



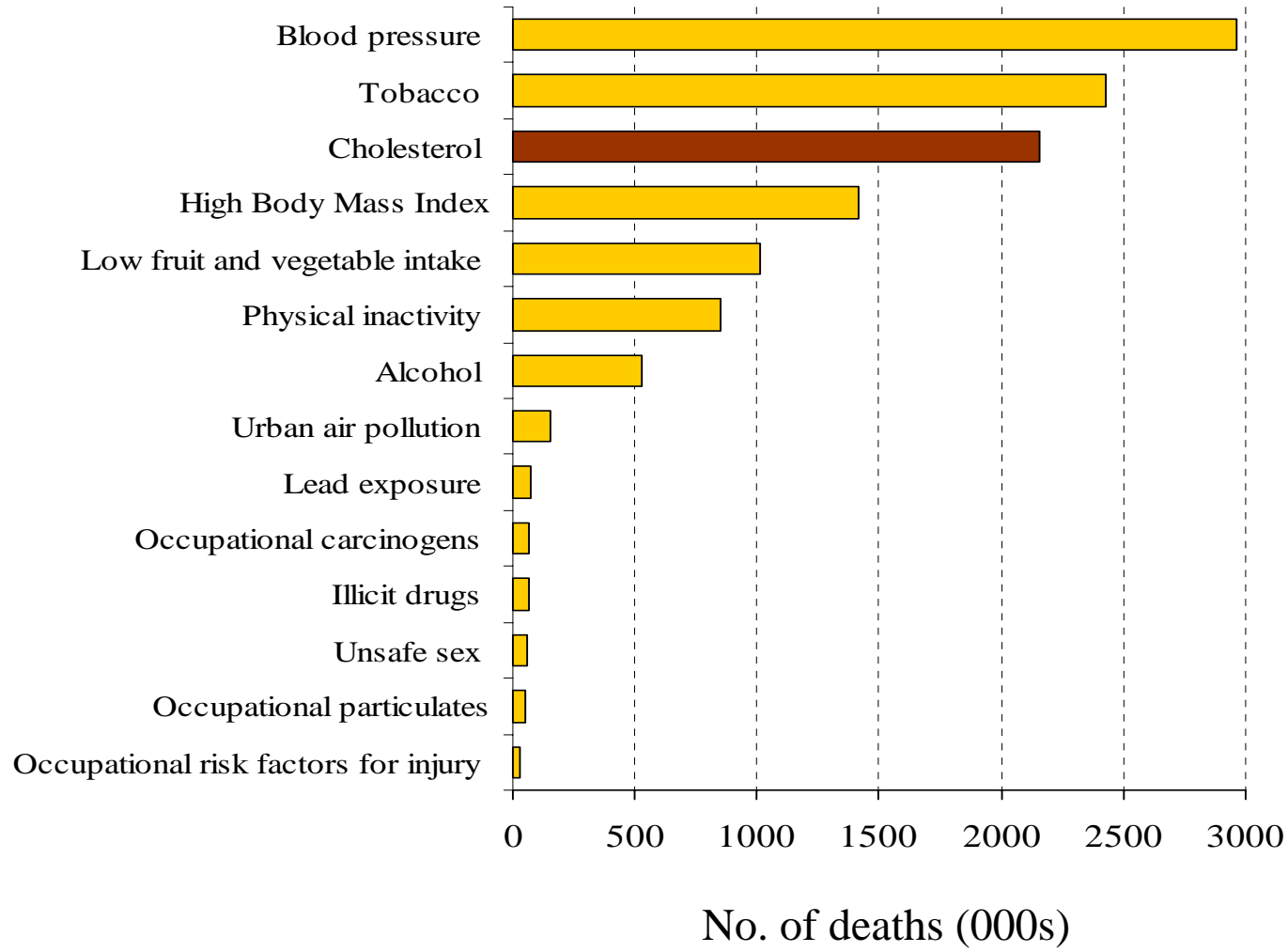
Breastfeeding and lipids

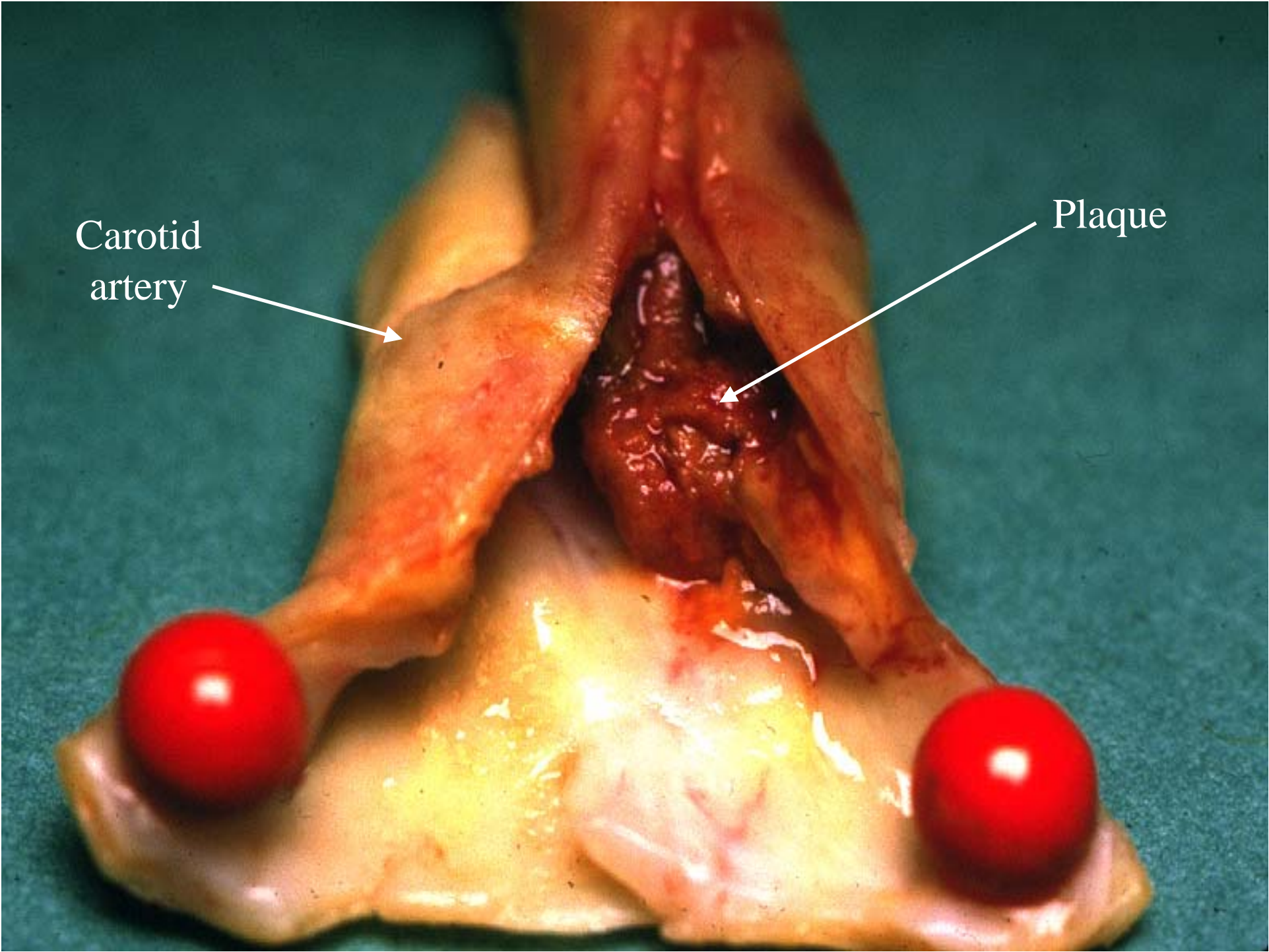
Dr Richard Martin, Department of Social
Medicine, University of Bristol

