

# CONGENITAL ANOMALIES

## Introduction

Congenital anomalies, also known as birth defects, congenital disorders or congenital malformations, are structural or functional anomalies that exist at or before birth (although they may not be detected until later in life).<sup>1</sup> They are major causes of fetal, infant and child deaths, and chronic illness and disability.<sup>1</sup> Congenital anomalies may occur in isolation or they may occur together in a pattern corresponding to a named syndrome, such as Down syndrome or achondroplasia (dwarfism).<sup>2</sup>

Congenital anomalies vary in severity from the inevitably lethal, such as absent kidneys, to minor abnormalities of cosmetic significance only. Major anomalies, those anomalies that have medical and/or social implications and often require surgical repair, occur in approximately three to four percent of all live births.<sup>3</sup> Common major anomalies include heart defects, cleft lip and palate, neural tube defects, and chromosomal abnormalities (the most common of which is Down syndrome).<sup>3</sup>

In at least half of all occurrences of congenital anomaly, no cause can be identified.<sup>1,4</sup> Genetic factors are important in many congenital anomalies, particularly syndromic anomalies.<sup>1</sup> Genetic factors cause around one third of all congenital anomalies and about 85% of those with known causes.<sup>5</sup> Environmental factors of various kinds can cause congenital anomalies, for example: insufficient maternal intake of folic acid increases the risk of neural tube defects; maternal infection with Zika virus seems to cause microcephaly; and poorly controlled pregestational maternal diabetes increases the risk of major anomalies in the cardiovascular and central nervous systems and in craniofacial structures.<sup>1,6</sup>

The following section uses data from the National Minimum Dataset to describe congenital anomalies in babies from 2000–2015 and concludes with a brief overview of some of the evidence relating to early diagnosis of these conditions.

### Data sources and methods

#### Indicators

- Prevalence of congenital anomalies
- Infant mortality associated with congenital anomalies

#### Definition

Anomalies diagnosed in stillbirths and liveborn babies up to one year of age are included, and cases identified based on codes adapted from those used by BINOCAR and by registers in Australia<sup>7</sup>

Stillbirths are of at least 400g birthweight or 20 weeks gestation (as defined by the Ministry of Health)

**Numerators:** Liveborn infants hospitalised: National Minimum Dataset  
Stillbirths: National Mortality Collection  
Infant deaths associated with congenital anomalies: National Mortality Collection

**Denominators:** Total births  
Livebirths: Birth Registration Dataset  
Stillbirths: National Mortality Collection

*Prevalence per 1,000 livebirths*

#### Additional information

Anomalies are year of birth; births are registration year.  
Codes used for identifying cases are documented in **Appendix 5**  
Maternal age was only available for 72% of cases.  
Prevalence rates presented for sex-specific anomalies are sex-specific rates.  
The confidence intervals are calculated using the Poisson distribution.

## National trends and distribution

The infant mortality rate in New Zealand between 2009 and 2013 was 5.14 per 1,000 live births. Over 27% of the infants who died had at least one congenital anomaly (**Table 1**). The infant mortality rate associated with congenital anomalies gradually decreased from 1990–91 to 2006–07 and from then on increased slightly from

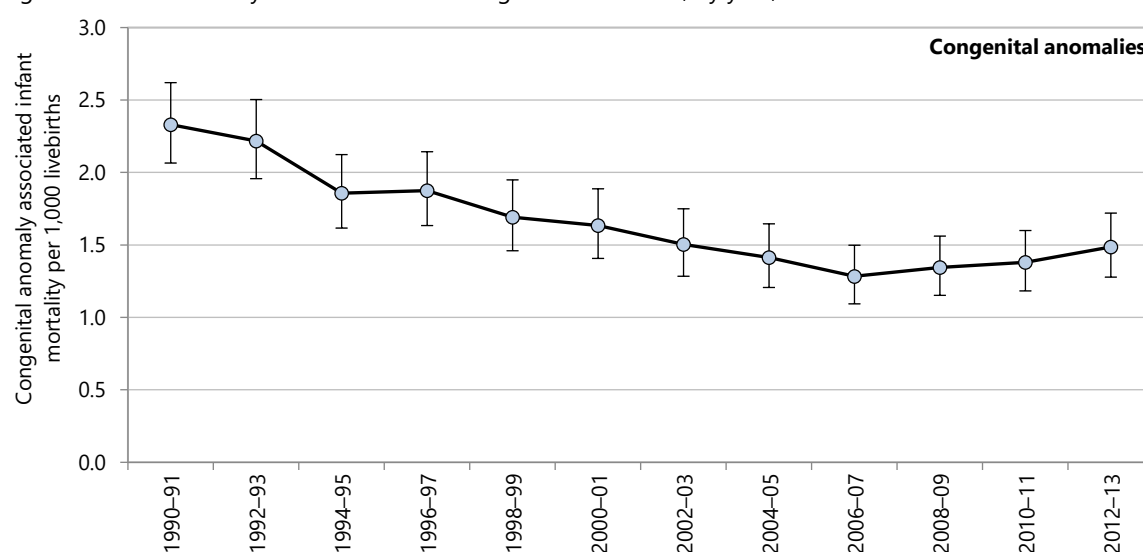
year to year (**Figure 1**). Congenital heart defects, nervous system defects, and chromosomal anomalies were the predominant congenital anomaly subgroups contributing to infant mortality (**Table 1**).

Table 1. Infant mortality with one or more congenital anomalies, by anomaly subgroup, New Zealand 2009–2013

2009–2013	<i>n</i>	Rate per 1,000 livebirths	95% CI
Congenital anomaly infant mortality			
New Zealand			
Infant mortality	1,603	5.14	4.89–5.40
Infant mortality with a congenital anomaly*	439	1.41	1.28–1.55
Congenital heart defects	181	0.58	0.50–0.67
Nervous system	82	0.26	0.21–0.33
Chromosomal anomalies	79	0.25	0.20–0.32
Digestive system	64	0.21	0.16–0.26
Urinary	54	0.17	0.13–0.23
Respiratory	48	0.15	0.11–0.20
Neural tube defects	33	0.11	0.07–0.15
Limb	20	0.06	0.04–0.10
Abdominal wall defects	11	0.04	0.02–0.06
Eye	<10	s	s
Orofacial clefts	<10	s	s
Genital	<10	s	s
Ear, Face and Neck	0	..	..

Numerator: National Mortality Collection, Denominator: Birth registration data. Congenital anomaly infant mortality per 1,000 livebirths. \*Infant mortality with one or more anomalies. One infant excluded for presence of single anomaly of minor severity; Some Infant mortality will have multiple anomalies and appear in more than one subgroup

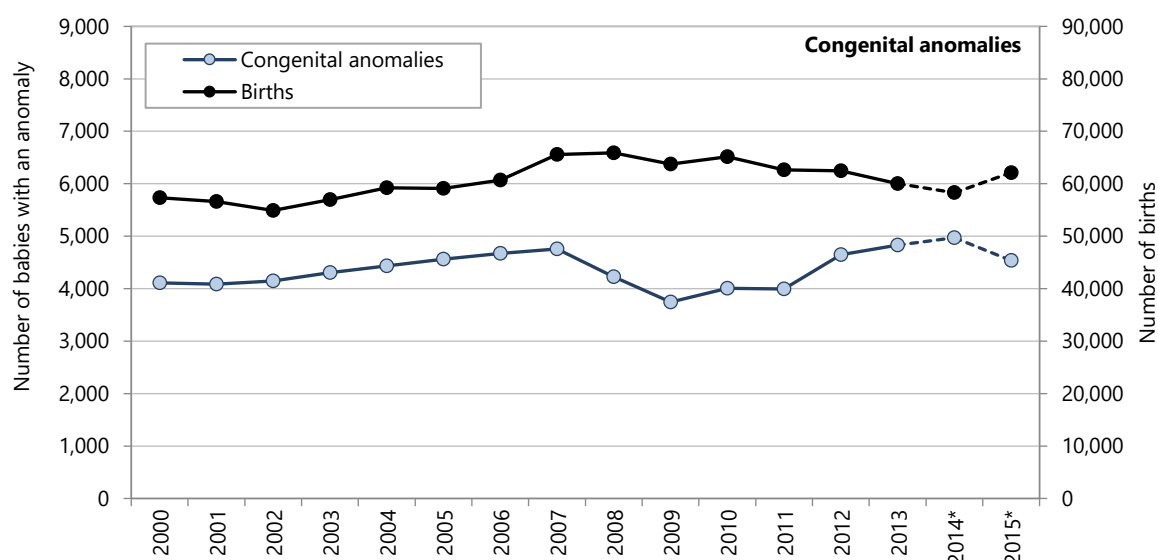
Figure 1. Infant mortality with one or more congenital anomalies, by year, New Zealand 1990–2013



Numerator: National Mortality Collection, Denominator: Birth registration dataset. Babies with one or more diagnosed anomalies

The number of babies with at least one congenital anomaly (including minor defects) gradually increased from 2000 to 2007. There was a noticeable dip between 2008 and 2011 which corresponded with a decrease in diagnoses of minor skin anomalies, such as tags and birth marks. From 2012 onwards numbers have been similar to those in 2007 (**Figure 2**). The proportion of babies born with one or more congenital anomalies has fluctuated slightly from year to year but, on average, has been around seven per cent (**Table 2**).

Figure 2. Number of babies born and those with one or more congenital anomalies, by year, New Zealand 2000-2015



Source: National Minimum Dataset, National Mortality Collection, Birth registration dataset. (Total) births corresponds to live births and fetal deaths, \* 2014 and 2015 are live births only

Table 2. Proportion of babies with one or more congenital anomalies, by year, New Zealand 2000–2015

Year	Babies with an anomaly (n)	Total births (n)	% of total births
New Zealand			
Congenital anomalies			
2000–2008	39,291	536,368	7.3
2009	3,744	63,767	5.9
2010	4,004	65,168	6.1
2011	3,991	62,624	6.4
2012	4,650	62,483	7.4
2013	4,830	60,026	8.0
2014*	4,971	58,285	8.5
2015*	4,535	62,122	7.3
Total	70,016	970,843	7.2

Source: National Minimum Dataset, National Mortality Collection, Birth registration dataset. Total births corresponds to live births and fetal deaths, \* 2014 and 2015 are live births only

## Diagnosis

**Table 3** presents the number of cases and prevalence for each congenital anomaly subgroup. The group of anomalies with the highest prevalence between 2009 and 2013 was digestive system anomalies, followed by congenital heart defects, and then limb anomalies.

