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Milk powder in relation to gluten intake and the risk of celiac disease during early childhood: a Swedish case-control study

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Study Objectives

To evaluate the association of milk powder in relation to gluten intake with the risk of celiac disease in Swedish genetically susceptible children.

Background

- Swedish genetically susceptible children are at a 2-fold risk of developing celiac disease before 3 years of age compared with at genetic risk children from the US (1).
- Milk powder and gluten are common components in the Swedish infant diet; almost 70% consumes milk cereal drink (2) and nearly 90% commercial porridge (3).
- High gluten intake during early childhood has been associated with increased risk of celiac disease in Swedish children (4), but not in other countries (5).

Methods

- The Environmental Determinants of Type 1 Diabetes in The Young (TEDDY) study screens children carrying HLA-risk genotypes for celiac disease.
- Tissue transglutaminase autoantibodies (tTGA) were measured annually from 2 years of age using radioligand binding assays. tTGA positive children were re-tested after 3-6 months and referred to a pediatrician for evaluation of celiac disease if being persistently positive. Previous serum samples were retrospectively analyzed to set the time-point of seroconversion.
- A 1-to-3 nested case-control study comprised of 207 Swedish children with celiac disease and 621 controls who were matched for sex, birth year, and HLA genotype.
- A 3-day food record collected at 6, 9, 12, 18 and 24 months of age, respectively, was used to estimate the mean intake of milk powder and gluten (g/day and g/kg body weight/day).

Statistical Analysis

- Conditional logistic regression calculated odds ratios (OR) at last intake, sum of all intakes and for each time-point prior to seroconversion of tTGA positivity.
- Data were adjusted for having a first-degree relative with celiac disease (FDR-CD) and milk powder intake adjusted for gluten intake.

References:

- Liu E et al NEJM (2014)
- Wibberger M et al SJPB (2014)
- Almquist-Tangen G et al Acta Paediatr (2013)
- Aronsson CA et al CGH (2016)
- Crespo-Escobar P et al AJCL (2017)

Conclusion

- Intake of milk powder during the first 2 years of life did not affect the risk of celiac disease in genetically susceptible children.
- Large intake of gluten increased the risk of celiac disease in early childhood.

Results

- Intake of milk powder did not affect the risk of celiac disease at last intake prior to seroconversion of tTGA positivity (OR=1.00; 95% CI=0.99-1.01; p=0.937) or at any given time (Table 1, Figure 1).
- Gluten intake increased the risk of celiac disease when estimated in grams/day (OR=1.09; 95% CI=1.03-1.16; p=0.004, Table 2, Figure 2) and grams/kg body weight/day (OR=2.78; 95% CI=1.38-5.62; p=0.004) prior to seroconversion of tTGA positivity.
- The highest risk of celiac disease was observed at 18 months of age for gluten intake in grams/day (OR=1.12; 95% CI=1.04-1.21; p=0.004, Table 2, Figure 2) and grams/kg body weight/day (OR=3.95; 95% CI=1.59-9.82; p=0.003).

Table 1. Mean daily intake of milk powder (g/day) and risk of celiac disease after adjusting for having a FDR-CD and gluten intake.

Food Data	Cases		Controls		OR (CI 95%)	p-value
	N	Mean g/day (SD)	N	Mean g/day (SD)		
Last intake ⁱ	207	17.5 (14.6)	621	17.4 (14.1)	1.0 (0.99-1.01)	0.937
Sum all intakes ⁱⁱ	207	93.3 (52.8)	621	88.6 (53.5)	1.0 (0.998-1.004)	0.662
Intake at:						
3 months	207	6.0 (9.6)	618	7.1 (10.5)	0.99 (0.97-1.01)	0.159
6 months	202	15.9 (12.9)	598	15.3 (12.7)	1.0 (0.99-1.02)	0.643
9 months	198	28.1 (17.1)	589	25.4 (16.6)	1.01 (1.0-1.02)	0.069
12 months	192	27.2 (15.1)	554	25.4 (14.8)	1.01 (1.0-1.02)	0.181
18 months	146	18.7 (13.2)	433	18.1 (13.1)	1.0 (0.98-1.02)	0.983
24 months	103	13.3 (13.9)	315	14.7 (12.6)	0.99 (0.97-1.01)	0.202

ⁱ Milk powder intake reported at the last visit prior to seroconversion of tTGA
ⁱⁱ Total intake prior of milk powder to seroconversion of tTGA

Table 2. Mean daily intake of gluten (g/day) and risk of celiac disease after adjusting for having a FDR-CD.

