PRETERM BIRTH

Introduction

Preterm birth is defined as the birth of a baby prior to 37 weeks completed gestation. It can be further subdivided into moderate/late preterm (32–36 completed weeks), very preterm (28–31 completed weeks) and extremely preterm (less than 28 weeks gestation) birth [1].

Preterm birth is not a single entity, but has a variety of causes (e.g. infections, stress, multiple pregnancy, cervical insufficiency), and pathways (e.g. inflammation, hormone activation, uterine over-distension) [1]. It is traditionally subdivided into three categories: births arising from 1) preterm labour with intact fetal membranes; 2) preterm rupture of the fetal membranes; and 3) iatrogenic preterm birth, where delivery is induced for maternal or fetal reasons [1]. In developed countries, it has been estimated that around 40–45% of preterm births follow preterm labour, 25–40% follow preterm premature rupture of the fetal membranes, and 30–35% are indicated deliveries [1].

Infants born prematurely may experience a range of adverse outcomes. When compared to term infants, preterm infants have higher rates of temperature instability, respiratory distress, infections, apnoea, low blood sugar, jaundice, and feeding difficulties. Preterm birth is also the leading cause of early neonatal death, with the risk increasing with decreasing gestational age [1]. Those born very or extremely prematurely (<32 weeks gestation) are also at an increased risk of developmental disabilities such as cerebral palsy, and intellectual disabilities [2].

Internationally, there have been large increases in preterm birth rates during the past two decades, largely confined to the late preterm (34–36 weeks) category. These increases have been attributed to increasing obstetric intervention, higher rates of twins as a result of assisted reproductive techniques, and delayed childbearing [2]. New Zealand also experienced an increase in preterm birth rates during the 1980s and 1990s, with the most rapid increases occurring amongst those living in the most affluent (NZDep deciles 1–2) areas, and in European/Other women [3,4].

The following section reviews preterm birth rates in the South Island DHBs using information from the Birth Registration Dataset. The section concludes with a brief overview of policy documents and evidence-based reviews which consider how preterm birth might be addressed at the population level.

Data Sources and Methods

Indicator

1. Preterm birth rates per 100 live births in singleton live born babies by gestational age

2. Preterm birth rates per 100 live births in live born babies by plurality (singletons, twins, triplets)

Data Sources

1. Numerator: Birth Registration Dataset: All singleton live born babies 20–36 weeks gestation. Gestational age categories include 20–27 weeks, 28–31 weeks, and 32–36 weeks.

Denominator: Birth Registration Dataset: All singleton live born babies 20+ weeks gestation.

2. Numerator: Birth Registration Dataset: All live born babies 20–36 weeks gestation by plurality (singletons, twins, triplets).

Denominator: Birth Registration Dataset: All live born babies 20+ weeks gestation by plurality.

Notes on Interpretation

Note 1: Year is year of registration, rather than year of birth.

Note 2: See Appendix 4 (The Birth Registration Dataset) for an overview of the Birth Registration Dataset

Note 3: In this analysis, stillborn babies have been excluded due to advice from the Ministry of Health that the Birth Registration dataset provides less reliable information on stillborn babies than the National Mortality Collection.

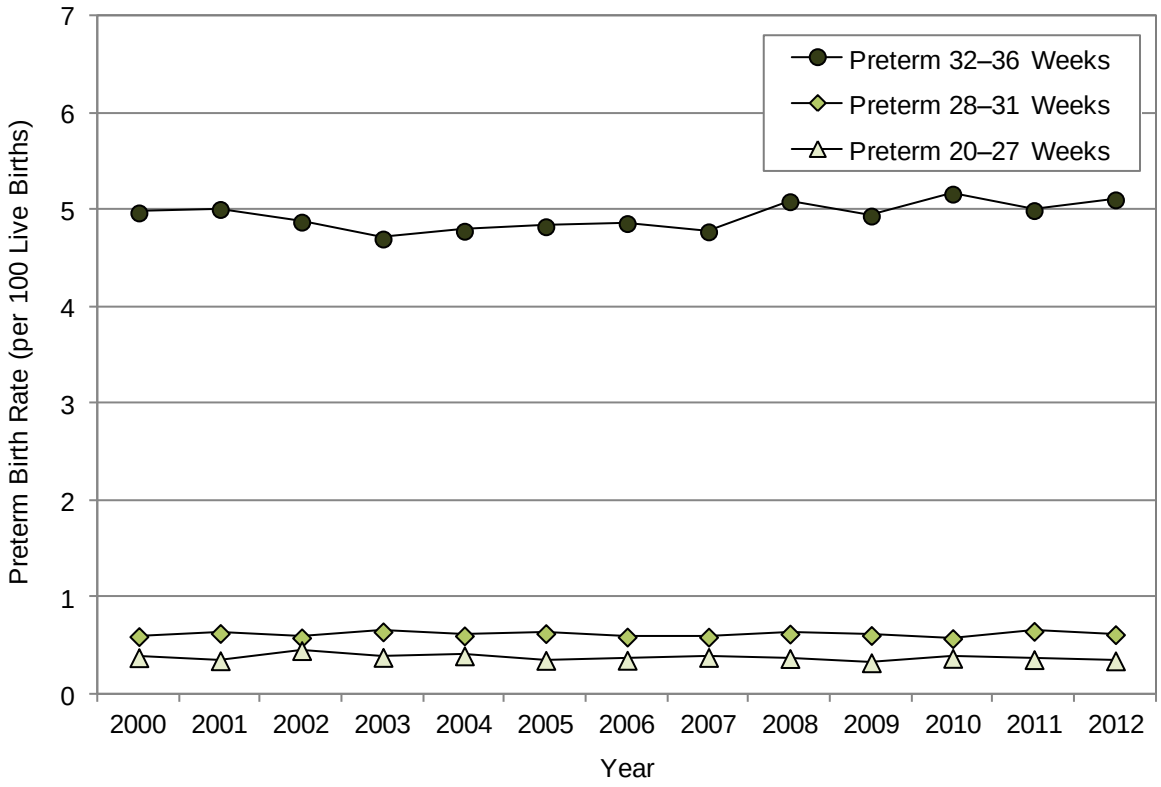
New Zealand Distribution and Trends

Preterm Births in Singleton Pregnancies

New Zealand Trends

Preterm Birth Rates: In New Zealand during 2000–2012, preterm birth rates were relatively static. Rates per 100 live births for those born at 20–27 weeks gestation were 0.38 in 2000 and 0.35 in 2012, while rates for those born at 28–31 weeks were 0.60 in 2000 and 0.62 in 2012, and rates for those born at 32–36 weeks were 5.0 in 2000 and 5.1 in 2012 (**Figure 1**).

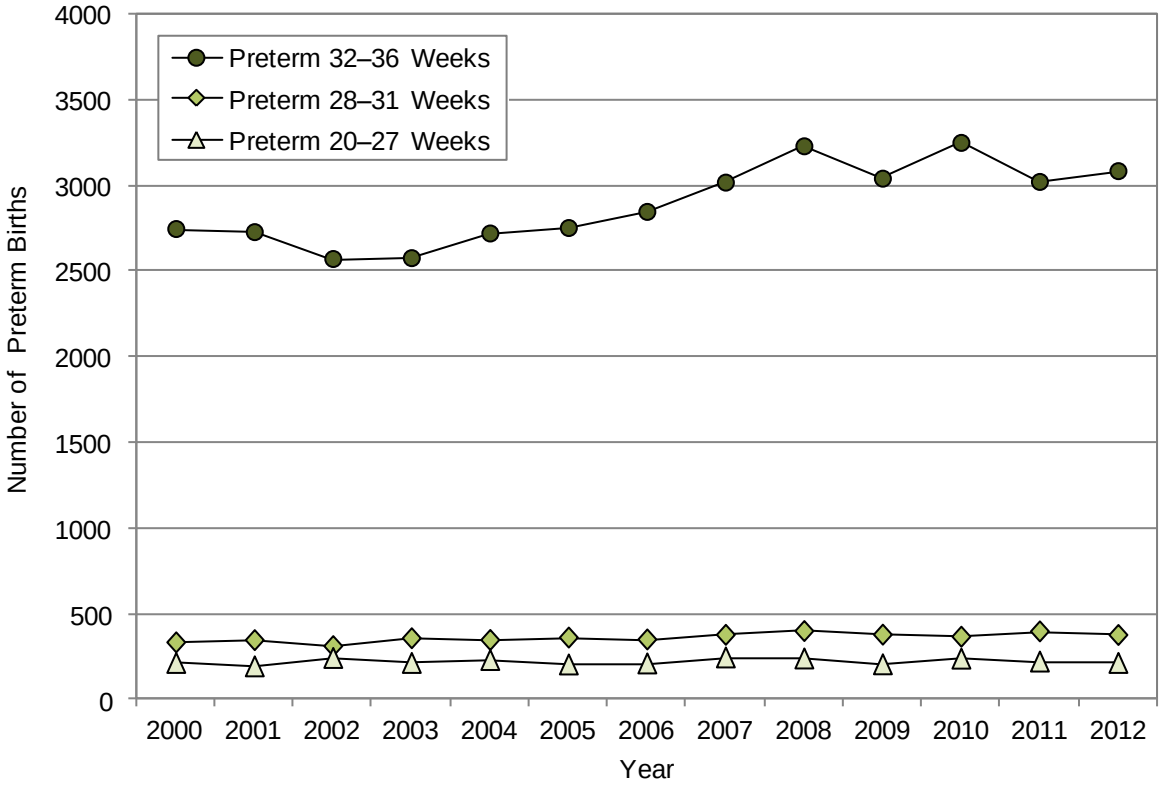
Figure 1. Preterm Birth Rates in Singleton Live Born Babies by Gestational Age, New Zealand 2000–2012



