

A descriptive observational study of B12 testing during pregnancy and infancy in New Zealand and suggested guidance for testing and treatment

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ABSTRACT

AIMS: Severe B12 deficiency is harmful to infants. This study describes the recent detection and treatment rates of antenatal and infant B12 deficiency in the Auckland–Northland region.

METHOD: Regional laboratory data on serum B12 levels were analysed. B12 deficient infants and pregnant women were identified and paired with their corresponding mother or infant, followed by a review of electronic health records.

RESULTS: Testing incidence was low in infants (5 per 1,000 infants per year). Among 529 infants tested over 5 years, 6% exhibited B12 deficiency (<148pmol/L). Antenatal B12 deficiency was found in 16% of 6,365 pregnant women tested over 1 year, with *high-risk* deficiency (<100pmol/L) found in 2%. Both infants and mothers with B12 deficiency had suboptimal rates of adequate treatment. Among infants of *high-risk* B12 deficient pregnancies, only 1% had serum B12 tested despite being at high risk of infant B12 deficiency.

CONCLUSION: Current guidelines and testing practices in Auckland–Northland inadequately detect and treat B12 deficiency in pregnancy and infancy. A risk-based screening approach is best suited to detect infants at risk of severe deficiency. Antenatal and post-natal recommendations for B12 testing and treatment of mothers and infants are made, along with nutritional advice in pregnancy and infancy.

B12 is an essential vitamin crucial to human neurodevelopment that is obtained almost exclusively from dietary animal products, fortified foods or supplementation. The mother is an infant's sole source of B12, provided antenatally via active transport across the placenta, and postnatally in breastmilk, until B12-rich foods or fortified milk formula are introduced to the infant's diet.¹ Low maternal serum B12 status correlates with increased risk of infant B12 deficiency.^{1,2}

The classic infant presentation of B12 deficiency occurs in the exclusively breastfed infant of a B12 deficient mother, manifesting between 4 and 9 months old as the infant's low B12 stores, already inadequate at birth following deficiency *in utero*, are steadily depleted and not replaced in the diet. In severe deficiency, the infant may present with anaemic pallor and fatigue, developmental delay, irritability, gastrointestinal symptoms, feeding difficulty and faltering growth. A high index of suspicion is required by the clinician, as these symptoms are common and nonspecific in infants, but the diagnosis is easily confirmed by

identifying low serum B12. Deficiency is treated with supplementation, and symptoms rapidly resolve with early intervention, but if left untreated the neurological consequences can be irreversible.¹

There is no gold standard definition of B12 deficiency at any age, and serum B12 levels alone are an imperfect measure of body stores. Various measurement methods of serum B12 are employed, including bacterial inhibition assays and various immunoassays, and these differing measurement techniques between laboratories may influence local deficiency thresholds. Defining antenatal B12 deficiency is further complicated by the gradual decline in measured serum B12 levels during pregnancy due to a combination of factors unrelated to B12 stores, especially a 20–30% reduction in the major B12 binding protein (haptocorrin) caused by increased oestrogens, along with haemodilution and increased glomerular filtration rate.^{1,2} The most commonly cited threshold for deficiency in pregnancy and infancy is a serum B12 <148pmol/L (200pg/mL), which is the third standard deviation value in non-pregnant North American adults as per

the National Health and Nutrition Examination Survey (NHANES).³ Global prevalence estimates of antenatal B12 insufficiency are approximately 25%, increasing up to 65% in ethnic groups where a vegetarian or vegan diet is common.⁴ A retrospective cohort study in Vancouver reported a prevalence of antenatal B12 deficiency (serum B12 <148pmol/L) in the first and second trimesters at 20.1% and 20.4% respectively and in women with South Asian ancestry 30.2% and 35.8% respectively.⁵

The prevalence of antenatal B12 deficiency in New Zealand is unknown. Recent estimates of the prevalence of vegetarian diet in New Zealand adults vary between 2–19%, with higher rates in women compared to men.^{6,7} The *2008/09 New Zealand Adult Nutrition Survey* reported inadequate dietary B12 intake using dietary questionnaires in 22.8% of women respondents aged between 19–30 and 16.1% of women aged between 31–50, along with B12 deficiency (<148pmol/L) in 2% of the subset of non-pregnant adults who had serum B12 measured, increasing to 3% among those of South Asian and NZ European ethnicity.^{8,9} The ethnic communities at highest risk of B12 deficiency in New Zealand are South Asians (defined as people with ancestral origins in the Indian subcontinent including India, Afghanistan, Pakistan, Sri Lanka, Nepal, Bangladesh, Bhutan and the Maldives) and Fijian Indians, related to cultural and religious dietary practices with the key dietary determinant being the consumption of red meat.⁸ Current New Zealand antenatal guidelines do not recommend routine B12 supplementation or measurement; however, they include dietary advice that encourages intake of lean meat and dairy products while recommending those with a vegan diet orally supplement B12 while pregnant and breastfeeding.¹⁰

The prevalence of symptomatic B12 deficiency among New Zealand infants is unknown. However, reports of the late detection of severely affected infants along with recently published findings of very low B12 levels (<50pmol/L) in the cord blood of otherwise healthy newborns in South Auckland suggests that deficiency may be under-recognised.^{11,12} Prevalence estimates of newborn B12 deficiency in demographically similar European countries range between 1:2,000 and 1:5,000.^{13,14} Assuming these estimates are comparable to New Zealand, with 60,000 births annually in New Zealand, this may represent a significant number of affected infants who could benefit from early detection and treatment.

