, fetal deaths, and TOPFA). Secondly, these data are coded and validated according to the recommendations of EUROCAT, ensuring their comparability with other European registries. Additionally, although these registries currently cover only about 16.4% of births in France, their presence in diverse and extensive territories, both in mainland France and in the Overseas Departments and Regions, allows for a geographically balanced distribution of cases with congenital anomalies.

Certain methodological limitations, however, must be highlighted. One is the heterogeneity in the duration of case inclusion. Specifically, the Parisian registry is limited to cases identified up to discharge from the maternity ward or neonatal hospital stay. This approach may lead to an underestimation of the prevalence of certain anomalies, such as cardiac or hypospadias, compared to other registries.

Also, as with EUROCAT, a minimum delay of two years is required to ensure the completeness and quality of the data (consolidation period), which limits their real-time updating.

Finally, registries rely on information available in medical records. Although maternal age is systematically recorded, other socio-economic and environmental factors—such as education level or exposure to chemical agents—are not consistently documented. This gap results in missing data and limits the study of environmental determinants. The systematic integration of these data into medical records would refine the analysis of territorial disparities, explore the social and environmental determinants of congenital anomalies, and guide etiological research. In this regard, the ATENA registry in Nouvelle-Aquitaine has implemented an additional environmental and medication questionnaire, collected directly from families. Assessing the feasibility, cost, and effectiveness of this method will be important for considering its extension to other registries.

Strengthening the registries, particularly through increased coordination within the RemaFrance collective, represents a structural advancement. This collaboration promotes the harmonization of practices, improves data quality, and enhances their scientific value, in synergy with Santé publique France and European partners.

CONCLUSION AND PERSPECTIVES

Congenital anomalies remain a major cause of perinatal morbidity and mortality, accounting for up to 27% of infant deaths in developed countries (33). They directly impact children's health and generate significant psychological, economic, and social consequences for families.

In this context, continuous epidemiological surveillance of congenital anomalies—recognized as a priority by the World Health Organization—is an essential public health tool (3). It enables rigorous quantification of the population impact, monitoring of temporal trends, identification of potential temporal clusters requiring targeted investigations, and evaluation of the effectiveness of screening and prevention strategies (34). This first national report on the surveillance of congenital anomalies in France, based on data from five population-based registries and standardized according to EUROCAT recommendations, provides updated reference data. These results are an indispensable foundation for guiding public health policies, improving the care of children with congenital anomalies, and supporting epidemiological research on their causes, care pathways, and outcomes (27).

Currently, population-based registries for congenital anomalies cover approximately 16.4% of births in France. Combining registry data, which remain the gold standard for epidemiological surveillance, with data from the SNDS presents an opportunity to enhance national coverage for certain congenital anomalies. In this regard, the MALFOSCAN feasibility study, led by Santé publique France in collaboration with the REGARDS network and based on data from four registries linked to the SNDS, aims to develop and validate algorithms for identifying six selected anomalies. Once the feasibility of this approach is assessed and validation is completed, these tools could expand surveillance to a national scale for the targeted anomalies. This could contribute to the analysis and validation of suspected spatiotemporal clusters in areas not covered by registries, thereby strengthening public health response capabilities. The feasibility of extending this approach to other anomalies will also be explored.

REFERENCES

1. Dolk H, Loane M, Garne E. The prevalence of congenital anomalies in Europe. Adv Exp Med Biol. 2010;686:349-64. doi:10.1007/978-90-481-9485-8_20 PubMed PMID: 20824455.

2. Perraud A, Garne, E., Morris, J. EUROCAT Monitoring of Congenital Anomalies. European Commission: Joint Research Centre; 2025. Rapport no.: JRC140903.

3. Christianson A, Howson CP, Modell B. March of Dimes global report on birth defects: The hidden toll of dying and disabled children. March of Dimes Birth Defects Foundation; 2006.

