

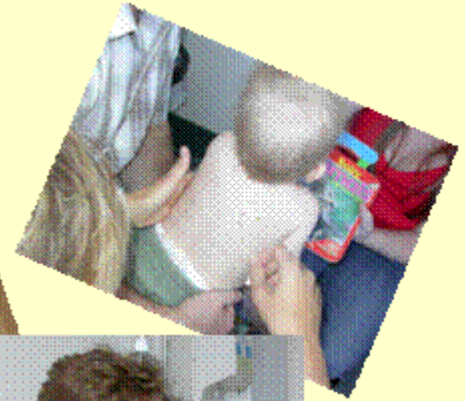
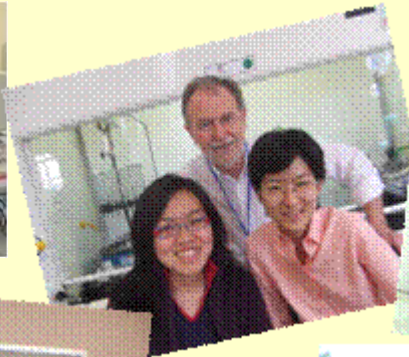
Meeting the nutritional needs of early life: the evidence and the myths

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I stand on the shoulders of many...



Context

- I am a dietitian/nutritionist researcher
- The ultimate aim of our research has been to establish practices and policies that will improve the health outcomes of women and their children
- What are the outcomes?
- Healthy children who develop well, grow appropriately and have a robust immune system

Fact or Myth?

- Pregnant women need iron
- Fish is brain food
- Breastfeeding women should avoid allergenic foods to stop their babies developing allergies

Pregnant women need iron

Iron during pregnancy

- Extra iron needed to support
 - expanded red cell mass
 - placenta
 - fetus
- Must be met from iron stores or from the diet
- RDI 30mg/day
- Average intake 12mg/day



Iron deficiency

- Continuum of depleted states to eventual iron deficiency anaemia
- In anaemia – not enough iron to produce Hb
- Consequences of iron deficiency anaemia (IDA)
 - Pallor, lethargy, reduction in work capacity
 - Increased susceptibility to infection
 - Adverse neurobehavioural outcomes, especially in young children

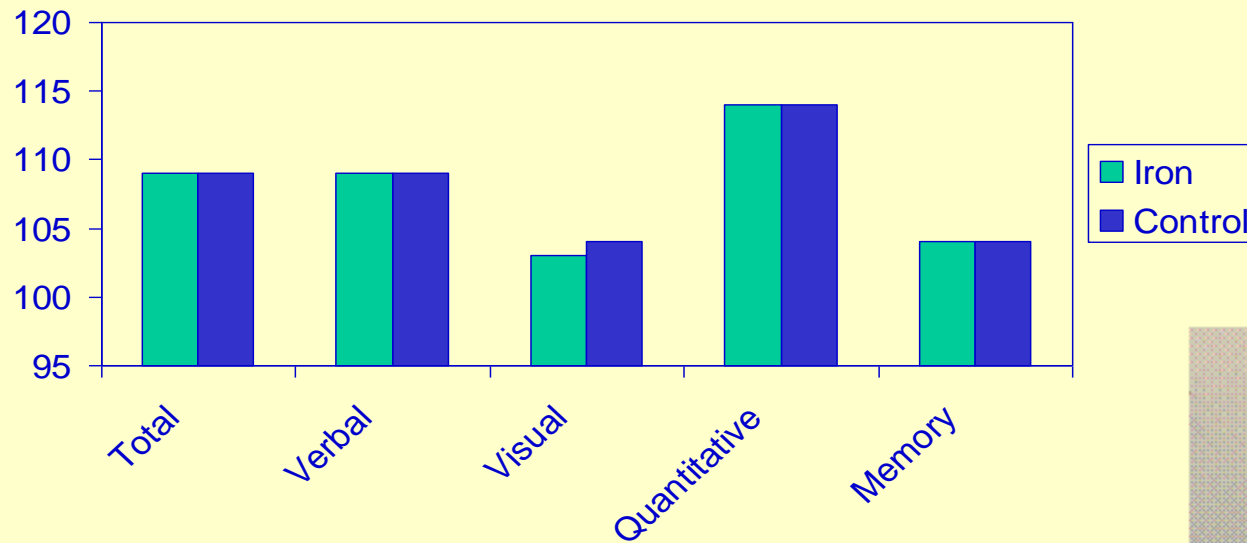
The debate: selective vs prophylactic
supplementation in pregnancy

Adelaide Mothers' and Babies' Iron Trial (AMBIT)

- Non-anaemic women from 20 weeks gestation
- 20mg iron or placebo per day to birth – designed to meet RDI for all women
- At end pregnancy,
ID ↓ 58% vs 35%
IDA ↓ 11% vs 3%
- No effect of supplementation on pregnancy outcomes



