DOI: 10.1111/mcn.12084

Original Article

Age at first introduction to complementary foods is associated with sociodemographic factors in children with increased genetic risk of developing type I diabetes

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Abstract

Infant's age at introduction to certain complementary foods (CF) has in previous studies been associated with islet autoimmunity, which is an early marker for type 1 diabetes (T1D). Various maternal sociodemographic factors have been found to be associated with early introduction to CF. The aims of this study were to describe early infant feeding and identify sociodemographic factors associated with early introduction to CF in a multinational cohort of infants with an increased genetic risk for T1D. The Environmental Determinants of Diabetes in the Young study is a prospective longitudinal birth cohort study. Infants (N = 6404) screened for T1D high risk human leucocyte antigen-DQ genotypes (DR3/4, DR4/4, DR4/8, DR3/3, DR4/4, DR4/1, DR4/13, DR4/9 and DR3/9) were followed for 2 years at six clinical research centres: three in the United States (Colorado, Georgia/Florida, Washington) and three in Europe (Sweden, Finland, Germany). Age at first introduction to any food was reported at clinical visits every third month from the age of 3 months. Maternal sociodemographic data were self-reported through questionnaires. Age at first introduction to CF was primarily associated with country of residence. Root vegetables and fruits were usually the first CF introduced in Finland and Sweden and cereals were usually the first CF introduced in the United States. Between 15% and 20% of the infants were introduced to solid foods before the age of 4 months. Young maternal age (<25 years), low educational level (<12 years) and smoking during pregnancy were significant predictors of early introduction to CF in this cohort. Infants with a relative with T1D were more likely to be introduced to CF later.

Keywords: complementary foods, breastfeeding, infant feeding, socioeconomic factors, TEDDY, newborn feeding behaviours.

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Introduction

Certain foods and food groups, such as milkcontaining foods, cereals, roots and fruits and berries, have been associated with increased risk for islet autoimmunity and the development of type 1 diabetes (T1D) in children (Knip *et al.* 2010), but studies on the relationship between timing of introduction to complementary foods and the risk for islet autoimmunity and T1D yielded inconsistent results (Knip *et al.* 2010). Currently, the World Health Organization (WHO) recommends that infants should be exclusively breastfed for 6 months and complementary feeding should start at around 6 months of age, while the infant is still breastfed (WHO 2001; Pan American Health Organization 2003). In a review, the Nutrition Committee for the European Society for Pediatric Gastroenterology, Hepatology and

Nutrition (ESPGHAN) recommended that complementary feeding should not be introduced before 17 weeks (4 months) and all infants should start complementary feeding by 26 weeks (6 months; Agostini et al. 2008). The ESPGHAN committee also highlights that it is wise to avoid both early and late introduction to gluten and to introduce gluten to the infant while it is still breastfed, to reduce the risk of T1D, celiac disease and wheat allergy (Agostini et al. 2008). Regardless of international recommendations, countries still have their own traditions and cultural habits and these may vary across regions. Furthermore, studies have reported that other factors may have an impact on timing of first introduction to solid foods i.e. complementary feeding (Alder et al. 2004; Gudnadottir et al. 2006; Scott et al. 2009; Scheiss et al. 2010; Erkkola et al. 2012). Both demographic factors (e.g. maternal age, maternal education and socioeconomic status) and behavioural factors (e.g. maternal smoking) are reported to influence breastfeeding duration and timing of first introduction to complementary foods (Yngve & Sjöström 2001; Wijndaele et al. 2009). Factors often described as predictors for non-adherence with international infant feeding recommendations, often resulting in earlier introduction to complementary foods and consequently shorter duration of exclusive breastfeeding, are young maternal age, low maternal education and smoking during pregnancy (Lande et al. 2003; Gudnadottir et al. 2006; Erkkola et al. 2012). Finally, timing of complementary food introduction may also be influenced by perinatal factors such as birthweight (Grote et al. 2011).

The aims of this study were to describe early infant feeding practices and to identify sociodemographic factors associated with duration of breastfeeding and early introduction to complementary foods in a multinational cohort of infants with an increased genetic risk for islet autoimmunity and T1D.

Methods and materials

The Environmental Determinants of Diabetes in the Young (TEDDY) is a prospective cohort study with a primary goal of identifying environmental causes of T1D. The study is comprised of six clinical research centres - three in the United States: Colorado, Georgia/Florida, Washington and three in Europe: Finland, Germany and Sweden. Detailed study design and methods have been previously published (TEDDY study group 2007, 2008). Infants are followed from birth until the T1D diagnosis is established, or until the child is 15 years old. A total of 424 788 newborns were screened at random for T1Dassociated human leucocyte antigen (HLA) genotypes, between September 2004 and February 2010 (Hagopian et al. 2011). HLA screening was performed by using either a dried blood spot punch or a small volume of whole blood. Screening blood sample was generally obtained at birth as a cord or as a capillary blood sample (heel, finger). Infants were eligible for the initial contact if they had one of the following HLA genotypes; DR3/4, DR4/4, DR4/8, DR3/3, DR4/4, DR4/1, DR4/13, DR4/9 and DR3/9. The last four genotypes were only applicable for infants with a first-degree relative (FDR i.e. mother, father or sibling) with T1D (Hagopian et al. 2011). The HLA screening at birth identified 21 589 eligible infants, of which 8677 were enrolled in the study (Hagopian et al. 2011). Infants were eligible for

Key messages

- Short breastfeeding duration is associated with determinants such as younger maternal age, low maternal education, smoking during pregnancy, single parenting and premature births.
- Age at first introduction to complementary foods are associated with country of residence, and early introduction (<4 months) to root vegetables, fruits and berries are common in Finland and Sweden.
- Early introduction to complementary foods is associated with smoking during pregnancy, younger maternal age, and low maternal education.
- In this study population at risk for TID, families with TID were more likely to delay timing of first introduction to solid foods compared with families with no TID history.

enrolment if they were less than 4 months of age and a parent or primary caregiver gave informed consent. The children were followed four times per year for diet, infectious agents, other environmental exposures and autoimmunity status based on interviews, questionnaires, food records and blood samples for laboratory tests (TEDDY study group 2007).

