Alberta Congenital Anomalies Surveillance System

Thirteenth Report:

Data for 1997 – 2018

Alberta Health Services

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ACRONYMS FOR JURISDICTIONS AND ORGANIZATIONS MENTIONED IN THE REPORT

AB	Alberta, Canada
ACASS	Alberta Congenital Anomalies Surveillance System
AHS	Alberta Health Services www.albertahealthservices.ca
AH	Alberta Health
BC	British Columbia, Canada
CCASN	Canadian Congenital Anomalies Surveillance Network http://www.phac-aspc.gc.ca/ccasn-rcsac/index-eng.php
CCASS	Canadian Congenital Anomalies Surveillance System
CPSS	Canadian Perinatal Surveillance System http://www.phac-aspc.gc.ca/rhs-ssg/
ICBDSR	International Clearinghouse for Birth Defects Surveillance and Research www.icbdsr.org
NBDPN	National Birth Defects Prevention Network www.nbdpn.org
NL	Newfoundland and Labrador, Canada
NS	Nova Scotia, Canada
PHAC	Public Health Agency of Canada www.phac-aspc.gc.ca/index-eng.php
RCPCH	Royal College of Paediatrics and Child Health

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1. ACASS Activities and Report Summary

1. This is the thirteenth in a series of reports detailing the birth prevalence of congenital anomalies in Alberta, for the years 1997–2018 inclusive.

2. The International Classification of Diseases – 10th Edition (ICD-10-CA) has been adopted by Alberta hospital reporting data systems, and ACASS uses the Royal College of Paediatrics and Child Health adaptation of ICD-10. Many of the anomalies outlined in the National Birth Defects Prevention Network's Guidelines for Conducting Birth Defects Surveillance (https://www.nbdpn.org/guidelines.php) are reported in this document along with others that might be of interest. It should be noted that notwithstanding the reported anomalies, all items from the ICD-10 "Q" codes as well as other sections such as disorders of metabolism are monitored by ACASS. Data on such disorders can be provided to interested parties upon request.

3. The numerator data include not only live births and stillbirths, but also fetal losses <20 weeks gestation with congenital anomalies. Denominator data include live births and stillbirths only. By including fetal losses in the numerator, the reported rates should be more representative of true congenital anomaly rates. Fetal losses have been ascertained since 1997. Data provided in this report include the years 1997-2018 however data from 1980 onward can be accessed at https://open.alberta.ca/dataset/1710-8594 and by request. Fetal losses will not be included in the numerators before 1997.

4. Microcephaly rates have been stable in Alberta. This report documents rates that, for the most part, precede the current concerns about Zika virus and its effect on the neurological development of the fetus and infant, specifically microcephaly. With the addition of 2017 and 2018 data, the rates continue to be stable. However, it is of value to have long-term baseline data from which to investigate potential rate changes over time **(p. 21-23)**.

5. Congenital anomaly rates have remained relatively stable over the years with fluctuations occurring on a year-to-year basis. There are, however, some exceptions:

    5.1. Gastroschisis rates have stabilized particularly in the <20 years maternal age group. The number of births in this age group has also decreased which may be driving the decrease of gastroschisis since this anomaly is significantly associated with younger maternal age. **(p. 36-39)**.

    5.2. Omphalocele rates are significantly increasing but these rates are driven by a higher frequency found in higher maternal ages (i.e. 40 years of age and older). Because omphalocele is more often associated with chromosome abnormalities, it is not unexpected that the rates would be higher in older mothers **(p. 39-41)**. In fact, 58% of cases with omphalocele in mothers over 40 years of age had a chromosome anomaly.

    5.3. The continued increase in Down syndrome is likely attributable to the increased number of women giving birth aged 35 years or older **(p. 41-44)**.

    5.4. Trisomy 13 and Trisomy 18 are increasing, again likely attributable to advanced maternal age at birth **(p. 41-43)**.

    5.5. Rates of anotia/microtia **(p. 25-28)** are significantly increasing.

5.6. Although the overall rates of orofacial clefts have remained stable, the rate of cleft palate without cleft lip decreased significantly from 1997-2018. This decrease was not maintained when only isolated cases were included (i.e. cases excluding known syndromes, teratogens, chromosome disorders or other major anomalies) **(p. 29-32)**.

5.7. Obstructive genitourinary defects are also increasing, perhaps related to better reporting and diagnostic imaging **(p. 32-34)**.

5.8. Anorectal malformation rates have continued to decline significantly since 1997 **(p. 48-51)**.

5.9. Hypospadias and undescended testes rates are significantly rising in Alberta. Rates vary world-wide with conflicting data whether trends are increasing, decreasing or remaining unchanged. Methodological issues such as ascertainment methods, definitions etc. can influence the results **(p. 57-59)**.

6. The percentage of births to women 35 years of age and over continues to increase with almost one quarter of women in this age category giving birth in 2018 compared to four per cent in 1980 **(p. 42)**.

7. The total number of Alberta births (live births and stillbirths) to Alberta mothers increased steadily from 36,797 in 1997 before peaking in 2015 at 56,524. Since 2015, the number has slowly decreased to 52,245 births in 2018.

8. Although the formal Canadian Congenital Anomalies Surveillance Network (CCASN) (https://www.canada.ca/en/public-health/services/health-promotion/what-is-ccasn.html) has been disbanded (a Public Health Agency of Canada (PHAC) initiative), T. Bedard has continued to be involved on an informal basis with the Canadian Congenital Anomalies Surveillance System (CCASS), administered by the Maternal and Infant Health Section of PHAC. R. B. Lowry and T. Bedard are members of the British Columbia Congenital Anomaly Surveillance System Advisory Committee. T. Bedard also participates with the Stakeholders Partnering for Arthrogryposis Research Client-Centred Care (SPARC) Network, which is funded by the Canadian Institutes of Health Research and Shriners Hospitals for Sick Children. With this funding, an international arthrogryposis registry has been established to align research priorities, and implement multi-site studies to promote evidence-based practice that will improve the overall health and well-being of individuals with arthrogryposis.

9. ACASS continues its affiliation with the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR) (http://www.icbdsr.org/) and has participated in group studies in a number of congenital anomalies including hypospadias, craniofacial defects, very rare defects, gastroschisis, holoprosencephaly and Down syndrome ascertainment (see Surveillance and Research Projects, **p. 61-64**). Currently, ACASS is participating in a Data Quality Indicator Project with ICBDSR to support a shared culture of quality assessment and improvement among member programs.

2. Introduction

This report provides updated data on congenital anomalies ascertained in Alberta from the years 1997–2018 inclusive. For the current release, the anomalies outlined in the National Birth Defects Prevention Network's (NBDPN) Guidelines for Conducting Birth Defects Surveillance (2004) are reported along with some others that might be of interest, however, data on other anomalies can be provided upon request.

The numerator data includes all fetal losses <20 weeks gestation with congenital anomalies. This differs from reports prior to 1997 where live births and stillbirths only were used. The reported rates are more representative of the true rates of congenital anomalies in Alberta. Fetal losses have been ascertained since 1997, thus aggregate data are reported from that year forward. Congenital anomalies data from 1980 onwards can be accessed from previous reports at https://open.alberta.ca/dataset/1710-8594; however fetal losses will not be included in the numerator. Denominator data includes live births and stillbirths only.

2.1 History

The history of the Alberta Congenital Anomalies Surveillance System (ACASS) has been described in previous reports. Between 1996 and 2017, funding was provided by Alberta Health. ACASS is now supported by Alberta Health Services but continues to work closely with Alberta Health as well as Alberta Vital Statistics relying on them for the provision of notifications of births, deaths and stillbirths (**see Case Ascertainment, p. 12**).

2.2 Purpose of a Surveillance System

Public health surveillance, in general, has been defined by the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia as the ongoing, systematic collection, analysis and interpretation of data (e.g., regarding agent/hazard, risk factor, exposure, health event) essential to the planning, implementation and evaluation of public health practice, closely integrated with the timely dissemination of these data to those responsible for prevention and control.

The purposes and objectives of surveillance for congenital anomalies (CAs) are to:

1) provide reliable and valid data on the birth prevalence of congenital anomalies in Alberta;
2) investigate any significant temporal or geographic changes in the frequency of congenital anomalies with a view to identifying environmental, and therefore, possibly preventable causes;
3) measure trends;
4) assess the effectiveness of prevention (e.g., folic acid fortification or antenatal screening);
5) assist with health related program planning and development through the provision of data;
6) participate in research into the etiology and natural history of birth defects;
7) assist with research through the provision of congenital anomalies data; and
8) provide advice to health care professionals about congenital anomalies, especially with respect to teaching and launching public health campaigns (e.g., folic acid campaign by Community Health in Calgary).

As well as the above, patterns or associations of malformations to determine whether they belong to an existing or new syndrome complex can be explored.

A principle feature of a surveillance system is timeliness; however, data collection and analysis should not be accomplished at the expense of an accurate diagnosis. Data are collected to the first birthday, and with the possibility of reporting delays, the data of a given calendar year may not be complete until at least December 31 of the subsequent year although the cases and anomalies are monitored as received. There can also be a lengthy delay in obtaining published data from Vital Statistics which is used for the denominators in our calculations.

3. Methodology

3.1 Case Definitions

A **congenital anomaly** is an abnormality that is present at birth, even if not diagnosed until months or years later. Most congenital anomalies are present long before the time of birth, some in the embryonic period (up to the end of the seventh week of gestation) and others in the fetal period (eighth week to term). The term "anomaly" covers all the major classes of abnormalities of development, of which there are four major categories as follows:

Malformation – a morphologic defect of an organ, part of an organ or a larger region of the body resulting from an intrinsically abnormal developmental process (e.g., spina bifida, cleft lip and palate).

Deformation – an abnormal form, shape or position of a part of the body caused by mechanical forces (e.g., extrinsic force such as intrauterine constraint causing some forms of clubfoot).

Disruption – a morphologic defect of an organ, part of an organ or a larger region of the body resulting from the extrinsic breakdown of, or interference with, an originally normal developmental process (e.g., an infection such as rubella or a teratogen such as thalidomide).

Dysplasia – the abnormal organization of cells into tissues and its morphologic result (e.g., Marfan Syndrome, osteogenesis imperfecta).

Other definitions related to pregnancy outcomes for the purposes of this report are as follows:

Live birth – a complete expulsion or extraction from the mother, *irrespective* of the duration of the pregnancy, of a fetus in which, after expulsion or extraction, there is breathing, beating of the heart, pulsation of the umbilical cord or definite movement of voluntary muscle (Alberta Vital Statistics Annual review, 2000).

Stillbirth – a complete expulsion or extraction from the mother, at 20 weeks of pregnancy or more ***or*** after attaining a weight of 500 grams or more, of a fetus in which, after the expulsion or extraction, there is no breathing, beating of the heart, pulsation of the umbilical cord or unmistakable movement of voluntary muscle (Alberta Vital Statistics Annual review, 2000).

Gestation – completed weeks of pregnancy at delivery.

Preterm birth (aka premature) – a birth before 37 weeks of gestation (<37 weeks).

Termination of Pregnancy (ToP) – for our purposes, includes any pregnancy loss before 20 weeks gestation (<20 weeks). Most cases are therapeutic terminations for congenital anomalies but spontaneous abortions or intrauterine fetal deaths with fetal anomalies could also be included.

Anomaly definitions are based, for the most part, on those provided by the ICBDSR and NBDPN.

3.2 Case Ascertainment

An infant can be ascertained at any time up to the first birthday. Multiple ascertainment of the same infant can occur and is encouraged, as this frequently improves the quality and reliability of the data.

As several malformations may occur in the same infant, it is advantageous to allow each to be reported so that groups of associated malformations may be studied. This, however, leads to difficulties since the final tabulations may be reported as total malformations (anomaly rates) or as the total number of malformed infants (case rates). The tables in **Appendix A.3 (p. 68-81)** report anomaly rates, which in most cases are similar to case rates (e.g. cleft palate, hypospadias, and microcephaly). Whereas with limb anomalies, there can be multiple different limb anomalies in the same infant.

ACASS obtains information about infants with congenital anomalies from a variety of independent sources. Acquisition of additional reporting agencies is always a priority since the use of multiple sources of information improves not only the ease but also completeness of ascertainment as well as for verification of the diagnostic data. **Appendix A.1 (p. 66**) indicates the process of data collection at ACASS.

ACASS screens many Alberta Health and Alberta Vital Statistics documents for the presence of a congenital anomaly including:

- Notice of a Live Birth or a Stillbirth and Newborn Record often referred to as the Physician's Notice of Birth (NOB)
- Medical Certificate of Stillbirth
- Medical Certificate of Death

Also, ACASS screens a notification called the Congenital Anomalies Reporting Form **(CARF, Appendix A.2, p. 67)** that is completed by all acute care hospitals in the province on live births, stillbirths, admissions or hospital deaths of infants under one year of age as well as pregnancy losses involving one or more congenital anomalies. This form serves as the single most important source of case ascertainment.

Since many children with congenital anomalies are not admitted to hospital, it is very important to obtain out-patient information such as from the Calgary and Edmonton Departments of Medical Genetics.

Ascertainment at a continued high level requires each hospital health records department and each health care provider to co-operate with the system by notifying us as promptly as possible. We are fortunate and grateful for having such co-operative agencies and personnel.

3.3 Quality Control Measures

When a copy of a reporting document reaches the ACASS office in Calgary, it is reviewed for content by the Research Assistant and Manager. If the information is unclear, the Manager, on behalf of the Medical Consultant, writes to the physician responsible for the case seeking clarification. A stamped, addressed envelope is included with the letter and the physician is asked to respond at the bottom of

the letter thus making the mechanics of replying easy. The response from physicians has been very satisfactory and usually this is sufficient to make a decision whether to accept or reject an anomaly or case. Any questionable diagnosis that is not confirmed is not entered into the database. Some cases also excluded, have diagnoses that do not belong in a congenital anomaly system or are part of a normal developmental process such as a patent ductus arteriosus or undescended testes in a premature infant. Any reports requiring a medical decision are reviewed with the Medical Consultants. Policy decisions with respect to the acceptance or rejection of a case and its coding are referred to the ACASS Advisory Committee. This body is comprised of a paediatric cardiologist, neonatologist/epidemiologist, paediatric pathologist, medical geneticists with occasional input from a paediatric neurologist, paediatric nephrologist, paediatric orthopaedic surgeon, paediatric general surgeon and a perinatologist/obstetrician.

3.4 Anomaly Coding

Coding is done at the Calgary office mainly using the Royal College of Paediatrics and Child Health (RCPCH) adaptation of the International Classification of Diseases, tenth edition (ICD-10). Difficult cases are referred to the Medical Consultants. In the past, we were able to code only six anomalies per case but since 1997 we have been coding all eligible anomalies reported to us. Of note, we have been updating our database as time permits, by going back to the original reports and reviewing all codes for consistency with current coding practices.

3.5 Data Linkage

Data from ACASS are linked to data from the Alberta Vital Statistics Birth Registry by the birth registration number ensuring a unique identifier for each case entered into the database. This is important to ACASS because we ascertain cases from multiple sources, thus the unique identifier reduces the risk of duplicate entries for a case.

Data linkage has been achieved with the Alberta Perinatal Health Programme (APHP) by way of the personal health number to ascertain maternal risk factor data, such as maternal smoking, drinking and use of street drugs during pregnancy for babies with congenital anomalies.

3.6 Confidentiality and Release of Data

Notifications of Congenital Anomalies are sent to the Analytics and Performance Reporting Branch, Alberta Health, and from there to the ACASS office in Calgary where the database is maintained. The notifications are handled by the Manager, Research Assistant, Secretary, Clerk and Medical Consultants. The data are treated in a completely confidential manner and the notifications are kept in locked files in a locked room. The database is secured by limited access and is password protected. Should further clarification about a case or anomaly become necessary, we communicate with the attending physician or the physician responsible for ongoing care. Direct contact is never made with the family. When data are requested from us, they are released in aggregate form with no personal identifiers.

3.7 Epidemiological and Statistical Measures

Unless otherwise stated, the birth defect rates presented in this report are calculated using the following formulae:

ANOMALY (DEFECT) RATE =

$$\frac{\text{Number of a particular congenital anomaly among live births + stillbirths + fetal losses}}{\text{Total number of live births and stillbirths}} \times 1000$$

CASE RATE =

$$\frac{\text{Number of individual infants (live or stillborn) or fetuses with} \geq \text{1 congenital anomaly}}{\text{Total number of live births and stillbirths}} \times 1000$$

Confidence intervals (95%) are also included because the rate obtained is actually only a point estimate of the unknown, true population rate. The confidence interval provides information about the precision of the estimate. Thus, the confidence intervals are an estimated range of values within which there is a 95% probability that the true population rate will fall.

Chi Squared Linear Trend Analysis was performed and presented as appropriate.

3.8 Limitations of Data and Analysis

One of the major limitations of the surveillance system is that on its own, the information provided does not allow us to determine etiology. If increasing trends indicate there is a potentially serious problem, then separate investigative studies need to be done. However, with appropriate approvals in place, it would be possible to conduct linkage studies with other data sources to explore potential causes of specific birth defects.

The ACASS data are collected passively from Vital Statistics, hospitals, and other agencies but are augmented by active ascertainment from physicians and labs, etc. The completeness and accuracy of data are largely dependent on reporting.

4. Patterns of Selected Congenital Anomalies in Alberta

4.1 Birth Prevalence – Time Trends

The following table and graphs of selected sentinel anomalies indicate the trends in congenital anomaly rates in Alberta from 1997 through 2018. Sentinel anomalies are those which the International Clearinghouse of Birth Defects Surveillance and Research (ICBDSR), of which we are a member, watches worldwide with the rationale that they are quite easily identified hence more accurately reported. See **Appendix A.5 (p. 83)** for other anomalies listed in the report**.**

Table 4.1.1 Chi Squared Linear Trend Analysis and p-values for Selected Anomalies 1997–2018 Inclusive (Live Births, Stillbirths & ToPs)

Anomaly	Trend Direction	Chi Squared Analysis (χ^2LT)	p-value
Neural Tube Defects	**Decreasing**	5.13	0.0235
Anencephaly	**Decreasing**	8.76	0.0031
Spina Bifida	No significant change	0.14	0.7083
Hydrocephalus	**Decreasing**	7.11	0.0077
Cleft Lip +/- Cleft Palate	No significant change	1.12	0.2899
Cleft Palate	**Decreasing**	3.88	0.0489
Oesophageal Atresia/Tracheo-oesophageal Fistula	No significant change	2.44	0.1183
Anorectal & Large Intestine Atresia/Stenosis	**Decreasing**	7.96	0.0048
Hypospadias*	**Increasing**	63.50	<0.0001
Undescended Testes*	**Increasing**	20.98	<0.0001
Renal Agenesis/Hypoplasia	**Increasing**	9.29	0.0023
Limb Reductions - upper	No significant change	1.30	0.2542
Limb Reductions - lower	No significant change	1.40	0.2367
Gastroschisis	No significant change	0.37	0.5430
Omphalocele	**Increasing**	10.43	0.0012
Down Syndrome	**Increasing**	22.94	<0.0001
Hypoplastic Left Heart Syndrome	No significant change	2.40	0.1213

*Hypospadias and Undescended Testes calculated for male births only

4.2 Selected Anomalies

4.2.1 Selected Anomaly Definitions

(Adapted from NBDPN guidelines: http://www.nbdpn.org/ and ICBDSR Reported Malformations Definitions: http://www.icbdsr.org/)

Abdominal Wall Defects

- ***Gastroschisis*** – a congenital opening or fissure in the anterior abdominal wall lateral to the umbilicus through which the small intestine, and occasionally the liver and spleen, may be herniated.
- ***Omphalocele*** – a defect in the anterior abdominal wall in which the umbilical ring is widened, allowing herniation of abdominal organs, including the small intestine, part of the large intestine, and occasionally the liver and spleen, into the umbilical cord. The herniating organs are covered by a nearly transparent sac.

Anorectal Atresia/Stenosis

Complete or partial occlusion of the lumen of one or more segments of the large intestine and/or rectum.

Anotia/Microtia

- ***Anotia –*** absence of external ear and canal
- ***Microtia –*** hypoplasia of external ear

Chromosome Anomalies

- ***Trisomy 13*** – *aka Patau syndrome* – the presence of three copies of all or a large part of chromosome 13.
- ***Trisomy 18*** – *aka Edwards syndrome* – the presence of three copies of all or a large part of chromosome 18.
- ***Trisomy 21*** – *aka Down syndrome* – the presence of three copies of all or a large part of chromosome 21.

Cleft Lip and Palate

- ***Cleft Lip*** – a defect in the upper lip resulting from incomplete fusion of the parts of the lip.
- ***Cleft palate*** – an opening in the roof of the mouth resulting from incomplete fusion of the shelves of the palate.

Congenital Heart Disease

- ***Aortic valve stenosis –*** obstruction or narrowing of the aortic valve impairing blood flow from the left ventricle to the aorta.
- ***Atrial Septal Defect (ASD) –*** opening in the septum that divides the right and left atria of the heart.
- ***Coarctation of the aorta –*** narrowing of the descending aorta obstructing blood flow from the heart to the rest of the body.
- ***Hypoplastic Left Heart Syndrome*** – a condition in which the structures on the left side of the heart and the aorta are extremely small. Classically, this condition includes hypoplasia of the

left ventricle, atresia or severe hypoplasia of the mitral and aortic valves, and hypoplasia and coarctation of the aorta.

- ***Tetralogy of Fallot*** – the simultaneous presence of a ventricular septal defect (VSD), pulmonic stenosis, a malpositioned aorta that overrides the ventricular septum and right ventricular hypertrophy.
- ***Ventricular Septal Defect (VSD) –*** opening in the septum that divides the right and left ventricles of the heart.

Hydrocephalus
An increase in the amount of cerebrospinal fluid within the brain resulting in enlargement of the cerebral ventricles and increased intracranial pressure.

Hypospadias
Displacement of the opening of the urethra ventrally and proximally (underneath and closer to the body) in relation to the glans of the penis.

Limb Reductions
Complete or partial absence of upper and/or lower limbs.

Microcephaly
Commonly defined as a head circumference less than 2 standard deviations (SD) from the mean, or less than the 3rd percentile for age and sex (some jurisdictions use less than 3 SD).

Neural tube defects

- ***Anencephaly*** – partial or complete absence of the brain and skull.
- ***Spina Bifida*** – incomplete closure of the vertebral spine through which spinal cord tissue and/or the membranes covering the spine (meninges) herniated.
- ***Encephalocele*** – herniation of brain tissue and/or meninges through a defect in the skull.

Obstructive genitourinary anomalies
Partial or complete obstruction of the flow of urine at any level of the genitourinary tract from the kidneys to the urethra.

Renal Agenesis/Hypoplasia
Complete absence or incomplete development of the kidney.

Undescended Testes
Bilateral or unilateral undescended testis in at term newborn.

4.2.2 Neural Tube Defects

The prevalence of neural tube defects (NTDs) as a group has significantly decreased (p=0.0235) from 1997-2018 (Figure 4.2.1). Since our last report (2019) there has been a significant decline in anencephaly**,** but not with spina bifida nor encephalocele (Figure 4.2.2). The decline in anencephaly rates started in 2016 and continued in 2017 and 2018 **(Appendix A.3, p. 68 and 69 data)** with the rates in those three years about half the previous 15 years (0.11 versus 0.24/1000 total births (TB)). It is only cases with isolated anencephaly, which have significantly declined, not those with associated anomalies.

The decline in the prevalence of isolated anencephaly may be true or attributed to the terminology used to report what is seen on first trimester prenatal ultrasounds. This affects the classification and the ICD-10 codes used by ACASS. In addition to "anencephaly", the terms "exencephaly", "acrania", and "absent calvarium" are commonly used to report first trimester ultrasound findings. While exencephaly is presumed to be the embryological precursor of anencephaly, and is thus classified as an NTD, acrania is absent calvarial bones and will often, but not always progress through the acrania-exencephaly-anencephaly sequence. Acrania and absent calvarium may be coded by ACASS with an ICD-10 code outside of the NTD section if there are no further reports of exencephaly or anencephaly. Since this can be diagnosed very early and if there is a subsequent termination of pregnancy, a more detailed and precise pathologic diagnosis may be impossible to ascertain due to the termination procedure. Further study is required to address this potential classification issue which may have contributed to the reported decline of anencephaly.

Spina bifida (SB) has remained relatively stable since the sharp decline following folic acid fortification (FAF) in 1998. A study of SB in AB for 2001-2013 (Lowry et al 2019), classified cases with SB and noted 58% were isolated. The prevalence of these isolated cases was 0.21/1000 TB compared with an overall SB prevalence of 0.37/1000 TB. Due to incomplete details for FA or multivitamin supplementation on the Notice of Birth forms in 69% of cases, the study by Lowry et al (2019) could not determine whether the continued prevalence was a factor in the lack of FA supplements.

A Canadian Health Measures Study showed that more than 20% of Canadian women of reproductive age had a red cell folate level below 906 nmol/L (Colapinto et al 2011), which is the minimum level necessary to prevent a NTDs. Suboptimal levels were also found in the Calgary-based APrON study (Fayyaz et al 2014), but they did not find a deficiency of vitamins B12 or B6. This is important because of the interrelationship between FA and vitamin B12, which was reviewed by Molloy (2018). She discussed the possibility of adding B12 to fortification but concluded there was insufficient evidence to justify fortification, but concluded that supplementation with B12 would probably be advantageous in reducing the prevalence of NTDs. Additionally, a pilot study by Greene et al (2016) reported that the addition of Inositol to folic acid supplementation may help prevent the recurrence of an NTD.