Methods

Aims

The aims of this descriptive observational study were to describe the recent detection and treatment rates of B12 deficiency in the Auckland–Northland region among pregnant mothers and infants who had serum B12 measured.

Study design

Awanui Labs (formerly Labtests Auckland [LTA]) provides almost all community laboratory services in the Auckland–Northland region. LTA provided data on serum B12 levels for analysis, along with approximate testing rates in the general population for comparison.¹⁵ Two patient cohorts were identified with the following inclusion criteria:

1. **Infant cohort:** infants aged less than 12 months who had B12 measured between 01/01/2017–01/06/2022 in the Auckland–Northland region. Infants with B12 deficiency (serum B12 <148pmol/L) were paired with the maternal national health index (NHI), and the electronic health record (EHR) of both mother and infant were reviewed. The longer timeframe was chosen to compensate for the lower rate of testing in this cohort.
2. **Antenatal cohort:** pregnant women who had B12 tested between 01/04/2021–01/04/2022 in the Auckland–Northland region. Mothers at highest risk of B12 deficiency (serum B12 <100pmol/L) were paired with the infant(s) NHI, and the EHR was reviewed.

Data collection categories included serum B12 levels of mother and infant, treatment prescribed and qualitative review of clinical records.

The EHR contains all prescriptions and laboratory test results for the study participants, along with documentation from hospital clinicians in the Auckland–Northland region. It includes antenatal documentation for women with complex pregnancies, but does not contain primary care documentation by community midwives or general practitioners providing care for women with low-risk pregnancies.

The New Zealand Ministry of Health – Manatū Hauora maternity database paired mothers and infants. Population statistics, including live births and city populations by year, were sourced from Statistics New Zealand.¹⁶ The number of live births

in 2022 represented completed pregnancies that followed antenatal blood tests collected between 01/04/2021 and 01/04/2022. Exclusion criteria were incomplete or duplicate records, non-liveborn babies and patients likely incorrectly coded as antenatal (male, <15 years old, >50 years old).

B12 deficiency and treatment thresholds

This study used the NHANES definition of B12 deficiency (<148pmol/L) for ease of comparison with other literature, but acknowledges this definition's limitations, particularly in the unique physiological states of pregnancy and infancy.^{1,2} Pregnant women in the study cohort with serum B12 <100pmol/L were deemed to have the highest likelihood of clinically significant B12 deficiency and are referred to here as *high-risk* pregnancies.

This study defined adequate treatment as "B12 treatment at any dose administered within 3 months of diagnosis, and if pregnant administered prior to delivery". Dietary advice alone did not meet this threshold. Both enteral and parenteral B12 administration were considered appropriate treatment modalities. In the absence of documented

treatment, a subsequent rise in serum B12 level to >400pmol/L on repeat testing was considered evidence that treatment was administered by alternative means, such as during a hospital admission or using a non-prescribed B12 supplement, as serum B12 is unlikely to spontaneously rise to this extent.