Focus of talk

- Background to the hypothesis
- Systematic review of observational evidence
- Experimental (trial) evidence
- Public health importance

Deaths in the developed world (2000) attributable to selected leading risk factors





Carotid
artery

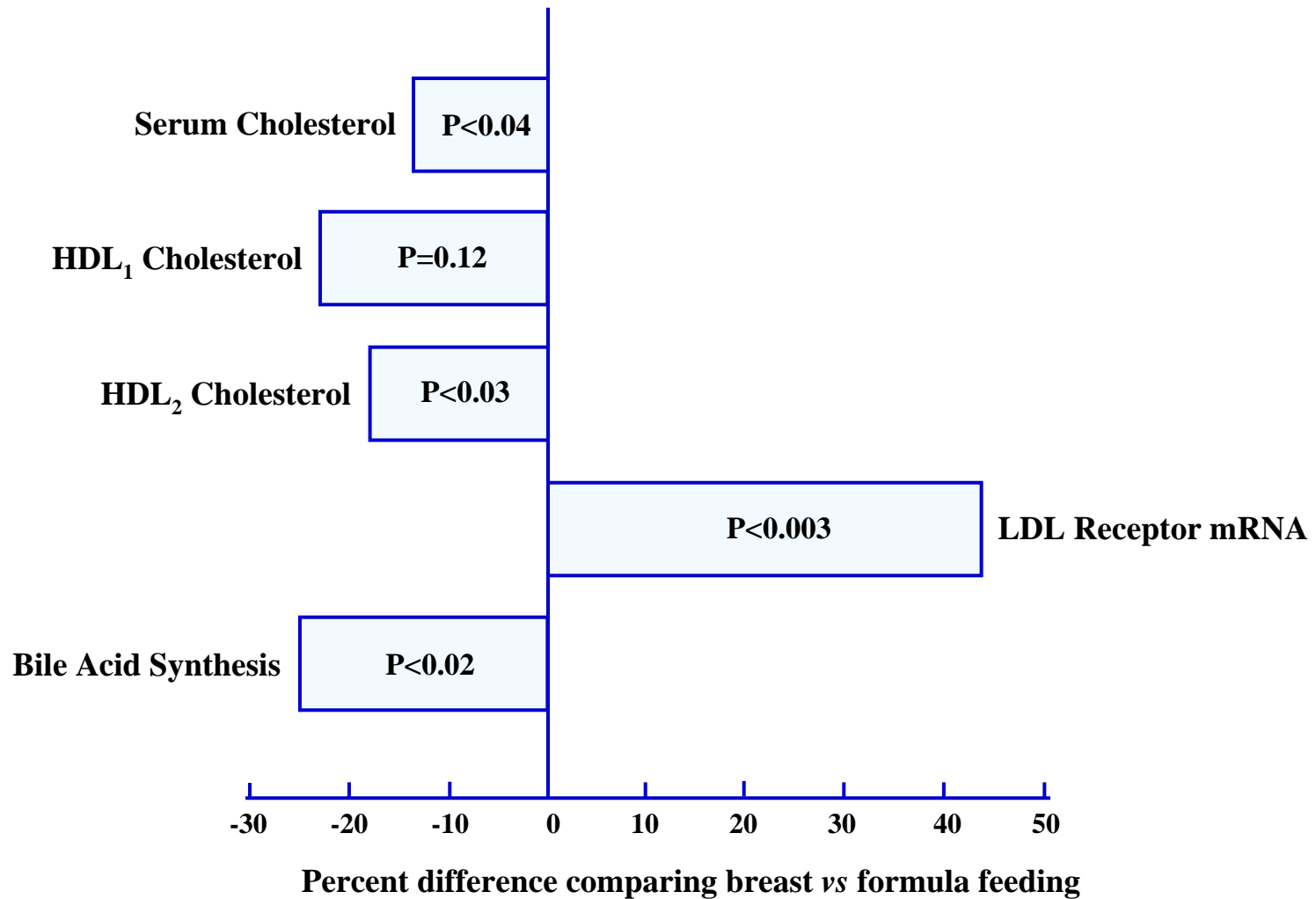
Plaque

STAGES IN DEVELOPMENT OF CORONARY
DISEASE OBSERVED FROM 1,500
YOUNG SUBJECTS.

