Optimising maternal nutrition

Investigating micronutrient deficiencies in women of childbearing age

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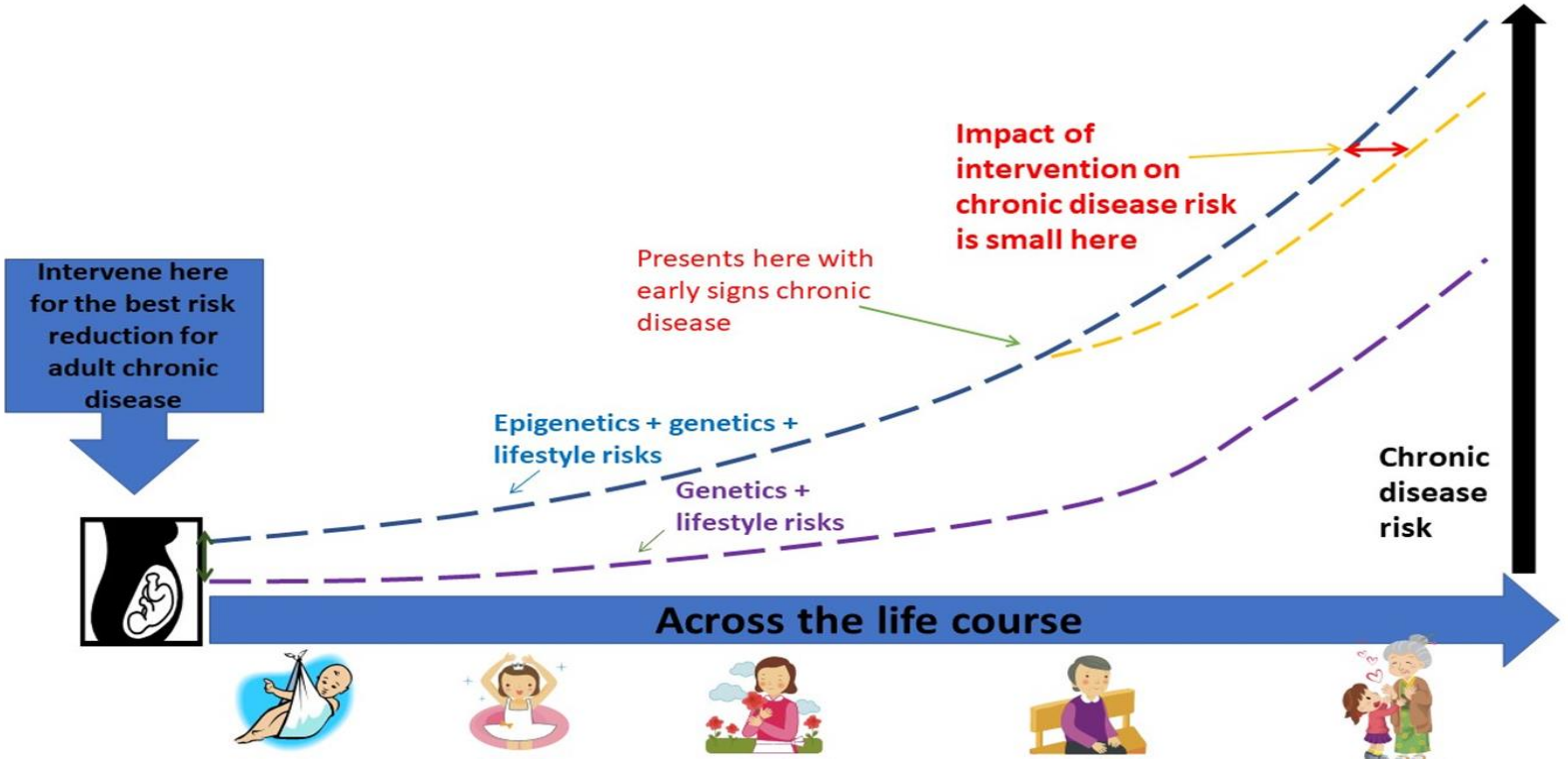
Developmental origins of health and disease –DoHAD (World Health Organisation)