In the present study, we analysed 6404/8677 (74%) children who had complete data. The following subjects were excluded: (i) subjects who left the study before the age of 2 years (n = 1935; 22%); and (ii) subjects with missing data on breastfeeding duration, age at introduction of new foods or maternal sociodemographic data (n = 338; 4%). Reasons for excluding subjects not followed for the specific length of time were that questions regarding first introduction to complementary foods and breastfeeding duration were asked at each clinic visit during the first 2 years. Demographic characteristics of the excluded subjects showed a majority of younger mothers (<25 years), lower maternal education, single parenting, living in crowded household and smoking during pregnancy (data not shown).

Written informed consents were obtained for all study children from a parent or primary caretaker, separately, for genetic screening and participation in prospective follow-up. The study was approved by local Institutional Review Boards and is monitored by an External Advisory Board formed by the National Institutes of Health.

Questionnaires

Information about duration of exclusive or any breastfeeding and age at first introduction to new foods were collected every third month from the age of 3 months, through a specific booklet that was given to the parents or primary caregiver at study entry. The booklet was reviewed at each visit (at 6, 9, 12, 15, 18, 21 and 24 months of age) by the clinical staff. Breastfeeding behaviours, both exclusive and any (overall) breastfeeding were studied. Exclusive breastfeeding could include small amounts of nonnutritious drinks such as water, oral electrolyte solutions, tea and nutritional supplements (such as dietary supplements). Parental report on feeding practice at

the delivery hospital was taken into account in determining the duration of exclusive breastfeeding. Any breastfeeding was defined as breastfeeding even in small amounts in combination with other foods. Breastfeeding duration was expressed in weeks. Food groups selected for analysis were: cow's milk (including infant formulas containing milk protein; nonhydrolysed and partially hydrolysed milk protein; commercial baby foods containing milk or milk powder and other milk based products); fruits and berries, potatoes and root vegetables; cereals (rice, wheat, rye, oats, barley, buckwheat and millet); and gluten-containing cereals (wheat, rye, and barley). The infant's age at first introduction of any given food was expressed in weeks. Categorical variables were created to define early vs. late introduction to solid foods according to the definitions by the ESPGHAN Committee (Agostini et al. 2008). Early introduction is defined as being introduced before 17 weeks (4 months) and late introduction is defined as being introduced after 26 weeks (6 months) of age.

Maternal sociodemographic data were collected through questionnaires distributed at the clinical visits. Maternal age was defined as the women's age at time of delivery (<25.0, 25-29.9, 30-34.9 and ≥35 years). Birth order of the child (first born vs. others) was determined by the question to the mother 'Is this your first child?'. Marital status was categorized as married, cohabited and others (single, separated, divorced and widowed). Maternal education was recorded on a 10-category scale to accommodate for different education systems in each country, and then aggregated into two categories - basic primary education (primary school through some trade school) and higher education (completed trade school or higher) - to achieve comparability across all countries. Smoking and drinking during pregnancy was defined as 'yes' if reported, regardless of frequency, amount and duration. Crowding (residence density) was defined as number of persons in the household divided by the number of rooms in the house. Birthweight of the child was reported by the parents and measured in grams (g). Low birthweight (LBW) was defined as below 2500 g and high birthweight was defined as above 4000 g. Gestational age was reported by the mothers and birth before 37 weeks was defined as premature birth. FDR status was considered positive if the child had a relative (mother, father or sibling) with T1D.

Statistics

Data were analysed using the Statistical Analysis System Software (Version 9.2, SAS Institute, Cary, NC, USA). Categorical variables were analysed using Pearson's χ^2 tests. Continuous variables were tested using analysis of variance for differences in means or the Kruskal-Wallis test for differences between medians. Medians are presented as median (quartile 1 - quartile 3). Stratified Cox proportional hazard models (stratified for country of residence) were used to estimate the hazards ratio for duration of breastfeeding (any or exclusive) and introduction of foods (cow's milk, root vegetables, fruits and berries, cereals, and gluten-containing cereals). The US population was chosen as reference variable because of being the largest sample population. Multivariable Cox models were adjusted for maternal age, birth order (first child or not), mother's marital status, maternal education, smoking during pregnancy, alcohol use during pregnancy, residence density (crowding), gender of child, child's birthweight, gestational age and T1D FDR-status. Efron's method for tied survival times were employed in the Cox analysis.

Results

The distribution of characteristics of the study population across four countries is provided in Table 1. The majority of the participating mothers (81%) had a high school degree or more. Nearly half of the women were primiparous, with the TEDDY child being their first child. Consumption of alcohol, even small amounts counted, was common during pregnancy, especially in Germany where 49% of the mothers reported having had alcoholic drinks during pregnancy. About 11% reported smoking either at some point or during the entire pregnancy. Only 8.6% lived in crowded conditions. Five per cent of the infants in the TEDDY-study were born premature, ranging from 4% in Finland to 7% in the United States.

Breastfeeding duration and associated factors

Breastfeeding duration (exclusive and any), measured in weeks, differed between the participating countries in TEDDY (Table 2). The exclusive breastfeeding duration in the United States was significantly shorter than in the European countries and the Swedish infants were exclusively breastfed for the longest period of time, 4 weeks (median). For any breastfeeding, the Finnish infants were breastfed for the longest duration, 38.7 weeks (8.9 months).