Stanford-Binet IQ of AMBIT children at 4 years of age



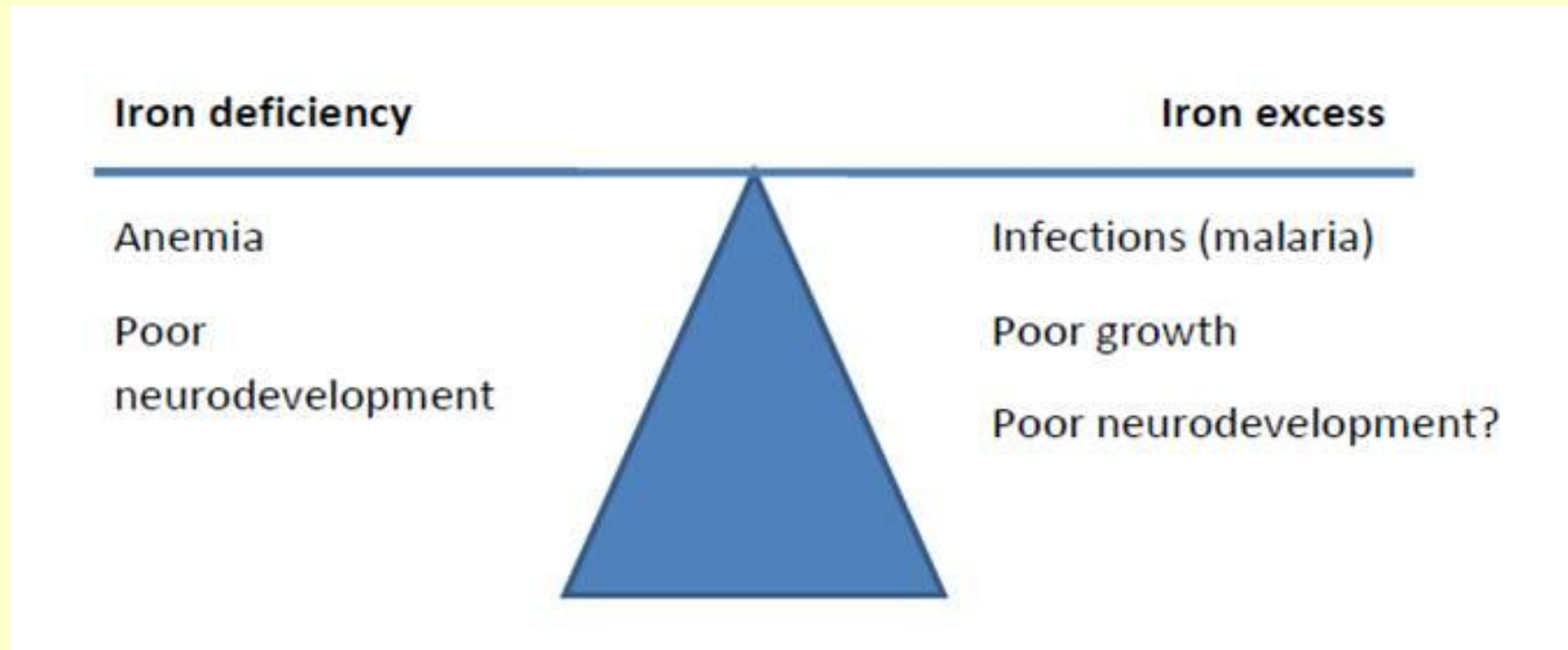
No benefit of routine iron supplementation in pregnancy on early childhood cognitive development



Childhood behaviour of AMBIT children at 4 & 8 years of age

- SDQ to assess emotion, conduct, hyperactivity, peer-problems, and total difficulties
- At 4 years, parents reported more children in iron group with high total difficulties score (12% vs 8%)
- At 8 years, teachers reported more children in the iron group with peer-problems (8% vs 2%)
- Needs cautious interpretation because it's a secondary outcome and there are relatively few children classified as “abnormal” **BUT.....**

Balance of benefit and harm



Do pregnant women need iron?

- Yes, if they are iron deficient
- No, if they are iron sufficient
- There is no reason for women to take iron supplements routinely during pregnancy
- Taking iron as “insurance” might not be such a good idea

