

FIGURE 2 Metrics of high-density lipoprotein (HDL) function. Isolated eosinophils of healthy, non-atopic volunteers were pretreated with HDL (50 µg/mL) of control subjects (n = 8) and atopic dermatitis (AD) patients (n = 16) (A-C) or indicated concentrations of lysophosphatidylcholine (LPC) 16:0 (D), LPC 18:0 (E) or LPC 18:1 (F). Samples were placed into transwell plate inserts with 5 µm pore size and allowed to migrate toward eotaxin-2/CCL24 (30 nM) into the bottom well for 1 h at 37°C. Bars indicate mean and SEM of duplicate measurements of the different test groups (A-C). Data are shown as mean and SEM from 5 individual donors (D-F). Isolated eosinophils of healthy, non-atopic volunteers were pretreated with HDL (50 µg/mL) of control subjects (n = 8) or AD patients (n = 16) (G-I), indicated concentrations of LPC 16:0 (J), LPC 18:0 (K), LPC 18:1 (L) or indicated concentrations of apolipoprotein (apo)-CIII (M) for 30 min and subsequently stimulated with eotaxin-2/CCL24 (10 nM) for 4 mins at 37°C. Shape change was analyzed by flow cytometry as increase of forward scatter. Bars indicate mean and SEM of duplicate measurements of the different test groups (G-I). Data are shown as mean and SEM of 5 individual donors (J-L). Values shown as mean and SEM are representative of two independent experiments measured in duplicates (M). Responses were expressed as percent of vehicle (eotaxin-2/CCL24 in the absence of HDL, apoC-III or LPC) treated cells (A-M). Arylesterase activity of HDL-associated paraoxonase 1 of control subjects (n = 8) and AD patients (n = 16) was measured using phenylacetate as substrate (N). [³H]-cholesterol-labeled J774 macrophages were incubated with HDL (50 µg/mL) of control subjects (n = 8) and AD patients (n = 16) for 4 h (O). Cholesterol efflux is expressed as radioactivity in the supernatant relative to total radioactivity (in supernatant and cells). Values shown represent means of two individual experiments measured in duplicates (N, O). Bars indicate mean and SEM of the different test groups. Levels of significance were calculated using Student's t-test or one-way ANOVA and Dunnett post-hoc test. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001 [Colour figure can be viewed at wileyonlinelibrary.com]

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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Milk and egg intervention during pregnancy and allergic disease in offspring up to 30 years of age

To the Editor,

The role of maternal ingestion of allergens during pregnancy for allergy development in the child is debated. In the 1980s, it was

hypothesized that avoidance of potent food allergens during pregnancy might prevent allergy-related disease in the child. In 2012, a Cochrane review concluded that there was no evidence in favor of

food avoidance during pregnancy.¹ In recent years, it has been suggested that allergen exposure through the maternal diet during pregnancy and/or lactation may reduce the risk of allergy development in the child^{2,3} but conflicting results have been presented. A recent review suggested that heterogeneous study designs with different foods and doses of intake, different periods of exposure, and different durations of follow-up as reasons for the conflicting results.⁴

The aim of this study was to investigate the association between high intake (daily intake of 0.5-1 one of cow's milk and at least one hen's egg) versus avoidance (all visible intake) of cow's milk and hen's egg, during the last trimester of pregnancy, and the development of allergic disease in the offspring up to 26-30 years of age. Pregnant women with self-reported allergy to airborne allergens were allocated either to high intake ("high" group) or to restricted intake ("avoidance" group) of hen's egg and cow's milk, during the third trimester of their pregnancy (Figure S1). Their children were followed through questionnaires, clinical examinations, Skin Prick Tests (SPTs), and IgE-analyses for a number of common food and airborne allergens at 18 months, and 5, 10, and 26-30 years. In the previously published 18 months follow-up, no association was found between the maternal diet and the development of allergic disease in the offspring.⁵

The study population consisted of all the individuals who attended the long-term follow-up, at which the individuals were between 26 and 30 years of age ($n = 136$, 86% of the original cohort), henceforth called 30 years follow-up. In a majority of these

participants, we also had information at ages 18 months ($n = 136$), 5 years ($n = 130$) and 10 years ($n = 123$). The study population was comparable to the original cohort in distribution of demographic categories (data not shown). Furthermore, the distribution of demographic characteristics was comparable between the two intervention groups (Table 1). Definitions of health outcomes (Table S1) and complete study methods can be found in the Data S1.