In the multivariate analysis, breastfeeding habits differed by country of residence (Table 3). Predictors for short duration of breastfeeding (both exclusive and any) were low maternal education, smoking during pregnancy, born premature and single parenting. LBW was only associated with short duration of any breastfeeding. A first-born infant was more likely to be exclusively breastfed for a shorter duration than infants with older siblings [hazards ratio (HR) 1.22, confidence interval (CI) 95% 1.16, 1.29]. Low maternal age (<25 years) was an additional predictor for shorter duration of any breastfeeding (HR 1.51, CI 95% 1.36, 1.67). Finally, if the mother were living in a crowded house, she was more likely to breastfeed longer (HR 0.81, CI 95% 0.74, 0.89).

Timing of introduction to complementary foods and associated factors

Age at first introduction to complementary foods differed between the participating countries in TEDDY (Table 2). Median age at first introduction to cow's milk was 3 weeks in this study. However, the infants in the United States were introduced to cow's milk significantly earlier (at the age of 1 week) than infants in the European countries. Root vegetables, fruits and berries, and cereals were introduced approximately at the same age to the infants, on average at 21 weeks (5 months). Swedish and Finnish infants were introduced the earliest to root vegetables, and fruit and berries compared with US and German infants. Cereals were first included into an infant's diet at the age of 19.6 weeks (4.5 months) in the United States and in Sweden, which was significantly earlier as compared with the other countries. Swedish infants were

	$\frac{\text{All}}{n = 6404}$	United States $n = 2540$	$\frac{\text{Sweden}}{n = 2005}$	$\frac{\text{Finland}}{n = 1445}$	$\frac{\text{Germany}}{n = 414}$	Р
Maternal age, n (%)						
<25.0	687 (10.7)	327 (12.9)	154 (7.7)	177 (12.2)	29 (7.0)	< 0.0001
25.0–29.9	1867 (29.1)	647 (25.5)	607 (30.3)	515 (35.6)	98 (23.7)	
30.0-34.9	2328 (36.4)	878 (34.5)	805 (40.1)	481 (33.3)	164 (39.6)	
≥35.0	1522 (23.8)	688 (27.1)	439 (21.9)	272 (18.8)	123 (29.7)	
Mothers first child, n (%)						
Yes	2879 (45.0)	1066 (42.0)	955 (47.6)	653 (45.2)	205 (49.5)	0.0004
Marital status, n (%)						
Married	4451 (69.5)	2168 (85.4)	966 (48.2)	980 (67.8)	337 (81.4)	< 0.0001
Cohabit	1709 (26.7)	232 (9.1)	998 (49.8)	416 (28.8)	63 (15.2)	
Single, divorced, widow	244 (3.8)	140 (5.5)	41 (2.0)	49 (3.4)	14 (3.4)	
Maternal education, n (%)						
Basic primary	1190 (18.6)	350 (13.8)	659 (32.9)	132 (9.1)	49 (11.8)	< 0.0001
High school or more	5214 (81.4)	2190 (86.2)	1346 (67.1)	1313 (90.9)	365 (88.2)	
Smoked during pregnancy, n (%)						
Yes	686 (10.7)	209 (8.2)	229 (11.4)	181 (12.5)	67 (16.2)	< 0.0001
Alcohol during pregnancy, n (%)						
Yes	2242 (35.0)	1027 (40.4)	570 (28.4)	444 (30.7)	201 (48.6)	< 0.0001
Crowding, n (%)						
≤1 people per room	5850 (91.4)	2342 (92.2)	1864 (93.0)	1284 (88.8)	360 (87.0)	< 0.0001
>1 people per room	554 (8.6)	198 (7.8)	141 (7.0)	161 (11.2)	54 (13.0)	
Sex, <i>n</i> (%)						
Girls	3114 (48.6)	1223 (48.1)	981 (48.9)	709 (49.1)	201 (48.6)	0.9368
Birthweight (g), n (%)						
<2500	365 (5.7)	252 (9.9)	50 (2.5)	47 (3.2)	16 (3.9)	< 0.0001
2500-3999	4991 (77.9)	1995 (78.6)	1522 (75.9)	1125 (77.9)	349 (84.3)	
≥4000	1048 (16.4)	293 (11.5)	433 (21.6)	273 (18.9)	49 (11.8)	
Gestational age, weeks, n (%)						
Premature (<37 weeks)	341 (5.3)	168 (7.1)	88 (4.4)	59 (4.1)	26 (6.3)	< 0.0001
Normal (37-42 weeks)	5932 (92.8)	2360 (93.1)	1823 (91.0)	1362 (94.3)	387 (93.7)	
Postmature (>42 weeks)	112 (1.9)	6 (0.2)	93 (4.6)	23 (1.6)	0 (0.0)	
Child with T1D FDR, n (%)						
Yes	742 (11.6)	296 (11.6)	137 (6.8)	136 (9.4)	173 (41.8)	< 0.0001

 Table 1. Sociodemographic characteristics of mothers and their infants participating in The Environmental Determinants of Diabetes in the Young

 Study for 2 years or more

T1D FDR, first-degree relative (i.e. mother, father or sibling) with type 1 diabetes.

introduced to gluten-containing cereals (wheat, rye, barley) significantly earlier compared with the other countries, at the age of 21.7 weeks (5 months; Table 2).

When using the ESPGHAN committee's cut-offs for defining early introduction to complementary foods, substantial country differences were seen in age at first introduction to foods (Fig. 1). The overall proportion of infants introduced to potatoes and roots early, before 4 months of age, was 17%, being higher in Finland (27.0%) and Sweden (22.0%) than in Germany (12.1%) and in the United States (9.1%). Before 4 months of age, 19.7% of the infants were introduced to fruit and berries, 16.4% to cereals, and 5.9% to gluten-containing cereals. In the United States, 25.4% of the infants were introduced to cereals before 4 months, compared with 14.0% in Sweden, and less than 10.0% in Finland (5.6%) and Germany (8.4%). In Germany, only 9% of the infants were introduced to fruits and berries before 4 months of age compared with the other countries: the United States (20.5%), Finland (24.0%) and Sweden (18.0%). In Sweden, 11% of the infants were introduced to gluten-containing cereals before 4 months of age, which is a clearly larger proportion compared with the United States (3.8%), Finland (3.2%) and Germany (4.6%).