Fish is brain food



Large scale epidemiological studies

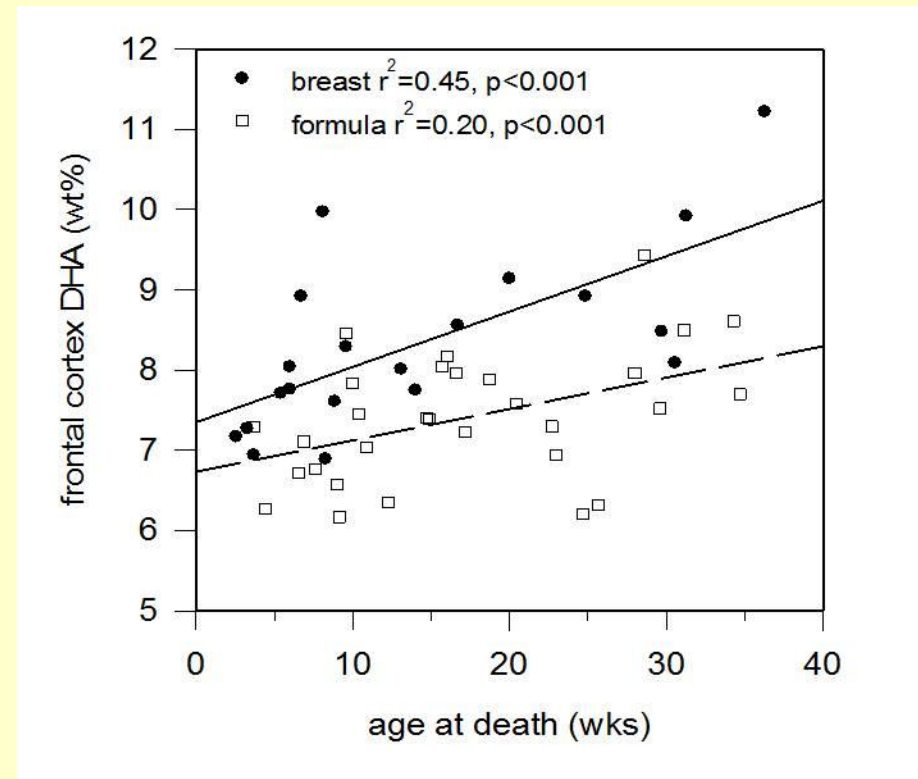
- High fish/seafood intake in pregnancy is associated with improved cognitive and behavioral outcomes
- Associations consistent across countries
- Intake of >340gm fish per week is needed to positively influence childhood development

Why would fish improve brain development?

- High fish intake and mercury?
- But other nutrients in fish may promote brain development
- Fish is the richest dietary source of the omega-3 fatty acid, DHA
- DHA makes up 30% of the lipid in the brain and plays an active role in neurotransmission and neuroprotection

Breastfeeding vs Formula Feeding

- Prior to mid-90's infant formulas did not have DHA
- Infants fed DHA have higher brain DHA than infant fed DHA-free diets
- Supplementing formulas with DHA increases blood levels
- But, does in change function



Makrides et al, AJCN 1994

DHA for Term Infants

- At least 15 trials that have tested the effect of adding DHA to infant formula on an aspect of infant development
- Some show modest, transient benefits to visual function
- No trials show benefits to global indices of development
- No evidence of harm



DHA for Preterm Infants

- Last trimester – very rapid growth and nutrient deposition
- Formula supplementation studies aimed at matching human milk, and showed visual and developmental benefits
- Calculations suggest that preterm infants need around 60mg DHA/kg/d (~1% of milk fats as DHA) compared with level in Western breast milk and formula of ~0.3% DHA
- Diet is the only feasible source of DHA – synthesis is slow and no body stores



DHA for the Improvement of Neurodevelopmental Outcome in preterm infants: DINO Trial