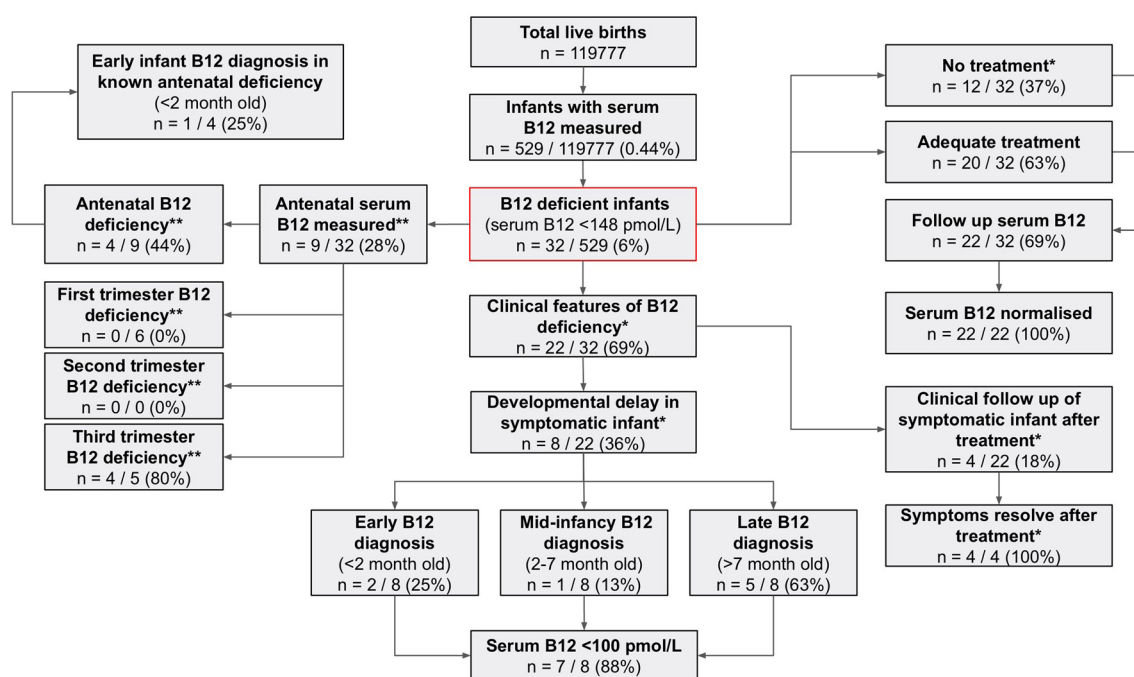
Biochemical analysis

Serum B12 was measured at LTA using the Siemens ADVIA Centaur between January 2017 and November 2020. From December 2020, the Roche cobas platform was used. The two assays closely correlate in accuracy in the normal and low range of serum B12; however, the Roche assay has a negative bias for very low levels compared to the Siemens method (e.g., Roche 100pmol/L approximated to Siemens 138pmol/L).

Ethics

This study was approved by the Auckland Health Research Ethics Committee (reference number AH25382).

Figure 1: Flowchart summary of infant cohort results.



*As documented in the electronic health record (EHR).

**Serum B12 levels were measured at varying gestations (see Table 3) and without important contextual information, which affects their interpretation. Normal antenatal B12 levels decline over time and antenatal B12 deficiency thresholds are debated.

Results

Infant cohort

In the 5-year period between 01/01/2017 and 31/12/2021 there were 119,777 live births registered in the Auckland–Northland region. Serum B12 was measured in 529 infants during this period (approximately 4 per 1,000 infants per year, or 0.44%), with 105 of these infants tested at 6 months of age or younger (approximately 1 per 1,000 infants per year, or 0.09%) (Figure 2). By comparison, 22% of the greater Auckland population had serum B12 measured at least once by LTA in 2022 (227 per 1,000 persons per year).¹⁵

B12 deficiency was found in 32 (6%) of tested infants, 22 of whom had clinical features documented in the EHR that may be caused by B12 deficiency (Table 1). The testing indication and/or symptoms of the remaining 10 infants were unavailable.

Seven out of the eight developmentally delayed infants had a serum B12 level less than 100pmol/L. Only two of these eight infants had B12 deficiency diagnosed in early infancy (<2 months old), with five diagnosed in late infancy (>7 months) (Table 2).

Among the 32 infants with B12 deficiency, 20 (63%) had evidence of adequate treatment.

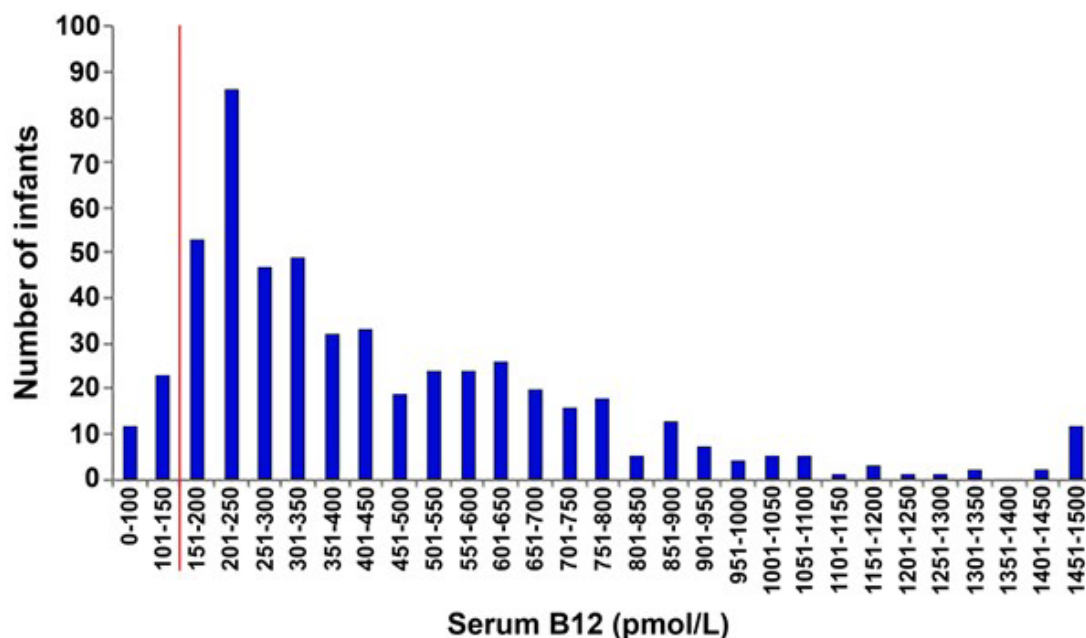
The dose varied widely, from low dose over-the-counter B12 drops in one infant to a cumulative 24mg of intramuscular B12 in another infant. The remaining 12 infants had no recorded treatment, but they may have been given dietary advice or over-the-counter B12 treatment.

A follow-up serum B12 level was checked at least 6 weeks after the initial test in 22 (69%) of the deficient infants. All B12 levels normalised on repeat measurement, including in two infants without documented treatment.

Four symptomatic treated infants had clinical follow-up documented in the EHR. All reported improved symptoms within 1 month of treatment, including rapid neurodevelopmental progress. One had long term follow-up that described normal neurodevelopment at age 2 years despite initial high-risk B12 deficiency (74pmol/L) at 10 months old. The remaining infants may have had clinical follow-up in primary care.