4. Congenital disorders [Internet]. Disponible sur: https://www.who.int/news-room/fact-sheets/detail/birth-defects

5. EUROCAT. JRC-EUROCAT Central Registry [Internet]. [cité 19 déc 2025]. Disponible sur: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-network/jrc-eurocat-central-registry_en

6. Tuppin P, Rudant J, Constantinou P, Gastaldi-Ménager C, Rachas A, de Roquefeuil L, *et al.* Value of a national administrative database to guide public decisions: From the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. Rev DÉpidémiologie Santé Publique. oct 2017;65:S149-67. doi:10.1016/j.respe.2017.05.004

7. Santé publique France. Santé publique France : qui sommes nous ? [Internet]. 2023. Disponible sur: https://www.santepubliquefrance.fr/a-propos/sante-publique-france-qui-sommes-nous

8. Ministère de la Santé. Santé publique France [Internet]. 2024. Disponible sur: https://sante.gouv.fr/ministere/acteurs/agences-et-operateurs/article/sante-publique-france

9. Santé publique France. Comités d'experts [Internet]. 2024. Disponible sur: https://www.santepubliquefrance.fr/a-propos/notre-organisation/comitologie/comites-d-experts

10. EUROCAT. European network of population-based registries for the epidemiological surveillance of congenital anomalies [Internet]. Disponible sur: https://eu-rd-platform.jrc.ec.europa.eu/eurocat_en

11. EUROCAT. Statistical Monitoring [Internet]. 2025. Disponible sur: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/statistical-monitoring_en

12. EUROCAT. Prenatal detection rates charts [Internet]. 2025. Disponible sur: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prenatal-screening-and-diagnosis_en

13. EUROCAT. Prevalence charts and tables [Internet]. 2025. Disponible sur: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prevalence_en

14. Bergman JE, Perraud A, Barišić I, Kinsner-Ovaskainen A, Morris JK, Tucker D, *et al.* Updated EUROCAT guidelines for classification of cases with congenital anomalies. Birth Defects Res. 2024;116(2):e2314.

15. Kinsner-Ovaskainen A, Perraud A, Barisic I, Bergman JE, Garne E. EUROCAT Guide 1.5 - Instructions for the registration of congenital anomalies - Updated Version - August 2025. Brussels: European Commission; 2025. Rapport no.: JRC143499.

16. Mason CA, Kirby RS, Sever LE, Langlois PH. Prevalence is the preferred measure of frequency of birth defects. Birt Defects Res A Clin Mol Teratol. oct 2005;73(10):690-2. doi:10.1002/bdra.20211 PubMed PMID: 16240384.

17. Mouquet MC, Rey S, Matet N, Barrois J. Le nouveau suivi de la mortinatalité en France depuis 2012. Études Résultats 901. 2014;6.

18. Cain M. Structural Equation Modeling using Stata. J Behav Data Sci. 2 déc 2021;1(2):156-77. doi:10.35566/jbds/v1n2/p7

19. Rouault K, Scotet V, Autret S, Gaucher F, Dubrana F, Tanguy D, *et al.* Evidence of association between GDF5 polymorphisms and congenital dislocation of the hip in a Caucasian population. Osteoarthritis Cartilage. sept 2010;18(9):1144-9. doi:10.1016/j.joca.2010.05.018 PubMed PMID: 20633687.

20. EUROCAT. Data quality indicators (2019-2023) [Internet]. 2025. Disponible sur: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/data-collection/data-quality_en

21. NHS England Digital [Internet]. NCARDRS Congenital Condition Official Statistics Report, 2022. Disponible sur: https://digital.nhs.uk/data-and-information/publications/statistical/ncardrs-congenital-anomaly-statistics-annual-data/ncardrs-congenital-condition-statistics-report-2022

22. Article L2213-1 - Code de la santé publique - Légifrance [Internet]. Disponible sur: https://www.legifrance.gouv.fr/codes/article_lc/LEGIARTI000043896164

23. Stallings EB, Isenburg JL, Rutkowski RE, Kirby RS, Nembhard WN, Sandidge T, *et al.* National population-based estimates for major birth defects, 2016-2020. Birth Defects Res. janv 2024;116(1):e2301. doi:10.1002/bdr2.2301 PubMed PMID: 38277408; PubMed Central PMCID: PMC10898112.

24. Dolk H, Loane M, Garne E. The prevalence of congenital anomalies in Europe. Adv Exp Med Biol. 2010;686:349-64. doi:10.1007/978-90-481-9485-8_20 PubMed PMID: 20824455.