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	All	United States	Sweden	Finland	Germany	P-value*
	<i>n</i> = 6404	<i>n</i> = 2540	n = 2005	n = 1445	<i>n</i> = 414	
	Median (Q1,Q3)					
Breastfeeding duration, weeks						
Exclusive	2.0 (0.07, 13.0)	1.0 (0.07, 8.0)	4.0 (0.07, 16.0)	3.0 (0.07, 13.0)	3.5 (0.07, 21.7)	< 0.0001
Any	33.0 (12.0, 52.1)	30.4 (8.0, 53.7)	31.6 (17.4, 43.4)	38.7 (21.0, 54.0)	32.1 (10.0, 48.1)	< 0.0001
Age at first introduction, weeks						
Cow's milk	3.0 (0.07, 17.4)	1.0 (0.07, 12.0)	4.0 (0.07, 17.4)	4.3 (1.0, 21.7)	6.0 (0.07, 26.1)	< 0.0001
Potatoes and roots	19.6 (17.4, 23.8)	23.8 (19.6, 26.1)	17.4 (17.4, 19.6)	17.4 (16.0, 21.7)	23.8 (19.6, 26.1)	< 0.0001
Fruits and berries	21.7 (17.4, 26.1)	21.7 (17.4, 26.1)	19.6 (17.4, 21.7)	19.6 (17.4, 23.8)	26.1 (21.7, 29.3)	< 0.0001
Cereals	21.7 (17.4, 23.8)	19.6 (16.0, 23.8)	19.6 (17.4, 21.7)	21.7 (21.7, 26.1)	26.1 (21.7, 30.4)	< 0.0001
Gluten-containing cereals	26.1 (21.7, 30.4)	30.4 (26.1, 34.8)	21.7 (17.4, 23.8)	26.1 (23.8, 30.4)	30.4 (26.1, 37.0)	< 0.0001

 Table 2. Breastfeeding duration (weeks) and age at first introduction to complementary foods (weeks), in children (0–24 months of age) in the multinational The Environmental Determinants of Diabetes in the Young study

*Kruskal-Wallis test was used to test the difference between countries. The earliest introduction to complementary food has been bolded.

Country of residence and smoking during pregnancy were two factors associated with early introduction to all selected food groups in this study (Table 4). Maternal age (<30 years) was associated with early introduction to all selected foods except for cow's milk; whereas the youngest age group (<25 years) had the highest probability to introduce cow's milk early to their infant's diet. Marital status such as single parenthood (single, divorced, widow) were a predictor for early introduction to cow's milk (HR 1.45, CI 95% 1.27, 1.65), root vegetables (HR 1.24, CI 95% 1.08, 1.41), fruits (HR 1.15, CI 95% 1.00, 1.32) and cereals (HR 1.24, CI 95% 1.08, 1.42). Low maternal education was a predictor for early introduction to cow's milk (HR 1.24, CI 95% 1.15, 1.33), fruits and berries (HR 1.21, CI 95% 1.13, 1.30), potatoes and roots (HR 1.10, CI 95% 1.03, 1.19), and cereals (HR 1.13, CI 95% 1.05, 1.21). Compared with girls, boys were more likely to be introduced earlier to foods like potatoes and roots, fruits and berries, and cereals. Premature infants (gestational age <37 weeks) were more likely to be introduced to cow's milk earlier than infants with gestational age \geq 37–42 weeks (HR 1.76, CI 95% 1.56, 1.99). LBW (<2500 g) was not associated with early introduction to complementary foods in this study. Infants with a family member with T1D (parent and/or sibling) were more likely to be introduced later to foods such as potatoes and roots (HR 0.87, CI 95% 0.80, 0.95), fruits and berries (HR

0.91, CI 95% 0.84, 0.99), cereals (HR 0.88, CI 95% 0.82, 0.96), and gluten-containing cereals (HR 0.89, CI 95% 0.82, 0.97).

Discussion

In this multinational prospective cohort study, we collected information about sociodemographic characteristics, breastfeeding duration and timing of first introduction to complementary foods during the first 2 years of life in infants that were screened for T1D high risk HLA-DQ genotypes.

International infant feeding recommendations were unchanged during the enrolment period in TEDDY (2004–2010); exclusive breastfeeding for 6 months with introduction of complementary foods and continued breastfeeding thereafter (WHO 2001). Also, all TEDDY countries have statements in their national recommendations that introduction to complementary feeding (tasting portions) should not occur earlier than 4 months of age and preferable when the child is still breastfed (Erkkola et al. 2005; Grummer-Strawn et al. 2008; Pflüger et al. 2010; Hörnell et al. 2013). Country of residence was the strongest determinant of early introduction to complementary foods. Both the age at first introduction to complementary foods (Table 2) and the proportion of infants introduced before the age of 4 months (Fig. 1) revealed country differences in first complementary

