

# Overview of Efficacy, Effectiveness and Safety of MNPs

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**SGHI**

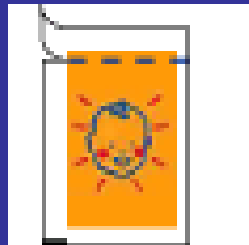
# Some definitions

- MNPs are **M**icronutrient **P**owders.
- ‘Sprinkles’ is the trademarked name for one particular brand of MNPs.
- Other brands of MNPs include ‘Anuka’, Babyfer, Chispitas, MixMe, MoniMix, etc.



# MNP Delivery Concept

- Single-serve sachets (packages) containing a premix powder of vitamins and minerals that are easily sprinkled once daily onto any semi-liquid foods without changing the colour, taste or texture of the food
- Home-fortification strategy enables families to instantly fortify prepared foods in the 'home':
  - Complementary foods for infants and young children
  - Fortified and un-fortified emergency rations such as CSBs
  - Homemade and prepared foods from local staples



# Advantages: Delivery Concept

- Easy to use and high acceptability among families and children; focus on ages 6 – 24 months
- A food-based rather than a medical approach;
- Does not require literacy;
- Does not conflict with breast-feeding practices;
- Used to promote the timely introduction of complementary foods at 6 months of age and proper weaning practices;
- Can be used for other ages throughout the life cycle;
- Light weight, easy to store and transport;
- Inexpensive and low tech to manufacture.



# Why Micronutrient Powders (MNPs)

- Drops and syrups for young children have been available for > 150 years, but....
  - Poor compliance because of the strong metallic taste, staining of teeth, difficulty in measurements (for illiterate caregivers), and medicinal approach.
  - No country-wide programs have been successfully implemented.
- Complementary or semi-liquid foods are a perfect vehicle for fortification (all infants eat them, rich and poor, rural and urban).



# Advantages: Coated Iron in MNPs



1. Can add MNPs directly to food
  - Coating prevents interactions between the micronutrient and the food
2. Easy to use
  - no literacy needed
  - relatively inexpensive to produce



# Sprinkles Formulations

## Nutritional Anemia Formulation

Micronutrient	Amount
Iron	12.5 mg
Zinc	5 mg
Folic Acid	160 µg
Vitamin A	300 µg RE
Vitamin C	30 mg

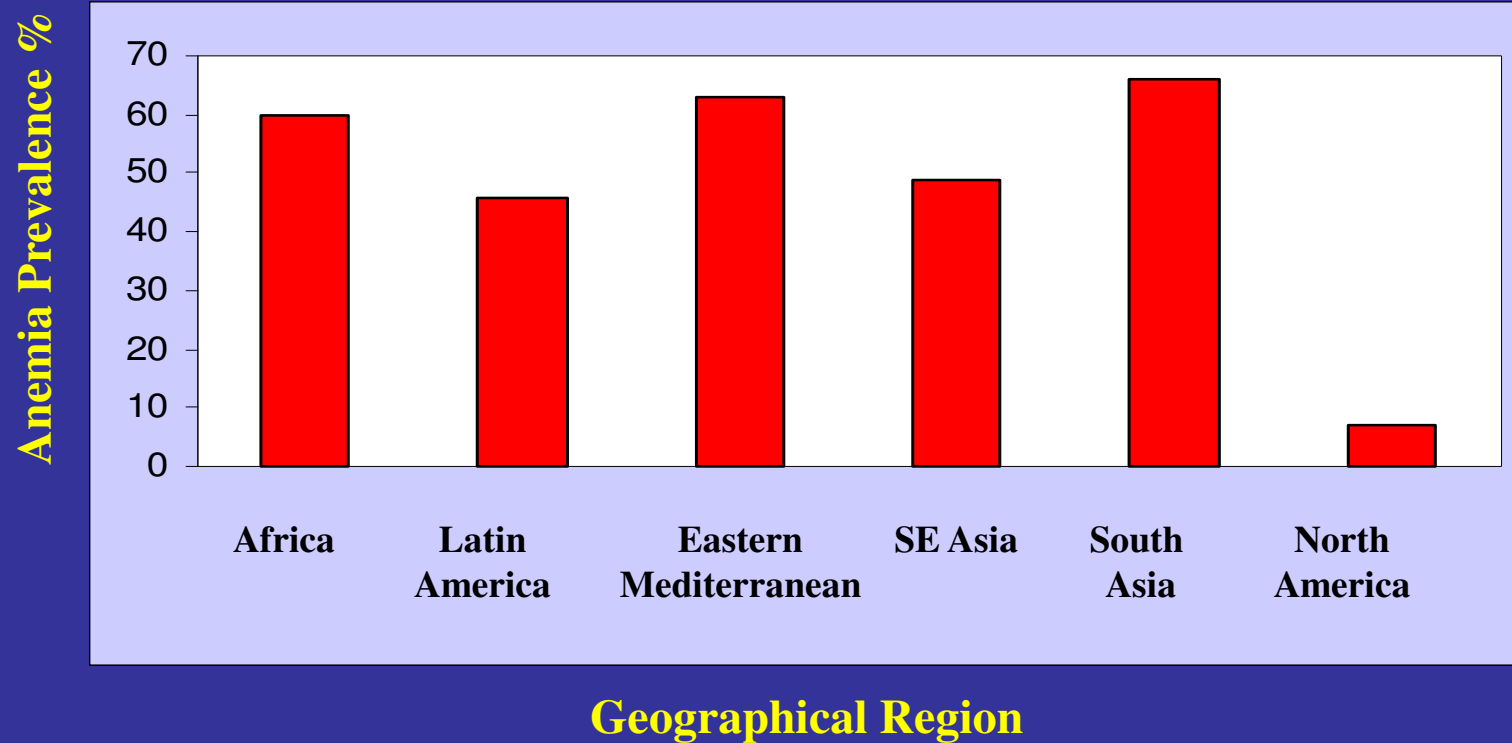
- Iron dose based on WHO/UNICEF/INACG recommendation for infants 6-24 mo, where the prevalence of anemia exceeds 40%
- Other nutrient levels based on WHO RNI and RDAs for children 6- 24 mo.