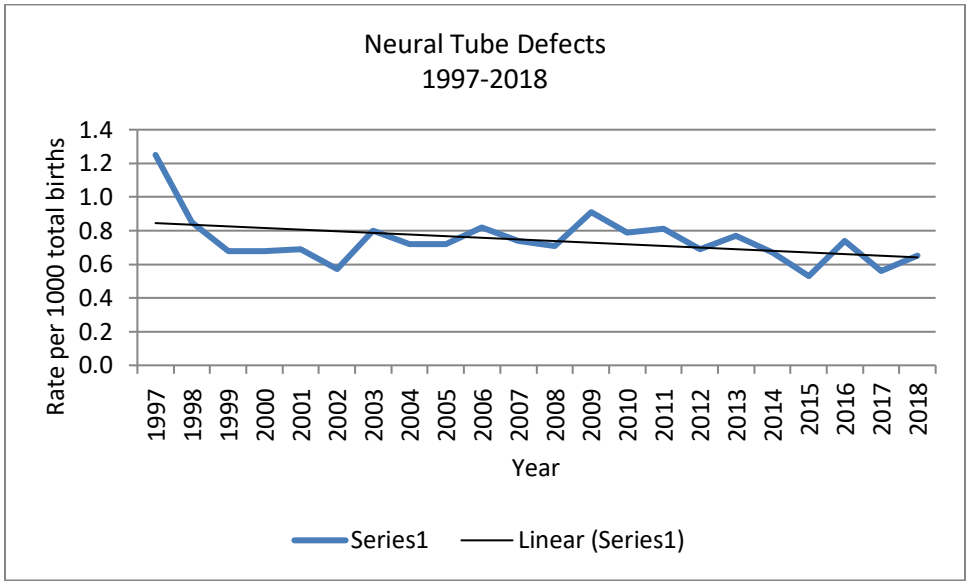
The most recent published prevalence study from South Carolina, covered a pre-fortification period (1992-1998) and a post fortification one (1999-2018) (Dean et al 2020). Their prevalence rate declined from 0.71/1000 TB to 0.56/1000 TB. The AB rate for 2000-2018 is 0.71/1000 TB but South Carolina has quite a high proportion of African–Americans whose prevalence rate is lower than Caucasians. There are no current rates from the Canadian Congenital Anomalies Surveillance System, with 2014 being the last reported year for NTD prevalence (0.57/1000 TB) (Public Health Agency of Canada, 2017).

Apart from a deficiency of FA and a potential B12 deficiency, the well-established risk factors for NTDs include maternal obesity, diabetes mellitus, and anticonvulsants (Valproic Acid and Carbamazepine). Less well-established factors are hyperthermia/maternal fever, low maternal education, and folic acid antagonists. Exposure to agricultural work as a risk factor for anencephaly was put forward for the three central States of Mexico (Lacasaña et al 2006), which might explain the higher risk of anencephaly in the Hutterite Brethren of Alberta despite a lower risk of SB (Lowry et al 2020).

Reece et al (2020) proposed that cannabis consumption patterns explained the East-West gradient in Canadian NTD incidence. While it is a statistical association, the East-West divide may be more reasonably explained by low red cell folate deficiency, which was corrected by mandatory FAF (De Wals et al 2007). This notable divide was perhaps exacerbated by differences in average income, being higher in the West, and ethnicity where on average there are more Irish-Scots in NL and NS versus more English-German in AB and BC. The increased odds ratio for the MTHFR 677 C > T polymorphism found in Ireland might apply to NL (Amorim et al 2007**).** This raises the question of ethnicity as something we should try to collect in future works. For example, there is a very high prevalence of NTDs in North Africa, Western Asia, and Eastern Asia (Blencowe et al 2018) where diets may not include meat and be FA and B12 deficient. Baird (1983) showed that the prevalence in the Sikh population in BC for NTDs was approximately double the BC general population rate (2.86 versus 1.26/1000 births). With an increased global movement of people, ethnicity is an important variable.

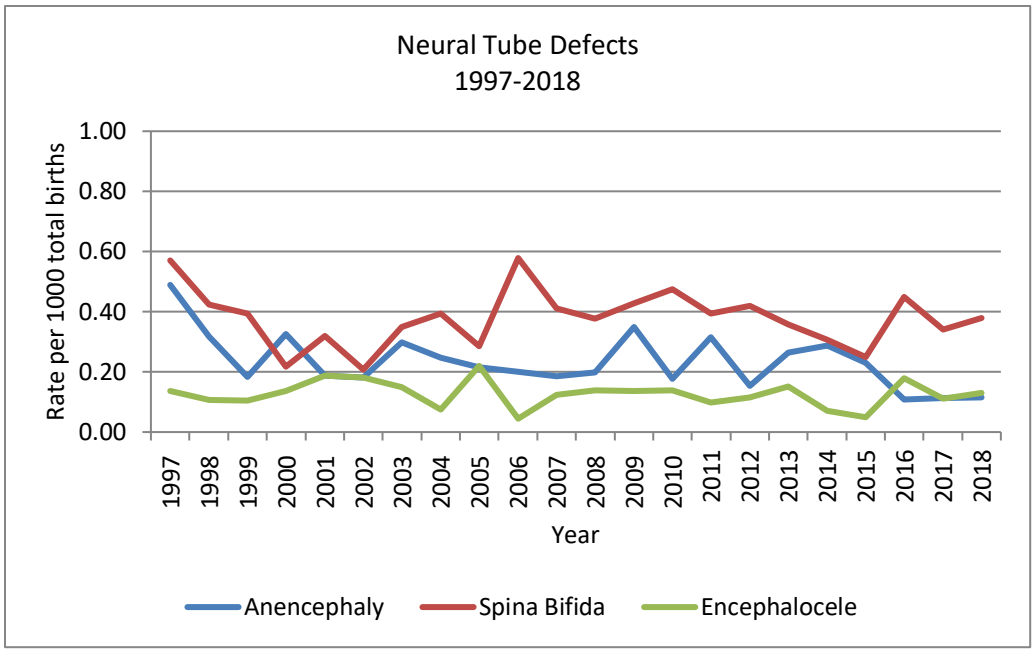
We should also strive to collect more specific details of the level and type of defect in the spine, which may differ in risk factors and responsiveness to primary prevention strategies.

Figure 4.2.1 All Neural Tube Defects, 1997-2018 (Rate per 1000 total births)



p = 0.0235

Figure 4.2.2 Neural Tube Defects: Spina Bifida, Anencephaly and Encephalocele, 1997-2018
(Rate per 1000 total births)



Anencephaly p = 0.0031; Spina Bifida p = 0.7083; Encephalocele p = 0.5323

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4.2.3 Microcephaly

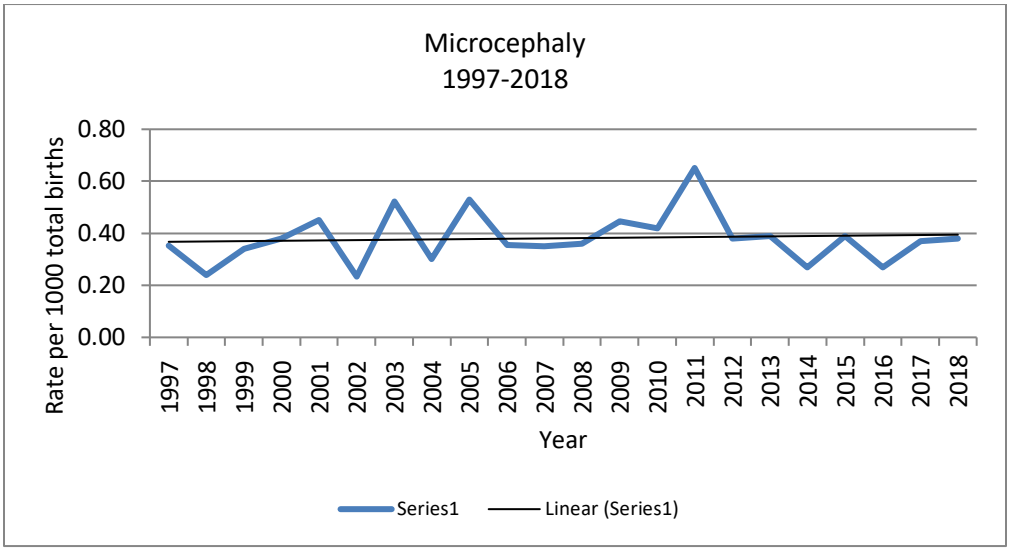
There are many known causes of microcephaly such as single gene disorders, chromosome abnormalities, teratogens (e.g. alcohol, rubella, cytomegalovirus), or other events including anoxia or haemorrhage, that disrupt the developing brain resulting in a smaller head circumference. There are also some cases for which we do not yet know or understand the cause for an unusually small head circumference. Although there are standard definitions for microcephaly, ACASS does not always have the head circumference measurement provided to us. We do accept a diagnosis of microcephaly when indicated. Nevertheless, despite our not receiving actual measurements in all cases, we can provide a useful guide to what is occurring in Alberta.

While there were concerns over the Zika virus causing microcephaly and other brain abnormalities, to date no such cases have been reported to ACASS. The first report of a Zika virus infection in a Canadian traveler returning from Thailand was reported from Calgary (Fonseca et al, 2014) but did not involve a pregnancy. The transmission rates have significantly decreased since late 2016 in the Americas, presumably due to sufficient herd immunity in areas where there was widespread transmission (Ribeiro et al, 2020).

The following graphs indicate that long-term microcephaly rates have been remarkably stable in the province over the 22 years between 1997 and 2018.

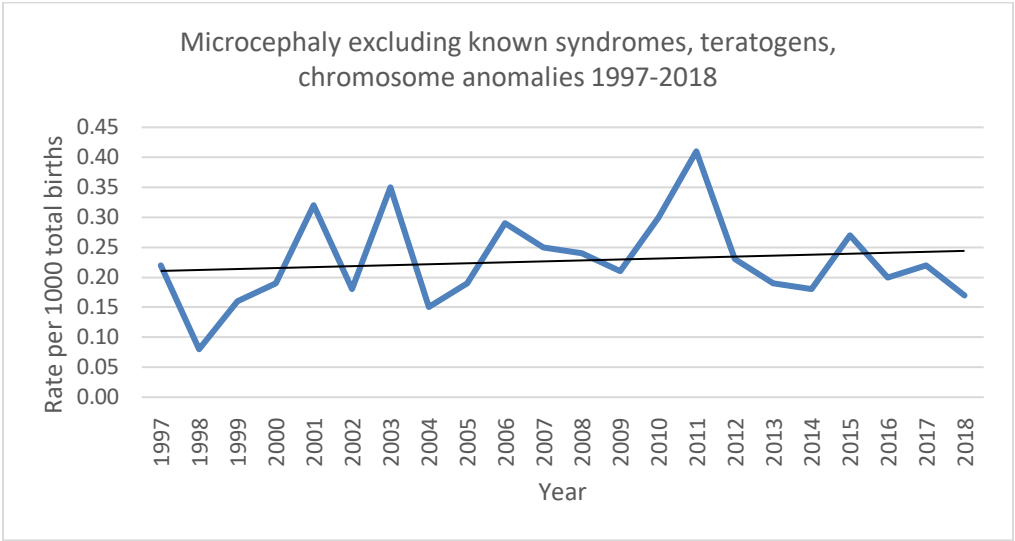
As the graphs demonstrate, whether or not we include known potential causes of the microcephaly, there have been no significant changes in the rates.

Figure 4.2.3 Microcephaly – all cases, 1997-2018 (Rate per 1000 total births)



p = 0.8065

Figure 4.2.4 Microcephaly – excluding known Syndromes, Teratogens, or Chromosome Anomalies, 1997-2018 (Rate per 1000 total births)



p=0.5598

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4.2.4 Hydrocephalus

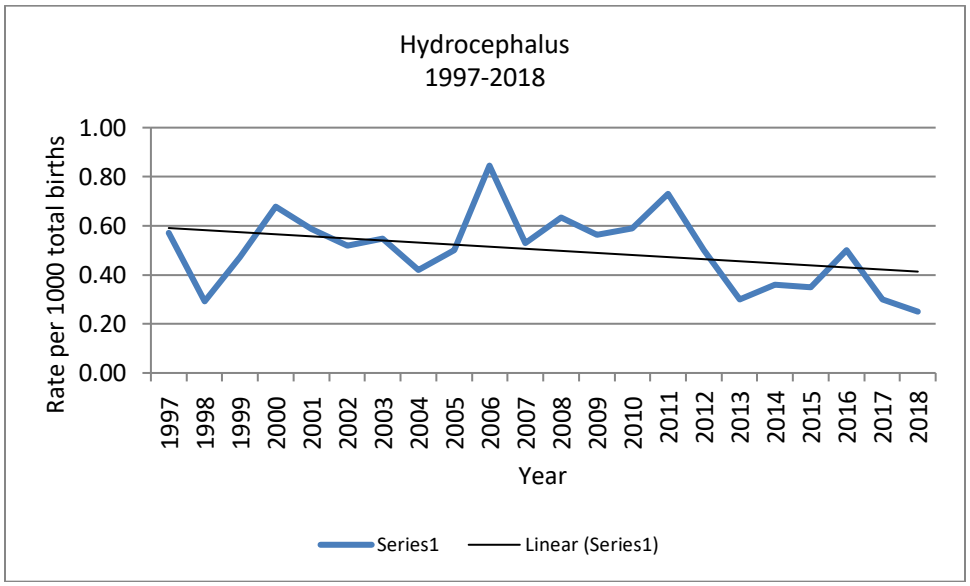
Rates of isolated hydrocephalus do fluctuate from year to year. However, since the last report, there has been a significant downward trend for 1997-2018 (p=0.0077) (Figure 4.2.5), with an overall prevalence of 0.50/1000 total births (TB) for the same period. These rates represent hydrocephalus without spina bifida or encephalocele.

There are no published data on similar downward trends globally in the same timeframe. However, Yi et al (2017) reported a decrease for 2005-2012 in China, although the study only included newborns >28 weeks gestation. The authors suggested that the decrease may be due to better prenatal diagnosis followed by termination of pregnancy. A systematic review and meta-analysis of the global incidence of hydrocephalus from 2003 to 2014, included data from the International Clearinghouse of Birth Defects Surveillance and Research (ICBDSR), which is comparable to the cases ascertained by ACASS. The reported rate of hydrocephalus was 0.50/1000 TB (Isaacs et al, 2018).

There is some evidence regarding folate supplementation being associated with lower rates of isolated hydrocephalus, particularly in regions with likely reduced folic acid intake (Liu et al, 2021). One limitation of this study is that it did not distinguish isolated cases, which are more responsive to folate, from syndromic or teratogen causes. A review and meta-analysis showed no difference in the rate of hydrocephalus between countries with and without folate fortification (Isaacs et al, 2018). There is no definitive evidence that folate fortification would account for the downward trend seen in ACASS rates.

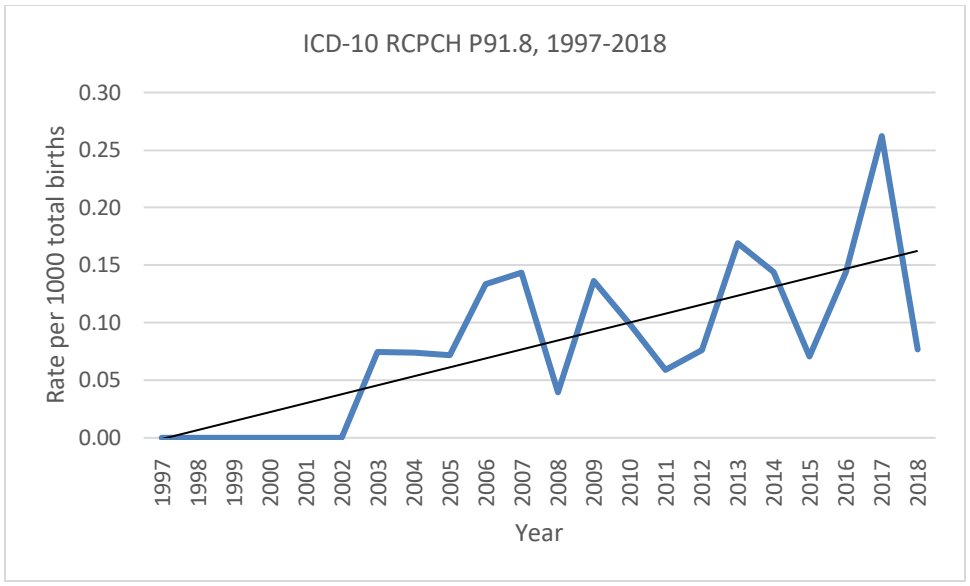
Ascertainment, classification, and coding may impact the observed rates. To address these potential factors, ACASS cases with the Royal College of Paediatrics and Child Health (RCPCH) ICD-10 code, P91.8, were reviewed. This code includes “persistent ventricular enlargement” when hydrocephalus is not specified, and is used by ACASS for cases with a prenatal diagnosis of ventriculomegaly without postnatal confirmation of hydrocephalus. Cases reported with mild ventriculomegaly are not eligible for ACASS. There has been a significant increasing trend in cases coded with P91.8 since 1997 (p<0001), (Figure 4.2.6). When cases coded with hydrocephalus or ventriculomegaly are combined, there is no change in trend and rates remain stable at just under 0.60/1000 TB, (Figure 4.2.7). Although this may explain the significant difference, rates of hydrocephalus will continue to be monitored by ACASS.

Figure 4.2.5 Hydrocephalus, 1997-2018 (Rate per 1000 total births)



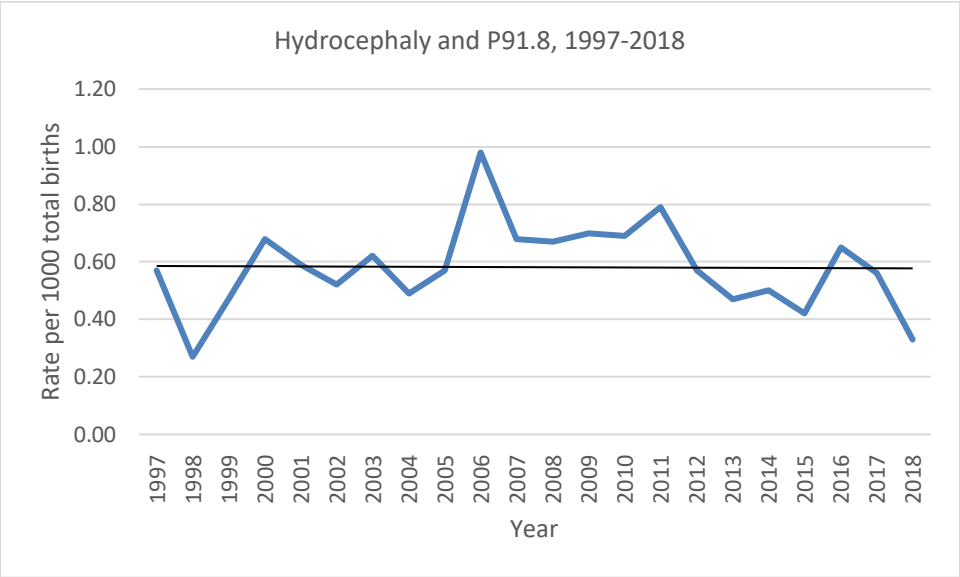
p = 0.0077

Figure 4.2.6 Persistent Ventricular Enlargement, 1997-2018 (Rate per 1000 total births)



p<0.0001

Figure 4.2.7 Hydrocephaly and Persistent Ventricular Enlargement (Rate per 1000 total births)



p=0.6315

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4.2.5 Anotia / Microtia

Major challenges with this entity include classification, ascertainment (e.g. active vs passive surveillance and hospital-based vs population surveillance), and inclusion differences between studies (e.g. isolated cases vs all cases including those with genetic diagnoses and established teratogens). Most clinicians and systems classify anotia / microtia (A/M) into four categories with Type 4 being anotia and Type 1 being a smaller ear with normal structure. Luquetti et al (2011) and Hunter et al (2009) outlined details about classifications. ACASS accepts any case with a diagnosis of microtia, which is probably Types 2 and 3 but might include some Type 1. If the ear is described as “small” on

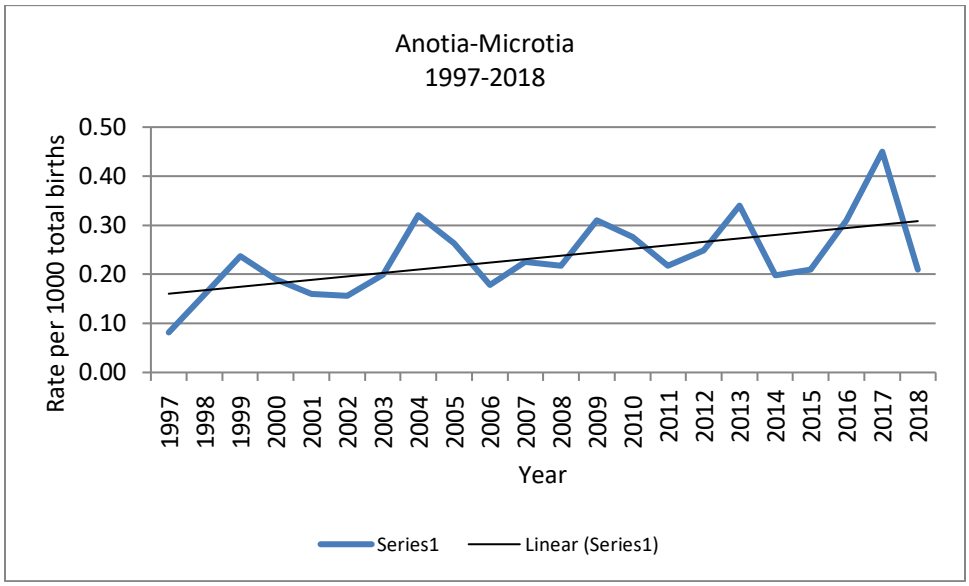
the reporting form, ACASS will try to verify if the size of the ear is within normal limits or if it is microtia. If the size cannot be verified and there is no further information, ACASS will not accept the case as microtia. Many studies collect Types 1-4 and like ACASS, the categories are not recorded. However, Texas (Canfield et al 2009) and Hawaii (Forrester and Merz 2005) specifically record Types 2-4, as did Ryan et al (2019).

Prevalence trends up to 2007 showed variability and were inconclusive (Luquetti et al 2011) although Deng et al (2016) showed an increasing trend in a specific geographic area of China and an increase in urban areas. The only recent published prevalence study is for the years 2011-2015 (Stallings et al 2018) which reported prevalence rates of 0.18/1000 live births (LB) from 30 States and 0.26/1000 LB from 12 States with active surveillance. The ACASS 19-year (2000-2018) average rate of 0.25/1000 total births (TB) (Appendix A.3) compares favorably with active surveillance rates but did show a rising trend up to 2017 (0.45/1000 TB) followed by a drop in 2018 (0.21/1000 TB). The overall significant increase shown in Figure 4.2.8 is unexplained.

It is difficult to compare risk factors from other studies because of the differences in inclusion, geographic areas, and years of study as outlined by Luquetti et al (2012), Liu et al (2018) and Ryan et al (2019). Nevertheless, some risk factors are common. These are male predominance, unilateral and right-sided occurrence in isolated cases, maternal diabetes, obesity, and Hispanic ethnicity. Other risk factors may include advanced maternal age, high parity, multifetal gestation, cold symptoms, virus infection, NSAIDS. Other ethnicities such as Asians, Pacific Islanders, Native/Alaskans, and Indigenous peoples may have higher risk. In contrast, African-Americans have low prevalence rates. Altitude above 2000m is a risk factor in South America (Castilla et al 1999), but is not a factor in Alberta with the two major population centres below this elevation (Calgary 1048m and Edmonton 645m). Tobacco and alcohol may contribute to increased risks of A/M, which have been reported among non-isolated cases exposed to smoking of at least five cigarettes/day (Ryan et al 2019) and isolated cases exposed to alcohol drinking (Luquetti et al 2012). Mothers taking peri-conception folic acid supplements and or high dietary folate may have a lower risk. Known teratogens include Thalidomide, Isotretinoin, and Mycophenolate Mofetil.

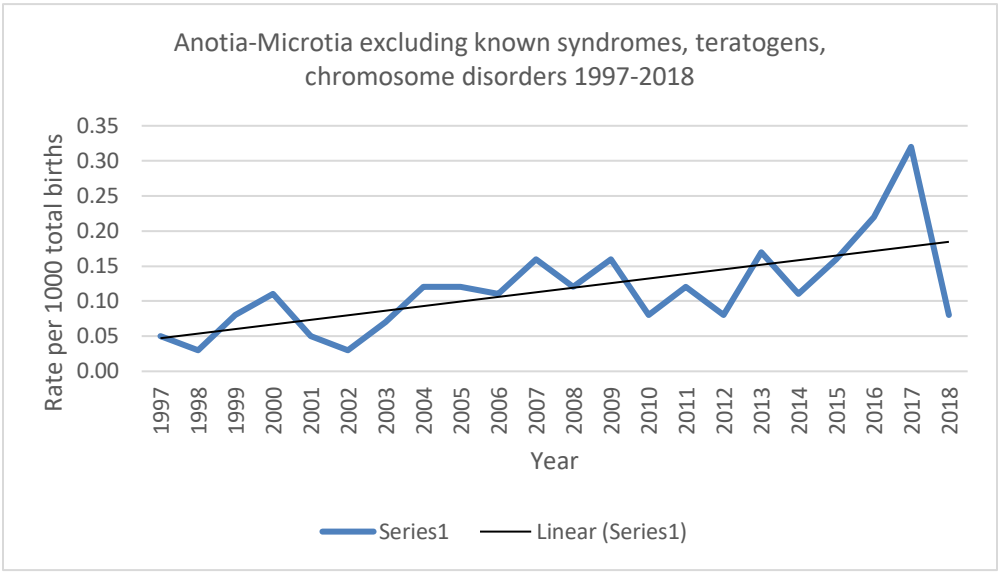
The etiology for isolated cases is presumed to be multifactorial although there are two reports of autosomal dominant inheritance with reduced penetrance (Gupta and Patton 1995; Klockars et al 2007). There are more than 20 syndromes with microtia plus many chromosomal aneuploidies (Luquetti et al 2012; Alasti and Van Camp 2009). Of interest is that significance was maintained after cases with known syndromes, teratogens, and chromosome anomalies were excluded (Figure 4.2.9).