Table 3. Babies with one or more congenital anomalies, by anomaly subgroup, New Zealand 2009–2013

Babies with an anomaly	(n)	Rate per 1,000 births	95% CI
Congenital anomalies			
New Zealand			
All cases**	21,219	67.56	66.66–68.48
Digestive system	7,075	22.53	22.01–23.06
Congenital heart defects	3,902	12.42	12.04–12.82
Limb	3,536	11.26	10.89–11.64
Genital	2,140	6.81	6.53–7.11
Urinary	1,322	4.21	3.99–4.44
Respiratory	1,186	3.78	3.56–4.00
Nervous system	748	2.38	2.21–2.56
Chromosomal anomalies	701	2.23	2.07–2.40
Ear, Face and Neck	689	2.19	2.03–2.36
Orofacial clefts	524	1.67	1.53–1.82
Eye	233	0.74	0.65–0.84
Abdominal wall defects	228	0.73	0.63–0.83
Neural tube defects	150	0.48	0.40–0.56

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly, Babies are counted once overall, once for each sub-group and for each anomaly documented; \*\* all cases

## Demographic distribution

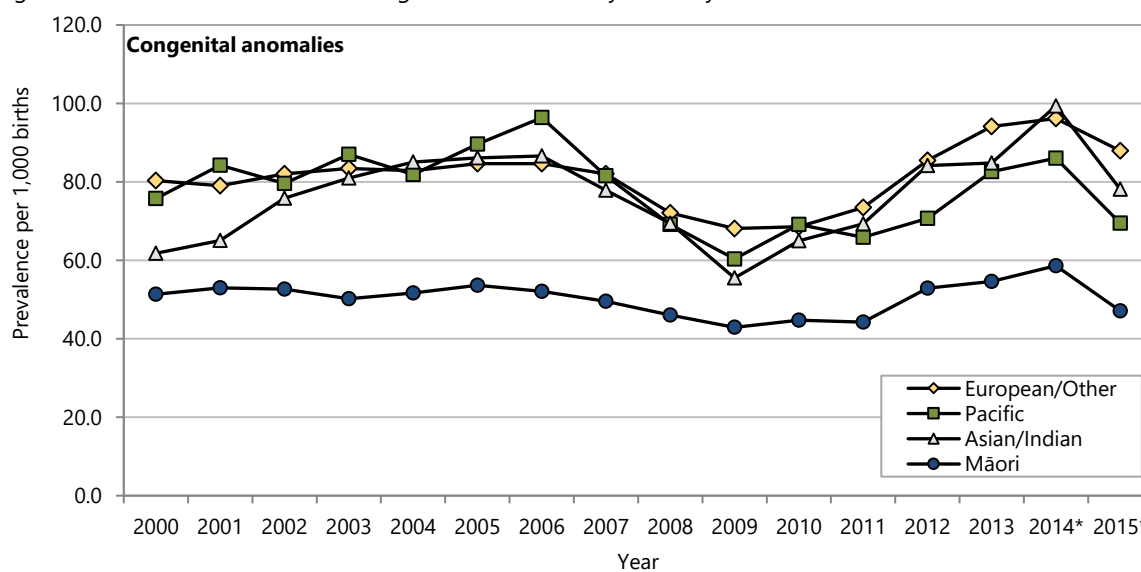
**Table 4** presents the demographic distribution of congenital anomalies in New Zealand between 2009 and 2013. There were no significant differences by New Zealand Deprivation Index quintile. The prevalence of anomalies was significantly higher for male babies. Māori, Pacific, Asian/Indian and MELAA babies all had statistically significantly lower congenital anomaly prevalence rates than babies of European/Other ethnicities but only the Māori rate was markedly lower than the European/Other rate. Compared to babies born to mothers aged 30–34 years, babies born to mothers aged 20–29 years had slightly but significantly lower rates while babies born to mothers aged over 35 years had significantly higher rates. Over the period 2000–2015, rates for the four largest ethnic groups were reasonably steady although there was a dip in rates between 2006 and 2012 (**Figure 3**). Rates for Māori babies were consistently considerably lower than rates for other babies (**Figure 3**).

Table 4. Babies with one or more congenital anomalies, by demographic factor, New Zealand 2009–2013

Variable	2009–2013 (n)	Prevalence per 1,000 births	Rate ratio	95% CI
<b>Congenital anomalies</b>				
NZ Deprivation Index quintile				
Deciles 1–2	3,088	67.77	1.00	
Deciles 3–4	3,430	68.06	1.00	0.96–1.05
Deciles 5–6	3,731	64.79	0.96	0.91–1.00
Deciles 7–8	4,737	68.61	1.01	0.97–1.06
Deciles 9–10	6,168	68.35	1.01	0.97–1.05
Prioritised ethnicity				
Māori	4,353	47.76	0.61	0.59–0.63
Pacific	2,445	69.47	0.89	0.85–0.93
Asian/Indian	2,865	72.82	0.93	0.90–0.97
MELAA	343	64.29	0.82	0.74–0.91
European/Other	11,144	77.97	1.00	
Gender				
Female	8,442	55.20	1.00	
Male	12,773	79.28	1.44	1.40–1.47
Maternal age				
<20 years	996	48.55	1.00	0.93–1.06
20–24 years	2,526	43.52	0.89	0.85–0.94
25–29 years	3,554	45.02	0.92	0.88–0.96
30–34 years	4,291	48.79	1.00	
35+ years	3,860	56.26	1.15	1.11–1.20

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly, Rate ratios are unadjusted, Ethnicity is level 1 prioritised, Decile is NZDep2013, Maternal age reported where available

Figure 3. Babies with one or more congenital anomalies, by ethnicity, New Zealand 2000–2015



Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. (Total) births corresponds to live births and fetal deaths, 2014 and 2015 are live births only. Ethnicity is level 1 prioritised

## Maternal age

The lowest prevalence rate of congenital anomalies between 2009 and 2013 was for babies born to mothers aged 20–24 years at delivery. Prevalence was significantly lower for babies born to mothers aged 20–29 years and significantly higher for babies born to mothers 35 years and over (compared to mothers aged 30–34 years; **Table 4, Table 5**). The prevalence of chromosomal anomalies increased with increasing maternal age with the highest prevalence being for babies born to mothers aged 35 years and over. Prevalence of non-chromosomal anomalies was highest for babies born to mothers aged under 20 years and 35 years and over (U-shaped

distribution across the maternal age groups). Most of the non-chromosomal anomaly subgroups had a U-shaped prevalence distribution except for abdominal defects, for which the prevalence was highest for the under 20 year maternal age group and decreased as maternal age increased (**Table 5**).

Table 5. Babies with one or more congenital anomalies, by maternal age and anomaly type, New Zealand 2009– 2013

2009–2013	Maternal age					
	Total	<20 years	20–24 years	25–29 years	30–34 years	35+ years
Congenital anomalies						
New Zealand						
Total births (n)	314,068	20,513	58,042	78,941	87,956	68,616
Babies with an anomaly (n)	21,219	996	2,526	3,554	4,291	3,860
Prevalence per 1,000 births (95% CI)						
All cases**	67.56 (66.66–68.48)	48.55 (45.59–51.67)	43.52 (41.84–45.25)	45.02 (43.55–46.53)	48.79 (47.34–50.27)	56.26 (54.49–58.06)
Non-chromosomal*	65.33 (64.44–66.23)	47.77 (44.83–50.86)	42.47 (40.81–44.18)	43.74 (42.29–45.23)	47.17 (45.75–48.63)	51.98 (50.29–53.72)
NS	2.23 (2.07–2.40)	2.73 (2.06–3.55)	1.91 (1.57–2.30)	1.24 (1.01–1.51)	1.49 (1.25–1.77)	1.92 (1.61–2.28)
CHD	11.45 (11.08–11.83)	10.38 (9.04–11.88)	7.87 (7.17–8.63)	7.64 (7.04–8.27)	8.07 (7.49–8.69)	9.71 (8.98–10.47)
Respiratory	3.56 (3.36–3.78)	1.71 (1.19–2.37)	1.19 (0.92–1.50)	1.33 (1.09–1.61)	1.36 (1.13–1.63)	1.85 (1.54–2.20)
OFC	1.58 (1.44–1.72)	1.85 (1.31–2.54)	1.12 (0.86–1.43)	1.05 (0.84–1.30)	1.08 (0.87–1.32)	1.50 (1.23–1.82)
Digestive	22.27 (21.75–22.79)	13.50 (11.96–15.19)	13.11 (12.20–14.08)	15.48 (14.62–16.37)	18.67 (17.78–19.59)	19.03 (18.02–20.09)
Abdominal	0.71 (0.62–0.81)	3.02 (2.32–3.87)	1.22 (0.96–1.54)	0.53 (0.38–0.72)	0.30 (0.19–0.43)	0.16 (0.08–0.29)
Urinary	4.13 (3.90–4.36)	2.83 (2.15–3.66)	2.52 (2.12–2.96)	2.85 (2.49–3.25)	3.39 (3.01–3.80)	3.86 (3.41–4.36)
Genital	6.66 (6.38–6.95)	5.26 (4.32–6.36)	4.67 (4.13–5.26)	4.24 (3.80–4.72)	4.63 (4.19–5.10)	4.74 (4.24–5.28)
Limb	11.10 (10.73–11.47)	8.48 (7.27–9.84)	8.82 (8.07–9.62)	8.36 (7.73–9.02)	7.84 (7.27–8.45)	8.80 (8.11–9.53)
Chromosomal	2.23 (2.07–2.40)	0.78 (0.45–1.27)	1.05 (0.80–1.35)	1.28 (1.04–1.55)	1.61 (1.36–1.90)	4.27 (3.80–4.79)

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. \*\*Babies are counted once overall, some babies will have multiple anomalies and appear in more than one row, Maternal age reported where available. \* Non-chromosomal anomalies exclude cases with chromosomal anomalies present, NS = Nervous system, CHD = Congenital heart defects, OFC = Oro-facial clefts, Abdominal = Abdominal wall defects

## Regional trends and distribution

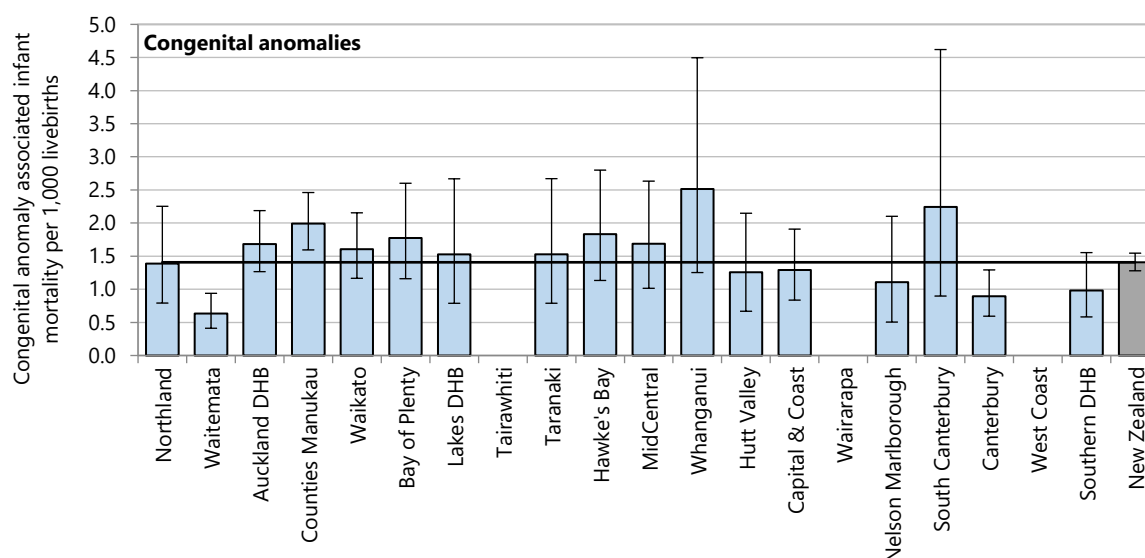
The proportion of infant deaths with at least one congenital anomaly in the South Island DHBs between 2009 and 2013 ranged from 19.9% in Canterbury to 32.1% in Nelson Marlborough (**Table 6**).

The congenital anomaly infant mortality rate in Canterbury DHB was significantly lower than the national rate between 2009 and 2013, and no significant difference in the remaining district health boards (**Figure 4, Table 6**).

Since 1990–91, there was considerable year-on-year variability in the infant mortality rate associated with congenital anomalies among the South Island DHBs. The rate has gradually decreased in Canterbury DHB and been highly variable in Southern DHB (

**Figure 5**). Trends have not been presented for Nelson Marlborough, South Canterbury and West Coast due to the small annual numbers. Total number of congenital anomaly associated infant mortality since 1990 was 46 in Nelson Marlborough, 25 in South Canterbury and 14 for West Coast DHB.