25. Wren C, Richmond S, Donaldson L. Temporal variability in birth prevalence of cardiovascular malformations. Heart Br Card Soc. avr 2000;83(4):414-9. doi:10.1136/heart.83.4.414 PubMed PMID: 10722540; PubMed Central PMCID: PMC1729354.

26. Bakker MK, Bergman JEH, Krikov S, Amar E, Cocchi G, Cragan J, *et al.* Prenatal diagnosis and prevalence of critical congenital heart defects: an international retrospective cohort study. BMJ Open. 2 juill 2019;9(7):e028139. doi:10.1136/bmjopen-2018-028139 PubMed PMID: 31270117; PubMed Central PMCID: PMC6609145.

27. Khoshnood B, De Vigan C, Vodovar V, Goujard J, Lhomme A, Bonnet D, *et al.* Trends in prenatal diagnosis, pregnancy termination, and perinatal mortality of newborns with congenital heart disease in France, 1983-2000: a population-based evaluation. Pediatrics. janv 2005;115(1):95-101. doi:10.1542/peds.2004-0516 PubMed PMID: 15629987.

28. Bonnet D, Coltri A, Butera G, Fermont L, Le Bidois J, Kachaner J, *et al.* Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation. 23 févr 1999;99(7):916-8. doi:10.1161/01.cir.99.7.916 PubMed PMID: 10027815.

29. Tomek V, Jicínská H, Pavlícek J, Kovanda J, Jehlicka P, Klásková E, *et al.* Pregnancy Termination and Postnatal Major Congenital Heart Defect Prevalence After Introduction of Prenatal Cardiac Screening. JAMA Netw Open. 5 sept 2023;6(9):e2334069. doi:10.1001/jamanetworkopen.2023.34069 PubMed PMID: 37713196; PubMed Central PMCID: PMC10504618.

30. Huang Q, Franklin RCG, Seale AN, Jowett V, Pagel C, Crowe S, *et al.* Congenital heart disease in England: a national cohort study from fetal diagnosis to end of infancy. Heart Br Card Soc. 21 oct 2025;heartjnl-2025-326369. doi:10.1136/heartjnl-2025-326369 PubMed PMID: 41125330.

31. Dommergues M, Mandelbrot L, Mahieu-Caputo D, Boudjema N, Durand-Zaleski I, Foetale and the IGC de médecine. Termination of pregnancy following prenatal diagnosis in France: how severe are the foetal anomalies? Prenat Diagn. 2010;30(6):531-9. doi:10.1002/pd.2510

32. Holmes LB, Nasri H, Hunt AT, Nasri HZ. Elective Terminations Because of Fetal Abnormalities: Findings in A Tertiary Maternity Center Over 41 Years (1972-2012). Am J Med Genet A. sept 2025;197(9):e64051. doi:10.1002/ajmg.a.64051 PubMed PMID: 40259542.

33. Syngelaki A, Chelemen T, Dagklis T, Allan L, Nicolaides KH. Challenges in the diagnosis of fetal non-chromosomal abnormalities at 11-13 weeks. Prenat Diagn. janv 2011;31(1):90-102. doi:10.1002/pd.2642 PubMed PMID: 21210483.

34. Article R2131-1 - Code de la santé publique - Légifrance [Internet]. Disponible sur: https://www.legifrance.gouv.fr/codes/article_lc/LEGIARTI000048395947

35. Article R2131-9-1 - Code de la santé publique - Légifrance [Internet]. Disponible sur: https://www.legifrance.gouv.fr/codes/article_lc/LEGIARTI000037663952

36. Haute Autorité de santé. Protocole National de Diagnostic et de Soins (PNDS) Trisomie 21. HAS; 2020.

37. Orphanet: Trisomie 21 [Internet]. Disponible sur: https://www.orpha.net/fr/disease/detail/870

38. Agence de la biomédecine. Rapport d'activité annuel de DPN 2023 [Internet]. [cité 18 déc 2025]. Disponible sur: https://rams-archives2023.agence-biomedecine.fr/activite-des-laboratoires-realisant-les-examens-de-recherche-daneuploidie-par-analyse-dadn-libre-0

39. Haute Autorité de Santé. Protocole national de diagnostic et de soins (PNDS) Syndrome de Turner. 2021.

40. Orphanet: Syndrome de Turner [Internet]. [cité 19 déc 2025]. Disponible sur: https://www.orpha.net/pdfs/data/patho/Pub/fr/Turner-FRfrPub44v02.pdf

41. Kancherla V. Neural tube defects: a review of global prevalence, causes, and primary prevention. Childs Nerv Syst ChNS Off J Int Soc Pediatr Neurosurg. juill 2023;39(7):1703-10. doi:10.1007/s00381-023-05910-7 PubMed PMID: 36882610.

