

What's New In Infant Nutrition?

Assoc Prof Maria Makrides

Director, Child Nutrition Research Centre
a joint venture of the Child Health Research Institute,
Women's and Children's Hospital
Flinders Medical Centre
Adelaide, Australia



The key goals of infant nutrition

- To grow appropriately
- To develop a strong immune system that protects from infection and allergy
- To support the developing brain to function to its full potential

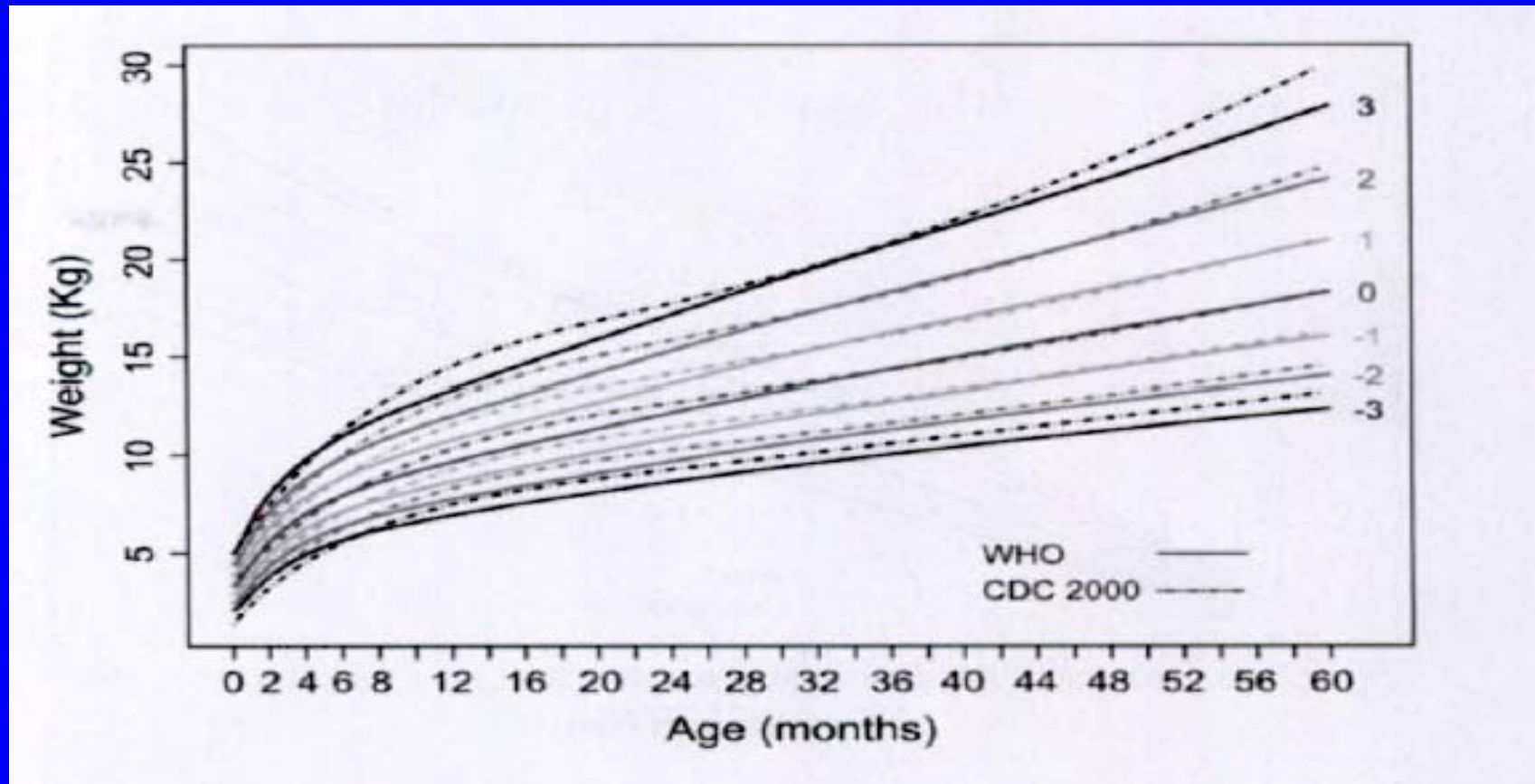
Why is growth at the top of the list?