Figure 4. Infant mortality with one or more congenital anomalies, by district health board, New Zealand 2009–2013



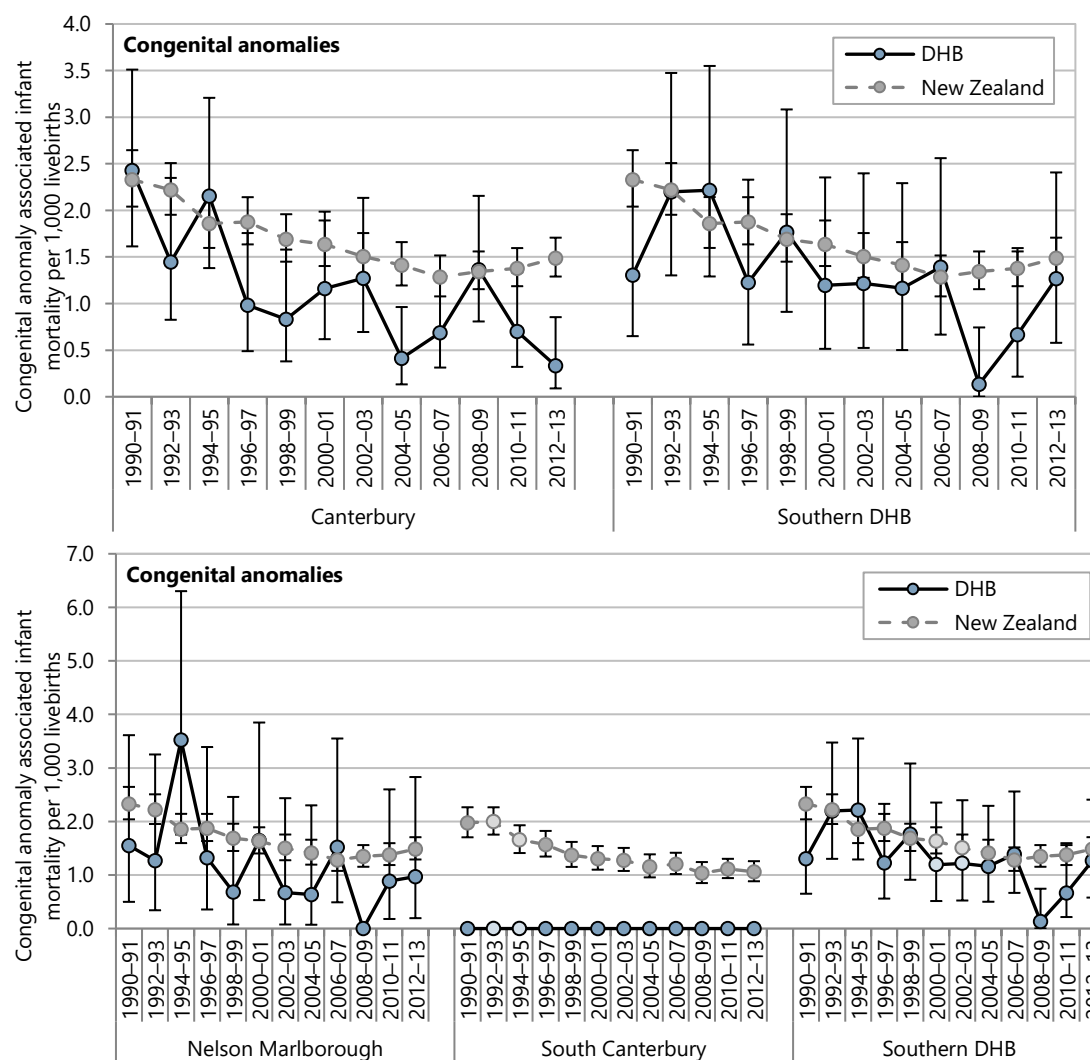
Numerator: National Mortality Collection, Denominator: Birth registration dataset. Infant mortality with one or more diagnosed anomalies; Congenital anomaly infant mortality per 1,000 livebirths

Table 6. Infant mortality with one or more congenital anomalies, by district health board, South Island DHBs vs New Zealand 2009–2013

2009–2013	Infant mortality with an anomaly ( <i>n</i> )	Rate	Rate ratio	95% CI	% of infant deaths
Congenital anomaly associated infant mortality					
Nelson Marlborough	9	1.11	0.79	0.41–1.52	32.1
South Canterbury	7	2.24	1.59	0.76–3.36	31.8
Canterbury	28	0.89	0.63	0.43–0.93	19.9
West Coast	<5	s	s	s	s
Southern DHB	18	0.98	0.70	0.44–1.12	25.4
New Zealand	439	1.41	1.00		27.4

Numerator: National Mortality Collection, Denominator: Birth registration dataset. Infant mortality with one or more diagnosed anomalies; Congenital anomaly infant mortality per 1,000 livebirths

Figure 5. Infant mortality with one or more congenital anomalies, by year, South Island DHBs vs New Zealand 1990–2013



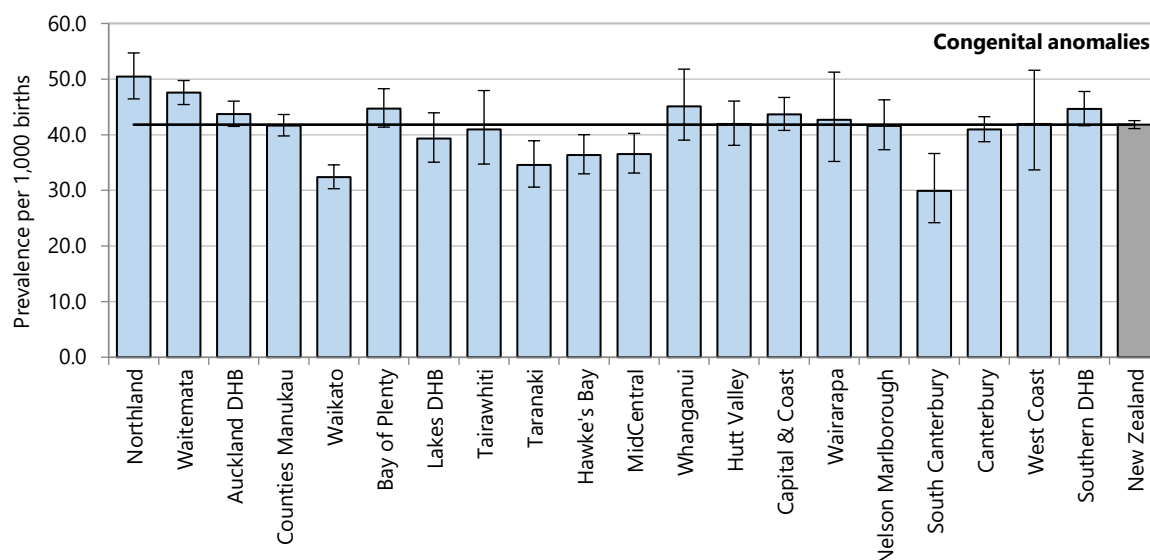
Numerator: National Mortality Collection, Denominator: Birth registration dataset. Babies with one or more diagnosed anomalies; Caution: DHB rates are based upon small numbers, rates suppressed due to small numbers for Nelson Marlborough, South Canterbury, and West Coast DHBs

The prevalence of babies with a congenital anomaly was significantly lower than the national rate between 2009 and 2013 in South Canterbury DHB, and not significantly different for the other South Island DHBs (**Figure 6, Table 7**).

The prevalence of babies with at least one congenital anomaly has gradually decreased since 2000 in Nelson Marlborough, South Canterbury, and Southern DHBs. There was year-on-year variability in the prevalence of babies with at least one congenital anomaly in Canterbury and West Coast DHBs (**Figure 7**).



Figure 6. Babies with one or more congenital anomalies, by district health board, New Zealand, 2009–2013



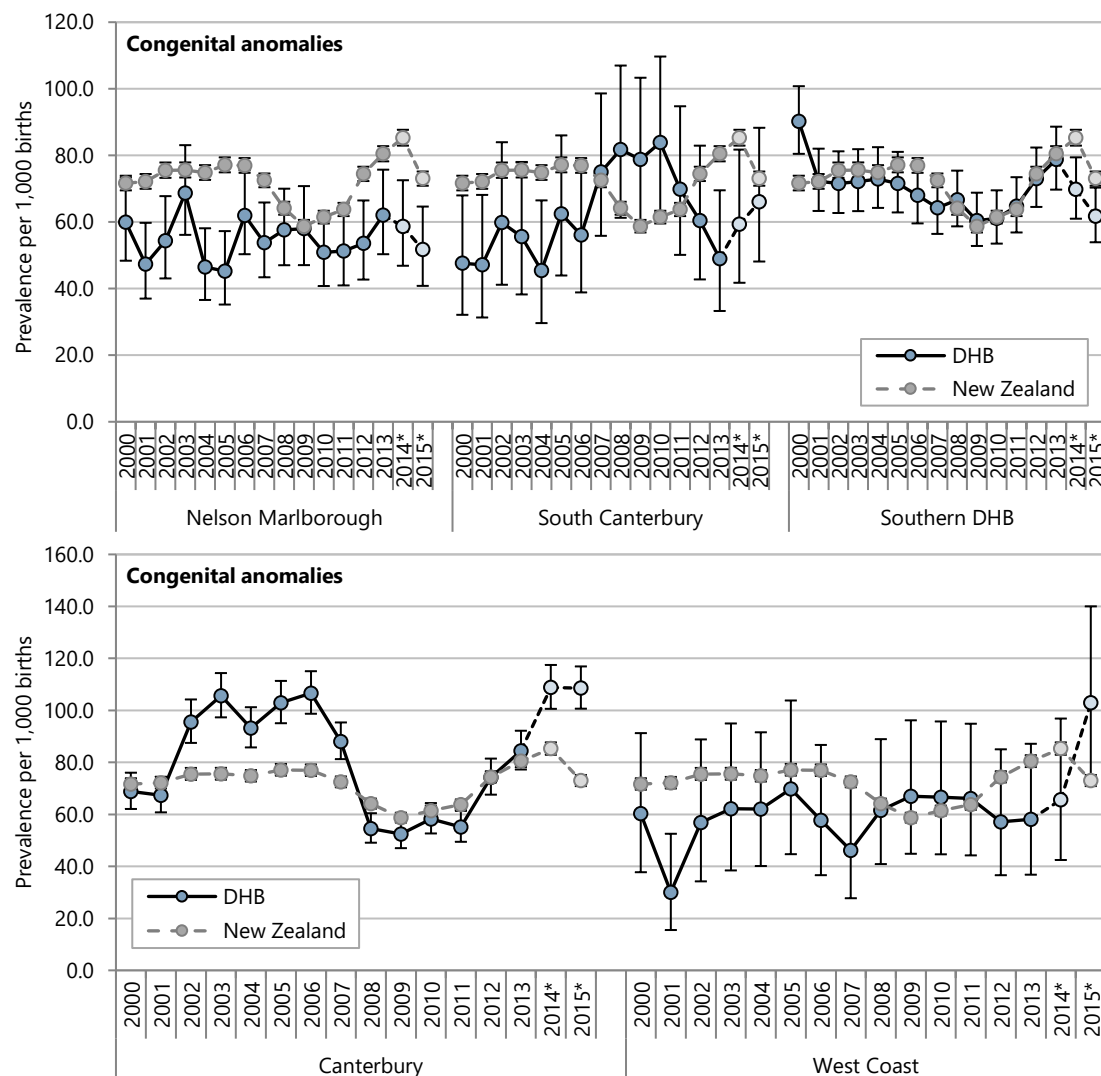
Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. (Total) births corresponds to live births and fetal death; Babies with one or more diagnosed anomalies

Table 7. Babies with one or more congenital anomalies, by district health board, South Island DHBs vs New Zealand 2009–2013

Babies with an anomaly	2009–2013 (n)	Rate per 1,000 births	Rate ratio	95% CI
<b>Congenital anomalies</b>				
Nelson Marlborough	450	55.07	0.82	0.74–0.89
South Canterbury	215	68.45	1.01	0.89–1.15
Canterbury	2,035	64.49	0.95	0.91–1.00
West Coast	134	63.12	0.93	0.79–1.10
Southern DHB	1,242	67.41	1.00	0.94–1.05
New Zealand	21,219	67.56	1.00	

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Prevalence per 1,000 births. (Total) births corresponds to live births and fetal death; Babies with one or more diagnosed anomalies

Figure 7. Babies with one or more congenital anomalies, by year, South Island DHBs vs New Zealand 2000–2015



Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration data and National Mortality Collection. Babies with at least one diagnosed anomaly; (Total) births corresponds to live births and fetal deaths, \* 2014 and 2015 are live births only

## Diagnosis

The number of babies with at least one congenital anomaly diagnosed before the age of one year between 2009 and 2013 and prevalence for each congenital anomaly subgroup are presented for each district health board in **Table 8** to **Table 12**. The anomaly subgroups with the highest prevalence rates were similar between the district health boards, namely congenital heart defects and limb anomalies. Canterbury also had high prevalence rates of digestive system and urinary anomalies.

