DOWN SYNDROME

Introduction

Down syndrome is the most common chromosomal anomaly in newborn babies and it results from extra genetic material from chromosome 21. In around 95% of cases there is an extra copy of chromosome 21 (Trisomy 21) and in about 4% there are 46 chromosomes as usual, but there is a translocation between chromosome 21q and another chromosome (usually chromosome 14 or 22). The risk of having a child with Trisomy 21, but not translocation Down syndrome, rises steeply with maternal age. There is a relatively high recurrence risk for translocation Down syndrome when a parent, especially the mother, is a carrier of the translocation [1].

In New Zealand, between 50 and 80 babies with Down syndrome are born each year [2]. Worldwide the incidence of Down syndrome is around 1 per 1,000 live births, with variations from country to country depending largely on average maternal age and attitudes to prenatal testing and termination [3].

In New Zealand, the Ministry of Health requires that all pregnant women be informed about antenatal screening for Down syndrome and that practitioners support and respect women's screening choices [4]. The antenatal screening guidelines published by the National Screening Unit recommend that women presenting in their first trimester be offered a nuchal translucency scan, plus a blood test measuring two maternal serum markers, while women who present later, be offered a blood test measuring four serum markers [4]. Women whose test results indicate an increased risk (> 1 in 300) are offered referral for more definitive testing [4].

Children born with Down syndrome usually have a distinctive facial appearance, low muscle tone and delayed development. They are at risk of a number of medical problems including hearing loss (75%), vision problems (severe refractive errors in 50% and cataracts in 15%), obstructive sleep apnoea (50–75%), congenital heart defects (50%), gastrointestinal atresias (12%), thyroid disease (4–18%) and seizures (1–13%) [5]. There are a number of guidelines on the clinical care of children with Down syndrome [3,5,6,7], including one from the Ministry of Health [8]. They suggest that in addition to continuing surveillance for medical, dental, developmental and behavioural problems, children with Down syndrome and their families also require a range of special education and disability support services.

The following section uses the National Minimum Dataset to review the number of babies born with Down syndrome. The section concludes with a brief overview of local policy documents and evidence-based reviews which are of relevance in this context.

Data Source and Methods

Definition

1. *Number of chromosomal anomalies identified at birth (by anomaly type)*

2. *Number of babies with Down syndrome identified at birth*

Data Source

1. National Minimum Dataset

Numerator: Hospital admissions with event type = birth and a chromosomal anomaly (ICD-10 Q90–Q99) listed in any of the first 15 diagnoses.

For this indicator, the unit of analysis is the number of chromosomal anomalies rather than the number of babies. Specific anomalies include: Down Syndrome (Q90), Edwards and Patau Syndromes (Q91), Other Autosomal Trisomies (Q92), Monosomies and Autosomal Deletions/Other Rearrangements (Q93, Q95), Turners Syndrome (Q96), Other Sex Chromosome Anomalies Female Phenotype (Q97), Sex Chromosome Anomalies Male Phenotype (Q98), Other Chromosome Anomalies (Q99)

2. National Minimum Dataset

Numerator: Hospital admissions with event type = birth and Down syndrome (Q90) listed in any of the first 15 diagnoses.

For this indicator, the unit of analysis is the number of babies with Down syndrome identified at birth.

Denominator: All hospital admissions with event type = birth

Notes on Interpretation

Note: This analysis includes all admissions in the National Minimum Dataset (NMDS) where the Event Type was listed as Birth. In the NMDS only one birth event is allowed per NHI number, with admissions for babies born prior to hospital admission, or readmitted shortly after discharge being listed as a routine inpatient event. Thus the analysis does not include babies born prior to hospital admission, babies born at home, or babies whose Down syndrome was overlooked at the time of discharge, but who re-presented shortly thereafter.

New Zealand Distribution and Trends

Chromosomal Anomalies Evident at Birth

In New Zealand during 2008–2012, Down syndrome was the most frequent chromosomal anomaly identified at birth, accounting for 65.6% of the chromosomal anomalies identified during this period. Such figures however, may significantly underestimate the prevalence of chromosomal anomalies, as in the absence of karyotyping, many anomalies (e.g. sex chromosome anomalies) may be undetectable by routine newborn examination (**Table 1**).

Table 1. Chromosomal Anomalies Evident at Birth, New Zealand 2008–2012

Chromosomal Anomaly	Number: Total 2008−2012	Number: Annual Average	Anomalies per 100,000 Births*
New Zealand			
Down Syndrome	257	51.4	85.01
Edwards and Patau Syndromes	40	8.0	13.23
Other Autosomal Trisomies	15	3.0	4.96
Turners Syndrome	10	2.0	3.31
Sex Chromosome Anomalies Male Phenotype	12	2.4	3.97
Monosomies/Autosomal Deletions/Other Rearrangements	25	5.0	8.27
Other Chromosome Anomalies	33	6.6	10.91
Total Chromosomal Anomalies	392	78.4	129.66

Source: National Minimum Dataset: Numerator: Hospitalisations with event type = birth and a chromosomal anomaly in any of first 15 diagnoses; Denominator: Hospitalisations with event type = birth; Note: *Anomalies per 100,000 births = number of anomalies rather than number of babies, as some babies have >1 anomaly

Babies with Down Syndrome and Other Congenital Anomalies

In New Zealand during 2008–2012, 45.9% of babies with Down syndrome identified at the time of birth had one or more co-existing cardiovascular anomalies, with the most frequent being patent ductus arteriosus and atrial septal defects. A smaller proportion had anomalies of other organ systems (**Table 2**).

New Zealand Trends

In New Zealand during 2000–2012, on average 53 babies per year were identified as having Down syndrome at the time of birth, with numbers fluctuating during this period (**Figure 1**).