Nine of the 32 mothers of infants with B12 deficiency had serum B12 measured during the pregnancy and four had B12 deficiency antenatally (<148pmol/L), each in the third trimester. In each case, contextual information including the reason for antenatal testing, the presence of antenatal risk factors for B12 deficiency and antenatal

Figure 2: Serum B12 levels of tested infants (n=529) born between 01/01/2017 and 01/06/2022 in Auckland and Northland.



*The red line indicates the approximate B12 deficiency threshold (<148pmol/L).

Table 1: Proportion of symptomatic B12 deficient infants with the corresponding clinical feature of B12 deficiency.*

Symptom	n/22 (%)
Feeding difficulties	15 (68%)
Faltering growth	13 (59%)
Developmental delay	8 (36%)
Anaemia and/or macrocytosis	5 (23%)
Raised urinary methylmalonic acid	1 (5%)
Tremor	1 (5%)

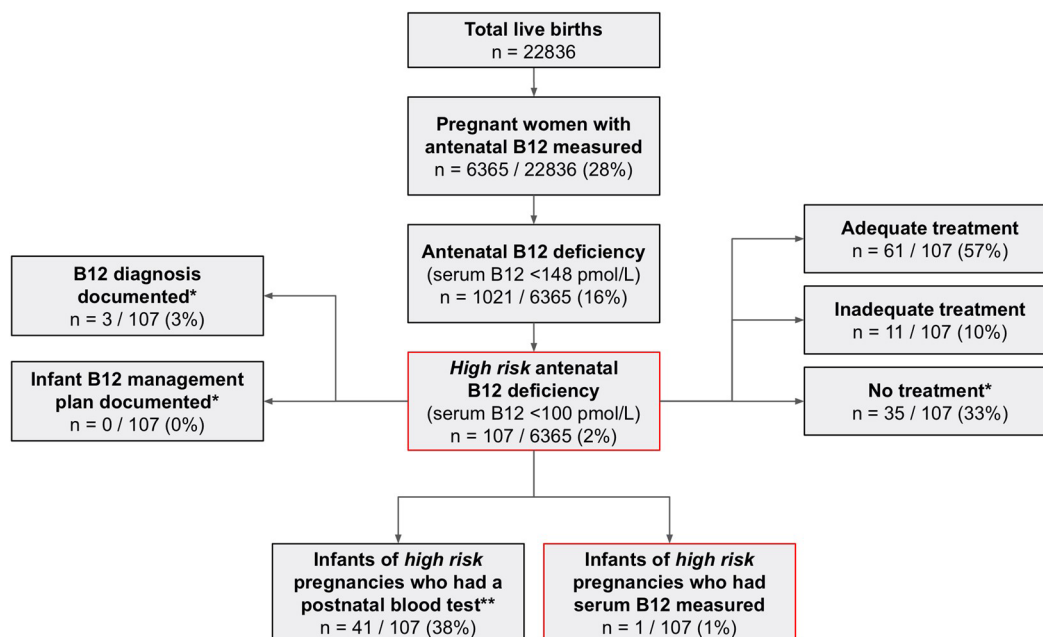
*As per available electronic health record (EHR) documentation. Some infants had several symptoms.

Table 2: Age of diagnosis and serum B12 level of B12 deficient infants with developmental delay.

Case number	Age at diagnosis (days)	B12 level (pmol/L)
1	212	52
2	322	74
3	319	74
4	347	74
5	148	83
6	37	94
7	48	99
8	345	143

Table 3: Age at diagnosis and maternal antenatal B12 levels of infants with B12 deficiency.

Case number	First trimester	Second trimester	Third trimester	Infant serum B12 (pmol/L)	Infant age at diagnosis (days)
1	219	-	-	92	240
2	-	-	219	94	37
3	-	-	92	97	291
4	165	-	-	99	164
5	198	-	111	101	240
6	-	-	126	111	32
7	347	-	133	119	310
8	385	-	-	132	121
9	172	-	-	145	205

Figure 3: Flowchart summary of antenatal cohort results.

*As documented in the electronic health record (EHR).

**Excluding newborn metabolic screen and blood sugar testing.

B12 treatment or supplementation could not be accurately determined from the EHR. Only one of these four infants was diagnosed in early infancy (<2 months) (Table 3).

Antenatal cohort

A total of 6,365 pregnant women in the Auckland–Northland region between 01/04/2021 and 01/04/2022 had serum B12 levels tested, which is approximately 28% of the 22,836 live births in Auckland and Northland in 2022. Antenatal B12 deficiency (<148pmol/L) was found in 1,021 (16%) of these women, with *high-risk* deficiency (<100pmol) in 107 (2%) of these pregnancies.

Among the *high-risk* pregnancies, 61 (57%) had evidence of adequate treatment. All but one were treated with intramuscular B12 with the cumulative dose ranging between 1 and 8mg. The remaining person was prescribed an oral multivitamin containing B12. Thirty-five women (33%) had no recorded treatment, but they may have been given dietary advice or over-the-counter B12 treatment. Eleven women (10%) were prescribed inadequate treatment; seven had treatment delayed either by >3 months after diagnosis or until postpartum, three had persistent deficiency on post-treatment

follow-up testing but did not receive further treatment, and two were prescribed a multivitamin that did not contain B12.