The anomaly subgroups with the highest prevalence rates were congenital heart defects and limb anomalies in Nelson Marlborough and congenital heart defects in South Canterbury.

Table 8. Babies with one or more congenital anomalies, by anomaly subgroup, Nelson Marlborough DHB 2009– 2013

	2009–2013 (n)	Rate per 1,000 births	95% CI
Congenital anomalies			
Nelson Marlborough			
All cases**	450	55.07	50.10–60.40
Nervous system	17	2.08	1.21–3.33
Neural tube defects	<10	s	s
Eye	<10	s	s
Ear, Face and Neck	11	1.35	0.67–2.41
Congenital heart defects	108	13.22	10.84–15.96
Respiratory	24	2.94	1.88–4.37
Orofacial clefts	10	1.22	0.59–2.25
Abdominal wall defects	<10	s	s
Digestive system	95	11.63	9.41–14.21
Urinary	30	3.67	2.48–5.24
Genital	48	5.87	4.33–7.79
Limb	93	11.38	9.19–13.94
Chromosomal anomalies	16	1.96	1.12–3.18

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly; Babies are counted once overall, once for each sub-group and for each anomaly documented

Table 9. Babies with one or more congenital anomalies, by anomaly subgroup, South Canterbury DHB 2009– 2013

	2009–2013 (n)	Rate per 1,000 births	95% CI
Congenital anomalies			
South Canterbury			
All cases**	215	68.45	59.60–78.24
Nervous system	<10	s	s
Neural tube defects	<10	s	s
Eye	<10	s	s
Ear, Face and Neck	<10	s	s
Congenital heart defects	29	9.23	6.18–13.26
Respiratory	11	3.50	1.75–6.27
Orofacial clefts	<10	s	s
Abdominal wall defects	<10	s	s
Digestive system	137	43.62	36.62–51.56
Urinary	<10	s	s
Genital	15	4.78	2.67–7.88
Limb	19	6.05	3.64–9.45
Chromosomal anomalies	<10	s	s

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly (excludes select minor anomalies; Babies are counted once overall, once for each sub-group and for each anomaly documented

Table 10. Babies with one or more congenital anomalies, by anomaly subgroup, Canterbury DHB 2009–2013

	2009–2013 (n)	Rate per 1,000 births	95% CI
Congenital anomalies			
Canterbury			
All cases**	2,035	64.49	61.72–67.36
Nervous system	78	2.47	1.95–3.09
Neural tube defects	15	0.48	0.27–0.78
Eye	27	0.86	0.56–1.25
Ear, Face and Neck	81	2.57	2.04–3.19
Congenital heart defects	432	13.69	12.43–15.04
Respiratory	110	3.49	2.87–4.20
Orofacial clefts	41	1.30	0.93–1.76
Abdominal wall defects	21	0.67	0.41–1.02
Digestive system	721	22.85	21.21–24.58
Urinary	143	4.53	3.82–5.34
Genital	148	4.69	3.97–5.51
Limb	297	9.41	8.37–10.55
Chromosomal anomalies	63	2.00	1.53–2.55

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly; Babies are counted once overall, once for each sub-group and for each anomaly documented

Table 11. Babies with one or more congenital anomalies, by anomaly subgroup, West Coast DHB 2009–2013

	2009–2013 (n)	Rate per 1,000 births	95% CI
Congenital anomalies			
West Coast			
All cases**	134	63.12	52.88–74.76
Nervous system	<10	s	s
Neural tube defects	<10	s	s
Eye	<10	s	s
Ear, Face and Neck	<10	s	s
Congenital heart defects	30	14.13	9.53–20.17
Respiratory	11	5.18	2.58–9.27
Orofacial clefts	<10	s	s
Abdominal wall defects	<10	s	s
Digestive system	42	19.78	14.26–26.74
Urinary	<10	s	s
Genital	<10	s	s
Limb	29	13.66	9.15–19.62
Chromosomal anomalies	<10	s	s

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly; Babies are counted once overall, once for each sub-group and for each anomaly documented

Table 12. Babies with one or more congenital anomalies, by anomaly subgroup, Southern DHB 2009–2013

	2009–2013 (n)	Rate per 1,000 births	95% CI
Congenital anomalies			
Southern DHB			
All cases**	1,242	67.41	63.71–71.26
Nervous system	36	1.95	1.37–2.71
Neural tube defects	<10	s	s
Eye	17	0.92	0.54–1.48
Ear, Face and Neck	22	1.19	0.75–1.81
Congenital heart defects	309	16.77	14.95–18.75
Respiratory	73	3.96	3.11–4.98
Orofacial clefts	30	1.63	1.10–2.32
Abdominal wall defects	13	0.71	0.38–1.21
Digestive system	442	23.99	21.80–26.33
Urinary	118	6.40	5.30–7.67
Genital	67	3.64	2.82–4.62
Limb	168	9.12	7.79–10.61
Chromosomal anomalies	36	1.95	1.37–2.71

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly; Babies are counted once overall, once for each sub-group and for each anomaly documented

## Demographic distribution

**Table 13** to **Table 17** present the demographic distribution of babies with at least one congenital anomaly for each district health board between 2009 and 2013.

The prevalence of anomalies was significantly higher for male babies, and among babies residing in areas with high deprivation scores (NZDep2013 deciles 7–10) in Canterbury, and Southern DHBs. There was no significant difference in the prevalence of anomalies by sex, or resident deprivation score in Nelson Marlborough, South Canterbury, and West Coast DHBs.

Māori babies had significantly lower congenital anomaly prevalence rates than babies of European/Other ethnicities in the South Island DHBs with the exception of the West Coast. Southern DHB also had significantly lower congenital anomaly prevalence rates among Asian/Indian babies.

Prevalence was significantly higher for babies born to mothers aged 35 years and over (compared to mothers aged 30–34 years) in Canterbury, and no significant difference for the other South Island DHBs.

Table 13. Babies with one or more congenital anomalies, by demographic factor, Nelson Marlborough DHB  
2009– 2013

Variable	<i>n</i>	Rate	Rate ratio	95% CI	Variable	<i>n</i>	Rate	Rate ratio	95% CI
Congenital anomalies									
Nelson Marlborough									
NZ Deprivation Index quintile					Prioritised ethnicity				
Deciles 1–2	33	54.55	1.00		Māori	54	31.27	0.50	0.38–0.67
Deciles 3–4	144	57.42	1.05	0.73–1.52	Pacific	16	62.02	1.00	0.61–1.62
Deciles 5–6	83	45.78	0.84	0.57–1.24	Asian/Indian	23	53.00	0.85	0.57–1.28
Deciles 7–8	169	62.20	1.14	0.79–1.64	MELAA	5	56.18	0.90	0.38–2.13
Deciles 9–10	21	39.70	0.73	0.43–1.24	European/Other	352	62.18	1.00	
Maternal age					Gender				
<20 years	25	55.43	1.30	0.85–1.99	Female	198	49.76	1.00	
20–24 years	52	36.88	0.87	0.62–1.20	Male	252	60.11	1.21	1.01–1.45
25–29 years	66	31.53	0.74	0.55–1.01					
30–34 years	100	42.57	1.00						
35+ years	77	41.20	0.97	0.72–1.29					

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly; Rate per 1,000 births, Rate ratios are unadjusted; Ethnicity is Level 1 prioritised; Decile is NZDep2013; Maternal age reported where available

Table 14. Babies with one or more congenital anomalies, by demographic factor, South Canterbury DHB  
2009– 2013

Variable	<i>n</i>	Rate	Rate ratio	95% CI	Variable	<i>n</i>	Rate	Rate ratio	95% CI
Congenital anomalies									
South Canterbury									
NZ Deprivation Index quintile					Prioritised ethnicity				
Deciles 1–2	33	79.52	1.00		Māori	18	32.85	0.41	0.26–0.67
Deciles 3–4	51	56.79	0.71	0.47–1.09	Pacific	<5	s	s	s
Deciles 5–6	70	78.65	0.99	0.66–1.47	Asian/Indian	<5	s	s	s
Deciles 7–8	51	61.74	0.78	0.51–1.18	MELAA	<5	s	s	s
Deciles 9–10	10	89.29	1.12	0.57–2.21	European/Other	189	79.21	1.00	
Maternal age					Gender				
<20 years	5	24.27	0.80	0.31–2.06	Female	75	49.70	1.00	
20–24 years	13	20.73	0.68	0.35–1.32	Male	140	85.78	1.73	1.32–2.26
25–29 years	20	23.87	0.79	0.44–1.40					
30–34 years	26	30.30	1.00						
35+ years	15	24.51	0.81	0.43–1.51					

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly; Rate per 1,000 births; Rate ratios are unadjusted; Ethnicity is Level 1 prioritised; Decile is NZDep2013; Maternal age reported where available

Table 15. Babies with one or more congenital anomalies, by demographic factor, Canterbury DHB 2009–2013

Variable	<i>n</i>	Rate	Rate ratio	95% CI	Variable	<i>n</i>	Rate	Rate ratio	95% CI
Congenital anomalies									
Canterbury									
NZ Deprivation Index quintile					Prioritised ethnicity				
Deciles 1–2	424	55.17	1.00		Māori	201	36.24	0.49	0.43–0.57
Deciles 3–4	470	64.99	1.18	1.04–1.34	Pacific	85	58.06	0.79	0.64–0.98
Deciles 5–6	351	65.19	1.18	1.03–1.36	Asian/Indian	181	56.72	0.77	0.66–0.90
Deciles 7–8	606	70.79	1.28	1.14–1.45	MELAA	27	48.91	0.67	0.46–0.97
Deciles 9–10	184	68.35	1.24	1.05–1.46	European/Other	1,527	73.46	1.00	
Maternal age					Gender				
<20 years	66	43.71	0.96	0.74–1.23	Female	774	50.13	1.00	
20–24 years	223	45.74	1.00	0.86–1.17	Male	1,260	78.20	1.56	1.43–1.70
25–29 years	339	43.35	0.95	0.83–1.09					
30–34 years	444	45.67	1.00						
35+ years	429	56.24	1.23	1.08–1.40					

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly; Rate per 1,000 births; Rate ratios are unadjusted; Ethnicity is Level 1 prioritised; Decile is NZDep2013; Maternal age reported where available

Table 16. Babies with one or more congenital anomalies, by demographic factor, West Coast DHB 2009–2013

Variable	<i>n</i>	Rate	Rate ratio	95% CI	Variable	<i>n</i>	Rate	Rate ratio	95% CI
Congenital anomalies									
West Coast									
NZ Deprivation Index quintile					Prioritised ethnicity				
Deciles 1–2	8	62.02	1.00		Māori	17	36.64	0.51	0.31–0.84
Deciles 3–4	30	67.26	1.08	0.51–2.31	Pacific	0	..	..	..
Deciles 5–6	29	70.39	1.14	0.53–2.42	Asian/Indian	5	79.37	1.10	0.47–2.60
Deciles 7–8	52	54.85	0.88	0.43–1.82	MELAA	0	..	..	..
Deciles 9–10	15	79.79	1.29	0.56–2.95	European/Other	111	72.12	1.00	
Maternal age					Gender				
<20 years	8	45.45	1.06	0.48–2.32	Female	62	58.05	1.00	
20–24 years	12	27.27	0.63	0.32–1.26	Male	72	68.31	1.18	0.85–1.63
25–29 years	19	34.61	0.80	0.44–1.46					
30–34 years	23	43.07	1.00						
35+ years	22	51.89	1.20	0.68–2.13					

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly; Rate per 1,000 births; Rate ratios are unadjusted; Ethnicity is Level 1 prioritised; Decile is NZDep2013; Maternal age reported where available

Table 17. Babies with one or more congenital anomalies, by demographic factor, Southern DHB 2009–2013