## Multiple Micronutrient Formulation

Micronutrient	Amount
Vitamin A	400 µg RE
Vitamin C	30 mg
Vitamin D	5.0 µg
Vitamin E	5 mg a-TE
Vitamin B1	0.5 mg
Vitamin B2	0.5 mg
Vitamin B6	0.5 mg
Vitamin B12	0.9 µg
Folic Acid	150 µg
Niacin	6 mg
Iron	10 mg
Zinc	4.1 mg
Copper	0.56 mg
Iodine	90 µg
Selenium	17.0



# Estimated anemia prevalence among children under-5 by world region



Source: INACG 2003



# The Adverse Effects of Anemia

Infants with *severe* anemia

- May develop congestive heart failure
- Are not able to deliver oxygen to all tissue of the body
- May die



# The Adverse Effects of Anemia

Infants with *mild to moderate* anemia:

- Show altered behaviour and cognition, such as increased fearfulness/wariness, irritability and unhappiness; lower IQ scores
- Demonstrate altered motor development, such as decreased exploration of environment, decreased willingness to leave a caregiver's side and increasing fatigue;
- May not be reversible



# Studies Have Compared Sprinkles to Drops or Placebo

1. To date, a total of 16 studies have evaluated the efficacy of Sprinkles.
2. The studies are from Africa, South Asia, South East Asia and North America.
3. The studies include infants and young children between 6 – 24 months.
4. A cumulative total of thousands of children have been studied.