Adapted from Hanson, M., & Gluckman, P. (2011). Developmental origins of noncommunicable disease: population and public health implications. *The American Journal of Clinical Nutrition, 94*(suppl_6), 1754S-1758S. doi:10.3945/ajcn.110.001206

Vitamin B12 – recommended daily intake 2.4mcg/day

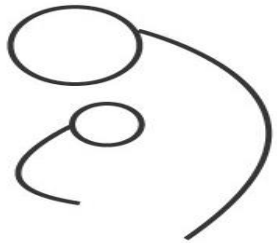
Natural food sources

- Fish
- Chicken
- Meat
- Eggs
- Milk
- Yoghurt
- Cheese

Fortified sources

- Soya, rice, almond milks
- Vegetarian meat analogues
- Marmite
- "Vegetarian" vegemite
- Energy drinks
- Meal replacements

Risks from Maternal B12 Deficiency



- Increased risk NTD (Molloy et al,2009; Ray et al., 2007)
- Impaired cognition/neurological deficit (Bhate et al., 2008)
- Maternal/neonatal macrocytic anaemia
- Low birthweight and preterm delivery (Muthayya et al., 2006)
- Insulin resistance & low muscle mass in child…
- …& increased risk of diabetes in adult life (Yajnik et al.,2008)

Prevalence of B12 deficiency

- Internationally – high rates of B12 deficiency South Asian populations
- Insufficient NZ research
  - NZNS 2008/9 –average of 20% of population low in B12 (Devi et al. 2018)
  - 50% South Asian women low in B12 (Gammon et al., 2013)
- US study - around 30 – 40% of older adults B12 insufficient/deficient (Andres, 2004)
  - 60 % of cases – due to food-bound cobalamin malabsorption
  - 15-20% due to pernicious anaemia – lack intrinsic factor
- US study -in younger adults –39% insufficient/deficient (Tucker et al., 2000)
  - more likely to be due to insufficient dietary intake, malabsorption or medications that inhibit B12 absorption (Tucker et al., 2000).
- Prevalence increasing with more vegan/vegetarian/low-meat–eating diets

Contributors to B12 deficiency

- Poor or incomplete absorption of B12 from food
  - Food – bound cobalamin absorption
  - Pernicious anaemia- loss of intrinsic factor binding for B12 absorption
  - GI inflammatory conditions- Crohn's, coeliac disease
  - GI infections – *H.Pylori*
- Inadequate dietary intake of B12
  - < RDI 2.4 mcg/day /2.6 mcg/day pregnancy
  - Low or non-meat eating dietary practices
- Medications that inhibit B12 absorption
  - e.g. Metformin, PPI