Variable	n	Rate	Rate ratio	95% CI	Variable	n	Rate	Rate ratio	95% CI
Congenital anomalies									
Southern DHB									
NZ Deprivation Index quintile					Prioritised ethnicity				
Deciles 1–2	250	55.58	1.00		Māori	137	37.30	0.49	0.41–0.58
Deciles 3–4	263	65.80	1.18	1.00–1.40	Pacific	45	69.44	0.91	0.68–1.22
Deciles 5–6	298	69.40	1.25	1.06–1.47	Asian/Indian	50	54.23	0.71	0.54–0.94
Deciles 7–8	281	77.77	1.40	1.19–1.65	MELAA	19	71.70	0.94	0.61–1.46
Deciles 9–10	148	73.16	1.32	1.08–1.60	European/Other	981	76.01	1.00	
Maternal age					Gender				
<20 years	42	42.64	0.86	0.62–1.18	Female	517	58.24	1.00	
20–24 years	132	42.48	0.85	0.70–1.05	Male	725	75.93	1.30	1.17–1.45
25–29 years	211	43.70	0.88	0.74–1.05					
30–34 years	277	49.71	1.00						
35+ years	243	61.78	1.24	1.05–1.47					

Numerator: National Minimum Dataset and National Mortality Collection, Denominator: Birth registration dataset and National Mortality Collection. Babies with at least one diagnosed anomaly; Rate per 1,000 births; Rate ratios are unadjusted; Ethnicity is Level 1 prioritised; Decile is NZDep2013; Maternal age reported where available

## Evidence for good practice

### Possibilities for prevention

The majority of congenital malformation have no known cause. For this reason, the avenues for prevention are limited and the effects of interventions modest. Some major structural malformations can be detected during pregnancy via ultrasound examination, and most chromosomal and some genetic disorders can be detected via amniocentesis or chorionic villus sampling. Prenatal diagnosis allows parents to choose termination when their fetus has a condition likely to be fatal or severely disabling, and delivery in a tertiary centre with appropriate surgical expertise when their baby will require surgery soon after birth.

**Table 18** indicates where prenatal detection is possible (to a variable degree), by ultrasound examination and/or genetic testing, where optimal health status before and during pregnancy and good antenatal care may reduce the incidence of the condition, and where early postnatal detection improves outcomes. For genetic conditions (including cystic fibrosis) pre-natal genetic testing is generally offered only in cases where there is a family history of the condition or where a genetic condition is suspected, for example, as a result of findings from maternal blood tests and/or prenatal ultrasound examination. The prenatal detection rate varies from condition to condition. The overall detection rate for structural anomalies via ultrasound in the first trimester is around 50%,<sup>8</sup> and for lethal anomalies the ultrasound detection rate in the second semester is over 80%.<sup>9,10</sup>

Table 18. Possibilities for prevention and early detection of genetic and congenital conditions

Condition	Potentially detectable prenatally	Incidence reduced by optimal health status before and during pregnancy and/or good antenatal care	Outcomes improved by early post-natal detection	References
Down syndrome and other chromosomal disorders	✓	x*	x	11,12
Cystic fibrosis	✓		✓	13-15
Neural tube defects	✓	✓	✓	16
Cardiovascular anomalies	✓	✓	✓	17-20
Other structural congenital anomalies	✓	✓	✓	8-10
Genetic metabolic disorders	✓	x	✓	21,22
Congenital hearing loss	✓	✓	✓	23-25

\*incidence is lower in younger women



## Brief notes relevant to the prevention of congenital anomalies

**Neural tube defects can be prevented by peri-conceptional folic acid supplementation:** The Ministry of Health recommends that women wishing to become pregnant who are at low risk of having a pregnancy affected by a neural tube defect should take 800 µg of folic acid daily for at least four weeks prior to conception and for 12 weeks after.<sup>26</sup> The 2015 Cochrane review on this topic found high quality evidence that daily folic acid supplementation prevents neural tube defects (risk ratio 0.31, 95% CI 0.17 to 0.58; five studies; 6708 births).<sup>16</sup>

**Maternal smoking is associated with an increased risk of non-chromosomal birth defects:** Odds ratios in the range 1.25–1.50 for limb reduction defects, clubfoot, oral clefts and defects of the eyes and gastrointestinal system (especially gastroschisis and abdominal hernias), and odds ratios in the range 1.09–1.19 for digit anomalies, cryptorchidism and defects of the heart and musculoskeletal system.<sup>27</sup>

**Heavy drinking in pregnancy,** especially binge drinking, can have severe effects on the developing fetus by disrupting brain development leading to cognitive, motor and behavioural disability with life-long consequences.<sup>28,29</sup> Fetal alcohol syndrome also produces distinctive facial anomalies and growth retardation and is associated with a greatly increased risk of vision and hearing impairments, and a wide variety of congenital malformations.<sup>28,30</sup>

**Maternal obesity** seems to be associated with a small increase in the rates of some congenital anomalies, including heart defects and neural tube defects, and the risk may increase with greater degree of obesity.<sup>31–33</sup> In addition, maternal obesity is associated with at least 20% lower rates of detection of fetal anomalies via ultrasound, in comparison to women with normal body mass index.<sup>34,35</sup>

**Diabetic women who become pregnant** have a risk of having a baby with a major congenital anomaly around that is twice that of other women<sup>36</sup> and a risk having a baby with a congenital heart defect that is almost four times higher.<sup>17</sup> These risks can be reduced by optimising maternal health in the peri-conception period especially by maintaining good control of blood glucose levels.<sup>20</sup>

**Maternal infections known to cause birth defects** include toxoplasmosis, rubella, cytomegalovirus, herpes, and syphilis (the TORCH infections), as well as varicella, influenza, Zika virus and Lymphocytic Choriomeningitis (the last two are not known to occur in New Zealand).<sup>37–40</sup>

**Common medications causing birth defects** include: angiotensin converting enzyme inhibitors (for hypertension), anticonvulsants (for epilepsy), anti-neoplastic agents (for cancer), and systemic retinoids (for acne and other skin conditions).<sup>37,41,42</sup> In general, medicines should be prescribed to pregnant women only when absolutely necessary, when the benefits outweigh the risks.

### Key points for achieving optimal pre-pregnancy health status to reduce congenital anomaly risk:<sup>43</sup>

- Take folic acid supplements (to prevent neural tube defects)
- Seek medical advice before becoming pregnant if you have a chronic condition such as diabetes, hypothyroidism, epilepsy or hypertension where the condition itself, or the medication used to treat it, may increase the risk of congenital anomalies in your baby
- Avoid smoking, alcohol and recreational drugs
- Lose weight if obese
- Seek medical advice before becoming pregnant if there is a family history of a genetic disorder
- Make sure you are immune to rubella, consider varicella vaccination if not already immune

### Key points for achieving optimal health status during pregnancy to reduce congenital anomaly risk:<sup>43–45</sup>

- Avoid smoking, alcohol and recreational drugs
- Take folic acid and iodine
- Do not take therapeutic drugs except on medical advice that the benefits outweigh the risks
- Register with a Lead Maternity Carer early in pregnancy (before 10 weeks' gestation)
- Make a decision about screening tests
- Take care with personal and food hygiene, wash hands before eating (especially if you have contact with young children), and avoid contact with cat faeces

Although listeria infection does not cause congenital anomalies, pregnant women should avoid eating soft cheeses, delicatessen meats, pâtés, hummus-based spreads, refrigerated smoked seafood and salad bar cold salads to prevent miscarriage, preterm birth and stillbirth due to listeria infection.<sup>46,47</sup>

The following section uses data from the National Minimum Dataset to describe congenital anomalies in babies from 2000–2015 and concludes with a brief overview of some of the evidence relating to early diagnosis of these conditions.

## **Evidence-based health care for children, young people and parents affected by congenital anomalies**

There are many thousands of different congenital anomalies so it is not practical to provide information here on the specific care each one requires. Instead, this section offers information on some new developments in prenatal and postnatal detection of congenital anomalies and highlights some of the findings from a review of the maternity care received by women who experienced perinatal deaths due to congenital anomalies in New Zealand in 2010.

In New Zealand, pregnant women are offered screening tests for Down syndrome and a fetal anatomy scan at 18–20 weeks' gestation.<sup>48</sup> The aim of fetal anomaly screening is to identify potential problems so that parents can make an informed choice about whether to continue the pregnancy if an anomaly is identified and have time to prepare for what is to come whether it is a termination, a baby who will need postnatal treatment or palliative care, or a child who will have long term disability.<sup>49</sup> Prenatal detection also allows planning for delivery in a specialist centre and, for a few conditions, intra-uterine therapy.<sup>49</sup> Ultrasound scanning to detect fetal malformations reduces perinatal mortality rates if there is a high level of diagnostic expertise and termination of pregnancy for fetal abnormality is widely accepted in the population.<sup>50</sup>

In New Zealand in 2010 there were 211 perinatal deaths due to congenital anomalies (30% of the 704 perinatal deaths in that year).<sup>51</sup> A review project based on the Perinatal and Maternal Mortality Review Committee dataset assessed the quality of the maternity care received by the women with one of the 137 perinatal deaths that were due to a congenital cardiovascular, central nervous system or chromosomal abnormality in that year.<sup>51</sup>

The review found that first contact with a health practitioner (most often a GP) occurred within 10 weeks of gestation in 74% of the women and within 14 weeks in 85% but there was often a significant delay in registering with a lead maternity carer (LMC). This meant that some women presented to a LMC too late for first trimester screening for Down syndrome. Of the 129 women who presented to a health professional at less than 20 weeks' gestation, 97 (71% of the 137) were offered first and/or second trimester screening and 82 (60% of the 137) had first and or second trimester screening. Fifteen women (11% of the 137) declined screening.

The review also found that only 7% of the women were documented as having taken folate supplements (to prevent neural tube defects) prior to pregnancy although 54% had taken them during pregnancy. On review of the women's ultrasound images it was found that some anomalies could have been detected earlier. The review made a number of recommendations, including those following. All women should receive preconception counselling to optimise their health and identify any risks for congenital anomalies resulting from previous obstetric history or family history. There should be a media campaign to promote peri-conceptional folate and the evidence on fortification of bread with folate should be further investigated. All women should be educated about the importance of booking before 10 weeks. GPs should be effective at offering first trimester screening since they are often a woman's first point of contact with maternity care and they should expedite booking with a LMC. If screening has not already been arranged then LMCs should offer all women first and second trimester screening, as required by the Ministry of Health, as this will enable the early diagnosis of a proportion of congenital anomalies.

It is now possible to test for Down, Edwards and Patau syndromes early in pregnancy using cell-free fetal DNA obtained from a sample of the mother's blood (non-invasive prenatal testing, NPIT).<sup>52</sup> A recent systematic review commissioned by the UK National Screening Committee, which included 41 studies relevant to Down syndrome, found that NPIT has very high sensitivity (99.3%) and specificity (99.9%) for Down syndrome.<sup>53</sup> Nevertheless, in the general obstetric population where the prevalence of Down syndrome is low, it could be expected that for every four Down syndrome cases detected there would be one false positive result so it is essential that, if a woman is considering a termination following a positive NPIT result, she has the diagnosis confirmed with an invasive diagnostic test (amniocentesis or chorionic villus sampling).<sup>53</sup> Non-invasive prenatal testing is available to New Zealand women on a user pays basis but is not part of publically funded ante-natal screening.<sup>54</sup>

Congenital heart disease (CHD) causes more early neonatal deaths than any other type of congenital anomaly, accounting for around 30% of all early neonatal deaths associated with congenital anomalies in EUROCAT (a European network of population-based registries) in 2008–2012.<sup>55</sup> In cases of major or critical CHD (defined as

cases requiring intervention or resulting in death within one year or within four weeks, respectively) delayed diagnosis is associated with increased mortality and morbidity.<sup>56</sup>

In New Zealand during 2006–2010 antenatal ultrasound picked up only 46% of critical CHD.<sup>57</sup> Postnatal physical examination cannot detect all babies with CHD as some do not display any physical symptoms until after hospital discharge.<sup>56</sup> Almost 20% of New Zealand infants with critical CHD are not diagnosed until after initial hospital discharge.<sup>57</sup>

Newborn pulse oximetry will detect hypoxaemic infants and is a simple and non-invasive method for screening for CHD which increases detection rates for CHD when used as an adjunct to physical examination.<sup>56</sup> A number of developed countries have such screening and a pulse oximetry pilot programme is currently underway in Auckland.<sup>58,59</sup>

These national and international guidelines, systematic reviews, other publications and websites relevant to the prevention and management of congenital anomalies are provided for further reading.