Figure 4.2.8 Anotia/Microtia – all cases, 1997-2018 (Rate per 1000 total births)



p = 0.0055

Figure 4.2.9 Anotia-Microtia – excluding known syndromes, teratogens, or chromosome disorders, 1997-2018 (Rate per 1000 total births)



p = 0.0003

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4.2.6 Orofacial Clefts

The rates for cleft lip with or without cleft palate (CL/P) (Figure 4.2.10) has remained stable in Alberta for more than 20 years and over 30-50 years in many other jurisdictions (summarized by Lowry et al 2014). The figures in Lowry et al (2019) show three 5-year periods: 1993-1997 for pre-folic acid fortification (FAF) and two post FAF periods, 2000-2004 and 2012-2016. No decline in prevalence was reported for total CL/P cases or those classified as isolated or with associated anomalies.

Two studies have reported a decline in prevalence for orofacial clefts (OFCs):

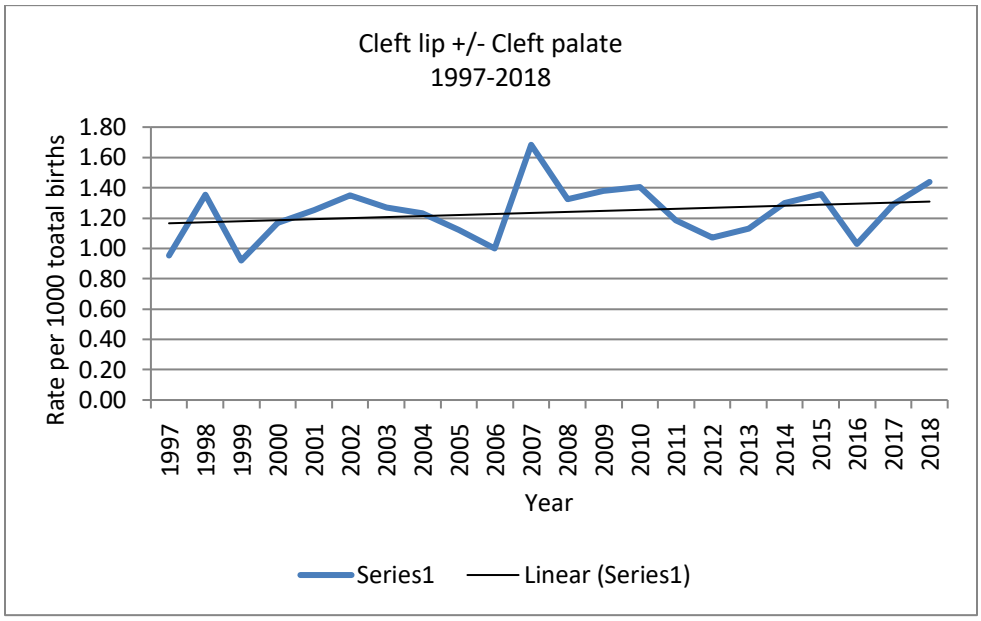
1. Andrew et al (2018) reported a decline in an eight-county area of California for CL/P but not cleft palate (CP) for the study years 1987-2010. The authors did not claim that it was the result of FAF or dietary supplements but pointed out that this decline has also been reported in other US studies (Yazdy et al 2007; Yang et al 2016). However, the authors speculate that there may be a greater proportion of CL/P terminations of pregnancy (ToPs) than CP ToPs because of increased sensitivity of antenatal diagnosis in the former compared to the latter. If these ToPs occurred in private clinics, they would not be ascertained by the California Birth Defects Programs, and this under-ascertainment may be a factor for the reported CL/P decline.
2. Malic et al (2020) reported a declining prevalence in OFCs from 1994 to 2017, especially for CP in Ontario. Although their study was population-based, it used health administrative data (Canadian Institute for Health Information (CIHI)) supplemented by Physician's Billings. It lacked data from stillbirths and terminations of pregnancy, which are essential for modern epidemiological studies. Furthermore, their study had wide differences in area prevalence rates: very low in the Greater Toronto Area (GTA) and very high in North and West Ontario. The former might be due to a large number of babies with Jamaican ethnicity (low prevalence group) and the latter, a high number of Indigenous babies (high prevalence group). Another potential explanation includes more prenatal diagnosis followed by termination in the GTA.

In contrast to CL/P, CP total rates have declined in Alberta, but there is no trend for isolated cases (Figures 4.2.11 and 4.2.12). We have no explanation for the decline and have no reason to believe that there is any change with ascertainment.

Risk factors for OFCs include smoking, both active and passive (Honein et al 2007; Sabbagh et al 2015; Hoyt et al, 2016). Alcohol risk is supported by some studies, especially binge drinking (De Roo et al 2016; Yin et al 2019). It is interesting that for the Hutterite Brethren, where smoking and alcohol are substantially limited, there were zero cases recorded of cleft lip with cleft palate from 1980-2016 (Lowry et al 2020). Maternal obesity is a risk factor for both CL/P and CP (Blanco et al 2015).

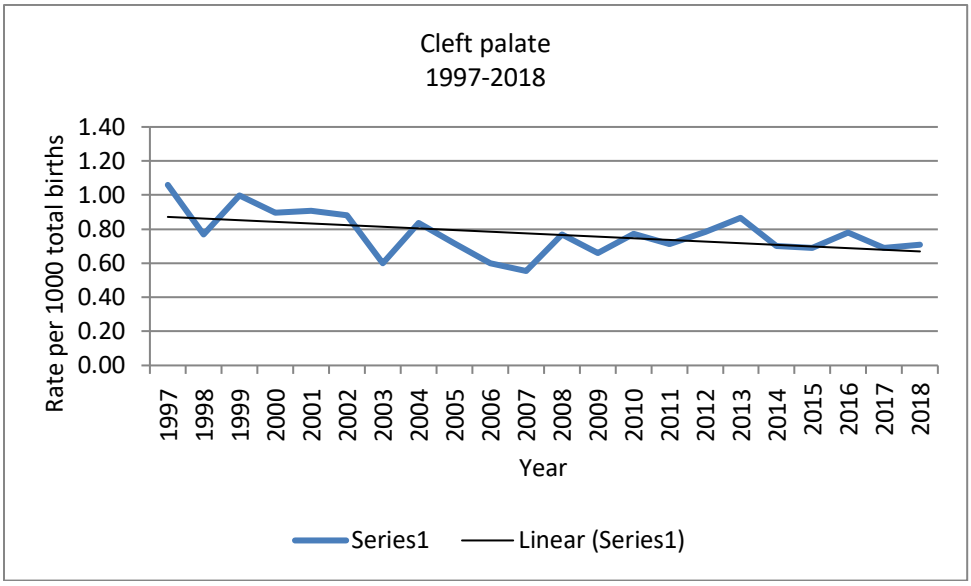
For Canada, the only data is from CIHI, and covers the years 2005-2014 (Public Health Agency of Canada, 2017). It shows no trend for CL/P, but a possible downward trend for CP.

Figure 4.2.10 Cleft Lip +/- Cleft Palate, 1997-2018 (Rate per 1000 total births)



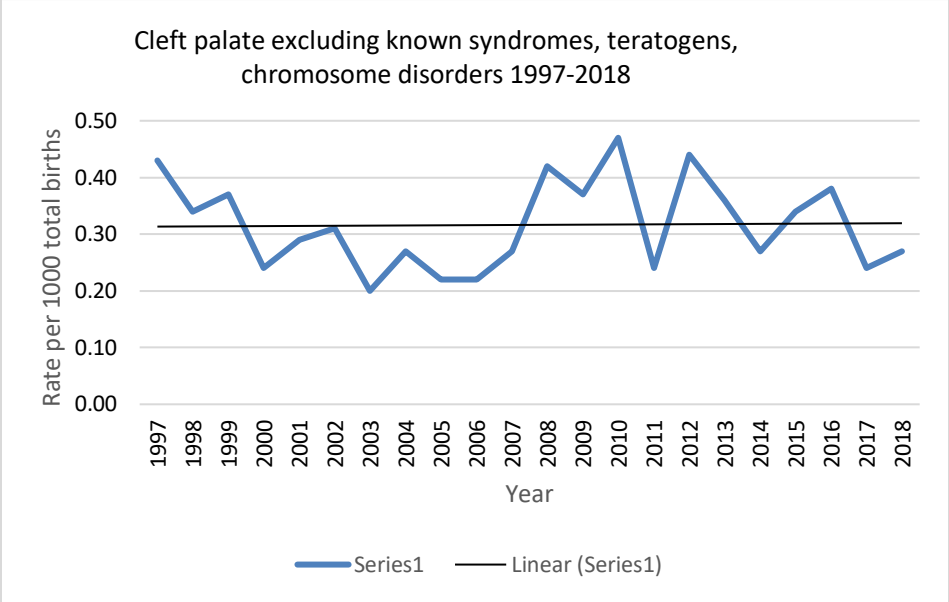
p = 0.2899

Figure 4.2.11 Cleft Palate Alone, 1997-2018 (Rate per 1000 total births)



p = 0.0489

Figure 4.2.12 Cleft palate – excluding known syndromes, teratogens or chromosome disorders, 1997-2018 (Rate per 1000 total births)



p = 0.9203

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4.2.7 Obstructive Genitourinary

A problem with analyzing or assessing the prevalence and risk factors for congenital anomalies of the kidney and urinary tract is that they are often grouped as one entity in the literature under Congenital Anomalies of the Kidney and Urinary Tract (CAKUT). We have separated Renal Agenesis and Hypoplasia (see Section 4.2.8).

The anomalies included in this section of our report, using ICD-10 RCPCH codes are: Q62.0-62.3 (includes hydronephrosis, atresia and stenosis of ureter, and other obstructive defects of the renal pelvis and ureter), Q64.2 (includes posterior urethral valves) and Q64.3 (includes other atresia and stenosis of urethra and bladder neck).

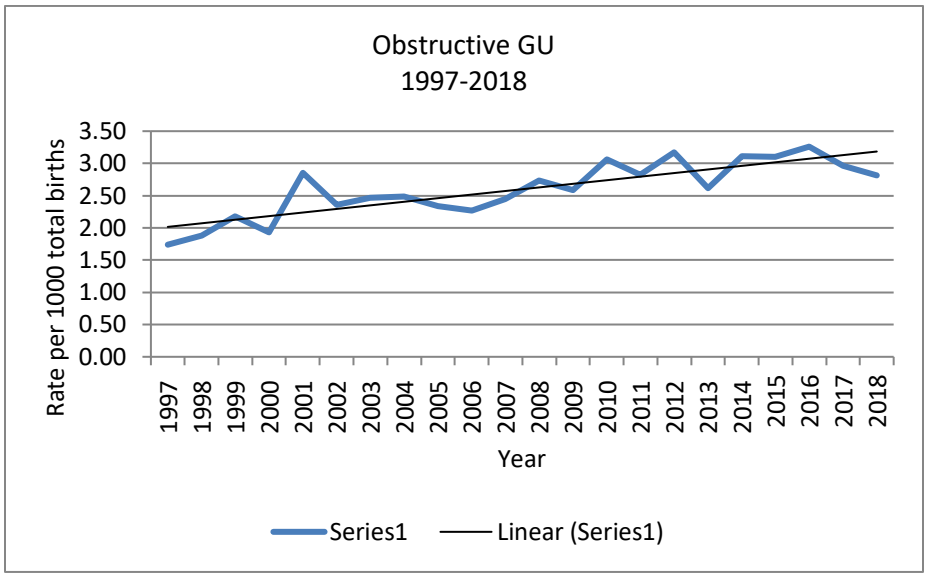
We report a statistically significant increase ($p<0.0001$) of congenital obstructive genitourinary tract anomalies from 1997-2018 (Fig. 4.2.13). The increase may be due to more frequent and accurate diagnostic imaging techniques. This combined with a lack of follow-up by ACASS, of cases that resolve spontaneously, may be contributing to the reported increase (Stonebrook et al 2019). As with the previous report, hydronephrosis continues to be the primary driver of the increase ($p<0.0001$).

Ureteropelvic junction (UPJ) obstruction also shows a significant upward trend ($p = 0.0016$). However unlike the previous report, versicoureteric junction (VUJ) obstruction, although increasing is no longer significant ($p = 0.1573$). There are only between 1 and 4 cases of VUJ reported annually, so an increase or decrease of only a few cases can make a significant difference.

Familial cases are well described with both autosomal dominant inheritance with reduced penetrance and/or variable expressivity, autosomal recessive, but probably most are multifactorial in origin (Yosypiv 2012). Recent reviews have isolated a number of genes such as signaling and epigenetic factors which are involved (Lee et al 2017; Sanna-Cherchi et al 2018).

Maternal risk factors for specific types of CAKUT were studied by Groen in 't Woud et al (2016) with variable results: e.g. folic acid alone increased the risk of vesicoureteric reflux (VUR) and duplex collecting systems. Obesity (BMI equal to or greater than 30 kg/m2) increased the risk for VUR, but smoking and alcohol were not found to increase the risk. Macumber et al (2017) confirmed that maternal obesity was a risk factor, especially for upper tract anomalies, such as hydronephrosis and UPJ obstruction.

Figure 4.2.13 Obstructive Genitourinary Tract Anomalies, 1997-2018 (Rate per 1000 total births)



p < 0.0001

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4.2.8 Renal Agenesis/Hypoplasia

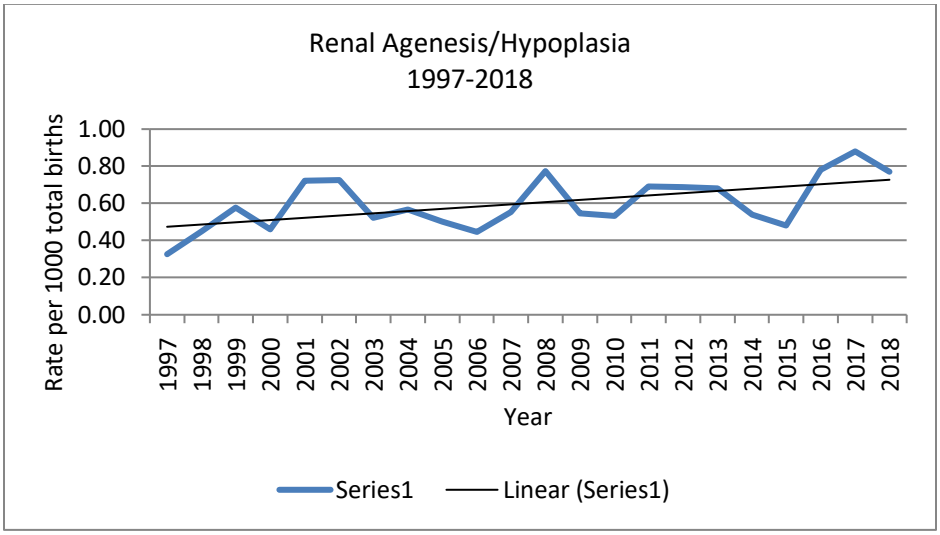
ACASS reports the prevalence of both renal agenesis and hypoplasia, affecting one or both kidneys. The total case load is 623 for the period 1997-2018, with a prevalence of 0.61/1000 total births. The trend is significantly increasing ($p = 0.0023$) (Figure 4.2.14).

Table 4.2.1 reports the prevalence and number of cases with renal agenesis or hypoplasia confirmed postnatally compared with those with only a prenatal ultrasound diagnosis, thus with no postnatal confirmation. Notably, those that are confirmed postnatally, may also have been prenatally diagnosed.

There are few reports in the literature and many group these renal anomalies with Congenital Anomalies of Kidney and Urinary Tracy (CAKUT). However, Li et al (2019) reported separate entities and recorded a prevalence for renal agenesis of 0.30/1000 live births with a male to female ratio of 0.89. Laurichesse Delmas et al (2017) reported a prevalence of 0.40/1000 total births and 0.33/1000 for live births, for unilateral renal agenesis. In the latter four years of their study the sensitivity for prenatal diagnosis reached 95.8%.

Risk factors for renal agenesis include: diabetes, both pre-gestation and gestational (Davis et al 2010); BMI > 30Kg/m^2; maternal smoking; and binge drinking (Slickers et al 2008).

Figure 4.2.14 Renal Agenesis-Hypoplasia, 1997-2018 (Rate per 1000 total births)



p = 0.0023

Table 4.2.1: Number of Cases and Prevalence of Renal Agenesis and Renal Hypoplasia with Postnatal Confirmation vs Prenatal Ultrasound Diagnosis Only

Renal Anomaly	Total Number of Cases with Postnatal Confirmed Diagnosis	Total Number of Cases with Prenatal Ultrasound Diagnosis Only	Prevalence of Cases with Postnatal Confirmed Diagnosis	Prevalence of Cases with Prenatal Ultrasound Diagnosis Only	Total Prevalence
Bilateral Renal Agenesis	96	22	0.09	0.02	0.12
Unilateral Renal Agenesis	400	20	0.39	0.02	0.41
Unspecified Renal Agenesis	24	0	0.02	0	0.02
Bilateral Renal Hypoplasia	22	1	0.02	0	0.02
Unilateral Renal Hypoplasia	37	0	0.04	0	0.04
Unspecified Renal Hypoplasia	1	0	0	0	0
Total Renal Agenesis	520	42	0.51	0.04	0.55
Total Renal Hypoplasia	60	1	0.06	0	0.06
Total Renal Agenesis/Hypoplasia	580	43	0.57	0.04	0.61

Total births for 1997-2018 = 1,023,435

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4.2.9 Abdominal Wall Defects

4.2.9a Gastroschisis

An increase in gastroschisis (GS) prevalence starting in the 1970's was noted in many jurisdictions including AB where prevalence rates rose from 0.15/1000 total births (TBs) in 1980 to 0.57/1000 TBs in 2011. The rates subsequently declined almost every year from 2011 (Figure 4.2.15). This decline has coincided in the same direction for teenage pregnancies (<20 yrs) which is a known risk factor for GS. In 2000, the percentage and number of births by mothers <20 yrs of age was 7.3% (2522/34475 births) with a declining rate every subsequent year to 2019 (1.8% - 908/50745 births) (APHP-Crawford 2021). Clark et al (2018) and others have also noted a decline in teenage pregnancies (El-Hassan et al 2020).

While GS commonly occurs as an isolated anomaly, it has been reported to occur with associated anomalies. The proportion of ACASS GS cases with co-occurring congenital anomalies is 28%, which is comparable to Stallings et al (2019) (33.6%) and Stoll et al (2021) (22.5%).

Other known risk factors for GS include maternal smoking, illicit drug use, consumption of alcohol, opioids, low BMI, poor nutrition and maternal genitourinary infections and socioeconomic disadvantage which were reviewed in a meta-analysis by Baldacci et al (2020). A healthy diet may also reduce the risk (Feldkamp et al 2014) as does maternal obesity or being overweight (Michikawa et al 2020; Raitio et al 2020).

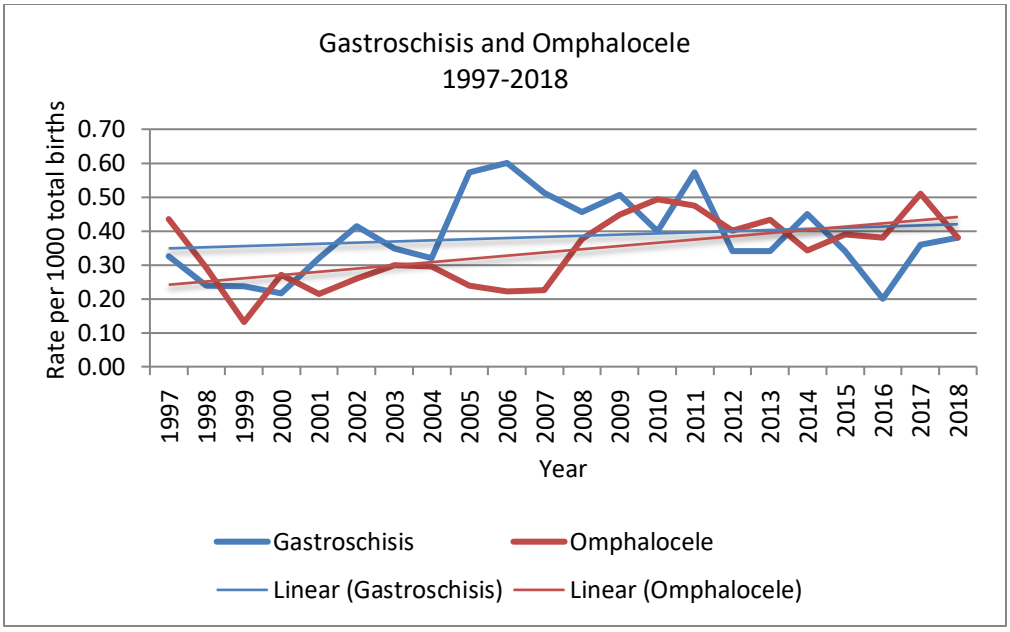
Although GS is largely sporadic, there are many reports of affected relations: Kohl (2010), Feldkamp et al (2011), Salinas-Torres et al (2018a). There are 3 reports of vertical transmission of parent to child and other reports of full sibs, twins, half sibs with different fathers or different mothers, and other degrees of relationship (Feldkamp et al 2011).

An increased risk for GS has also been shown to be associated with genetic variations and polymorphisms associated with blood pressure regulation, cell-cell interactions, coagulation and inflammatory responses (Salinas-Torres, 2018b). Feldkamp et al (2019) identified shared genomic

segments in multigenerational pedigrees with GS in the Utah registry. The regions were different in each pedigree but all contained immune pathway genes (Feldkamp et al 2019).

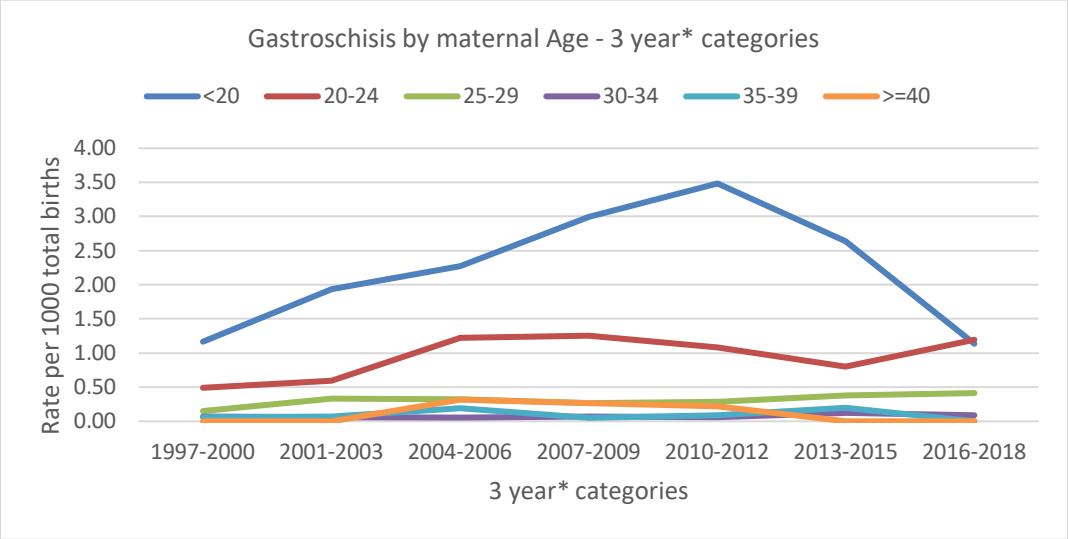
There have been reports of clusters of GS with geospatial studies in the USA (Yazdy 2015), Canada (Bassil et al 2016), Poland (Materna-Kiryluk et al 2016) and Mexico (Salinas-Torres et al 2018). Some were significant, others not significant or inconclusive. Urban/rural differences were noted in Poland and Mexico with urban rates higher. A recent study in the Hutterite Brethren (HB) (Lowry et al 2020) found zero cases of GS from 1980-2016 which is not too surprising given the likely absence of many of the risk factors, such as teen pregnancies, alcohol, smoking, illegal drugs and poor nutrition.