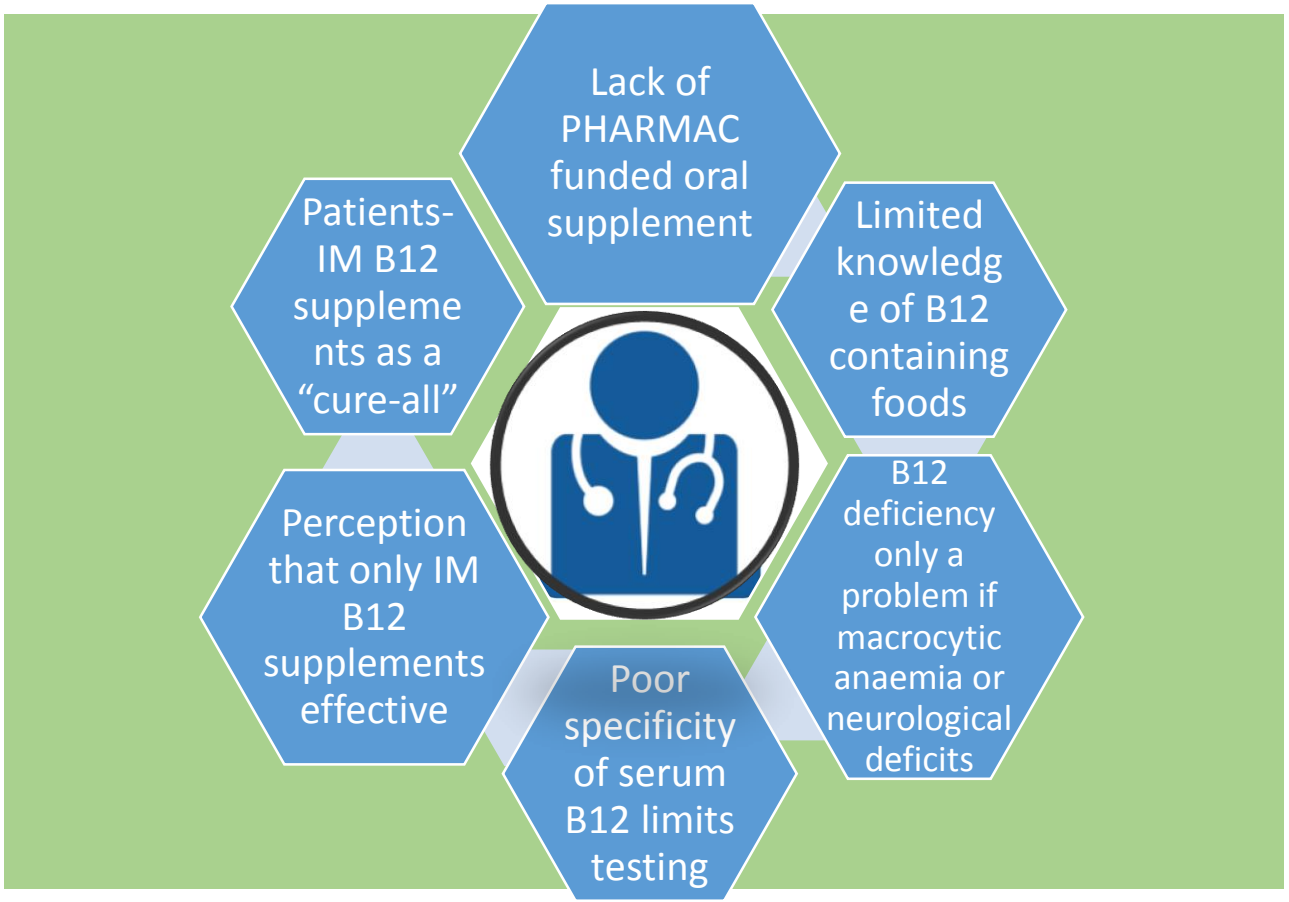
South Asian community perspectives on B12 deficiency - a qualitative descriptive study

South Asian community perspectives on B12 deficiency

Six community focus groups

One health professional focus group

Key findings health professional focus groups



Key findings from South Asian Community

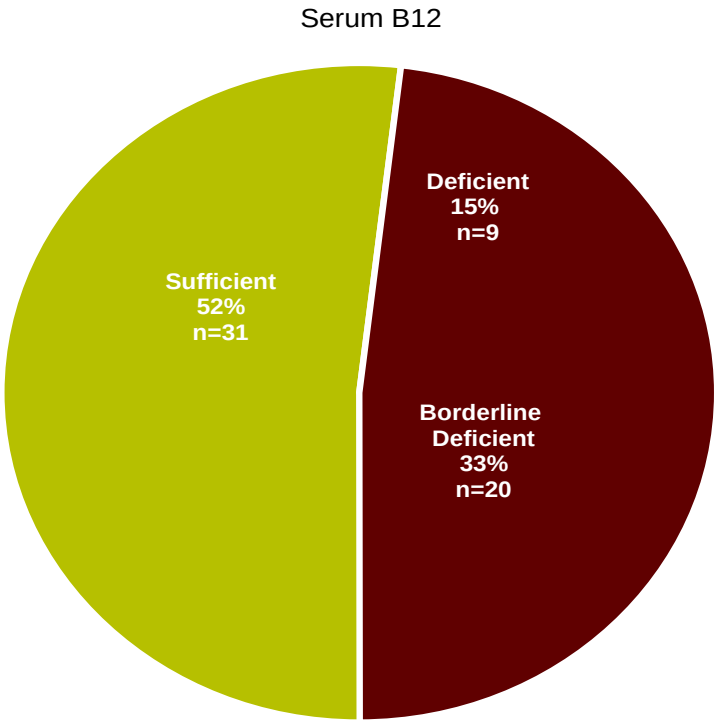
Pharmacological vs. physiological doses for B12 deficiency