RELATIONSHIP OF HYPOTENSION
AND INFANT FEEDING TO AETIOLOGY

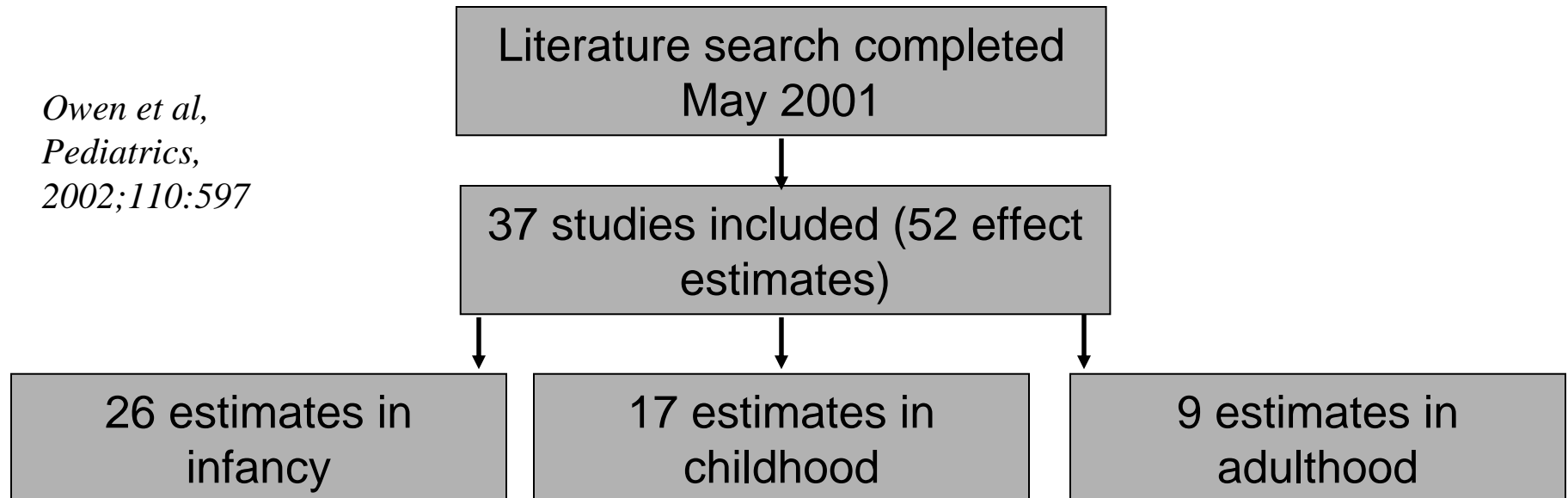
G. R. OSBORN

Cholesterol metabolism in juvenile baboons

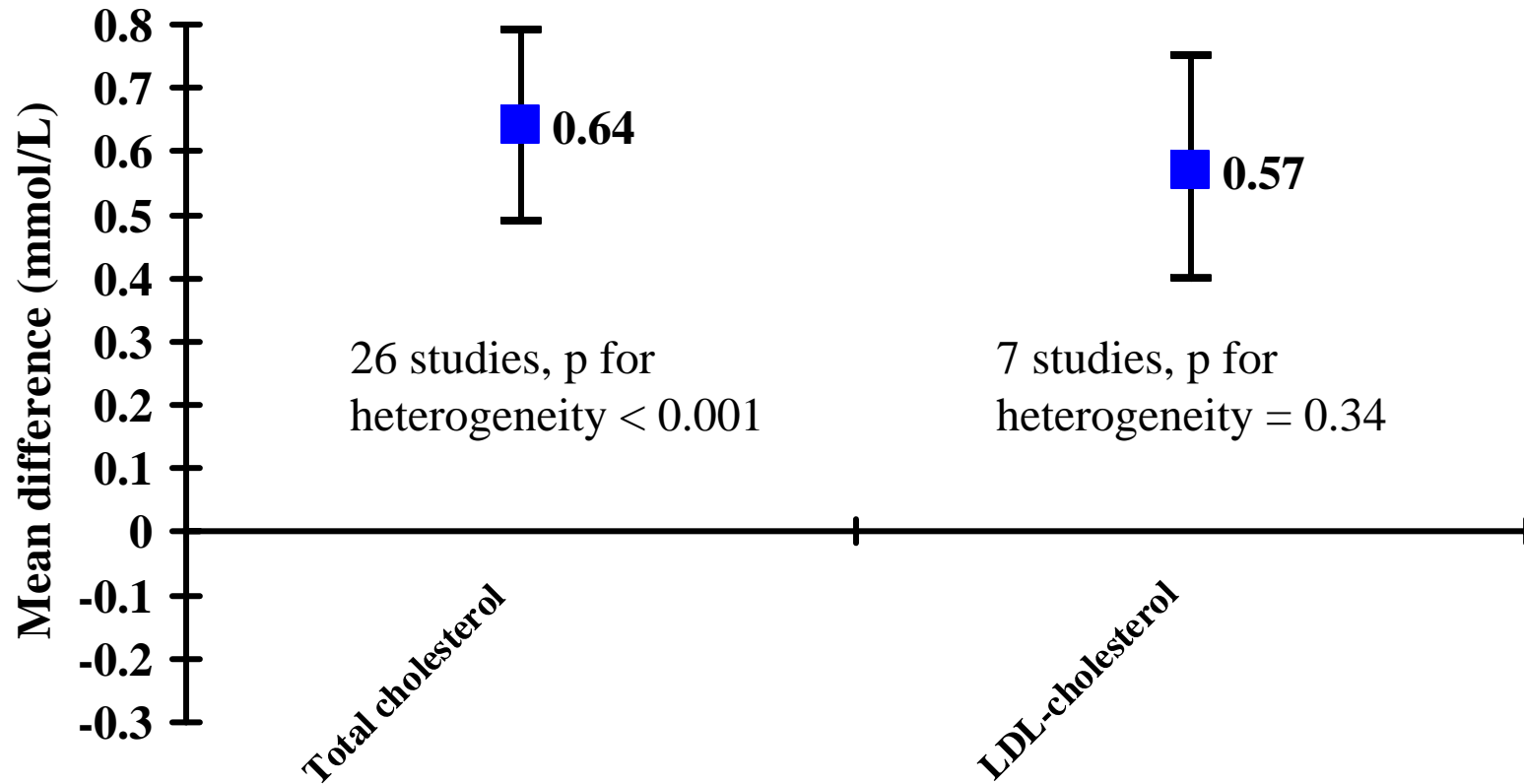


Systematic review of infant feeding and lipid profile

*Owen et al,
Pediatrics,
2002;110:597*

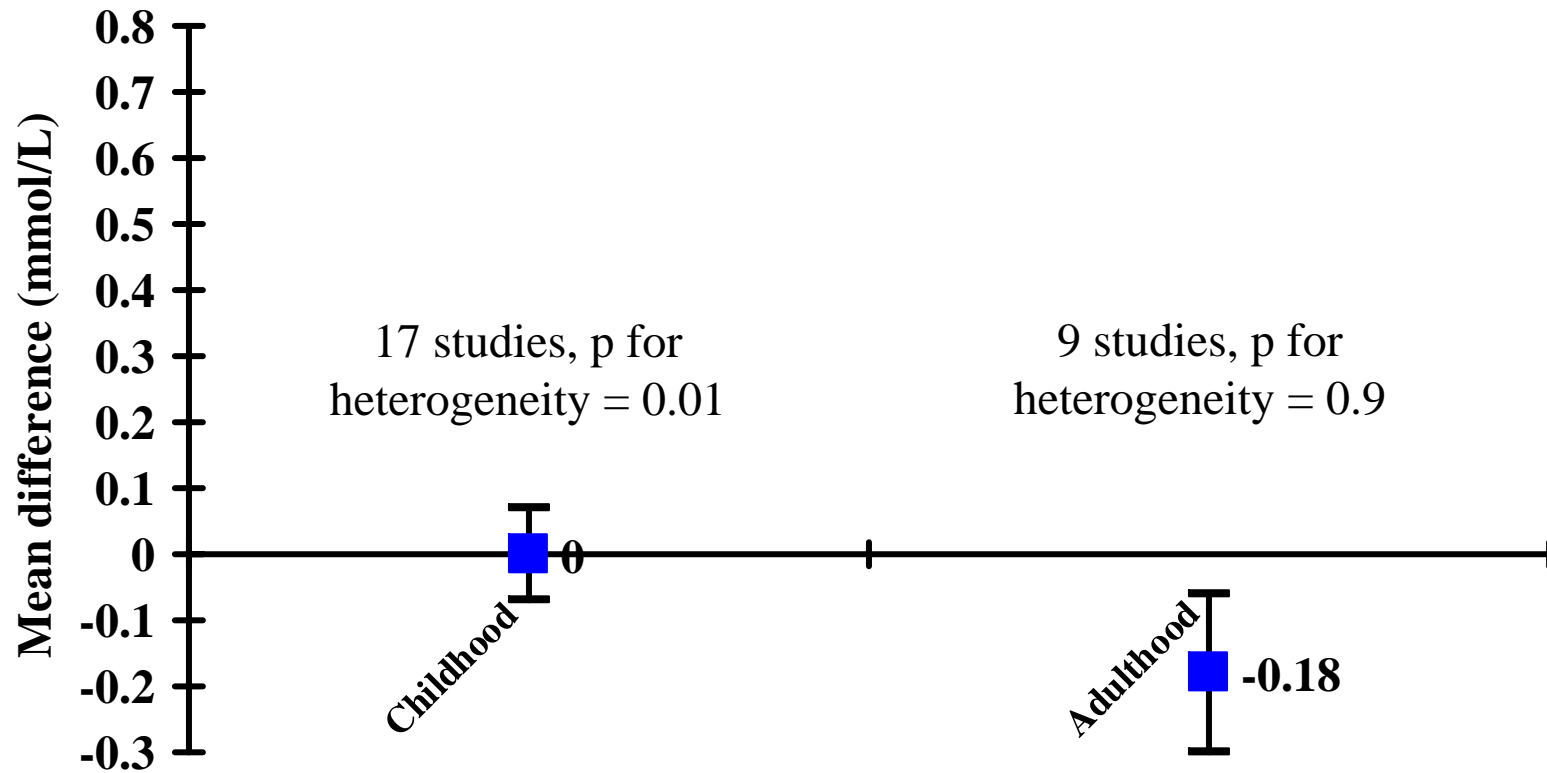


Difference in mean total and LDL cholesterol levels in infants (< 1 yr) breastfed vs formula fed



Owen et al, Pediatrics, 2002;110:597

Difference in mean total cholesterol levels in children (1-16 yrs) & adults (≥ 17 yrs), breastfed vs formula fed