Distribution by Maternal Age

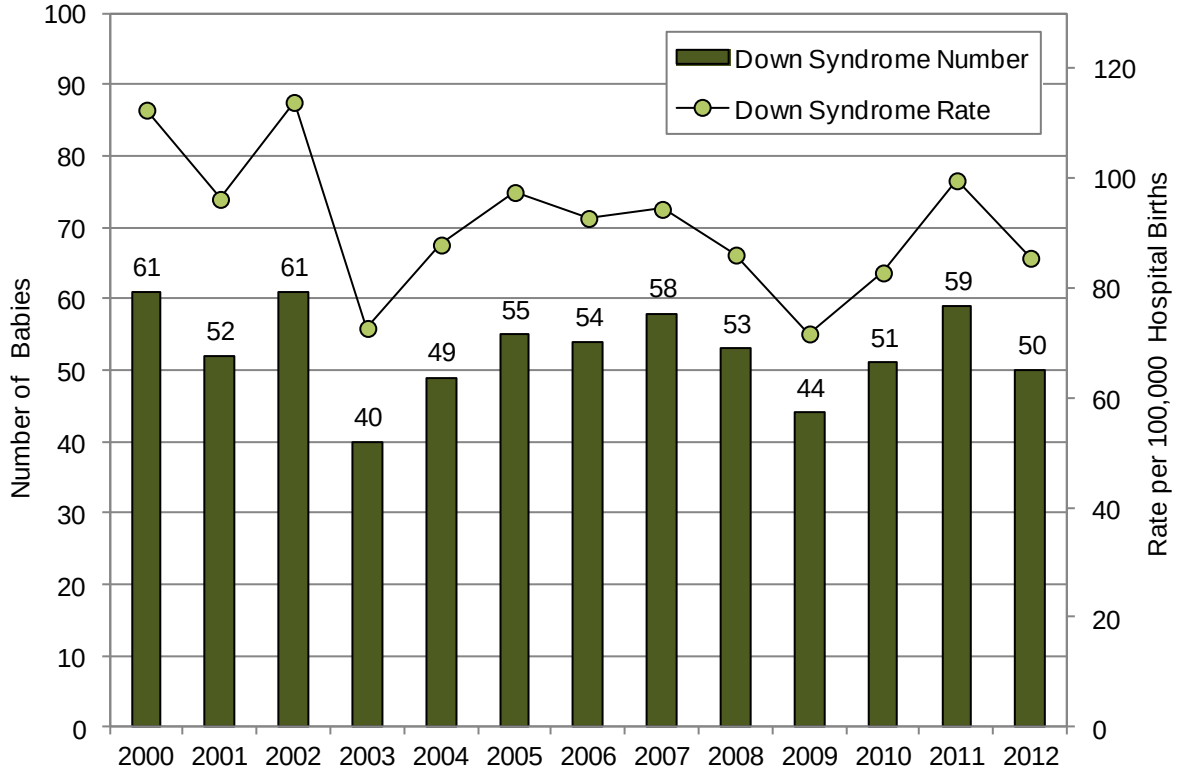
In New Zealand during 2008–2012, while the largest absolute number of babies with Down syndrome were born to women aged 35–39 years, Down syndrome rates rose exponentially with increasing maternal age, with the highest rates being seen in the babies of mothers aged 40+ years (**Figure 2**).

Table 2. Babies with Down Syndrome who also had Other Congenital Anomalies Evident at Birth, New Zealand Hospital Births 2008–2012

Congenital Anomaly	Number: Total 2008−2012	% of Babies with Down Syndrome
Babies with Down Syndrome (n=257)		
One or more Malformations of the Nervous System	4	1.6
One or more Malformations of Eye, Ear, Face and Neck	9	3.5
One or more Malformations of the Circulatory System*	118	45.9
One or more Malformations of the Respiratory System	5	1.9
One or more Other Malformations of the Digestive System	18	7.0
One or more Malformations of the Genital Organs	8	3.1
One or more Malformations of the Urinary System	3	1.2
One or more Malformations of the Musculoskeletal System	13	5.1
One or more Other Congenital Malformations	5	1.9
*Babies with Down Syndrome and a Circulatory System Anomaly (n= 118)		
Ventricular Septal Defect	19	7.4
Atrial Septal Defect	55	21.4
Atrioventricular Septal Defect	24	9.3
Tetralogy of Fallot	5	1.9
One or more Pulmonary/Tricuspid Valve Malformations	5	1.9
One or more Aortic/Mitral Valve Malformations	3	1.2
One or more Other Heart Malformations	7	2.7
Patent Ductus Arteriosus (PDA)	56	21.8
One or more Malformations Great Arteries (Excluding PDA)	8	3.1
One or more Other Circulatory Malformations	<3	s