- Best way to assess well-being of a preverbal child
- Nutritional deprivation as well as infection, illness and inappropriate environments will all cause growth faltering
- Therefore growth charts are fundamental to evaluating child growth trajectories and the interventions designed to improve child health

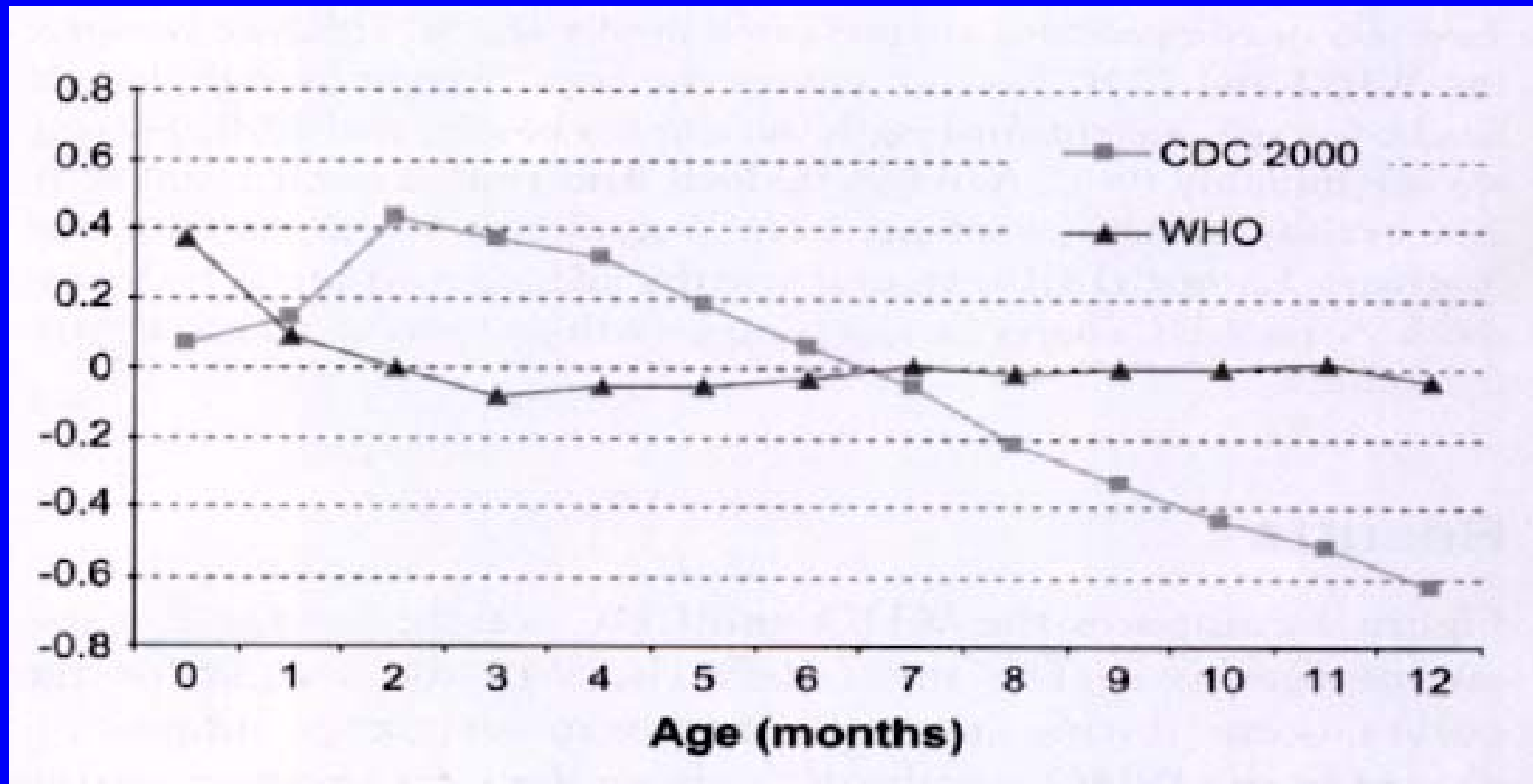
New growth charts to replace 1977 NCHS

- CDC
 - Released May 2000
 - For infancy based on NHANES II (1976-80) and III (1988-94)
 - Weight collected from 2 mo and length from 3 mo
 - Used birth vital stats
 - Relatively few fully breastfed infants
- WHO
 - Released April 2006
 - Data from WHO MGRS
 - Data collected in Brazil, Ghana, India, Norway, Oman and USA 1997-2003
 - Birth to 5 years of age only
 - All infants exclusively or predominately breastfed for at least 4mo