Food Data	Cases		Controls		OR (CI 95%)	p-value
	N	Mean g/day (SD)	N	Mean g/day (SD)		
Last intake ⁱ	207	5.5 (2.7)	621	4.9 (2.6)	1.09 (1.03-1.16)	0.004
Sum all intakes ⁱⁱ	207	14.1 (7.2)	207	13.0 (7.0)	1.03 (1.01-1.06)	0.021
Intake at:						
3 months	207	0.0 (0.1)	618	0.0 (0.0)	2.94 (0.17-51.4)	0.461
6 months	202	0.6 (0.9)	598	0.6 (1.0)	1.03 (0.86-1.22)	0.779
9 months	198	2.6 (1.5)	589	2.5 (1.7)	1.02 (0.93-1.13)	0.642
12 months	192	4.2 (2.0)	554	4.1 (2.1)	1.02 (0.94-1.11)	0.592
18 months	146	5.8 (2.7)	433	5.0 (2.3)	1.12 (1.04-1.21)	0.004
24 months	103	6.0 (2.7)	315	5.6 (2.5)	1.04 (0.96-1.14)	0.340

ⁱ Gluten intake reported at the last visit prior to seroconversion of tTGA
ⁱⁱ Total intake of gluten prior to seroconversion of tTGA

Figure 1. Milk powder intake and risk of celiac disease, adjusted for having a FDR-CD and gluten intake.