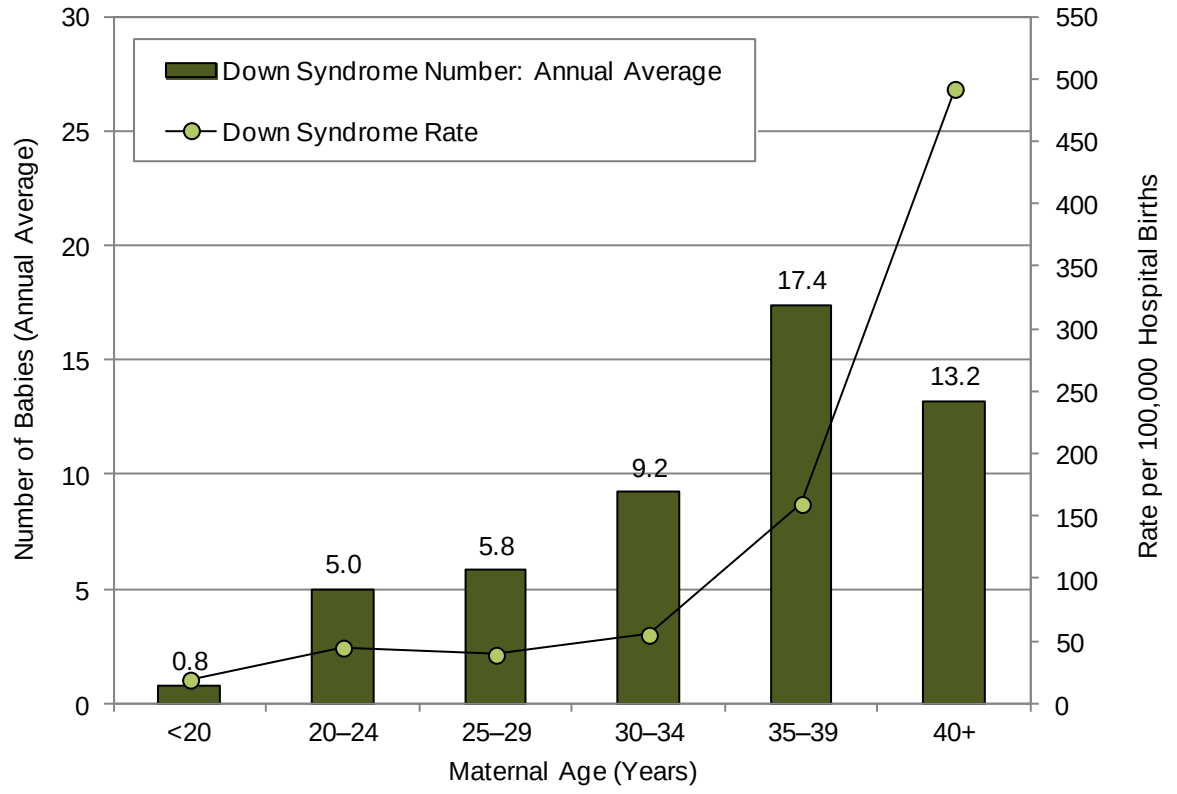
Source: National Minimum Dataset: Numerator: Hospitalisations with event type = birth and Down syndrome listed in any of the first 15 diagnoses, plus another congenital anomaly listed in first 15 diagnoses; Denominator: All hospitalisations with event type = birth and Down syndrome listed in any of the first 15 diagnoses; Note: Numbers and percentages do not sum to 100%, as some babies have more than one anomaly for each of the systems listed; s: suppressed due to small numbers

Figure 1. Babies with Down Syndrome Evident at Birth, New Zealand Hospital Births 2000–2012



Source: National Minimum Dataset: Numerator: Hospitalisations with event type = birth and Down syndrome listed in any of first 15 diagnoses; Denominator: All hospitalisations with event type = birth

Figure 2. Babies with Down Syndrome Evident at Birth by Maternal Age, New Zealand Hospital Births 2008–2012



Source: National Minimum Dataset: Numerator: Hospitalisations with event type = birth and Down syndrome listed in any of first 15 diagnoses; Denominator: All hospitalisations with event type = birth

Distribution by Prioritised Ethnicity, NZDep Index Decile and Gender

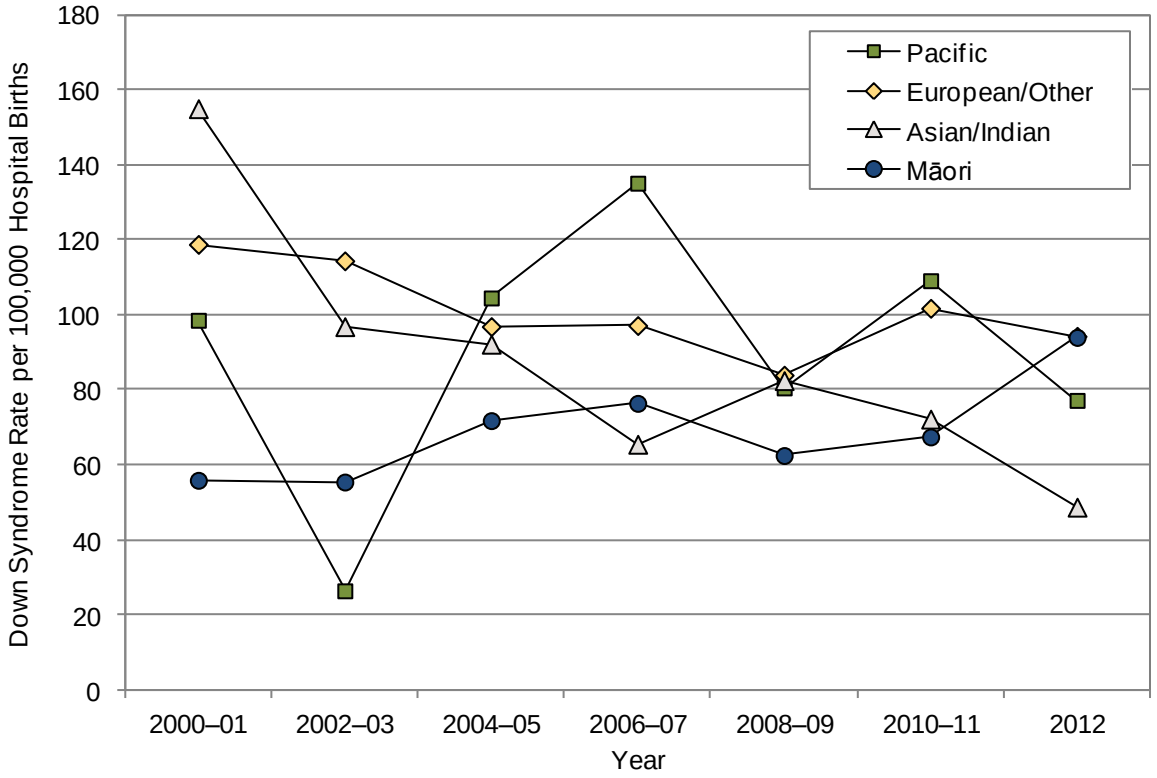
In New Zealand during 2008–2012, there were no statistically significant socioeconomic, (as measured by NZDep06 quintile), ethnic or gender differences in the proportion of babies identified with Down syndrome at the time of birth. Rates however, were *significantly* higher for the babies of older women, with rates for the babies of mothers aged 40+ years being 25.68 (95% CI 9.36–70.45) times higher than for the babies of teenage mothers (**Table 3**). During 2000–2012, large variations in rates (possibly as the result of small numbers) made ethnic specific trends difficult to interpret, although rates were generally lower for Māori, than for European babies, for the majority of this period (**Figure 3**).