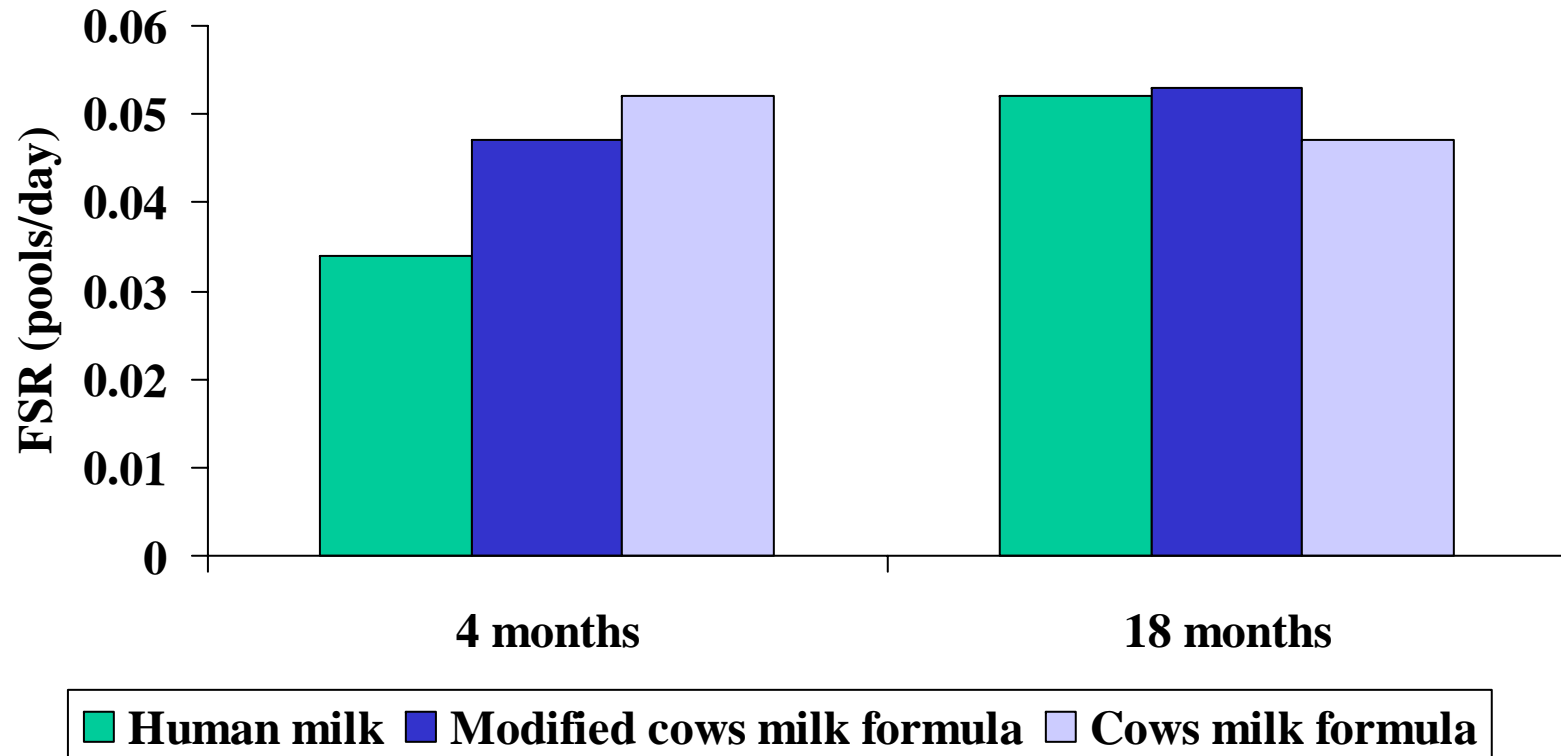


Studies in adults published since the Owen et al review

Author	N	Age	Mean difference in total cholesterol, breast minus formula
Victoria <i>JECH</i> 2006;60:621	822	18	Men = - 0.07 mmol/l, p = 0.2
Williams <i>JECH</i> 2006;60:146	2250	26	Men = -0.11 mmol/l, p = 0.8 Women = -0.42, p = 0.01
Martin. <i>JECH</i> 2005;59:121	1538	45-59	Men = + 0.04, p = 0.6

Victoria and Martin compare ever vs never breastfed; Williams compares breastfed ≥ 6 months vs never breastfed

Effect of infant diet on fractional synthesis rate of endogenous cholesterol at 4 & 18 months (n=47)