### Government publications and websites

- Ministry of Health. 2016. Zika virus. <https://www.health.govt.nz/our-work/diseases-and-conditions/zika-virus>
- Ministry of Health. 2014. Quality Standards for Diabetes Care Toolkit. Wellington: Ministry of Health. <https://www.health.govt.nz/publication/quality-standards-diabetes-care-toolkit-2014> (standard 20 deals with pregnant women and women planning a pregnancy)
- Ministry of Health. 2014. Well Child / Tamariki Ora Programme Practitioner Handbook: Supporting families and whānau to promote their child's health and development. Revised 2014. Wellington: Ministry of Health. <https://www.health.govt.nz/publication/well-child-tamariki-ora-programme-practitioner-handbook-2013> (provides guidance on health and development assessments, one purpose of which is to detect congenital anomalies)
- National Screening Unit. 2012. Antenatal Screening for Down Syndrome and Other Conditions: Guidelines for health practitioners. Wellington: Ministry of Health. <https://www.health.govt.nz/publication/antenatal-screening-down-syndrome-and-other-conditions-guidelines-health-practitioners>
- Farquar C, Arroll N, Sadler L, et al. 2013. Improving quality and safety in maternity services: can we improve prevention, detection and management of congenital abnormalities in pregnancy? Wellington: Health Quality and Safety Commission of New Zealand. <https://www.hqsc.govt.nz/assets/Other-Topics/QS-challenge-reports/Detecting-abnormalities-earlier-in-pregnancy-Final-Report.pdf>
- Ministry of Health. 2010. Alcohol and Pregnancy: A practical guide for health professionals. Wellington: Ministry of Health. <https://www.health.govt.nz/publication/alcohol-and-pregnancy-practical-guide-health-professionals>

### New Zealand guidelines and websites

- National Screening Unit. 2012. Antenatal Screening for Down syndrome and other conditions: Guidelines for health practitioners. Wellington: Ministry of Health. [https://www.nsu.govt.nz/system/files/page/antenatal\\_screening\\_for\\_down\\_syndrome\\_and\\_other\\_conditions\\_guidelines\\_for\\_health\\_practitioners.pdf](https://www.nsu.govt.nz/system/files/page/antenatal_screening_for_down_syndrome_and_other_conditions_guidelines_for_health_practitioners.pdf)
- National Screening Unit. Antenatal Screening for Down syndrome and other conditions. <https://www.nsu.govt.nz/health-professionals/antenatal-screening-down-syndrome-and-other-conditions> (links to a range of resources)
- National Screening unit. Newborn Metabolic Screening Programme. <https://www.nsu.govt.nz/health-professionals/newborn-metabolic-screening-programme> (links to a range of resources)
- National Screening unit. Universal Newborn Hearing Screening Programme. <https://www.nsu.govt.nz/health-professionals/universal-newborn-hearing-screening-programme> (links to a range of resources)

### International guidelines

- McLafferty LP, Becker M, Dresner N, et al. 2016. Guidelines for the management of pregnant women with substance use disorders. *Psychosomatics*, 57(2) 115-30 <http://dx.doi.org/10.1016/j.psych.2015.12.001>
- National Collaborating Centre for Women's and Children's Health. 2015. Diabetes in pregnancy: Management of diabetes and its complications from preconception to the postnatal period. London: National Institute for Health and Care Excellence (UK). <https://www.ncbi.nlm.nih.gov/pubmed/25950069>

- Shawe J, Delbaere I, Ekstrand M, et al. 2015. Preconception care policy, guidelines, recommendations and services across six European countries: Belgium (Flanders), Denmark, Italy, the Netherlands, Sweden and the United Kingdom. *European Journal of Contraception and Reproductive Health Care*, 20(2) 77–87 <http://dx.doi.org/10.3109/13625187.2014.990088>
- Kolon TF, Herndon CD, Baker LA, et al. 2014. Evaluation and treatment of cryptorchidism: AUA guideline. *Journal of Urology*, 192(2) 337–45 <http://dx.doi.org/10.1016/j.juro.2014.05.005>
- Kantor PF, Loughheed J, Dancea A, et al. 2013. Presentation, diagnosis, and medical management of heart failure in children: Canadian Cardiovascular Society guidelines. *Canadian Journal of Cardiology*, 29(12) 1535–52 <http://dx.doi.org/10.1016/j.cjca.2013.08.008>
- Wilson RD, Audibert F, Brock JA, et al. 2011. Genetic considerations for a woman's pre-conception evaluation. *Journal of Obstetrics and Gynaecology Canada*, 33(1) 57–64 [http://www.jogc.com/article/S1701-2163\(16\)34774-0/pdf](http://www.jogc.com/article/S1701-2163(16)34774-0/pdf)
- Bull MJ. 2011. Health supervision for children with Down syndrome. *Pediatrics*, 128(2) 393–406. <http://dx.doi.org/10.1542/peds.2011-1605>
- Harden CL, Meador KJ, Pennell PB, et al. 2009. Practice parameter update: management issues for women with epilepsy--focus on pregnancy (an evidence-based review): teratogenesis and perinatal outcomes: report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society. *Neurology*, 73(2) 133–41 <http://dx.doi.org/10.1212/WNL.0b013e3181a6b312>

#### **Evidence-based medicine reviews**

- Taylor-Phillips S, Freeman K, Geppert J, et al. 2016. Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis. *BMJ Open*, 6(1) e010002 <http://dx.doi.org/10.1136/bmjopen-2015-010002>
- Weston J, Bromley R, Jackson CF, et al. 2016. Monotherapy treatment of epilepsy in pregnancy: congenital malformation outcomes in the child. *Cochrane Database Systematic Reviews*, 11 <http://dx.doi.org/10.1002/14651858.CD010224.pub2>
- Karim JN, Roberts NW, Salomon LJ, et al. 2016. Systematic review of first trimester ultrasound screening in detecting fetal structural anomalies and factors affecting screening performance. *Ultrasound in Obstetrics and Gynecology*, <http://dx.doi.org/10.1002/uog.17246>
- D'Antonio F, Familiari A, Thilaganathan B, et al. 2016. Sensitivity of first-trimester ultrasound in the detection of congenital anomalies in twin pregnancies: population study and systematic review. *Acta Obstetrica et Gynecologica Scandinavica*, <http://dx.doi.org/10.1111/aogs.13017>
- Araujo Junior E, Tonni G, Chung M, et al. 2016. Perinatal outcomes and intrauterine complications following fetal intervention for congenital heart disease: systematic review and meta-analysis of observational studies. *Ultrasound in Obstetrics and Gynecology*, 48(4) 426–33 <http://dx.doi.org/10.1002/uog.15867>
- Brown KL, Wray J, Knowles RL, et al. 2016. Infant deaths in the UK community following successful cardiac surgery: building the evidence base for optimal surveillance, a mixed-methods study. *Health Services and Delivery Research*, 4(19) <http://dx.doi.org/10.3310/hsdr04190>
- Narayan IC, Blom NA, Ewer AK, et al. 2016. Aspects of pulse oximetry screening for critical congenital heart defects: when, how and why? *Archives of Disease in Childhood. Fetal Neonatal Edition*, 101(2) F162–7 <http://dx.doi.org/10.1136/archdischild-2015-309205>
- Tanoshima M, Kobayashi T, Tanoshima R, et al. 2015. Risks of congenital malformations in offspring exposed to valproic acid in utero: A systematic review and cumulative meta-analysis. *Clinical Pharmacology and Therapeutics*, 98(4) 417–41 <http://dx.doi.org/10.1002/cpt.158>
- Liu H, Zhou J, Feng QL, et al. 2015. Fetal echocardiography for congenital heart disease diagnosis: a meta-analysis, power analysis and missing data analysis. *European Journal of Preventive Cardiology*, 22(12) 1531–47 <http://dx.doi.org/10.1177/2047487314551547>
- Whitworth M, Bricker L, Mullan C. 2015. Ultrasound for fetal assessment in early pregnancy. *Cochrane Database Systematic Reviews*, (7) <http://dx.doi.org/10.1002/14651858.CD007058.pub3>
- Alldred SK, Guo B, Takwoingi Y, et al. 2015. Urine tests for Down's syndrome screening. *Cochrane Database of Systematic Reviews*, (12) <http://dx.doi.org/10.1002/14651858.cd011984>

- Alldred SK, Takwoingi Y, Guo B, et al. 2015. First trimester serum tests for Down's syndrome screening. *Cochrane Database of Systematic Reviews*, (11) <http://dx.doi.org/10.1002/14651858.cd011975>
- De-Regil LM, Pena-Rosas JP, Fernandez-Gaxiola AC, et al. 2015. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database of Systematic Reviews*, (12) <http://dx.doi.org/10.1002/14651858.CD007950.pub3>
- Crawford-Williams F, Fielder A, Mikocka-Walus A, et al. 2015. A critical review of public health interventions aimed at reducing alcohol consumption and/or increasing knowledge among pregnant women. *Drug and Alcohol Review*, 34(2) 154-61 <http://dx.doi.org/10.1111/dar.12152>
- DiMiceli-Zsigmond M, Williams AK, Richardson MG. 2015. Expecting the Unexpected: Perspectives on Stillbirth and Late Termination of Pregnancy for Fetal Anomalies. *Anesthesia & Analgesia*, 121(2) 457-64 <http://dx.doi.org/10.1213/ane.0000000000000785>
- Drakouli M, Petsios K, Giannakopoulou M, et al. 2015. Determinants of quality of life in children and adolescents with CHD: a systematic review. *Cardiology in the Young*, 25(6) 1027-36 <http://dx.doi.org/10.1017/s1047951115000086>
- Liu H, Zhou J, Feng QL, et al. 2015. Fetal echocardiography for congenital heart disease diagnosis: a meta-analysis, power analysis and missing data analysis. *European Journal of Preventive Cardiology*, 22(12) 1531-47 <http://dx.doi.org/10.1177/2047487314551547>
- Di Mario S, Basevi V, Gagliotti C, et al. 2015. Prenatal education for congenital toxoplasmosis. *Cochrane Database of Systematic Reviews*, (10) <http://dx.doi.org/10.1002/14651858.CD006171.pub4>
- Grivell RM, Andersen C, Dodd JM. 2015. Prenatal interventions for congenital diaphragmatic hernia for improving outcomes. *Cochrane Database Systematic Reviews*, (11) <http://dx.doi.org/10.1002/14651858.CD008925.pub2>
- Verrotti A, Mencaroni E, Castagnino M, et al. 2015. Foetal safety of old and new antiepileptic drugs. *Expert Opinion on Drug Safety*, 14(10) 1563-71 <http://dx.doi.org/10.1517/14740338.2015.1084288>
- Wei H, Roscigno CI, Hanson CC, et al. 2015. Families of children with congenital heart disease: A literature review. *Heart & Lung*, 44(6) 494-511 <http://dx.doi.org/10.1016/j.hrtlng.2015.08.005>
- Bruno CJ, Havranek T. 2015. Screening for Critical Congenital Heart Disease in Newborns. *Advances in Pediatrics*, 62(1) 211-26 <http://dx.doi.org/10.1016/j.yapd.2015.04.002>
- Smith WG. 2015. Interventions for congenital talipes equinovarus (clubfoot). *Paediatrics and Child Health*, 20(6) 307-08 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4578470/>
- Puligandla PS, Grabowski J, Austin M, et al. 2015. Management of congenital diaphragmatic hernia: A systematic review from the APSA outcomes and evidence based practice committee. *Journal of Pediatric Surgery*, 50(11) 1958-70 <http://dx.doi.org/10.1016/j.jpedsurg.2015.09.010>
- Olney RS, Ailes EC, Sontag MK. 2015. Detection of critical congenital heart defects: Review of contributions from prenatal and newborn screening. *Seminars in Perinatology*, 39(3) 230-7 <http://dx.doi.org/10.1053/j.semperi.2015.03.007>
- Shannon GD, Alberg C, Nacul L, et al. 2014. Preconception healthcare and congenital disorders: systematic review of the effectiveness of preconception care programs in the prevention of congenital disorders. *Maternal and Child Health Journal*, 18(6), 1354-79 <http://dx.doi.org/10.1007/s10995-013-1370-2>
- Temel S, van Voorst SF, Jack BW, et al. 2014. Evidence-based preconceptional lifestyle interventions. *Epidemiology Reviews*, 36, 19-30. <http://dx.doi.org/10.1093/epirev/mxt003>
- Lassi ZS, Imam AM, Dean SV, et al. 2014. Preconception care: screening and management of chronic disease and promoting psychological health. *Reproductive Health*, 11 Suppl 3 S5 <http://dx.doi.org/10.1186/1742-4755-11-s3-s5>
- Gray K, Pacey V, Gibbons P, et al. 2014. Interventions for congenital talipes equinovarus (clubfoot). *Cochrane Database Systematic Reviews*, (8) <http://dx.doi.org/10.1002/14651858.CD008602.pub3>
- Hamilton ST, van Zuylen W, Shand A, et al. 2014. Prevention of congenital cytomegalovirus complications by maternal and neonatal treatments: a systematic review. *Reviews in Medical Virology*, 24(6) 420-33 <http://dx.doi.org/10.1002/rmv.1814>
- Turner J, Preston L, Booth A, et al. 2014. What evidence is there for a relationship between organisational features and patient outcomes in congenital heart disease services? A rapid review. *Health Services and Delivery Research*, 2(43) [http://www.journalslibrary.nihr.ac.uk/\\_data/assets/pdf\\_file/0017/130085/FullReport-hsdr02430.pdf](http://www.journalslibrary.nihr.ac.uk/_data/assets/pdf_file/0017/130085/FullReport-hsdr02430.pdf)