Table 3. Babies with Down Syndrome Evident at Birth by Ethnicity, NZ Deprivation Index Decile, Gender and Maternal Age, New Zealand Hospital Births 2008–2012

Variable	Number of Babies: Annual Average	Rate per 100,000 Births	Rate Ratio	95% CI
Down Syndrome				
Prioritised Ethnicity				
Māori	9.4	70.45	0.76	0.55–1.05
Pacific	6.2	91.44	0.98	0.67–1.45
European/Other	30.8	92.89	1.00	
Asian/Indian	4.8	70.16	0.76	0.49–1.16
NZ Deprivation Index				
Deciles 1–2	8.0	94.29	1.00	
Deciles 3–4	8.2	90.92	0.96	0.62–1.49
Deciles 5–6	8.2	72.79	0.77	0.50–1.19
Deciles 7–8	11.6	82.23	0.87	0.58–1.30
Deciles 9–10	15.2	86.79	0.92	0.63–1.35
Gender				
Female	22.8	77.57	1.00	
Male	28.6	92.06	1.19	0.93–1.52
Maternal Age				
<20 Years	0.8	19.16	1.00	
20–24 Years	5.0	44.78	2.34	0.81–6.71
25–29 Years	5.8	39.08	2.04	0.72–5.80
30–34 Years	9.2	55.06	2.87	1.03–7.98
35–39 Years	17.4	159.76	8.34	3.06–22.71
40+ Years	13.2	492.17	25.68	9.36–70.45

Source: National Minimum Dataset: Numerator: Hospitalisations with event type = birth and Down syndrome listed in any of first 15 diagnoses; Denominator: All hospitalisations with event type = birth; Note: Rate Ratios are unadjusted

Figure 3. Babies with Down Syndrome Evident at Birth by Ethnicity, New Zealand Hospital Births 2000–2012



Source: National Minimum Dataset: Numerator: Hospitalisations with event type = birth and Down syndrome listed in any of first 15 diagnoses; Denominator: All hospitalisations with event type = birth; Note: Ethnicity is Level 1 Prioritised

South Island DHBs Distribution

South Island DHBs Distribution

During 2008–2012, 4 Nelson Marlborough, <3 South Canterbury, 23 Canterbury, 4 West Coast, 11 Otago and 8 Southland babies were identified as having Down syndrome at the time of birth, with a small number of babies also having other chromosomal anomalies. The proportion of babies with Down syndrome in each of the South Island DHBs/areas was not *significantly* different from the New Zealand rate (**Table 4**, **Table 5**).

Table 4. Babies with Down Syndrome Evident at Birth, South Island DHBs vs. New Zealand Hospital Births 2008–2012

DHB/Area	Number: Total 2008−2012	Number: Annual Average	Rate per 100,000 Births	Rate Ratio	95% CI
Down Syndrome					
Nelson Marlborough	4	0.8	50.98	0.60	0.22–1.61
South Canterbury	<3	s	s	s	s
Canterbury	23	4.6	75.80	0.89	0.58–1.37
West Coast	4	0.8	217.39	2.56	0.95–6.86
Otago	11	2.2	114.79	1.35	0.74–2.47
Southland	8	1.6	104.59	1.23	0.61–2.49
New Zealand	257	51.4	85.01	1.00	

Source: National Minimum Dataset: Numerator: Hospitalisations with event type = birth and Down syndrome listed in any of first 15 diagnoses; Denominator: All hospitalisations with event type = birth; Note: Rate Ratios are compared to New Zealand rates and have not been adjusted for population demographics; s: suppressed due to small numbers