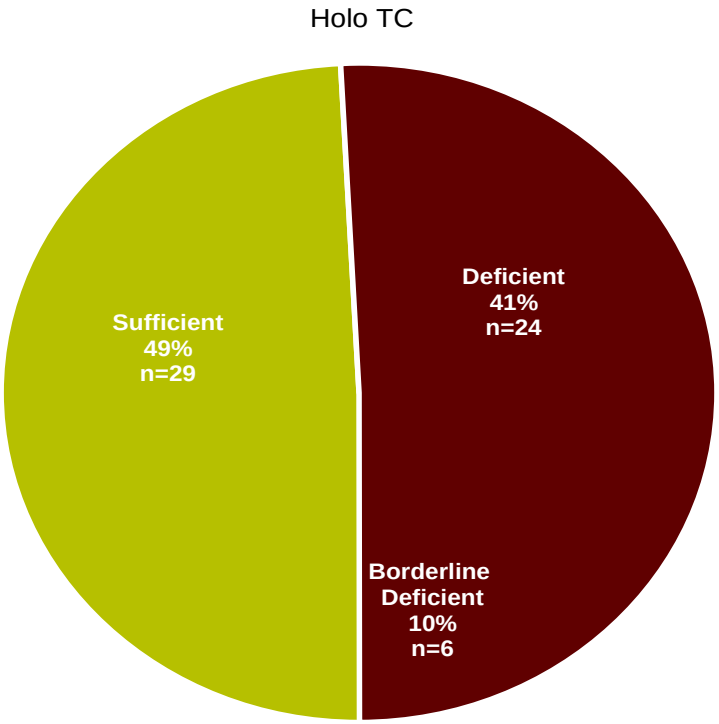
- B12 deficiency due to malabsorption
  - **Large pharmacological** doses of B12 (high dose oral B12 or B12 injections - 1000mcg x 3-5 doses)
  - Enterohepatic recycling of B12 affected -1-2% still absorbed by passive diffusion
  - Deficiency can become profound
- Low or non meat eaters at risk of B12 deficiency:
  - Absorb B12 well
  - **Require only physiological** oral dose supplement
  - ??What is an appropriate dose?
  - Oral B12 supplements - B12 not bound – easily absorbed even in lack of gastric acid
  - Enterohepatic recycling of B12 intact
  - Deficiency not profound

VitB12 study

- **6-month trial 63 South Asian women**
  - **oral B12 supplementation 6 mcg**
  - **vs placebo**
  - **OR dietary advice**
- **Tested at baseline, 6weeks, 3 months, 6 months**
- **Registered clinical trial:** ACTRN12610000262000

VitB12 study- approx. 50% of South Asian women B12 insufficient/deficient (Mearns et al., 2014)