A clinician documented the diagnosis of antenatal B12 deficiency in three (3%) of the *high-risk* pregnancies. There was no documented plan in any *high-risk* pregnancy to screen the infant for B12 deficiency after birth, but there may have been documentation in primary care.

Of the 109 children born of *high-risk* pregnancies only one (1%) had serum B12 measured in infancy. By comparison, 41 (38%) had blood tests (not including newborn metabolic screening or blood sugar testing) performed in infancy unrelated to B12.

Discussion

This study found that serum B12 was measured in over a quarter of pregnancies despite not being recommended as a routine screening test. However, when pregnant women were diagnosed with B12 deficiency they were frequently under-treated and there was little testing of their at-risk infants. Serum B12 was measured 50-fold less frequently in infants than in the general population. B12

deficient infants were usually not diagnosed until late infancy. When neurodevelopmental delay was present in a B12 deficient infant, it was almost exclusively in those with the lowest B12 levels (<100pmol) and resolved with supplemental B12 treatment where developmental data was available. Despite the known causal link between antenatal and infant B12 deficiency, it was uncommon to find cases where a mother and infant both had serum B12 measured. These findings suggest there may be an unrecognised burden of treatable B12 deficiency in infants in the Auckland–Northland region.

The key strengths of this study lie in the large study population from which the B12 deficient cohorts were identified. During the study period LTA was effectively the sole provider of the test in the region; therefore, this large dataset was a representative sample and allowed for focussed analysis of a significant number of *high-risk* pregnancies and infants. However, there were significant limitations. Database linkage analysis may have incompletely or inaccurately identified patient records. The EHR is not a comprehensive medical record and therefore relevant clinical information recorded elsewhere would have been overlooked. Interpretation of paired antenatal–infant B12 levels were particularly confounded by this limitation. The study contained participants in the Auckland–Northland region and due to demographic differences, as well as potential regional differences in clinical and laboratory practice, these findings may not apply to other regions of New Zealand. Furthermore, these data cannot determine the prevalence or effect of B12 deficiency on infant neurodevelopment, as they are confounded by the absence of randomisation, the low testing incidence and the comparatively high prevalence of developmental delay in infants.

Infants of B12 deficient mothers were rarely tested for deficiency, and the reason is unclear. A large proportion of these infants had blood tests performed for other reasons, and thus a reluctance by clinicians to test due to the painful nature or technical difficulty of blood sampling in infancy cannot be the sole explanation. The disruption to care continuity during the transition from pregnancy to infancy may be contributory. There is usually no single practitioner that oversees both the pregnancy and infancy in New Zealand. Antenatal and early postnatal care is led by the lead maternity carer (LMC), usually a midwife. As B12 deficiency is asymptomatic in the first weeks of life, there may be no clinical concerns when the

mother and baby's care is transferred to a general practitioner at 4–6 weeks postnatally. By the time they present to primary care with neurodevelopmental symptoms in later infancy, the antenatal risk factor may be overlooked or assumed not to be relevant.

Several large prospective cohort studies and small randomised trials have suggested that mild to moderate B12 deficiency either antenatally or in infancy may have a detrimental effect on infant neurodevelopment.^{17–21} However, a recent large randomised controlled trial of antenatal B12 supplementation in a Nepalese population with endemic B12 deficiency demonstrated no difference in infant neurodevelopment outcomes between the treated and untreated groups despite improved B12 status in the treated group.²² These latter findings support the current World Health Organization (WHO) recommendation against routine antenatal B12 supplementation.²³

However, there remains a threshold of severity where B12 deficiency becomes unequivocally and irreversibly harmful to an infant. The New Zealand National Metabolic Service is notified of between one and three such cases annually in New Zealand, typically presenting with severe anaemia and neurological impairment, which can be life-threatening.²⁴ These infants remain a priority for early detection and treatment, particularly when comparing the relative ease and low cost of treatment against the high cost of neurodevelopmental impairment to both the patient and the healthcare system over a lifetime.

The New Zealand Newborn Metabolic Screening Programme (NMSP) occasionally detects incidental B12 deficiency via raised propionylcarnitine (C3) levels while screening for methylmalonic and propionic acidaemia, which has led to NMSP considering implementation of universal newborn screening (NBS) in New Zealand.²⁴ Several European NBS centres have recently published pilot studies implementing systematic newborn B12 bloodspot screening by adapting the screening thresholds of the B12 metabolites classically used to detect these acidaemias. They reported an unexpectedly high prevalence of B12 deficiency (1:1989–1:5355); however, the approach appears limited by suboptimal sensitivity and specificity.^{13,14,25}

Since universal newborn screening appears impractical, targeted screening must be considered. However, symptoms of infant B12 deficiency such as poor feeding and irritability are common and non-specific in infancy, and there is a high

prevalence of developmental delay in New Zealand children.^{26,27} Using the third percentile cutoff for developmental milestones, approximately 2,000 of the 60,000 infants born annually in New Zealand will be expected to have some degree of developmental delay. Symptomatic B12 deficiency will rarely be the cause of these symptoms, particularly in populations with regular dietary intake of animal products, thereby rendering indiscriminate testing of serum B12 of these infants inefficient and impractical.