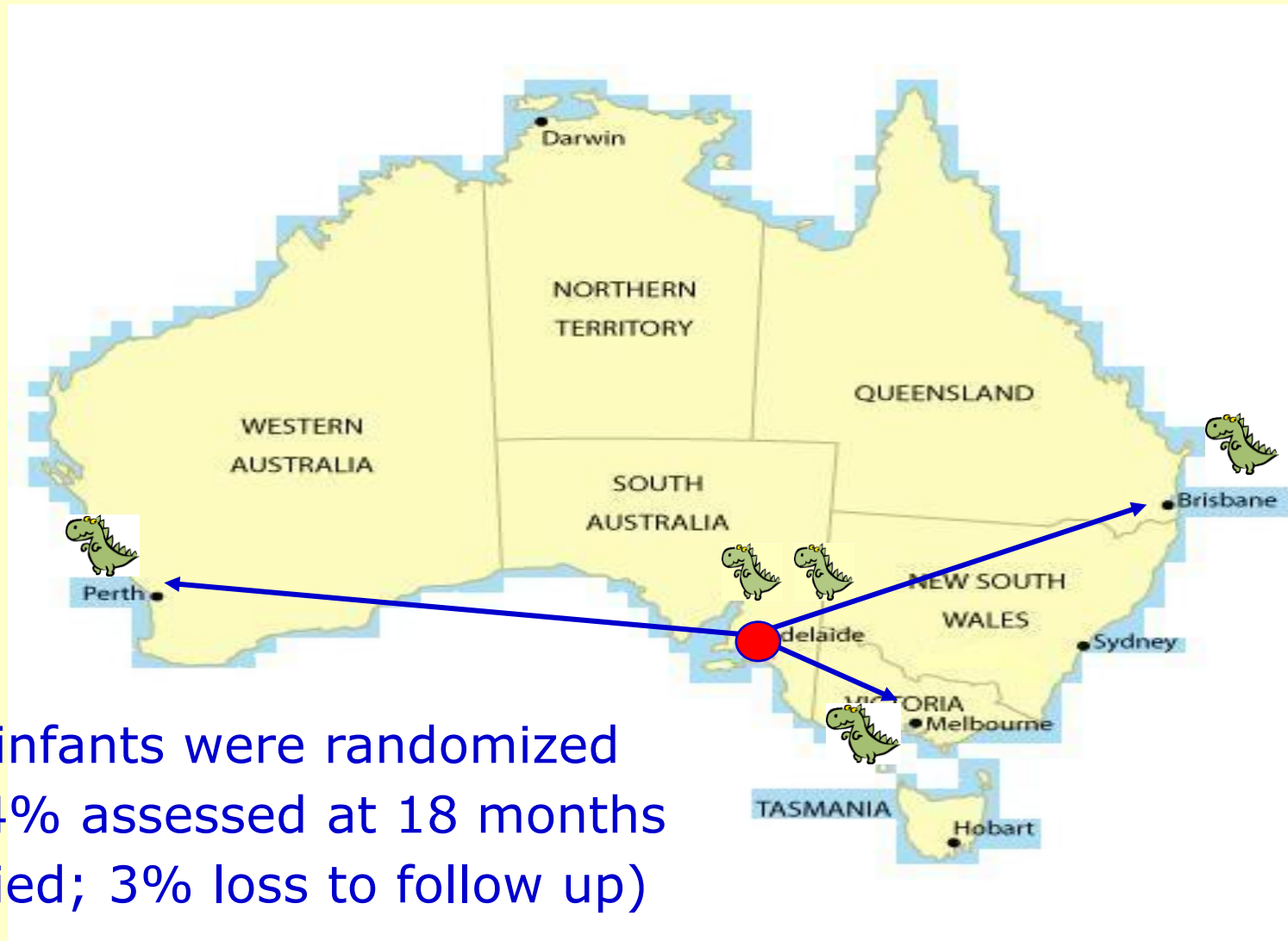


DINO Dietary Treatments

- High-DHA feeding practice ($\approx 1\%$ total fat)
 - Breast milk: Mothers - 6x500mg tuna oil capsules/day
 - if formula required, assign one with matching DHA composition
- Standard-DHA feeding practice ($\approx 0.3\%$ total fat)
 - Breast milk: Mothers - 6x500mg soy oil capsules/day
 - if formula required, assign one with matching DHA composition
- Intervene to 40 weeks PMA
- All receive standard DHA post-term

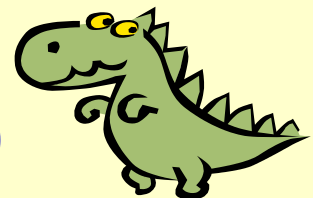
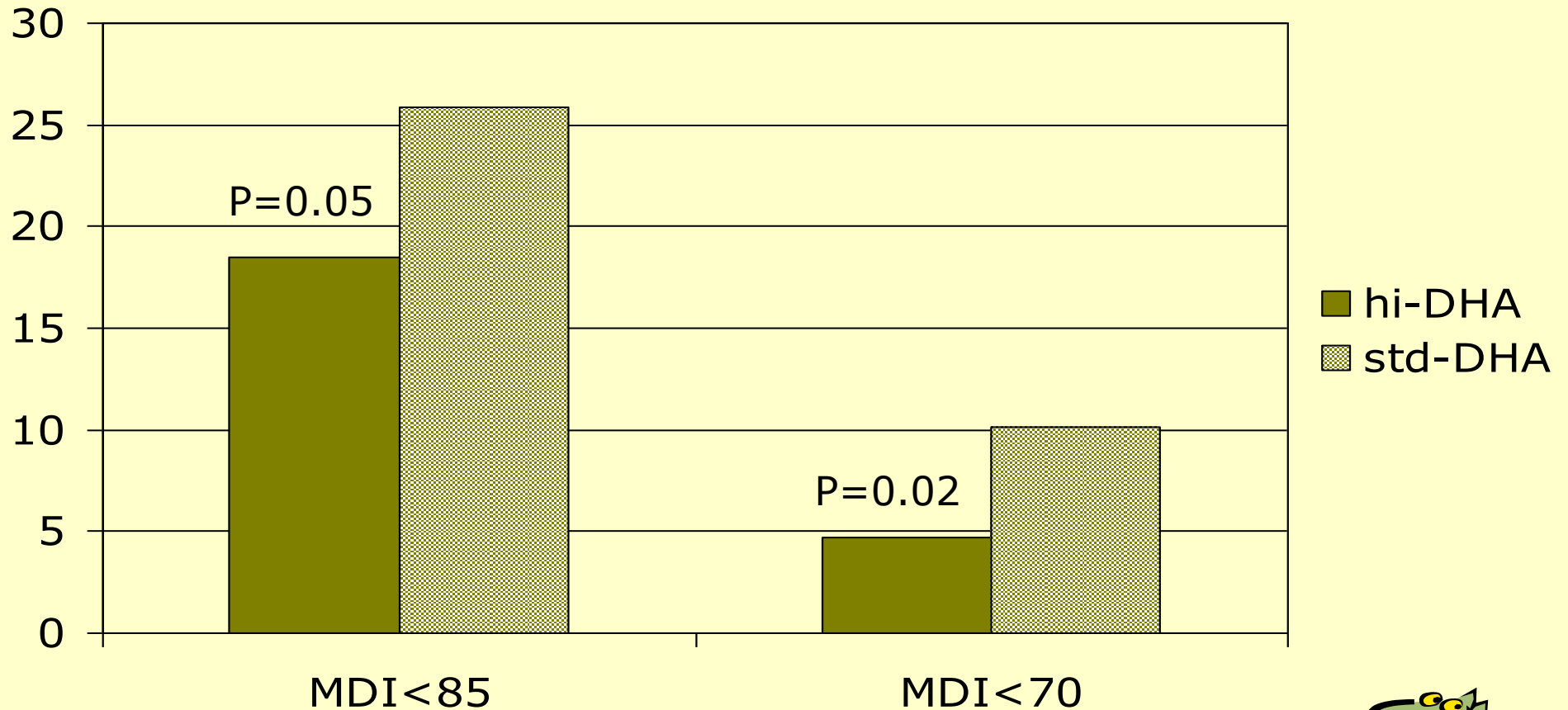