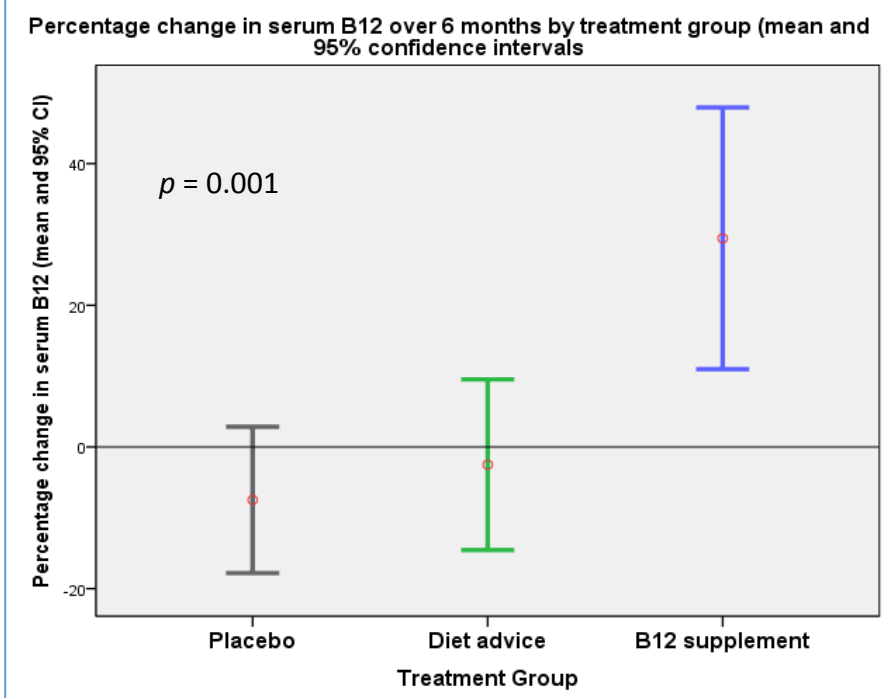




Response in B12 biomarkers to study treatments over 6 months (Mearns et al.,2014)

% change in serum B12 over 6 months

% change in holo TC over 6 months



Conclusions of VitB12 RCT

- Low vitamin B12 status common in sample population
- 6 mcg B12 supplement capsule effective treatment for increasing B12 biomarkers
- Adherence with supplements decreased over time –reduced efficacy of oral supplement
  - relook at dose and frequency
- B12 dietary advice: insignificant effect on increasing B12 intake or serum B12
  - relook at effective ways to increase B12 intake via dietary advice/support

Vitamin B12 Food Frequency Questionnaire

- Estimates vitamin B12 intake from dietary recall of foods consumed

Food frequency questionnaire (B12FFQ)

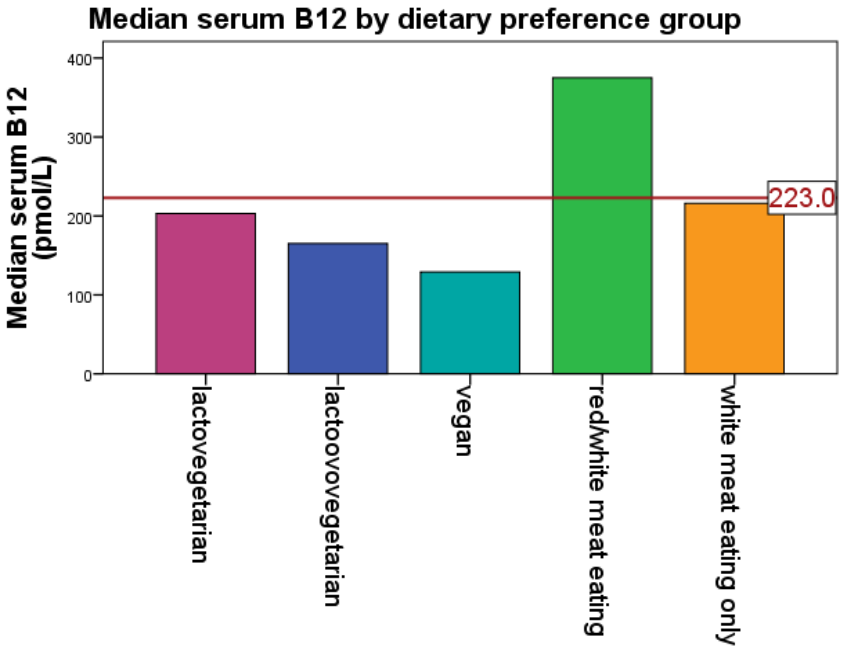
- 30 questions
- Included B12 containing food and beverages
- Recall of frequency and portion of foods eaten
- Approximated average B12 (mcg) consumed per day
- Compared with serum B12 and holoTC biomarkers