Targeted testing of B12 status in infants and

their mothers based on risk factors for deficiency is therefore recommended. If B12 deficiency is diagnosed in either group, it should be managed primarily with the goal of reducing the infant's risk of severe deficiency and neurodevelopmental harm. If a mother and infant are at risk of B12 deficiency, this must be included in the handover of care between antenatal and primary care providers. The following screening recommendations aim to guide the management of at-risk pregnant women and infants while increasing awareness of this complex issue among clinicians.

COMPETING INTERESTS

DW is Vice President of the International Society for Neonatal Screening (ISNS).

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Appendix

There are currently no formal consensus screening or treatment guidelines in managing the risk of B12 deficiency in the infants of B12 deficient mothers. This shortfall may be contributing to the results described in this study. The recommendations that follow are not systematic guidelines, but rather intend to provide pragmatic advice to the clinician managing a pregnancy or infancy at risk of B12 deficiency in New Zealand based on the local context described in this study and other recent emerging evidence.

These recommendations specifically target infants at high risk of B12 deficiency; they do not provide comprehensive guidance regarding the investigation and management of B12 deficiency in pregnant women. For systematic guidelines regarding the management of B12 deficiency in adults, refer to the National Institute for Care and Excellence (NICE) guideline *Vitamin B12 deficiency in over 16s: diagnosis and management*.²⁸

A) Screening recommendations

Recent evidence suggests that the vast majority of infants at risk of B12 deficiency will experience normal neurodevelopment with no medical consequences, including those who are mild–moderately deficient.²² However, B12 deficiency that is severe and prolonged can cause irreversible neurological harm to an infant. The goal of these recommendations is to identify these infants with the highest risk for severe deficiency, and to effectively reduce their risk through dietary and pharmacological intervention both before and after birth. Where dietary/supplementation advice is recommended, refer to *B) Nutrition and treatment recommendations*. Allowing for the margin of error of the laboratory assay and the lack of consensus definition for deficiency, thresholds have been rounded up to the nearest 10pmol/L for simplicity.

Pregnancy (see Appendix Figure 1)

1. **Take a medical and dietary history in the first trimester to identify risk factors for deficiency.** See Appendix Table 1 and *Appendix—B) Nutrition and treatment recommendations*.
2. **If a woman has no risk factors, then testing is not recommended.** Most women do not require B12 testing or supplementation in pregnancy.

3. **If a woman has any risk factor for B12 deficiency, provide dietary/supplementation advice and measure serum B12 alongside other routine antenatal screening blood tests at the first booking appointment (ideally in the first trimester).** Antenatal serum B12 levels trend downwards as gestation progresses due to normal physiological changes in pregnancy; therefore, early antenatal serum B12 levels are a more representative screening test for deficiency in the mother.^{1,2}
4. **Recommended management according to antenatal serum B12 level (ideally measured first trimester):**
 - A. **>400pmol/L:** no further testing or treatment is recommended due to the low risk for infant deficiency.²
 - B. **150–400pmol/L:** reiterate diet/supplementation advice. Further testing or treatment has not been shown to improve infant neurodevelopmental outcomes.²²
 - C. **100–149pmol/L:** recommend antenatal oral or intramuscular B12 treatment to reduce the infant's risk of deficiency. Reiterate diet/supplementation advice.
 - D. **<100pmol/L:** recommend administration of intramuscular B12 treatment to reduce the infant's risk of deficiency. Reiterate diet/supplementation advice.
5. **If B12 deficiency is appropriately treated antenatally, then follow-up testing of the mother is not required.**
6. **If serum B12 level is <150pmol/L at any gestation, refer to the “Infancy” recommendations to guide management of the infant** (see Appendix Figure 2). Refer to the NICE Guidelines for advice regarding investigation of the underlying cause of B12 deficiency in pregnant adults.²⁸

Infancy (see Appendix Figure 2)