Figure 4.2.15 Abdominal Wall Defects – Gastroschisis and Omphalocele, 1997-2018 (Rate per 1000 total births)



Gastroschisis p = 0.5430; Omphalocele p = 0.0012

Figure 4.2.16 Gastroschisis by Maternal Age Groups - 3 Year* Increments 1997–2018 (Rate per 1000 total births)



*except 4 years for 1997-2000

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4.2.9b Omphalocele

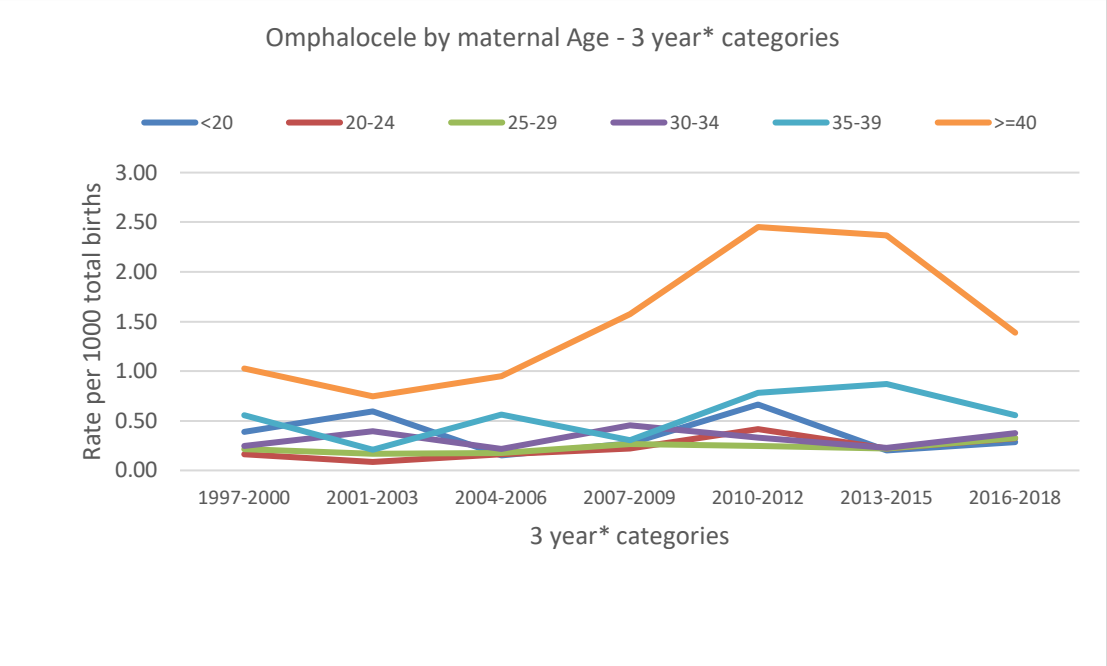
The linear trend for omphalocele is significantly increasing (p = 0.0012). Omphalocele by maternal age groups are shown in Figure 4.2.17 which again peaked in 2010 for 40 and over age groups (2.50/1000), dropping to 1.49/1000 for 2018.

In contrast to gastroschisis, omphalocele often occurs with associated anomalies. The proportion of ACASS omphalocele cases with co-occurring congenital anomalies is 77%, which is comparable with Stalling et al (2019) (71.8%) and Stoll et al (2021) (74.3%). These anomalies involve chromosome aneuploidies and other chromosome defects as well as malformations in many systems such as heart, gastrointestinal, genitourinary and neural tube defects. Many syndromes have omphalocele as one of their features, e.g. Beckwith-Wiedemann, Cantrell and OEIS (Adams et al 2021; Frolov et al 2010).

While isolated omphalocele is usually a sporadic event, nevertheless, there are reports of familial cases (Hershey et al 1989) but of course, the recurrence risk to be cited depends on the diagnosis such as a syndrome.

Risk factors are advanced maternal age equal to or greater than 35 years or a very young age (less than 20 years), certain ethnic groups (e.g. higher in African Americans and lower in North American Indigenous peoples), maternal obesity, and multiple gestations. There is frequently a 2:1 male predominance. No teratogens have been implicated for omphalocele, although Feldkamp et al (2014) in a self-reported maternal smoking study found no association but did find a possible association with second-hand smoke. Botto et al (2002) suggested that periconceptional use of folic acid and multivitamins reduced the risk while Canfield et al (2005) suggested that mandatory fortified grain products also resulted in a reduced risk but these results have not been replicated. Certainly mandatory folic acid fortification in Alberta has had no influence on the prevalence.

Figure 4.2.17 Omphalocele by Maternal Age Groups – 3 year* increments 1997–2018 (Rate per 1000 total births)



*except 4 years for 1997-2000

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4.2.10 Chromosome Anomalies

Down syndrome (Trisomy 21) is the most commonly ascertained chromosome anomaly. As previously reported, rates of Down syndrome, Trisomy 13 and Trisomy 18 are increasing significantly (χ trend analyses: T21 $p<0.0001$; T13 $p=0.0123$; T18 $p<0.0001$) (Appendix A.5; Figure 4.2.20) and are strongly correlated with increasing maternal age (Table 4.2.2). In 1983, approximately 4% of mothers were 35 years of age or over at the birth of their infant whereas, in 2018, there were almost 23% in the same age category (Figure 4.2.19).

Infants with Down syndrome often have associated anomalies. As previously noted in earlier reports, ACASS does not code minor anomalies associated with Down syndrome such as single palmar crease, upslanting palpebral fissures, and increased space between the first and second toes. On the other hand, major malformations are entered routinely into the database as most live born infants with Trisomy 21 survive and require ongoing health services. Major malformations are entered into the database for Trisomies 13 and 18 as well. Although mortality is high among infants born with Trisomies 13 and 18, some infants survive and require medical care and treatment thus counting the anomalies associated with these diagnoses can help with future health care planning.

Figure 4.2.18 Maternal Age at birth as a percent of total births, 1983-2018

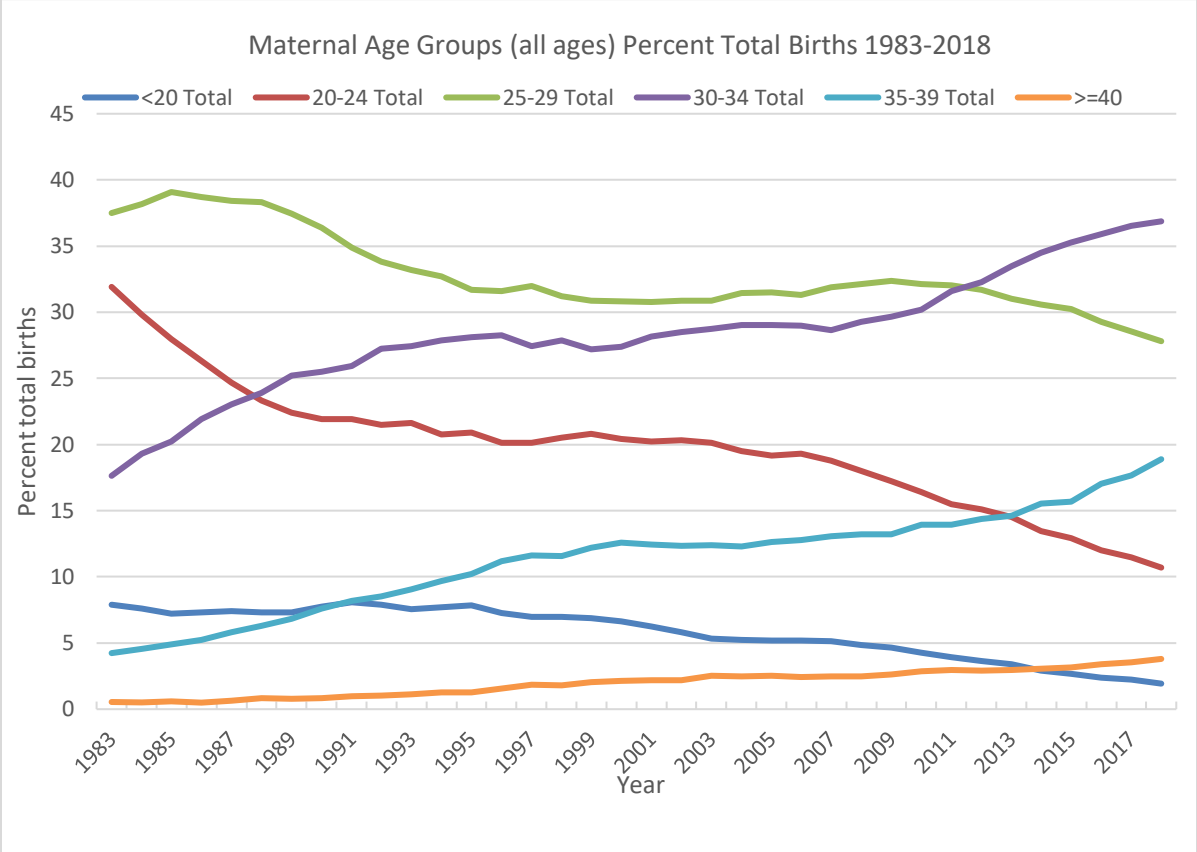


Figure 4.2.19 Maternal Age (>=35 years) at birth as a percent of total births, 1983-2018

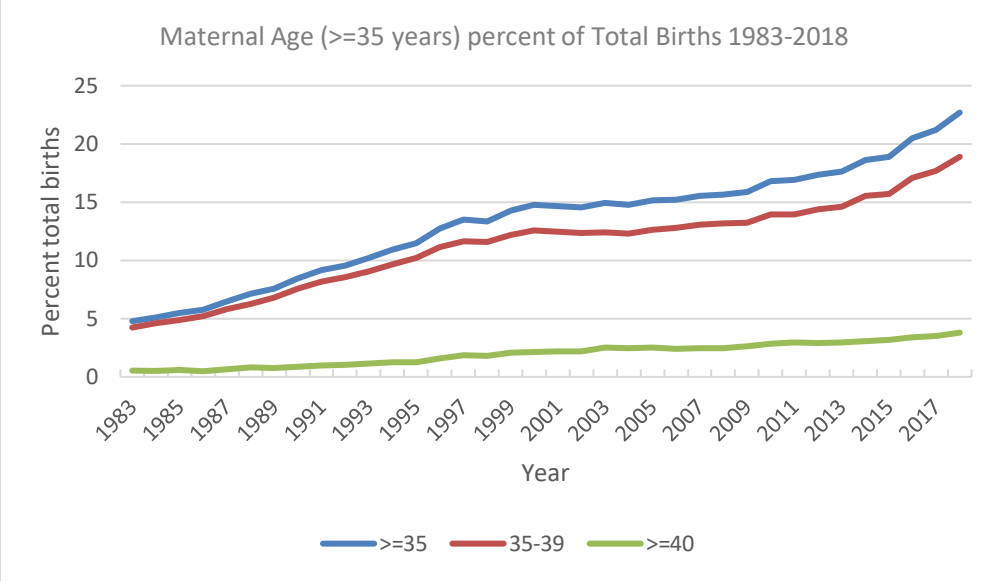
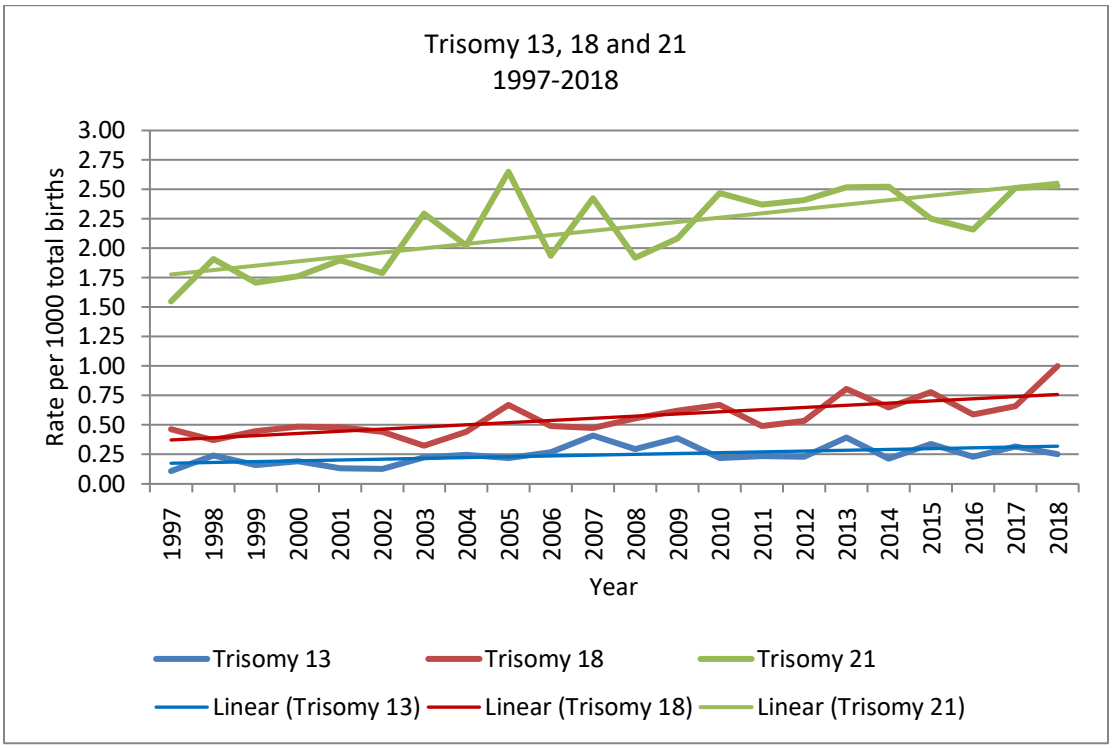


Figure 4.2.20 Chromosome Anomalies: Trisomy 13, Trisomy 18, Trisomy 21, 1997-2018
(Rate per 1000 total births)

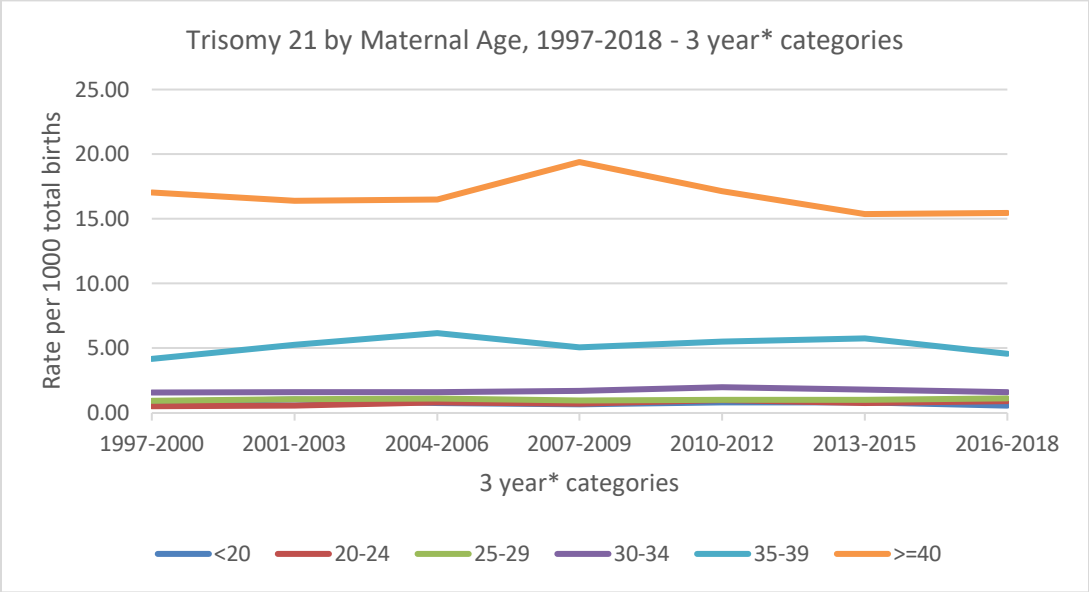


Trisomy 13 p = 0.0123; Trisomy 18 p < 0.0001; Trisomy 21 p < 0.0001

Table 4.2.2 Trisomy 21 by Maternal Age, 2010-2018 (Rate per 1000 total births)

Maternal Age	Year								
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**
<20	1.39	0	1.06	1.66	0.62	0	0.76	0.84	0
20–24	0.84	1.02	1.14	1.30	0.67	0.27	0.60	0.81	1.43
25–29	1.17	0.99	0.84	0.85	1.24	0.99	0.80	1.05	1.58
30–34	2.29	1.62	2.07	1.68	2.25	1.55	1.56	1.69	1.56
35–39	4.67	5.80	6.11	6.81	4.99	5.64	4.76	5.51	3.55
≥40	19.38	19.22	13.05	15.18	15.88	15.07	13.75	14.37	18.15
All ages	2.47	2.37	2.41	2.52	2.52	2.25	2.16	2.51	2.53

Figure 4.2.21 Trisomy 21 by Maternal Age, 3 year* increments, 1997–2018 (Rate per 1000 total births)



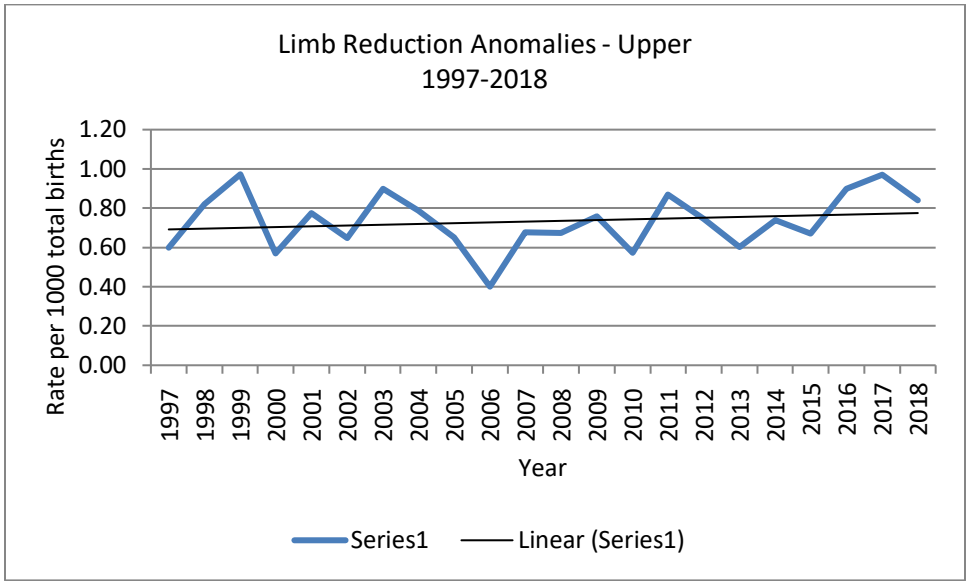
*except 4 years for 1997-2000

4.2.11 Limb Reductions

Since 1980 there have been many episodes of fluctuating rates but no overall trend for 1997-2018, nor after separating these anomalies into upper limb and lower limb categories. In most cases the cause or causes are unknown. For best ascertainment it is helpful to have x-rays, photographs, autopsies and detailed clinical descriptions as outlined by Bedard et al (2015). ACASS has legal access to these source documents. Since one case may have multiple limb reduction anomalies, we report both anomaly rates (Figures 4.2.22, 4.2.23 and 4.2.24) and case rates (Figures 4.2.25 and 4.2.26). ACASS case rates for 1997-2018 are 6.8/10,000 total births (TBs) which excludes those with an ultrasound diagnosis rising to 7.3/10,000 if the latter are included. Our case rates are comparable to many previous studies as outlined by Bedard et al (2015) but higher than a recent study from Norway that reported a rate of 4.6/10,000 for 1999-2016 (Klungsøyr et al 2019).

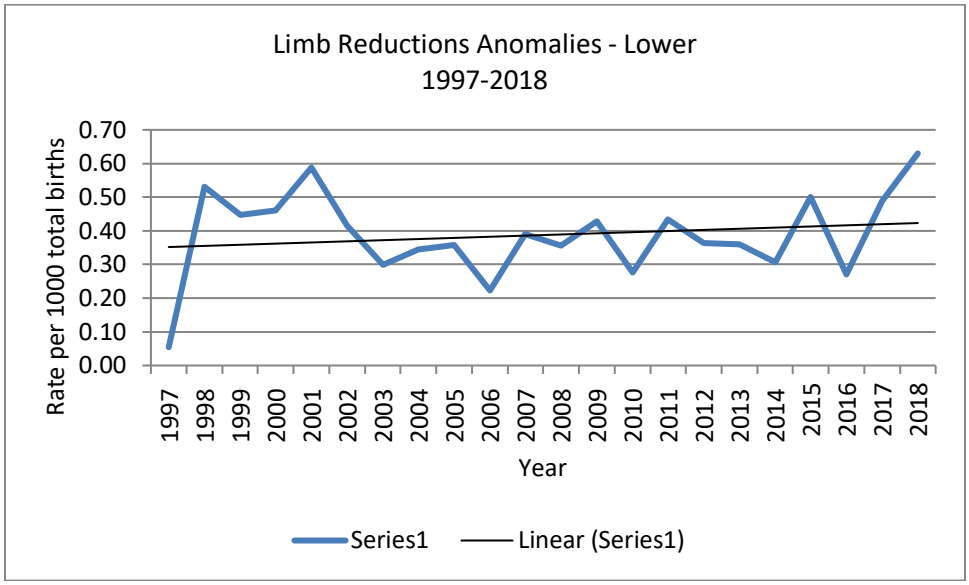
Whether folic acid plus/minus supplements reduces the risk is uncertain, as there are both positive and negative studies as discussed by Klungsøyr et al (2019) and by Liu et al (2019). The latter authors found a significant difference in China with a positive effect of folic acid fortification in Northern China but no effect in Southern China which they suggested was due to very low red blood cell folate levels in the North. It is clear that folic acid fortification has had no effect in Alberta which was also found in three South American countries (López-Camelo 2010). Classification is often an issue when comparing studies as outlined by Lowry and Bedard (2016). Geospatial data is very important, especially when investigating a cluster as emphasized in a region in France (Gnansia et al 2021). The recent Hutterite Brethren study found no cases of LRDs (Lowry et al 2020) except for two syndrome cases of the Alveolar Capillary Dysplasia with LRDs (Innes et al 2009).

Figure 4.2.22 Limb Reductions – Upper, Anomaly Rates, 1997-2018 **(Rate per 1000 total births)**



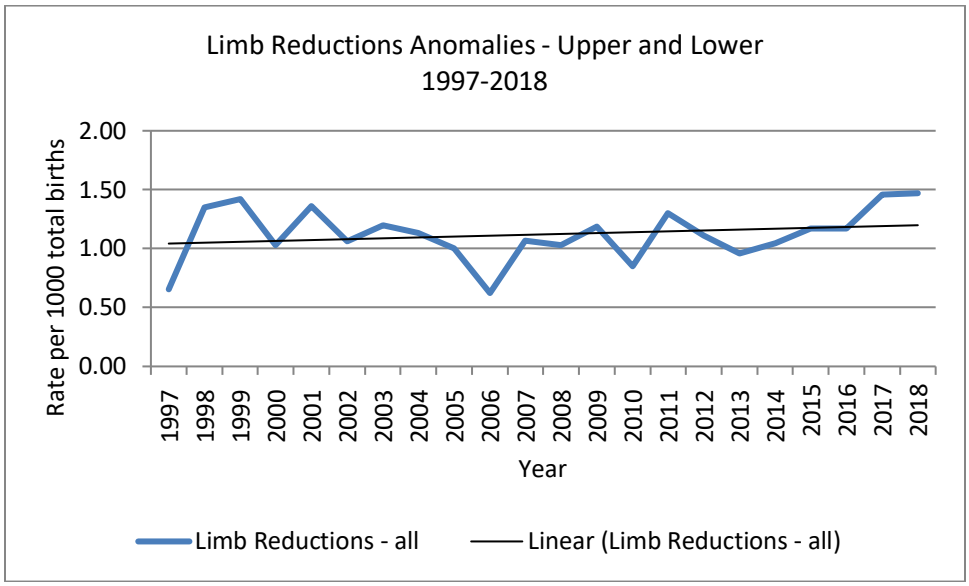
p=0.2542

Figure 4.2.23 Limb Reductions – Lower, Anomaly Rates, 1997-2018 **(Rate per 1000 total births)**



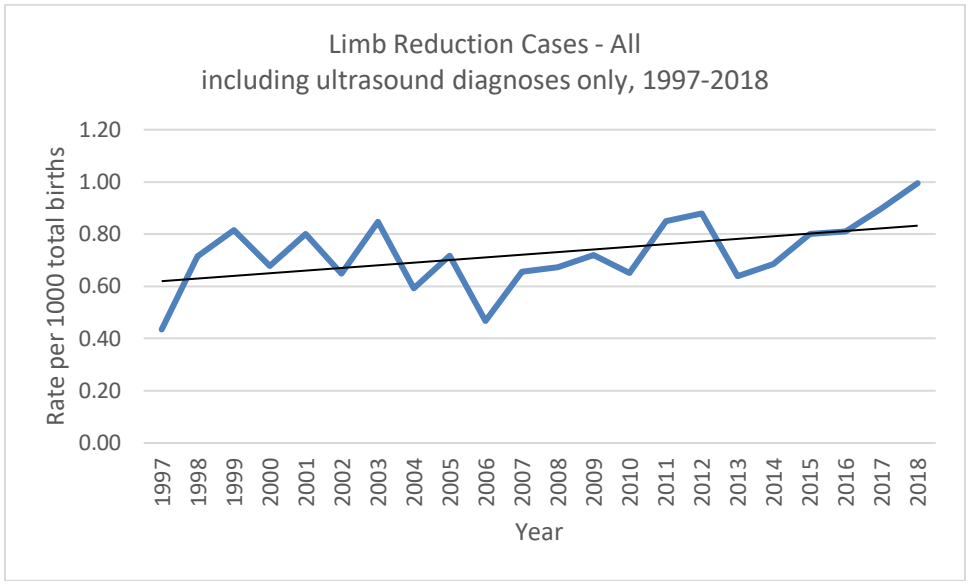
p=0.2367

Figure 4.2.24 Limb Reductions – Upper and Lower, Anomaly Rates, 1997-2018
(Rate per 1000 total births)



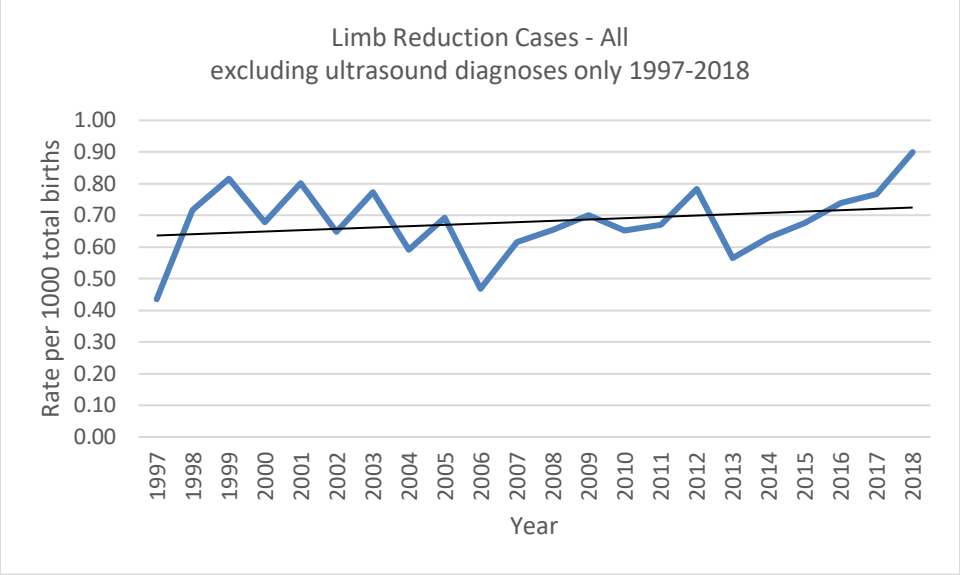
p=0.1055

Figure 4.2.25 Limb Reduction – All, Case Rates Including Cases with Ultrasound Diagnoses Only, 1997-2018 (Rate per 1000 total births)



p = 0.0131

Figure 4.2.26 Limb Reduction – All, Case Rates Excluding Cases with Ultrasound Diagnoses Only, 1997-2018 (Rate per 1000 total births)



p = 0.2636

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Lowry RB, Bedard T, Crawford S, Grevers X, Bernier FP, Thomas MA. 2020. Prevalence rates study of selected isolated non-Mendelian congenital anomalies in the Hutterite population of Alberta, 1980-2016. Am J Med Genet A, 182(11):2594-2604.