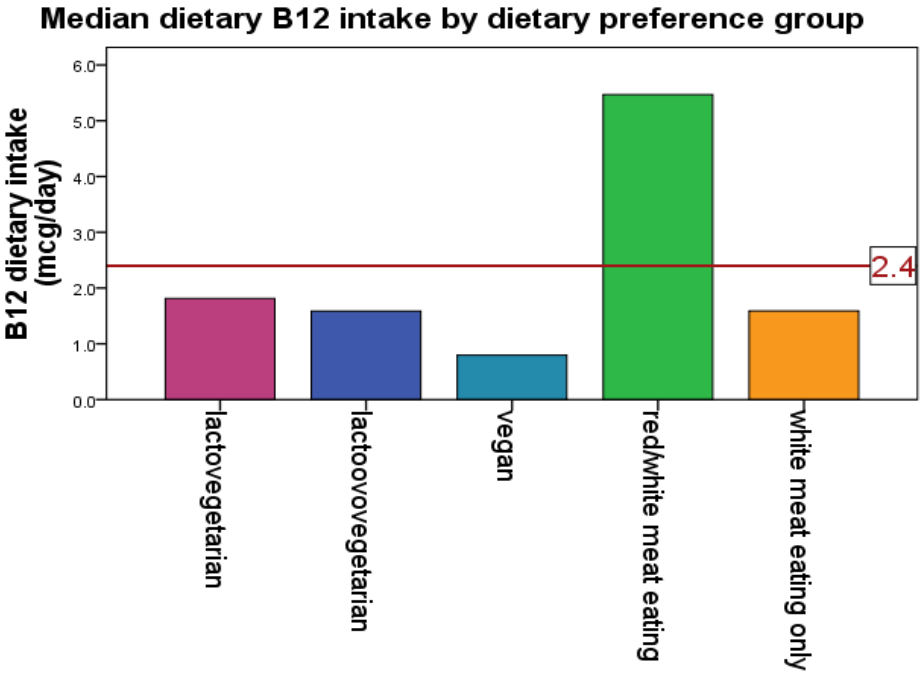
Vitamin B12 study
Vitamin B12 Foods Questionnaire

GENERAL INSTRUCTIONS

- Answer each question as best you can. Estimate if you are not sure. A guess is better than leaving a blank.
- Put an X in the box next to your answer.
- If you make any changes, cross out the incorrect answer and put an X in the box next to the correct answer. Also draw a circle around the correct answer.
- If you mark NEVER, NO, or DON'T KNOW for a question, please follow any arrows or instructions that direct you to the next question.

Relationship between B12 dietary intake and serum B12 biomarkers





Summary of B12 FFQ findings (Mearns & Rush, 2017)

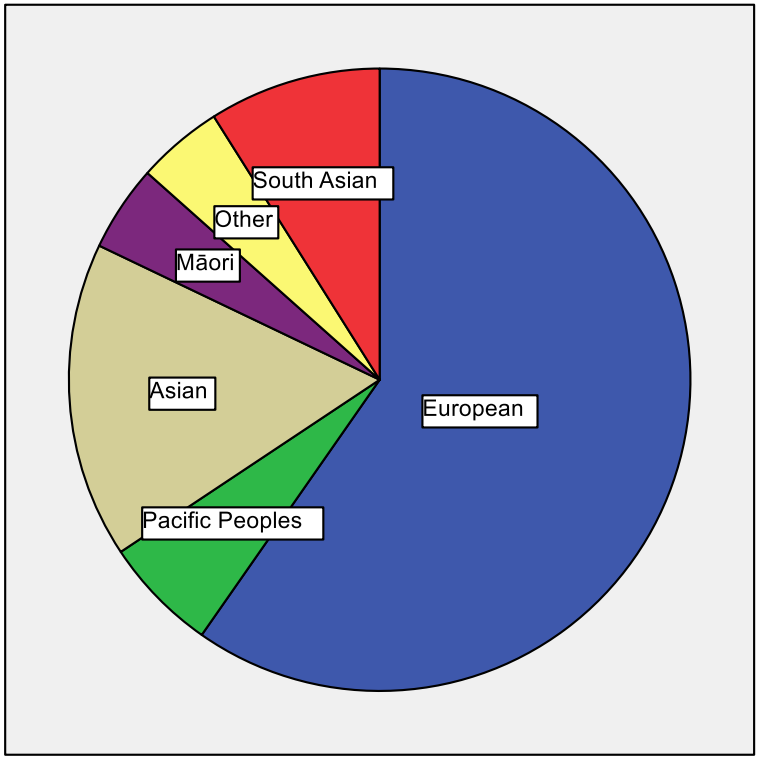
- B12 FFQ a valid measure of dietary B12 intake