Cholesterol contents of HM, MCF, and CF were 120, 80, and 40 mg/L, respectively

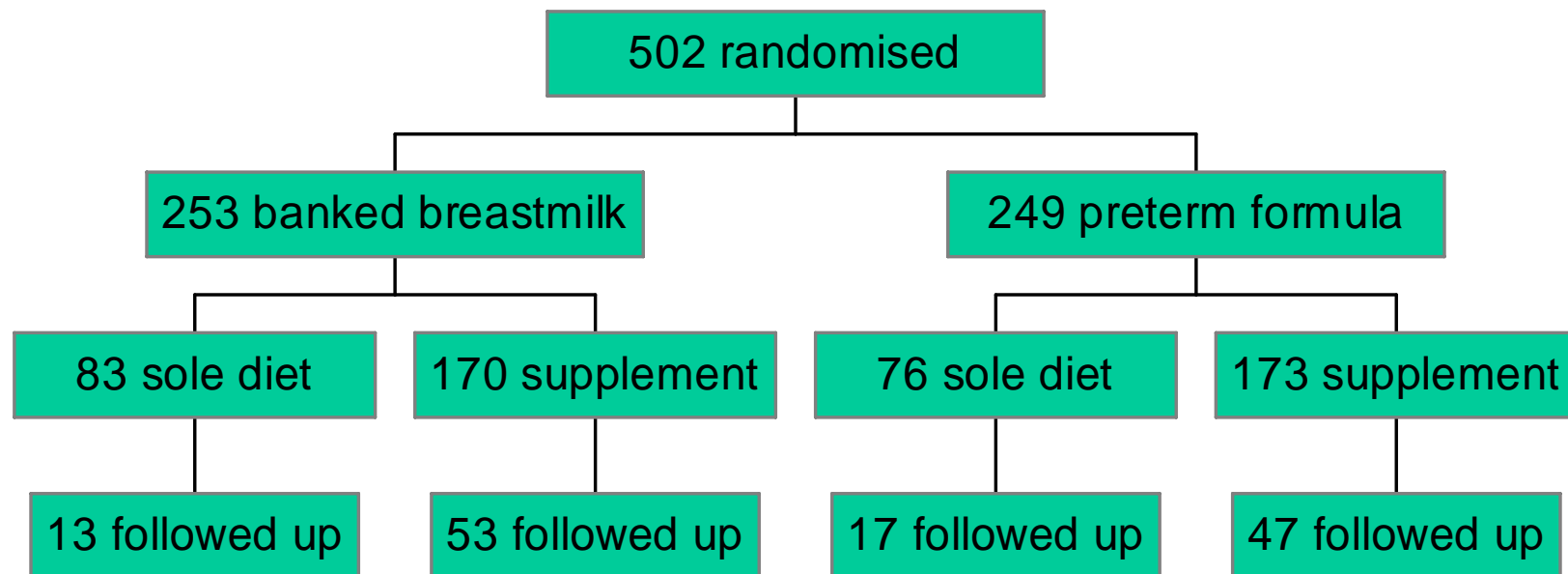
Problems with the evidence base

- Evidence is based on observational studies
- Residual confounding?
 - Difficult/impossible to measure and control for
- Selection bias (breast milk output sufficient for slower-growing infants)?
- Publication bias may have affected evidence base
- Biological effect of breast milk or of the alternatives to breastfeeding?

Solution: RCT

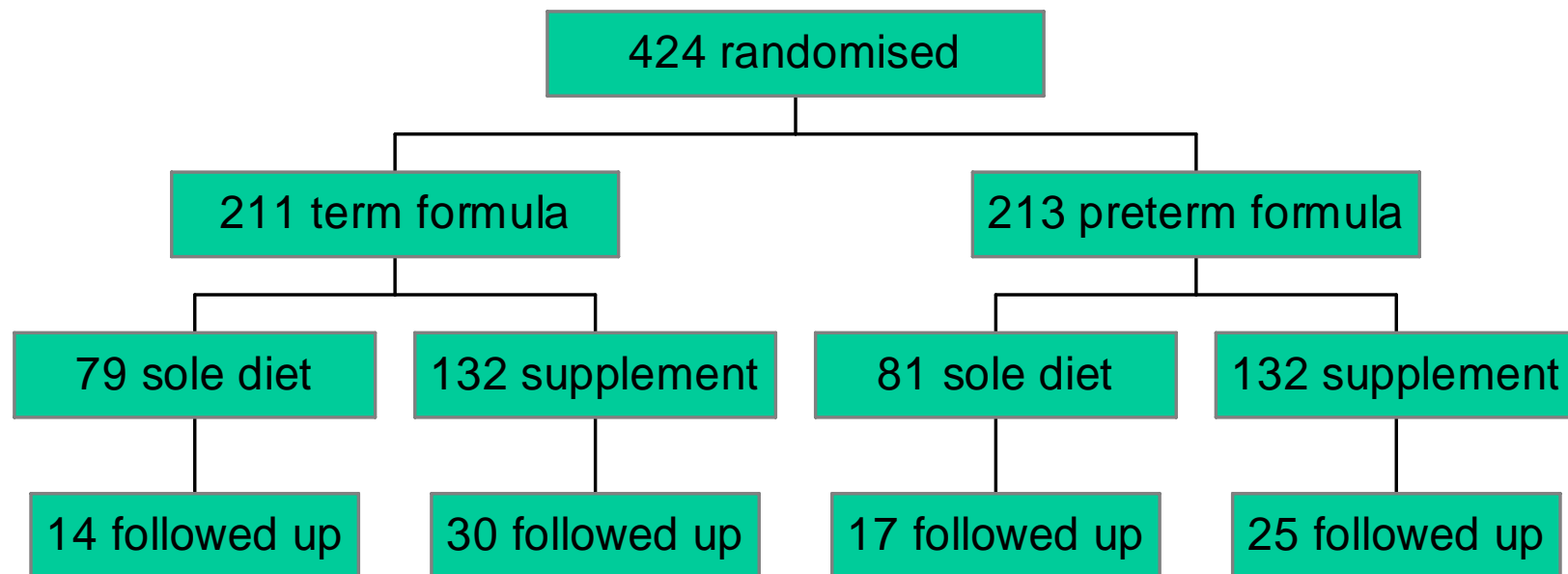
- But randomization to breast- vs formula feeding is not feasible and may be unethical
- Randomisation has been feasible in special situations
 - Randomised trial of different diets at birth in preterm infants < 1850g, initiated by Lucas in 1982
 - RCT of an intervention to promote breastfeeding exclusivity and duration (PROBIT)
- These trials resulted in cohorts created by *randomization*, not the choice of the mother
 - Analysis by “intention to treat” enables *strong causal inferences* with respect to breastfeeding effects on long-term outcomes