Weight for age Z-score curves for boys



Mean weight for age z-score of healthy breastfed infants relative to CDC and WHO standards



Summary

- WHO and CDC 2000 growth charts differ
- Difference relate to study design (sample size and measurement interval) and characteristics of the sample (mainly differences in mode of feeding)
- Implications for the definitions of failure to thrive and estimates of overweight and obesity
- Locally, in the process of changing from 1977 NCHS to CDC 2000

Could there be a nutritional reason for growth differences between breastfed and formula fed infants?

- Protein content of mature human milk is about 1g/100mL
- Traditionally most infant formulas 1.5g/100mL
- Why?
- To meet the minimum requirements for individual amino acids (protein quality)

The response

- Pressure on the formula industry to improve protein quality while reducing protein quantity
- A change in the regulations has also encouraged change
- In Australia we now have at least two infant formulas with lower protein contents that better approximate the amino acid profiles of breast milk in the first month of lactation

The immune system with an allergy focus

- Incidence of allergic disease has increased and is now estimated to be at least 20%, with some estimates as high as 40%
- Cost to the health care system and the burden to the family are high
- Estimated at \$18billion annually in the US alone
- Prevention is the key and there is a natural focus on the perinatal period where there is opportunity to modulate the developing immune system

Breastfeeding and immune outcomes

- Evidence of beneficial effects based almost exclusively on observational studies
- Potential sources of bias in such studies has made the extent of benefit difficult to quantify in industrialized countries
- Promotion of Breastfeeding Intervention Trial (PROBIT)
- Cluster RCT comparing an intervention modelled on the BFHI vs current practice in Belarus (1996-7)

PROBIT breastfeeding outcomes

- 16 sites with 8865 mother-infant pairs enrolled in the intervention
- 16 sites with 8930 mother infant pairs enrolled in the standard care group
- Table shows frequency of any breastfeeding

Infant age	Interven tion	Control
3mo	72%	60%
6mo	50%	36%
9mo	36%	24%
12mo	20%	11%

PROBIT health outcomes

Outcome	Intervention	Control
≥ 1 GI infection in first year	9.1%	13.2%*
Any rash in first year	12.3%	18.3%*
Atopic eczema in first year	3.3%	6.3%*

- No differences in
 - Respiratory tract infections in the first year
 - Otitis media in the first year
 - Eczema, asthma or hay-fever at 6.5 years
 - Positive skin prick test to HDM, cat, birch pollen, grasses or *Alternaria* at 6.5 years

When and what solids to introduce? Sensitisation vs Tolerance

- The “old” school
 - Avoidance
 - No solids until 6 months
 - Avoid allergenic foods such as peanuts, other nuts, shellfish in the first years of life
- The “new” school
 - Introduce low levels early to induce tolerance
 - Introduce solids between 4 and 6 months of life
 - No need to avoid the introduction of allergenic foods