	Exclusive	Any	
	breastfeeding	breastfeeding	
	HR (95% CI)	HR (95% CI)	
Maternal factors			
Country			
United States	1.0	1.0	
Sweden	0.85 (0.80, 0.90)***	1.28 (1.21, 1.36)***	
Finland	$0.81 (0.76, 0.86)^{***}$	0.99 (0.93, 1.06)	
Germany	0.54 (0.49, 0.61)***	1.12 (1.01, 1.25)*	
Maternal age, years			
<25.0	0.99 (0.90, 1.10)	1.51 (1.36, 1.67)***	
25.0-29.9	0.97 (0.91, 1.05)	1.34 (1.25, 1.44)***	
30.0-34.9	0.94 (0.88, 1.00)	1.17 (1.10, 1.25)***	
≥35.0	1.0	1.0	
Mothers first child			
Yes	1.22 (1.16, 1.29)***	1.04 (0.99, 1.10)	
No	1.0	1.0	
Marital status			
Married	1.0	1.0	
Cohabit	1.07 (1.01, 1.14)*	1.06 (0.99, 1.13)	
Others	1.37 (1.20, 1.57)***	1.18 (1.03, 1.35)*	
Maternal education			
Basic primary	1.24 (1.15, 1.33)***	1.34 (1.24, 1.44)***	
Trade school or higher	1.0	1.0	
Smoking during pregnancy			
Yes	1.22 (1.12, 1.32)***	1.38 (1.27, 1.50)***	
No	1.0	1.0	
Alcohol during pregnancy			
Yes	0.92 (0.88, 0.97)**	0.96 (0.91, 1.01)	
No	1.0	1.0	
Crowding			
≤1 people per room	1.0	1.0	
>1 people per room	0.96 (0.88, 1.05)	0.81 (0.74, 0.89)***	
Infant factors			
Sex			
Girls	1.0	1.0	
Boys	1.05 (0.99, 1.10)	1.00 (0.96, 1.06)	
Birthweight (g)			
<2500	1.10 (0.98, 1.24)	1.28 (1.14, 1.43)***	
2500-3999	1.0	1.0	
≥4000	1.03 (0.96, 1.11)	0.96 (0.90, 1.03)	
Gestational age			
Premature (<37 weeks)	1.75 (1.55, 1.98)***	1.32 (1.18, 1.49)***	
Normal (37-42 weeks)	1.0	1.0	
Postmature (>42 weeks)	1.15 (0.96, 1.38)	0.89 (0.75, 1.07)	
Child with T1D FDR			
Yes	0.99 (0.92, 1.08)	0.99 (0.91, 1.07)	
No	1.0	1.0	

 Table 3. Multivariable analysis of sociodemographic predictors for shorter duration of breastfeeding (exclusive and any)

T1D FDR, first-degree relative (i.e. mother, father or sibling) with type 1 diabetes; HR, hazards ratio; CI, confidence interval. *P < 0.05, **P < 0.01, ***P < 0.0001. The models included all covariates presented in the table.

foods. In Finland and Sweden, it was common to introduce potatoes or other root vegetables, and fruits and berries, around the age of 4 months. In the United States, most often rice cereals were the first comple-

mentary foods introduced. Less than 10% of the infants from Germany were introduced to complementary foods before the age of 4 months. This corresponds well with a German report, which showed that only 16% of the infants in Bavaria, a German region, were introduced to complementary foods before the age of 5 months (Rebhan et al. 2009). The most noticeable country difference was seen in introduction to gluten-containing cereals. Infants in Sweden were four times more likely to be introduced earlier to gluten-containing cereals than infants in the United States. This is probably due to the Swedish tradition to feed infants with wheat- and rye-based porridges and gruels. So, despite international and national recommendations and guidelines, the timing of first introduction of complementary foods differs by country.

Maternal smoking is a strong determinant for shorter duration of breastfeeding and consequently early introduction to complementary foods. Smoking is also associated with sociodemographic factors such as low education level and low socioeconomic status. A study from the United States, describing psychosocial differences between smokers and non-smokers during pregnancy found that women who smoked during pregnancy were more likely to report that they experienced stress, negative paternal support, low self-efficacy, less social support and conscientiousness, and that they had lower perceived social standing compared with those who did not smoke (Maxson et al. 2012). The association between smoking and short duration of breastfeeding and early introduction to complementary foods may originate from both psychosocial and biological factors. Smoking mothers are often less health conscious, but they may also be unable to produce adequate amounts of breast milk during pregnancy and post-partum (Vio et al. 1991). The findings in our study regarding smoking during pregnancy and early infant feeding practices are consistent with other studies (Lande et al. 2003; Gudnadottir et al. 2006: Rebhan et al. 2009: Scott et al. 2009; Erkkola et al. 2012). Results from a systematic review lists maternal smoking as one of the strongest predictors associated with early introduction to complementary foods (Wijndaele et al. 2009). In a German study with a similar study population as



Fig. 1. Country-specific differences in timing of introduction to complementary foods with cut-offs defined by the European Society for Pediatric Gastroenterology, Hepatology and Nutrition's complementary feeding recommendations.

TEDDY, i.e. infants with increased genetic and familiar risk for T1D, it was shown that infants to mothers who smoked were introduced to complementary foods earlier than infants of non-smoking mothers (Pflüger *et al.* 2010.)

Male gender has been associated with early introduction of complementary foods in some studies (Lande *et al.* 2003; Alder *et al.* 2004; Virtanen *et al.* 2006; Grote *et al.* 2011; Erkkola *et al.* 2012), but not in all (Rebhan *et al.* 2009; Scott *et al.* 2009). The Diabetes Prediction and Prevention study from Finland (Virtanen *et al.* 2006) found that boys were introduced to roots, fruits and berries earlier than girls and in four other studies, boys were more likely to receive complementary foods earlier than girls (Lande *et al.* 2003; Alder *et al.* 2004; Grote *et al.* 2011; Erkkola *et al.* 2012). Mother's reasons for earlier introduction to complementary foods to boys may vary. The expression 'boys need more' has been mentioned in some reports and refers to mother's perception of their infant's needs (Wijndaele *et al.* 2009). Scott *et al.* (2009) reported that the main reason for the mothers to introduce complementary foods before 4 months was that they thought that their infants needed complementary foods or that they were ready for them (i.e. a 'baby-led' reason). In our study, foods like roots,

