Anaemia & IDA of Young Children in Malaysia: The latest findings of Iron Strong Study

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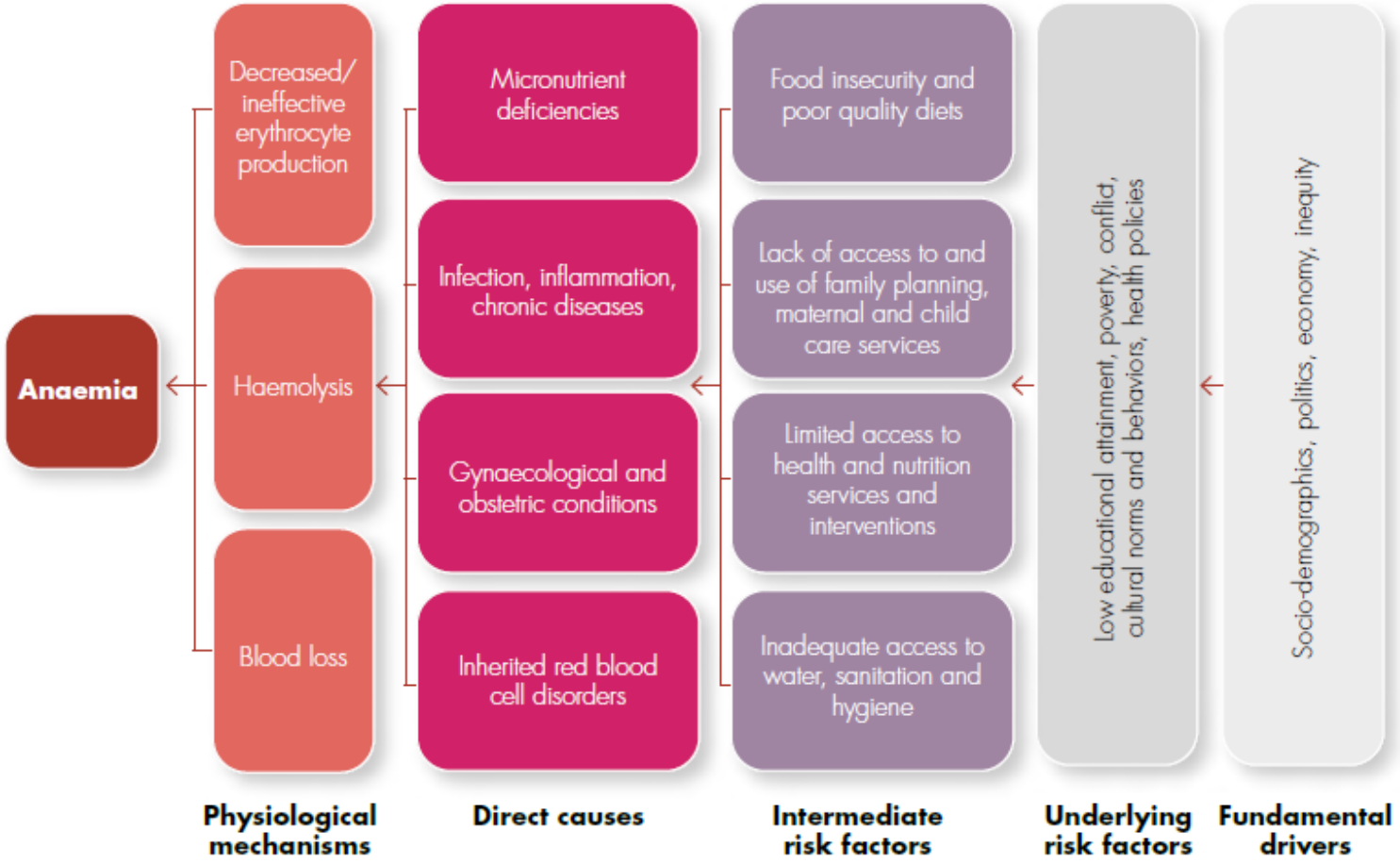
- Past President of Asia Pacific Paediatric Endocrine Society (2018-2020)

What is Anaemia?

- Anaemia is a condition in which the number of red blood cells or the haemoglobin concentration within them is lower than normal.
- Causes of Anaemia



References:
- WHO, Accelerating anaemia reduction: a comprehensive framework for action, 2023.

Anaemia Diagnosis: Hb Cut Off

- Haemoglobin and haematocrit levels below which anaemia is present

Table 1
Haemoglobin levels to diagnose anaemia at sea level (g/l)±

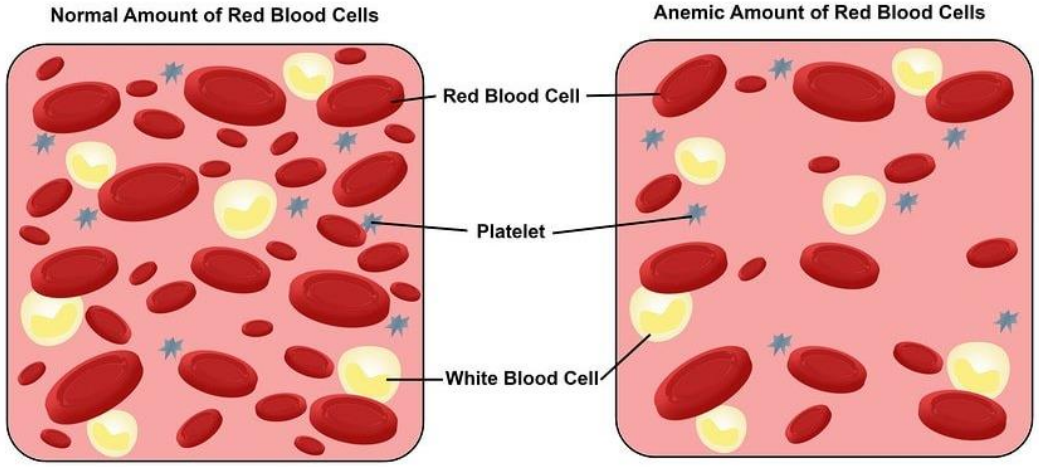
Population	Non -Anaemia*	Anaemia*		
		Mild[a]	Moderate	Severe
Children 6 - 59 months of age	110 or higher	100-109	70-99	lower than 70
Children 5 - 11 years of age	115 or higher	110-114	80-109	lower than 80
Children 12 - 14 years of age	120 or higher	110-119	80-109	lower than 80
Non-pregnant women (15 years of age and above)	120 or higher	110-119	80-109	lower than 80
Pregnant women	110 or higher	100-109	70-99	lower than 70
Men (15 years of age and above)	130 or higher	110-129	80-109	lower than 80

± Adapted from references 5 and 6
* Haemoglobin in grams per litre
a "Mild" is a misnomer: iron deficiency is already advanced by the time anaemia is detected. The deficiency has consequences even when no anaemia is clinically apparent.

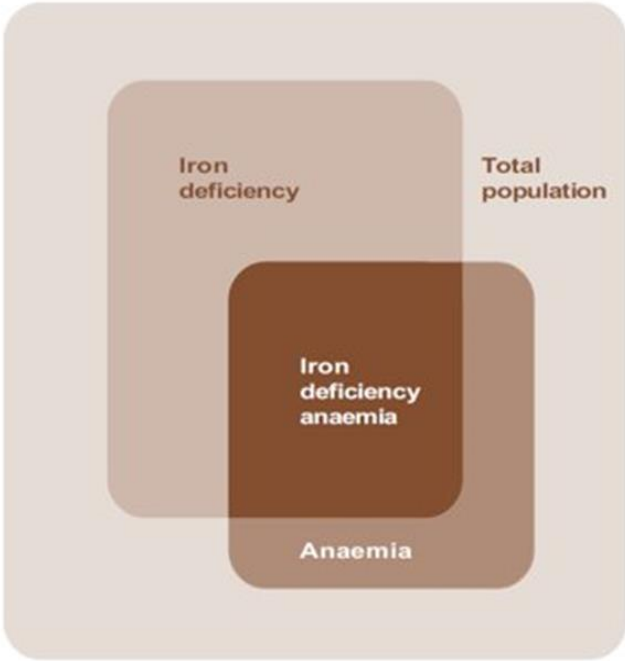
References:
- WHO. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Vitamin and Mineral Nutrition Information System. Geneva, World Health Organization, 2011 (WHO/NMH/NHD/MNM/11.1) (http://www.who.int/vmnis/indicators/haemoglobin. pdf, accessed 31 May 23).

