

Type 1 Diabetes and the Environment: a Focus on Dietary Factors

CHE Partnership Call
November 12, 2014

Jill M. Norris, MPH, PhD
Professor and Chair
Department of Epidemiology
Colorado School of Public Health

Epidemiology of Type 1 Diabetes (T1D)

- Peak incidence at 10-12 years of age
- US Incidence: approx. 16 per 100,000/yr
- 1 in 300 children will develop T1D before age 20 yrs
- No major gender difference in risk
- Northern Europeans have highest risk

Candidate Environmental Factors

- Viruses
 - Enteroviruses
- Hygiene
 - Day care/social crowding
 - Gut microbiota
- Psychosocial Stress
- Growth and Dietary factors

Candidate Dietary Risk Factors in T1D

- Nitrates, nitrites, nitrosamines ↑
- Cod liver oil ↓
- Vitamin D ↓
- Potatoes/vegetables ↓

- Breast-feeding (BF) ↓
- BF when introducing solids ↓
- Early/late exposure to:
 - cow's milk ↑
 - cereals/gluten ↑
 - solid foods ↑
 - root vegetables ↑
 - berries ↑
- Vitamin D ↓
- Cod liver oil ↓

- Cow's milk ↑
- Nitrates, nitrites, nitrosamines ↑
- Vitamin D ↓
- Omega-3 fatty acids ↓



In Utero



Infancy



Childhood





Based on existing evidence regarding dietary factors in type 1 diabetes, we are confident of the following....

- (no dietary factor)

We believe the following specific questions should be pursued in future investigations based on strength of the current data...