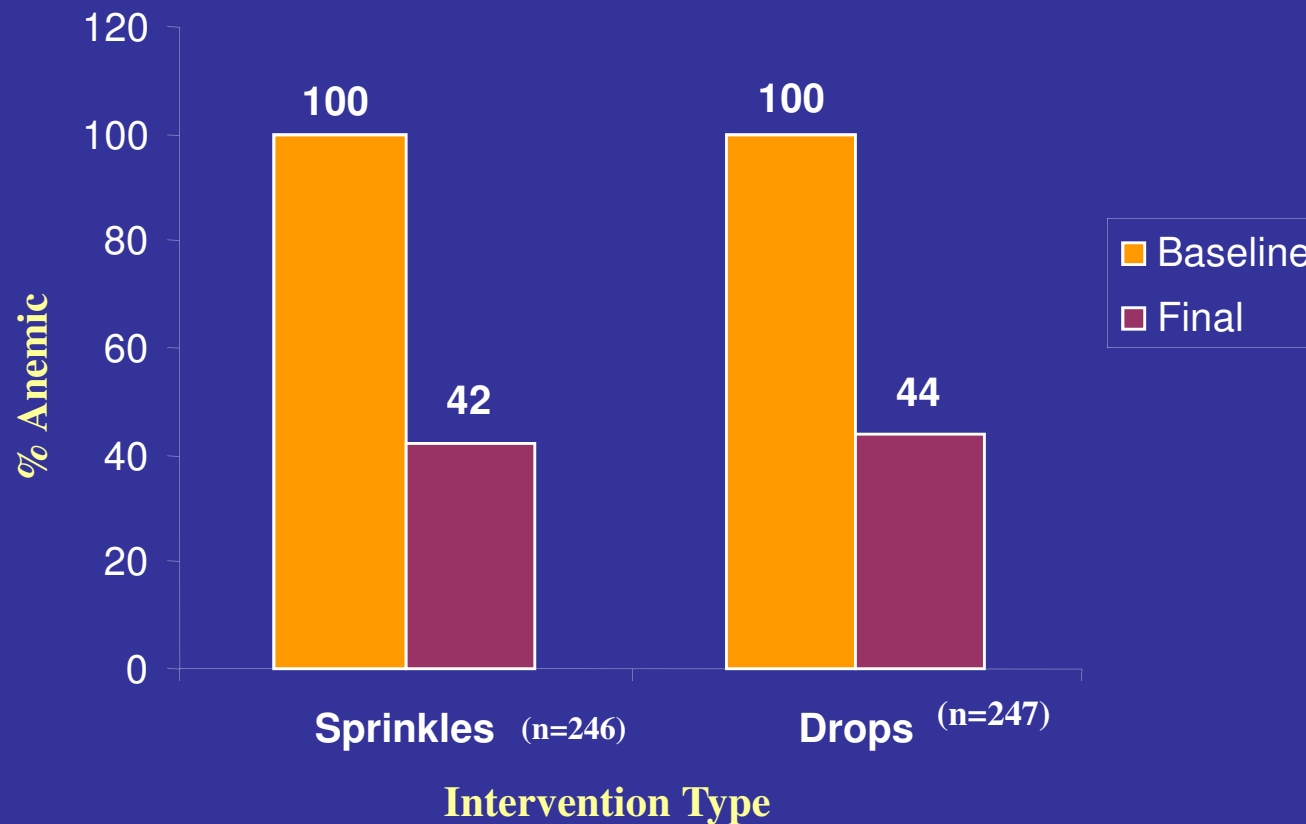
# Research on Efficacy: Do Sprinkles Work?

1. Completed 4 efficacy studies ( 2 large and 2 small) in Ghana
  - Also completed 2 stable isotope studies defining iron and zinc absorption;
2. A moderately large study in China;
3. Small studies in Bolivia, Sri Lanka and Israel;
4. Effectiveness and efficacy trials in Pakistan;
5. One study in aboriginal Canadians;
6. One study in India;
7. Three studies in Bangladesh (including a formative research);
8. A large effectiveness trial in Mongolia;
9. Added to CSB in Haiti;
10. Placebo controlled trial in Cambodia.



# Findings from Rural Ghana

Anemia prevalence before and after receiving 60 sachets over 2 months in 6-18 month old infants



(Modified from Zlotkin et al. AJCN 2001; 74:791-5)



# Acceptability

- High acceptability among families and children in many cultural settings:
  - **Bangladesh: Clinical Trial** → On a four-point scale, 60% of mothers 'extremely liked', 30% 'liked' and 10% somewhat liked Sprinkles
    - Compliance 88-98%
    - Reasons for acceptability included 'easy to use', perceived improvements in child's health, improved appetite
  - **China: AC Nielsen survey** → among 1375 households, across 5 cities found 70% of mothers 'extremely or somewhat' liked the product
    - 60% intent to purchase after a 4 week product evaluation.
    - 60% reported positive behavioural and physical changes in their child that they attributed to Sprinkles.