Iron Deficiency Anaemia

- **Iron Deficiency** is a condition when there is not enough iron in the body.
- **Iron Deficiency Anaemia** is a condition when iron stores in the body is too low to support normal red blood cells production (Haemoglobin)
- **Iron Deficiency Anaemia** is the most common form of Anaemia.



Normal **Anaemia**



- **Thalassemia** are genetic disorder that results in abnormal Haemoglobin. Prevalence of alpha-thalassaemia in SEA ranges Vietnam 51.5%, Cambodia 39.5%, Laos 26.8%, Thailand 20.1%, Malaysia 17.3%; Myanmar 10-56.9%

References:
- UNCF, UNU, WHO. Iron Deficiency Anaemia-Assessment, Prevention, and Control, A guide for programme managers.
- Adapted from Yip R. Iron nutritional status defined. In: Filer IJ, ed. Dietary Iron: birth to two years. New York, Raven Press, 1989:19-36.
- Manuel Olivares, Tomds Walter, Eva Hertrampf and Fernando Pizarro, Anaemia and iron deficiency disease in children, Institute of Nutrition and Food Technology, British Medical Bulletin 1999; 55 (No. 3): 534-543.
- Lucky Poh Wah Goh, et al, Prevalence of Alpha(α)-Thalassemia in Southeast Asia (2010-2020): A Meta-Analysis Involving 83,674 Subjects, Int J Environ Res Public Health, 2020 Oct 9;17(20):7354.

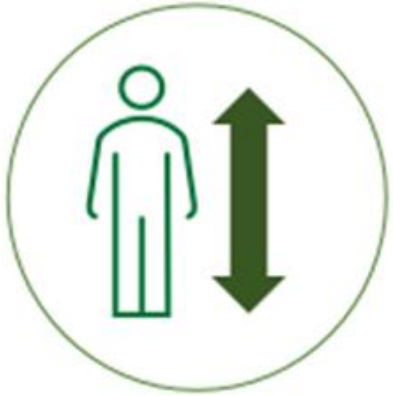
Signs of Iron Deficiency Anaemia

Fatigue

Headache

Pale skin
Cold hands and Feet

Consequences of Iron Deficiency Anaemia



Growth and development

Cognitive and motor function

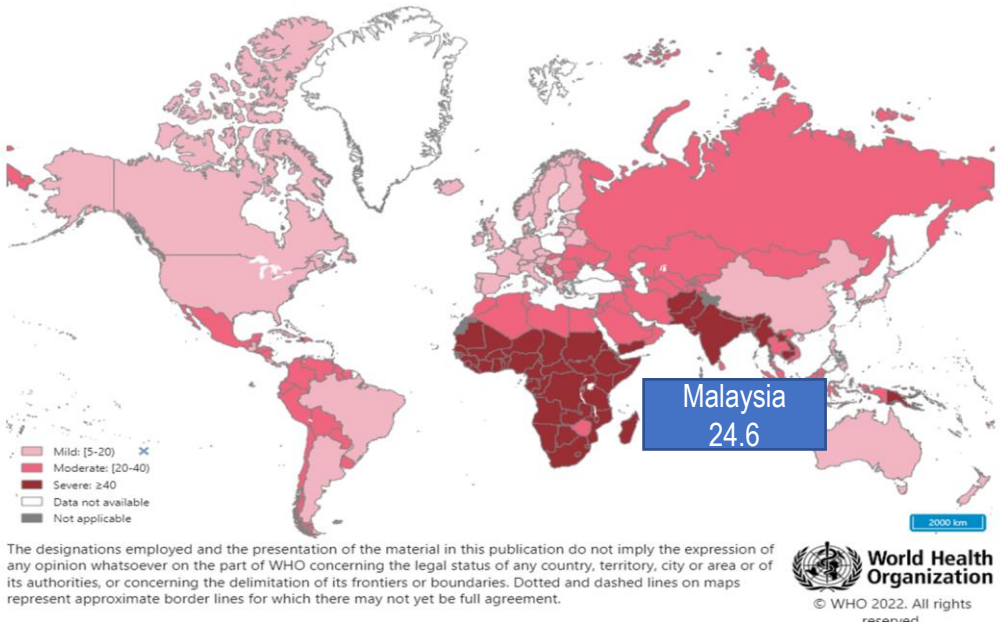
Fatigue and Lethargy

Impaired immune system

Prevalence of Anaemia in Malaysian Children

WHO

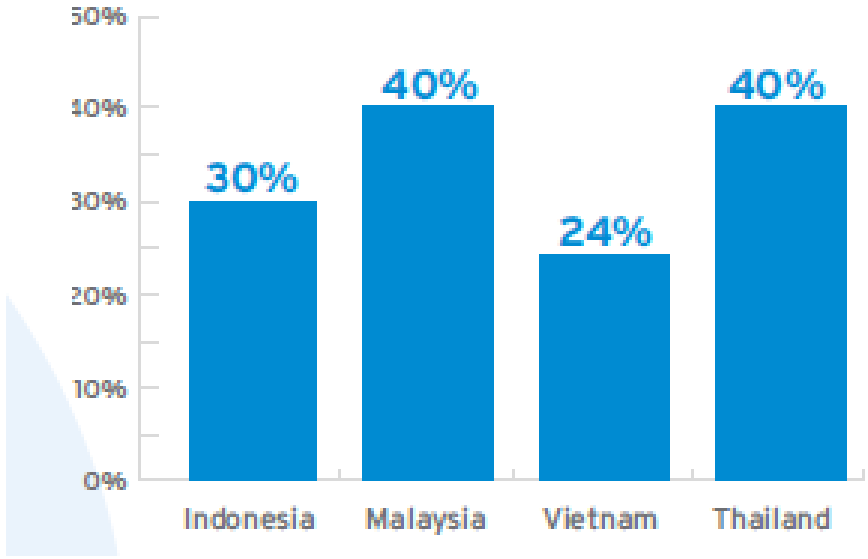
1 in 4 of Malaysian children **younger than 5 years old** have Anemia (2019)



- Using blood hemoglobin concentrations, cyanmethemoglobin method

SEANUTS II

4 in 10 of Malaysian children **younger than 4 years old** have Anaemia (2022)



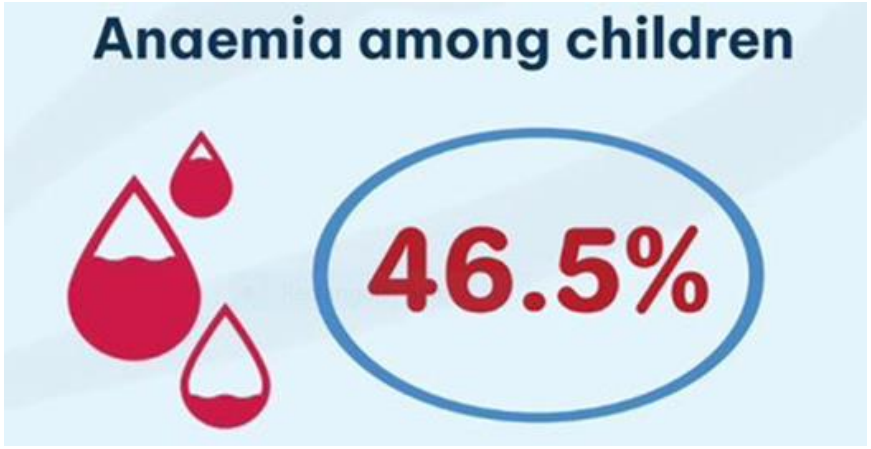
- Biochemistry data was collected from finger prick <below 4 years> or venepuncture blood samples
- Assessed based on World Health Organization (WHO) cut-off values

References:
-World Health Organization, Prevalence of anaemia in children aged 6–59 months (%) (who.int)
-The FrieslandCampina Institute, RESULTS OF SEANUTS II: New research for a positive impact on tomorrow's society, 2022.