4.2.12 Anorectal Malformations

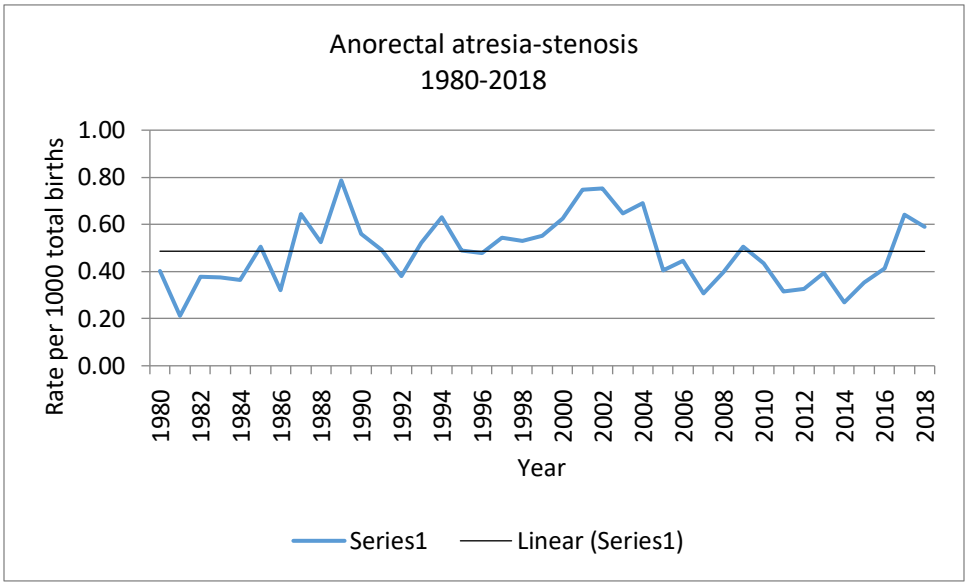
The malformations included in this category are accessed using the ICD-10 RCPCH codes Q42.0 (congenital absence, atresia and stenosis of rectum with fistula), Q42.1 (congenital absence, atresia and stenosis of rectum without fistula), Q42.2 (congenital absence, atresia and stenosis of anus with fistula) and Q42.3 (congenital absence, atresia, stenosis of anus without fistula), but data for fistulae defect level is not always available to us. A previous ACASS study for the years 1990-2004 showed stable rates (Lowry et al 2007) and compared favourably with other studies of that time (Jenetzky 2007). Figure 4.2.27 combines data from 1980 to 2018. While it shows a mild decreasing trend, it essentially shows marked fluctuations from time to time which could be true or ascertainment issues. The latter is always a concern though we have no reason to believe it is any less. If anything, it should be improved since the acquisition of termination of pregnancy (ToP) cases from 1997. It should be noted that for the 1997-2018 cohort (Figures 4.2.28, 4.2.29, 4.2.30) there has been a slight decline for both isolated and associated cases.

Risk factors include maternal smoking, maternal BMI greater than 30 kg/m^2, assisted reproductive techniques, maternal chronic respiratory disease, maternal use of anti-asthmatic medications, SSRIs, and benzodiazepine (Zwink et al 2012; Svenningsson et al 2018; Zwink et al 2016; Zwink and Jenetzky 2018). There are inconsistent results for folic acid supplements (Zwink and Janetzky 2018) and no association with the MTHFR polymorphism (Wijers et al 2014).

In the majority of studies, about 60% of anorectal malformations (ARMs) have an associated anomaly, which was lower than the ACASS study of 76% (Lowry et al 2007). The authors included live births, stillbirths, and ToPs whereas other studies only include live born, surgically treated cases (Zwink et al 2016, Svenningsson et al 2018, Oh et al 2020).

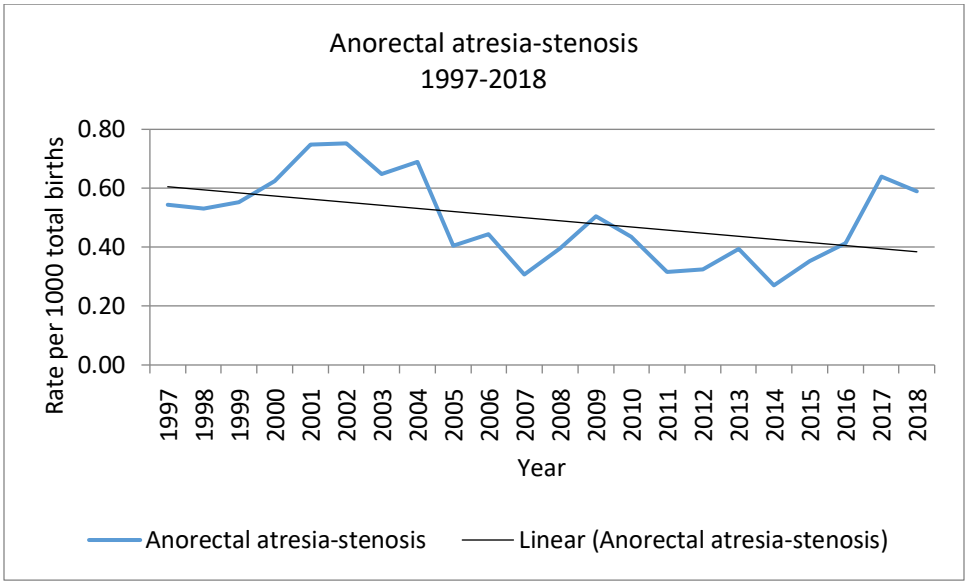
Many of the associated cases can be categorized as syndromes or chromosomal defects (Lowry et al 2007; Wang et al 2015; Khanna et al 2018) but are excluded from other studies which are for live born cases (Zwink et al 2016; Svenningsson et al 2018). While the majority of ARMs are probably the result of multifactorial inheritance with a male preponderance in most studies, cases due to autosomal dominant inheritance were reported by Dworschak et al (2017). Khanna et al (2018) reviewed candidate genes which may be partially responsible for ARMs.

Figure 4.2.27 Anorectal Malformations, 1980-2018 (Rate per 1000 Total Births)



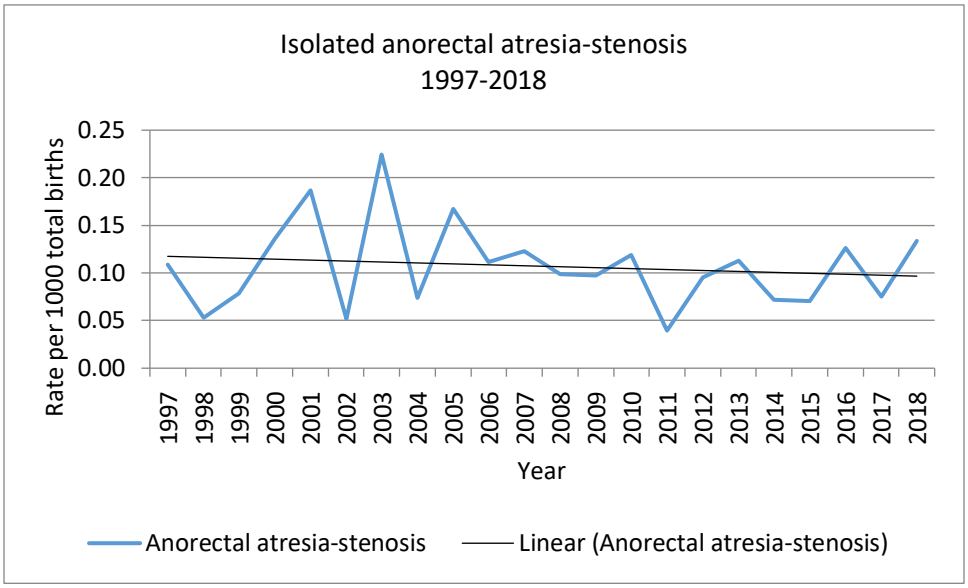
p=0.1659

Figure 4.2.28 Anorectal Malformations, 1997-2018 (Rate per 1000 Total Births)



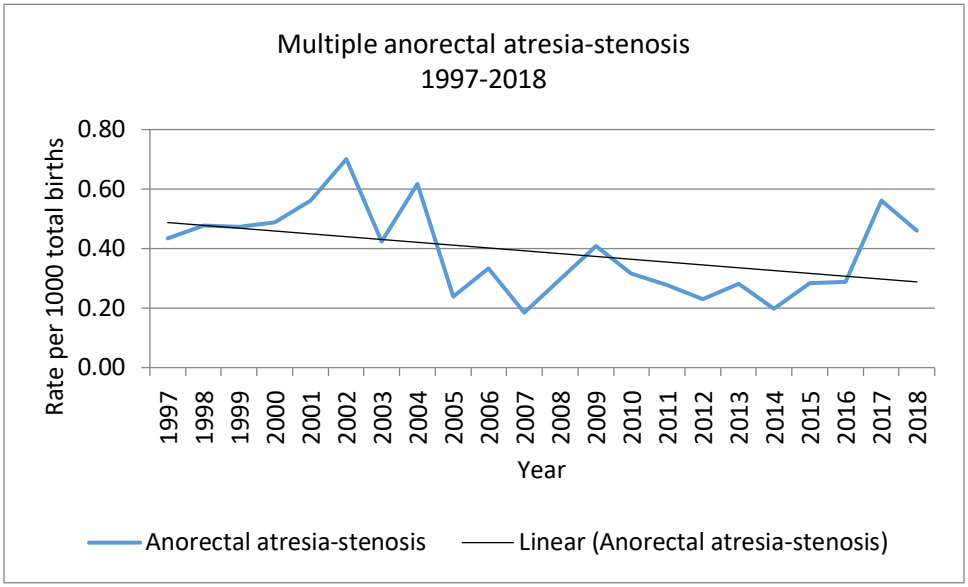
p = 0.0048

Figure 4.2.29 Anorectal Malformations – Isolated, 1997-2018 (Rate per 1000 Total Births)



p=0.5071

Figure 4.2.30 Anorectal Malformations with Multiple Anomalies, 1997-2018 (Rate per 1000 Total Births)



p=0.0045

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4.2.13 Congenital Heart Disease (CHD)

Congenital heart disease (CHD) has significantly increased from 1997-2018 ($p < 0.0001$). However, CHD is a heterogeneous group of anomalies. This includes easily managed atrial septal defects (ASDs) that may not require intervention and close spontaneously, to severe defects such as hypoplastic left heart syndrome (HLHS) which require multiple operations and has life-long morbidity.

While the majority of CHDs are multifactorial, single-gene disorders are associated with 3-5%, chromosomal anomalies/aneuploidies 8-10%, and pathogenic copy number variants 3-25% (Pierpont et al 2018). van Nisselrooij et al (2020) reported genetic diagnoses in 15.7% of their study population born between 2012 and 2016, with a severe CHD requiring surgery or therapeutic intervention in the first year of life. They excluded those with a known aneuploidy. Copy number variants were identified in 9.9% and sequence variants in 5.8%. The most commonly associated CHDs with a genetic diagnosis were interrupted aortic arch, pulmonary valve atresia with ventricular septal defect (VSD), and atrioventricular septal defects (AVSDs) (van Nisselrooij et al 2020).

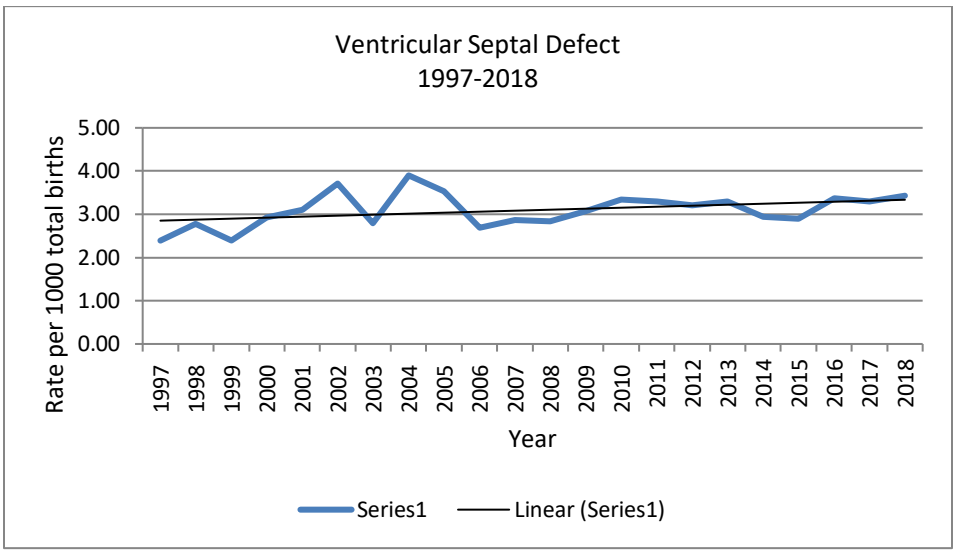
There are established syndromes associated with CHDs, particularly Down syndrome (cardiac septal defects are common), Turner syndrome (left outflow tract defects, are common), 22q11 deletion syndrome (outflow tract defects, are common), and Alagille syndrome caused by JAG1 gene mutation is associated with pulmonary artery stenosis and tetralogy of Fallot (Lin et al 2021). In the past two decades, genetic variants have been reportedly associated with non-syndromic or isolated CHDs, particularly for highly conserved transcription factors essential for cardiac development (e.g. GATA4 variants associated with tetralogy of Fallot, ASDs, VSDs, AVSDs, and pulmonary stenosis) (Lin et al 2021).

Reported risk factors for CHDs include teratogens (e.g. thalidomide, isotretinoin, anticonvulsants, potassium channel blockers, lithium, alcohol), nutritional deficiencies (e.g. vitamin A, vitamin B3), and maternal conditions (diabetes, obesity, phenylketonuria, viral infections and hyperthermia) (Kalisch-Smith et al 2020). Dolk et al (2020) reported significant associations for low maternal education, vaginal infections, maternal clotting disorders, and prescriptions for the anticlotting medication enoxaparin. More research is needed to confirm the latter, since there is no previous evidence to support an increased risk with enoxaparin, albeit the evidence base is limited. Although recent reports do not support a protective effect from folic acid supplementation (Øyen et al 2019; Dolk et al 2020), the latter group of authors reported a significant increased risk for those with poor maternal diet particularly low in fruits and vegetables. The authors emphasized the need to consider the entire dietary context to determine risk, as well as to study specific CHD subtype associations.

While the prevalence of ASDs has remained stable between 1997 and 2018 ($p=0.6892$), there is a statistically significant increase of ventricular septal defects (VSDs), $p=0.0144$, during the same period (Figure 4.2.31). Although more minor CHDs, such as small septal defects are better diagnosed due to advances in echocardiography and heart ultrasound, ACASS has stricter eligibility criteria for ASDs when compared with VSDs. ACASS does not accept patent foramen ovale as a CHD, an ASD in a premature infant, or if the defect is < 3mm and spontaneously closes. There are no such restrictions for VSDs, which is accepted regardless of the size of the defect, or if the defect needs intervention or spontaneously closes.

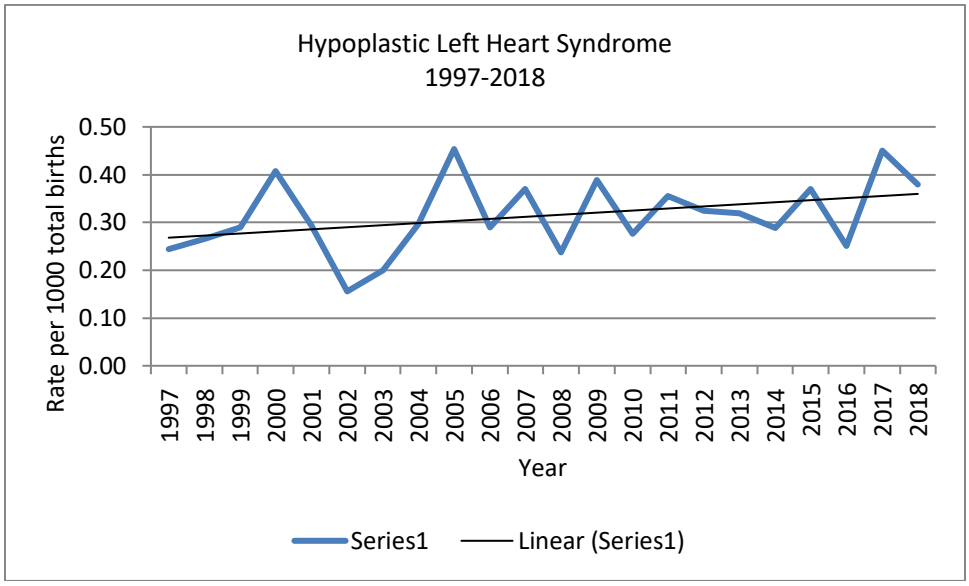
The prevalence rates of the more severe CHDs, although not statistically significant, show a slight increase from 1997-2018, including that of HLHS ($p=0.1213$)(Figure 4.2.32) transposition of the great vessels ($p=0.2334$), tetralogy of Fallot ($p=0.2733$) (Figure 4.2.33), and truncus arteriosus ($p=0.1213$). Öhman et al (2019) reported a decrease of live births with HLHS in Sweden, and suggested that the decrease was due to increased prenatal detection and an increase in termination of pregnancy, highlighting the importance of ascertaining ToPs to determine more accurate estimates of prevalence.

Figure 4.2.31 Ventricular Septal Defect, 1997-2018 (Rate per 1000 Total Births)



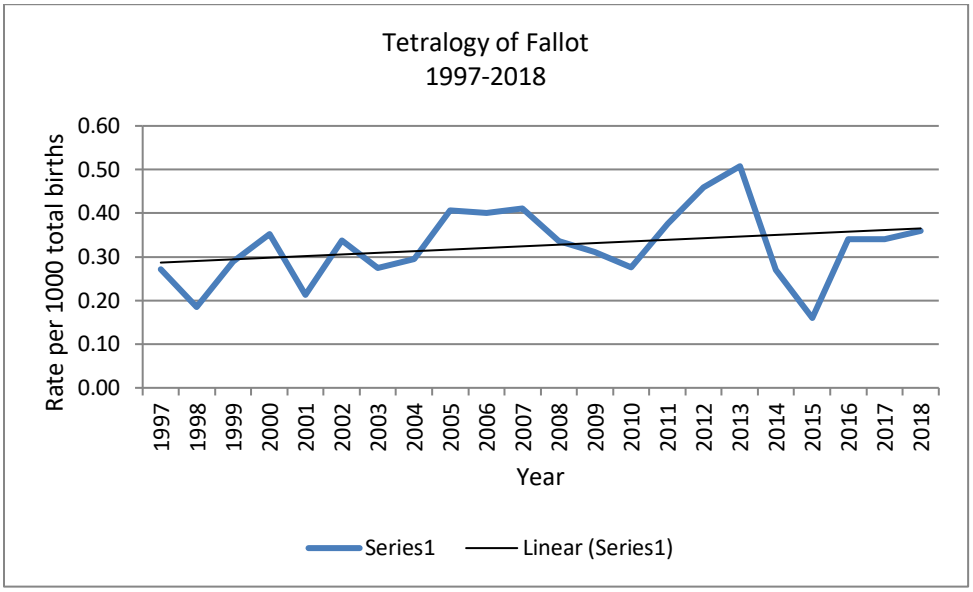
p = 0.0144

Figure 4.2.32 Hypoplastic Left Heart Syndrome, 1997-2018 (Rate per 1000 Total Births)



p = 0.1213

Figure 4.2.33 Tetralogy of Fallot, 1997-2018 (Rate per 1000 Total Births)



p = 0.2733

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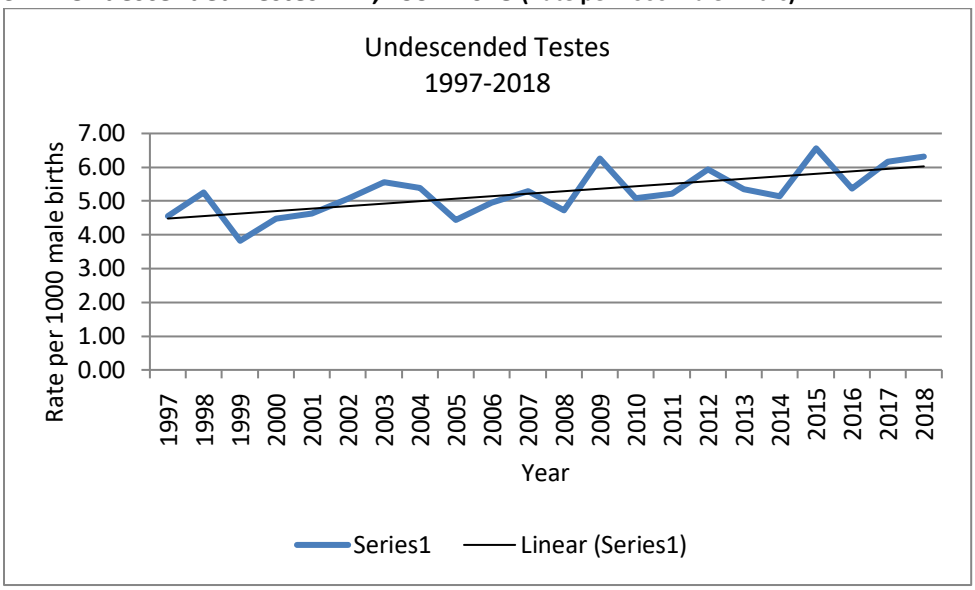
4.2.14 Undescended Testes

Although the prevalence rates of all males with undescended testes (UT) and males with UT excluding known syndromes, teratogens, and chromosome disorders for 1997-2018 (Figures 4.2.34 and 4.2.35) show statistically significant increases ($p < 0.0001$), the trends need to be interpreted with caution. Many cases resolve spontaneously while others may be misdiagnosed and actually have retractile testes. A more accurate prevalence would be determined by knowing which cases came to orchidopexy. This would require a special study with a longer follow-up of cases. ACASS does not accept cases born before 37 weeks gestation or a birth weight less than 2500g since these cases commonly have UT.