# Safety

- *Bland taste* of product and packaging discourages accidental overdosing and reduces risk of toxicity;
- *No adverse events* reported in children (6 mo – 5 yrs) from 7 community-based efficacy trials in 4 countries;
- *No evidence of iron-overload* in iron replete or deplete children as measured by serum ferritin;
- *No negative impact on growth* in iron replete children 4-18 mo receiving Sprinkles for 6 mo in placebo-controlled RCT in Northern Canada;
- *Less than 1% of caregivers* reported an increase in diarrhea, vomiting, harder stools or stomach upset in children receiving Sprinkles through relief activities conducted by ACF in Haiti.



# Frequency of Use

- Choices
  - Daily
  - Every second day
  - Every week
  - Flexible approach
- Give a consistent message...be clear.





# Frequency of Use

- | Choices            | Advantages/Disadvantages  |
|--------------------|---|
| – Daily            | Hard to remember/missed doses   |
| – Every second day | Even harder to remember   |
| – Every week       | Easier to remember/may not work; missed doses are very serious  |
| – Flexible         | It works well; does not matter if one or more doses are missed; message to use all that are given to you. |



## Number of MNP Sachets to Provide to Children (age 6 to 24 months)....General Principles

- WHO recommends an iron supplement of 12.5 mg per day from 6 to 24 months (thus, maximum 540 doses)
- Research supports the use of Sprinkles (12.5 mg Fe) to control anemia (safely) using either:
  - **Daily** – one sachet/day for 60, 90 or 120 days **OR**
  - **Flexibly and intermittently**, 60 sachets over a period of 90 or 120 days, with no more than 1 sachet/day
  - Two studies (Bangladesh and Haiti) demonstrate a significant reduction of anemia with 60 sachets with the impact lasting at least for the following 6-7 months.



# Haiti Study

## Results at 7 months post-intervention (follow-up 2)

<i>Indicator</i>	<i>Baseline</i>	<i>Follow-up 1</i>	<i>Follow-up 2</i>
Mean adjusted Hb (g/L) (SE)	98.9 (2.4)	104.4 (0.8)**	109.8 (0.6)**
Anemia prevalence, adjusted (%)	53.7	24.5**	14.3**

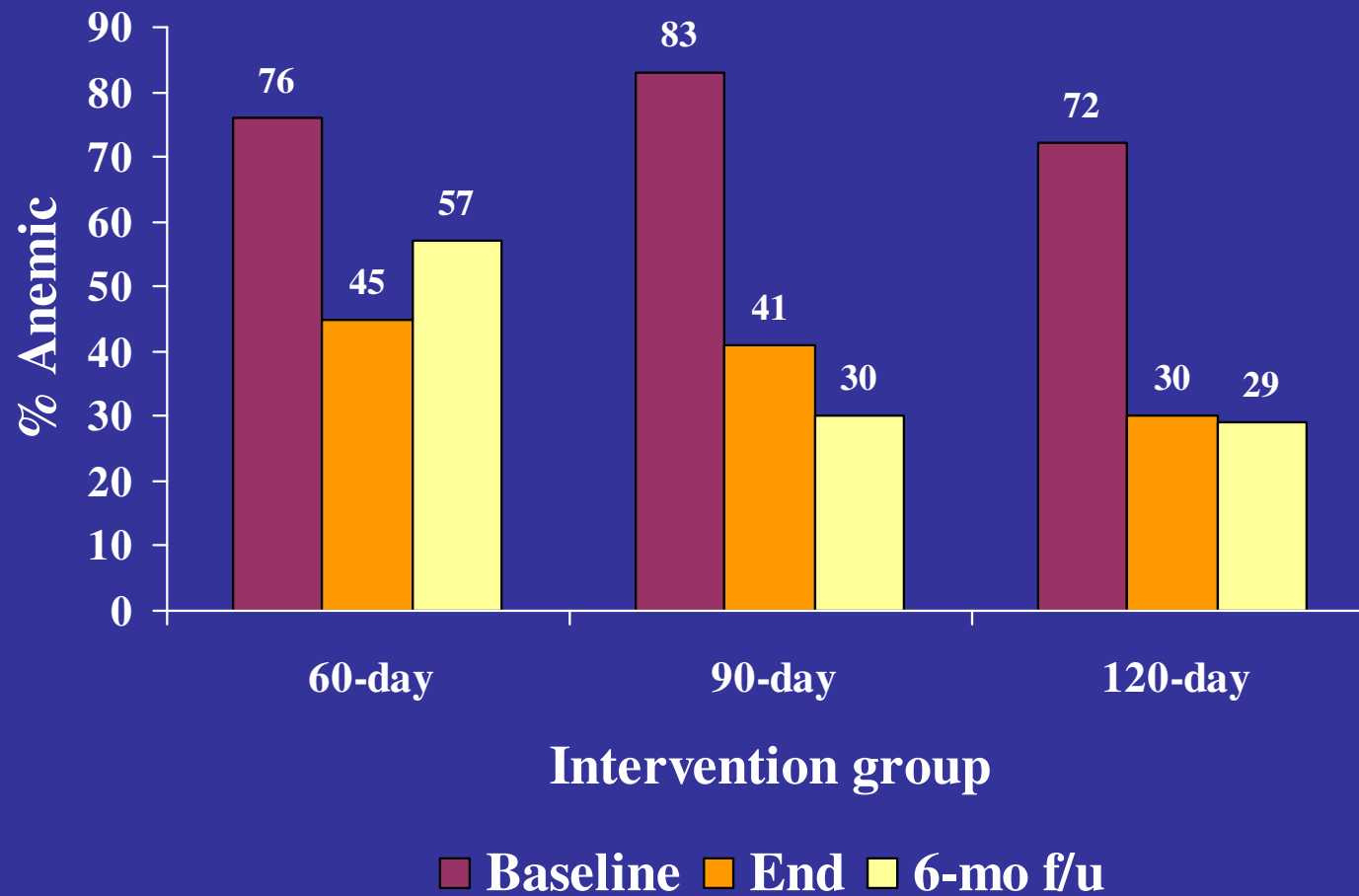
Follow-up 2 only done in Sprinkles-WSB group since WSB group received Sprinkles at the end of Follow-up 1; Mean Hb and anemia prevalence were adjusted for child age, sex and baseline Hb using random effects regression models.