Prevalence of Anaemia in Malaysian children

NHMS 2022

About Half of Malaysian children have Anaemia (2022)



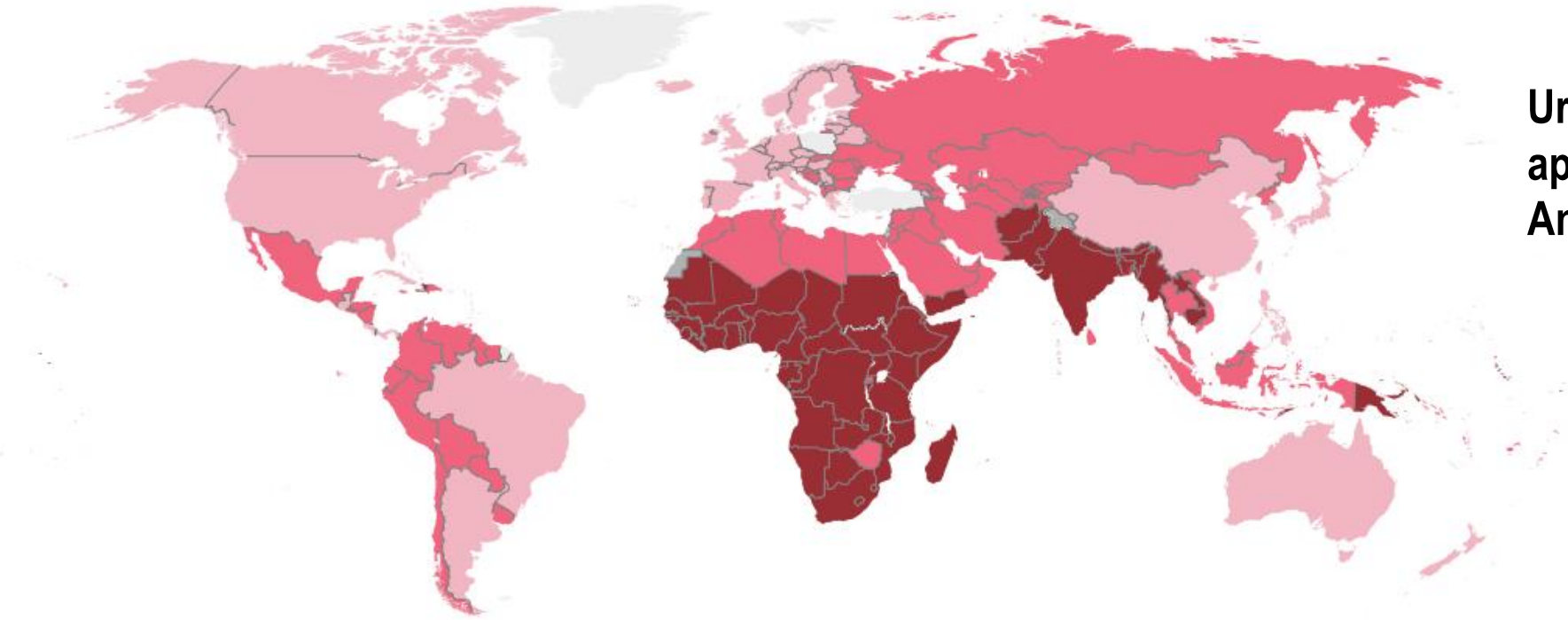
Prevalence of anaemia among children aged <59 months

- Mild : 24.3
- Moderate: 21.9%
- Severe: 0.3%
- Non-Anaemia 53.5%

References:
-Ministry of health malaysia institute for public health, NHMS 2022: Maternal and Child Health; www.iku.gov.my/nhms

Anaemia in Malaysia increasing over the years & categorised as moderate-severe public health significance

Fig. 1. Prevalence of anaemia in children 6–59 months of age, 2019

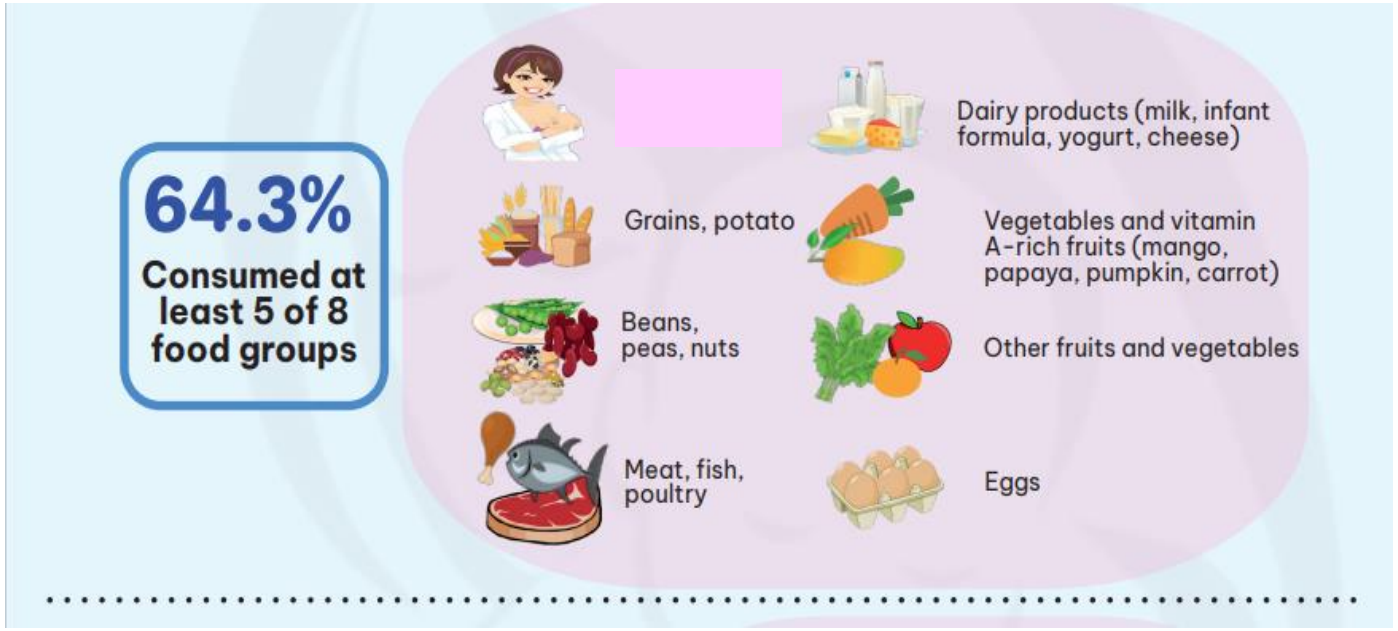


Source: Global Health Observatory, World Health Organization, 2023 *(11)*.