Source: Birth Registration Dataset: Numerator: all singleton live born babies 20–36 weeks gestation; Denominator: all singleton live born babies 20+ weeks gestation

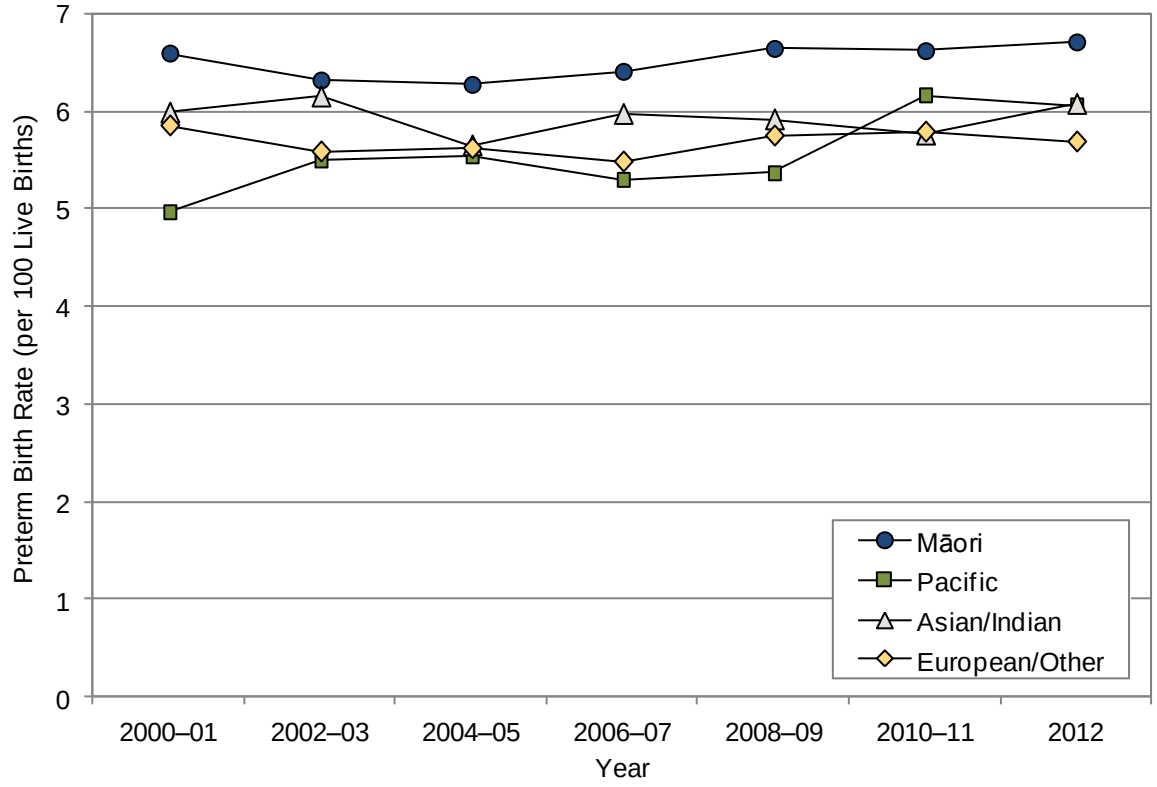
Number of Preterm Births: During the same period however, the actual number of preterm babies born increased, as the result of a rising birth rate, with the majority of this increase occurring between 2003 and 2008. The largest increases were seen in those born at 32–36 weeks, with numbers in this category rising from 2,744 in 2000 to 3,082 in 2012. While the number of babies born at 28–31 weeks gestation also rose, from 331 in 2000 to 374 in 2012, the number of babies born at 20–27 weeks gestation did not change (211 in both 2000 and 2012) (**Figure 2**).

Figure 2. Number of Preterm Births in Singleton Live Born Babies by Gestational Age, New Zealand 2000–2012



Source: Birth Registration Dataset, All singleton live born babies 20–36 weeks gestation

Figure 3. Preterm Birth Rates in Singleton Live Born Babies by Baby's Ethnicity, New Zealand 2000–2012



Source: Birth Registration Dataset: Numerator: All singleton live born babies 20–36 weeks gestation; Denominator: All singleton live born babies 20+ weeks gestation; Note: Ethnicity is Level 1 Prioritised

Distribution by Ethnicity, NZDep Decile, Gender and Maternal Age

All Preterm Births (20–36 Weeks): In New Zealand during 2008–2012, preterm birth rates were *significantly* higher for males and for Māori babies than for Asian/Indian, European/Other and Pacific babies. Rates were also *significantly* higher for those living in more deprived (NZDep deciles 7–10) areas, and for the babies of younger (<25 years) and older (35+ years) mothers, than for the babies of mothers aged 25–29 years (**Table 1**). Similarly, during 2000–2012, preterm birth rates for Māori babies were consistently higher than for Asian/Indian, European/Other and Pacific babies (**Figure 3**).

Table 1. Preterm Birth Rates in Singleton Live Born Babies by Ethnicity, NZ Deprivation Index Decile, Gender and Maternal Age, New Zealand 2008–2012

Variable	Rate	Rate Ratio	95% CI	Variable	Rate	Rate Ratio	95% CI
All Preterm Singletons (20–36 Weeks)							
NZ Deprivation Index Decile				Maternal Age			
Deciles 1–2	5.58	1.00		<20 Years	7.51	1.34	1.26–1.41
Deciles 3–4	5.63	1.01	0.96–1.06	20–24 Years	6.14	1.09	1.05–1.14
Deciles 5–6	5.75	1.03	0.98–1.08	25–29 Years	5.62	1.00	
Deciles 7–8	6.15	1.10	1.05–1.16	30–34 Years	5.65	1.01	0.97–1.05
Deciles 9–10	6.61	1.19	1.13–1.24	35+ Years	6.46	1.15	1.10–1.20
Baby's Ethnicity				Gender			
Asian/Indian	5.89	1.02	0.98–1.07	Female	5.53	1.00	
European/Other	5.76	1.00		Male	6.52	1.18	1.15–1.21
Māori	6.64	1.15	1.12–1.19				
Pacific	5.83	1.01	0.97–1.06				

Source: Birth Registration Dataset: Numerator: All singleton live born babies 20–36 weeks gestation; Denominator: All singleton live born babies 20+ weeks gestation; Note: Rates are per 100 live births; Baby's Ethnicity is Level 1 prioritised; Decile is NZDep2006

When broken down by gestational age, a common theme emerged, with the magnitude of the excess risk of preterm birth seen for Māori, Pacific and Asian/Indian babies, the babies of teenage mothers, and those from the more deprived areas, being most marked amongst births at lower gestations (**Table 2**). Specifically:

20–27 Weeks: During 2008–2012, preterm birth rates at 20–27 weeks gestation were *significantly* higher for males, and for those living in more deprived (NZDep deciles 7–10) areas. Rates were also *significantly* higher for Māori, Pacific and Asian/Indian babies than for European/Other babies, and for the babies of teenage mothers, followed by those aged 20–24 years (**Table 2**).

28–31 Weeks: During 2008–2012, preterm birth rates at 28–31 weeks gestation were also *significantly* higher for males and for those living in average and more deprived (NZDep deciles 3–4 and 7–10) areas. Rates were also *significantly* higher for Pacific and Māori babies than for European/Other babies, and for the babies of teenage mothers, followed by those aged 20–24 years (**Table 2**).

32–36 Weeks: During 2008–2012, preterm birth rates at 32–36 weeks gestation were *significantly* higher for males, for Māori babies than for European/Other, Asian/Indian and Pacific babies, and for those living in the most deprived (NZDep deciles 9–10) areas. Preterm birth rates were also *significantly* higher for the babies of younger (<25 years) and older (35+ years) mothers than for the babies of mothers aged 25–29 years (**Table 2**).