- The timing of introduction of specific complex foods
- Omega-3 fatty acids

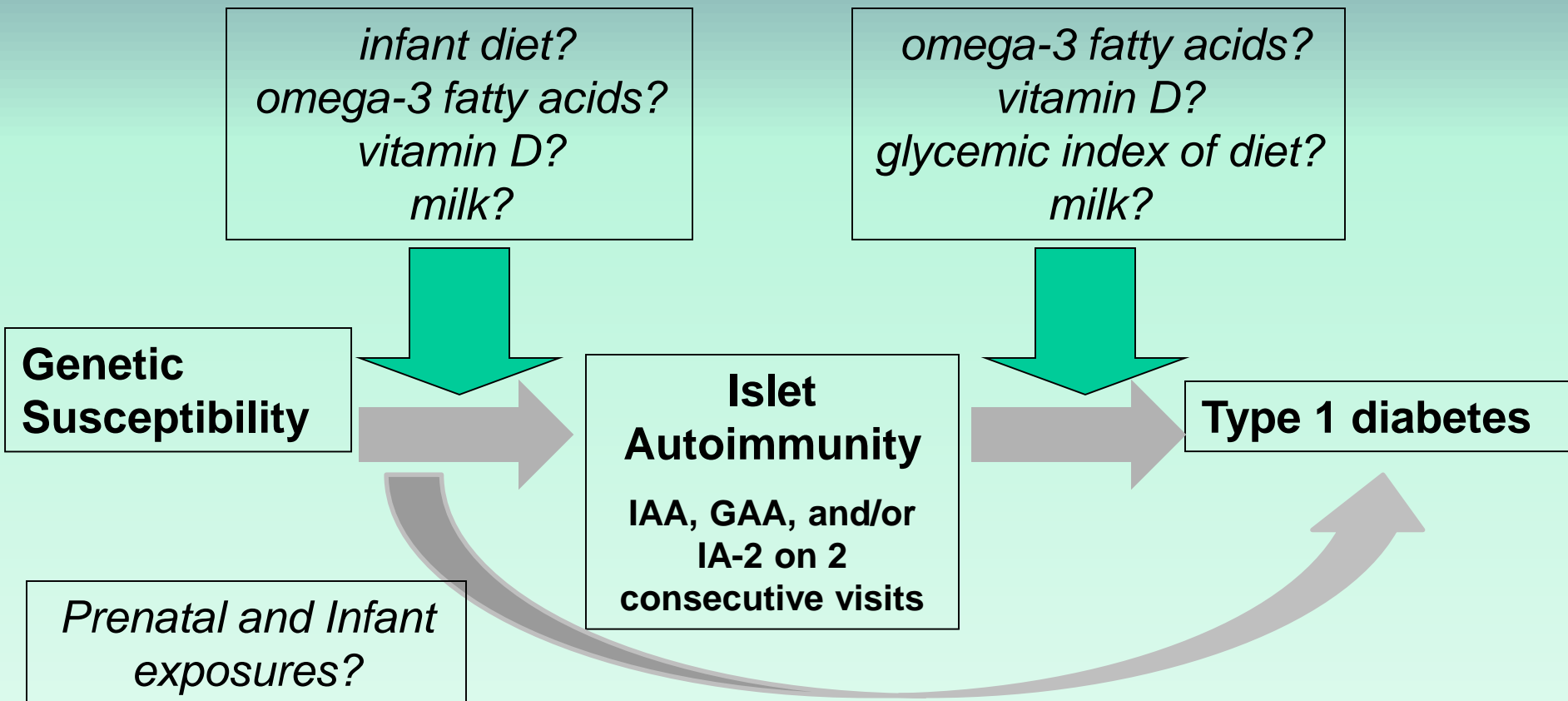


Panel Conclusions

- More research into phenotypes, genotypes (gene-environment interaction), multiple exposures and mechanisms are needed
- Understanding the effects of the timing of exposures (life-course, latencies) and dose-response effects are critical