Urgency to call for different approach to address Anaemia & IDA in children

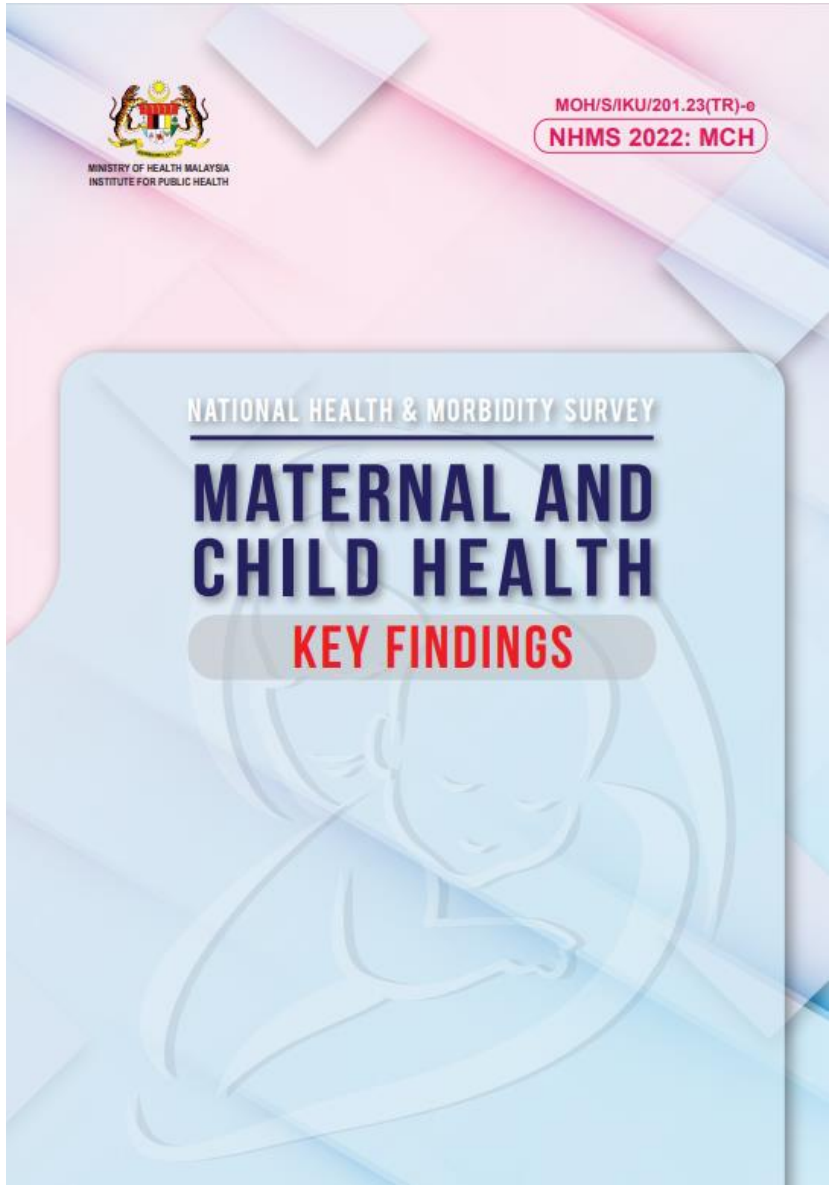
YOUNG CHILD FEEDING PRACTICE

Complementary feeding practice (<2 years)



78.6%

Children received solid, semi-solid and soft food a minimum number of times.



References:
-Ministry of health malaysia institute for public health, NHMS 2022: Maternal and Child Health; www.iku.gov.my/nhms

STRATEGIES TO PREVENT ANAEMIA IN CHILDREN

Screening

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REVIEW ARTICLE

Gynecology

GYNECOLOGY OBSTETRICS FIGO WILEY

Expert consensus on improving iron deficiency anemia management in obstetrics and gynecology in Asia

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Abstract

Iron deficiency anemia (IDA) is a major health burden among women in Asia. Key issues in IDA management in Asia are under-diagnosis and under-treatment. The lack of Asia-specific guidelines, and suboptimal utilization of treatment compounds the management of IDA. To address these gaps, a panel of 12 experts in obstetrics, gynecology, and hematology from six regions in Asia convened to review current practices and clinical evidence and provide practical guidance on IDA diagnosis and management in Asian women. The Delphi approach was used to obtain objective opinions and attain consensus on statements pertaining to awareness, diagnosis, and management of IDA. In total, 79 statements attained consensus and are summarized to provide guidance on raising awareness of IDA and approaches for improved diagnosis and treatment of IDA among women in various settings: pregnancy, postpartum, heavy menstrual bleeding, gynecologic cancers, and perioperative care. This clinician-led consensus integrates appropriate recommendations based on clinical evidence and best practices and is intended to guide decision making in the management of iron deficiency/IDA in women. The expert panel raises a call for timely diagnosis and utilization of appropriate treatment, including use of high-dose intravenous iron, stringent blood management, and interdisciplinary collaboration, for optimization of IDA management among women in Asia.

KEYWORDS

Asia, consensus, gynecology, iron deficiency anemia, obstetrics

TABLE 5 Consensus on management of IDA in pregnancy.

1. Anemia in pregnancy should be defined as Hb < 11 g/dL.
2. Pregnant women should be screened for anemia at the first prenatal visit and at the beginning of the third trimester. If anemia is detected, further investigations should be conducted to determine its underlying cause. Women should also be monitored for response after treatment.
3. Pregnant women with IDA should receive iron supplementation as IDA increases the risk of maternal morbidity, preterm delivery, and low-birth-weight babies.
4. Oral iron is the current standard of care for treatment of IDA in pregnancy as it is convenient, inexpensive, and easily available.
5. Oral iron should be the first-line therapy for mild anemia (Hb 9–10.5 g/dL) in the first and second trimester, with a target Hb of ≥11 g/dL.
6. Patients should receive counseling on the correct way to take oral iron to allow better absorption and avoid food interactions. It should be taken on an empty stomach, with water.
7. Over-the-counter prenatal multivitamins may not contain sufficient elemental iron to be adequate as sole therapy for IDA. Furthermore, multivitamins may have minerals that interfere with iron absorption. Identifying the amount of elemental iron in these preparations is important.
8. Judicious dosing of oral iron is essential. Daily or twice daily dosing of oral elemental iron >60 mg may increase hepcidin levels and decrease absorption of iron. Alternate-day dosing should be considered to optimize iron absorption.
9. Follow-up Hb levels should be measured after 2–3 weeks of oral iron therapy. Once Hb is normalized, oral iron should be continued for another 3 months or until at least 6 weeks postpartum to replenish iron stores.
10. A patient may be considered a poor responder to oral iron if the level of Hb does not increase by 1 g/dL after 2–3 weeks. After addressing causes for poor response, intravenous iron may be considered.
11. Intravenous iron can be considered in the second and third trimester if oral iron is not well tolerated, ineffective (increase in Hb < 1 g/dL, or Hb remains <10 g/dL after 2–3 weeks of treatment), or if there is lack of compliance.
12. Intravenous iron should be recommended as first-line therapy in women presenting with IDA (Hb < 10 g/dL) after 34 weeks of pregnancy. Rapid and effective anemia correction in these women is necessary to avoid the need for blood transfusion.
13. Intravenous iron may be considered when rapid repletion is necessary, in patients with risk factors such as coagulation disorders or placenta previa, and when complicated obstetrical surgery is anticipated.
14. Clinicians should be aware of the importance of judicious blood transfusion in anemic pregnant women as there is a higher risk of alloimmunization during pregnancy.
15. Blood transfusion may be considered in non-bleeding pregnant patients with symptomatic severe anemia, after taking clinical signs and symptoms into consideration.
16. If blood transfusion is deemed necessary in pregnant women with IDA, a single-unit transfusion should be followed by a clinical re-assessment to determine further management strategies.

Abbreviations: Hb, hemoglobin; IDA, iron deficiency anemia.

STRATEGIES TO PREVENT ANAEMIA IN CHILDREN

Screening

- WHO recommendation: Screening (invasive method) recommended when **prevalence > 5%**
- AAP; American Academy of Pediatrics recommends **universal screening** (invasive method) for anaemia **at 1 year of age**
- The AAP also recommends **selective screening** (invasive method) **at any age in children** with risk factors for anaemia
  e.g. Feeding problems, Poor growth, Inadequate nutrition, Low socioeconomic status
- CDC; Centers for Disease Control and Prevention recommends screening (invasive method) for IDA **at ages 9-12 months**, **6 months later**, and then annually from **ages 2 to 5 years** in children who are at high risk for IDA.

References:
- Baker RD, Greer FR, Committee on Nutrition. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0–3 years of age). Pediatrics. 2010 Nov;126(5):1040-50.
- UNCF, UNU, WHO. Iron Deficiency Anaemia-Assessment, Prevention, and Control, A guide for programme managers.
- McDonagh M, Blazina I, Dana T, et al. Routine iron supplementation and screening for iron deficiency anemia In children ages 6 to 24 months: A systematic review to update the U.S. Preventive Services Task Force Recommendation. 2015. Available at https://www.ncbi.nlm.nih.gov/books/NBK285661/. Accessed on 20 June 2023.

STRATEGIES TO PREVENT ANAEMIA IN CHILDREN

Screening

- **Haemoglobin & Nutritional Screening test can help identify children at risk of IDA**

- **Invasive:**
  - Blood sampling
  - Capillary blood: Portable Hb test based on capillary blood obtained from the fingertip

- **Non-invasive:** Fast & portable hemoglobin Monitoring
  - Masimo

Reference:
-E.M. DeMaeyer et.al., 1989. PREVENTING AND CONTROLLING IRON DEFICIENCY ANAEMIA THROUGH PRIMARY HEALTH CARE. WHO, Geneva, Switizerland
-Steven J. Barker, PhD, MD et.al., 2016. Continuous Noninvasive Hemoglobin Monitoring: A Measured Response to a Critical Review. International Anesthesia Research Society

STRATEGIES TO PREVENT ANAEMIA IN CHILDREN

Dietary Improvement

- Improve the year-round availability of micronutrient-rich foods
- Ensure the access of households, especially those at risk to these foods
- Change feeding practices with respect to these foods
- Food fortification
- Children need an additional source of iron to maintain adequate iron nutrition and prevent iron deficiency anaemia

References:
- Baker RD, Greer FR, Committee on Nutrition. Diagnosis and prevention of iron deficiency and iron-deficiency anemia in infants and young children (0–3 years of age). Pediatrics. 2010 Nov;126(5):1040-50.