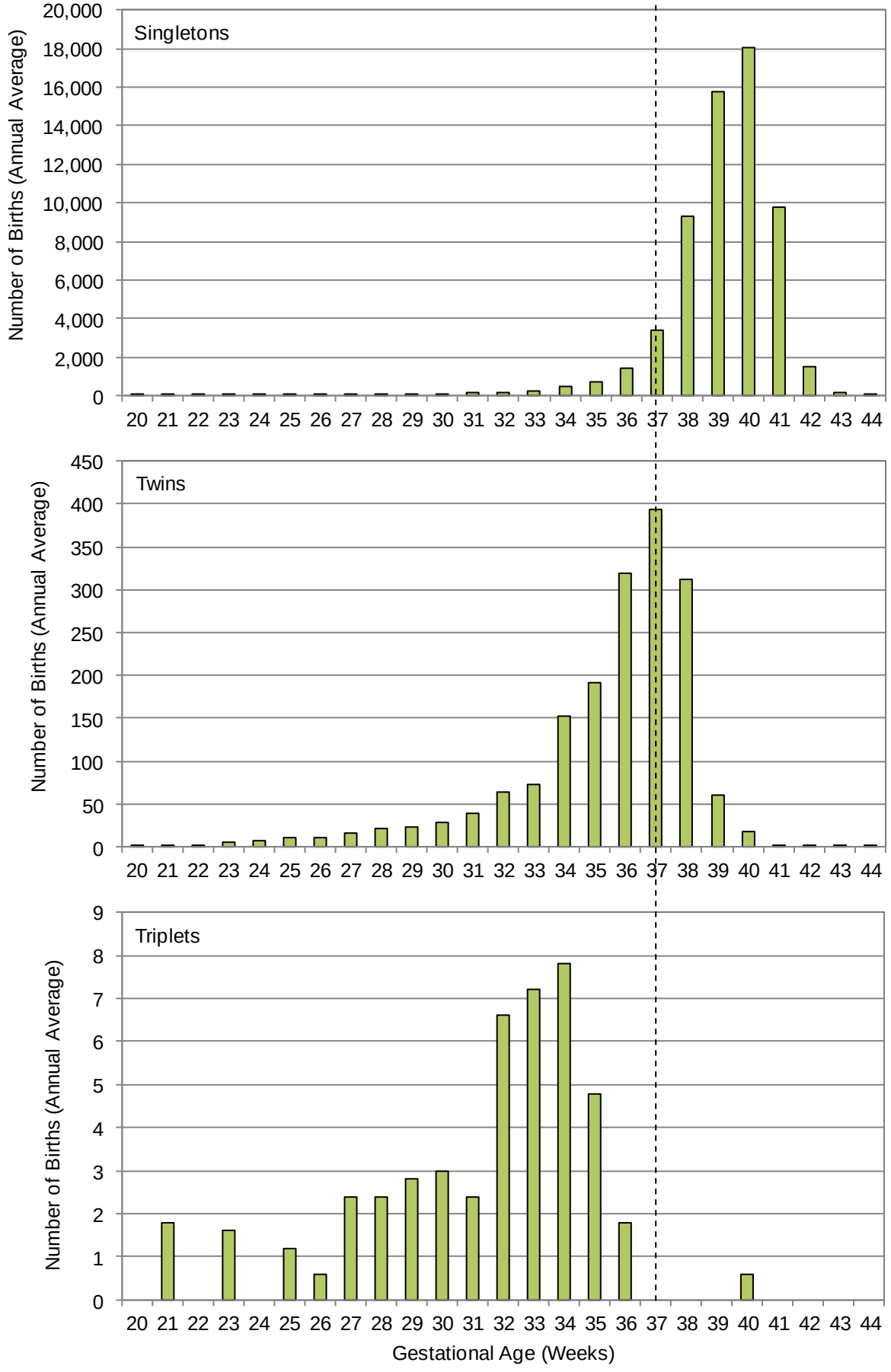
Table 2. Preterm Birth Rates in Singleton Live Born Babies by Ethnicity, NZ Deprivation Index Decile, Gender, Maternal Age and Gestational Age, New Zealand 2008–2012

Variable	Rate	Rate Ratio	95% CI	Variable	Rate	Rate Ratio	95% CI
Preterm Singletons 20–27 Weeks							
NZ Deprivation Index Decile				Maternal Age			
Deciles 1–2	0.26	1.00		<20 Years	0.69	2.14	1.75–2.62
Deciles 3–4	0.29	1.11	0.87–1.42	20–24 Years	0.43	1.34	1.12–1.60
Deciles 5–6	0.29	1.13	0.89–1.43	25–29 Years	0.32	1.00	
Deciles 7–8	0.36	1.37	1.10–1.70	30–34 Years	0.28	0.87	0.73–1.04
Deciles 9–10	0.50	1.92	1.57–2.36	35+ Years	0.33	1.02	0.85–1.22
Baby's Ethnicity				Gender			
Asian/Indian	0.39	1.42	1.17–1.72	Female	0.33	1.00	
European/Other	0.27	1.00		Male	0.38	1.14	1.02–1.29
Māori	0.46	1.66	1.45–1.91				
Pacific	0.44	1.59	1.32–1.91				
Preterm Singletons 28–31 Weeks							
NZ Deprivation Index Decile				Maternal Age			
Deciles 1–2	0.45	1.00		<20 Years	0.78	1.36	1.14–1.62
Deciles 3–4	0.56	1.23	1.03–1.47	20–24 Years	0.69	1.19	1.04–1.37
Deciles 5–6	0.54	1.18	0.99–1.41	25–29 Years	0.58	1.00	
Deciles 7–8	0.64	1.41	1.20–1.67	30–34 Years	0.54	0.93	0.81–1.06
Deciles 9–10	0.77	1.70	1.45–1.99	35+ Years	0.66	1.14	1.00–1.30
Baby's Ethnicity				Gender			
Asian/Indian	0.60	1.11	0.96–1.29	Female	0.57	1.00	
European/Other	0.54	1.00		Male	0.66	1.16	1.06–1.27
Māori	0.71	1.32	1.19–1.46				
Pacific	0.72	1.33	1.16–1.54				
Preterm Singletons 32–36 Weeks							
NZ Deprivation Index Decile				Maternal Age			
Deciles 1–2	4.87	1.00		<20 Years	6.03	1.28	1.20–1.36
Deciles 3–4	4.78	0.98	0.93–1.04	20–24 Years	5.02	1.06	1.01–1.12
Deciles 5–6	4.92	1.01	0.96–1.07	25–29 Years	4.72	1.00	
Deciles 7–8	5.15	1.06	1.00–1.11	30–34 Years	4.84	1.02	0.98–1.07
Deciles 9–10	5.34	1.10	1.05–1.15	35+ Years	5.47	1.16	1.11–1.21
Baby's Ethnicity				Gender			
Asian/Indian	4.90	0.99	0.94–1.04	Female	4.63	1.00	
European/Other	4.94	1.00		Male	5.48	1.18	1.15–1.22
Māori	5.48	1.11	1.07–1.15				
Pacific	4.67	0.94	0.90–1.00				

Source: Birth Registration Dataset: Numerator: All singleton live born babies 20–36 weeks gestation; Denominator: All singleton live born babies 20+ weeks gestation; Note: Rates are per 100 live births; Baby's Ethnicity is Level 1 prioritised; Decile is NZDep2006

Preterm Births in Multiple Pregnancies

Figure 4. Gestational Age at Delivery by Plurality, New Zealand Live Births 2008–2012



Source: Birth Registration Dataset, All live born babies 20–36 weeks gestation

Distribution by Gestational Age

In New Zealand during 2008–2012, 94.0% of singleton babies were born after 36 weeks gestation, as compared to only 44.9% of twins and 1.3% of triplets, with the gestational age curve shifting increasingly towards the left (i.e. towards younger gestational ages) as the number of babies increased. During this period, the most frequent gestational age for the delivery of a singleton baby was 40 weeks, as compared to 37 weeks for twins and 34 weeks for triplets (**Figure 4**).

Risk of Preterm Birth by Plurality

In New Zealand during 2008–2012, preterm birth rates per 100 live births were 6.0 for singletons, 55.1 for twins and 98.7 for triplets, with the risk of preterm birth being 9.13 (95% CI 8.92–9.35) times higher for twins and 16.34 (95% CI 16.02–16.68) times higher for triplets, than for singleton babies (**Table 3**).

Table 3. Preterm Birth Rates by Plurality, New Zealand 2008–2012

Plurality	Number Preterm Births: Total 2008–2012	Number Preterm Births: Annual Average	Number Live Births: Annual Average	Preterm Birth Rate	Rate Ratio	95% CI
Preterm Births 20–36 Weeks						
Singleton	18,625	3,725	61,664	6.04	1.00	
Twin	4,840	968	1,755	55.14	9.13	8.92–9.35
Triplet	232	46	47	98.72	16.34	16.02–16.68

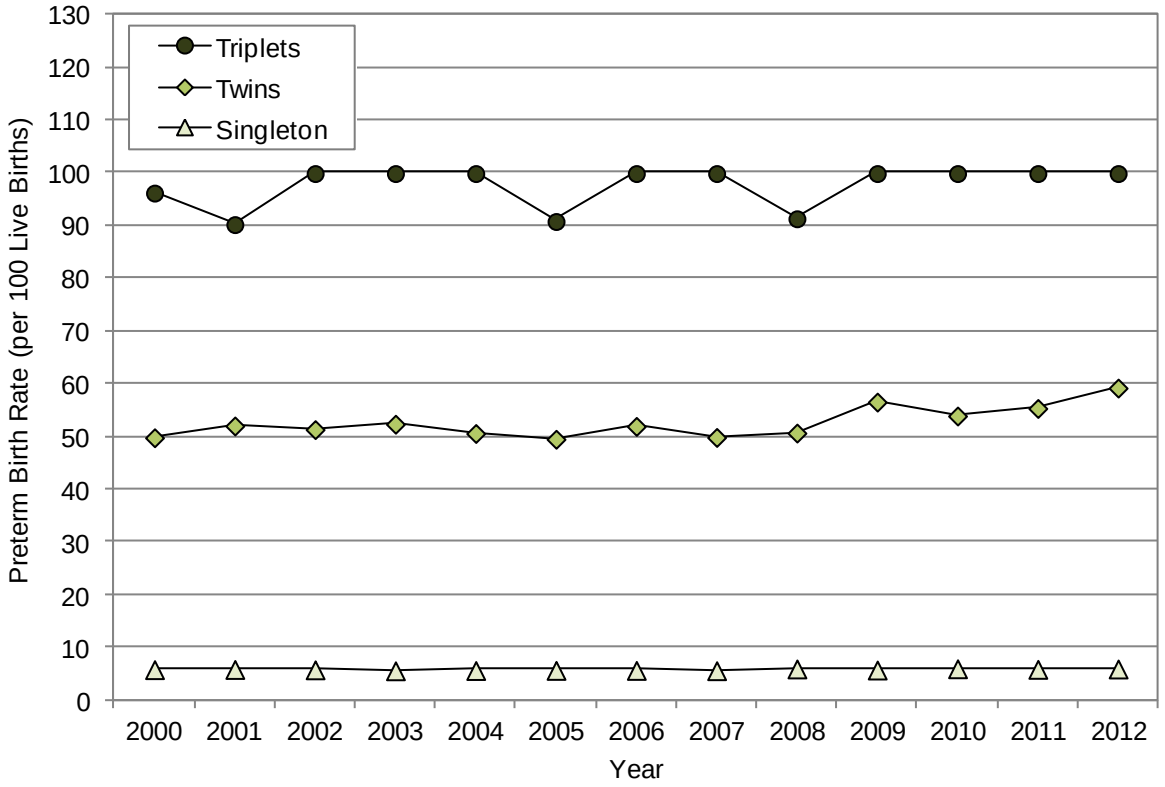
Source: Birth Registration Dataset: Numerator: All live born babies 20–36 weeks gestation; Denominator: All live born babies 20+ weeks gestation; Note: Preterm birth rates are per 100 live births

New Zealand Trends

Preterm Birth Rates: In New Zealand during 2000–2012, preterm birth rates per 100 live births were relatively static in singletons and triplets, with rates for singletons being 6.0 in 2000 and 6.1 in 2012. Similarly rates for triplets were 96.3 in 2000 and 100.0 in 2012. In contrast, preterm birth rates in twins increased, from 49.9 in 2000 to 59.3 in 2000, with the majority of this increase occurring after 2008 (**Figure 5**).