DINO Trial Across Australia



657 infants were randomized
and 94% assessed at 18 months
(3% died; 3% loss to follow up)

Percentage of Infants with Mild and Major Mental Delay



DINO Results Summary

- 30% reduction in mild and 50% reduction in major cognitive delay in hi-DHA group, although the mean DQ did not differ between groups
- Significant interactions between DHA treatment and birth weight and DHA treatment and sex
- Babies with birth weight <1250g and girls responded to the DHA treatment





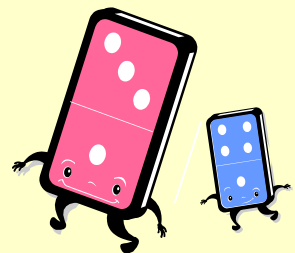
Implications of the DINO trial to preterm children

- 7 year follow up: are the cognitive effects permanent?
- More fully understanding the effects of DHA
 - Why the sex differences?
 - Other organ systems
 - Better delivery systems
- Implications for clinical practice

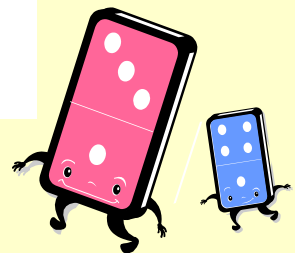
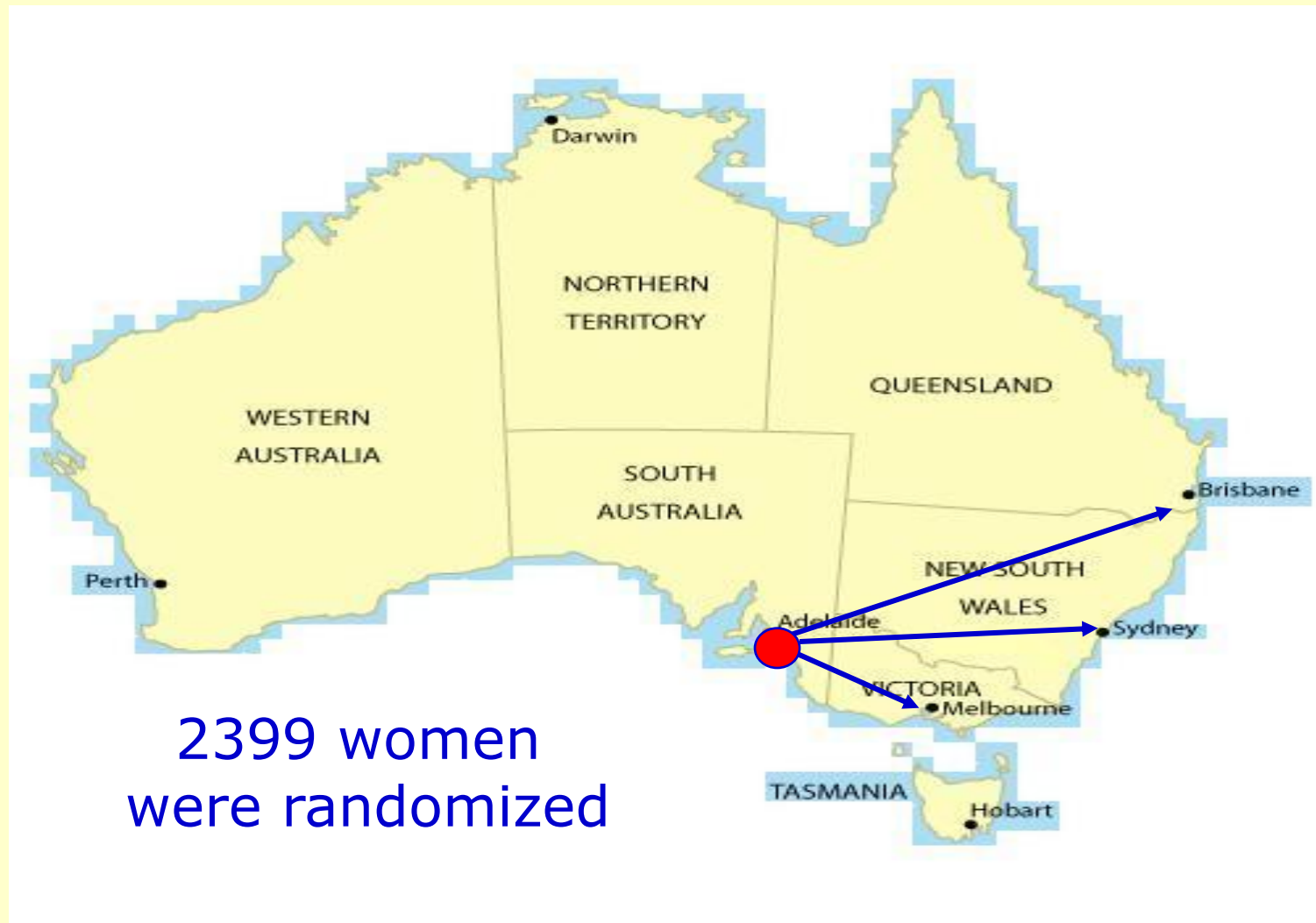