STRATEGIES TO PREVENT ANAEMIA IN CHILDREN

Iron Supplementation

- WHO: Dosage schedules for iron supplementation to prevent IDA

Age groups	Indications for supplementation	Dosage schedule	Duration
Low-birth-weight infants	Universal supplementation	Iron: 2 mg/kg body weight/day	From 2 months of age up to 23 months of age
Children from 6 to 23 months of age	Where the diet does not include foods fortified with iron or where anaemia prevalence is above 40%	Iron: 2 mg/kg body weight/day	From 6 months of age up to 23 months of age
Children from 24 to 59 months of age	Where anaemia prevalence is above 40 %	Iron: 2 mg/kg body weight/day up to 30 mg	3 months
School-aged children (above 60 months)	Where anaemia prevalence is above 40 %	Iron: 30 mg/day Folic acid: 250 µg/day	3 months

- Malaysia: Iron supplementation, 100 mg iron/day is recommended for pregnant women

References:
- UNCF, UNU, WHO. Iron Deficiency Anaemia-Assessment, Prevention, and Control, A guide for programme managers.

STRATEGIES TO PREVENT ANAEMIA IN CHILDREN

Food and Milk Fortification

➢ Food fortification

WHO:

- Reinforces and supports ongoing nutrition improvement programmes
- Complementing other approaches to improve micronutrient status
- Iron in the fortified sauce was reported to be very effective in the treatment of iron-deficiency anaemia in children; positive effects were seen within 3 months of the start of the intervention

➢ Milk fortification

WHO:

- Iron fortification of formulas has been associated with a fall in the prevalence of anaemia in children aged under 5 years in the United States
- Fortification of milk with iron and vitamin C (ascorbic acid) in Chile produced a rapid reduction in the prevalence of iron deficiency in infants and young children

References:
- Lindsay Allen, et al, Guidelines on food fortification with micronutrients, WHO and FAO, 2006.

STRATEGIES TO PREVENT ANAEMIA IN CHILDREN

Milk Fortification

➢ Systematic review of 18 studies from Peru, UK, South Africa, Zambia, Ireland, Ghana, China, Spain, Mexico, India, Guatemala, Sweden, Chile (n = 5468 children):

- Iron multi micronutrient fortification increases haemoglobin levels by 0.87 g/dL and **reduces risk of anaemia by 57%.**
- **Multi micronutrient fortified milk and cereal products can be an effective option to reduce anaemia in children up to three years of age** in developing countries.

➢Systematic review and meta-analysis of 19 studies from low- or middle-income countries :

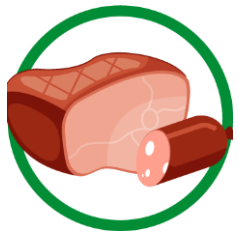
- Large-scale food fortification (LSFF) with iron was associated with a small, but significant, increase in the haemoglobin concentration for combined populations (preschool children, school-age children, and women of reproductive age [WRA]).
- LSFF with iron was associated with a **34% decline in anaemia prevalence** for combined groups, with the greatest impact noted for WRA, followed by **school-age children.**
- There was also a statistically **significant change in anaemia prevalence among the youngest children (<7 years).**
- The **prevalence of iron deficiency declined by 58%** among all population subsets.

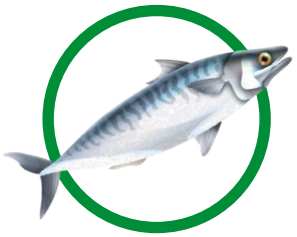
References:
- Eichler K, Wieser S, Rüthemann I, Brügger U. Effects of micronutrient fortified milk and cereal food for infants and children: a systematic review. Bmc public health. 2012 Dec;12:1-3.¥
- Keats EC, Neufeld LM, Garrett GS, Mbuya MN, Bhutta ZA. Improved micronutrient status and health outcomes in low-and middle-income countries following large-scale fortification: evidence from a systematic review and meta-analysis. The American journal of clinical nutrition. 2019 Jun 1;109(6):1696-708.

STRATEGIES TO PREVENT ANAEMIA IN CHILDREN

Dietary Improvement

Choose the right food





Food:	Beef	Salmon	Mackerel	Broccoli	Iron fortified milk	Iron fortified milk	Iron fortified milk
Iron per serving/day:	2.25 mg	1.1 mg	0.6-0.9 mg	0.33 mg	6.73 mg	5.1 mg	6 mg
	2 pieces 45 g	1 whole egg	20g to ½ piece	½ cup	6 serves	4 serves	3 serves Step 3
Recommended Nutrient Intake (RNI):	37.5%RNI**	18.3%RNI**	10-15%RNI**	5.5% RNI**	Breastmilk is the best		100%RNI**

***RNI iron for < 12 months is 9mg/day**
****RNI iron for 1-3 years is 6mg/day**

Choose the right time

Complementary feeding should be given

Too early may lead to digestive issues & risk of developing food allergies.

Too late can increase iron & malnutrition risk leading to stunting

References:
- Malaysian Dietary Guidelines for Children and Adolescents- Summary - National Coordinating Committee on Food and Nutrition Ministry of Health Malaysia 2013 - Cover 1 Upload (moh.gov.my)
- MALAYSIAN FOOD COMPOSITION DATABASE (MYFCD) 1997 - Food Compositon Database Module Industry (moh.gov.my)
- National Coordinating Committee on Food and Nutrition, Ministry of Health Malaysia, 2017 Untitled-1 (moh.gov.my)

FOOD SOURCES: HEME & NON HEME IRON

Heme Iron: From Animal

- More Bioavailable

Beef

Lamb

Salmon

Chicken

Tuna

Sardine

Egg

Non-Heme Iron: From Plant

- Less bioavailable

Tofu

Wheat

Grains

Chickpeas

Peanuts

Brown rice

Spinach

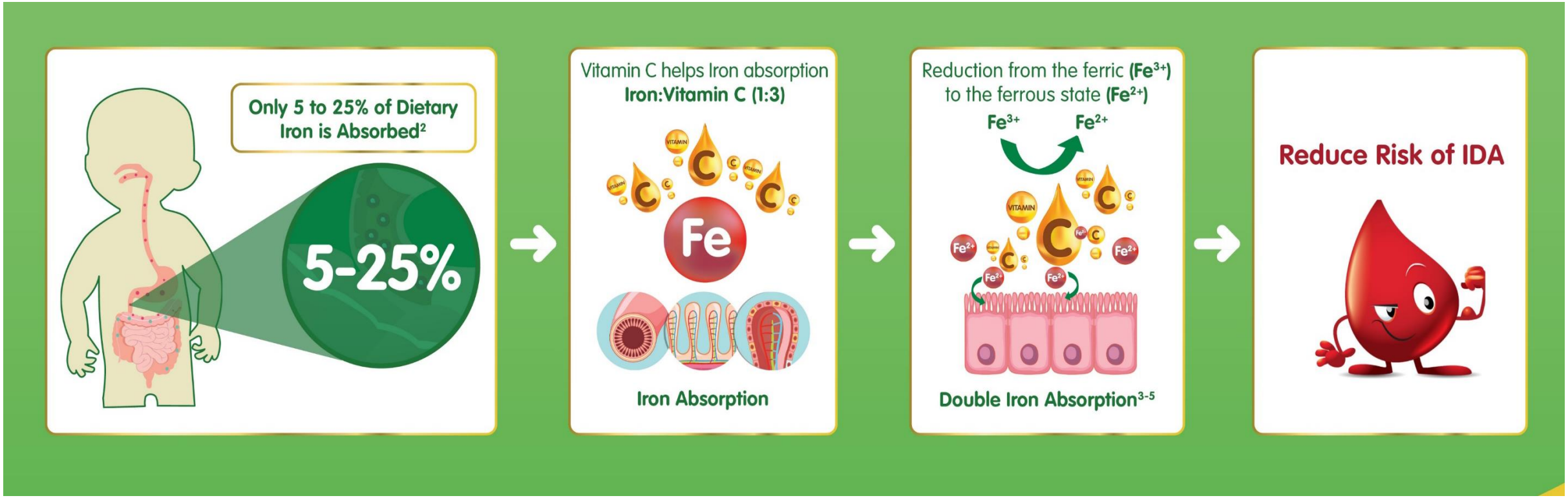
Dried Fruit

Fortified Milk

COMBINING IRON & VITAMIN C ENHANCED IRON ABSORPTION

WHO recommendation

- ❑ Vitamin C: Iron >> 2:1 ratio increase iron absorption from food 2-3 folds in children
- ❑ Vitamin C: Iron >> 4:1 ratio can be used for high phytate foods (cereals, whole grains, seeds, legumes) which inhibit iron absorption