Investigating Dietary Factors in Type 1 Diabetes Prospectively

DAISY/DIPP/BabyDiab/TEDDY



Early and Late First Solid Food Exposure Increases Risk of T1D

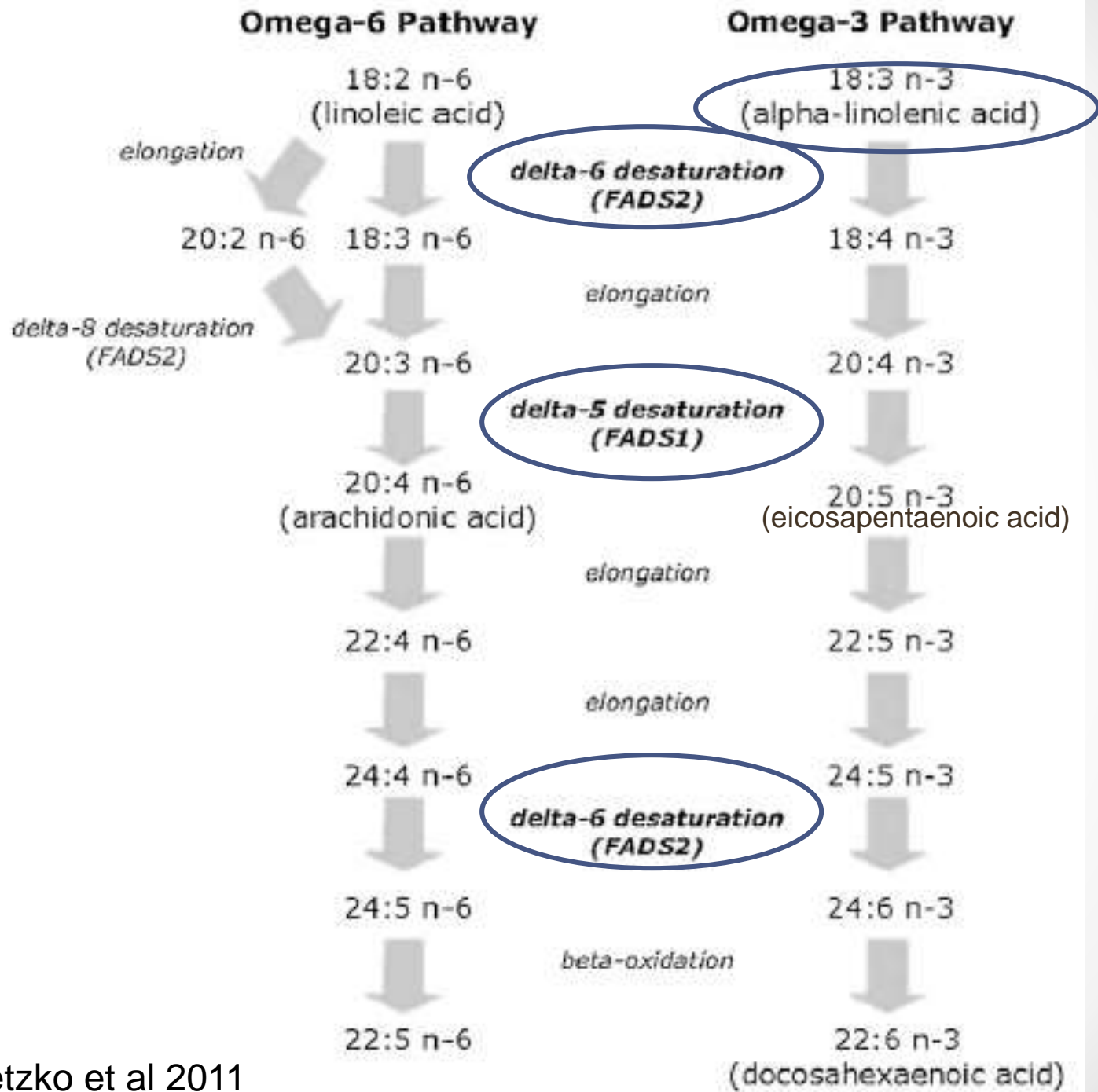
DAISY Birth Cohort

	HR (95% CI)
Age first exposed to solid foods	
< 4 months	1.9 (1.04-3.51)
4-5 months	Referent
≥ 6 months	3.0 (1.26-7.24)
Breast-fed when first exposed to gluten	0.5 (0.26-0.86)

Survival analyses were adjusted for HLA, family history of T1D, maternal education and birth delivery type.