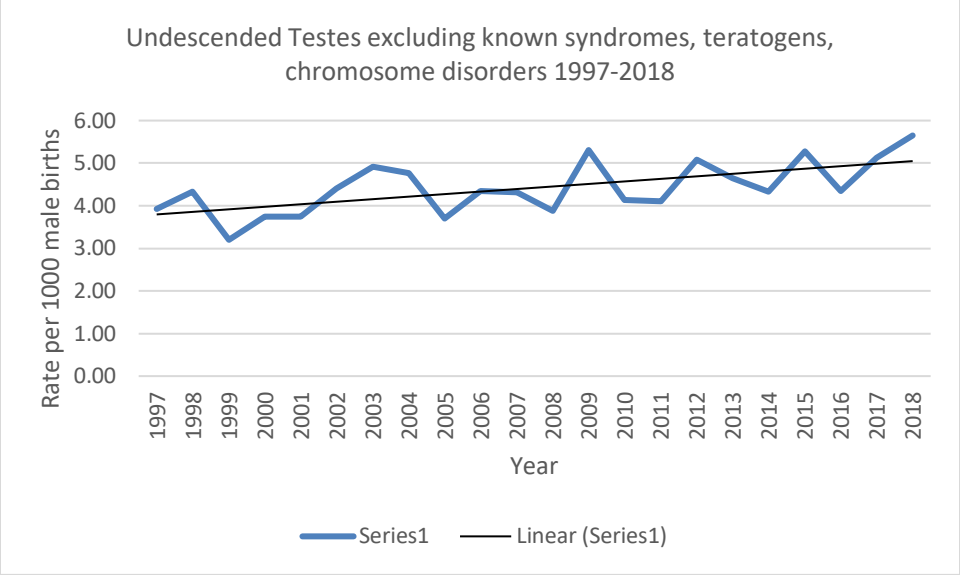
While the precise etiology is largely unknown, it is thought to be multifactorial since familial cases have been observed as well as multiple susceptibility genes (Barthold et al 2016). The most consistent risk factor is maternal smoking. Other risk factors which have been implicated are inconsistent between studies. These include: maternal obesity, alcohol, use of analgesics and exposure to endocrine-disrupting chemicals such as agricultural pesticides (Gurney et al 2017; Hurtado-Gonzalez et al 2017; Yu et al 2019). Although agricultural exposure was suggested as a risk for hypospadias by Lowry et al (2020) there was no increase in the prevalence of UT in the Hutterite population. This suggests the etiology of these two congenital anomalies may be different.

Figure 4.2.34 Undescended Testes - All, 1997-2018 (Rate per 1000 Male Births)



$p < 0.0001$

Figure 4.2.35 Undescended Testes excluding known syndromes, teratogens, chromosome disorders, 1997-2018 (Rate per 1000 Male Births)



$p < 0.0001$

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4.2.15 Hypospadias

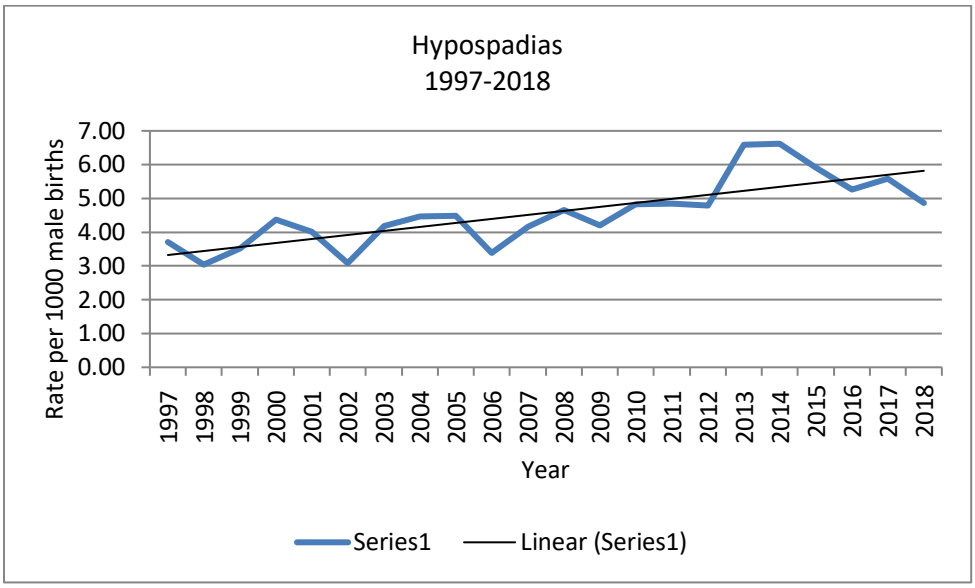
Prevalence rates for hypospadias for both isolated and nonisolated cases, including syndromes and multiple anomalies, continued to increase steadily from 1997 until 2017 with a sharp drop for 2018 (Figures 4.2.36 and 4.2.37). Nevertheless, the rate of increase is significant ($p < 0.0001$).

Risk factors include a positive family history, low birth weight and/or small gestational age, maternal hypertension, preeclampsia, multiple gestations, placental insufficiency, diabetes mellitus, and certain drug exposures such as to Progesterone derivatives or Valproic acid. There is inconsistent evidence regarding risk factors like maternal age and weight, paternal or maternal occupations, and agriculture practices including residential proximity to agricultural land. A review of genetic and environmental factors by George et al (2015) summarizes some of the issues pertaining to the strengths of associations to determine the etiology of hypospadias.

Most cases are probably the result of multifactorial inheritance since there are very few reports of single gene inheritance, although there have been two reports of autosomal recessive and five of autosomal dominant inheritance cases (Harris 1990). More recently, studies of genetic variants and/or polymorphisms have shown these to be significant risk factors. The first report on the diacylglycerol kinase kappa (DGKK) variant was by van der Zanden et al (2011) and later summarized by Bouty et al (2015) and Joodi et al (2019). Carmichael et al (2016) reported an area of California where residential proximity to pesticide application plus cases with the DGKK variant had the highest odds ratios for hypospadias. Similar findings were reported from Poland (Hozyasz et al 2018).

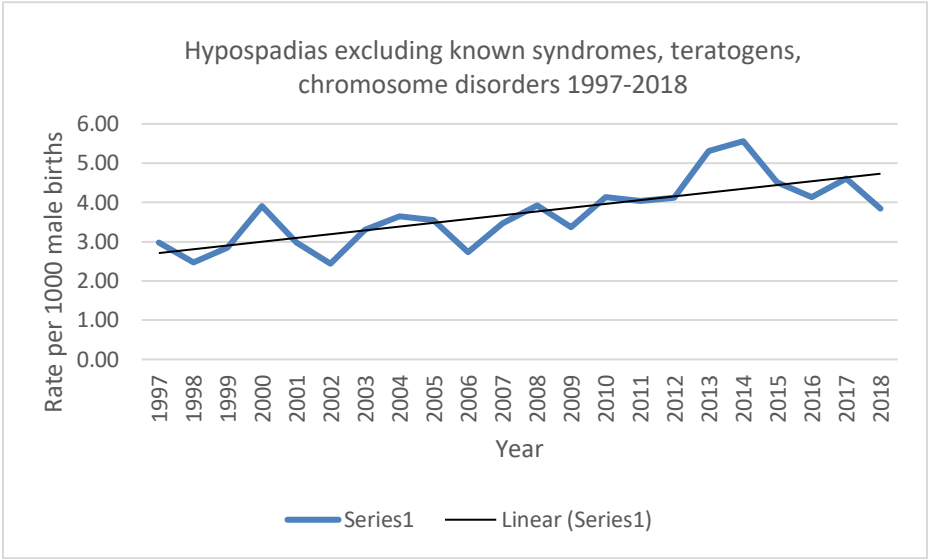
In Nova Scotia, the highest prevalence rate of hypospadias was found in two counties that were associated with intense farming (Lane et al 2017). Lowry et al (2020), showed that the Hutterite Brethren (HB) have about double the prevalence rate of isolated hypospadias compared to the general Alberta population. For the years 1997-2016, the HB rate was 7.7/1000 male births compared to the Alberta provincial prevalence rate of 3.80/1000 male births. Since the HB are a farming and agriculture community, it does suggest that the overall rate, which is rising in Alberta, may be related to agricultural practices and requires further study.

Figure 4.2.36 Hypospadias - All, 1997-2018 (Rate per 1000 Male Births)



p < 0.0001

Figure 4.2.37 Hypospadias excluding known syndromes, teratogens, chromosome disorders, 1997-2018 (Rate per 1000 Male Births)



p < 0.0001

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Summary

ACASS reviews anomalies that have been entered into the database on a regular basis. Detailed studies of some individual anomalies or anomaly groups aid in the assessment and maintenance of the data quality. With intensive review, some cases might be reassigned, recoded or discarded altogether from the database. This continuing review might explain some discrepancies in the data from earlier reports.

5. Surveillance and Research Projects since 2001

5.1 Surveillance and Research Projects/Collaborations and Consultations/Papers

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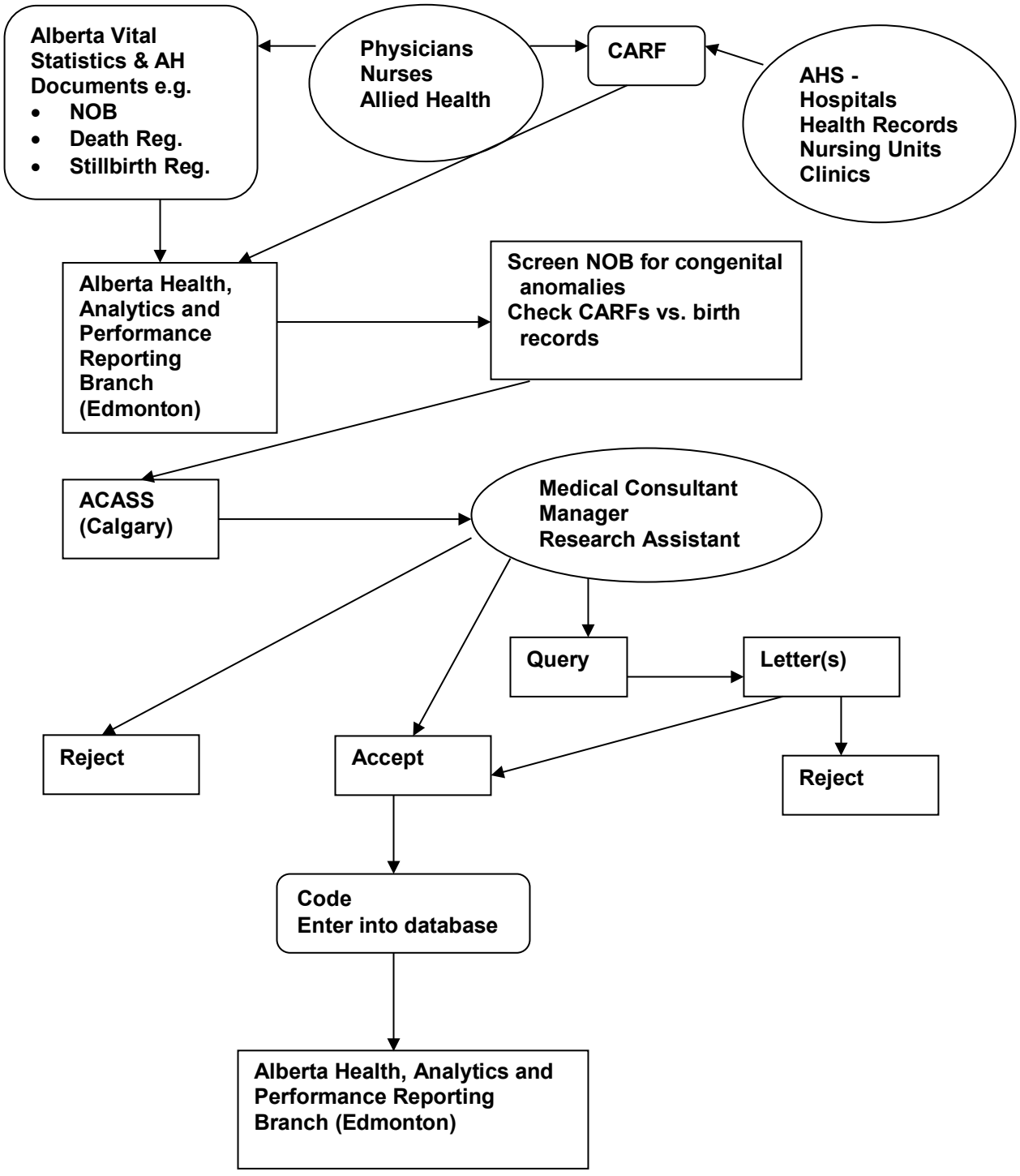
ii. Sibbald B and Lowry RB Abdominal wall defects- Alberta 1980–2002 (winter 2004) http://www.phac-aspc.gc.ca/ccasn-rcsac/ct2004/awd-alb.html
iii. Sibbald B and Lowry RB Down Syndrome in Alberta: Alberta Congenital Anomalies Surveillance System (fall 2003) http://www.phac-aspc.gc.ca/ccasn-rcsac/ct2003/abds_e.html

Alberta Congenital Anomalies Surveillance System

6. Appendices

Appendix A.1 Flowchart of the Process of ACASS Data Collection



Appendix A.2 Congenital Anomaly(ies) Reporting Form (CARF)

Alberta Health and Wellness

Death Reg No	Birth Reg No

Addressograph

Mail parts one and two to:
Alberta Health and Wellness
Surveillance and Environmental Health Branch
PO Box 1360 Stn Main
Edmonton AB T5J 2N3

Congenital Anomaly(ies) Reporting

Fetus / Infant — **PLEASE PRINT CLEARLY**

Name *(Last, First, Initial)*	**Date of Birth** *Month by Name* Day Year

Gender ☐ Male ☐ Female ☐ Unknown	Type of Birth ☐ Livebirth ☐ Stillbirth ☐ Fetus less than 20 weeks gestation	Name of Hospital of Birth
Birthweight *Grams*	Gestation Age *(Completed Weeks)*	Location of Hospital of Birth *(City/Town)*
Child's Personal Health Number		Attending Physician's Name
Plurality of Birth ☐ Single ☐ Twin ☐ First ☐ Second ☐ Triplets ☐ First ☐ Second ☐ Third		Physician Responsible for Ongoing Care *(if different from above)*

Parents

Mother's Name *(Last, First, Maiden)*	**Date of Birth or Age** *(if DOB unavailable)* *Month by Name* Day Year	**Total Number of**
Permanent Address	Mother's Personal Health Number	Livebirths
City/Town	Postal Code	Stillbirths
Father's Name *(Last, First, Initial)*	**Date of Birth or Age** *(if DOB unavailable)* *Month by Name* Day Year	Spontaneous Abortions
		Therapeutic Abortions

Reporting Hospital/Agency/Clinic

Name	Infant's Admission *(If different from birthdate)*	Infant's Discharge *Month by Name* Day Year
Location *(City/Town)*	*Month by Name* Day Year	Infant's Death *(If Applicable)* *Month by Name* Day Year

Full description of Congenital Anomaly(ies) and/or **SYNDROME DIAGNOSES** *(If necessary, please attach supporting documents.)*

OFFICE USE ONLY

Completed by	Position	Date

HS0020-112 (2008/06)

Send to Surveillance and Environmental Health

Appendix A.3 Alberta Congenital Anomalies Surveillance System Anomaly Rates
RCPCH version ICD-10 Q-Chapter (Q00-Q99)
Single Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Anencephaly	NUMBER	10	18	9	16	8	14	16	13	6	6	6
	RATE	**0.20**	**0.35**	**0.18**	**0.32**	**0.15**	**0.26**	**0.29**	**0.23**	**0.11**	**0.11**	**0.11**
	Lower CI	0.10	0.21	0.08	0.18	0.07	0.14	0.17	0.12	0.04	0.04	0.04
ICD-10 Q00.00, Q00.01, Q00.1	Upper CI	0.36	0.55	0.34	0.51	0.30	0.44	0.47	0.39	0.23	0.24	0.25
Spina Bifida without Anencephaly	NUMBER	19	22	24	20	22	19	17	14	25	18	20
	RATE	**0.38**	**0.43**	**0.47**	**0.39**	**0.42**	**0.36**	**0.31**	**0.25**	**0.45**	**0.34**	**0.38**
	Lower CI	0.23	0.27	0.30	0.24	0.26	0.22	0.18	0.14	0.29	0.20	0.23
ICD-10 Q05..	Upper CI	0.59	0.65	0.71	0.61	0.64	0.56	0.49	0.41	0.67	0.53	0.59
Encephalocele	NUMBER	7	7	7	5	6	8	4	3	10	6	7
	RATE	**0.14**	**0.14**	**0.14**	**0.10**	**0.11**	**0.15**	**0.07**	**0.05**	**0.18**	**0.11**	**0.13**
	Lower CI	0.06	0.05	0.06	0.03	0.04	0.06	0.02	0.01	0.09	0.04	0.05
ICD-10 Q01..	Upper CI	0.28	0.28	0.28	0.23	0.25	0.29	0.18	0.15	0.33	0.24	0.27
Neural Tube Defects (all)	NUMBER	36	47	40	41	36	41	37	30	41	30	34
	RATE	**0.71**	**0.91**	**0.79**	**0.81**	**0.69**	**0.77**	**0.67**	**0.53**	**0.74**	**0.56**	**0.65**
	Lower CI	0.50	0.67	0.57	0.58	0.48	0.55	0.47	0.36	0.53	0.38	0.45
ICD-10 Q00.., Q01.., Q05..	Upper CI	0.99	1.22	1.08	1.10	0.95	1.05	0.92	0.76	1.00	0.80	0.91
Hydrocephalus without Spina Bifida	NUMBER	32	29	30	37	26	16	20	20	28	16	13
	RATE	**0.63**	**0.56**	**0.59**	**0.73**	**0.50**	**0.30**	**0.36**	**0.35**	**0.50**	**0.30**	**0.25**
(Excludes hydranencephaly)	Lower CI	0.43	0.38	0.40	0.51	0.33	0.17	0.22	0.22	0.34	0.17	0.13
ICD-10 Q03	Upper CI	0.89	0.81	0.85	1.01	0.73	0.49	0.56	0.55	0.73	0.49	0.42
Arrhinencephaly/ Holoprosencephaly	NUMBER	16	16	9	11	12	18	8	15	17	22	11
	RATE	**0.32**	**0.31**	**0.18**	**0.22**	**0.23**	**0.34**	**0.14**	**0.27**	**0.31**	**0.41**	**0.21**
	Lower CI	0.18	0.18	0.08	0.11	0.12	0.20	0.06	0.15	0.18	0.26	0.11
ICD-10 Q04.1, Q04.2, Q87.03	Upper CI	0.51	0.50	0.34	0.39	0.40	0.53	0.28	0.44	0.49	0.62	0.38
Microcephaly	NUMBER	18	23	21	33	20	21	15	22	15	20	20
	RATE	**036**	**0.45**	**0.42**	**0.65**	**0.38**	**0.39**	**0.27**	**0.39**	**0.27**	**0.37**	**0.38**
	Lower CI	0.21	0.28	0.26	0.45	0.23	0.24	0.15	0.24	0.15	0.23	0.23
ICD-10 Q02	Upper CI	0.56	0.67	0.63	0.92	0.59	0.60	0.44	0.59	0.45	0.58	0.59
Anophthalmia/microphthalmia	NUMBER	10	4	6	8	7	9	6	6	10	13	10
	RATE	**0.20**	**0.08**	**0.12**	**0.16**	**0.13**	**0.17**	**0.11**	**0.11**	**0.18**	**0.24**	**0.19**
	Lower CI	0.10	0.02	0.04	0.07	0.05	0.08	0.04	0.04	0.09	0.13	0.09
ICD-10 Q11.0, Q11.1, Q11.2	Upper CI	0.36	0.19	0.26	0.31	0.27	0.32	0.23	0.23	0.33	0.42	0.35
Congenital cataract	NUMBER	4	11	13	7	6	9	10	4	8	8	13
	RATE	**0.08**	**0.21**	**0.26**	**0.14**	**0.11**	**0.17**	**0.18**	**0.07**	**0.14**	**0.15**	**0.25**
	Lower CI	0.02	0.11	0.14	0.06	0.04	0.08	0.09	0.02	0.06	0.06	0.13
ICD-10 Q12.0	Upper CI	0.20	0.38	0.44	0.28	0.25	0.32	0.33	0.18	0.28	0.29	0.42

Appendix A.3 Alberta Congenital Anomalies Surveillance System
RCPCH version ICD-10 Q-Chapter (Q00-Q99)
Aggregate Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		00-04 (5 years)	05-09 (5 years)	10-14 (5 years)	15-18 (4 years)	00-18 (19 years)
Anencephaly	NUMBER	48	55	63	31	197
	RATE	**0.25**	**0.23**	**0.24**	**0.14**	**0.22**
	Lower CI	0.18	0.17	0.18	0.10	0.19
ICD-10 Q00.00, Q00.01, Q00.1	Upper CI	0.33	0.30	0.31	0.20	0.25
Spina Bifida without Anencephaly	NUMBER	58	99	102	77	336
	RATE	**0.30**	**0.42**	**0.39**	**0.35**	**0.37**
	Lower CI	0.23	0.34	0.32	0.28	0.33
ICD-10 Q05..	Upper CI	0.39	0.51	0.47	0.44	0.41
Encephalocele	NUMBER	28	31	30	26	115
	RATE	**0.14**	**0.13**	**0.11**	**0.12**	**0.13**
	Lower CI	0.10	0.09	0.08	0.08	0.10
ICD-10 Q01..	Upper CI	0.21	0.18	0.16	0.18	0.15
Neural Tube Defects (all)	NUMBER	134	186	195	135	650
	RATE	**0.69**	**0.78**	**0.74**	**0.62**	**0.71**
	Lower CI	0.58	0.67	0.64	0.52	0.66
ICD-10 Q00.., Q01.., Q05..	Upper CI	0.82	0.90	0.86	0.73	0.77
Hydrocephalus without Spina Bifida	NUMBER	106	146	129	77	458
	RATE	**0.55**	**0.61**	**0.49**	**0.35**	**0.50**
(Excludes hydranencephaly)	Lower CI	0.45	0.52	0.41	0.28	0.46
ICD-10 Q03	Upper CI	0.66	0.72	0.58	0.44	0.55
Arrhinencephaly/ Holoprosencephaly	NUMBER	37	59	58	65	219
	RATE	**0.19**	**0.25**	**0.22**	**0.30**	**0.24**
	Lower CI	0.13	0.19	0.17	0.23	0.21
ICD-10 Q04.1, Q04.2, Q87.03	Upper CI	0.26	0.32	0.29	0.38	0.27
Microcephaly	NUMBER	77	96	110	77	356
	RATE	**0.38**	**0.40**	**0.42**	**0.35**	**0.39**
	Lower CI	0.30	0.33	0.34	0.28	0.35
ICD-10 Q02	Upper CI	0.47	0.49	0.51	0.44	0.43
Anophthalmia/microphthalmia	NUMBER	28	39	36	39	142
	RATE	**0.14**	**0.16**	**0.14**	**0.18**	**0.16**
	Lower CI	0.10	0.12	0.10	0.13	0.13
ICD-10 Q11.0, Q11.1, Q11.2	Upper CI	0.21	0.22	0.19	0.25	0.18
Congenital cataract	NUMBER	16	34	45	33	128
	RATE	**0.08**	**0.14**	**0.17**	**0.15**	**0.14**
	Lower CI	0.05	0.10	0.13	0.10	0.12
ICD-10 Q12.0	Upper CI	0.13	0.20	0.23	0.21	0.17

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Single Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Anotia/microtia	NUMBER	11	16	14	11	13	18	11	12	17	24	11
	RATE	**0.22**	**0.31**	**0.28**	**0.22**	**0.25**	**0.34**	**0.20**	**0.21**	**0.31**	**0.45**	**0.21**
	Lower CI	0.11	0.18	0.15	0.11	0.13	0.20	0.10	0.11	0.18	0.29	0.11
ICD-10 Q16.0, Q17.2	Upper CI	0.39	0.50	0.46	0.39	0.42	0.53	0.35	0.37	0.49	0.67	0.38
Congenital Heart Defects (all)	NUMBER	528	586	661	643	690	747	682	757	725	676	755
	RATE	**10.45**	**11.40**	**13.07**	**12.69**	**13.19**	**14.05**	**12.29**	**13.39**	**13.07**	**12.66**	**14.45**
	Lower CI	9.58	10.49	12.09	11.73	12.22	13.06	11.38	12.46	12.13	11.72	13.44
ICD-10 Q20.. to Q26..	Upper CI	11.38	12.36	14.10	13.71	14.21	15.09	13.25	14.38	14.05	13.65	15.52
Common Truncus	NUMBER	3	2	4	2	5	8	3	3	8	7	3
Excludes AP window	**RATE**	**0.06**	**0.04**	**0.08**	**0.04**	**0.10**	**0.15**	**0.05**	**0.05**	**0.14**	**0.13**	**0.06**
	Lower CI	0.01	0.00	0.02	0.00	0.03	0.06	0.01	0.15	0.06	0.05	0.01
ICD-10 Q20.0	Upper CI	0.17	0.13	0.20	0.14	0.22	0.29	0.15	0.15	0.28	0.27	0.16
Transposition of Great Arteries	NUMBER	14	13	13	20	21	23	29	25	22	19	26
	RATE	**0.28**	**0.25**	**0.26**	**0.39**	**0.40**	**0.43**	**0.52**	**0.44**	**0.40**	**0.36**	**0.50**
	Lower CI	0.15	0.13	0.14	0.24	0.25	0.27	0.35	0.29	0.25	0.21	0.33
ICD-10 Q20.11, Q20.3, Q20.5	Upper CI	0.46	0.43	0.44	0.61	0.61	0.65	0.75	0.65	0.60	0.56	0.73
Tetralogy of Fallot	NUMBER	17	16	14	19	24	27	15	9	19	18	19
(Includes Tetralogy with ASD	**RATE**	**0.34**	**0.31**	**0.28**	**0.38**	**0.46**	**0.51**	**0.27**	**0.16**	**0.34**	**0.34**	**0.36**
aka Pentalogy of Fallot)	Lower CI	0.20	0.18	0.15	0.23	0.29	0.34	0.15	0.07	0.21	0.20	0.22
ICD-10 Q21.3.., Q21.82	Upper CI	0.54	0.50	0.46	0.59	0.68	0.74	0.44	0.30	0.53	0.53	0.57
Ventricular Septal Defect	NUMBER	143	158	169	167	168	175	163	164	187	176	179
	RATE	**2.83**	**3.07**	**3.34**	**3.30**	**3.21**	**3.29**	**2.94**	**2.90**	**3.37**	**3.30**	**3.43**
	Lower CI	2.39	2.61	2.86	2.82	2.74	2.82	2.50	2.48	2.91	2.83	2.94
ICD-10 Q21.0	Upper CI	3.34	3.59	3.89	3.34	3.73	3.82	3.42	3.38	3.89	3.82	3.97
Atrial Septal Defect	NUMBER	74	95	111	99	107	117	127	135	108	116	107
	RATE	**1.46**	**1.85**	**2.19**	**1.95**	**2.05**	**2.20**	**2.29**	**2.39**	**1.95**	**2.17**	**2.05**
	Lower CI	1.15	1.50	1.81	1.59	1.68	1.82	1.91	2.00	1.60	1.80	1.68
ICD-10 Q21.1..	Upper CI	1.84	2.26	2.64	2.38	2.47	2.64	2.72	2.83	2.35	2.61	2.47
Endocardial Cushion Defect	NUMBER	25	20	32	26	30	33	33	30	25	23	34
	RATE	**0.49**	**0.39**	**0.63**	**0.51**	**0.57**	**0.62**	**0.59**	**0.53**	**0.45**	**0.43**	**0.65**
	Lower CI	0.32	0.24	0.43	0.34	0.39	0.43	0.41	0.36	0.29	0.27	0.45
ICD-10 Q21.2..	Upper CI	0.73	0.60	0.89	0.75	0.82	0.87	0.84	0.76	0.67	0.65	0.91
Pulmonary Valve Atresia And Stenosis	NUMBER	24	29	36	29	33	31	41	38	33	35	50
	RATE	**0.48**	**0.56**	**0.71**	**0.57**	**0.63**	**0.58**	**0.74**	**0.67**	**0.59**	**0.66**	**0.96**
	Lower CI	0.30	0.38	0.50	0.38	0.43	0.40	0.53	0.48	0.41	0.46	0.71
ICD-10 Q22.0, Q22.1	Upper CI	0.71	0.81	0.99	0.82	0.89	0.83	1.00	0.92	0.84	0.91	1.26