IRON & VITAMIN C FOOD PAIRING
ENHANCED IRON ABSORPTION

PB + Watermelon
.6 mg iron

Chicken + Strawberries
.3 mg iron

Fortified O's + Oranges
2.3 mg iron

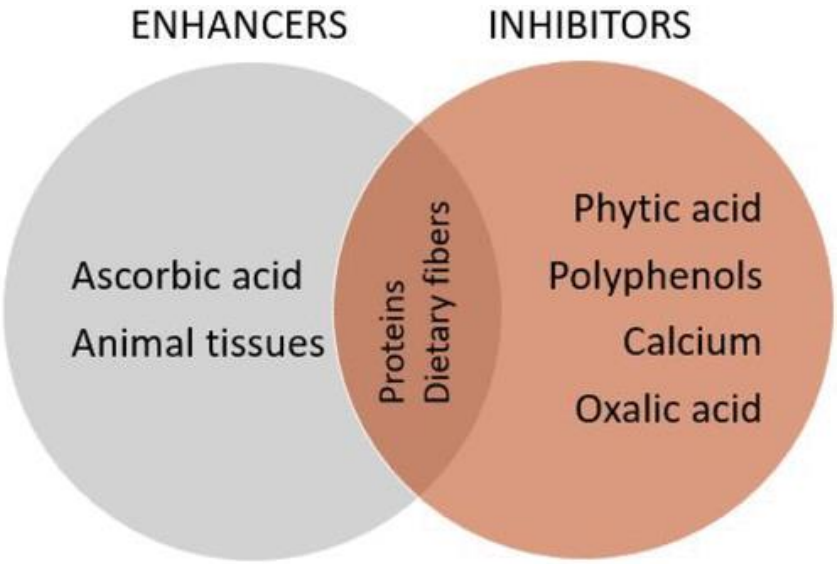
Spinach + Mango
.75 mg iron

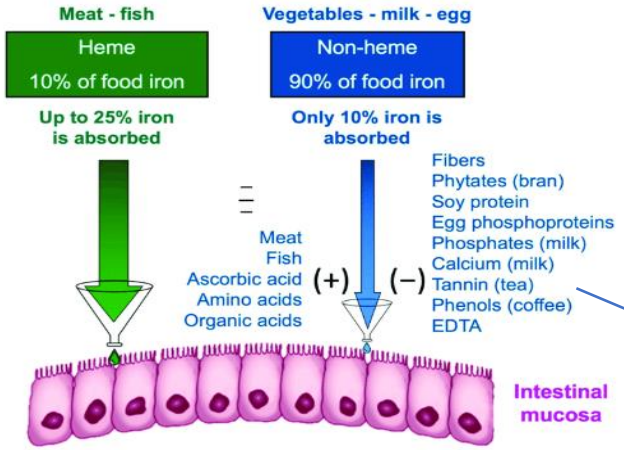
Steak + broccoli

Raisins + Pineapple
.5 mg iron

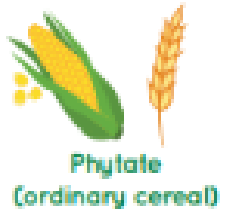
LIMIT FOOD WITH IRON ABSORPTION INHIBITORS

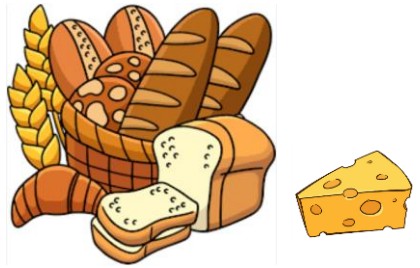
VITAMIN C CAN COUNTERACT INHIBITORY IMPACT





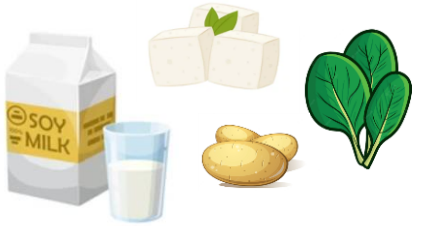
Chelate with iron and form insoluble chemical complexes in the gastrointestinal tract that cannot be digested or absorbed





Dairy & cheese

Calcium



spinach, potatoes, soy milk, tofu

Oxalic acid

THE LATEST FINDINGS OF IRON STRONG STUDY

Study Design — FIRST LARGE-SCALE MULTI-SITE CLINICAL STUDY IN MALAYSIA PREVALENCE OF ANAEMIA RISK IN 1200 CHILDREN 6-36 MO

Objective	To determine the prevalence of Malaysian children aged ≥ 6 - ≤ 36 months at risk of anaemia by measuring Total Haemoglobin (SpHb) using Masimo Rad-67
Main deliverables	**Primary** • To estimate the percentage of Malaysian Children aged ≥ 6 - ≤ 36 at risk of anaemia (SpHb <12g/dL) using non-invasive haemoglobin assessment. **Secondary** • To compare the socio-demographic characteristics of children with and without risk of anaemia. • To compare and identify the nutritional status and dietary intake of children with and without risk of anaemia. • To identify socio-demographic and nutritional factors associated with risk of anaemia.
Subjects	1200 Children aged ≥ 6 Months - ≤ 36 Months, receive routine immunization at Mother and Child Health Clinic (MCHC).
Study Design	Cross-sectional Five Sites 1) KK Bandar Botanic, Klang, Selangor 2) KK Luyang, Kota Kinabalu, Sabah 3) KK Endau, Mersing, Johore 4) KK Wakaf Bharu, Tumpat, Kelantan, 5) KK Simpang Kuala, Alor Setar, Kedah Duration: 12 weeks

➢ Masimo Rad-67

Finger Application

➢ Iron-Strong App: D-Lab

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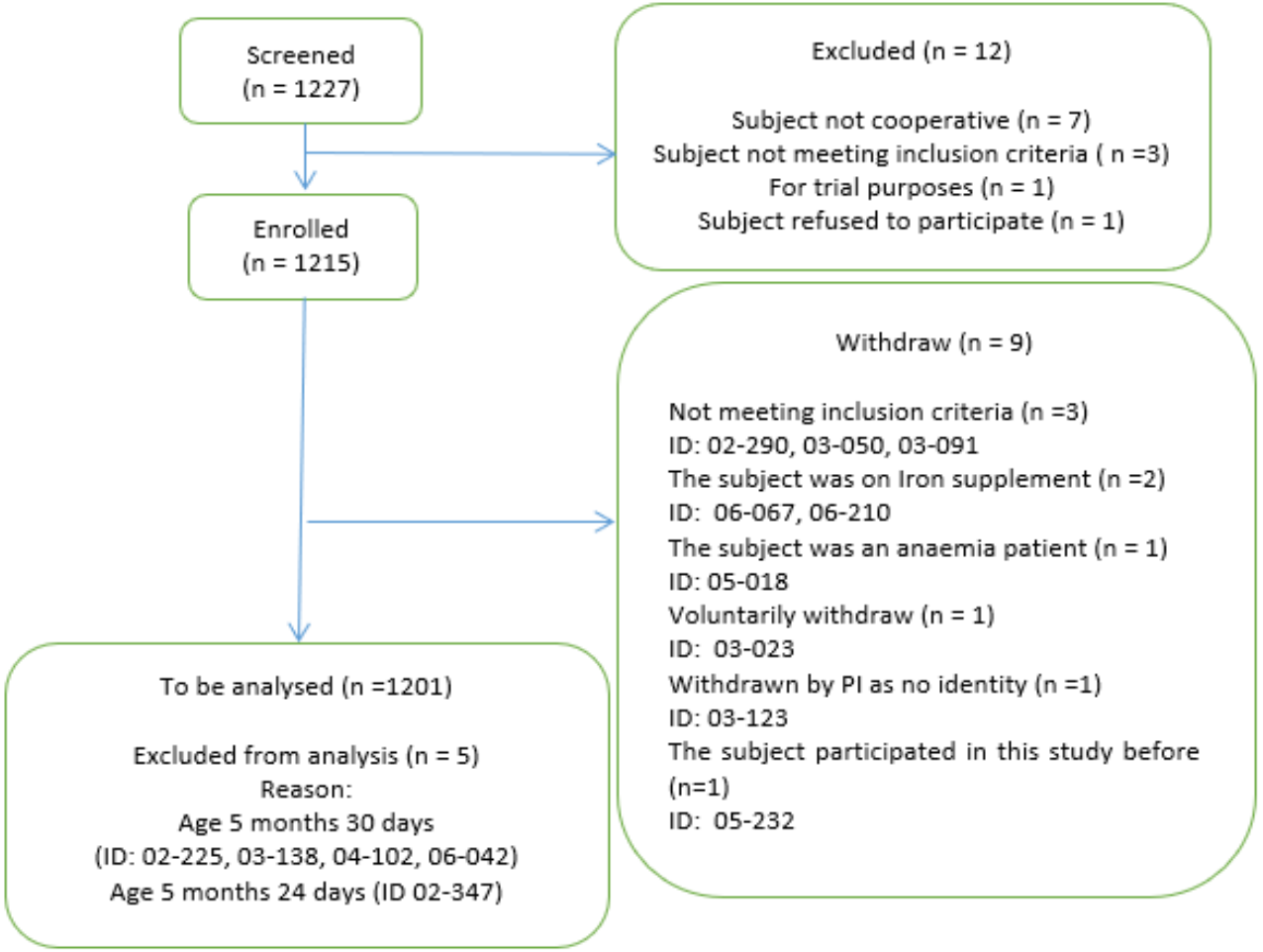
UNIVERSITY OF MALAYA MEDICAL CENTRE