	Cow milk	Potatoes and roots	Fruit and berries	Cereals	Gluten HR (95% CI)	
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)		
Maternal factors						
Country						
United States	1.0	1.0	1.0	1.0	1.0	
Sweden	1.03 (0.97, 1.10)	3.35 (3.15, 3.58)***	1.68 (1.58, 1.78)***	1.23 (1.16, 1.31)***	4.48 (4.20, 4.78)***	
Finland	0.78 (0.73, 0.83)***	2.29 (2.14, 2.44)***	1.55 (1.45, 1.65)***	0.59 (0.56, 0.64)***	1.38 (1.29, 1.48)***	
Germany	0.72 (0.65, 0.80)***	0.99 (0.89, 1.10)	0.59 (0.53, 0.65)***	0.35 (0.31, 0.39)***	0.79 (0.71, 0.88)***	
Maternal age, years						
<25.0	1.01 (0.92, 1.12)	1.38 (1.24, 1.52)***	1.44 (1.30, 1.60)***	1.46 (1.32, 1.61)***	1.44 (1.30, 1.59)***	
25.0-29.9	1.00 (0.93, 1.08)	1.22 (1.13, 1.30)***	1.23 (1.14, 1.32)***	1.26 (1.17, 1.35)***	1.15 (1.08, 1.24)***	
30.0-34.9	0.96 (0.90, 1.03)	1.04 (0.98, 1.11)	1.04 (0.98, 1.11)	1.07 (1.00, 1.14)*	1.04 (0.98, 1.12)	
≥35.0	1.0	1.0	1.0	1.0	1.0	
Mothers first child						
Yes	1.17 (1.10, 1.23)***	1.10 (1.05, 1.16)**	1.02 (0.97, 1.08)	1.04 (0.99, 1.00)	0.96 (0.91, 1.01)	
No	1.0	1.0	1.0	1.0	1.0	
Marital status						
Married	1.0	1.0	1.0	1.0	1.0	
Cohabit	1.10 (1.03, 1.17)**	1.05 (0.99, 1.12)	1.02 (0.96, 1.09)	1.00 (0.94, 1.07)	1.07 (1.00, 1.14)*	
Others	1.45 (1.27, 1.65)***	1.24 (1.08, 1.41)**	1.15 (1.00, 1.32)*	1.24 (1.08, 1.42)**	0.99 (0.86, 1.14)	
Maternal education						
Basic primary	1.24 (1.15, 1.33)***	1.10 (1.03, 1.19)**	1.21 (1.13, 1.30)***	1.13 (1.05, 1.21)**	1.05 (0.98, 1.12)	
Trade school or higher	1.0	1.0	1.0	1.0	1.0	
Smoking during pregnancy						
Yes	1.23 (1.13, 1.34)***	1.34 (1.24, 1.46)***	1.45 (1.33, 1.58)***	1.29 (1.18, 1.40)***	1.22 (1.12, 1.32)***	
No	1.0	1.0	1.0	1.0	1.0	
Alcohol during pregnancy						
Yes	0.94 (0.89, 0.99)*	1.01 (0.96, 1.07)	0.99 (0.94, 1.04)	1.00 (0.95, 1.06)	1.01 (0.96, 1.07)	
No	1.0	1.0	1.0	1.0	1.0	
Crowding						
≤1 of people / room	1.0	1.0	1.0	1.0	1.0	
>1 of people / room	1.0 (0.87, 1.04)	0.93 (0.85, 1.02)	0.97 (0.89, 1.07)	0.90 (0.83, 0.99)*	0.94 (0.86, 1.03)	
Infant factors						
Sex						
Girls	1.0	1.0	1.0	1.0	1.0	
Boys	1.05 (1.00, 1.10)	1.08 (1.03, 1.14)**	1.08 (1.02, 1.13)**	1.09 (1.04, 1.15)**	1.01 (0.96, 1.06)	
Birthweight (g)						
<2500	1.09 (0.97, 1.23)	1.01 (0.90, 1.14)	1.00 (0.90, 1.13)	0.99 (0.88, 1.10)	0.91 (0.81, 1.03)	
2500-3999	10	10	10	10	10	

1.04 (0.97, 1.11)

0.92 (0.81, 1.04)

1.06 (0.88, 1.28)

0.91 (0.84, 0.99)*

1.0

1.0

1.00 (0.93, 1.07)

1.06 (0.94, 1.20)

1.05 (0.88, 1.26)

0.88 (0.82, 0.96)**

1.0

1.0

1.04 (0.97, 1.11)

0.98 (0.87, 1.11)

0.83 (0.69, 1.00)

0.89 (0.82, 0.97)**

1.0

1.0

Table 4. Multivariable analysis of sociodemographic predictors for early introduction to complementary foods

≥4000

Yes

No

Gestational age (weeks)

Child with T1D FDR

Premature (<37 weeks) Normal (37–42 weeks)

Postmature (>42 weeks)

T1D FDR, first-degree relative (i.e. mother, father or sibling) with type 1 diabetes; HR, hazards ratio; CI, confidence interval. *P<0.05, **P < 0.01, ***P < 0.0001. The models included all covariates presented in the table.

1.05 (0.98, 1.13)

1.02 (0.90, 1.14)

1.04 (0.87, 1.25)

0.87 (0.80, 0.95)**

1.0

1.0

1.02 (0.95, 1.09)

0.96 (0.80, 1.15)

0.94 (0.87, 1.02)

1.0

1.0

1.76 (1.56, 1.99)***

fruits and berries, and cereals were introduced somewhat earlier to boys than to girls. However, we did not observe any gender differences in duration of breastfeeding.