DHA to Optimise Mother Infant Outcome: DOMInO trial

- To assess the effect of DHA supplementation during pregnancy on:
 - Risk of maternal postnatal depression
 - Early childhood development
 - Allergy (high-risk children)
 - Growth and fat mass in children



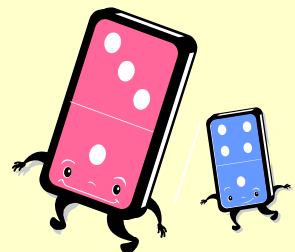
DOMInO Centres across Australia



DOMInO dietary treatment



- DHA group – 3x500mg capsules of DHA-rich fish oil concentrate providing **800mg of DHA/day**
- Control group – 3x500mg capsules containing a blend of 3 vegetable oils (to match Australian diet) with **no DHA**
- Intervene from study entry to birth
- No intervention post birth



DOMInO data will soon be available...

- DHA supplementation did increase the level of DHA in cord blood and therefore DHA delivery to the baby
- But the level in the control group was pretty high anyway despite the mother eating no fish – why is this so?
- Adaptions in pregnancy. Mobilization of fat stores. Typical pregnant women would have about 20g in fat stores. Estimated fetal need is about 6g during last trimester

Is fish brain food?

- Depends.....
- Most work relates to DHA, but DHA is not fish
- Term babies: Any effects of DHA probably small and may not be of clinical significance
- Preterm babies: Definite role for DHA
- Pregnant women: We will soon know

Breastfeeding women should avoid
allergenic foods to stop their babies
developing allergies

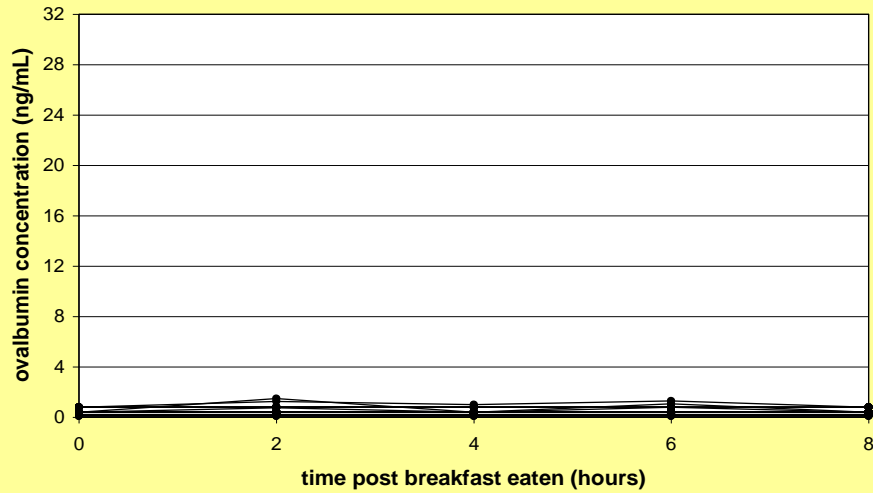


Does egg ingested by women appear in their breast milk?

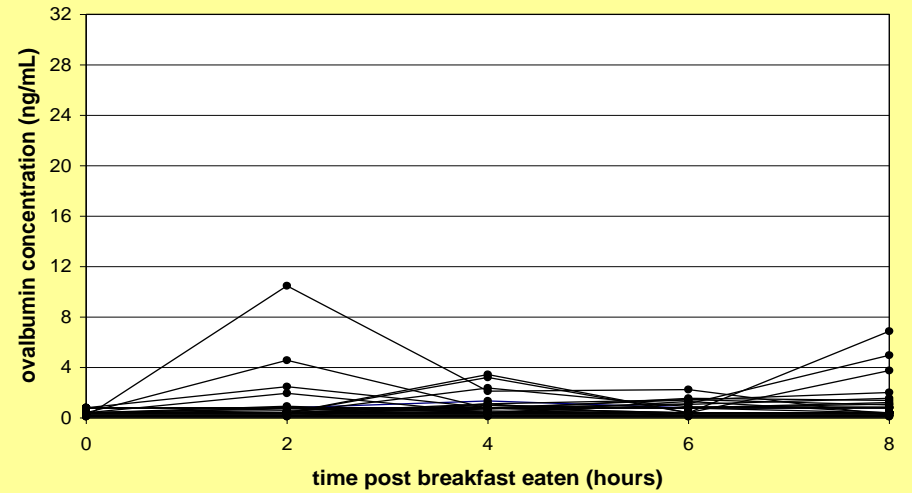
- Women followed an egg free diet
- Randomly allocated to 1 of 4 test breakfasts each week
- Each test breakfast: muffin and milkshake
- 4 test breakfasts: no egg, 1/2 cooked egg, 1 cooked egg or 1 raw egg
- Recipe development: indistinguishable taste and appearance
- Kinetic study to measure egg excretion in breast milk