IRON STRONG STUDY CONSORT FLOW DIAGRAM

Non-invasive anaemia screening is feasible approach: Only 7 out of 1227 not cooperative and cannot complete the test



Total screened subjects: 1227
Total enrolled subjects : 1215
Total subjects withdraw and excluded for analysis: 14
Total subjects with data to be analysed: 1201

THE LATEST FINDINGS OF IRON STRONG STUDY

Results

IRONSTRONG STUDY SHOWS

1 IN 3

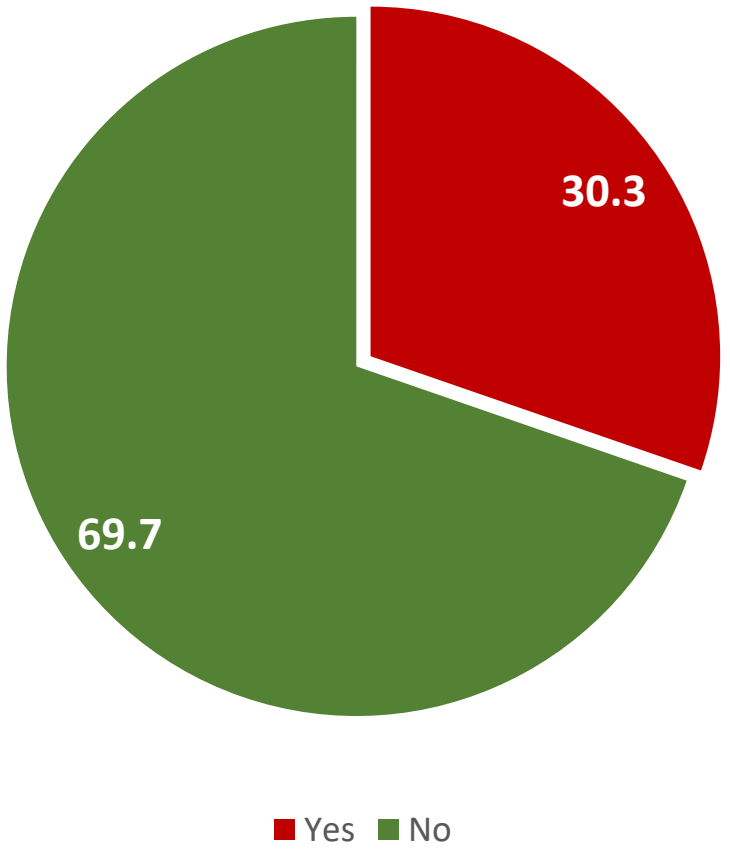
MALAYSIAN CHILDREN AT RISK OF ANAEMIA*

1,201 subjects from 5 sites

In line with WHO 2022 pooled-analysis Population Report, 24.6% Anaemia in Malaysia children