Dietary components to modulate the development of allergies

- Pro-biotics
- Pre-biotics
- Long chain omega-3 fatty acids

Nutrition and the Developing Brain

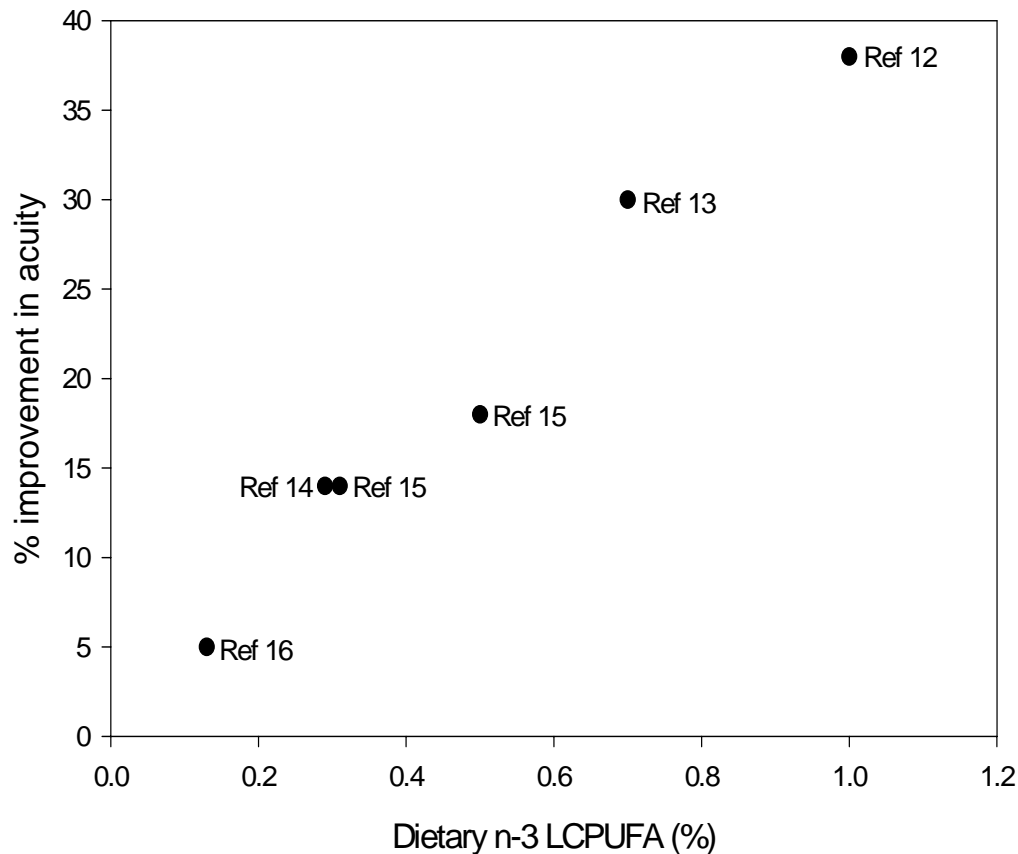
- Breastfeeding vs formula feeding
- Extent of benefit in healthy term infants?
- Confounding in observational studies
- Studies with adjustment for maternal IQ and the quality of the home environment generally show no difference in DQ or IQ between children who were breastfed or formula fed as infants

Nutrition and the Developing Brain

- A special focus on preterm infants
- Denied the in utero accretion of many nutrients in the last trimester of pregnancy
- Poor postnatal growth and nutrition associated with poor neurodevelopment



DHA and developmental outcome in preterm infants



RCTs involving formula fed infants

Mostly visual acuity data

Difficult to combine but when expressed as a percentage improvement over placebo there is a suggestion of a dose effect

DINO Trial

DHA for the Improvement of
Neurodevelopmental Outcome in
preterm infants

Makrides, Gibson, McPhee, Davis, Simmer, Morris
(NHMRC 2003-2007)

Makrides, Gibson, Doyle, Anderson, Ryan, Collins
(NHMRC 2008-2012)



Why this trial?

- Previous trials have compared exclusively formula fed infants and studied only “healthy” preterm infants. This represents <5% of preterm population in Australia and many Western countries
- Previous trials have assessed doses of DHA that approximate the level of DHA in the breast milk of women in industrialised countries, which a 3-5 fold lower than DHA exposure in utero



Objective

- To evaluate the effect of providing the *in utero* accretion rate of DHA compared with current feeding practice on
 - the Bayley Scales of Development at 18 months corrected age
 - IQ and executive function at 7 years corrected age



Eligibility criteria

- **Inclusion**

- Infants born <33 weeks and parents speak English

- **Exclusion**

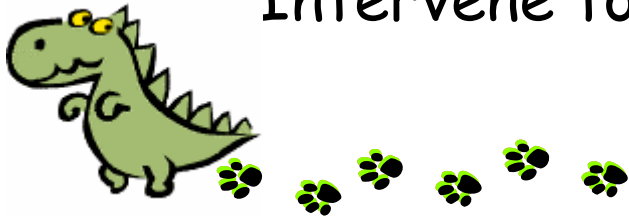
- Infants with major congenital or chromosomal abnormalities
- Lactating mothers with bleeding disorders or on regular anticoagulant therapy
- Multiple birth where all live born infants not eligible
- Participation in another trial involving fatty acid intervention