Table 5. Chromosomal Anomalies Evident at Birth, South Island DHBs 2008–2012

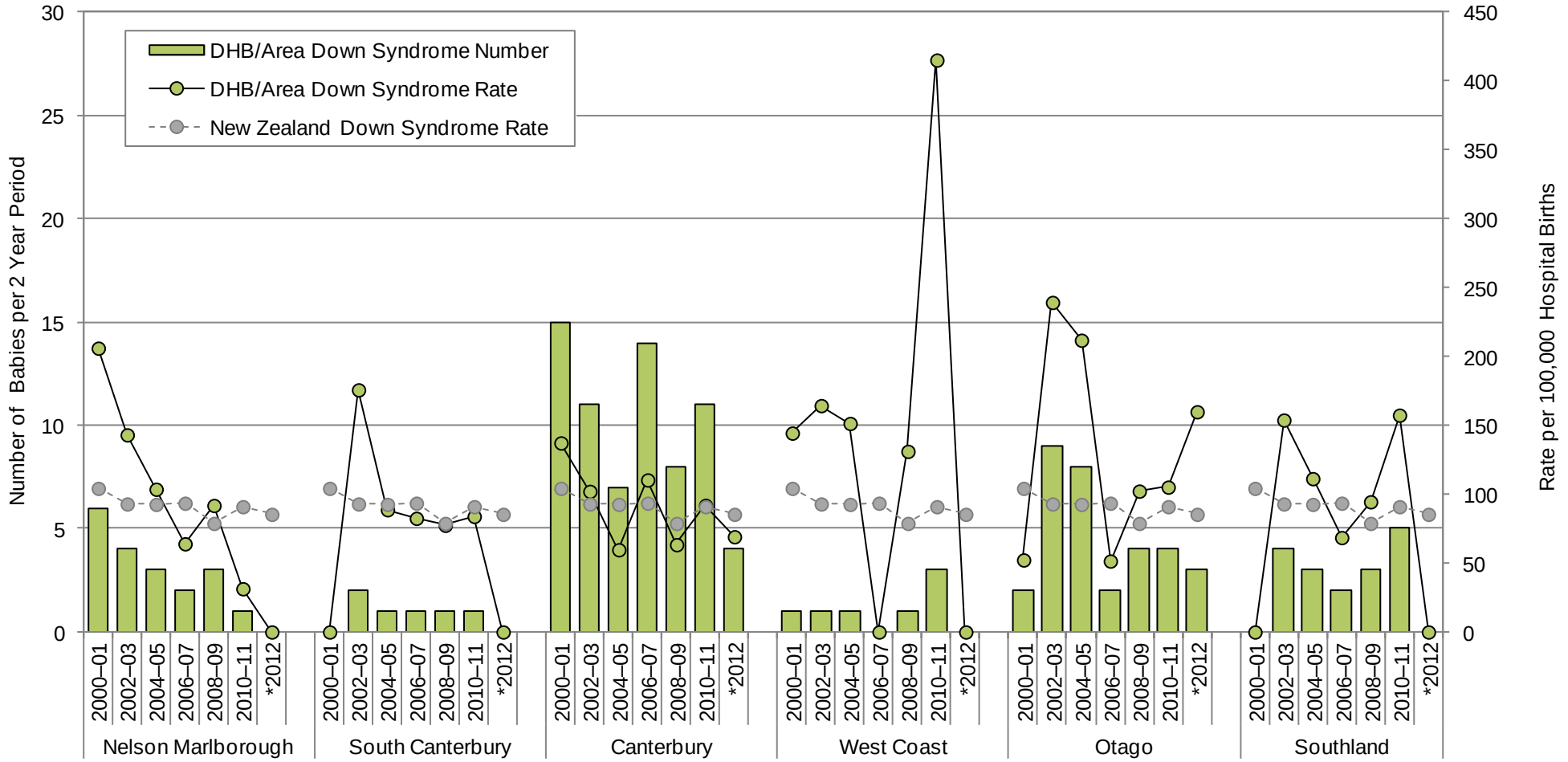
Chromosomal Anomaly	Number: Total 2008−2012	Number: Annual Average	Number of Anomalies per 100,000 Births*
Nelson Marlborough			
Down Syndrome	4	0.8	50.98
Other Chromosomal Anomalies	5	1.0	63.74
Total Chromosomal Anomalies	9	1.8	114.72
South Canterbury			
Down Syndrome	<3	s	s
Other Chromosomal Anomalies	<3	s	s
Total Chromosomal Anomalies	4	0.8	128.75
Canterbury			
Down Syndrome	23	4.6	75.80
Edwards and Patau Syndromes	3	0.6	9.89
Turners Syndrome/Other Female Chromosome Anomalies	4	0.8	13.18
Monosomies/Autosomal Deletions/Rearrangements	3	0.6	9.89
Other Chromosomal Anomalies	5	1.0	16.48
Total Chromosomal Anomalies	38	7.6	125.24
West Coast			
Down Syndrome	4	0.8	217.39
Other Chromosomal Anomalies	<3	s	s
Total Chromosomal Anomalies	5	1.0	271.74
Otago			
Down Syndrome	11	2.2	114.79
Other Chromosomal Anomalies	5	1.0	52.20
Total Chromosomal Anomalies	16	3.2	166.99
Southland			
Down Syndrome	8	1.6	104.59
Total Chromosomal Anomalies	8	1.6	104.59

Source: National Minimum Dataset: Numerator: Hospitalisations with event type = birth and a chromosomal anomaly in any of the first 15 diagnoses; Denominator: Hospitalisations with event type = birth; Note: *Anomalies per 100,000 births = number of anomalies rather than number of babies, as some babies have >1 anomaly; s: suppressed due to small numbers

South Island DHBs Trends

In the South Island DHBs during 2000–2012, large year to year variations (likely as the result of small numbers) made trends in Down syndrome rates difficult to interpret (**Figure 4**).

Figure 4. Babies with Down Syndrome Evident at Birth, South Island DHBs vs. New Zealand Hospital Births 2000–2012



Source: National Minimum Dataset: Numerator: Hospitalisations with event type = birth and Down syndrome listed in any of first 15 diagnoses; Denominator: All hospitalisations with event type = birth; Note: *Numbers are per 2 year period except for 2012 which is for a single year only

Local Policy Documents and Evidence-Based Reviews Relevant to Down Syndrome and Other Chromosomal Anomalies

In New Zealand there are a number of policy documents relevant to the diagnosis and management of those with Down syndrome. These are summarized in **Table 6,** along with a range of reviews which consider these issues in the overseas context. In addition, **Table 16** (Local Policy Documents and Evidence-Based Reviews Relevant to Antenatal and Newborn Screening) on **Page 81** considers publications relevant to antenatal and newborn screening, while **Table 32** (Local Policy Documents and Evidence-Based Reviews Relevant to Congenital Anomalies) on **Page 105** considers congenital anomalies collectively, and **Table 38** (Policy Documents and Evidence-Based Reviews Relevant to Cardiovascular Anomalies) on **Page 118** considers cardiovascular anomalies, which are known to be much higher in those with Down syndrome.