By analyzing the data primarily by intention to treat (ITT), we emphasize the allocation, rather than the individual choice of a few mothers, in an attempt to exclude other unknown confounders. Secondly, we performed analysis per protocol, where women that did not follow the allocated diet were excluded (eight women from avoidance and 12 from high group), as was done in the evaluation of the 18 months follow-up.⁵

Chi-squared tests or Fisher's exact test when applicable were used to study the significant differences in clinical outcomes and IgE-sensitization between the intervention groups (significant P -value set at < 0.05). Logistic regression was used to investigate the association between high versus no maternal intake of cow's milk and hen's egg during the third trimester, in relation to allergy-related symptoms and IgE-sensitization in the child, presented as odds ratios (OR) with a 95% CI. Based upon known risk factors for development of allergic disease, we adjusted for heredity of allergic disease from both parents, and for parental smoking in the infancy period. Exclusive breastfeeding (≥ 4 vs < 4 months) influenced the observed OR $< 10\%$, and was therefore not included in the model.

TABLE 1 Background characteristics in the study populations' interventions groups

Characteristics	Intention to treat			Per protocol		
	High intake ($n = 63$)	Avoidance group ($n = 73$)	P -value	High intake ($n = 51$)	Avoidance group ($n = 65$)	P -value
Parental characteristics						
Maternal age (y)	28.8 $\pm$ 4.7	28.6 $\pm$ 3.7		28.3 $\pm$ 4.5	28.5 $\pm$ 3.8	
Maternal asthma	29 (46.0)	33 (45.2)	0.923	22 (43.1)	30 (46.2)	0.746
Maternal eczema	31 (49.2)	41 (56.2)	0.418	22 (43.1)	37 (56.9)	0.140
Maternal rhinitis	60 (95.2)	71 (97.3)	0.532	48 (94.1)	63 (96.9)	0.460
Maternal smoking at 18 mos	10 (15.9)	9 (12.5)	0.574	10 (19.6)	9 (13.9)	0.405
Paternal age (y)	32.0 $\pm$ 5.3	30.3 $\pm$ 4.9		31.3 $\pm$ 4.9	30.3 $\pm$ 5.1	
Paternal asthma	6 (9.5)	6 (8.2)	0.789	5 (9.8)	5 (7.7)	0.688
Paternal eczema	8 (12.7)	12 (16.4)	0.539	8 (15.7)	11 (16.9)	0.858
Paternal rhinitis	22 (34.9)	21 (28.8)	0.442	16 (31.4)	16 (24.6)	0.419
Paternal smoking at 18 mos	16 (25.4)	17 (23.6)	0.810	11 (21.6)	21 (26.2)	0.567
Any parental smoking in infancy (at 18 mos)	21 (33.3)	19 (26.4)	0.378	16 (31.4)	19 (29.2)	0.803
Double heredity of allergic disease	27 (42.9)	28 (38.4)	0.594	21 (41.2)	23 (35.4)	0.523
Child characteristics						
Gender, boy	40 (63.5)	41 (56.2)	0.385	32 (62.8)	36 (55.4)	0.424
Birth weight (g)	3436 $\pm$ 380	3399 $\pm$ 514		3418 $\pm$ 372	3394 $\pm$ 518	
Exclusive breast feeding, ≥ 4 mos	44 (69.8)	50 (68.5)	0.865	33 (64.7)	44 (67.7)	0.735
Older siblings	29 (46.0)	33 (45.8)	0.982	23 (45.1)	31 (48.4)	0.721

Values n (%) or mean $\pm$ SD.

One individual missing data for maternal and paternal smoking in avoidance group (ITT, $n = 72$), and for older siblings in the avoidance group (ITT, $n = 72$)/(per protocol, $n = 64$).

TABLE 2 Odds ratios of developing eczema, asthma, and rhinitis at 18 mos, 5, 10, and 30 y in relation to maternal intake of egg and milk during third trimester of pregnancy according to (A) Intention to treat (ITT); (B) Per protocol (PP)