Premature births (<37 weeks) were associated with shorter duration of breastfeeding (exclusive and any) and earlier introduction to cow's milk. These associations were likely due to complications that typically occur among premature infants, such as separation from the mother because of intensive care, as well as immature suckling and swallow coordination. In this population, LBW was only associated with shorter duration of any breastfeeding. Neither premature births nor LBW were associated with earlier introduction to solid foods in this study.

Many of our findings on sociodemographic factors and infant feeding practices were consistent with previous studies, especially young maternal age (<25 years) and low maternal education (<12 years). These factors has often been reported to be associated with both short duration of breastfeeding and early introduction of solid foods (Gudnadottir *et al.* 2006; Rebhan *et al.* 2009; Scheiss *et al.* 2010; Erkkola *et al.* 2012). Both determinants are also used as characteristics of lower socioeconomic status.

Single parenting has been described as a potential factor for short breastfeeding duration and early introduction to complementary foods in the systemic review by Wijndaele *et al.* (2009). In our study, a similar association was seen. Infants living with a single mother were more likely to be breastfeed for a shorter duration (exclusive and any) and to be introduced to complementary foods (cow's milk, root vegetables, cereals) earlier. This may be a consequence of lack of social support (and paternal support) and increased stress because of single parenting.

Almost 12% of the infants in our study population have a mother, father or a sibling with T1D. The presence of T1D in a FDR was not associated with breastfeeding habits, although we did observe that infants with T1D relatives were introduced later to complementary foods such as roots and potatoes, fruits and berries, cereals, and gluten-containing cereals than infants without a T1D relative. Cow's milk, gluten and fruits, berries, and roots have been associated with an increased risk for islet autoimmunity and T1D (Norris et al. 2003; Ziegler et al. 2003; Virtanen et al. 2006; Holmberg et al. 2007). These reports on risk for T1D may have affected decisions of when to start introducing complementary foods to the infant in our study population. We observed that complementary feeding were started later in Germany compared with the other TEDDY countries. This difference in behaviour may be explained by the fact that there is a much larger proportion of infants with a relative with T1D in Germany (42%) compared with other TEDDY countries. On the other hand, Hummel et al. (2007) reported that reduced breastfeeding duration in a FDR population was only associated with the maternal T1D status, and not with the paternal or sibling FDR status. A European multicentre study also describes later introduction to complementary foods in a German general population compared with similar populations in four other European countries (Scheiss et al. 2010).

The limitation of this study was that the study population represented children who were genetically at elevated risk for T1D and the parents knew it by the time when complementary feeding was started. This may have had an impact on food introduction pattern and overall generalizability because of existing literature and recommendations related to feeding and T1D risk. However, very few studies have compared breastfeeding and complementary food introduction and associated sociodemographic characteristics of the family between countries and continents using similar populations and the same methods. The results were well in concordance with earlier knowledge of country-specific infant feeding patterns, e.g. early introduction to gluten in Sweden. Our results also confirmed that the infants of younger, less educated, smoking mothers are still at higher risk of being fed in ways that are not in compliance with infant feeding recommendations.

In conclusion, it has been shown that both cultural and sociodemographic factors were associated with short duration of breastfeeding and early introduction to complementary foods in this multinational cohort study. Country of residence was an important determinant for both the duration of breastfeeding and for the timing of first introduction to complementary foods. Almost 20% of our study population was introduced to complementary before 4 months of age. Smoking during pregnancy, young maternal age, and low maternal education were all predictors of short duration of breastfeeding and of early introduction to complementary foods. Families with a history of T1D seem to delay the introduction of foods that had earlier been implicated in increasing the risk for islet autoimmunity. Given the cited association between early food introduction and risk for T1D observed in other similar cohorts, these findings may be used as preventive tools within the public health area.

Acknowledgement

The authors express their gratitude to the children and parents who participated, and wish to thank the TEDDY staff for excellent collaboration over the years.

Source of funding

This study is funded by U01 DK63829, U01 DK63861, U01 DK63821, U01 DK63865, U01 DK63863, U01 DK63836, U01 DK63790, UC4 DK63863, UC4 DK63861, UC4 DK63821, UC4 DK63865, UC4 DK63863, UC4 DK63836 and UC4 DK95300, and contract no. HHSN267200700014C from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Child Health and Human Development (NICHD), National Institute of Environmental Health Sciences (NIEHS), Juvenile Diabetes Research Foundation (JDRF), and Centers for Disease Control and Prevention (CDC).

Conflicts of interest

The authors declare that they have no conflicts of interest.

Contributions

CAA drafted and wrote the manuscript. KV conducted the statistical analysis. CAA, UU, JY, SMV and JMN contributed to the interpretation of the results. SMV and JMN contributed in the study design and the overall academic supervision. All authors contributed in the results presentation and were involved in preparing the final manuscript.