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Aggregate Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		00-04 (5 years)	05-09 (5 years)	10-14 (5 years)	15-18 (4 years)	00-18 (19 years)
Anotia/microtia	NUMBER	40	57	67	64	228
	RATE	**0.21**	**0.24**	**0.26**	**0.29**	**0.25**
	Lower CI	0.15	0.18	0.20	0.23	0.22
ICD-10 Q16.0, Q17.2	Upper CI	0.28	0.31	0.32	0.38	0.28
Congenital Heart Defects (all)	NUMBER	2495	2582	3423	2913	11413
	RATE	**12.89**	**10.87**	**13.05**	**13.38**	**12.53**
	Lower CI	12.39	10.46	12.62	12.90	12.30
ICD-10 Q20.., Q26..	Upper CI	13.41	11.30	13.50	13.88	12.76
Common Truncus	NUMBER	14	14	22	21	71
Excludes AP window	**RATE**	**0.07**	**0.06**	**0.08**	**0.10**	**0.08**
	Lower CI	0.04	0.03	0.05	0.06	0.06
ICD-10 Q20.0	Upper CI	0.12	0.10	0.13	0.15	0.10
Transposition of Great Arteries	NUMBER	78	74	106	92	350
	RATE	**0.40**	**0.31**	**0.40**	**0.42**	**0.38**
	Lower CI	0.32	0.24	0.33	0.34	0.35
ICD-10 Q20.11, Q20.3, Q20.5	Upper CI	0.50	0.39	0.49	0.52	0.43
Tetralogy of Fallot	NUMBER	57	88	99	65	309
(Includes Tetralogy with ASD aka	**RATE**	**0.29**	**0.37**	**0.38**	**0.30**	**0.34**
Pentalogy of Fallot)	Lower CI	0.22	0.30	0.31	0.23	0.30
ICD-10 Q21.3.., Q21.82	Upper CI	0.38	0.46	0.46	0.38	0.38
Ventricular Septal Defect	NUMBER	637	710	842	706	2895
	RATE	**3.29**	**2.99**	**3.21**	**3.24**	**3.18**
	Lower CI	3.04	2.77	3.00	3.01	3.06
ICD-10 Q21.0	Upper CI	3.56	3.22	3.44	3.49	3.30
Atrial Septal Defect	NUMBER	433	387	561	466	1847
	RATE	**2.24**	**1.63**	**2.14**	**2.14**	**2.03**
	Lower CI	2.03	1.47	1.97	1.95	1.94
ICD-10 Q21.1..	Upper CI	2.46	1.80	2.32	2.34	2.12
Endocardial Cushion Defect	NUMBER	100	99	154	112	465
	RATE	**0.52**	**0.42**	**0.59**	**0.51**	**0.51**
	Lower CI	0.42	0.34	0.50	0.42	0.47
ICD-10 Q21.2..	Upper CI	0.63	0.51	0.69	0.62	0.56
Pulmonary Valve Atresia and Stenosis	NUMBER	124	133	170	156	583
	RATE	**0.64**	**0.56**	**0.65**	**0.72**	**0.64**
	Lower CI	0.53	0.47	0.55	0.61	0.59
ICD-10 Q22.0, Q22.1	Upper CI	0.76	0.66	0.75	0.84	0.69

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Single Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Tricuspid Valve Atresia and Stenosis	NUMBER	4	5	8	2	3	3	6	5	6	6	4
	RATE	**0.08**	**0.10**	**0.16**	**0.04**	**0.06**	**0.06**	**0.11**	**0.09**	**0.11**	**0.11**	**0.08**
	Lower CI	0.02	0.03	0.07	0.00	0.01	0.01	0.04	0.03	0.04	0.04	0.02
ICD-10 Q22.4	Upper CI	0.20	0.22	0.31	0.14	0.16	0.16	0.23	0.20	0.23	0.24	0.19
Ebstein's Anomaly	NUMBER	3	3	4	3	3	8	8	3	1	0	5
	RATE	**0.06**	**0.06**	**0.08**	**0.06**	**0.06**	**0.15**	**0.14**	**0.05**	**0.02**	**0.00**	**0.10**
	Lower CI	0.01	0.01	0.02	0.01	0.01	0.06	0.06	0.01	0.00		0.03
ICD-10 Q22.5	Upper CI	0.17	0.17	0.20	0.17	0.16	0.29	0.28	0.15	0.09		0.22
Aortic Valve Atresia/Stenosis	NUMBER	7	6	11	5	9	10	13	9	11	9	6
(excludes sub & supra aortic stenosis &	**RATE**	**0.14**	**0.12**	**0.22**	**0.10**	**0.17**	**0.19**	**0.23**	**0.16**	**0.20**	**0.17**	**0.11**
Aortic stenosis found with HLHS)	Lower CI	0.06	0.04	0.11	0.03	0.08	0.09	0.12	0.07	0.10	0.08	0.04
ICD-10 Q23.0	Upper CI	0.28	0.25	0.39	0.23	0.32	0.34	0.40	0.30	0.35	0.32	0.25
Hypoplastic Left Heart Syndrome (HLHS)	NUMBER	12	20	14	18	17	17	16	21	14	24	20
	RATE	**0.24**	**0.39**	**0.28**	**0.36**	**0.32**	**0.32**	**0.29**	**0.37**	**0.25**	**0.45**	**0.38**
	Lower CI	0.12	0.24	0.15	0.21	0.19	0.19	0.17	0.23	0.14	0.29	0.23
ICD-10 Q23.4	Upper CI	0.41	0.60	0.46	0.56	0.52	0.51	0.47	0.57	0.42	0.67	0.59
Coarctation of the Aorta	NUMBER	30	21	26	23	27	25	22	27	33	22	32
	RATE	**0.59**	**0.41**	**0.51**	**0.45**	**0.52**	**0.47**	**0.40**	**0.48**	**0.59**	**0.41**	**0.61**
	Lower CI	0.40	0.25	0.34	0.29	0.34	0.30	0.25	0.32	0.41	0.26	0.42
ICD-10 Q25.1..	Upper CI	0.85	0.62	0.75	0.68	0.75	0.69	0.60	0.70	0.84	0.62	0.86
Cleft Palate without Cleft Lip	NUMBER	39	34	39	36	41	46	39	39	43	37	37
(i.e. cleft palate alone)	**RATE**	**0.77**	**0.66**	**0.77**	**0.71**	**0.78**	**0.86**	**0.70**	**0.69**	**0.78**	**0.69**	**0.71**
	Lower CI	0.55	0.46	0.55	0.50	0.56	0.63	0.50	0.49	0.56	0.49	0.50
ICD-10 Q35..	Upper CI	1.06	0.92	1.05	0.98	1.06	1.15	0.96	0.94	1.04	0.96	0.98
Cleft Lip without Cleft Palate	NUMBER	32	26	17	21	25	25	27	20	21	22	30
(i.e. cleft lip alone)	**RATE**	**0.63**	**0.51**	**0.34**	**0.41**	**0.48**	**0.47**	**0.49**	**0.35**	**0.38**	**0.41**	**0.57**
	Lower CI	0.43	0.33	0.20	0.26	0.31	0.30	0.32	0.22	0.23	0.26	0.39
ICD-10 Q36..	Upper CI	0.89	0.74	0.54	0.63	0.71	0.69	0.71	0.55	0.58	0.62	0.82
Cleft Lip and Cleft Palate	NUMBER	35	45	54	39	31	35	45	57	36	47	45
	RATE	**0.69**	**0.88**	**1.07**	**0.77**	**0.59**	**0.66**	**0.81**	**1.01**	**0.65**	**0.88**	**0.86**
	Lower CI	0.48	0.64	0.80	0.55	0.40	0.46	0.59	0.76	0.45	0.65	0.63
ICD-10 Q37..	Upper CI	0.96	1.17	1.39	1.05	0.84	0.92	1.09	1.31	0.90	1.17	1.15
Cleft Lip with and without Cleft Palate	NUMBER	67	71	71	60	56	60	72	77	57	69	75
	RATE	**1.33**	**1.38**	**1.40**	**1.18**	**1.07**	**1.13**	**1.30**	**1.36**	**1.03**	**1.29**	**1.44**
	Lower CI	1.03	1.08	1.10	0.90	0.81	0.86	1.02	1.08	0.78	1.01	1.13
ICD-10 Q36.., Q37..	Upper CI	1.68	1.74	1.77	1.52	1.39	1.45	1.63	1.70	1.33	1.63	1.80

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Aggregate Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		00-04 (5 years)	05-09 (5 years)	10-14 (5 years)	15-18 (4 years)	00-18 (19 years)
Tricuspid Valve Atresia and Stenosis	NUMBER	13	21	22	21	77
	RATE	**0.07**	**0.09**	**0.08**	**0.10**	**0.08**
	Lower CI	0.04	0.05	0.05	0.06	0.07
ICD-10 Q22.4	Upper CI	0.11	0.14	0.13	0.15	0.11
Ebstein's Anomaly	NUMBER	14	13	26	9	62
	RATE	**0.07**	**0.05**	**0.10**	**0.04**	**0.07**
	Lower CI	0.04	0.03	0.06	0.02	0.05
ICD-10 Q22.5	Upper CI	0.12	0.09	0.15	0.08	0.09
Aortic Valve Atresia/Stenosis	NUMBER	50	32	48	35	165
(excludes sub & supra aortic stenosis &	**RATE**	**0.26**	**0.13**	**0.18**	**0.16**	**0.18**
Aortic stenosis found with HLHS)	Lower CI	0.19	0.09	0.14	0.11	0.15
ICD-10 Q23.0	Upper CI	0.34	0.19	0.24	0.22	0.21
Hypoplastic Left Heart Syndrome	NUMBER	52	82	82	79	295
	RATE	**0.27**	**0.35**	**0.31**	**0.36**	**0.32**
	Lower CI	0.20	0.27	0.25	0.29	0.29
ICD-10 Q23.4	Upper CI	0.35	0.43	0.39	0.45	0.36
Coarctation of the Aorta	NUMBER	64	99	123	114	400
	RATE	**0.33**	**0.42**	**0.47**	**0.52**	**0.44**
	Lower CI	0.25	0.34	0.39	0.43	0.40
ICD-10 Q25.1..	Upper CI	0.42	0.51	0.56	0.63	0.48
Cleft Palate without Cleft Lip	NUMBER	159	157	201	156	673
(i.e. cleft palate alone)	**RATE**	**0.82**	**0.66**	**0.77**	**0.72**	**0.74**
	Lower CI	0.70	0.56	0.66	0.61	0.68
ICD-10 Q35..	Upper CI	0.96	0.77	0.88	0.84	0.80
Cleft Lip without Cleft Palate	NUMBER	82	122	115	63	412
(i.e. cleft lip alone)	**RATE**	**0.42**	**0.51**	**0.44**	**0.43**	**0.45**
	Lower CI	0.34	0.43	0.36	0.35	0.41
ICD-10 Q35..	Upper CI	0.53	0.61	0.53	0.52	0.50
Cleft Lip and Cleft Palate	NUMBER	161	190	204	185	740
	RATE	**0.83**	**0.80**	**0.78**	**0.85**	**0.81**
	Lower CI	0.71	0.69	0.67	0.73	0.75
ICD-10 Q35..	Upper CI	0.97	0.92	0.89	0.98	0.87
Cleft Lip with and without Cleft Palate	NUMBER	243	312	319	278	1152
	RATE	**1.26**	**1.31**	**1.22**	**1.28**	**1.26**
	Lower CI	1.10	1.17	1.09	1.13	1.19
ICD-10 Q36.., Q37..	Upper CI	1.42	1.47	1.36	1.44	1.34

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Single Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Choanal Atresia/Stenosis	NUMBER	6	9	8	1	10	8	14	5	9	5	6
	RATE	**0.12**	**0.18**	**0.16**	**0.02**	**0.19**	**0.15**	**0.25**	**0.09**	**0.16**	**0.09**	**0.11**
	Lower CI	0.04	0.08	0.07	0.00	0.09	0.06	0.14	0.03	0.07	0.03	0.04
ICD-10 Q30.0..	Upper CI	0.26	0.33	0.31	0.10	0.35	0.29	0.42	0.20	0.31	0.22	0.25
Oesophageal Atresia/	NUMBER	14	12	13	20	11	16	15	7	13	20	26
Tracheo-oesphageal Fistula	**RATE**	**0.28**	**0.23**	**0.26**	**0.39**	**0.21**	**0.30**	**0.27**	**0.12**	**0.23**	**0.37**	**0.50**
	Lower CI	0.15	0.12	0.14	0.24	0.11	0.17	0.15	0.05	0.12	0.23	0.33
ICD-10 Q39.0 – Q39.4	Upper CI	0.46	0.41	0.44	0.61	0.37	0.49	0.44	0.25	0.40	0.58	0.73
Pyloric Stenosis	NUMBER	57	53	44	44	51	33	49	35	29	29	25
	RATE	**1.13**	**1.03**	**0.87**	**0.87**	**0.97**	**0.62**	**0.88**	**0.62**	**0.52**	**0.54**	**0.48**
	Lower CI	0.86	0.77	0.63	0.63	0.73	0.43	0.65	0.43	0.35	0.36	0.31
ICD-10 Q40.0	Upper CI	1.46	1.35	1.17	1.17	1.28	0.87	1.17	0.86	0.75	0.78	0.71
Small Intestinal	NUMBER	24	14	18	22	24	18	22	20	18	28	16
Atresia/Stenosis (all)	**RATE**	**0.48**	**0.27**	**0.36**	**0.43**	**0.46**	**0.34**	**0.40**	**0.35**	**0.32**	**0.52**	**0.31**
	Lower CI	0.30	0.15	0.21	0.27	0.29	0.20	0.25	0.22	0.19	0.35	0.18
ICD-10 Q41…	Upper CI	0.71	0.46	0.56	0.66	0.68	0.53	0.60	0.55	0.51	0.76	0.50
Duodenal Atresia/Stenosis	NUMBER	16	3	11	14	15	9	14	12	9	14	9
	RATE	**0.32**	**0.06**	**0.22**	**0.28**	**0.29**	**0.17**	**0.25**	**0.21**	**0.16**	**0.26**	**0.17**
	Lower CI	0.18	0.01	0.11	0.15	0.16	0.08	0.14	0.11	0.07	0.14	0.08
ICD-10 Q41.0…	Upper CI	0.51	0.17	0.39	0.46	0.47	0.32	0.42	0.37	0.31	0.44	0.33
Rectal and Large Intestinal	NUMBER	22	31	24	18	19	22	18	21	27	38	34
Atresia/Stenosis (all)	**RATE**	**0.44**	**0.60**	**0.47**	**0.36**	**0.36**	**0.41**	**0.32**	**0.37**	**0.49**	**0.71**	**0.65**
	Lower CI	0.27	0.41	0.30	0.21	0.22	0.26	0.19	0.23	0.32	0.50	0.45
ICD-10 Q42..	Upper CI	0.66	0.86	0.71	0.56	0.57	0.63	0.51	0.57	0.71	0.98	0.91
Rectal Atresia/Stenosis	NUMBER	1	1	0	1	2	2	1	1	2	2	4
	RATE	**0.02**	**0.02**	**0.00**	**0.02**	**0.04**	**0.04**	**0.02**	**0.02**	**0.04**	**0.04**	**0.08**
	Lower CI	0.00	0.00		0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.02
ICD-10 Q42.0…, Q42.1…	Upper CI	0.10	0.10		0.10	0.13	0.13	0.09	0.09	0.12	0.13	0.19
Anal Atresia/Stenosis	NUMBER	19	25	22	15	15	19	14	19	21	32	27
	RATE	**0.38**	**0.49**	**0.43**	**0.30**	**0.29**	**0.36**	**0.25**	**0.34**	**0.38**	**0.60**	**0.52**
	Lower CI	0.23	0.32	0.27	0.17	0.16	0.22	0.14	0.20	0.23	0.41	0.34
ICD-10 Q42.2…, Q42.3…	Upper CI	0.59	0.72	0.66	0.49	0.47	0.56	0.42	0.52	0.58	0.85	0.75
Other Large Intestinal	NUMBER	2	5	2	2	2	1	3	1	4	4	3
Atresia/Stenosis	**RATE**	**0.04**	**0.10**	**0.04**	**0.04**	**0.04**	**0.02**	**0.05**	**0.02**	**0.07**	**0.07**	**0.06**
	Lower CI	0.00	0.03	0.00	0.00	0.00	0.00	0.01	0.00	0.02	0.02	0.01
ICD-10 Q42.8…, Q42.9…	Upper CI	0.14	0.22	0.14	0.14	0.13	0.10	0.15	0.09	0.18	0.19	0.16

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Aggregate Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		00-04 (5 years)	05-09 (5 years)	10-14 (5 years)	15-18 (4 years)	00-18 (19 years)
Choanal Atresia/Stenosis	NUMBER	41	35	41	25	142
	RATE	**0.21**	**0.15**	**0.16**	**0.11**	**0.16**
	Lower CI	0.15	0.10	0.11	0.07	0.13
ICD-10 Q30.0..	Upper CI	0.29	0.21	0.21	0.17	0.18
Oesophageal Atresia/	NUMBER	40	52	75	66	233
Tracheo-oesphageal Fistula	**RATE**	**0.21**	**0.22**	**0.29**	**0.30**	**0.26**
	Lower CI	0.15	0.16	0.23	0.23	0.22
ICD-10 Q39.0 – Q39.4	Upper CI	0.28	0.29	0.36	0.39	0.29
Pyloric Stenosis	NUMBER	179	247	221	118	765
	RATE	**0.92**	**1.04**	**0.84**	**0.54**	**0.84**
	Lower CI	0.79	0.91	0.74	0.45	0.78
ICD-10 Q40.0	Upper CI	1.07	1.81	0.96	0.65	0.90
Small Intestinal Atresia/	NUMBER	66	72	104	82	324
Stenosis (all)	**RATE**	**0.34**	**0.30**	**0.40**	**0.38**	**0.36**
	Lower CI	0.26	0.24	0.32	0.30	0.32
ICD-10 Q41…	Upper CI	0.43	0.38	0.48	0.47	0.40
Duodenal Atresia/Stenosis	NUMBER	34	36	63	44	177
	RATE	**0.18**	**0.15**	**0.24**	**0.20**	**0.19**
	Lower CI	0.12	0.11	0.18	0.15	0.17
ICD-10 Q41.0…	Upper CI	0.25	0.21	0.31	0.27	0.23
Rectal and Large Intestinal	NUMBER	146	113	101	120	480
Atresia/Stenosis (all)	**RATE**	**0.75**	**0.48**	**0.39**	**0.55**	**0.53**
	Lower CI	0.64	0.39	0.31	0.46	0.48
ICD-10 Q42..	Upper CI	0.89	0.57	0.47	0.66	0.58
Rectal Atresia/Stenosis	NUMBER	14	7	6	9	36
	RATE	**0.07**	**0.03**	**0.02**	**0.04**	**0.04**
	Lower CI	0.04	0.01	0.01	0.02	0.03
ICD-10 Q42.0…., Q42.1….	Upper CI	0.12	0.06	0.05	0.08	0.05
Anal Atresia/Stenosis	NUMBER	120	91	85	99	395
	RATE	**0.62**	**0.38**	**0.32**	**0.45**	**0.43**
	Lower CI	0.51	0.31	0.26	0.37	0.39
ICD-10 Q42.2…., Q42.3….	Upper CI	0.74	0.47	0.40	0.55	0.48
Other Large Intestinal	NUMBER	12	15	10	12	49
Atresia/Stenosis	**RATE**	**0.06**	**0.06**	**0.04**	**0.06**	**0.05**
	Lower CI	0.03	0.04	0.02	0.03	0.04
ICD-10 Q42.8…., Q42.9….	Upper CI	0.11	0.10	0.07	0.10	0.07

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Single Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Hirschsprung Disease	NUMBER	6	8	10	7	9	13	6	6	7	7	8
	RATE	**0.12**	**0.16**	**0.20**	**0.14**	**0.17**	**0.24**	**0.11**	**0.11**	**0.13**	**0.13**	**0.15**
	Lower CI	0.04	0.07	0.09	0.06	0.08	0.13	0.04	0.04	0.05	0.05	0.07
ICD-10 Q43.1..	Upper CI	0.26	0.30	0.36	0.28	0.32	0.42	0.23	0.23	0.26	0.27	0.30
Biliary Atresia	NUMBER	2	5	1	5	3	4	4	3	5	2	4
	RATE	**0.04**	**0.10**	**0.02**	**0.10**	**0.06**	**0.08**	**0.07**	**0.05**	**0.09**	**0.04**	**0.08**
	Lower CI	0.00	0.03	0.00	0.03	0.01	0.02	0.02	0.01	0.03	0.00	0.02
ICD-10 Q44.2	Upper CI	0.14	0.22	0.10	0.23	0.16	0.19	0.18	0.15	0.21	0.13	0.19
Undescended Testes	NUMBER	123	165	133	136	160	146	146	189	152	170	169
(denominator MALE births only)	**RATE**	**4.73**	**6.25**	**5.09**	**5.22**	**5.93**	**5.34**	**5.14**	**6.56**	**5.37**	**6.17**	**6.32**
(>36 weeks gestation)	Lower CI	3.93	5.34	4.27	4.39	5.05	4.51	4.34	5.66	4.55	5.28	5.41
ICD-10 Q53…	Upper CI	5.64	7.28	6.03	6.18	6.93	6.28	6.04	7.56	6.30	7.17	7.35
Hypospadias	NUMBER	121	111	126	126	129	180	188	170	149	154	130
(denominator MALE births only)	**RATE**	**4.65**	**4.21**	**4.82**	**4.84**	**4.78**	**6.59**	**6.62**	**5.90**	**5.27**	**5.59**	**4.86**
	Lower CI	3.86	3.46	4.02	4.03	3.99	5.66	5.71	5.05	4.46	4.74	4.06
ICD-10 Q54 (excl. Q54.4)	Upper CI	5.56	5.07	5.74	5.76	5.68	7.62	7.63	6.85	6.18	6.54	5.77
Epispadias	NUMBER	4	3	5	5	1	5	3	3	2	0	0
(denominator MALE births only)	**RATE**	**0.15**	**0.11**	**0.19**	**0.19**	**0.04**	**0.18**	**0.11**	**0.10**	**0.07**	**0.00**	**0.00**
	Lower CI	0.04	0.02	0.06	0.06	0.00	0.06	0.02	0.02	0.01		
ICD-10 Q64.0	Upper CI	0.39	0.32	0.44	0.44	0.19	0.42	0.30	0.29	0.24		
Renal Agenesis/Hypoplasia	NUMBER	39	28	27	35	36	36	30	27	43	47	40
	RATE	**0.77**	**0.54**	**0.53**	**0.69**	**0.69**	**0.68**	**0.54**	**0.48**	**0.78**	**0.88**	**0.77**
	Lower CI	0.55	0.36	0.35	0.48	0.48	0.47	0.37	0.32	0.56	0.65	0.55
ICD-10 Q60..	Upper CI	1.06	0.79	0.78	0.96	0.95	0.94	0.77	0.70	1.04	1.17	1.04
Cystic Kidney	NUMBER	30	37	44	35	43	37	36	51	41	39	47
(exclude single renal cyst	**RATE**	**0.59**	**0.72**	**0.87**	**0.69**	**0.82**	**0.70**	**0.65**	**0.90**	**0.74**	**0.73**	**0.90**
Q61.0)	Lower CI	0.40	0.51	0.63	0.48	0.60	0.49	0.45	0.67	0.53	0.52	0.66
Q61..	Upper CI	0.85	0.99	1.17	0.96	1.11	0.96	0.90	1.19	1.00	1.00	1.20
Bladder Exstrophy	NUMBER	1	1	3	0	1	1	2	2	1	1	1
	RATE	**0.02**	**0.02**	**0.06**	**0.00**	**0.02**	**0.02**	**0.04**	**0.04**	**0.02**	**0.02**	**0.02**
	Lower CI	0.00	0.00	0.01		0.00	0.00	0.00	0.00	0.00	0.00	0.00
ICD-10 Q64.1 (excl Q64.10)	Upper CI	0.10	0.10	0.19		0.10	0.10	0.12	0.12	0.09	0.09	0.10
Obstructive Genitourinary	NUMBER	138	133	155	143	166	139	173	175	181	158	147
Defects (All)	**RATE**	**2.73**	**2.59**	**3.06**	**2.82**	**3.17**	**2.61**	**3.12**	**3.10**	**3.26**	**2.96**	**2.81**
	Lower CI	2.30	2.17	2.60	2.38	2.71	2.20	2.67	2.66	2.81	2.52	2.38
ICD-10 Q62.0 – Q62.3, Q64.2, Q64.3	Upper CI	3.23	3.07	3.59	3.32	3.69	3.09	3.62	3.59	3.77	3.46	3.31