- Hom LA, Martin GR. 2014. U.S. international efforts on critical congenital heart disease screening: can we have a uniform recommendation for Europe? *Early Human Development*, 90 Suppl 2 S11-4  
[http://dx.doi.org/10.1016/s0378-3782\(14\)50004-7](http://dx.doi.org/10.1016/s0378-3782(14)50004-7)
- Tassone F. 2014. Newborn screening for fragile X syndrome. *JAMA Neurology*, 71(3) 355–9  
<http://dx.doi.org/10.1001/jamaneurol.2013.4808>
- Grivell RM, Andersen C, Dodd JM. 2014. Prenatal versus postnatal repair procedures for spina bifida for improving infant and maternal outcomes. *Cochrane Database of Systematic Reviews*, (10)  
<http://dx.doi.org/10.1002/14651858.CD008825.pub2>
- Conner SN, Longman RE, Cahill AG. 2014. The role of ultrasound in the diagnosis of fetal genetic syndromes. *Best Practice & Research Clinical Obstetrics & Gynaecology*, 28(3) 417-28  
<http://dx.doi.org/10.1016/j.bpobgyn.2014.01.005>
- Wax J, Minkoff H, Johnson A, et al. 2014. Consensus report on the detailed fetal anatomic ultrasound examination: indications, components, and qualifications. *Journal of Ultrasound in Medicine*, 33(2) 189-95  
<http://dx.doi.org/10.7863/ultra.33.2.189>
- Pinto NM, Nelson R, Puchalski M, et al. 2014. Cost-effectiveness of prenatal screening strategies for congenital heart disease. *Ultrasound in Obstetrics & Gynecology*, 44(1) 50-7  
<http://dx.doi.org/10.1002/uog.13287>
- Peterson C, Grosse SD, Oster ME, et al. 2013. Cost-Effectiveness of Routine Screening for Critical Congenital Heart Disease in US Newborns. *Pediatrics*, 132(3) e595-e603  
<http://dx.doi.org/10.1542/peds.2013-0332>
- Grant NH, Dorling J, Thornton JG. 2013. Elective preterm birth for fetal gastroschisis. *Cochrane Database Systematic Reviews*, (6) <http://dx.doi.org/10.1002/14651858.CD009394.pub2>
- Grigoriadis S, VonderPorten EH, Mamisashvili L, et al. 2013. Antidepressant exposure during pregnancy and congenital malformations: is there an association? A systematic review and meta-analysis of the best evidence. *Journal of Clinical Psychiatry*, 74(4) e293-308 <http://dx.doi.org/10.4088/JCP.12r07966>
- Mongua-Rodriguez N, Diaz-Ortega JL, Garcia-Garcia L, et al. 2013. A systematic review of rubella vaccination strategies implemented in the Americas: impact on the incidence and seroprevalence rates of rubella and congenital rubella syndrome. *Vaccine*, 31(17) 2145-51  
<http://dx.doi.org/10.1016/j.vaccine.2013.02.047>
- Diwakar L, Morris RK, Barton P, et al. 2013. Evaluation of the cost effectiveness of vesico-amniotic shunting in the management of congenital lower urinary tract obstruction (based on data from the PLUTO Trial). *PLoS One*, 8(12) e82564 <http://dx.doi.org/10.1371/journal.pone.0082564>
- Sotiropoulos A, Papatheodorou S, Eleftheriades M, et al. 2013. Nuchal translucency and major congenital heart defects in fetuses with normal karyotype: a meta-analysis. *Ultrasound in Obstetrics & Gynecology*, 42(4) 383-9 <http://dx.doi.org/10.1002/uog.12488>
- Lane DA, Millane TA, Lip GYH. 2013. Psychological interventions for depression in adolescent and adult congenital heart disease. *Cochrane Database of Systematic Reviews*, (10)  
<http://dx.doi.org/10.1002/14651858.CD004372.pub2>
- Alldred SK, Deeks JJ, Guo B, et al. 2012. Second trimester serum tests for Down's Syndrome screening. *Cochrane Database Systematic Reviews*, (6) <http://dx.doi.org/10.1002/14651858.cd009925>
- Marino BS, Lipkin PH, Newburger JW, et al. 2012. Neurodevelopmental outcomes in children with congenital heart disease: evaluation and management: a scientific statement from the American Heart Association. *Circulation*, 126(9) 1143-72 <http://dx.doi.org/10.1161/CIR.0b013e318265ee8a>
- Wahabi HA, Alzeidan RA, Esmaeil SA. 2012. Pre-pregnancy care for women with pre-gestational diabetes mellitus: a systematic review and meta-analysis. *BMC Public Health*, 12 792  
<http://dx.doi.org/10.1186/1471-2458-12-792>
- Racusin D, Stevens B, Campbell G, et al. 2012. Obesity and the risk and detection of fetal malformations. *Seminars in Perinatology*, 36(3) 213-21 <http://dx.doi.org/10.1053/j.semperi.2012.05.001>
- Choi H, Van Riper M, Thoyre S. 2012. Decision making following a prenatal diagnosis of Down syndrome: an integrative review. *Journal of Midwifery & Women's Health*, 57(2) 156-64  
<http://dx.doi.org/10.1111/j.1542-2011.2011.00109.x>
- National Collaborating Centre for Women's and Children's Health. 2008. Antenatal Care: Routine Care for the Healthy Pregnant Woman. NICE Clinical Guidelines, No. 62. London: RCOG Press.



<https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0009601> (Chapter 9 covers screening for fetal anomalies)

- Bricker L, Garcia J, Henderson J, et al. 2000. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. *Health Technology Assessment*, 4(16) i-vi, 1-193 <http://dx.doi.org/10.3310/hta4160>

### Other relevant publications

- Khoshnood B, Greenlees R, Loane M, et al. 2011. Paper 2: EUROCAT public health indicators for congenital anomalies in Europe. *Birth Defects Research Part A: Clinical and Molecular Teratology*, 91 Suppl 1 S16-22 <http://dx.doi.org/10.1002/bdra.20776>
- Dodge-Khatami A. 2016. Advances and research in congenital heart disease. *Translational Pediatrics*, 5(3) 109-11 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC5035758/>
- Gaynor JW, Stopp C, Wypij D, et al. 2015. Neurodevelopmental outcomes after cardiac surgery in infancy. *Pediatrics*, 135(5) 816-25 <http://dx.doi.org/10.1542/peds.2014-3825>
- Andersson IM, Christensson K, Gemzell-Danielsson K. 2014. Experiences, feelings and thoughts of women undergoing second trimester medical termination of pregnancy. *PLoS One*, 9(12) e115957 <http://dx.doi.org/10.1371/journal.pone.0115957>
- Arroll N, Farquhar C, Sadler L, et al. 2013. Can we improve the prevention and detection of congenital abnormalities? An audit of early pregnancy care in New Zealand. *New Zealand Medical Journal*, 126(1380) <https://www.nzma.org.nz/journal/read-the-journal/all-issues/2010-2019/2013/vol-126-no-1380/article-arroll>
- Royal College of Obstetricians and Gynaecologists working party. 2010. Termination of pregnancy for fetal abnormality in England, Scotland and Wales. London: Royal College of Obstetricians and Gynaecologists. <https://www.rcog.org.uk/globalassets/documents/guidelines/terminationpregnancyreport18may2010.pdf>

## References

1. World Health Organization. 2016. Congenital anomalies fact sheet <http://www.who.int/mediacentre/factsheets/fs370/en/> accessed November, 2016
2. Slavotinek A, Ali M. 2015. Recognizable syndromes in the newborn period. *Clinics in Perinatology*, 42(2) 263-80, viii. <http://dx.doi.org/10.1016/j.clp.2015.02.003>
3. Dolk H, Loane M, Garne E. 2010. The prevalence of congenital anomalies in Europe. *Advances in Experimental Medicine and Biology*, 686 349-64. [http://dx.doi.org/10.1007/978-90-481-9485-8\\_20](http://dx.doi.org/10.1007/978-90-481-9485-8_20)
4. Chaabane S, Berard A. 2013. Epidemiology of major congenital malformations with specific focus on teratogens. *Current Drug Safety*, 8(2) 128-40.
5. Moore KL, Persaud TVM. 2008. Human birth defects. Before we are born: Essentials of embryology and birth defects. 7 th ed. Philadelphia, PA: Saunders Elsevier.
6. Ornoy A, Reece EA, Pavlinkova G, et al. 2015. Effect of maternal diabetes on the embryo, fetus, and children: Congenital anomalies, genetic and epigenetic changes and developmental outcomes. *Birth Defects Research Part C: Embryo Today: Reviews*, 105(1) 53-72. <http://dx.doi.org/10.1002/bdrc.21090>
7. Springett A, Budd J, Draper E, et al. 2014. Congenital anomaly statistics 2012. England and Wales [http://www.binocar.org/content/Annual%20report%202012\\_FINAL\\_nologo.pdf](http://www.binocar.org/content/Annual%20report%202012_FINAL_nologo.pdf) accessed September, 2016
8. Rossi AC, Prefumo F. 2013. Accuracy of ultrasonography at 11-14 weeks of gestation for detection of fetal structural anomalies: a systematic review. *Obstetrics & Gynecology*, 122(6) 1160-7. <http://dx.doi.org/10.1097/AOG.0000000000000015>
9. National Collaborating Centre for Women's and Children's Health. 2008. Antenatal care: Routine care for the healthy pregnant woman. London: RCOG Press. <http://www.nice.org.uk/nicemedia/live/11947/40145/40145.pdf>
10. Reddy UM, Abuhamad AZ, Levine D, et al. 2014. Fetal imaging: Executive summary of a joint Eunice Kennedy Shriver National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Institute of Ultrasound in Medicine, American College of Obstetricians and Gynecologists, American College of Radiology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound Fetal Imaging Workshop. *Journal of Ultrasound in Medicine*, 33(5) 745-57. <http://dx.doi.org/10.7863/ultra.33.5.745>
11. Mersy E, Smits LJ, van Winden LA, et al. 2013. Noninvasive detection of fetal trisomy 21: systematic review and report of quality and outcomes of diagnostic accuracy studies performed between 1997 and 2012. *Human Reproduction Update*, 19(4) 318-29. <http://dx.doi.org/10.1093/humupd/dmt001>