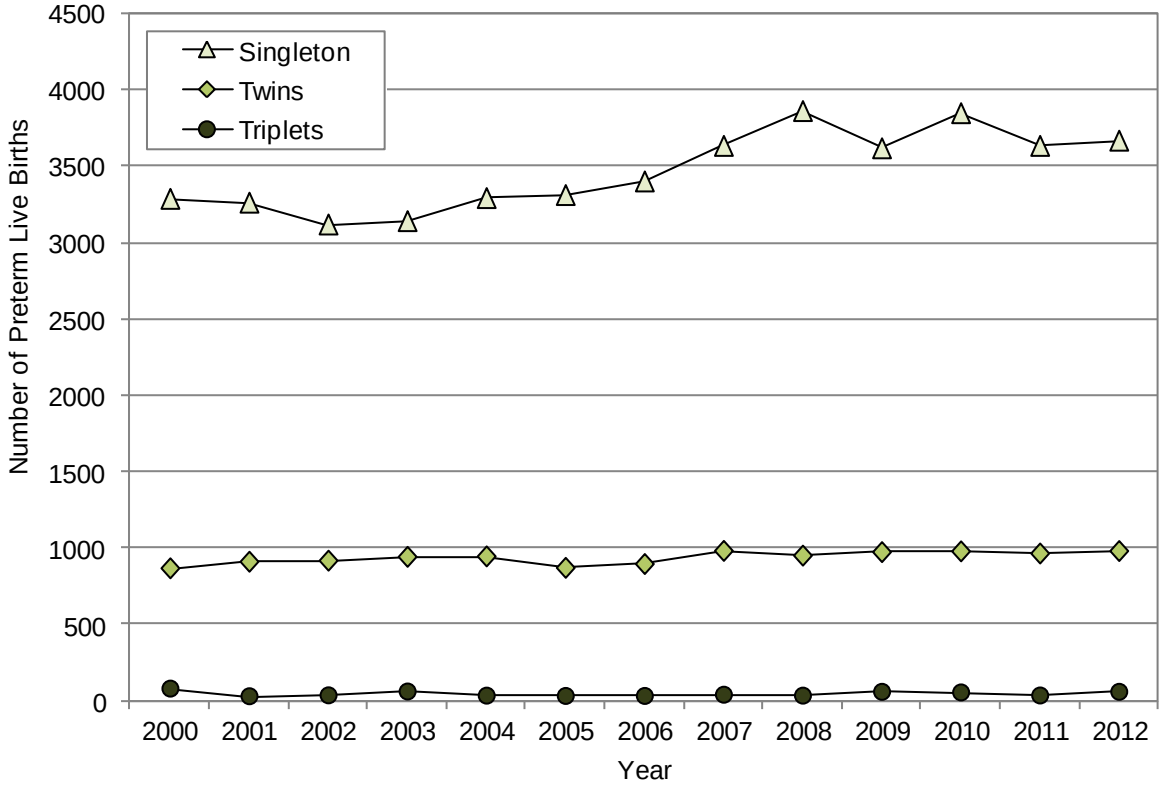
Number of Preterm Births: During the same period, the actual number of singleton preterm babies born increased (from 3,286 in 2000 to 3,667 in 2012), as the result of a rising birth rate, with the majority of this increase being between 2003 and 2008. Similarly, the number of twin preterm births increased, from 866 in 2000 to 979 in 2012. The number of triplet births however was more static (**Figure 6**).

Figure 5. Preterm Birth Rates in Live Born Babies by Plurality, New Zealand 2000–2012



Source: Birth Registration Dataset: Numerator: All live born babies 20–36 weeks gestation; Denominator: All live born babies 20+ weeks gestation

Figure 6. Number of Preterm Live Births by Plurality, New Zealand 2000–2012



Source: Birth Registration Dataset, All live born babies 20–36 weeks gestation

Distribution by Ethnicity, NZDep Decile, Gender and Maternal Age

In New Zealand during 2008–2012, there were no *significant* gender, socioeconomic (as measured by NZDep06), or maternal age-related differences in preterm birth rates amongst twins. Preterm birth rates for Pacific twins however, were *significantly* (albeit only marginally) lower than for European/Other babies (**Table 4**).

Table 4. Preterm Birth Rates in Live Born Twins by Ethnicity, NZ Deprivation Index Decile, Gender and Maternal Age, New Zealand 2008–2012

Variable	Rate	Rate Ratio	95% CI	Variable	Rate	Rate Ratio	95% CI
Preterm Twins 20–36 Weeks							
NZ Deprivation Index Decile				Maternal Age			
Deciles 1–2	57.07	1.00		<20 Years	59.72	1.08	0.98–1.18
Deciles 3–4	54.90	0.96	0.90–1.03	20–24 Years	55.65	1.00	0.94–1.07
Deciles 5–6	54.78	0.96	0.90–1.02	25–29 Years	55.53	1.00	
Deciles 7–8	55.49	0.97	0.92–1.03	30–34 Years	52.94	0.95	0.90–1.01
Deciles 9–10	53.98	0.95	0.89–1.00	35+ Years	56.17	1.01	0.96–1.07
Baby's Ethnicity				Gender			
Asian/Indian	59.32	1.06	1.00–1.14	Female	55.87	1.00	
European/Other	55.73	1.00		Male	54.41	0.97	0.94–1.01
Māori	54.56	0.98	0.94–1.02				
Pacific	50.91	0.91	0.85–0.98				

Source: Birth Registration Dataset: Numerator: All live born babies 20–36 weeks gestation; Denominator: All live born babies 20+ weeks gestation; Note: Rates are per 100 live births; Baby's Ethnicity is Level 1 prioritised; Decile is NZDep2006

South Island DHBs Distribution and Trends

South Island DHBs Distribution

In the South Island during 2008–2012, on average 82 Nelson Marlborough, 35 South Canterbury, 379 Canterbury, 26 West Coast and 248 Southern babies per year were born prior to 37 weeks gestation, with the majority of births being in the 32–36 weeks category (**Table 5**).

Preterm birth rates at 20–27 weeks, 28–31 weeks and 32–36 weeks in South Canterbury, Canterbury, the West Coast and Southland were not *significantly* different from the New Zealand rates. Preterm birth rates at 32–36 weeks in Nelson Marlborough however, were *significantly* lower than the New Zealand rate, while in Otago rates were *significantly* higher (**Table 5**).

South Island DHBs Trends

In the South Island during 2000–2012, there was considerable year to year variability in preterm birth rates. Rates in Nelson Marlborough however, were lower than the New Zealand rate for the majority of this period, while rates in Otago were generally higher (**Figure 7**).