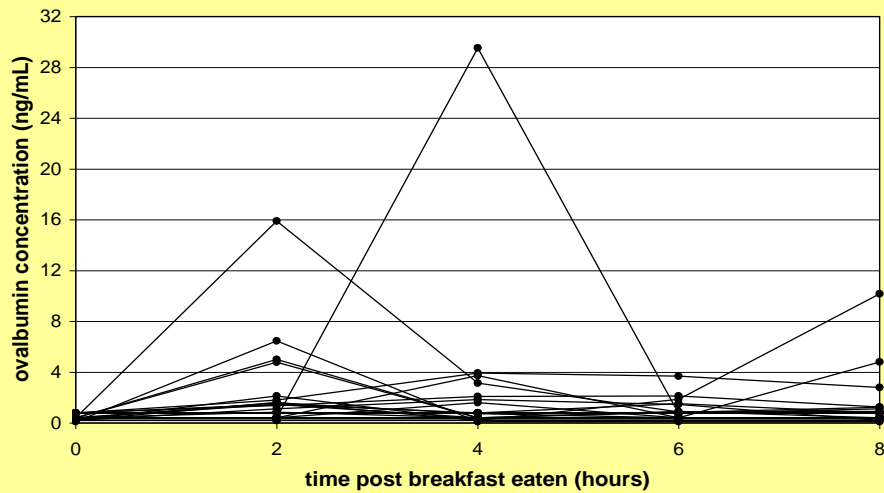
Breakfast: no egg (n=41)



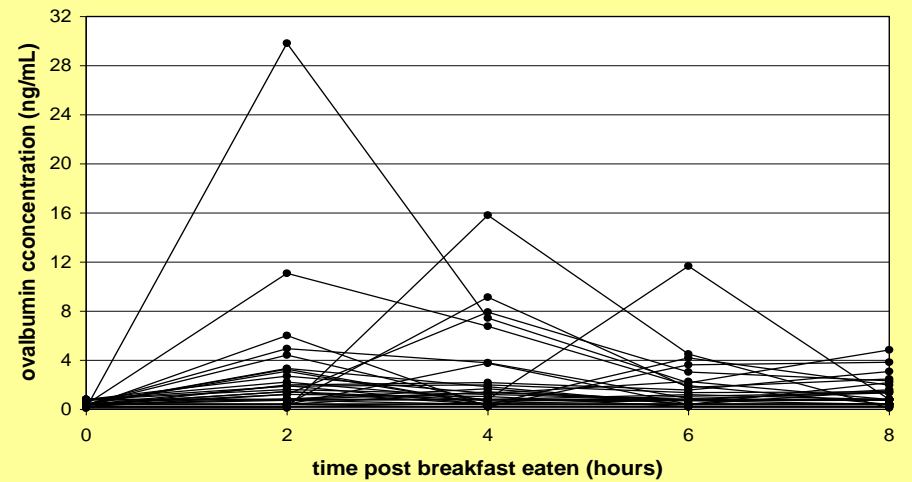
Breakfast: 1 raw egg (n=41)



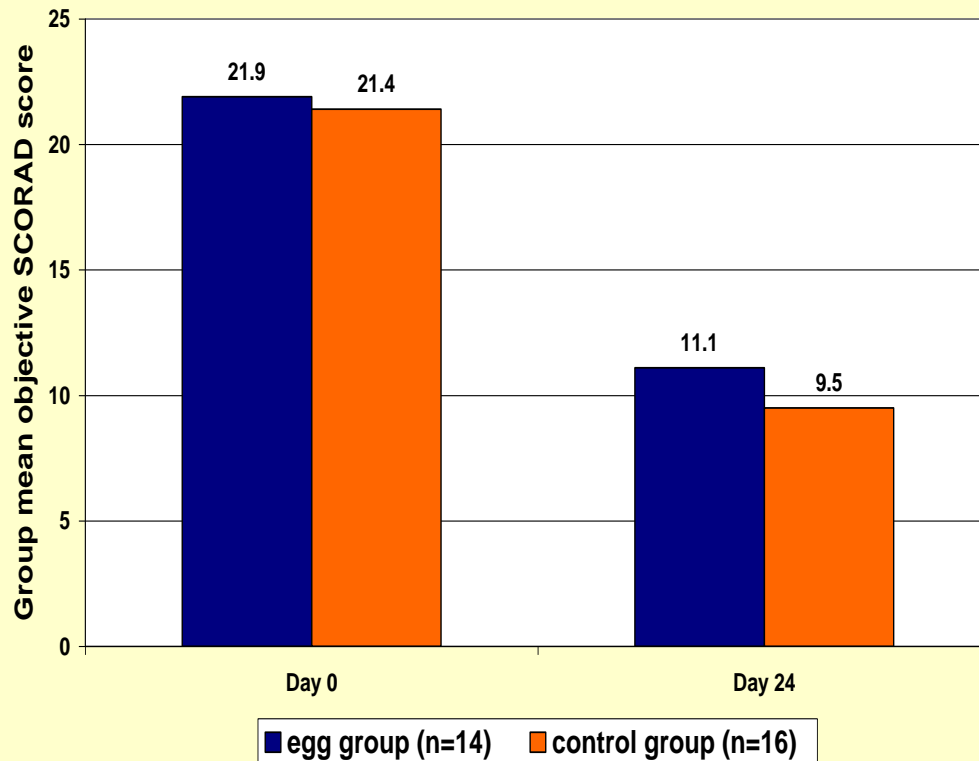
Breakfast: 1/2 cooked egg (n=41)