42. Cinelli H, Lelong N, Le Ray C et ENP2021 Study group. Rapport de l'Enquête Nationale Périnatale 2021 en France métropolitaine : Les naissances, le suivi à 2 mois et les établissements – Situation et évolution depuis 2016 [Internet]. Inserm; oct 2022. Disponible sur: https://enp.inserm.fr/

43. Unité de surveillance et d'épidémiologie nutritionnelle (Usen). Étude nationale nutrition santé (ENNS, 2006) – Situation nutritionnelle en France en 2006 selon les indicateurs d'objectif et les repères du Programme national nutrition santé (PNNS). Saint-Maurice Cedex France: Institut de veille sanitaire, Université de Paris 13, Conservatoire national des arts et métiers; 2007.

44. Équipe de surveillance et d'épidémiologie nutritionnelle (Esen). Étude de santé sur l'environnement, la biosurveillance, l'activité physique et la nutrition (Esteban), 2014-2016. Volet Nutrition. Chapitre Dosages biologiques : vitamines et minéraux [Internet]. Saint-Maurice Cedex France: Santé publique France; 2019. Disponible sur: Disponible à partir de l'URL : www.santepubliquefrance.fr

45. Morris JK, Addor MC, Ballardini E, Barisic I, Barrachina-Bonet L, Braz P, *et al.* Prevention of Neural Tube Defects in Europe: A Public Health Failure. Front Pediatr. 2021;9:647038. doi:10.3389/fped.2021.647038 PubMed PMID: 34249803; PubMed Central PMCID: PMC8264257.

46. Anses. AVIS de l'Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail relatif à l'actualisation de l'état des connaissances sur la prévention des anomalies de fermeture du tube neural par les folates. Maisons-Alfort: Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail; 2024. Rapport Saisine n° 2023-SA-0019.

47. de la Fournière B, Dhombres F, Maurice P, de Foucaud S, Lallemant P, Zérah M, *et al.* Prevention of Neural Tube Defects by Folic Acid Supplementation: A National Population-Based Study. Nutrients. 16 oct 2020;12(10):3170. doi:10.3390/nu12103170 PubMed PMID: 33081287; PubMed Central PMCID: PMC7603060.

48. Dhombres F, Guilbaud L, de Saint-Denis T, Jouannic JM. [Prevention of dysraphism in France through mandatory food fortification with folic acid]. Gynecol Obstet Fertil Senol. janv 2024;52(1):60-2. doi:10.1016/j.gofs.2023.10.007 PubMed PMID: 37918686.

49. Bergman JEH, Loane M, Vrijheid M, Pierini A, Nijman RJM, Addor MC, *et al.* Epidemiology of hypospadias in Europe: a registry-based study. World J Urol. déc 2015;33(12):2159-67. doi:10.1007/s00345-015-1507-6 PubMed PMID: 25712311; PubMed Central PMCID: PMC4655014.

50. Yu X, Nassar N, Mastroiacovo P, Canfield M, Groisman B, Bermejo-Sánchez E, *et al.* Hypospadias Prevalence and Trends in International Birth Defect Surveillance Systems, 1980-2010. Eur Urol. oct 2019;76(4):482-90. doi:10.1016/j.eururo.2019.06.027 PubMed PMID: 31300237; PubMed Central PMCID: PMC7265200.

51. Toppari J, Kaleva M, Virtanen HE. Trends in the incidence of cryptorchidism and hypospadias, and methodological limitations of registry-based data. Hum Reprod Update. 2001;7(3):282-6. doi:10.1093/humupd/7.3.282 PubMed PMID: 11392374.