Lucas trial with prospective follow-up at 13-16 years: Trial 1



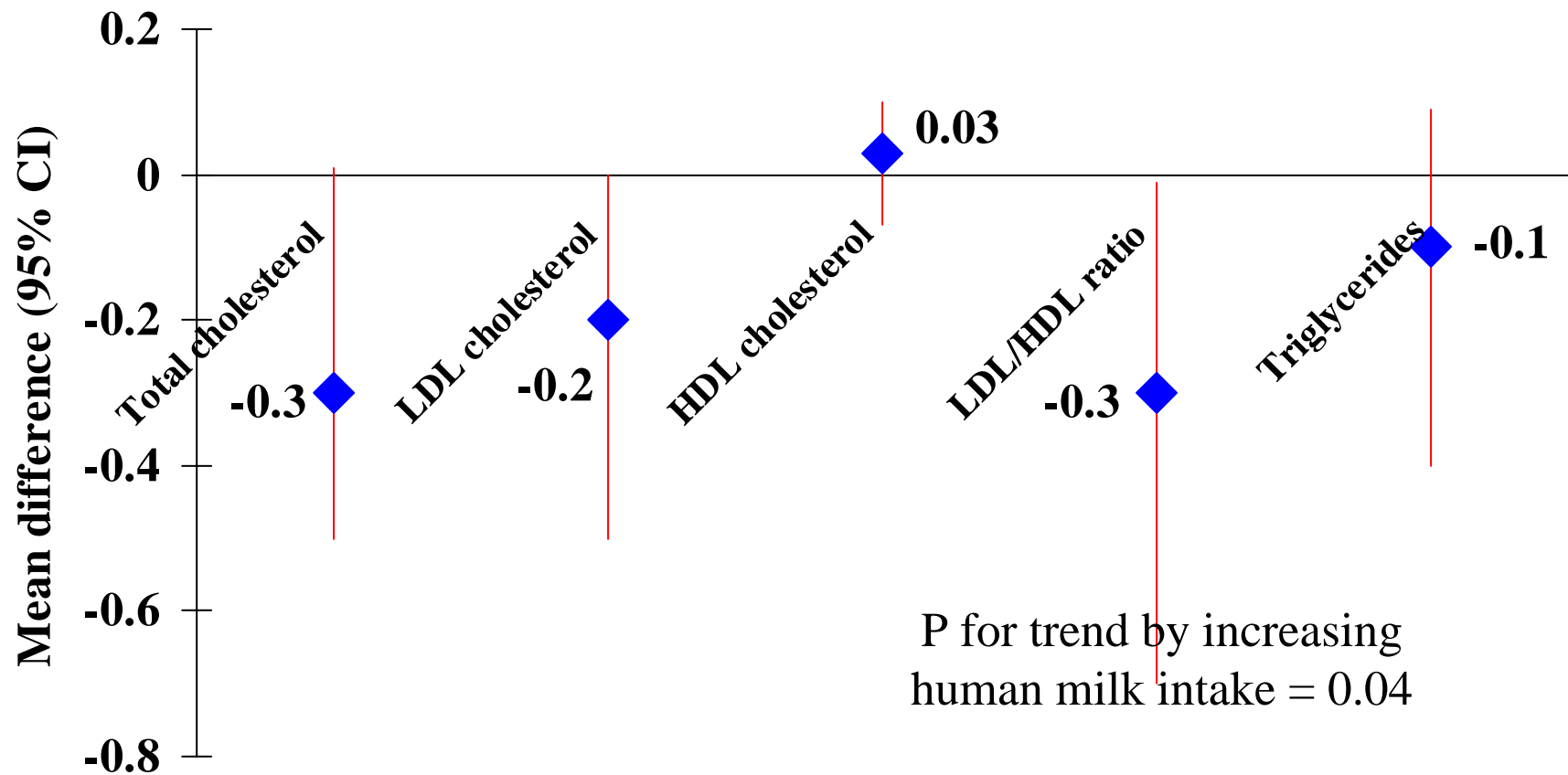
Mean gestation = 31 weeks; mean birthweight = 1.4 kg

Lucas trial with prospective follow-up at 13-16 years: Trial 2



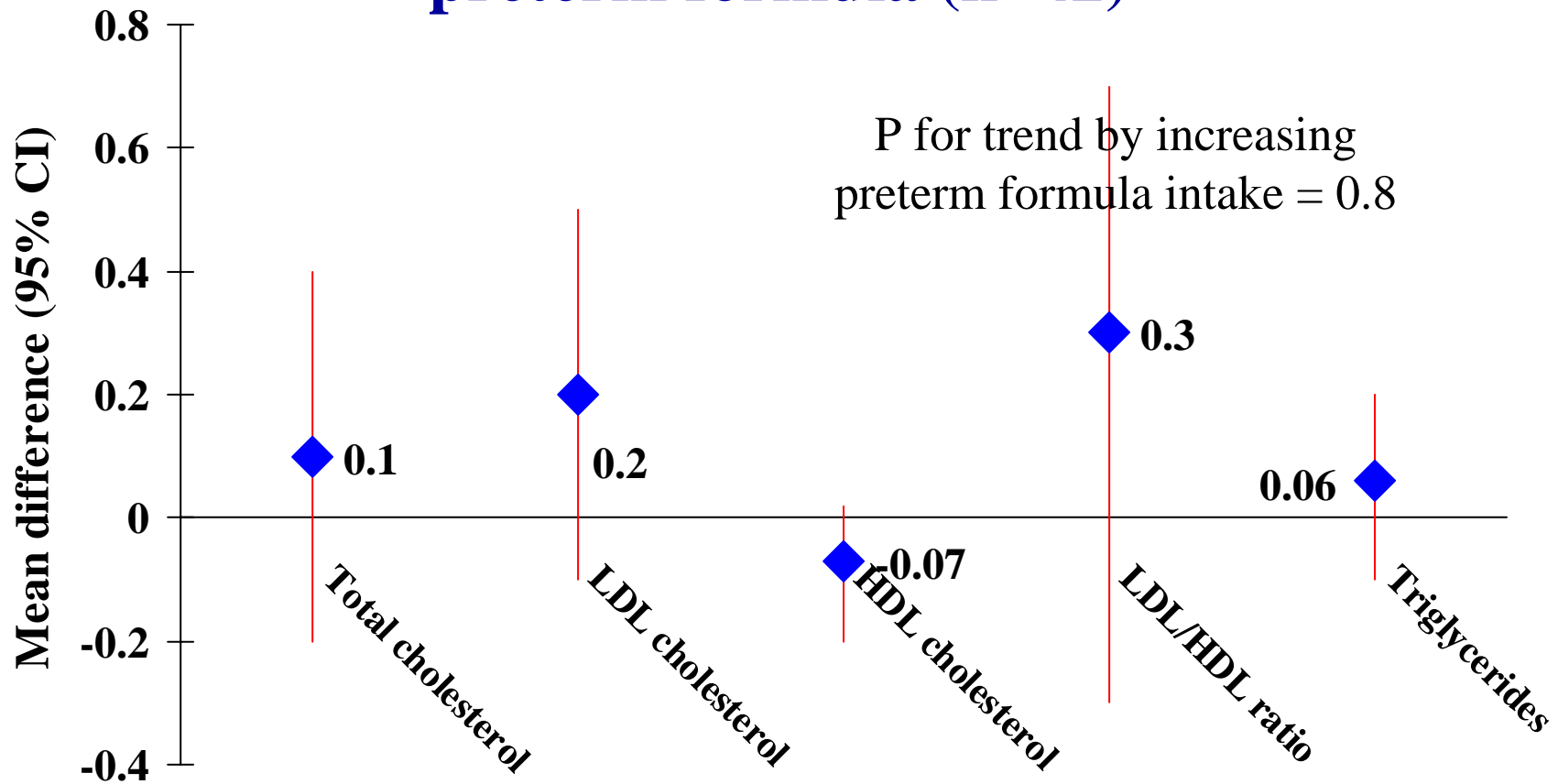
Mean gestation = 31 weeks; mean birthweight = 1.4 kg