Breakfast: 1 cooked egg (n=41)



What happens when breastfed infants with egg allergy are exposed to egg through breast milk?



Significant reduction in eczema severity for both groups over time, but no difference between the groups



Breastfeeding women should avoid allergenic foods to stop their babies developing allergies

- More work needs to be done
- But, our work and that of others is increasingly suggesting that tolerance may best be achieved through regular exposure of food antigens and preferably in the presence of breast milk

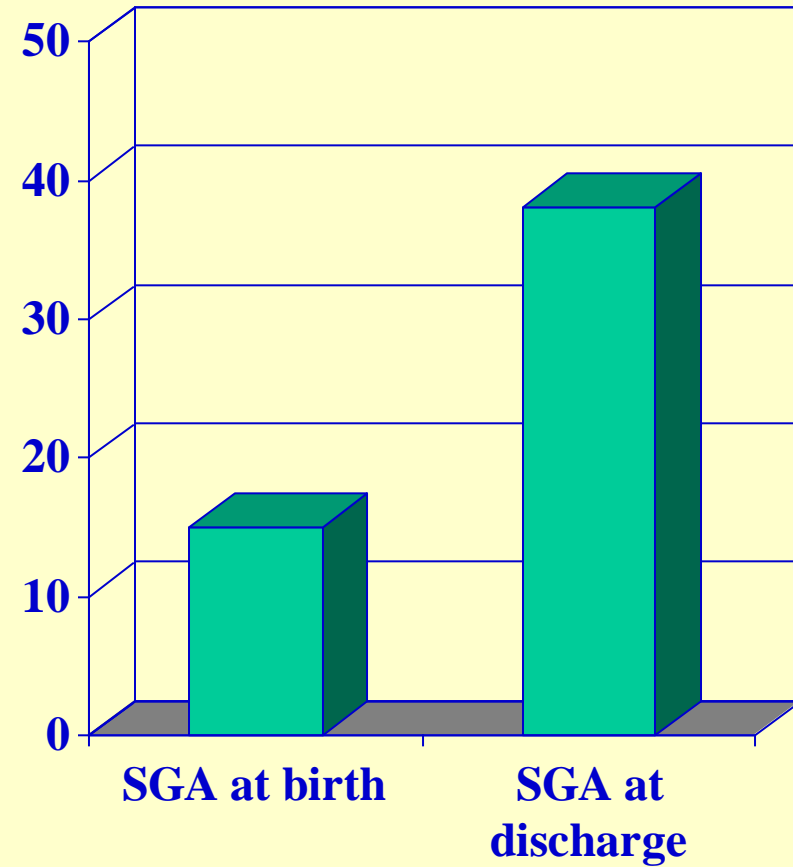


Challenges for the next decade

- Back to basics, perhaps with the odd hi-tech assessment
 - Growth – too little, too much
 - Nutrient-environment interactions
 - Degree of nutrient insufficiency and effect on functional and clinical outcomes



Growth of preterm infants



Allergies: food-environment interactions

- Egg allergy is the most common food allergy in Australian young children affecting about 4% of children <3 years of age
- Conflicting advice regarding the introduction of allergenic foods like egg
- The STEP (Start Time of Egg Protein) trial compares early introduction (4 months) with later introduction (10 months) on egg allergy



Is supplementation needed in regions of mild iodine deficiency?



- Mandatory iodine fortification of bread in Australia & NZ from Sept 2009 (FSANZ)
- Do pregnant women need extra iodine?
- RCT in Australia and NZ to determine whether routine iodine supplementation of pregnant women will enhance neurodevelopmental outcome of the off-spring



Finally...

- Many more exciting things to conquer in nutritional science
- None would be possible without
 - National clinical collaborators with the same commitment to clinical trial excellence
 - Outstanding statistical and data management collaborations, DMAC
 - Great team committed to excellence
 - Wonderful hospitals where research is encouraged
 - An altruistic public
 - Government funding that leaves the investigator free
- Important that we extend the capacity building of nutritional science across different disciplines