South Island DHBs Distribution by Ethnicity

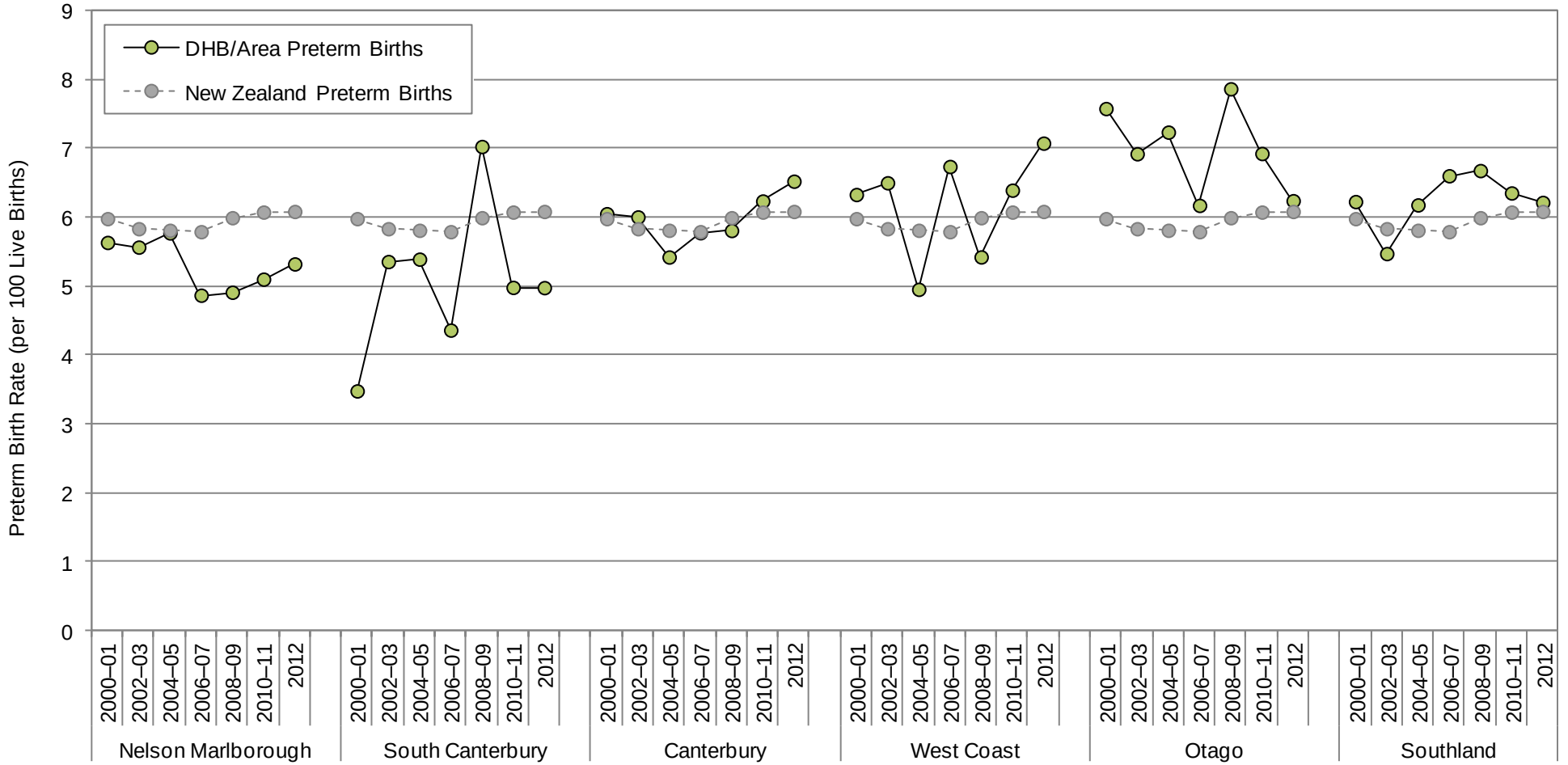
In the South Island DHBs during 2000–2012, there were no consistent differences in preterm birth rates between Māori and European/Other babies (**Figure 8**).

Table 5. Preterm Birth Rates in Singleton Live Born Babies by Gestational Age, South Island DHBs vs. New Zealand 2008–2012

Gestational Age	Number: Total 2008−2012	Number: Annual Average	Preterm Birth Rate	Rate Ratio	95% CI
Preterm Births					
Nelson Marlborough					
20–27 weeks	30	6	0.37	1.03	0.72–1.49
28–31 weeks	43	9	0.53	0.86	0.64–1.16
32–36 weeks	336	67	4.16	0.82	0.74–0.91
37+ weeks	7,672	1,534	94.94		
Nelson Marlborough Total	8,081	1,616	100.00		
South Canterbury					
20–27 weeks	8	2	0.26	0.73	0.37–1.47
28–31 weeks	19	4	0.63	1.01	0.65–1.59
32–36 weeks	150	30.	4.94	0.98	0.83–1.14
37+ weeks	2,858	572	94.17		
South Canterbury Total	3,035	607	100.00		
Canterbury					
20–27 weeks	96	19	0.31	0.86	0.70–1.06
28–31 weeks	195	39	0.63	1.02	0.88–1.18
32–36 weeks	1,604	321	5.17	1.02	0.97–1.07
37+ weeks	29,114	5,823	93.89		
Canterbury Total	31,009	6,202	100.00		
West Coast					
20–27 weeks	4	1	0.19	0.53	0.20–1.40
28–31 weeks	20	4	0.94	1.52	0.98–2.36
32–36 weeks	106	21	5.00	0.99	0.82–1.19
37+ weeks	1,992	398	93.87		
West Coast Total	2,122	424	100.00		
Otago					
20–27 weeks	26	5	0.26	0.71	0.48–1.05
28–31 weeks	76	15	0.75	1.21	0.96–1.52
32–36 weeks	625	125	6.16	1.22	1.13–1.31
37+ weeks	9,422	1,884	92.84		
Total Otago	10,149	2,030	100.00		
Southland					
20–27 weeks	27	5	0.34	0.95	0.65–1.39
28–31 weeks	48	10	0.61	0.98	0.74–1.31
32–36 weeks	436	87	5.51	1.09	0.99–1.19
37+ weeks	7,405	1,481	93.54		
Total Southland	7,916	1,583	100.00		
New Zealand					
20–27 weeks	1,106	221	0.36	1.00	
28–31 weeks	1,906	381	0.62	1.00	
32–36 weeks	15,613	3,123	5.06	1.00	
37+ weeks	289,694	57,939	93.96		
New Zealand Total	308,319	61,664	100.00		

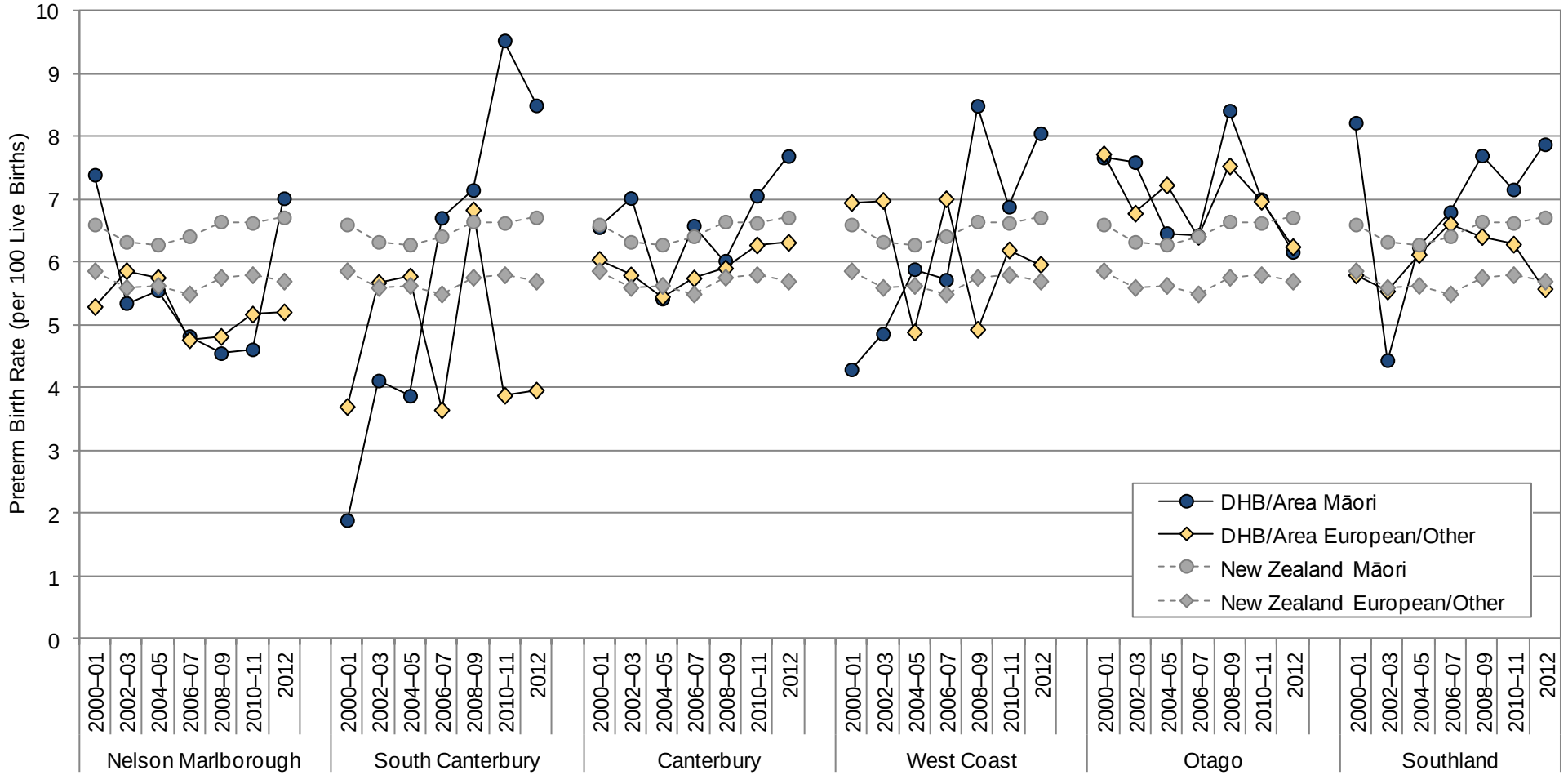
Source: Birth Registration Dataset: Numerator: All singleton live born babies 20–36 weeks gestation; Denominator: All singleton live born babies 20+ weeks gestation; Note: Preterm birth rates are per 100 live births

Figure 7. Preterm Birth Rates in Singleton Live Born Babies, South Island DHBs vs. New Zealand 2000–2012



Source: Birth Registration Dataset: Numerator: All singleton live born babies 20–36 weeks gestation; Denominator: All singleton live born babies 20+ weeks gestation

Figure 8. Preterm Birth Rates in Singleton Live Born Babies by Baby's Ethnicity, South Island DHBs vs. New Zealand 2000–2012



Source: Birth Registration Dataset: Numerator: All singleton live born babies 20–36 weeks gestation; Denominator: All singleton live born babies 20+ weeks gestation; Note: Ethnicity is Level 1 Prioritised

Local Policy Documents and Evidence-Based Reviews Relevant to Preterm Birth

In New Zealand at present, there is no single strategy which focuses on the prevention of preterm birth, and thus any local strategies developed will need to incorporate evidence from a variety of sources. **Table 6** provides an overview of a range of New Zealand policy documents and overseas evidence-based reviews which may be useful in this context.