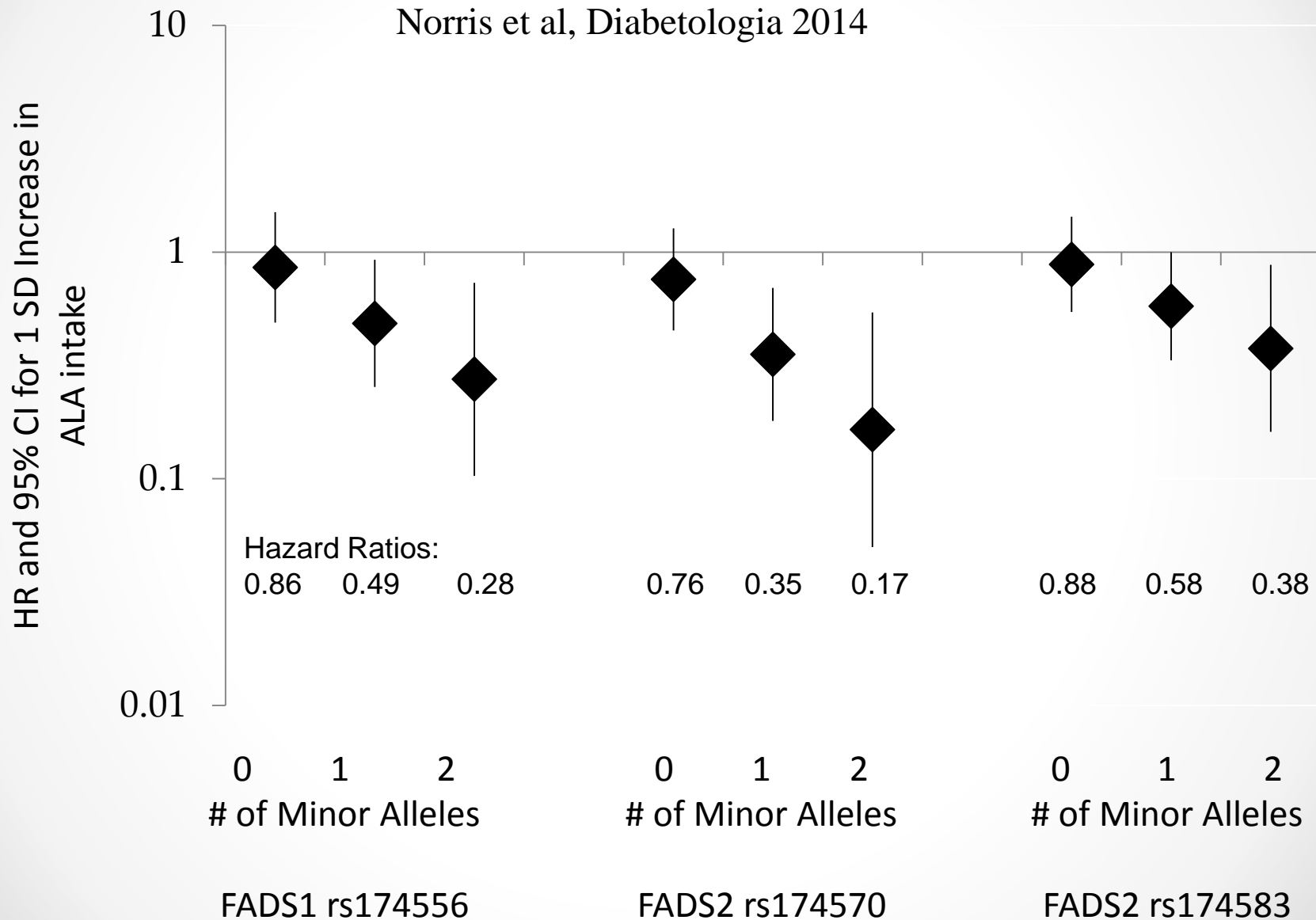
Omega-3 Fatty Acids and T1D and IA

- A study in Norway showed that children with T1D were less likely to have gotten cod liver oil during infancy than children without T1D (Stene et al 2001).
- Cod liver oil is an excellent source of the 'fish oil' omega-3 fatty acids, docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).
- In DAISY, intake of alpha-linolenic acid (ALA) was associated with lower risk of islet autoimmunity (IA) (Hazard Ratio (HR): 0.72, 95% Confidence Interval (CI): 0.55-0.98). DHA and EPA intake were not associated. (Norris et al, 2014)



The Decreased Risk of IA with Increased ALA Intake Differs by Number of *FADS1* and *FADS2* Minor Alleles

Norris et al, Diabetologia 2014



Adjusted for HLA, family history of T1D, ethnicity, total energy intake and FFQ type.

Vitamin D



- Vitamin D supplementation at age 1 year associated with decreased T1D risk in Finnish birth-cohort study (Hypponen *et al.*, 2001)
- A case-control study across 7 European countries found vitamin D supplementation in infancy associated with decreased T1D risk (The EURODIAB Substudy 2 Study Group, 1999)
- A meta-analysis of 5 retrospective studies showed that vitamin D supplementation in infancy was associated with a reduced risk of T1D (Zipitis and Akoberg, 2008)

DAISY Results Re: Vitamin D



- Dietary vitamin D intake was not associated with risk of IA nor T1D.
 - Kids who developed autoimmunity were eating just as much vitamin D as those who didn't develop autoimmunity
 - Same for progression to diabetes
- Vitamin D levels were not associated with risk of IA nor T1D.
 - Kids who developed autoimmunity had the same levels of 25[OH]D in their blood than those who didn't develop autoimmunity
 - Same for progression to diabetes