Table 6. Local Policy Documents and Evidence-Based Reviews Relevant to Down Syndrome and Other Chromosomal Anomalies

New Zealand Policy Documents and Publications
National Screening Unit. 2012. **Antenatal screening for Down syndrome and other conditions: guidelines for health practitioners**. Wellington: Ministry of Health. http://www.nsu.govt.nz/files/ANNB/antenatal_screening_for_down_syndrome_and_other_conditions_guidelines_for_health_practitioners.pdf These guidelines are intended for all practitioners who have involvement in any part of the antenatal screening process for Down syndrome and other conditions. Under the Primary Maternity Services Notice 2007, issued pursuant to section 88 of the New Zealand Public Health and Disability Act 2000, all health practitioners advising women about maternity care are obliged to provide advice about the available screening services that are endorsed by the Ministry of Health, including antenatal screening for Down syndrome and other conditions. The advice must include up to date information about the risks, benefits and harms of screening so that a woman can make an informed choice about whether to participate in screening or not and a woman's choice must be respected. Specific guidelines for first trimester ultrasound reports can be found here: http://www.nsu.govt.nz/health-professionals/3814.aspx.
Antenatal Down Syndrome Advisory Group. **Antenatal Down syndrome screening in New Zealand 2007**. Wellington: National Screening Unit, 2007. http://www.health.govt.nz/system/files/documents/publications/antenatal-down-syndrome-screening-in-nz-2007-apr07.pdf This report reviewed the main issues relating to antenatal screening for Down syndrome and considered possible screening options. The members of the advisory group agreed that the opportunistic screening practice current in 2007 was unsafe, inequitable, not in accord with international best practice and resulted in women unnecessarily being referred for invasive diagnostic tests (chorionic villus sampling and amniocentesis) which have a risk of miscarriage. The members of the group were not able to agree on the best way to proceed with screening. A large majority wished to continue to offer screening and to improve the quality and safety of screening tests by means of a nationally organised screening programme. They offered suggestions on the best practice screening methods in particular situations. A minority of group members did not support the introduction of a national screening programme as they felt it would imply an intention to reduce the incidence of Down syndrome. They considered that the best option was to recommend additional funding for disability support services.
O'Connell R, Stephenson M, Weir R. 2006.**Screening strategies for antenatal Down syndrome screening**. Christchurch: New Zealand Health Technology Assessment (NZHTA). http://www.otago.ac.nz/christchurch/otago014075.pdf (Part 1) http://www.otago.ac.nz/christchurch/otago014076.pdf (Part 2) This literature review was performed at the request of the Ministry of Health to assist with assessing options for antenatal Down syndrome screening and determining whether or not New Zealand should have a national antenatal screening programme. The review appraised the international evidence on screening technologies and strategies. Key results of the literature review are presented under the following headings: Accuracy of screening methods, Difficulties in implementing any screening strategies, Uptake of invasive testing following receipt of screening results, Changes in the rate of invasive testing with the introduction of a screening programme and Rates of fetal loss associated with invasive testing procedures.
Ministry of Health. 2001. **The clinical assessment and management of children, young people and adults with Down syndrome: recommended clinical practice**. Wellington: Ministry of Health. http://www.health.govt.nz/system/files/documents/publications/downssyndrome.pdf This document provides information and guidance on the medical management of Down syndrome throughout the lifespan as well as on therapy, education, vocational and social support for people with Down syndrome and their families. Part 1 provides a general overview of Down syndrome including the major clinical features, incidence, genetics and a brief Māori perspective. Part 2 provides recommendations for care at the various stages of life.