Breast milk feeding and lipoprotein profile in adolescents born preterm: banked breast milk (n=66) vs preterm formula (n=64)



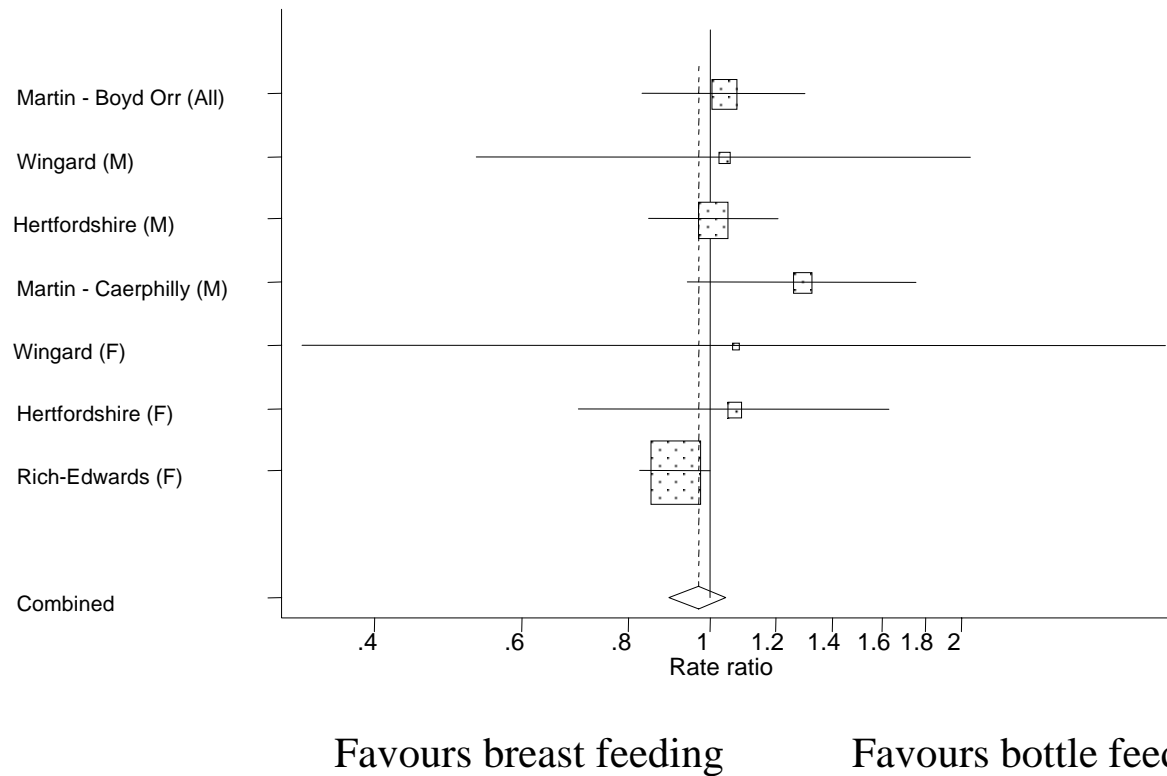
Source: Singhal et al. *Lancet*, 2004;363:1571

Formula feeding and lipoprotein profile in adolescents born preterm: term formula (n=44) vs preterm formula (n=42)



Source: Singhal et al. Lancet, 2004;363:1571

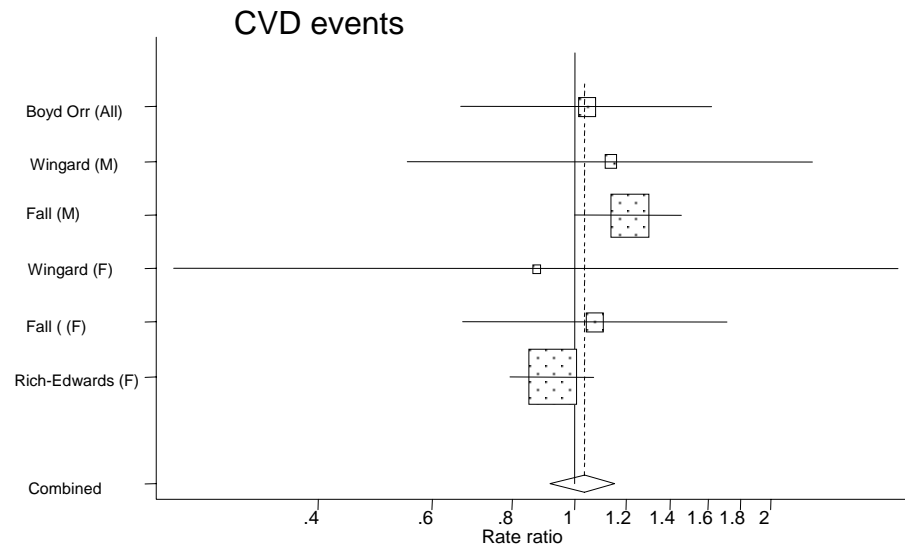
Pooled rate ratio (95% CI) for CVD comparing breastfeeding vs bottle-feeding