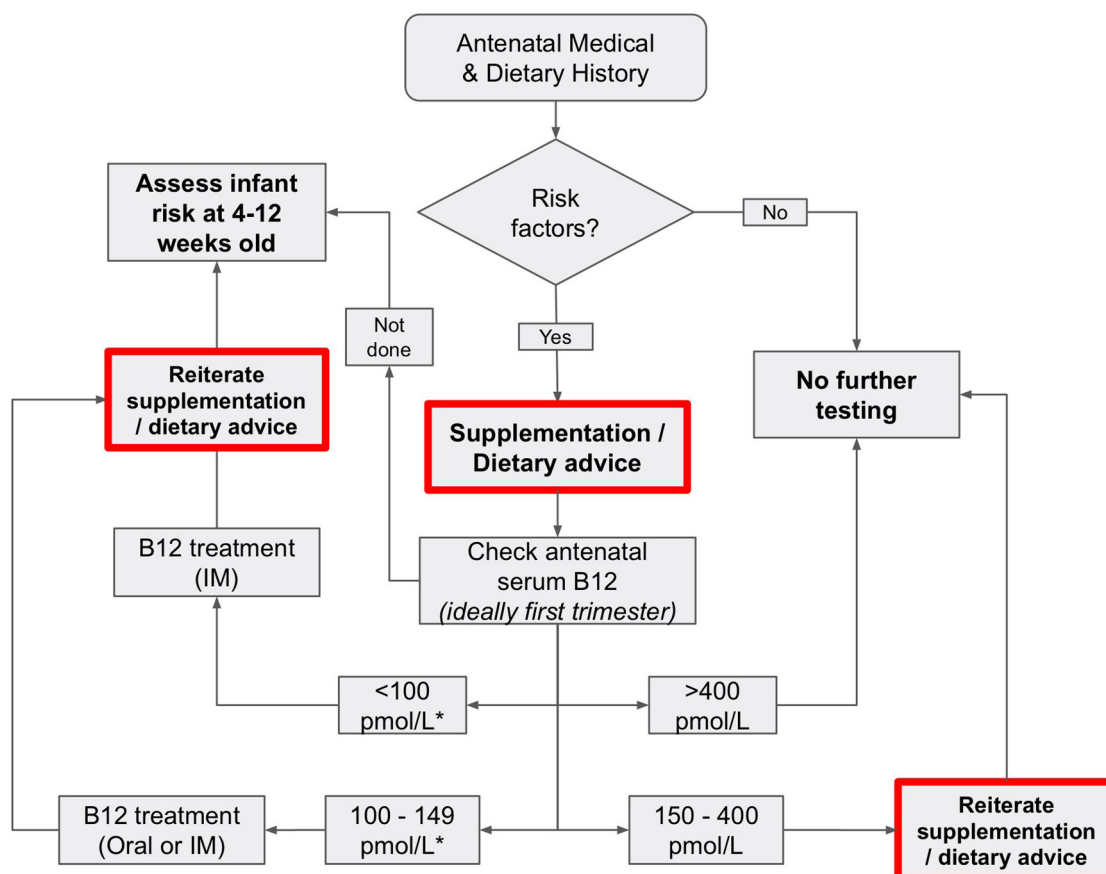
1. **If antenatal serum B12 was <150pmol/L at any gestation, or if any maternal risk factors for deficiency were present but antenatal serum B12 levels were not measured, then the infant is at risk of B12 deficiency.** Provide dietary/supplementation advice. This risk factor must be included in any handover of care from antenatal care to primary care (e.g., general practitioner).
2. **Reassess infant risk between 4–12 weeks old** (e.g., at time of discharge from lead

Appendix Table 1: Maternal risk factors for infant B12 deficiency.^{1,8}

Previous antenatal B12 deficiency
Previous child with B12 deficiency
Limited consumption of animal products, particularly red meat (vegetarian/vegan diet, socio-economic factors, eating disorders)*
Gastrointestinal condition causing B12 malabsorption (pernicious anaemia, significant disease or surgery affecting the stomach, ileum or pancreas, inflammatory bowel disease)
Unexplained or macrocytic anaemia
Genetic disorder of B12 metabolism
Chronic use of medications/substances that affect B12 absorption or metabolism (e.g., metformin, proton pump inhibitor, H2-receptor antagonists, excess alcohol)
History of autoimmune disease (e.g., Coeliac, autoimmune thyroiditis, type 1 diabetes)

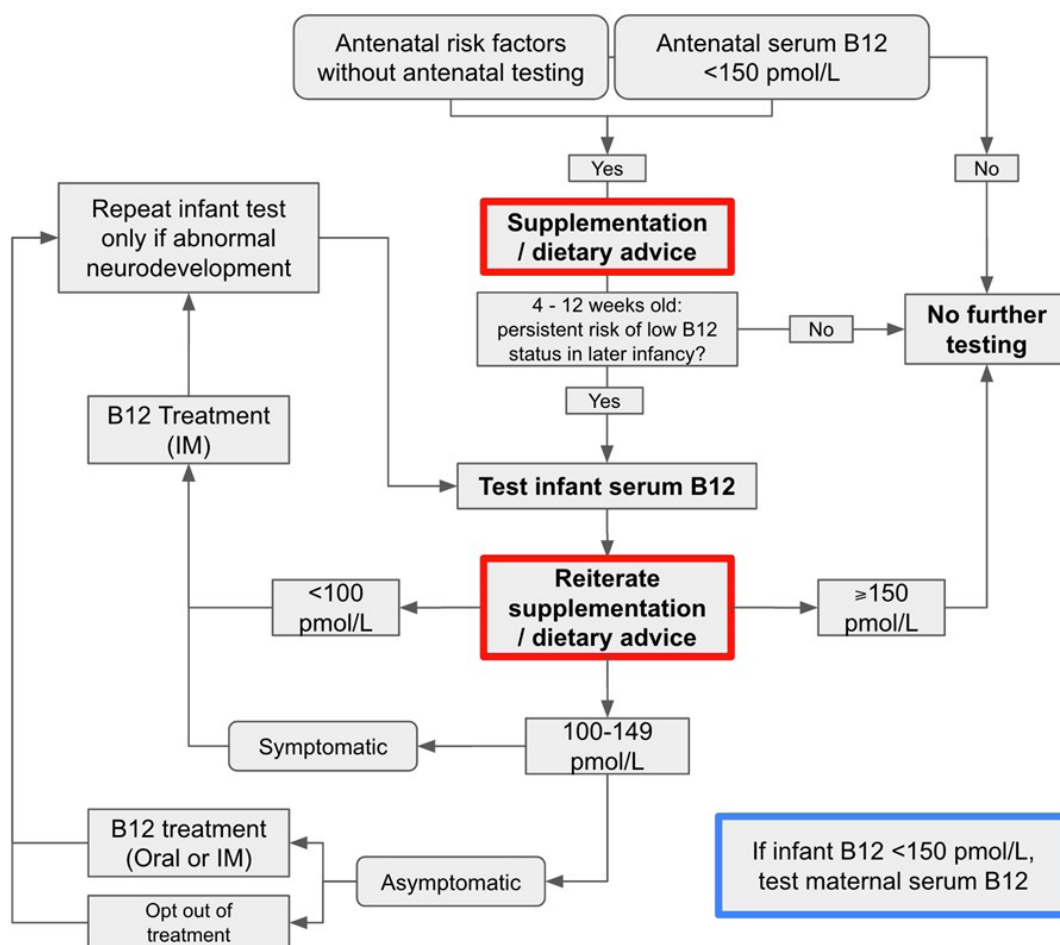
*See Appendix—B) Nutrition and treatment recommendations.