Feeding Schedule

- High-DHA feeding practice ($\approx 1\%$ total fat)
 - 6x500mg tuna oil capsules per day
 - if formula required, assign one with matching DHA composition
- Standard feeding practice ($\approx 0.3\%$ total fat)
 - 6x500mg soy oil capsules per day
 - if formula required, assign one with matching DHA composition

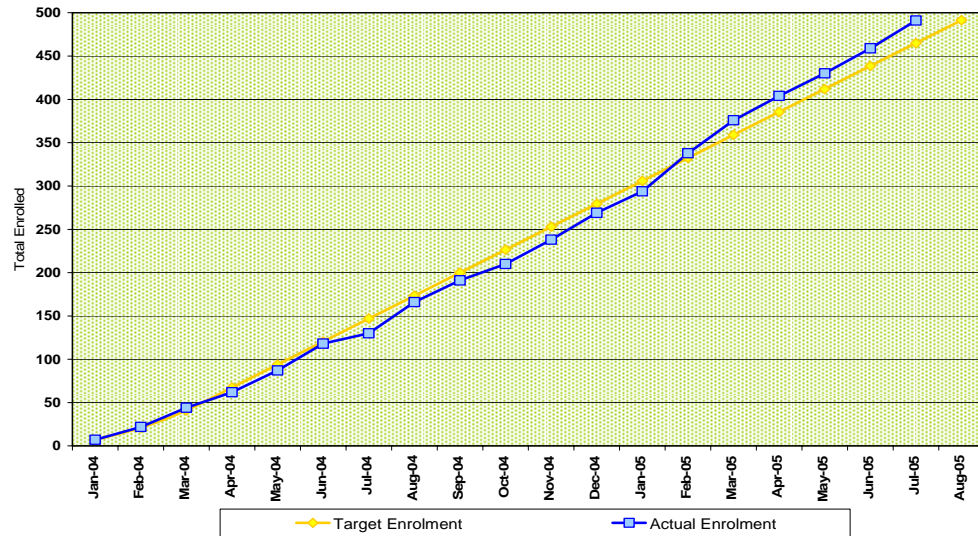
Intervene to 40 weeks PMA



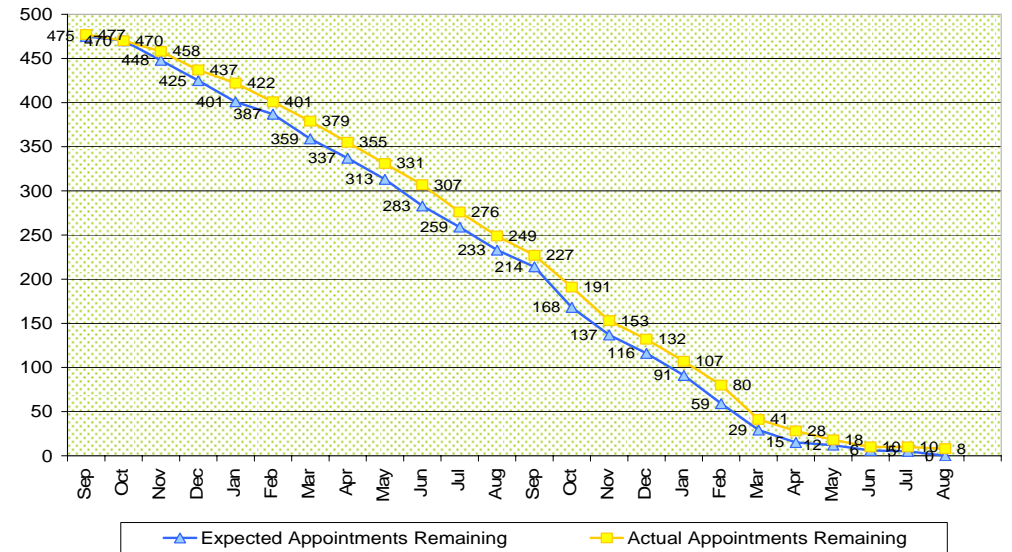
Progress to date

(last baby assessed 2 weeks ago!)

DINO RECRUITMENT



DINO - Total 18 Month Appointments - Expected vs Actual



To appropriately grown,
robust, bright kids!



Source: Anne Geddes Photo