Table 6. Local Policy Documents and Evidence-Based Reviews Relevant to Preterm Birth

Ministry of Health Policy Documents
In New Zealand a number of Government policy documents identify and are beginning to report on clinical indicators related to the quality and delivery of maternity services including preterm births.
Ministry of Health. 2013.**New Zealand maternity clinical indicators 2011.** Wellington. Ministry of Health http://www.health.govt.nz/publication/new-zealand-maternity-clinical-indicators-2011 A set of twelve maternity clinical indicators have been established for the New Zealand setting that can be drawn from available data collections. The intent of these clinical indicators is to assist DHBs and maternity stakeholders to use national benchmarked data in local maternity quality and safety programmes. Indicator 12 is premature birth (32–36 weeks gestation).
National Maternity Monitoring Group. 2013. **National Maternity Monitoring Group Annual Report** Auckland, Health Improvement and Innovation Research Centre. http://www.health.govt.nz/publication/national-maternity-monitoring-group-annual-report-2013 This is the report for the first year of operation by the New Zealand National Maternity Monitoring Group (NMMG). The NMMG was established to oversee the implementation of the NZ Maternity Standards. It contains a chapter that reports on the monitoring conducted on late preterm birth (34-36 weeks gestation) and a further chapter on smoking amongst pregnant women. Each chapter includes a set of expectations for DHBs with respect to the indicators to be collected in the coming year and how they will meet the Ministry of Health's targets. Preterm births varied by DHB, and the report identifies changes the NMMG expects to see: specifically that each DHB audit preterm births in their region, particularly those from 34 to 36 weeks. The proportion of mothers smoking at both delivery and 2 weeks post-delivery differed significantly across DHBs. The report notes that the NMMG expects changes from the Ministry, proposing it expand its data collection from primary care providers. Changes are expected from DHBs too. It is proposed that they work with all aspects of maternity services to meet the Ministry's target on advice and support for pregnant women to quit smoking.
International Guidelines
National Collaborating Centre for Women's and Children's Health. 2011. **Multiple pregnancy: the management of twin and triplet pregnancies in the antenatal period**. London: National Institute for Health and Clinical Excellence. http://www.nice.org.uk/nicemedia/live/13571/56497/56497.pdf Women with twin and triplet pregnancies have a higher risk of preterm birth. This guideline is complementary to the NICE guideline 'Antenatal care: routine care for the healthy pregnant woman' (NICE clinical guideline 62) and it specifies the additional or different care that women with twin or triplet pregnancies should receive. Chapter 8 deals specifically with preterm birth. Following discussion of the research evidence, the following recommendations are made regarding the prevention of preterm birth and its associated risks: • Be aware that women who have had a previous premature singleton birth are at increased risk • Do not use fibronectin testing alone, home uterine activity monitoring, or routine cervical length measuring (with or without fetal fibronectin) to predict the risk of spontaneous preterm birth in twin and triplet pregnancies. • Do not use the following interventions (either alone or in combination) routinely to prevent spontaneous preterm birth in twin and triplet pregnancies: bed rest (either at home or in hospital), intramuscular or vaginal progesterone, cervical cerclage or oral tocolytics. • Inform women with twin and triplet pregnancies their risk of preterm birth and about the benefits of targeted (i.e. when birth is imminent) corticosteroids. • Do not use single or multiple untargeted (routine) courses of corticosteroids and inform women that there is no benefit from using untargeted corticosteroids. The guideline appendices, which include the details of the evidence review (including the evidence tables) can be found at http://guidance.nice.org.uk/CG129/Guidance/Appendices In 2013, priority statements to drive measurable quality improvements were issued: Multiple Pregnancy Quality Standards (QS46). These are available at http://publications.nice.org.uk/multiple-pregnancy-qs46 A *NICE Pathways* is available on multiple pregnancy. It provides a very accessible and rapid reference to information for patients and the public, information and guidance for professionals, and quality standards and practice resources for professionals and health systems. It is available at http://pathways.nice.org.uk/pathways/multiple-pregnancy

Systematic and Other Reviews from the International Literature
Liem SM, van Pampus MG, Mol BW, Bekedam DJ. 2013. **Cervical pessaries for the prevention of preterm birth: A systematic review.** Obstet Gynecol Int.: ID576723. doi: 10.1155/2013/576723. http://dx.doi.org/10.1155/2013/576723 This systematic review of randomised controlled trials and cohort studies on the effectiveness of cervical pessaries to prevent preterm birth concluded that while there is some potential effectiveness in the intervention, more RCTs are required before pessaries could be used in practice. Data from six cohort studies and four RCTs were examined in this review. One RCT (n=380) indicated a lower delivery rate prior to 34 weeks (RR 0.24; 95% CI, 0.13–0.43) while another smaller trial (n=108) did not show any positive effect at this stage (RR 1.73; 95% CI 0.43–6.88).
Chamberlain C, O'Mara-Eves A, Oliver S, Caird JR, et al. 2013. **Psychosocial interventions for supporting women to stop smoking in pregnancy.** Cochrane Database of Systematic Reviews, Issue 10. Art. No.: CD001055. DOI:10.1002/14651858.CD001055.pub4 Smoking during pregnancy increases the risk of the mother having complications during pregnancy and the baby being born preterm (before 37 weeks). This updated systematic review identifies that psychosocial interventions to support women to stop smoking in pregnancy can increase the proportion of women who stop smoking in late pregnancy and reduce low birthweight and preterm births. Eighty six trials were included in the review with 79 of them involving 29,000 women providing data on smoking abstinence in late pregnancy. Most were conducted in high income countries. Detailed results are provided in the review, with the key findings being that interventions that provided an incentive to stop smoking appeared to support the most women to quit (one study; RR 3.64, 95% CI 1.84–7.23) and an alternative intervention (one study; RR 4.05,95% CI 1.48–11.11). In studies comparing counselling and usual care (the largest comparison), it was unclear whether interventions prevented smoking relapse among women who had stopped smoking spontaneously in early pregnancy (eight studies; average RR 1.06, 95% CI 0.93–1.21). However, a clear effect was seen in smoking abstinence at zero to five months postpartum (10 studies; average RR 1.76, 95% CI 1.05–2.95), a borderline effect at six to 11 months (six studies; average RR 1.33, 95% CI 1.00–1.77), and a significant effect at 12 to 17 months (two studies, average RR 2.20, 95% CI 1.23–3.96), but not in the longer term. Feedback interventions had a significant effect only when compared with usual care and provided in conjunction with other strategies, such as counselling (two studies; average RR 4.39, 95% CI 1.89–10.21), but the effect was unclear when compared with a less intensive intervention (two studies; average RR 1.19, 95% CI 0.45–3.12). Peer provided social support appeared effective (five studies; average RR 1.49, 95% CI 1.01–2.19), but the effect of partner support was not clear (one study).
Brocklehurst P, Gordon A, Heatley E, Milan SJ. 2013. **Antibiotics for treating bacterial vaginosis in pregnancy.** Cochrane Database of Systematic Reviews Issue 1:CD000262. doi: 10.1002/14651858.CD000262.pub4. Bacterial vaginosis is an overgrowth of anaerobic bacteria and a lack of normal lactobacillary vaginal flora. It has been associated with preterm birth and other poor perinatal outcomes. This updated review aimed to assess the effects of antibiotic treatment of bacterial vaginosis in pregnancy. Twenty one good quality RCTs (7847 women) were included. Antibiotic therapy was effective at eradicating bacterial vaginosis during pregnancy (average RR 0.42; 95% CI 0.31–0.56) and reduced the risk of late miscarriage (RR 0.20; 95% CI 0.05–0.76).Treatment did not reduce the risk of preterm birth before 37 weeks (average RR 0.88; 95% CI 0.71–1.09), or the risk of preterm pre-labour rupture of membranes (RR 0.74; 95% CI 0.30–1.84). It did increase the risk of side-effects sufficient to stop or change treatment (RR 1.66; 95% CI 1.02–2.68). Treatment before 20 weeks' gestation did not reduce the risk of preterm birth (average RR 0.85; 95% CI 0.62–1.17). In women with a previous preterm birth, treatment did not affect the risk of subsequent preterm birth (average RR 0.78; 95% CI 0.42–1.48).In women with abnormal vaginal flora (intermediate flora or bacterial vaginosis), treatment may reduce the risk of preterm birth (RR 0.53; 95% CI 0.34–0.84).One small trial of 156 women compared metronidazole and clindamycin, both oral and vaginal, with no significant differences seen for any of the pre-specified primary outcomes. Statistically significant differences were seen for the outcomes of prolongation of gestational age (days) (mean difference (MD) 1.00; 95% CI 0.26–1.74) and birthweight (grams) (MD 75.18; 95% CI 25.37–124.99) however these represent relatively small differences in the clinical setting. The authors concluded that antibiotic treatment can eradicate bacterial vaginosis in pregnancy; however, the overall risk to preterm birth was not significantly reduced. There was little evidence that screening and treating all pregnant women with bacterial vaginosis will prevent preterm birth and its consequences.
Alfirevic Z, Stampalija T, Roberts D, Jorgensen AL. 2012. **Cervical stitch (cerclage) for preventing preterm birth in singleton pregnancy.** Cochrane Database of Systematic Reviews. Issue 4:CD008991. DOI: 10.1002/14651858.CD008991.pub2. The use of cervical cerclage, in which a stitch is positioned around the neck of the cervix intended to reduce the risk of preterm birth, is still considered controversial for safety and effectiveness reasons. This review is a further assessment of this procedure, specifically focusing on whether the use of such a stitch in singleton pregnancy at high risk of loss based on a woman's history and/or ultrasound finding of a short cervix or physical examination improves subsequent obstetric care and fetal outcome. Twelve trials were included (n = 3328 women). Compared to no treatment, cervical cerclage made no significant difference to perinatal death (8.4% versus 10.7%) (RR 0.78; 95% CI 0.61–1.00) and neonatal morbidity (9.6% versus 10.2%) (RR 0.95; 95% CI 0.63–1.43), but did show significant reduction in preterm births (average RR 0.80; 95% CI 0.69–0.95). Cervical cerclage was associated with significantly higher rates of caesarean sections (RR 1.19; 95% CI 1.01–1.40) and higher rates of maternal side effects (vaginal discharge and bleeding, pyrexia) (average RR 2.25; 95% CI 0.89 to 5.69). The review concluded that cerclage reduces the incidence of preterm birth in women at risk of recurrent preterm birth, although there was no significant reduction in perinatal mortality or neonatal morbidity and it was unclear about the effect long term on the baby. Caesarean section is more likely where cervical cerclage has been utilised. The authors' advice is that decisions should be 'personalised', based on the woman's informed choice, the clinical circumstances and the expertise of the clinical team.