International Guidelines and Systematic and Other Reviews
Alldred SK, Deeks Jonathan J, Guo B, et al. 2012. **Second trimester serum tests for Down's syndrome screening**. Cochrane Database of Systematic Reviews doi:10.1002/14651858.CD009925 (assessed as up to date 31 OCT 2007) http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009925/abstract Amniocentesis and chorionic villus sampling allow definitive antenatal testing for Down syndrome but carry a risk of miscarriage (c. 1%) so these invasive tests are not satisfactory as screening tests in low risk populations. There are a number of biochemical markers in maternal serum for which unusually low or high levels are associated with Down syndrome. The measured marker values can be used individually or in combination with each other together with maternal age to estimate the risk of a fetus having Down syndrome. Where multiple markers are measured risk estimates are calculated by computer software using risk equations that take account of the known correlations between different markers in affected and unaffected populations. This review aimed to estimate and compare the accuracy of second trimester serum markers for detecting Down syndrome. It included 59 studies (342,261 pregnancies including 1,994 with Down syndrome) which were generally of high quality. Fifty four test combinations (of 12 different tests and maternal age) were evaluated. Meta-analysis of 12 frequently evaluated or best performing test combinations indicated that double or triple tests perform significantly better than single marker tests, detecting 6 to 7 out of ten Down syndrome pregnancies with a false positive rate of 5%. Combination tests were significantly less sensitive in women aged over 35 years. Test combinations which included inhibin or four or more markers did not perform significantly better than standard triple tests in direct comparisons.
Audibert F, Gagnon A. 2011. **Prenatal screening for and diagnosis of aneuploidy in twin pregnancies**. J Obstet Gynaecol Can, 33(7), 754-67. http://www.sogc.org/guidelines/documents/gui262CPG1107E.pdf There is a higher risk of chromosomal abnormalities in twin pregnancies, mostly because twin pregnancies are more common in older mothers. Screening for Down syndrome is more complicated in twin pregnancies. Twin pregnancies may be either monozygotic (a single fertilized oocyte splits in two producing genetically identical twins) or dizygotic (when two separate oocytes are fertilized). Dizygotic twins are always dichorionic (a separate placenta for each twin) but monozygotic twins may be either dichorionic (about 33% of cases) or monochorionic (both twins share one placenta, about 66% of cases). Chorionicity has a major impact on the screening process and so needs to be determined by ultrasound in the first trimester. These Canadian guidelines provide evidence-based recommendations on prenatal screening for and diagnosis of fetal aneuploidy (e.g. Down syndrome and trisomy 18) in twin pregnancies. The evidence is graded and the recommendations are classified using criteria adapted from those described in the Canadian Task Force on Preventive Health Care.
Bull M J, the Committee on Genetics. 2011. **Health supervision for children with Down syndrome**. Pediatrics, 128(2), 393-406. http://pediatrics.aappublications.org/content/128/2/393.full.pdf+html The guidelines from the American Academy of Pediatrics are intended for paediatricians who care for children with Down syndrome or may be involved in counselling a pregnant woman who has received a prenatal diagnosis of Down syndrome. They provide recommendations for health supervision at different stages: prenatally, newborn, infancy, early childhood, late childhood, and adolescence to early adulthood. There is a comprehensive list of references and links to resources for parents.
Bryant L, et al. 2010. **Literature survey for the review of Down's syndrome screening policy 2010**. Plymouth, U.K.: Socio-economic Research and Intelligence Observatory, University of Plymouth. http://fetalanomaly.screening.nhs.uk/getdata.php?id=11367 This literature survey was commissioned by the Fetal Anomaly Screening Programme Steering Group (FASPSG) to inform the policy review of Down Syndrome screening in the U.K. taking place in 2010. It covers screening strategies, specific ultrasound features and serum markers, screening between 8 and 10 weeks gestation, and screening for trisomy 13 and trisomy 18 both prior to 14 weeks of gestation and at 18 to 21 weeks (for comparison purposes).
Chitayat D, Wyatt PR, Wilson RD, et al. 2008. **Fragile X testing in obstetrics and gynaecology in Canada**. J Obstet Gynaecol Can, 30(9), 837-46 http://www.sogc.org/guidelines/documents/gui216CPG0809.pdf These concise document prepared by committees of the Society of Obstetricians and Gynaecologists of Canada and the Canadian College of Medical Geneticists provides evidence-based recommendations on screening for Fragile X in women receiving obstetric or gynaecological healthcare. The evidence and the recommendations are graded according to the criteria of the Canadian Taskforce on Preventive Health Care.
Bondy CA, for The Turner Syndrome Consensus Study Group. **Care of girls and women with Turner syndrome: A guideline of the Turner Syndrome Study Group**. Journal of Clinical Endocrinology & Metabolism 2007; 92(1): 10-25. http://pediatrics.aappublications.org/content/123/5/1423.full.pdf+html These guidelines are the result of a meeting of the Turners Syndrome Consensus Study Group (multidisciplinary panel of experts with relevant clinical and research experience) that met in Maryland in April 2006. The group used peer reviewed published information as the basis for its recommendations and expert opinion where evidence was lacking. The guidelines cover genetic, cardiological, growth-related, psychological, gynaecological, and general medical concerns.

Alfirevic Z, Mujezinovic F, Sundberg K. 2003. **Amniocentesis and chorionic villus sampling for prenatal diagnosis**. Cochrane Database of Systematic Reviews doi:10.1002/14651858.CD003252 http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003252/abstract

Fetal cells for genetic testing can be obtained from amniotic fluid or the placenta (chorionic villus tissue). Amniocentesis involves inserting a needle through the abdominal wall to withdraw a sample of amniotic fluid (usually under ultrasound guidance). It is usually done at around 16 weeks' gestation but can be done earlier (at 9–14 weeks). Chorionic villus sampling (CVS) involves aspiration of placental tissue via either a transabdominal or a transcervical approach. It is usually done late in the first trimester. This review assessed the comparative safety and accuracy of second trimester amniocentesis, early amniocentesis, transabdominal and transcervical CVS. Sixteen RCTs were included. One study in a low-risk population (4606 women aged between 25 and 34) found that amniocentesis (compared to routine antenatal care) was associated with an increase of 1% in total pregnancy loss (3.2% vs. 2.2%), which was not statistically significant (1.41; 95% CI 0.99 to 2.00), and an increase in spontaneous miscarriages of 0.8% (2.1% vs. 1.3%) which was statistically significant (RR 1.60; 95% CI 1.02 to 2.52). Compared to second trimester amniocentesis, early amniocentesis is associated with greater total pregnancy loss (RR 1.29; 95% CI 1.03 to 1.61) and a higher number of babies with talipes equinovarus (clubfoot), 1.3% vs. 0.09%. Compared to second trimester amniocentesis, transcervical CVS increased the risk of total pregnancy loss, mainly due to spontaneous miscarriages although there was heterogeneity between studies. The one study that compared second trimester amniocentesis with transabdominal CVS found no significant difference in pregnancy loss rates between the two procedures. Compared to transabdominal CVS, transcervical CVS is more technically demanding and more likely to cause vaginal bleeding immediately after the procedure. The authors were unable to assess the diagnostic accuracies of the various techniques because of incomplete karyotype data in most studies. They concluded that amniocentesis the preferred procedure for second trimester testing and transabdominal CVS is the first choice procedure for testing before 15 weeks gestation.