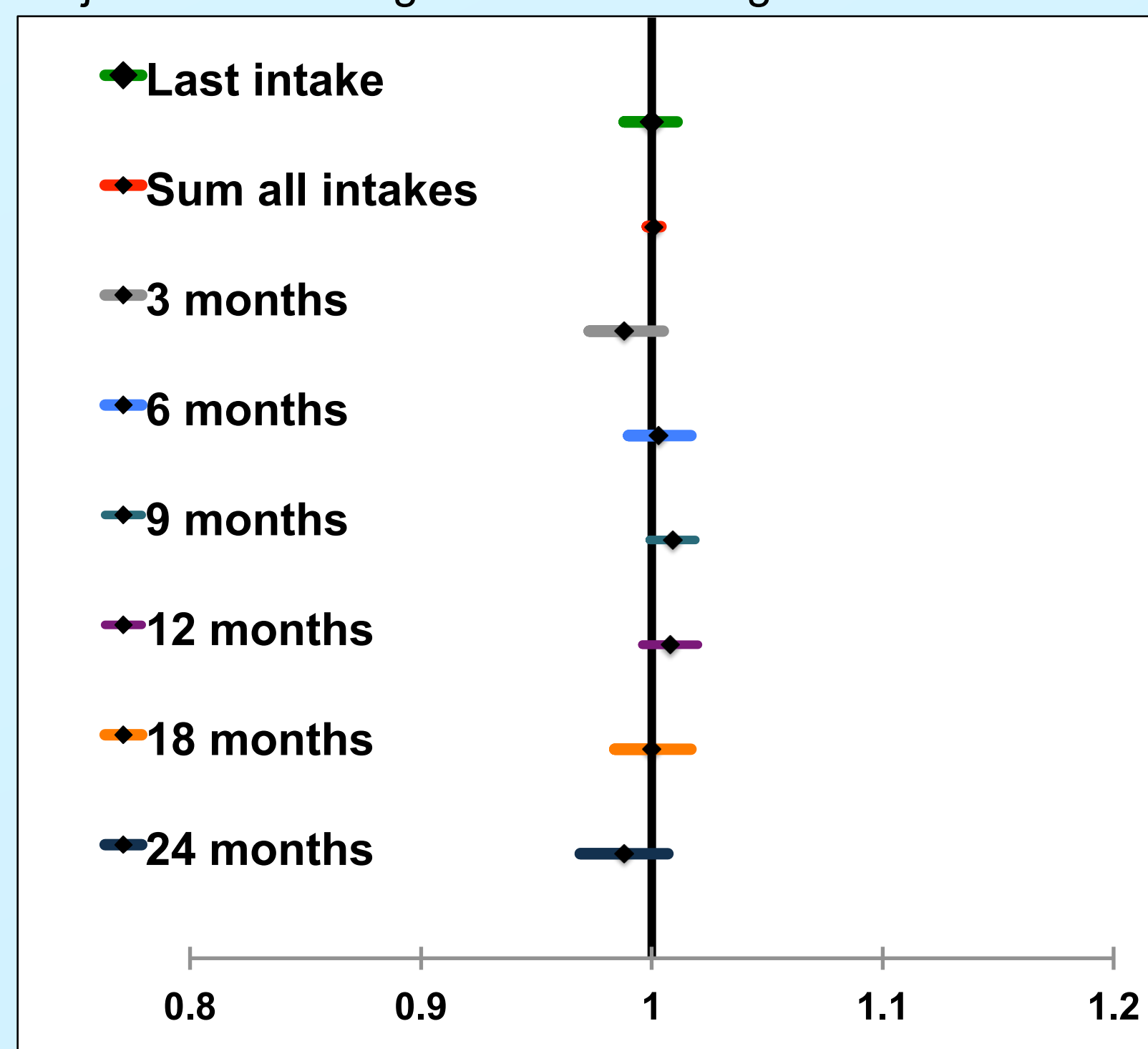
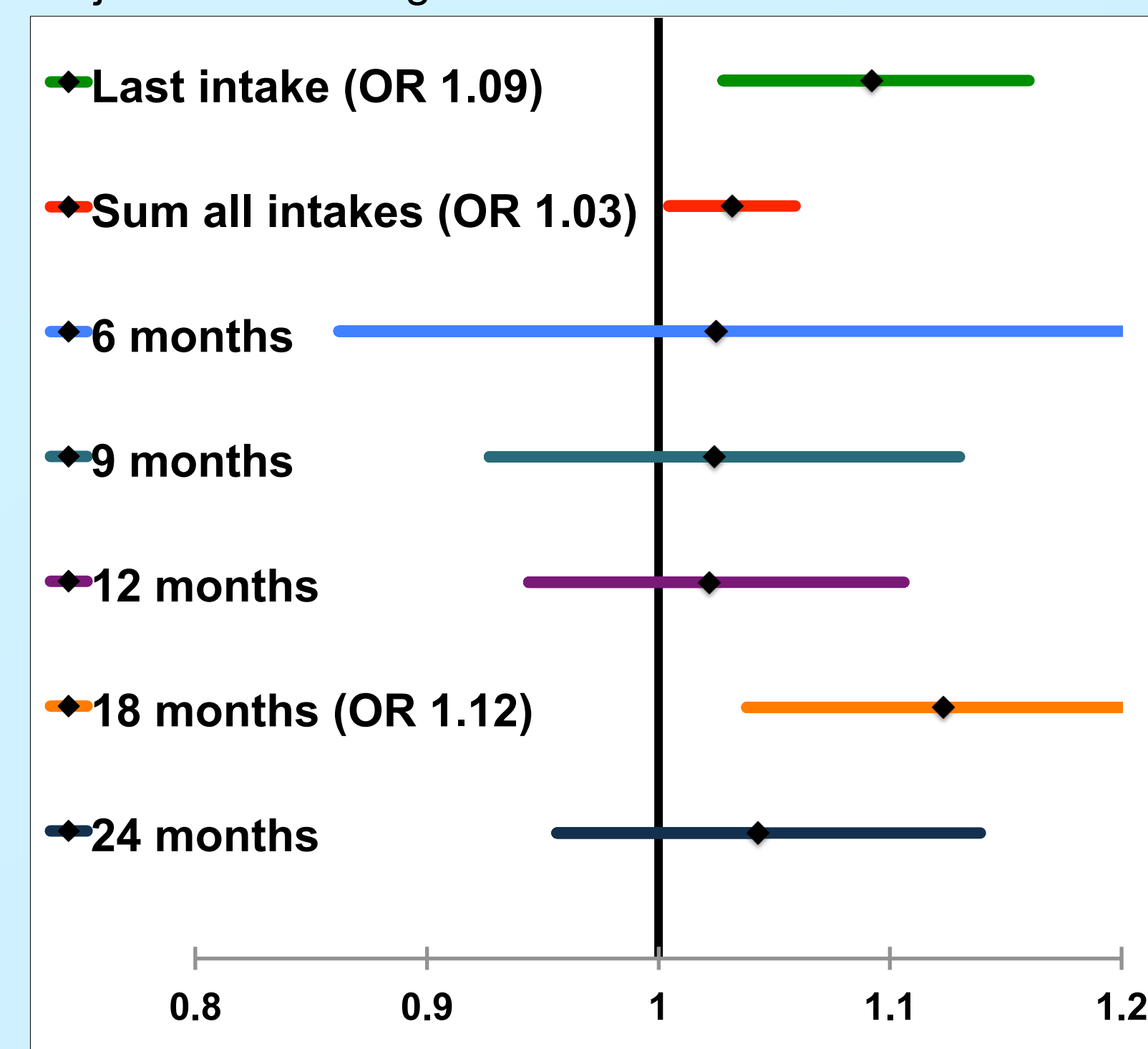


Figure 2. Gluten intake and risk of celiac disease, adjusted for having a FDR-CD.



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