Pooled rate ratio: 0.97 (95% CI: 0.90-1.05), $I^2 = 0\%$

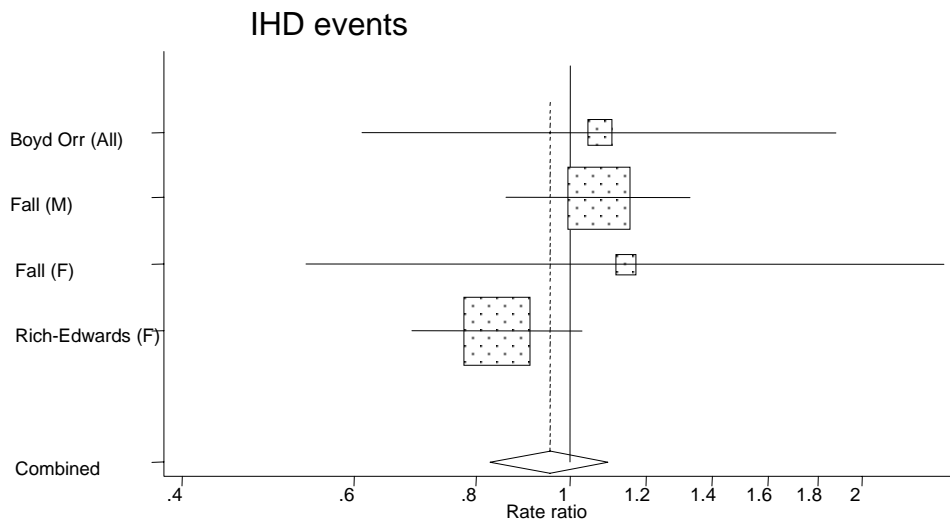
Source: Martin RM et al. Eur Heart Journal, 2004;25:778-786 (meta-analysis updated 2005)

Influence of prolonged breastfeeding (> 9-12 mo)



Pooled rate ratio: 1.03 (0.92-1.15)

I²: 4%



Pooled rate ratio: 0.95 (0.83-1.10)

I²: 0%

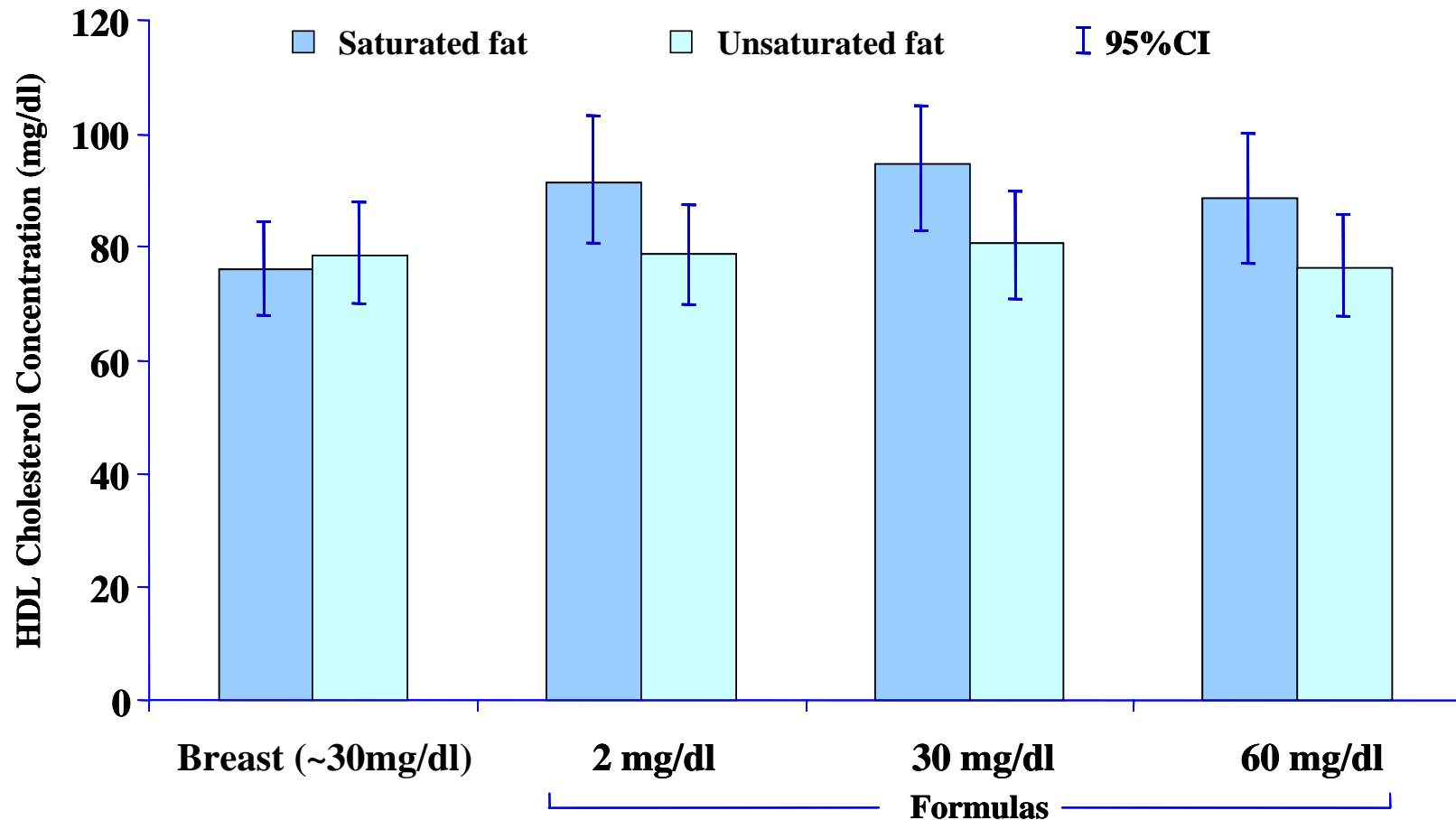
Conclusions

- In observational studies, breastfeeding was associated with a small reduction in total and LDL cholesterol in adulthood
- A trial of preterm infants provides experimental support for the hypothesis
- However, there is little consistent evidence that any effect of breastfeeding on lipid profile translates into a reduced risk of CVD in later life
- The mechanistic basis for a programming effect of breastfeeding on adult lipid profile remains to be established in humans

Acknowledgements

- 6th Framework Programme (EARNEST) & CIHR
- George Davey Smith, David Gunnell, Stephen Frankel, Jeff Holly, Andy Ness (Bristol)
- Chris Owen, Peter Whincup, Derek Cook (St George's)
- Mike Kramer, Matt Gillman (PROBIT PIs)
- Irina Vanilivich, Konstantin Vilchuck, Rita Patel, Irina Mitroshenka, Irina Mezen, Nina Gusina, Ying Foo and the PROBIT team

Interaction of infant and adult diet in juvenile baboons



P for interaction of infant feeding mode with type of adult dietary fat < 0.04

Growth acceleration hypothesis

- There was a 0.2 unit (0.03 to 0.4) increase in LDL:HDL ratio per 100g weight change in the first 2 weeks of life
- Faster early postnatal weight gain explained the association of breast milk feeding on later lipid profile
- Similar findings for insulin resistance & blood pressure led to the growth acceleration hypothesis proposed by Singhal and Lucas:
 - the possibility that faster growth as a result of a nutrient enriched diet adversely programmes the principal components of the metabolic syndrome (vice versa for breastfeeding)