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Aggregate Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		00-04 (5 years)	05-09 (5 years)	10-14 (5 years)	15-18 (4 years)	00-18 (19 years)
Hirschsprung Disease	NUMBER	23	37	45	28	133
	RATE	**0.12**	**0.16**	**0.17**	**0.13**	**0.15**
	Lower CI	0.08	0.11	0.13	0.09	0.12
ICD-10 Q43.1..	Upper CI	0.18	0.21	0.23	0.19	0.17
Biliary Atresia	NUMBER	12	17	17	14	60
	RATE	**0.06**	**0.07**	**0.06**	**0.06**	**0.07**
	Lower CI	0.03	0.04	0.04	0.04	0.05
ICD-10 Q44.2	Upper CI	0.11	0.11	0.10	0.11	0.08
Undescended Testes	NUMBER	499	628	721	680	2528
(denominator MALE births only)	**RATE**	**5.04**	**5.17**	**5.35**	**6.10**	**5.42**
(>36 weeks gestation)	Lower CI	4.61	4.77	4.96	5.65	5.21
ICD-10 Q53….	Upper CI	5.50	5.59	5.75	6.58	5.63
Hypospadias	NUMBER	399	509	749	603	2260
(denominator MALE births only)	**RATE**	**4.03**	**4.19**	**5.55**	**5.41**	**4.84**
	Lower CI	3.64	3.83	5.16	4.99	4.64
ICD-10 Q54 (excl. Q54.4)	Upper CI	4.45	4.57	5.97	5.86	5.04
Epispadias	NUMBER	14	19	19	5	57
(denominator MALE births only)	**RATE**	**0.14**	**0.16**	**0.14**	**0.04**	**0.12**
	Lower CI	0.08	0.09	0.08	0.01	0.09
ICD-10 Q64.0	Upper CI	0.24	0.24	0.22	0.10	0.16
Renal Agenesis/Hypoplasia	NUMBER	116	135	164	157	572
	RATE	**0.60**	**0.57**	**0.63**	**0.72**	**0.63**
	Lower CI	0.50	0.48	0.53	0.61	0.58
ICD-10 Q60..	Upper CI	0.72	0.67	0.73	0.84	0.68
Cystic Kidney	NUMBER	156	168	195	178	697
(excludes single renal cyst Q61.0)	**RATE**	**0.81**	**0.71**	**0.74**	**0.82**	**0.77**
	Lower CI	0.68	0.60	0.64	0.70	0.71
ICD-10 Q61..	Upper CI	0.94	0.82	0.86	0.95	0.82
Bladder Exstrophy	NUMBER	9	6	7	5	27
	RATE	**0.05**	**0.03**	**0.03**	**0.02**	**0.03**
	Lower CI	0.02	0.01	0.01	0.01	0.02
ICD-10 Q64.1 (excl Q64.10)	Upper CI	0.09	0.05	0.05	0.05	0.04
Obstructive Genitourinary	NUMBER	469	590	776	661	2496
Defects (All)	**RATE**	**2.42**	**2.48**	**2.96**	**3.04**	**2.74**
	Lower CI	2.21	2.29	2.75	2.81	2.63
ICD-10 Q62.0 – Q62.3, Q64.2, Q64.3	Upper CI	2.65	2.69	3.17	3.28	2.85

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Single Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Hydronephrosis	NUMBER	90	95	103	96	111	98	99	104	106	101	86
	RATE	**1.78**	**1.85**	**2.04**	**1.89**	**2.12**	**1.84**	**1.78**	**1.84**	**1.91**	**1.89**	**1.65**
	Lower CI	1.43	1.50	1.66	1.54	1.75	1.50	1.45	1.50	1.56	1.54	1.32
ICD-10 Q62.0..	Upper CI	2.19	2.26	2.47	2.31	2.55	2.25	2.17	2.23	2.31	2.30	2.03
Pelviureteric Junction Obstruction	NUMBER	12	9	7	11	10	9	12	18	19	17	16
	RATE	**0.24**	**0.18**	**0.14**	**0.22**	**0.19**	**0.17**	**0.22**	**0.32**	**0.34**	**0.32**	**0.31**
	Lower CI	0.12	0.08	0.06	0.11	0.09	0.08	0.11	0.19	0.21	0.19	0.18
ICD-10 Q62.10 & Q62.11	Upper CI	0.41	0.33	0.28	0.39	0.35	0.32	0.38	0.50	0.53	0.51	0.50
Vesicoureteric Junction Obstruction	NUMBER	4	4	0	4	2	2	0	2	3	1	1
	RATE	**0.08**	**0.08**	**0.00**	**0.08**	**0.04**	**0.04**	**0.00**	**0.04**	**0.05**	**0.02**	**0.02**
	Lower CI	0.02	0.02		0.02	0.00	0.00		0.00	0.01	0.00	0.00
ICD-10 Q62.12 & Q62.13	Upper CI	0.20	0.19		0.20	0.13	0.13		0.12	0.15	0.09	0.10
Posterior Urethral Valves	NUMBER	7	2	5	3	3	4	9	8	2	1	5
(denominator MALE births only)	**RATE**	**0.27**	**0.08**	**0.19**	**0.12**	**0.11**	**0.15**	**0.32**	**0.28**	**0.07**	**0.04**	**0.19**
	Lower CI	0.11	0.01	0.06	0.02	0.02	0.04	0.15	0.12	0.01	0.00	0.06
ICD-10 Q64.20	Upper CI	0.55	0.26	0.44	0.33	0.31	0.37	0.60	0.54	0.24	0.18	0.43
Congenital Deformities Hip (All)	NUMBER	123	108	119	103	125	96	76	79	50	54	50
	RATE	**2.43**	**2.10**	**2.35**	**2.03**	**2.39**	**1.81**	**1.37**	**1.40**	**0.90**	**1.01**	**0.96**
	Lower CI	2.02	1.72	1.95	1.66	1.99	1.46	1.08	1.11	0.67	0.76	0.71
ICD-10 Q65	Upper CI	2.90	2.54	2.81	2.47	2.85	2.20	1.71	1.74	1.19	1.32	1.26
Congenital Hip Dislocation Subluxation and Dysplasia	NUMBER	85	74	84	72	85	66	60	70	45	49	41
	RATE	**1.68**	**1.44**	**1.66**	**1.42**	**1.62**	**1.24**	**1.08**	**1.24**	**0.81**	**0.92**	**0.78**
ICD-10 Q65.0-Q65.5 & Q65.80-Q65.81	Lower CI	1.34	1.13	1.33	1.11	1.30	0.96	0.83	0.97	0.59	0.68	0.56
	Upper CI	2.08	1.81	2.06	1.79	2.01	1.58	1.39	1.56	1.09	1.21	1.07
Reduction Deformity, Upper Limbs	NUMBER	34	39	29	44	39	32	41	38	50	52	44
	RATE	**0.67**	**0.76**	**0.57**	**0.87**	**0.75**	**0.60**	**0.74**	**0.67**	**0.90**	**0.97**	**0.84**
	Lower CI	0.47	0.54	0.38	0.63	0.53	0.41	0.53	0.48	0.67	0.73	0.61
ICD-10 Q71..	Upper CI	0.94	1.04	0.82	1.17	1.02	0.85	1.00	0.92	1.19	1.28	1.13
Reduction Deformity, Lower Limbs	NUMBER	18	22	14	22	19	19	17	28	15	26	33
	RATE	**0.36**	**0.43**	**0.28**	**0.43**	**0.36**	**0.36**	**0.31**	**0.50**	**0.27**	**0.49**	**0.63**
	Lower CI	0.21	0.27	0.15	0.27	0.22	0.22	0.18	0.33	0.15	0.32	0.44
ICD-10 Q72..	Upper CI	0.56	0.65	0.46	0.66	0.57	0.56	0.49	0.72	0.45	0.71	0.89
Diaphragmatic Hernia	NUMBER	18	20	17	18	23	12	15	18	17	20	13
	RATE	**0.36**	**0.39**	**0.34**	**0.36**	**0.44**	**0.23**	**0.27**	**0.32**	**0.31**	**0.37**	**0.25**
	Lower CI	0.21	0.24	0.20	0.21	0.28	0.12	0.15	0.19	0.18	0.23	0.13
ICD-10 Q79.0, Q79.11, Q79.12	Upper CI	0.56	0.60	0.54	0.56	0.66	0.39	0.44	0.50	0.49	0.58	0.42

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Aggregate Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		00-04 (5 years)	05-09 (5 years)	10-14 (5 years)	15-18 (4 years)	00-18 (19 years)
Hydronephrosis	NUMBER	292	389	507	397	1585
	RATE	**1.51**	**1.64**	**1.93**	**1.82**	**1.74**
	Lower CI	1.34	1.48	1.77	1.65	1.66
ICD-10 Q62.0..	Upper CI	1.69	1.81	2.11	2.01	1.83
Pelviureteric Junction Obstruction	NUMBER	41	45	49	70	205
	RATE	**0.21**	**0.19**	**0.19**	**0.32**	**0.23**
	Lower CI	0.15	0.14	0.14	0.25	0.20
ICD-10 Q62.10 & Q62.11	Upper CI	0.29	0.25	0.25	0.41	0.26
Vesicoureteric Junction Obstruction	NUMBER	4	14	8	7	33
	RATE	**0.02**	**0.06**	**0.03**	**0.03**	**0.04**
	Lower CI	0.01	0.03	0.01	0.01	0.02
ICD-10 Q62.12 & Q62.13	Upper CI	0.05	0.10	0.06	0.07	0.05
Posterior Urethral Valves	NUMBER	15	22	24	16	77
	RATE	**0.15**	**0.18**	**0.18**	**0.14**	**0.16**
	Lower CI	0.08	0.11	0.11	0.08	0.13
ICD-10 Q64.20	Upper CI	0.25	0.27	0.26	0.23	0.21
Congenital Deformities Hip (All)	NUMBER	418	470	519	233	1640
	RATE	**2.16**	**1.98**	**1.98**	**1.07**	**1.80**
	Lower CI	1.96	1.80	1.81	0.94	1.71
ICD-10 Q65	Upper CI	2.38	2.17	2.16	1.22	1.89
Congenital Hip Dislocation, Subluxation and Dysplasia	NUMBER	285	331	367	205	1188
	RATE	**1.47**	**1.39**	**1.40**	**0.94**	**1.30**
ICD-10 Q65.0-Q65.5 & Q65.80-Q65.81	Lower CI	1.31	1.25	1.26	0.82	1.23
	Upper CI	1.65	1.55	1.55	1.08	1.38
Reduction Deformity, Upper Limbs	NUMBER	143	151	185	184	663
	RATE	**0.74**	**0.64**	**0.71**	**0.85**	**0.73**
	Lower CI	062	0.54	0.61	0.73	0.67
ICD-10 Q71..	Upper CI	0.87	0.75	0.81	0.98	0.79
Reduction Deformity, Lower Limbs	NUMBER	81	84	91	102	358
	RATE	**0.42**	**0.35**	**0.35**	**0.47**	**0.39**
	Lower CI	0.33	0.28	0.28	0.38	0.35
ICD-10 Q72..	Upper CI	0.52	0.44	0.43	0.57	0.44
Diaphragmatic Hernia	NUMBER	80	85	85	68	318
	RATE	**0.41**	**0.36**	**0.32**	**0.31**	**0.35**
	Lower CI	0.33	0.29	0.26	0.24	0.31
ICD-10 Q79.0.., Q79.11, Q79.12	Upper CI	0.51	0.44	0.40	0.40	0.39

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Single Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Abdominal Wall Defects (all)	NUMBER	48	52	52	57	48	47	48	48	45	52	45
	RATE	**0.95**	**1.01**	**1.03**	**1.13**	**0.92**	**0.88**	**0.86**	**0.85**	**0.81**	**0.97**	**0.86**
	Lower CI	0.70	0.76	0.77	0.85	0.68	0.65	0.64	0.63	0.59	0.73	0.63
ICD-10 Q79.2 to Q79.5	Upper CI	1.26	1.33	1.35	1.46	1.22	1.18	1.15	1.13	1.09	1.28	1.15
Omphalocele	NUMBER	19	23	25	24	21	23	19	22	21	27	20
	RATE	**0.38**	**0.45**	**0.49**	**0.47**	**0.40**	**0.43**	**0.34**	**0.39**	**0.38**	**0.51**	**0.38**
	Lower CI	0.23	0.28	0.32	0.30	0.25	0.27	0.21	0.24	0.23	0.33	0.23
ICD-10 Q79.2	Upper CI	0.59	0.67	0.73	0.70	0.61	0.65	0.53	0.59	0.58	0.74	0.59
Gastroschisis	NUMBER	23	26	20	29	18	18	25	19	11	19	20
	RATE	**0.46**	**0.51**	**0.40**	**0.57**	**0.34**	**0.34**	**0.45**	**0.34**	**0.20**	**0.36**	**0.38**
	Lower CI	0.29	0.33	0.24	0.38	0.20	0.20	0.29	0.20	0.10	0.21	0.23
ICD-10 Q79.3	Upper CI	0.68	0.74	0.61	0.82	0.54	0.53	0.66	0.52	0.35	0.56	0.59
All Chromosome Anomalies	NUMBER	225	254	244	230	241	284	287	274	279	310	319
	RATE	**4.45**	**4.94**	**4.82**	**4.54**	**4.61**	**5.34**	**5.17**	**4.85**	**5.03**	**5.81**	**6.11**
	Lower CI	3.89	4.35	4.24	3.97	4.04	4.74	4.59	4.29	4.46	5.18	5.45
ICD-10 Q90-Q99	Upper CI	5.08	5.59	5.47	5.17	5.23	6.00	5.80	5.46	5.65	6.49	6.81
Trisomy 13	NUMBER	15	20	11	12	12	21	12	19	13	17	13
	RATE	**0.30**	**0.39**	**0.22**	**0.24**	**0.23**	**0.39**	**0.22**	**0.34**	**0.23**	**0.32**	**0.25**
	Lower CI	0.17	0.24	0.11	0.12	0.12	0.24	0.11	0.20	0.12	0.19	0.13
ICD-10 Q91.4-Q91.7	Upper CI	0.49	0.60	0.39	0.41	0.40	0.60	0.38	0.52	0.40	0.51	0.42
Trisomy 18	NUMBER	28	32	34	25	28	43	36	44	33	35	52
	RATE	**0.55**	**0.62**	**0.67**	**0.49**	**0.54**	**0.81**	**0.65**	**0.78**	**0.59**	**0.66**	**1.00**
	Lower CI	0.37	0.43	0.47	0.32	0.36	0.59	0.45	0.57	0.41	0.46	0.74
ICD-10 Q91.0-Q91.3	Upper CI	0.80	0.88	0.94	0.73	0.77	1.09	0.90	1.05	0.84	0.91	1.30
Down Syndrome (Trisomy 21)	NUMBER	97	107	125	120	126	134	140	127	120	134	132
	RATE	**1.92**	**2.08**	**2.47**	**2.37**	**2.41**	**2.52**	**2.52**	**2.25**	**2.16**	**2.51**	**2.53**
	Lower CI	1.56	1.71	2.06	1.96	2.01	2.11	2.12	1.87	1.79	2.10	2.11
ICD-10 Q90..	Upper CI	2.34	2.51	2.94	2.83	2.87	2.98	2.98	2.67	2.59	2.97	3.00

Appendix A.3 **Alberta Congenital Anomalies Surveillance System**
RCPCH version ICD-10 Q Chapter (Q00-Q99)
Aggregate Year Anomaly Rates per 1,000 Total Births (live births + stillbirths)
Numerator (live births, stillbirths and fetal losses)

Diagnostic Category and ICD-10 RCPCH Code		00-04 (5 years)	05-09 (5 years)	10-14 (5 years)	15-18 (4 years)	00-18 (19 years)
Abdominal Wall Defects (all)	NUMBER	143	220	252	190	805
	RATE	**0.74**	**0.93**	**0.96**	**0.87**	**0.88**
	Lower CI	0.62	0.81	0.85	0.75	0.82
ICD-10 Q79.2-Q79.5	Upper CI	0.87	1.06	1.09	1.01	0.95
Omphalocele	NUMBER	52	73	112	90	327
	RATE	**0.27**	**0.31**	**0.43**	**0.41**	**0.36**
	Lower CI	0.20	0.24	0.35	0.33	0.32
ICD-10 Q79.2	Upper CI	0.35	0.39	0.51	0.51	0.40
Gastroschisis	NUMBER	63	125	110	69	367
	RATE	**0.33**	**0.53**	**0.42**	**0.32**	**0.40**
	Lower CI	0.25	0.44	0.34	0.25	0.36
ICD-10 Q79.3	Upper CI	0.42	0.63	0.51	0.40	0.45
All Chromosome Anomalies	NUMBER	779	1136	1286	1182	4383
	RATE	**4.03**	**4.78**	**4.90**	**5.43**	**4.81**
	Lower CI	3.75	4.51	4.64	5.13	4.67
ICD-10 Q90-Q99	Upper CI	4.32	5.07	5.18	5.75	4.96
Trisomy 13	NUMBER	36	76	68	62	242
	RATE	**0.19**	**0.32**	**0.26**	**0.28**	**0.27**
	Lower CI	0.13	0.25	0.20	0.22	0.23
ICD-10 Q91.4-Q91.7	Upper CI	0.26	0.40	0.33	0.36	0.30
Trisomy 18	NUMBER	84	133	166	164	547
	RATE	**0.43**	**0.56**	**0.63**	**0.75**	**0.60**
	Lower CI	0.35	0.47	0.54	0.64	0.55
ICD-10 Q91.0-Q91.3	Upper CI	0.54	0.66	0.74	0.88	0.65
Down Syndrome (Trisomy 21)	NUMBER	379	520	645	513	2057
	RATE	**1.96**	**2.19**	**2.46**	**2.36**	**2.26**
	Lower CI	1.77	2.01	2.27	2.16	2.16
ICD-10 Q90..	Upper CI	2.17	2.39	2.66	2.57	2.36

Appendix A.4 Numbers of Cases, Anomalies and Anomalies per Case 1997–2018
Live Births (L), Stillbirths (S) and Fetal losses <20 weeks (T)

Year	Alberta Total Births (L & S)	# Cases (L, S & T)	Case Rate/1000 Total Births	# Anomalies (L, S & T)	Anomaly Rate/1000 Total Births	Average # Anomalies/ Case
1997	36797	1126	30.60	1980	53.81	1.76
1998	37715	1193	31.63	2183	57.88	1.83
1999	38044	1222	32.12	2419	63.58	1.98
2000	36860	1288	34.94	2362	64.08	1.83
2001	37460	1384	36.95	2600	69.41	1.88
2002	38532	1373	35.63	2548	66.13	1.86
2003	40118	1516	37.79	2609	65.03	1.72
2004	40557	1550	38.22	2893	71.33	1.87
2005	41856	1609	38.44	2889	69.02	1.80
2006	44947	1620	36.04	2718	60.47	1.68
2007	48708	1872	38.43	3149	64.65	1.68
2008	50516	2005	39.69	3460	68.49	1.73
2009	51420	2091	40.67	3644	70.87	1.74
2010	50590	2188	43.25	3701	73.16	1.69
2011	50665	2087	41.19	3648	72.01	1.75
2012	52318	2133	40.77	3730	71.29	1.75
2013	53180	2158	40.58	3796	71.38	1.76
2014	55506	2196	39.56	3875	69.81	1.76
2015	56524	2171	38.59	4040	71.82	1.86
2016	55481	2209	39.82	4033	72.69	1.83
2017	53399	2283	42.75	4241	79.42	1.86
2018	52245	2083	39.87	4173	79.87	2.00
1997–2018	**1023168**	**39357**	**38.46**	**70691**	**69.07**	**1.80**

Alberta Total Births from: Alberta Vital Statistics Annual Reviews for 1980-2018

Appendix A.5 Chi Trend Table for Reported Anomalies 1997–2018

Anomaly	X^2	p Value	Direction*
Anencephaly	8.76	0.0031	↓
Spina bifida without anencephaly	0.14	0.7083	↔
Encephalocele	0.39	0.5323	↔
Neural tube defects (all)	5.13	0.0235	↓
Hydrocephalus without spina bifida	7.11	0.0077	↓
Arhinencephaly/ Holoprosencephaly	6.16	0.0131	↑
Microcephaly	0.06	0.8065	↔
Anophthalmia/Microphthalmia	0.53	0.4666	?↓
Congenital cataract	1.20	0.2733	?↑
Anotia/Microtia	7.70	0.0055	↑
Congenital heart defects (all)	15.69	<0.0001	↑
Common truncus	2.40	0.1213	?↑
Transposition of great arteries	1.42	0.2334	?↑
Tetralogy of Fallot	1.20	0.2733	?↑
Ventricular septal defect	5.99	0.0144	↑
Atrial septal defect	0.16	0.6892	↔
Endocardial cushion defect	1.81	0.1785	?↑
Pulmonary valve atresia/stenosis	0.85	0.3566	?↑
Tricuspid valve atresia/stenosis	0.44	0.5071	?↑
Ebstein's anomaly	0.00	1.00	↔
Aortic valve atresia/stenosis	5.73	0.0167	↓
Hypoplastic left heart syndrome	2.40	0.1213	?↑
Coarctation of the aorta	11.65	0.0006	↑
Cleft palate without cleft lip (CPO)	3.88	0.0489	↓
Cleft lip without cleft palate (CLO)	0.55	0.4583	?↑
Cleft lip and cleft palate (CL+CP)	0.58	0.4463	?↑
Cleft lip with and without cleft palate (CL+/-CP)	1.12	0.2899	?↑
Choanal atresia/stenosis	0.98	0.3222	?↓
Oesophageal atresia/trachea-oesophageal fistula	2.44	0.1183	?↑
Pyloric stenosis	8.11	0.0044	↓
Small intestinal atresia/stenosis (all)	0.39	0.5323	↔

Anomaly	X^2	p Value	Direction*
Duodenal atresia/stenosis	1.25	0.2636	?↑
Rectal and large intestinal atresia/stenosis (all)	10.45	0.0012	↓
Rectal atresia/stenosis	4.32	0.0377	↓
Anal atresia/stenosis	5.31	0.0212	↓
Ano-rectal atresia/stenosis	7.96	0.0048	↓
Other large intestinal atresia/stenosis	2.95	0.0859	?↓
Hirschsprung's disease	0.52	0.4708	?↑
Biliary atresia	0.05	0.8231	↔
Undescended testes (male denominator)	20.98	<0.0001	↑
Hypospadias (male denominator)	63.50	<0.0001	↑
Epispadias (male denominator)	1.29	0.2560	?↓
Renal agenesis/hypoplasia	9.29	0.0023	↑
Cystic kidney	2.67	0.1023	?↑
Bladder exstrophy	1.39	0.2384	?↓
Obstructive genitourinary defects (all)	45.59	<0.0001	↑
Hydronephrosis	30.32	<0.0001	↑
UPJ obstruction	9.96	0.0016	↑
VUJ obstruction (based on very few cases per yr. - range 0-4)	2.00	0.1573	?↑
Posterior urethral valves (male denominator)	0.01	0.9203	↔
Congenital deformities of hip (all)	41.30	<0.0001	↓
Congenital hip dislocation, subluxation, dysplasia	16.49	<0.0001	↓
Reduction deformity, upper	1.30	0.2542	?↑
Reduction deformity, lower	1.40	0.2367	?↑
Diaphragmatic hernia	1.08	0.2987	?↓
Abdominal wall defects (all)	5.85	0.0156	↑
Omphalocele	10.43	0.0012	↑
Gastroschisis	0.37	0.5430	↔
All chromosome anomalies	90.59	<0.0001	↑
Trisomy 13	6.27	0.0123	↑
Trisomy 18	23.92	<0.0001	↑
Trisomy 21	22.94	<0.0001	↑

*Direction:↑(up); ↓(down); ↔ (no change); ?↑ or ?↓ (not statistically significant but a possible trend to watch)

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