52. Dolk H, Vrijheid M, Scott JES, Addor MC, Botting B, de Vigan C, *et al.* Toward the effective surveillance of hypospadias. Environ Health Perspect. mars 2004;112(3):398-402. doi:10.1289/ehp.6398 PubMed PMID: 14998760; PubMed Central PMCID: PMC1241874.

53. Manson JM, Carr MC. Molecular epidemiology of hypospadias: review of genetic and environmental risk factors. Birt Defects Res A Clin Mol Teratol. oct 2003;67(10):825-36. doi:10.1002/bdra.10084 PubMed PMID: 14745936.

54. Marrocco G, Grammatico P, Vallasciani S, Gulia C, Zangari A, Marrocco F, *et al.* Environmental, parental and gestational factors that influence the occurrence of hypospadias in male patients. J Pediatr Urol. févr 2015;11(1):12-9. doi:10.1016/j.jpurol.2014.10.003 PubMed PMID: 25725611.

55. Wu Y, Wang J, Wei Y, Chen J, Kang L, Long C, *et al.* Contribution of prenatal endocrine-disrupting chemical exposure to genital anomalies in males: The pooled results from current evidence. Chemosphere. janv 2022;286(Pt 3):131844. doi:10.1016/j.chemosphere.2021.131844 PubMed PMID: 34392196.

56. Mattiske DM, Pask AJ. Endocrine disrupting chemicals in the pathogenesis of hypospadias; developmental and toxicological perspectives. Curr Res Toxicol. 2021;2:179-91. doi:10.1016/j.crtox.2021.03.004 PubMed PMID: 34345859; PubMed Central PMCID: PMC8320613.

57. Le Moal J, Rigou A, De Crouy-Chanel P, Goria S, Rolland M, Wagner V. Analyse combinée des quatre indicateurs du syndrome de dysgénésie testiculaire en France, dans le contexte de l'exposition aux perturbateurs endocriniens : cryptorchidies, hypospadias, cancer du testicule et qualité du sperme. Bull Epidémiol Hebd. 2018;452-63:22-3.

58. Paty AC, Gomes Do Esperito Santo E, Suzan F. Étude des cryptorchidies et hypospadias opérés en France de 1998 à 2008 chez le petit garçon âgé de moins de sept ans à partir des données du Programme de médicalisation des systèmes d'information (PMSI). Rev DÉpidémiologie Santé Publique. 1 mars 2012;60:S30. doi:10.1016/j.respe.2011.12.052

59. Kinsner-Ovaskainen A, Perraud A, Barisic I, Bergman JE, Garne, E. EUROCAT Subgroups of Congenital Anomalies. In: EUROCAT Guide 1.5 - Instructions for the registration of congenital anomalies - Updated Version - August 2025. JRC143499 éd. Brussels: European Commission; 2025.

APPENDICES

Appendix 1. List of congenital anomalies by groups of anomalies according to EUROCAT classification (14,59)

EUROCAT Classfication
Nervous sytem anomalies
Neural tube defects
Anencephaly and similar
Encephalocele and meningocele
Spina bifida
Hydrocephaly
Severe microcephaly
Arhinencephaly / holoprosencephaly
Agenesie of corpus callosum
Eye anomalies
Anophtalmos / microphtalmos
Anophtalmos
Congenital cataract
Congenital glaucoma
Ear, face and neck anomalies
Anotia and atresia / stenosis / structure of external auditory canal
Cardiac anomalies
Severe congenital heart defects
Common arterial truncus
Double outlet right ventricle
Double outlet left ventricle
Complete transposition of great arteries
Single ventricle
Corrected transposition of great arteries
Ventricular septal defect
Atrial septal defect
Atrioventricular septal defect
Tetralogy and pentalogy of Fallot
Triscuspid atresia and stenosis