McCormick MC, Litt JS, Smith VC, et al. 2011. **Prematurity: an overview and public health implications**. Annual Review of Public Health, 32, 367-79.

This review article explains that, largely because of the limited understanding of the basic biology underlying preterm delivery, there are few opportunities for prevention. Two strategies which could have a very small effect in reducing rates of preterm birth are decreasing higher-order multiple births resulting from the use of assisted reproductive technology and improving estimates of gestational age in early pregnancy in order to reduce the number of infants inadvertently delivered preterm because of inaccurate dates. Public health approaches to prematurity include ensuring that premature infants are delivered in a suitable facility able to deal with neonatal complications, minimising variations in quality of care between institutions, early developmental support for such infants and support for families.

Davey M-A, Watson L, Rayner Jo A, et al. 2011. **Risk scoring systems for predicting preterm birth with the aim of reducing associated adverse outcomes**. Cochrane Database of Systematic Reviews, Issue 11, Art. No.: CD004902. DOI:10.1002/14651858.CD004902.pub4.

There have been many scoring systems designed to facilitate prediction of preterm birth so that appropriate interventions might reduce the incidence of preterm and very preterm birth and the associated adverse outcomes. Extensive searching by the authors of this review failed to reveal any RCTs evaluating such scoring systems. The value of scoring systems is thus unknown. Prospective studies are needed, followed by RCTs of promising systems.

Raynes-Greenow Camille H, Roberts Christine L, Bell Jane C, et al. 2011. **Antibiotics for ureaplasma in the vagina in pregnancy**. Cochrane Database of Systematic Reviews, Issue9, Art. No.: CD003767. DOI: 10.1002/14651858.CD003767.pub3.

Heavy vaginal colonisation with ureaplasma is suspected of playing a role in preterm rupture of membranes and preterm birth but the benefits of treating it with antibiotics are unclear. Based on a review of one RCT of 3 types antibiotic treatment vs. placebo in 1105 pregnant women (between 22 and 33 weeks gestation), which did not report on rates of preterm birth, the authors concluded that there was insufficient evidence to either support or refute the use of antibiotics for ureaplasma infection to prevent preterm birth.

Whitworth M, Quenby S, Cockerill Ruth O, et al. 2011. **Specialised antenatal clinics for women with a pregnancy at high risk of preterm birth (excluding multiple pregnancy) to improve maternal and infant outcomes**. Cochrane Database of Systematic Reviews, Issue9, Art. No.: CD006760. DOI: 10.1002/14651858.CD006760.pub2.

Previous preterm delivery is strong predictor of preterm delivery and for this reason specialised care for women with a previous history of preterm delivery is common practice. This review considered three RCTs conducted in the 1980s comparing specialised care with standard care in women with a singleton pregnancy who were considered to be at high risk of preterm labour (3400 women all in the U.S.). The authors reported that overall there was very little difference in outcomes between specialised and standard care groups, but due to differences in study designs most outcomes were only reported by one study which limited statistical power to detect significant differences. All three studies reported on preterm birth before 37 weeks and a pooled analysis of the results suggested that there may have been fewer preterm births in the specialised care mothers but the difference was not statistically significant (RR 0.87, 95% CI 0.69–1.08).

Rubens CE, Victora CG, Gravett MG, et al. 2010. **Global report on preterm birth & stillbirth: The foundation for innovative solutions and improved outcomes**. BMC Pregnancy and Childbirth, 10(Suppl 1), http://www.biomedcentral.com/bmcpregnancychildbirth/supplements/10/S1

This series of seven reviews provides a global perspective on preterm birth. The third review in the series is:

Barros F, Bhutta Z, Batra M, et al. 2010. **Global report on preterm birth and stillbirth (3 of 7): Evidence for effectiveness of interventions**. BMC Pregnancy and Childbirth, 10(Suppl 1), S3.

This systematic review discusses the evidence for the effectiveness of interventions to prevent preterm birth and to improve survival among preterm newborns particularly those applicable to low-to-middle income countries. Recommendations are rated in four categories (from strong in favour to strong against) based on the quality of evidence, how the evidence may be translated to practice in a specific setting such as low-to-middle income countries, the level of baseline risk, and on potential trade-offs between expected benefits, harms and costs. The two interventions strongly recommended for preventing preterm births are smoking cessation and the use of progesterone. The authors note that since specialised clinics are now an accepted part of antenatal services in many countries it is unlikely that further RCTs will be carried out. They suggest that further research should focus on service development.

Hodnett ED, Fredericks S, Weston J. 2010. **Support during pregnancy for women at increased risk of low birthweight babies**. Cochrane Database of Systematic Reviews, Issue 6, Art. No.: CD000198. DOI: 10.1002/14651858.CD000198.pub2.

Numerous studies have consistently shown a relationship between social disadvantage and low birthweight (<2500g). Many countries have programmes to assist women who are thought to be at risk of having a low birthweight baby and these may include advice and counselling, practical assistance (e.g. transport to clinic appointments or help with household responsibilities and care of other children), and emotional support. This review included 17 RCTs (12,264 women) of additional support, provided by either a professional (social worker, midwife or nurse) or a trained lay person, compared to routine care. Programmes of extra support made no difference to rates of either low birthweight or preterm births but they were associated with a reduced likelihood of antenatal hospital admission (3 trials, 737 women, RR 0.79, 95% CI 0.68–0.92) and of caesarean birth (9 trials, 4522 women, RR 0.87, 95% CI 0.78–0.97).

Alexander S, Boulvain M, Ceysens G, et al. 2010. **Repeat digital cervical assessment in pregnancy for identifying women at risk of preterm labour**. Cochrane Database of Systematic Reviews, Issue6, Art. No.: CD005940. DOI:10.1002/14651858.CD005940.pub2.

Based on a review of two RCTs (7163 women) the authors of this review concluded that there was no evidence to support the use of repeat digital cervical assessment to reduce numbers of preterm births.

Crowther CA, Han S. 2010. **Hospitalisation and bed rest for multiple pregnancy**. Cochrane Database of Systematic Reviews, Issue 7, Art. No.: CD000110. DOI: 10.1002/14651858.CD000110.pub2.

Bed rest used to be commonly advised for women with multiple pregnancy. This review included seven trials (713 women and 1452 babies) comparing outcomes in women who were offered bed rest in hospital with those in women who were only admitted to hospital if complications occurred. There was no reduction in the risk of preterm birth or perinatal death but there may have been a decrease in the number of low birthweight (<2500g) infants in the bed rest women (risk ratio 0.92, 95% CI 0.85–1.0) although there was no difference in the number of very low birthweight infants (<1500g). There was no difference in the proportions of mothers developing hypertension or needing a caesarean. When the results for subgroups of women were analysed, there were no differences between the bed rest and the controls groups in any of the groups. The results of this review indicate that there is no benefit to be obtained from routine bed rest for women with an uncomplicated twin pregnancy.

Honest H, Forbes CA, Duree KH, et al. 2009. **Screening to prevent spontaneous preterm birth: systematic reviews of accuracy and effectiveness literature with economic modelling**. Health Technology Assessment (Winchester, England), 13(43), 1-627. http://www.hta.ac.uk/fullmono/mon1343.pdf

This is the report for a very sizeable project which aimed to identify combinations of tests and treatments to predict and prevent preterm labour. It includes both two systematic reviews and a decision analysis (health economic evaluation). One systematic review aimed to determine the accuracy of 22 different tests for the prediction of preterm birth in asymptomatic women in early pregnancy and in women symptomatic with threatened preterm labour in later pregnancy and the other review assessed the effectiveness of interventions with potential to reduce spontaneous preterm births in asymptomatic women in early pregnancy and to reduce spontaneous preterm births or improve neonatal outcomes in women with a viable pregnancy and symptoms of threatened preterm labour. The economic evaluation incorporated the combined effects of test and treatments and costs in a model-based analysis.

Berghella V, Baxter JK, Hendrix NW. 2013. **Cervical assessment by ultrasound for preventing preterm delivery**. Cochrane Database Systematic Review. Issue 1:CD007235. doi: 10.1002/14651858.CD007235.pub3.