  (r=0.55, p <0.001, 95 % CI [0.34, 0.71])
- 44% of women had a dietary intake <RDI of 2.4 mcg B12/day
- Women who did not consume red meat were 2.2 and 2.8 times more likely to be B12 deficient or insufficient (p=0.005, 95% CI [1.4,5.9])

Nurses Nutrition Study

Micronutrient status and associations with dietary patterns

Ethnicity of study participants



67 female students age 18-45 years

- European n=40 (58%)
- Māori n=3 (4.3%)
- Pacific n=4 (5.8%)
- Asian n=11 (15.9%)
- South Asian n=6 (8.7%)
- Other n=3 (5.3%)

NNS: Micronutrient biomarker status (n=67)

	Median (25^{th}/75th)	Range Lower/upper limit	n (%) low or deficient
Hb Low<115 g/L	135 (129/142)	104/166	5(7.5%)
MCV (f/L) Low < 80 f/L	87 (85/90)	62/95	13(19.4%)
Serum ferritin (ug/L) Low <20 ug/L	24 (12/28)	2/300	29(43%)
Serum vitamin B12 Low <222pmol/L)	320 (237/407)	99/794	13(19.4%)
Serum folate (nmol/L) Low <7nmol/L	26 (11/36)	6/45	1(1.4%)

Dietary practices

Reported dietary practices: Non meat-eating n=4(6%), white meat-eating only n=5(7.5%), red and white meat eating n=58 (86.5%)

Factor analysis of dietary patterns

Three dominant patterns in this group

- **Discretionary/junk:** deserts/sweets, snacks, takeaways, milk, pasta, starchy vegetables.
- **Flexitarian:** non starchy and starchy veges, fruit, nuts & seeds
- **Traditional:** all meats, dairy, eggs, bread and crackers, fruit

Analysis of dietary intake/patterns

- **Significant associations**
  - *Traditional pattern-meat eating/dairy &eggs/bread pattern*
    - More likely to be ferritin replete in this pattern (r = 0.26, p=0.035)
  - *Discretionary/junk food patterns* (r=-0.289, p=0.018)
    - More likely to be B12 deficient with this pattern

Regression and correlation analysis

- Only significant association
  - Serum B12 and servings of red meat/day (rho=0.38, p=0.003)
  - No association found between ethnicity and micronutrient deficiency
  - No association found between self-reported menstrual blood flow and ferritin

Challenges in screening for, preventing and managing B12 deficiency

- A more sensitive, specific and affordable test of B12 status needed
- Identifying and working with dietary ‘at-risk’ groups
- Treatment options appropriate for the cause of B12 deficiency

A more sensitive, specific and affordable test of B12 status needed for high risk