Ebstein’s anomaly
Pulmonary valve stenosis
Pulmonary valve atresia
Aortic valve atresia /stenosis
Mitral valve atresia / stenosis
Hypoplastic left heart
Hypoplastic right heart
Coarctation of aorta
Aortic atresia / interrupted aortic arch
Total anomalous pulmonary venous return
Patent Ductus arteriosus as only CHD in term infants (GA +37 weeks)
Respiratory anomalies
Choanal stenosis or atresia
Congenital pulmonary airway malformations
Oro-facial clefts
Cleft lip with or without cleft palate
Cleft palate
Gastro-intestinal anomalies
Oesophageal atresia with or without tracheo-oesophageal fistula
Duodenal atresia or stenosis
Atresia or stenosis of other parts of small intestine
Ano-rectal atresia or stenosis
Hirschsprung’s disease
Atresia of bile ducts
Annular pancreas
Anomalies of intestinal fixation
Diaphragmatic hernia
Abdominal wall defects
Gastroschisis
Omphalocele
Congenital anomalies of kidney and urinary tract
Unilateral renal agenesis
Bilateral renal agenesis including Potter sequence
Multicystic renal dysplasia
Congenital hydronephrosis including ureter obstruction

Lobulated, fused and horseshoe kidney and ectopic kidney
Bladder exstrophy and / or epispadias
Posterior urethral valves
Prune belly syndrome
Genital anomalies
Hypospadias
Indeterminate sex
Limb anomalies
Limb reduction defects (LRD)
Transverse LRD
Longitudinal preaxial LRD
Longitudinal postaxial LRD
Longitudinal central LRD
Intercalary LRD
Club foot – talipes equinovarus
Hip dislocation
Polydactyly
Syndactyly
Other anomalies / syndromes
Craniosynostosis
Congenital constriction bands / Amniotic band sequence resulting in major malformations
Situs inversus
Conjoined twins
VATER / VACTERL association
Pierre-Robin Sequence
Caudal regression sequence
Sirenomelia
Septo-optic dysplasia
Vascular disruption anomalies
Laterality anomalies
Teratogenic syndromes resulting in major malformations
Valproate syndrome
Maternal infections resulting in major malformations

Genetic disorders (genetic syndromes, hereditary skin disorders, skeletal dysplasias and chromosomal anomalies)
Skeletal dysplasias
Down syndrome / Trisomy 21
Patau syndrome / Trisomy 13
Edwards syndrome / Trisomy 18
Turner syndrome

Appendix 2. List of congenital anomalies classified as chromosomal and genetic disorders according to EUROCAT coding guidelines (14,59)

- 22q11 deletion syndrome
- Alagille syndrome
- Meckel-Gruber syndrome
- Larsen syndrome
- Crouzon syndrome / Craniofacial dysostosis
- Mandibulofacial dysostosis including Treacher-Collins syndrome
- Frontonasal dysplasia
- Ehlers-Danlos syndrome
- Neurofibromatosis type 1
- Tuberous sclerosis
- Sturge–Weber syndrome
- Congenital malformation syndromes (associations and sequences are excluded)
- Kartagener syndrome
- Chromosomal anomalies
- Hereditary skin disorders
- Skeletal dysplasias
- Trisomy 21
- Trisomy 13
- Trisomy 18
- Turner syndrome
- Triploidy and polyploidy

Notes:
* Polycystic kidney disease was not included in the genetic disorders subgroup, as many cases in the EUROCAT database associated with these codes appeared to correspond to unilateral multicystic dysplastic kidney disease, which is not part of this subgroup.
* The Klinefelter subgroup was removed, as cases of Klinefelter syndrome rarely present with congenital anomalies and diagnosis may be delayed until puberty, leading to significant underreporting.

Appendix 3. Classification of severe cardiac anomalies according to EUROCAT coding rules (59)

- Single ventricle,
- Hypoplastic right heart
- Hypoplastic left heart
- Tricuspid atresia and stenosis
- Ebstein’s anomaly
- Common arterial truncus
- Double outlet right ventricle
- Double outlet left ventricle
- Complete and corrected transposition of the great arteries
- Atrioventricular septal defect
- Tetra and pentalogy of Fallot
- Pulmonary valve atresia
- Tricuspid valve stenosis
- Aortic valve atresia/stenosis
- Mitral valve atresia/stenosis
- Coarctation of aorta
- Aortic atresia/interrupted aortic arch
- Total and partial anomalous pulmonary venous return
- Ivemark atrial isomerism
- Aortopulmonary window
- Cor triatriatum
- Subaortic valve stenosis
- Supravalvular aortic stenosis
- Malformations of the coronary arteries