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## Dietary patterns during early childhood confer different risk of celiac disease autoimmunity and celiac disease in children at genetic risk: TEDDY study

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# Dietary patterns in early childhood confer different risks of celiac disease autoimmunity and celiac disease in children at genetic risk: TEDDY study

Hård af Segerstad EM, Mramba L, Liu X, Uusitalo U, Yang J, Norris J, Virtanen SM, Liu E, Kurppa K, Koletzko S, Ziegler AG, Toppari J, Hagopian WA, Rewers M, McIndoe RA, Akolkar B, Krischer JP, Aronsson CA, Agardh D for the TEDDY study group

## 1. Study Objectives

To explore associations of early life dietary patterns with the risk of celiac disease autoimmunity and celiac disease in genetically at-risk children.

## 2. Background

- Differences between countries in incidence of celiac disease (CD), despite shared genetic background<sup>1</sup>, are not fully explained by variation in gluten intake<sup>2</sup>.
- Diet is a complex exposure incorporating a large number of active components. Examining dietary patterns closer resembles real life dietary exposures and behaviors.
- A “prudent” dietary pattern with high intake of vegetables, potatoes, pasta and rice, and low intake of refined cereals was associated with lower risk of celiac disease autoimmunity (CDA) in Dutch children<sup>3</sup>.

## 3. Methods and analysis

- 3-day food records were collected at age 9, 12, 18 and 24 months. Total food intake was aggregated into 27 food groups.
- Principal components analysis was used to construct simplified dietary patterns (including only food groups with factor loadings  $\geq 0.2$  and  $\leq -0.2$ )<sup>4</sup>.
- Annual screening for tissue transglutaminase autoantibodies (tTGA) started at age 2.
- Definition of study outcomes:  
CDA: having at least 2 consecutive, positive tTGA.  
CD: a small intestine biopsy of Marsh  $\geq 2$ , or mean tTGA  $\geq 100$  U/L in 2 consecutive samples.
- Cox regression examined associations between dietary patterns and risk of CDA, as well as of CD.
- Analyses were adjusted for country of residence, sex, HLA genotype, family history of CD, energy and gluten intake.

## 4. Results

- In 6677 enrolled children, 1287 (19.3%) developed CDA and 527 (7.9%) were diagnosed with celiac disease during mean follow-up of 11.0 years (SD 3.6)
- The dietary pattern “*Unsaturated fats and wheat*” at age 9 months was associated with reduced risk of CDA (HR 0.88, 95% CI 0.79, 0.98), but at age 24 months with increased risk of CDA (HR 1.18, 95% CI 1.05, 1.33) as well as CD (HR 1.24, 95% CI 1.03, 1.50) for every 5 unit increase in adherence.
- At age 18 months, the dietary pattern “*Potatoes and meat*” was associated with reduced risk of CD (HR 0.83, 95% CI 0.70, 0.99) for every 5 unit increase in adherence.

## 5. Conclusion

This explorative study indicates that common foods, or combination of foods, besides the gluten amount in the diet, may modify the risk of CDA and CD.

There is a need to further study early life dietary patterns to elucidate which combinations are harmful as well as protective to better understand the role of the diet in the development of CD.

Age months	Dietary pattern	High intakes	Low intakes	CDA HR (95% CI)	p-value	CD HR (95% CI)	p-value
9	<i>Unsaturated fats and wheat</i>	Unsaturated fats, wheat, milk, rice and GF grains, oats, potatoes, juices	Infant formula, breastmilk, legumes	0.88 (0.79, 0.98)	0.019	0.90 (0.77, 1.06)	0.222
	<i>Potatoes and meat</i>	Potatoes, meat, oats, rye and barley, rice and GF grains, root vegetables, sugar and sweets, vegetables	Cheese	1.03 (0.92, 1.15)	0.595	1.04 (0.88, 1.24)	0.641
	<i>Fruit and vegetables</i>	Fruit and berries, vegetables, root vegetables, legumes, wheat, animal fats, cheese, fermented dairy		1.02 (0.93, 1.12)	0.652	1.03 (0.89, 1.19)	0.711
12	<i>Unsaturated fats and wheat</i>	Unsaturated fats, wheat, milk, rice and GF grains, rye and barley, processed meat, fish and seafood, juices	Infant formula, legumes, root vegetables	0.96 (0.87, 1.05)	0.344	1.03 (0.90, 1.19)	0.673
	<i>Potatoes and meat</i>	Potatoes, meat, oats, rye and barley, rice and GF grains, root vegetables, fish and seafood	Cheese, wheat, legumes, processed meat, eggs	0.97 (0.88, 1.06)	0.438	0.95 (0.83, 1.09)	0.483
	<i>Fruit and vegetables</i>	Fruit and berries, vegetables, root vegetables, juices, wheat, rice and GF grains	Milk, fermented dairy	0.96 (0.87, 1.07)	0.450	0.92 (0.79, 1.08)	0.310
18	<i>Unsaturated fats and wheat</i>	Unsaturated fats, wheat, rye and barley processed meats, juices	Legumes, oats, meat, milk	1.03 (0.91, 1.17)	0.626	0.95 (0.78, 1.16)	0.620
	<i>Potatoes and meat</i>	Meat, rice and GF grains, potatoes, root vegetables, sweet beverages	Cheese, wheat, milk	0.96 (0.86, 1.07)	0.475	0.83 (0.70, 0.99)	0.035
	<i>Fruit and vegetables</i>	Fruit and berries, vegetables, root vegetables, legumes, fish and seafood	Sugar and sweets, sweet beverages	1.03 (0.93, 1.14)	0.551	0.93 (0.79, 1.10)	0.393
	<i>Rye, barley, unsaturated fats</i>	Rye and barley, unsaturated fats, potatoes, milk, oats, fish and seafood, fermented dairy	Saturated fats, sweet beverages, eggs, cheese, legumes, nuts and seeds, sugar and sweets	1.01 (0.92, 1.10)	0.906	1.09 (0.95, 1.25)	0.235
24	<i>Unsaturated fats and wheat</i>	Unsaturated fats, wheat, rye and barley, processed meats, juices	Legumes, root vegetables, oats, meat, milk	1.18 (1.05, 1.33)	0.006	1.24 (1.03, 1.50)	0.027
	<i>Potatoes and meat</i>	Potatoes, meat, oats, rye and barley, rice and GF grains, root vegetables, fish and seafood, unsaturated fats, fermented dairy, vegetables	Sugar and sweets, lite beverages, nuts and seeds, cheese, eggs, legumes	1.07 (0.98, 1.16)	0.126	1.06 (0.93, 1.21)	0.382
	<i>Fruit and vegetables</i>	Fruit and berries, vegetables, root vegetables, legumes, nuts and seeds, cheese	Milk, sweet beverages, potatoes, ice cream	1.02 (0.92, 1.12)	0.745	0.90 (0.78, 1.06)	0.203

References: <sup>1</sup> Liu et al: N Engl J Med. 2015. <sup>2</sup>Andrén Aronsson et al. JAMA. 2019. <sup>3</sup>Barroso et al. Gastroenterology. 2018. <sup>4</sup>Schultze et al. Br J Nutr. 2003.

Author correspondence: elin.malmberg\_hard\_af\_segerstad@med.lu.se (Lund university)