12. Hixson L, Goel S, Schuber P, et al. 2015. An overview on prenatal screening for chromosomal aberrations. *Journal of Laboratory Automation*, 20(5) 562-73. <http://dx.doi.org/10.1177/2211068214564595>
13. Massie J, Ioannou L, Delatycki M. 2014. Prenatal and preconception population carrier screening for cystic fibrosis in Australia: where are we up to? *The Australian & New Zealand Journal Of Obstetrics & Gynaecology*, 54(6) 503-9. <http://dx.doi.org/10.1111/ajo.12255>
14. The Human Genetics Society of Australasia. 2013. Population-based carrier screening for cystic fibrosis. <http://www.hgsa.org.au/documents/item/1282>
15. Gaskin KJ. 2013. Nutritional care in children with cystic fibrosis: are our patients becoming better? *European Journal of Clinical Nutrition*, 67(5) 558-64. <http://dx.doi.org/10.1038/ejcn.2013.20>
16. De-Regil Luz M, Peña-Rosas Juan P, Fernández-Gaxiola Ana C, et al. 2015. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database of Systematic Reviews*, (12) <http://dx.doi.org/10.1002/14651858.CD007950.pub3>
17. Simeone RM, Devine OJ, Marcinkevage JA, et al. 2015. Diabetes and congenital heart defects: a systematic review, meta-analysis, and modeling project. *American Journal of Preventive Medicine*, 48(2) 195-204. <http://dx.doi.org/10.1016/j.amepre.2014.09.002>
18. Eckersley L, Sadler L, Parry E, et al. 2015. Timing of diagnosis affects mortality in critical congenital heart disease. *Archives of Disease in Childhood*, 101 516–20. <http://dx.doi.org/10.1136/archdischild-2014-307691>
19. Sanapo L, Moon-Grady AJ, Donofrio MT. 2016. Perinatal and delivery management of infants with congenital heart disease. *Clinics in Perinatology*, 43(1) 55-71. <http://dx.doi.org/10.1016/j.clp.2015.11.004>
20. Wahabi HA, Alzeidan RA, Bawazeer GA, et al. 2010. Preconception care for diabetic women for improving maternal and fetal outcomes: a systematic review and meta-analysis. *BMC Pregnancy Childbirth*, 10 63. <http://dx.doi.org/10.1186/1471-2393-10-63>
21. Pollak A, Kasper DC. 2014. Austrian Newborn Screening Program: a perspective of five decades. *Journal of Perinatal Medicine*, 42(2) 151-8. <http://dx.doi.org/10.1515/jpm-2013-0113>
22. Wilcken B, Wiley V. 2008. Newborn screening. *Pathology*, 40(2) 104-15. <http://dx.doi.org/10.1080/00313020701813743>
23. Nikolopoulos TP. 2015. Neonatal hearing screening: what we have achieved and what needs to be improved. *Journal of Pediatric Otorhinolaryngology*, 79(5) 635-7. <http://dx.doi.org/10.1016/j.jiporl.2015.02.010>
24. Colgan S, Gold L, Wirth K, et al. 2012. The cost-effectiveness of universal newborn screening for bilateral permanent congenital hearing impairment: systematic review. *Academic Pediatrics*, 12(3) 171-80. <http://dx.doi.org/10.1016/j.acap.2012.02.002>
25. Pimperton H, Kennedy CR. 2012. The impact of early identification of permanent childhood hearing impairment on speech and language outcomes. *Archives of disease in childhood - Education & practice edition*, 97(7) 648-53. <http://dx.doi.org/10.1136/archdischild-2011-301501>
26. Ministry of Health. 2016. Folate/folic acid [http://www.health.govt.nz/our-work/preventative-health-wellness/nutrition/folate-folic-acid#current\\_policy](http://www.health.govt.nz/our-work/preventative-health-wellness/nutrition/folate-folic-acid#current_policy) accessed March, 2016.
27. Hackshaw A, Rodeck C, Boniface S. 2011. Maternal smoking in pregnancy and birth defects: a systematic review based on 173 687 malformed cases and 11.7 million controls. *Human Reproduction Update*, 17(5) 589-604. <http://dx.doi.org/10.1093/humupd/dmr022>
28. Riley EP, Infante MA, Warren KR. 2011. Fetal alcohol spectrum disorders: an overview. *Neuropsychology Review*, 21(2) 73-80. <http://dx.doi.org/10.1007/s11065-011-9166-x>
29. Flak AL, Su S, Bertrand J, et al. 2014. The association of mild, moderate, and binge prenatal alcohol exposure and child neuropsychological outcomes: a meta-analysis. *Alcoholism, Clinical and Experimental Research*, 38(1) 214-26. <http://dx.doi.org/10.1111/acer.12214>
30. Popova S, Lange S, Shield K, et al. 2016. Comorbidity of fetal alcohol spectrum disorder: a systematic review and meta-analysis. *The Lancet*, 387(10022) 978-87. [http://dx.doi.org/10.1016/s0140-6736\(15\)01345-8](http://dx.doi.org/10.1016/s0140-6736(15)01345-8)
31. Stothard KJ, Tennant PW, Bell R, et al. 2009. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *JAMA*, 301(6) 636-50. <http://dx.doi.org/10.1001/jama.2009.113>
32. Rasmussen SA, Chu SY, Kim SY, et al. 2008. Maternal obesity and risk of neural tube defects: a metaanalysis. *American Journal of Obstetrics and Gynecology*, 198(6) 611-9. <http://dx.doi.org/10.1016/j.ajog.2008.04.021>
33. Gilboa SM, Correa A, Botto LD, et al. 2010. Association between prepregnancy body mass index and congenital heart defects. *American journal of Obstetrics and Gynecology*, 202(1) 51 e1-51 e10. <http://dx.doi.org/10.1016/j.ajog.2009.08.005>



34. Dashe J S, McIntire D D, Twickler D M. 2009. Effect of maternal obesity on the ultrasound detection of anomalous fetuses. *Obstetrics & Gynecology*, 113(5) 1001–07.
35. Aagaard-Tillery KM, Flint Porter T, Malone FD, et al. 2010. Influence of maternal BMI on genetic sonography in the FaSTER trial. *Prenatal Diagnosis*, 30(1) 14-22. <http://dx.doi.org/10.1002/pd.2399>
36. Confidential Enquiry into Maternal and Child Health (CEMACH). 2005. Pregnancy in women with type 1 and type 2 diabetes in 2002-2003, England Wales and Northern Ireland. London: CEMACH. <http://www.bathdiabetes.org/resources/254.pdf>
37. Ostrer H. 2016. Genetic and environmental causes of birth defects. In Barbieri R L (Ed.), UpToDate®. Waltham, MA (cited March, 2016).
38. Mody R M. 2014. Lymphocytic choriomeningitis epidemiology. Medscape. <http://emedicine.medscape.com/article/220796-overview#a6>
39. Centers for Disease Control and Prevention. 2016. Preventing infections in pregnancy <http://www.cdc.gov/pregnancy/infections.html> accessed March, 2016.
40. Centers for Disease Control and Prevention. 2016. All countries and territories with active Zika virus transmission <http://www.cdc.gov/zika/geo/active-countries.html> accessed March, 2016.
41. Stephens S, Hodson K, Thomas SHL. 2009. Prescribing in pregnancy. *Medicine*, 37(9) 500-05. <http://dx.doi.org/10.1016/j.mpmed.2009.03.010>
42. van Gelder MMHJ, de Jong-van den Berg LTW, Roeleveld N. 2014. Drugs associated with teratogenic mechanisms. Part II: a literature review of the evidence on human risks. *Human Reproduction*, 29(1) 168-83. <http://dx.doi.org/10.1093/humrep/det370>
43. Centers for Disease Control and Prevention. 2015. Make a PACT for prevention. Commit to healthy choices to help prevent birth defects <http://www.cdc.gov/ncbddd/birthdefects/prevention.html> accessed May, 2016.
44. Ministry of Health. 2016. Folic acid, iodine and vitamin D <http://www.health.govt.nz/your-health/pregnancy-and-kids/pregnancy/helpful-advice-during-pregnancy/folic-acid-iodine-and-vitamin-d> accessed November, 2016.
45. West Coast DHB. Pregnant? 5 things to do within the first 10 weeks. <http://www.westcoastdhb.org.nz/publications/services/maternity/im-pregnant-what-next/5-things-to-do-within-first-10-weeks-poster.pdf>
46. Mateus T, Silva J, Maia RL, et al. 2013. Listeriosis during pregnancy: A public health concern. *ISRN Obstetrics and Gynecology*, 2013 851712. <http://dx.doi.org/10.1155/2013/851712>
47. Ministry of Health. 2016. Listeria <http://www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/food-and-water-borne-diseases/listeria> accessed May, 2016.
48. Ministry of Health. 2015. Screening tests and scans: week 14–30 <http://www.health.govt.nz/your-health/pregnancy-and-kids/pregnancy/weeks-14-30/screening-tests-and-scans-week-14-30> accessed November, 2016.
49. National Collaborating Centre for Women's and Children's Health. 2008. Antenatal Care: Routine care for the healthy pregnant woman. NICE Clinical Guidelines, No. 62. London: RCOG Press. <https://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0009601>
50. Bricker L, Garcia J, Henderson J, et al. 2000. Ultrasound screening in pregnancy: a systematic review of the clinical effectiveness, cost-effectiveness and women's views. *Health Technology Assessment*, 4(16) i-vi, 1-193. <http://dx.doi.org/10.3310/hta4160>
51. Farquar C, Arroll N, Sadler L, et al. 2013. Improving quality and safety in maternity services: can we improve prevention, detection and management of congenital abnormalities in pregnancy? Wellington: Health Quality and Safety Commission of New Zealand. <https://www.hqsc.govt.nz/assets/Other-Topics/QS-challenge-reports/Detecting-abnormalities-earlier-in-pregnancy-Final-Report.pdf>
52. Chandrasekharan, Subhashini, Minear MA, Hung A, et al. 2014. Noninvasive prenatal testing goes global. *Science Translational Medicine*, 6(231) 231fs15-31fs15. <http://dx.doi.org/10.1126/scitranslmed.3008704>
53. Taylor-Phillips S, Freeman K, Geppert J, et al. 2016. Accuracy of non-invasive prenatal testing using cell-free DNA for detection of Down, Edwards and Patau syndromes: a systematic review and meta-analysis. *BMJ Open*, 6(1) e010002. <http://dx.doi.org/10.1136/bmjopen-2015-010002>
54. National Screening Unit. 2013. Position statement on non-invasive prenatal testing. [https://www.nsu.govt.nz/system/files/page/nipt\\_revised\\_statement.pdf](https://www.nsu.govt.nz/system/files/page/nipt_revised_statement.pdf)
55. EUROCAT. Perinatal mortality associated with congenital anomalies in EUROCAT full member registries, 2008-2012, by type of anomaly <http://www.eurocat-network.eu/content/EUROCAT-Perinatal-Mortality-Table-1v.pdf> accessed November, 2016.
56. Mahle WT, Newburger JW, Matherne GP, et al. 2009. Role of pulse oximetry in examining newborns for congenital heart disease: a scientific statement from the American Heart Association and American

- Academy of Pediatrics. *Circulation*, 120(5) 447-58.  
<http://dx.doi.org/10.1161/circulationaha.109.192576>
57. Eckersley L, Sadler L, Parry E, et al. 2016. Timing of diagnosis affects mortality in critical congenital heart disease. *Archives of Disease in Childhood*, 101(6) 516-20.  
<http://dx.doi.org/10.1136/archdischild-2014-307691>
58. Starship clinical guidelines. 2016. Pulse oximetry screening in the newborn  
<https://www.starship.org.nz/for-health-professionals/starship-clinical-guidelines/p/pulse-oximetry-screening-in-the-newborn/> accessed November, 2016.
59. Starship Foundation. 2016. Newborn pulse oximetry trial  
<https://www.starship.org.nz/foundation/latest-news/newborn-pulse-oximetry-trial/> accessed November, 2016.