Appendix Figure 1: Antenatal recommendations flowchart.



*Refer to NICE guidelines regarding investigation of cause of B12 deficiency.²⁸

Appendix Figure 2: Infant recommendations flowchart.



maternity carer [LMC] care, or during the “6-week infant check” in primary care). If a risk reduction strategy has been put in place (e.g., infant/maternal B12 supplementation, plan for prioritised introduction of animal products into diet when the infant starts solids—see *Appendix*), then no further testing is needed. However, if no risk reduction strategy is in place, the infant remains at risk of B12 deficiency; **test serum B12 in these selected infants while reiterating dietary/supplementation advice.**

3. Recommended management according to infant serum B12 level:

A. <100pmol/L: strongly recommend B12 treatment via the intramuscular route.

B. 100–149pmol/L: if symptomatic, treat as per (A) above. If asymptomatic, provide treatment based on family preference. If they opt out of treatment, monitor the infant

clinically for symptoms of B12 deficiency, particularly abnormal neurodevelopment.

C. ≥150pmol/L: no treatment is required.

- 4. Follow-up testing is not required in most infants, regardless of treatment.** The exception is when specific symptoms develop in later infancy suggestive of severe B12 deficiency, particularly abnormal neurodevelopment.
- 5. If an infant’s serum B12 is <150pmol/L, measure the B12 status of the mother.** If she is also found to be B12 deficient, treat as per NICE guidelines.²⁸

B) Nutrition and treatment recommendations

Diet is the most important determinant of a person’s B12 status. The consumption of red meat is the main dietary factor correlating to serum B12 concentration in the New Zealand population.⁸ When taking an antenatal dietary history,

specifically ask about consumption of animal products, with particular attention in patients of South Asian (defined as people with ancestral origins in the Indian subcontinent including India, Afghanistan, Pakistan, Sri Lanka, Nepal, Bangladesh, Bhutan and the Maldives) and Fijian Indian ethnicities, where reduced animal product consumption is more prevalent due to cultural and religious practices.⁸ Other factors causing food restriction (such as socio-economic deprivation or eating disorders) may also limit a person's ability to regularly consume animal products or B12 supplementation.¹

The antenatal recommended daily intake (RDI) for B12 is 2.6mcg/day (increased from 2.4mcg/day for non-pregnant adults due to placental and foetal demand), and further increases to 2.8mcg/day when breastfeeding.²⁹ Pregnant women with a diet inclusive of animal products will usually meet this requirement by following the Ministry of Health guidance on *Safe and healthy eating in pregnancy*, consuming at least three servings per day from the following food groups: lean meat, poultry, seafood, eggs, nuts, seeds and legumes, while prioritising the consumption of animal products.¹⁰ If a pregnant woman is vegetarian or vegan, they are recommended to take an oral supplement providing at least the RDI of vitamin B12 due to the variable levels of B12 in fortified food products.¹⁰ There are numerous inexpensive oral vitamin supplements containing B12 that are commercially available in New Zealand, although none are currently subsidised for pregnant women or infants.

In infants with risk factors or a confirmed diagnosis of B12 deficiency, do not delay introducing solids beyond 6 months of age, and consider introduction of solids from 4 months of age if the infant is developmentally ready. Prioritise B12-rich foods such as well-cooked and pureed meat, seafood and egg. B12 supplementation is recommended in children older than 6 months who transition to a diet that restricts animal products, or have a malabsorptive medical condition, or have not introduced solids or fortified milk formula into the diet. Refer to a New Zealand Registered Dietitian for individualised advice.

If treatment doses of B12 are required for either a mother or infant, both oral and parenteral B12 are considered equally effective unless enteral dosing is contraindicated (e.g., pernicious anaemia or other malabsorptive condition).³⁰ B12 has minimal risk of toxicity even in large doses.^{1,30} In severe deficiency, considering the potential for neurodevelopmental impairment, we have advised intramuscular B12 be given in alignment with NICE guidelines as it guarantees adherence, has high bioavailability and is subsidised.^{28,30} Refer to the New Zealand Formulary for intramuscular dosing. Alternatively, high dose oral B12 can be given; there is no standard dose, but a several week course of high dose oral B12 at 500–1,000mcg per day can be safely administered in both women and infants.^{1,13,28,30}

Measuring follow-up serum B12 levels within 3 months of intramuscular B12 treatment is not useful as these levels are often misleadingly elevated and do not accurately reflect body stores.²⁸