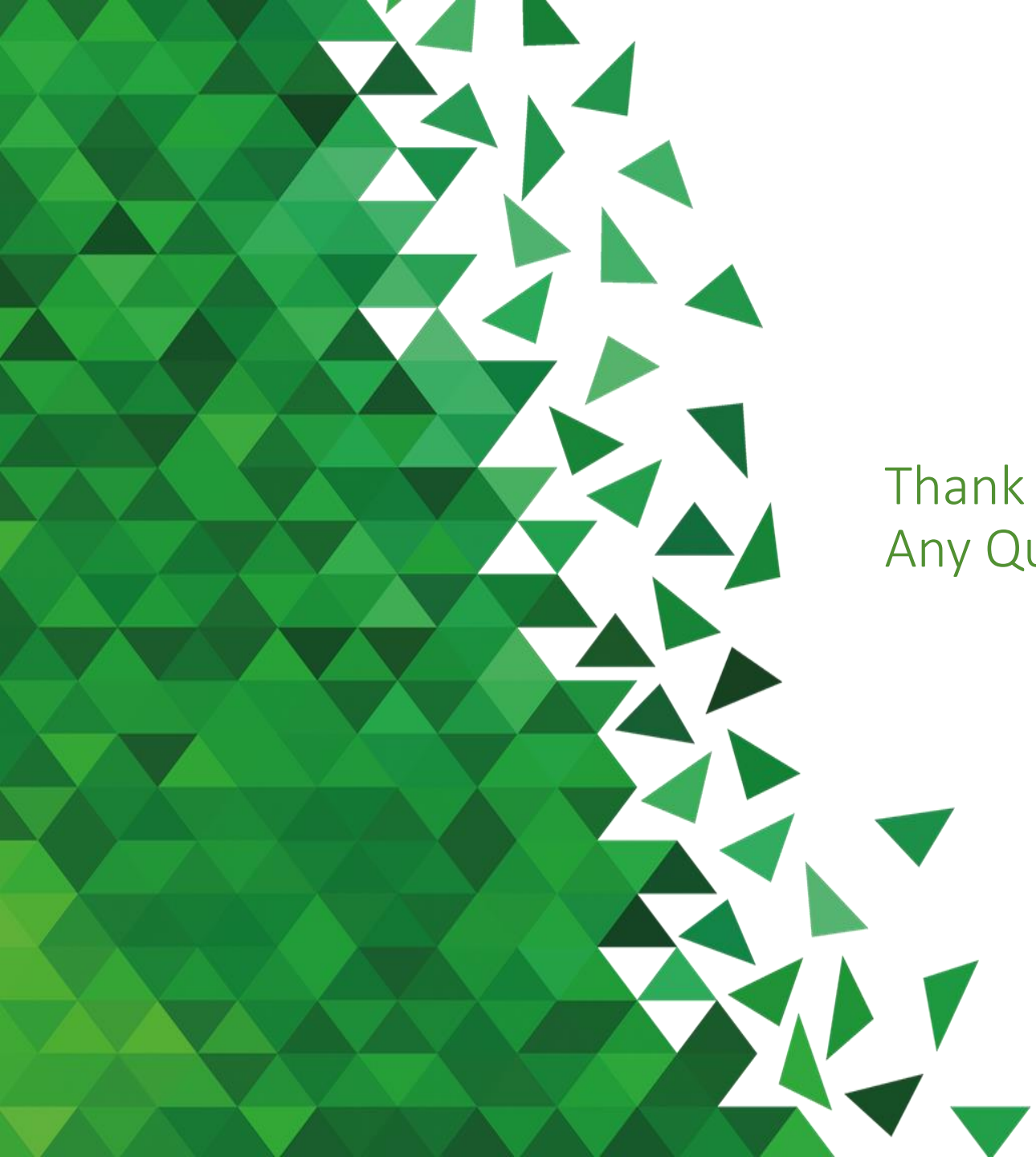
- Serum B12 – low specificity and sensitivity –especially in pregnancy (Morbak, 2007)
- HoloTC – reflects active B12 available for metabolism
  - Remains stable over pregnancy
- Testing for metabolites produced in B12 deficiency more accurate
  - Homocysteine and Methylmalonic acid (MMA)expensive and only tested in specialist laboratories
- Issues with transport of samples to specialist laboratories
  - MMA and Homocysteine

Future research –DBS-MMA testing

- Assistant Prof. Yvonne Lamers at the University of British Columbia (UBC) validated novel methods for testing DBS-MMA (Schroder et al., 2014)
- Convenient dried blood spot method (DBS) for sampling and tandem mass-spectrometry for testing.
- DBS-MMA measures methylmalonic acid (MMA), a metabolite specific to B12 deficiency.
- This DBS-MMA test has potential to aid more sensitive and reliable testing for B12 deficiency - complement the currently used serum B12 assay test
- Proposed AUT project includes evaluation of DBS-MMA testing; cost, convenience, and sensitivity.

Summary

- Low B12 status is common in women of child bearing age – needs better recognition and prevention
- Align management of B12 deficiency with the contributors of deficiency
- Identify appropriate physiological oral B12 supplement dose
- More focus on dietary patterns for risk of deficiecny
- MoH dietary guidelines - recommended food groups- discretionary/ junk eating patterns- increased risk of B12 deficiency.
- Better resources needed on sources of dietary B12 and when supplementation indicated
- More sensitive and specific tests needed to test for B12 deficiency
- PHARMAC funding of an oral B12 supplement



Thank you
Any Questions?

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