Vitamin D Metabolism Genes

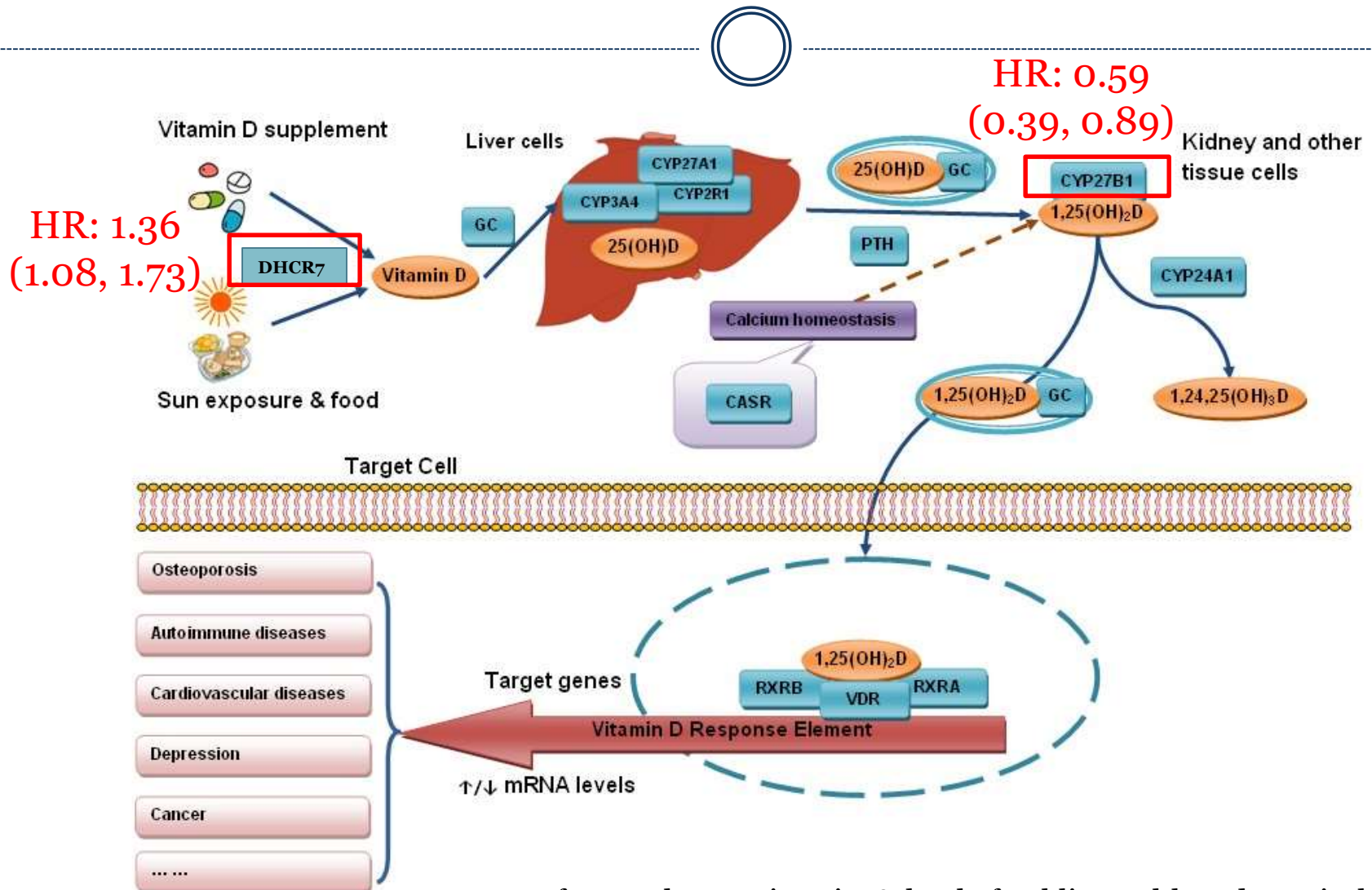
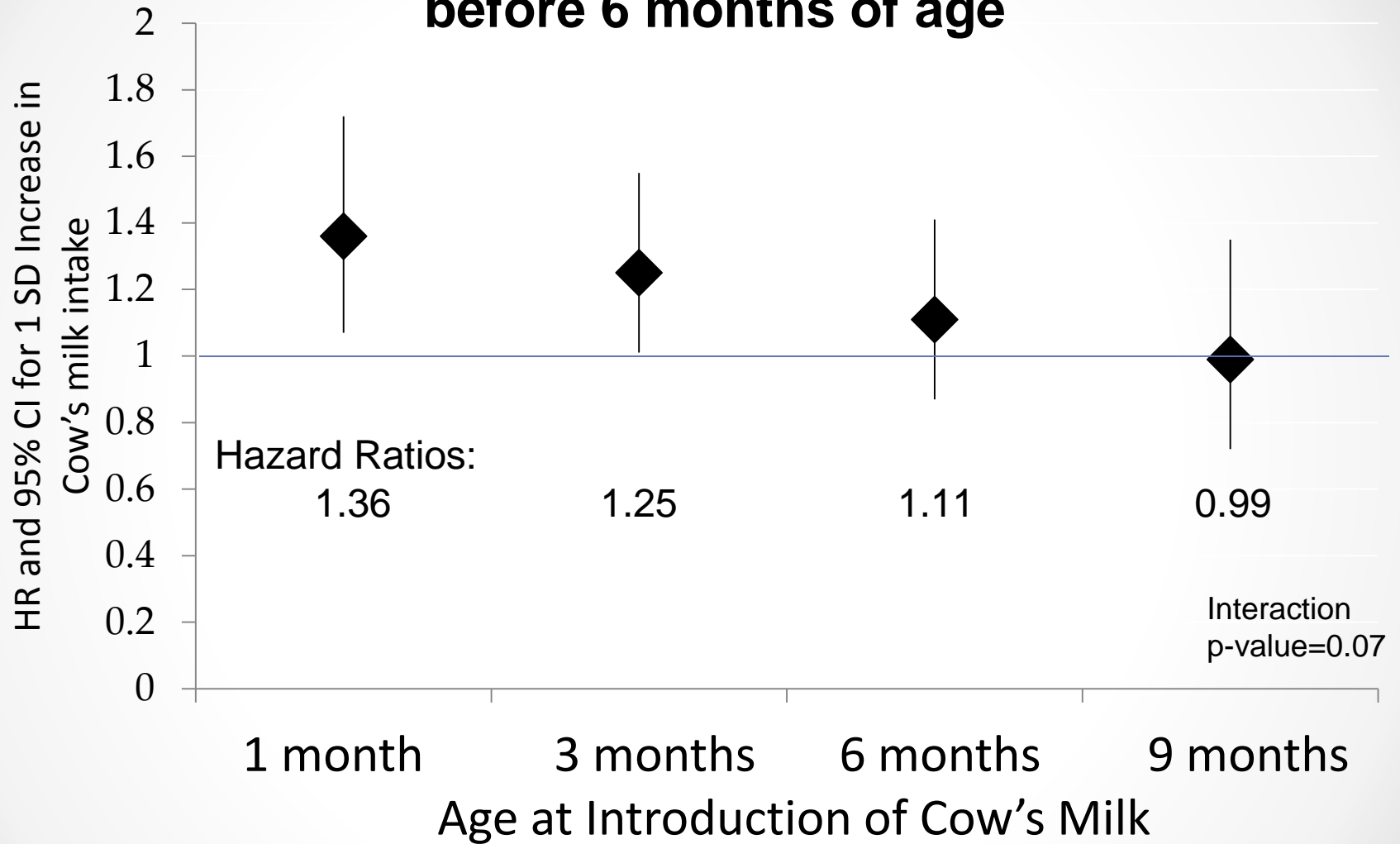


Image from Tulane University School of Public Health and Tropical Medicine

The increased risk for IA with increased cow's milk consumption is only seen in children introduced to milk before 6 months of age



Lamb et al, 2014

Adjusted for HLA, family history of T1D, ethnicity, total energy intake and FFQ type.

Thank-you.