Menon et al., *J Nutr* 2007



# Findings from rural Bangladesh

Effectiveness of the three Sprinkles administration models delivering 60 sachets of Sprinkles in children 6-24 months



# Number of Doses to Provide and Frequency of Distribution

- Depends on objectives of the program (WHO, RDA or anemia control)
  - Should be linked to distribution strategy

Example 1:    **Goal** – anemia control  
                  **Distribution strategy** - monthly distribution

- Total number** of doses to provide:
- at least 60 sachets (30 per month x 2 months);
  - repeat every 6 months (3 repeats)

Product Cost  $60 \times \$0.025 \times 3 = \text{US\$}4.50$   
Total 6-24 mo.



# Number of Doses to Provide and Frequency of Distribution

- Depends on objectives of the program
- Should be linked to distribution strategy

Example 2:     **Goal** – anemia control

**Distribution strategy** – biannual distribution

**Total number** of sachets to provide: at least 60 sachets (use flexible or daily)

Repeat biannually (3 repeats)

Product Cost  $60 \times \$0.025 \times 3 = \text{US\$}4.50$

Total 6 – 24 mo.



# Number of Doses to Provide and Frequency of Distribution

- Depends on objectives of the program
- Should be linked to distribution strategy

Example 3: **Goal** – meeting RDA for minerals/vit

**Distribution strategy** – monthly distribution

Repeat every month

**Total** number of sachets to provide:  
maximum 365/year (total 550 for 6-24 mo)

Cost = 550 X \$0.025 = US\$13.75

Total 6 – 24 mo.



# Research Agenda

- Unresolved issues:
  - (i) Use of iron containing MNPs (sprinkles) in areas with very high prevalence of malaria;
    - SGHI recommends malaria control efforts and continued use of food-based MNPs.
  - (ii) Environmental impact of MNP packaging;
  - (iii) Optimal methods for improving adherence to use.





# Summary

- Frequency of use – recommendation is daily but flexible likely to be successful;
- Number of doses:
  - Depends on objectives of the program
  - Linked to distribution strategy
    - Minimum – 60 sachets (total)/per 6 months, 180 total
    - Maximum – daily for 18 months (540 total)



# Conclusion

There has been more research on ***Sprinkles*** showing that they ***work*** (efficacy), that they ***are acceptable*** and that they ***are safe***, than probably any other new product in the past decade.