While measurement of cervical length by trans-vaginal ultrasound (TVU) can be used to predict preterm birth (the shorter the cervical length, the higher the risk) it is uncertain if it is useful as a screening test for the prevention of preterm birth. This review aimed to assess the effect of knowledge of cervical length on the effectiveness of antenatal management in preventing preterm birth. This review included five RCTs (507 women) of knowledge of cervical length (obtained by TVU) vs. no knowledge of cervical length. In the three trials (290 women) involving singleton gestations with preterm labour, knowledge of cervical length was associated with a non-significant decrease in preterm birth at < 37 weeks (22.3% versus 34.7%, respectively; risk ratio 0.59, 95% CI 0.26–1.32) and delivery occurred on average 0.64 weeks later (95% CI 0.03–1.25 weeks). There were no differences in other outcomes measured. One trial in singleton gestations with premature rupture of membranes (92 women) evaluated the safety of TVU in this situation and found no difference in maternal or neonatal infection rates between the group that had TVU and the group that did not. In the one trial in twin gestations (125 women, with or without preterm labour) there was no difference between the TVU and no TVU groups in preterm birth at 36, 34 or 30 weeks, or in gestational age at delivery or other perinatal and maternal outcomes. Life table analysis showed significantly less (p= 0.02) preterm birth at <35 weeks in the TVU group compared to the no TVU group. The authors of this review concluded that there is insufficient evidence to recommend routine screening of either symptomatic or asymptomatic pregnant women with cervical length measurement via TVU.

Berghella V, Hayes E, Visintine J, et al. 2008. **Fetal fibronectin testing for reducing the risk of preterm birth**. Cochrane Database of Systematic Reviews, Issue 4, Art. No.: CD006843. DOI: 10.1002/14651858.CD006843.pub2.

Fetal fibronectin (FFN) is a protein which is localised at the maternal-fetal interface of the amniotic membranes and is normally found only at very low levels in cervico-vaginal secretions. Levels greater ≥ 50 ng/l at or after 22 weeks have been associated with an increased risk of preterm birth and high FFN levels have been found to be one of the best predictors of preterm birth in all populations studied to date. The aim of this review was to assess the effectiveness of management based on knowledge of FFN levels, compared to management without such knowledge, for the prevention of preterm birth. This review included five RCTs (474 women) of knowledge vs. no knowledge of FNN. There was a significant decrease in preterm birth at <37 weeks in the knowledge group compared to the no-knowledge group (15.6% vs.28.6%, RR 0.54, 95% CI 0.34–0.87). All other outcomes measured were similar in both groups (preterm birth at <34, 32, or 28 weeks; gestational age at delivery; birthweight < 2500 grams; perinatal death; maternal hospitalization; tocolysis; steroids for fetal lung maturity; and time to evaluate i.e. time between hospital arrival and a management decision being made). The authors of this review concluded that, although FFN measurements are commonly used in labour and delivery units, there is currently little evidence to recommend such measurements. Given the association found in this review between knowledge of FNN results and a lower incidence of preterm birth before 37 weeks, further research is worthwhile and should be encouraged.

Swadpanich U, Lumbiganon P, Prasertcharoensook W, et al. 2008. **Antenatal lower genital tract infection screening and treatment programs for preventing preterm delivery**. Cochrane Database of Systematic Reviews, Issue 2, Art. No.:CD006178. DOI: 10.1002/14651858.CD006178.pub2.

Genital tract infection is a cause of preterm birth and infection screening has been used as a means of preventing preterm birth. There are some adverse effects from treating such infections including cost and increased antibiotic resistance. The authors of this review identified one high quality RCT (4155 women). In the intervention group the results of screening for bacterial vaginosis, trichomonas vaginalis and candidiasis were reported and women received treatment if tests were positive, and in the control group results of tests were not reported. There were significantly fewer preterm births in the intervention group (3% vs. 5%, relative risk 0.55, 95% CI 0.41–0.75) and also fewer preterm very low birthweight (<1500g) infants (RR 0.34, 95% CI 0.15–0.75) and preterm low birthweight (<2500g) infants (RR 0.48, 95% CI 0.34–0.66). The review authors concluded that infection screening and treatment programmes in pregnant women before 20 weeks gestation reduce both preterm births and preterm low birthweights.

Flenady V, Macphail J, New K, Devenish-Meares P, Smith J. 2008. **Implementation of a clinical practice guideline for smoking cessation in a public antenatal care setting.** Aust N Z J Obstet Gynaecol. 48(6):552-8. doi: 10.1111/j.1479-828X.2008.00907.x.

Despite high level evidence showing that antenatal smoking cessation programmes are effective in reducing the number of women who smoke during pregnancy and the number of low birthweight and preterm births, few Australian hospitals have adopted a systematic approach to assist pregnant women to stop smoking. This study aimed to assess the effectiveness of a smoking cessation guideline, developed specifically for clinicians providing antenatal care in public maternity hospitals, combined with an implementation program on the uptake of evidence-based practice. A clinical practice guideline was developed and an implementation strategy was tested, using a prospective before-and-after study design. Women were surveyed in late pregnancy, pre- and post-implementation. The primary outcome measures were women's report of appropriate smoking cessation support received, specifically, information brochures and referral to Quitline. Secondary outcome measures included women's report of smoking status in late pregnancy and relapse rates. Post-implementation, more women reported receiving written materials on smoking cessation (76% vs. 35%; relative risk (RR) 3.4; 95% CI 2.7, 4.2) and referral to Quitline (67% vs. 14%; RR 4.9; 95% CI 3.0, 8.0). While not statistically significant, fewer women post-implementation reported smoking in late pregnancy (19.5% vs. 16.7%) and fewer reported smoking >10 cigarettes per day (38% vs. 25%). The authors concluded that clinical practice guidelines specifically designed for a public maternity care setting combined with an implementation program resulted in an increase in evidence-based practice with some indication of improved smoking behaviour for women.

Smaill F, Vazquez JC. 2007. **Antibiotics for asymptomatic bacteriuria in pregnancy**. Cochrane Database of Systematic Reviews, Issue 2, Art. No.: CD000490. DOI: 10.1002/14651858.CD000490.pub2.

Asymptomatic bacteriuria is relatively common in pregnancy (2–10% of women) and, if this is untreated, about 30% of those affected will develop acute pyelonephritis. Asymptomatic bacteriuria has been associated with both low birthweight and preterm birth. This review aimed to assess the effect of antibiotic treatment on bacteriuria detected by screening in asymptomatic pregnant women. It included 14 RCTs of generally poor quality comparing antibiotics to placebo. Compared to placebo, antibiotics were effective at clearing symptomatic bacteriuria (risk ratio (RR) 0.25, 95% CI 0.14 to 0.48) and reducing the incidence of pyelonephritis (RR 0.23, 95% CI 0.13–0.41). Antibiotic treatment was also associated with a reduction in the proportion of low birthweight babies (RR 0.66, 95% CI 0.49–0.89) but not in the proportion of deliveries that were preterm. The review authors concluded that antibiotics were effective in reducing the risk of pyelonephritis in pregnancy and that, although the observed effect on reducing low birthweight is consistent with accepted theories about the role of infection in adverse pregnancy outcomes, this association should be viewed cautiously in view of the poor qualities of the included studies.

Dodd Jodie M, Flenady V, Cincotta R, et al. 2006. **Prenatal administration of progesterone for preventing preterm birth in women considered to be at risk of preterm birth**. Cochrane Database of Systematic Reviews, Issue 1, Art. No.: CD004947. DOI:10.1002/14651858.CD004947.pub2. Content updated after new search for studies (no change to conclusions), assessed as up to date in December 2008, published in Issue 2, 2009.

Progesterone has a role in maintaining pregnancy and the mechanism is thought to be inhibition of uterine smooth muscle contraction. It may be given either by intramuscular injection or as a vaginal pessary. There is little long term safety data and little information about the optimal dose, route of administration, gestation to begin therapy, or duration of therapy. This review included 36 RCTs (8523 women and 12,515 infants) involving comparison of progesterone vs. placebo in a variety of situations. In women with past history of spontaneous preterm birth progesterone was associated with a statistically significant reduction in the risk of preterm birth less than 34 weeks (average RR 0.31, 95% CI 0.14–0.69), preterm birth less than 37 weeks (average RR 0.55, 95% CI 0.42 to 0.74) and infant birthweight less than 2500 g (RR 0.58, 95% CI 0.42–0.79). Also noted was a statistically significant increase in pregnancy prolongation in weeks (mean difference (MD) 4.47, 95% CI 2.15–6.79). For women with a short cervix identified on ultrasound, progesterone was associated with a statistically significant reduction in the risk of preterm birth < 34 weeks (RR 0.64, 95% CI 0.45–0.90) and preterm birth at less than 28 weeks' gestation (RR 0.59, 95% CI 0.37–0.93). An increased risk of urticaria in women when compared with placebo was noted (RR 5.03, 95% CI 1.11–22.78). In women with a threatened labour, progesterone was associated with significant reduction in the risk of infant birthweight < 2500 grams (RR 0.52; 95% CI 0.28–0.98); In women with “other” risk factors for preterm birth progesterone was associated with a statistically significant reduction in the risk of infant birthweight less than 2500 g (RR 0.48, 95% CI 0.25–0.91).No statistically significant differences were noted in the reported outcomes for women with a multiple pregnancy. The authors state that further research is required to determine the optimal timing, mode of administration and dose of progesterone.

Note: The publications listed were identified using the search methodology outlined in Appendix 1 (Search Methods for Policy Documents and Evidence-Based Reviews)

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