References

- Agostini C., Desci T., Fewtrell M., Goulet O., Kolacek S., Koletzko B. *et al.* (2008) Complementary feeding: a commentary by the ESPGHAN Committee on Nutrition. *Journal of Pediatric Gastroenterology and Nutrition* **46**, 99–110.
- Alder E.M., Williams F.L.R., Anderson A.S., Forsyth S., Florey C.du V. & van der Velde P. (2004) What influences the timing of the introduction of solid foods to infants? *The British Journal of Nutrition* 92, 527–531.
- Erkkola M., Pigg H.-M., Virta-Autio P., Hekkala A., Hyppönen E., Knip M. *et al.* (2005) Infant feeding patterns in the Finnish type 1 diabetes prediction and prevention nutrition study cohort. *European Journal of Clinical Nutrition* **59**, 107–113.
- Erkkola M., Salmenhaara M., Nwaru B.I., Uusitalo L.,
 Kronberg-Kippliä C., Ahonen S. *et al.* (2012)
 Sociodemographic determinants of early weaning: a
 Finnish birth cohort study in infants with human leucocyte antigen-conferred susceptibility to type 1 diabetes. *Public Health Nutrition* 16, 296–304.
- Grote V., Schiess S.A., Closa-Monasterolo R., Escribano J., Giovannini M., Scaglioni S. *et al.* (2011) The introduction of solid food and growth in the first 2 y of life in the formula-fed children: analysis of data from a European cohort study. *The American Journal of Clinical Nutrition* **94**, 1785S–1793S.
- Grummer-Strawn L., Scanlon K. & Fein S. (2008) Infant feeding and feeding transitions during the first year of life. *Pediatrics* **122**, S36–S42.
- Gudnadottir M., Gunnarsson B.S. & Thorsdottir I. (2006) Effects of sociodemographic factors on adherence to breastfeeding and other important infant dietary recommendations. *Acta Paediatrica* 95 (4), 419–424.
- Hagopian W.A., Erlich H., Lernmark Å., Rewers M., Ziegler A.G., Simell O. *et al.* (2011) The Environmental Determinants of Diabetes in the Young (TEDDY): genetic criteria and international diabetes risk screening of 421 000 infants. *Pediatric Diabetes* **12**, 733–743.
- Holmberg H., Wahlberg J., Vaarala O., Ludvigsson J. & ABIS Study Group (2007) Short duration of breastfeeding as a risk-factor for β -cell autoantibodies in 5-year old children from the general population. *The British Journal of Nutrition* **97**, 111–116.
- Hörnell A., Hernell O. & Silfverdal S.A. (2013) Breastfeeding and adaption to solid foods for healthy

full-term infants. A review from the Swedish Paediatric Society and the National Food Agency. *Lakartidningen* **110**, 405–409.

- Hummel S., Winkler C., Schoen S., Knopff A., Marienfeld S., Bonifacio E. *et al.* (2007) Breastfeeding habits in families with Type 1 diabetes. *Diabetic Medicine* **24**, 671–676.
- Knip M., Virtanen S.M. & Åkerblom H. (2010) Infant feeding and the risk of type 1 diabetes. *The American Journal of Clinical Nutrition* **91**, 1506S–1513S.
- Lande B., Andersen L.F., Bærug A., Trygg K., Lund-Larsen K., Veierød M. *et al.* (2003) Infant feeding practices and associated factors in the first six months of life: the Norwegian Infant Nutrition Survey. *Acta Paediatrica* 92, 152–161.
- Maxson P.J., Edwards S.E., Ingram A. & Miranda M.L. (2012) Psychosocial differences between smokers and non-smokers during pregnancy. *Addictive Behaviors* 37, 153–159.
- Norris J.M., Barriga K., Klingensmith G., Hoffman M., Eisenbarth G.S., Erlich H.A. *et al.* (2003) Timing of initial cereal exposure in infancy and risk of islet autoimmunity. *JAMA* 290, 1713–1720.
- Pan American Health Organization (PAHO) (2003) Guiding Principles for Complementary Feeding of the Breastfed Child. Pan American Health Organization: Washington, DC. Available at: http://whqlibdoc.who.int/ paho/2003/a85622.pdf (Accessed 16 April 2013).
- Pflüger M., Winkler C., Hummel S. & Ziegler A. (2010) Early infant diet in children at high risk for type 1 diabetes. *Hormone and Metabolic Research* 42, 143–148.
- Rebhan B., Kohlhuber M., Schwegler U., Koletzko B.V. & Fromme H. (2009) Infant feeding practices and associated factors through the first 9 months of life in Bavaria, Germany. *Journal of Pediatric Gastroenterology and Nutrition* 49, 467–473.
- Scheiss S., Grote V., Scagloni S., Luque V., Martin F., Stolarczyk A. *et al.* (2010) Introduction of complementary feeding in 5 European countries. *Journal of Pediatric Gastroenterology and Nutrition* 50, 92–98.
- Scott J.A., Binns C.W., Graham K.I. & Oddy W.H. (2009) Predictors of early introduction of solid foods in infants:

results of a cohort study. *BMC Pediatrics* **9**, 60. doi: 10.1186/1471-2431-9-60.

- TEDDY Study Group (2007) The environmental determinants of diabetes in the young (TEDDY) study: study design. *Pediatric Diabetes* **8**, 286–298.
- TEDDY Study Group (2008) The environmental determinants of diabetes in the young (TEDDY) study. *Annals of the New York Academy of Sciences* **1150**, 1–13.
- Vio F., Salazar G. & Infante C. (1991) Smoking during pregnancy and lactation and its effects on breast milk volume. *The American Journal of Clinical Nutrition* 54, 1011–1016.
- Virtanen S.M., Kenward M., Erkkola M., Kautiainen S., Kronberg-Kippilä C., Hakulinen T. *et al.* (2006) Age at introduction of new foods and advanced beta cell autoimmunity in young children with HLA-conferred susceptibility to type 1 diabetes. *Diabetologia* 49, 1512– 1521.
- Wijndaele K., Lakshman R., Landsbaugh J., Ong K. & Ogilvie D. (2009) Determinants of early weaning and use of unmodified cow's milk in infants: a systemic review. *Journal of the American Dietetic Association* **109**, 2017–2028.
- World Health Organization (WHO) (2001) The optimal duration of exclusive breastfeeding: report of an Expert Consultation. Available at: http://www.who.int/nutrition/ publications/optimal_duration_of_exc_bfeeding_report_ eng.pdf (Accessed 16 April 2013).
- Yngve A. & Sjöström M. (2001) Breastfeeding determinants and suggested framework for action in Europe. *Public Health Nutrition* 4, 729–739.
- Ziegler A.G., Schmid S., Huber D., Hummel M. & Bonifacio E. (2003) Early infant feeding and risk of developing type 1 diabetes-associated autoantibodies. *JAMA* 290, 1721–1728.

Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher's web-site:

Appendix. The Teddy Study Group