*cut off Hb<12g/dL and using Masimo device for screening

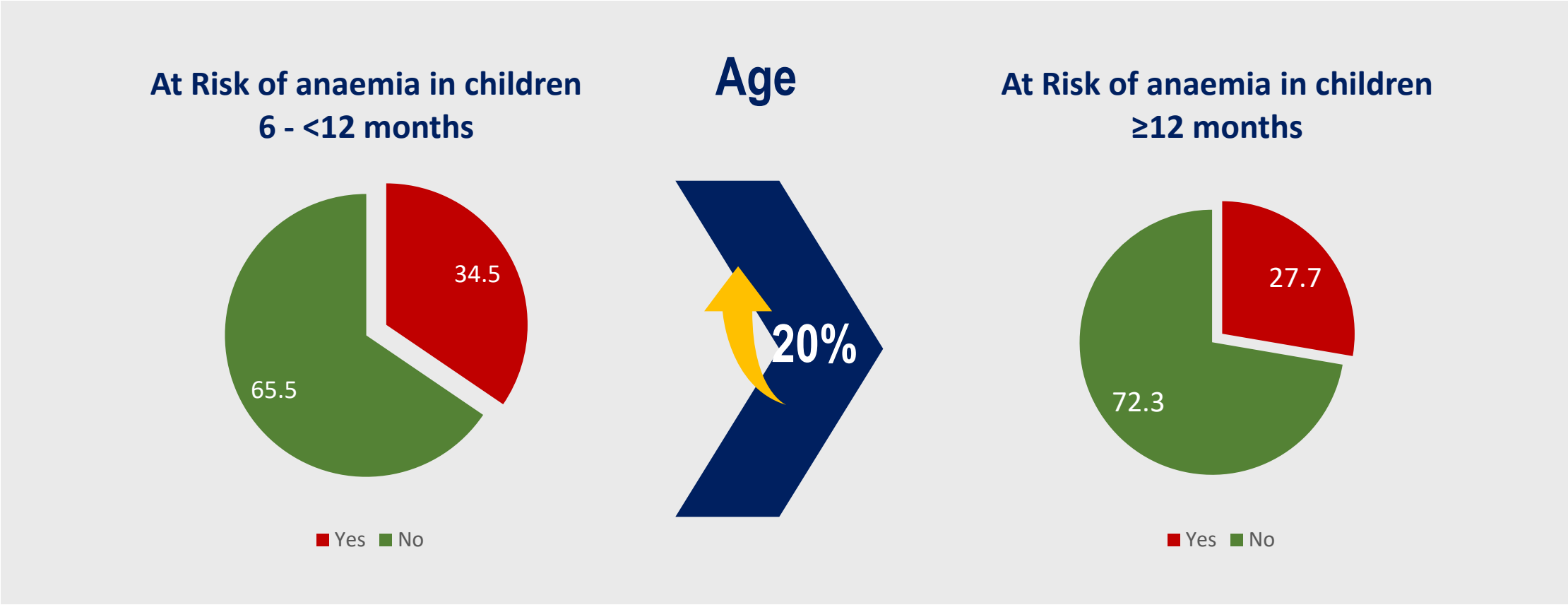
Risk of anemia in children 6-36 months



THE LATEST FINDINGS OF IRON STRONG STUDY

Results

Higher prevalent of anaemia in younger children

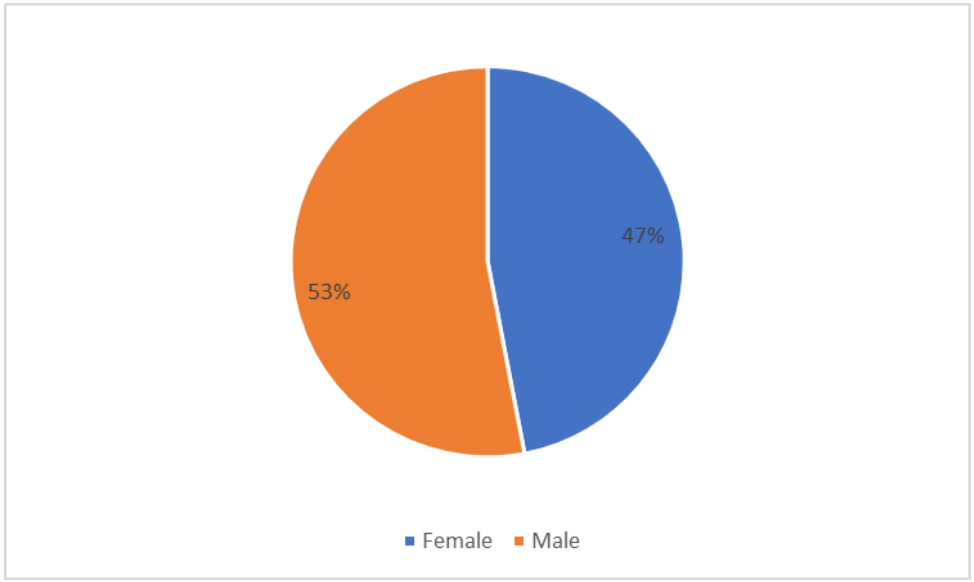


THE LATEST FINDINGS OF IRON STRONG STUDY

Results

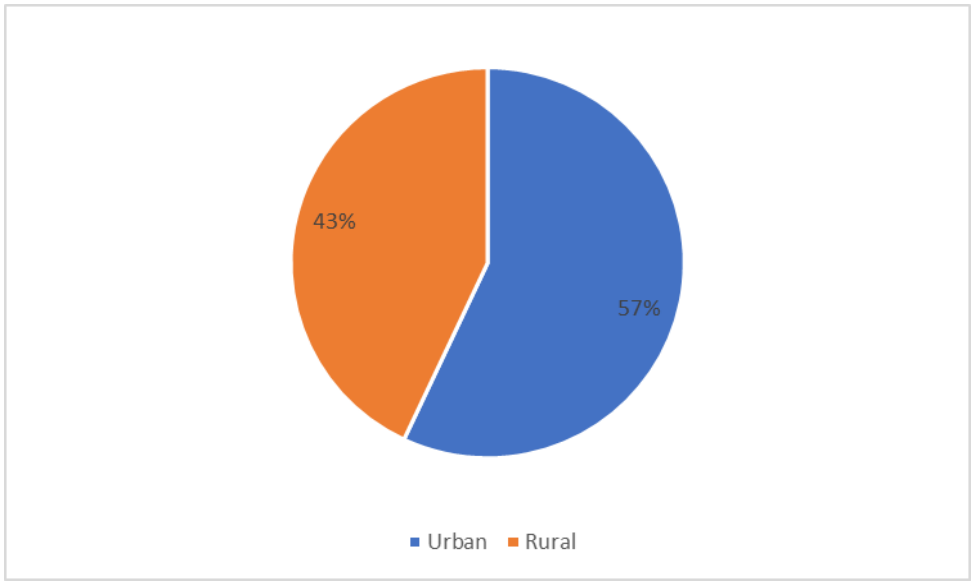
Gender does not impact anaemia

Gender

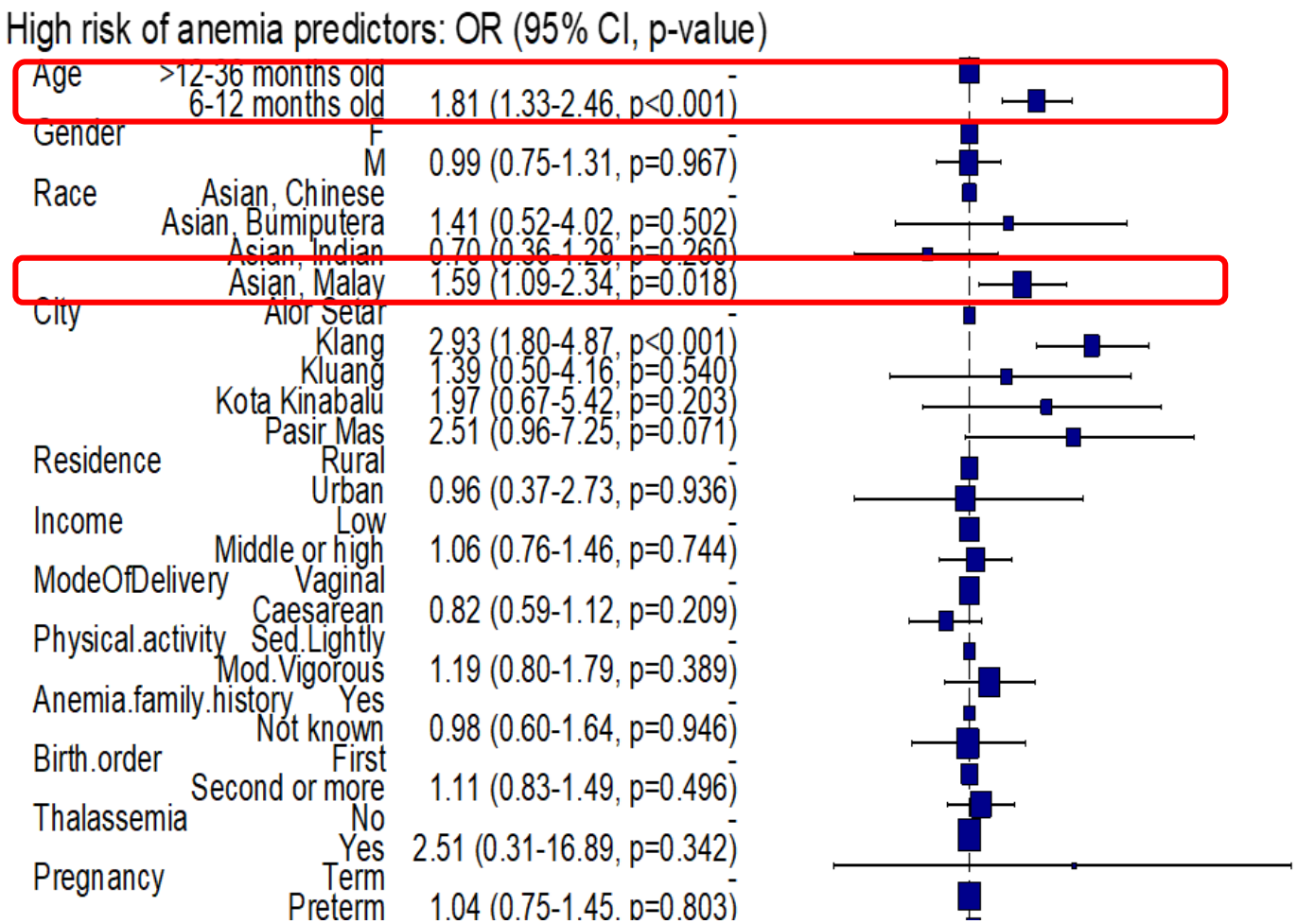


Urban and rural children are both susceptible to anaemia

Urban vs Rural



LOGISTIC REGRESSION PLOT & T-TEST : YOUNG AGE (<12 MONTHS), RACE & WFA PREDICTORS OF HIGH RISK OF ANAEMIA AMOUNG CHILDREN PARTICIPATEING IN THE STUDY



DEMOGRAPHIC CHARACTERISTICS DISTRIBUTED ACROSS THOS WHO HAVE RISK OF ANEMIA AND THOSE WHO HAVE NOT

Demographic characteristics of the study participants	Risk of anaemia		**p-value**[2]
	No, N = 837[1]	**Yes**, N = 364[1]	
Weight for age Z score	-0.62±1.35	-0.78±1.15	0.033

[2] Pearson's Chi-squared test; Fisher's exact test; Welch Two Sample t-test

KEY TAKEOUT

- ✓ Prevalence of Anaemia in children remains high in Malaysia
- ✓ Iron deficiency is the main cause of anaemia
- ✓ Early screening and improve nutrition awareness & dietary habits can alleviate IDA
- ✓ Proactive Non-Invasive Screening might be beneficial to Children
- ✓ Result of IRON STRONG study:
  - ✓ Feasibility of using non-invasive method is high
  - ✓ Prevalence of anaemia in Malaysian children is comparable with WHO report
  - ✓ Children 6 -12 months are at higher risk (higher prevalence)

Q&A

THANK YOU