Other Relevant Publications and Websites

Ministry of Health. 2013. **Antenatal screening and testing for Down syndrome and other conditions in pregnancy**. Wellington: Ministry of Health. https://www.healthed.govt.nz/system/files/resource-files/HE2382_0.pdf

This is a brief publication intended for pregnant women with information about antenatal screening and testing for Down Syndrome and other conditions.

Auckland District Health Board. 2013. **Management of babies with Down syndrome**. www.adhb.govt.nz/newborn/Guidelines/Anomalies/DownSyndrome.htm accessed April 2013.

This webpage provides concise clinical guidelines on the Management of Babies with Down syndrome covering background, assessment in the neonatal period, investigations, referrals and other issues.

2012. **Noninvasive prenatal testing for fetal aneuploidy. Committee Opinion No. 545. American College of Obstetricians and Gynecologists**. Obstet Gynecol, 120, 1532–4. http://www.acog.org/Resources%20And%20Publications/Committee%20Opinions/Committee%20on%20Genetics/Noninvasive%20Prenatal%20Testing%20for%20Fetal%20Aneuploidy.aspx

Maternal serum contains cell free DNA and a small proportion of this is fetal cell free DNA, thought to be derived primarily from the placenta. There is new technology known as massively parallel genomic sequencing which can detect trisomy 21 (Down syndrome), trisomy 13 and trisomy 18 as early as the 10th week of pregnancy via a maternal blood test. This has the advantages of reducing the need for amniocentesis and allowing termination early in pregnancy (if desired). This committee opinion from the American College of Obstetricians and Gynecologists (ACOG) notes the great potential of this technology as a screening tool. It recommends that such testing should not be part of routine antenatal care for low risk women or women with multiple pregnancies because it has not been sufficiently well evaluated in these groups, but offered to women at increased risk of aneuploidy. In these women several large studies have shown detection rates for trisomy 13, trisomy 18, and trisomy 21 of greater than 98% with very low false-positive rates (less than 0.5%). Women at increased risk of aneuploidy include women aged over 35 years, women with suspicious ultrasound findings, women with a previous affected child, and cases where a parent carries a balanced robertsonian translocation with increased risk of trisomy 13 or trisomy 21.The AGOG states that the test can also be used as a follow up test for patients who have abnormal results on current first or second trimester screening tests. It recommends that women with positive cell free DNA test should be referred for genetic counselling and offered invasive testing to confirm the test results (amniocentesis or chorionic villus sampling). This publication includes references to the relevant studies.

The test referred to above is commercially available as **MateriT21 PLUS^{TM}**. Information about the test from Sequenom, the company that developed the test, can be found here: http://www.sequenomcmm.com/Home/Health-Care-Professionals/Trisomy-21/About-the-Test .

The Down's Syndrome Medical Interest Group. http://www.dsmig.org.uk/ accessed April 2013.

The Down's Syndrome Medical Interest Group (DSMIG) is a network of doctors from the UK and the Republic of Ireland who have a specialist interest in Down's syndrome. The DSMIG has produced evidence-based surveillance guidelines for cardiac disease, thyroid dysfunction, hearing and vision disorders, growth and cervical spine instability as well as number of other useful publications. Also on their website is a library of relevant publications from the medical literature.

European Down Syndrome Association. http://www.edsa.eu/index.html accessed April 2013.

Useful publications on this website include:

- EDSA Essentials 2 Health Care Guidelines for People with Down Syndrome
- EDSA Essentials 3 The Person with Down Syndrome: Orientations for Families

Down Syndrome Education International. http://www.dseinternational.org/en-gb/ accessed April 2013

Down Syndrome Education International is a UK-based charity that works to improve education for young people with Down syndrome through scientific research and global information and advice services. It publishes the journal Down Syndrome Research and Practice.

Note: The publications listed were identified using the search methodology outlined in **Appendix 1**

References

1. 2007. Chapter 6 – Clinical Cytogenetics: Disorders of the autosomes and the sex chromosomes. In Nussbaum R L, McInnes R R Willard H F (Eds.), Thompson & Thompson Genetics in Medicine (7th ed.). Philadelphia: Elsevier Saunders.
2. New Zealand Birth Defects Registry. 2013. Liveborn cases of birth defects reported to the New Zealand Birth Defects Registry, 2000–2009. http://nzbdr.ac.nz/assets/FILES/Final%20published%20table%202000-2009.pdf accessed June 2013
3. Weijerman M E, de Winte J P. 2010. Clinical practice: The care of children with Down syndrome. *European Journal of Pediatrics* 169(12) 1445-52.
4. National Screening Unit. 2012. Antenatal screening for Down syndrome and other conditions: Guidelines for health practitioners. Wellington: Ministry of Health http://www.nsu.govt.nz/files/ANNB/antenatal_screening_for_down_syndrome_and_other_conditions_guidelines_for_health_practitioners.pdf
5. Bull M J, the Committee on Genetics. 2011. Health supervision for children with Down syndrome. *Pediatrics* 128(2) 393-406.
6. Davidson MA. 2008. Primary care for children and adolescents with Down syndrome. *Pediatric Clinics of North America* 55(5) 1099-111.
7. The Down Syndrome Medical Interest Group. Guidelines for essential medical surveillance. http://www.dsmig.org.uk/publications/guidelines.html accessed June 2013
8. Ministry of Health. 2001. The clinical assessment and management of children, young people and adults with Down syndrome: recommended clinical practice. Wellington: Ministry of Health http://www.moh.govt.nz/notebook/nbbooks.nsf/0/3B99EDCA116487C4CC256B05006A5346/$file/DownsSyndrome.pdf