Allergy-related symptoms	Number of individuals at follow up	Prevalence of disease (ITT) n (%)		High vs Avoidance crOR (95% CI)	High vs Avoidance adjOR (95% CI)
		"High"	"Avoidance"		
(A)					
Eczema					
18 mos	135	11 (17.5)	15 (20.8)	0.80 (0.34-1.91)	0.75 (0.31-1.81)
5 y	130	15 (25.4)	26 (36.6)	0.59 (0.28-1.26)	0.54 (0.24-1.17)
10 y	123	9 (16.1)	16 (23.9)	0.61 (0.25-1.51)	0.60 (0.24-1.50)
30 y	136	15 (23.8)	18 (24.7)	0.95 (0.43-2.10)	0.94 (0.43-2.09)
Asthma					
18 mos	135	5 (7.9)	7 (9.7)	0.80 (0.24-2.66)	0.73 (0.22-2.45)
5 y	130	11 (18.3)	13 (18.3)	1.02 (0.42-2.49)	0.90 (0.36-2.28)
10 y	123	12 (21.4)	14 (20.9)	1.03 (0.43-2.46)	0.91 (0.36-2.29)
30 y	136	7 (11.1)	20 (27.4)*	0.33 (0.13-0.85)	0.25 (0.09-0.69)
Rhinitis					
18 mos	135	0	1 (1.4)	1	1
5 y	130	8 (13.6)	11 (15.5)	0.86 (0.32-2.29)	0.75 (0.27-2.10)
10 y	122	15 (27.3)	22 (32.8)	0.77 (0.35-1.68)	0.70 (0.31-1.58)
30 y	136	36 (57.1)	47 (64.4)	0.74 (0.37-1.47)	0.74 (0.37-1.50)
(B)					
Eczema					
18 mos	115	9 (17.7)	13 (20.3)	0.84 (0.33-2.16)	0.79 (0.30-2.07)
5 y	113	12 (24.0)	23 (36.5)	0.55 (0.24-1.26)	0.50 (0.21-1.18)
10 y	106	8 (17.0)	14 (23.7)	0.66 (0.25-1.74)	0.65 (0.24-1.72)
30 y	116	13 (25.5)	16 (24.6)	1.05 (0.45-2.44)	1.04 (0.45-2.43)
Asthma					
18 mos	115	4 (7.8)	7 (10.9)	0.69 (0.19-2.52)	0.66 (0.18-2.43)
5 y	113	10 (20.0)	11 (17.5)	1.18 (0.46-3.06)	1.10 (0.41-2.94)
10 y	106	11 (23.4)	12 (20.3)	1.20 (0.47-3.02)	1.13 (0.42-3.01)
30 y	116	7 (13.7)	17 (26.2)	0.45 (0.17-1.19)	0.37 (0.13-1.04)
Rhinitis					
18 mos	115	0	1 (1.6)	1	1
5 y	113	8 (16.0)	10 (15.9)	1.01 (0.37-2.78)	0.88 (0.30-2.57)
10 y	105	15 (32.6)	19 (32.2)	1.02 (0.45-2.32)	0.97 (0.42-2.26)
30 y	116	31 (60.8)	40 (61.5)	0.97 (0.46-2.06)	0.93 (0.43-2.00)

Reference group in analysis are "Avoidance group".

Double heredity of allergic disease and any parental smoking in the infancy period (at 18 mos) were adjusted for.

One individual missing in diagnosis of rhinitis at 10 y (A) n = 122, (B) n = 105.

*No statistical significant differences were seen in prevalence between the groups, besides for asthma at 30 y ($P = 0.018$).

All analysis was performed with STATA Statistical Software (13.1; StataCorp, College Station, TX, USA).

Intake of egg and milk in late pregnancy was not associated with eczema, asthma or rhinitis, except at 30 years, where 11.1% ($n = 7$) had asthma in the "high" group, versus 27.4% ($n = 20$) in the "avoidance" group ($P = 0.018$) (Table 2A). In the ITT analysis, there was a reduced odds of asthma at 30 years in the "high" group (adjOR 0.25; 95% CI 0.09-0.69). When analyzed per

protocol, the association with asthma was no longer statistically significant (adjOR 0.37; 95% CI 0.13-1.04) (Table 2B). There was no significant association between the maternal diet and overall sensitization at any of the follow-ups in neither the ITT nor the per protocol analysis.

The present study is, to our knowledge, the first long-term follow-up to 30 years of age on the effects of the maternal diet during pregnancy on the child's allergic outcome. Strengths in our study

are multiple follow-ups using objective biological markers for the definition of allergy and sensitization, as well as high participation rates at the follow-up at 30 years. In addition, maternal compliance to the allocated diets was validated by repeated food registrations of egg and milk intake during the third trimester,⁵ and by testing of milk- and egg-specific IgG levels in some of the mothers during the intervention, which were found to be in accordance to the allocated diet.⁶

Bunyavanich et al³ found that milk intake during early pregnancy was inversely associated with mid-childhood asthma. While we cannot confirm these results during childhood, we found the same inverse association at the long-term follow-up. Possibly, the higher prevalence of asthma at 30 years compared to previous ages may explain why we observe our strongest association at this age. We also study a high-risk population, and possibly this strong risk factor reduces the protective effect of exposure on allergy development. Few individuals were sensitized to milk and egg, or had egg or milk allergy, at the different follow-ups (Table S2). This prevalence seems to be in accordance with observations from a Swedish population-based cohort followed up to adolescence.⁷

In conclusion, the results of this intervention study do not support an avoidance diet during pregnancy among mothers with airborne allergy. In contrast, our study indicates that high intake of cow's milk and hen's egg during pregnancy may be associated with a reduced prevalence of asthma in the offspring at age 30 years. Due to the limited sample size this needs to be further investigated. Given this was an intervention study, with a very high follow-up frequency after 30 years, we believe this study contributes to improve understanding of the role of prenatal allergen exposure on allergy development in the offspring.

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AUTHOR CONTRIBUTION

CF and GL carried out the data acquisition and analysis together with IK. CF, AB, AN, GL and IK participated in the design, planning and execution of the study, as well as in the interpretation of the results. CF led the drafting of the manuscript, and all authors commented on the drafts of the manuscript and approved the final version.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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SUPPORTING INFORMATION

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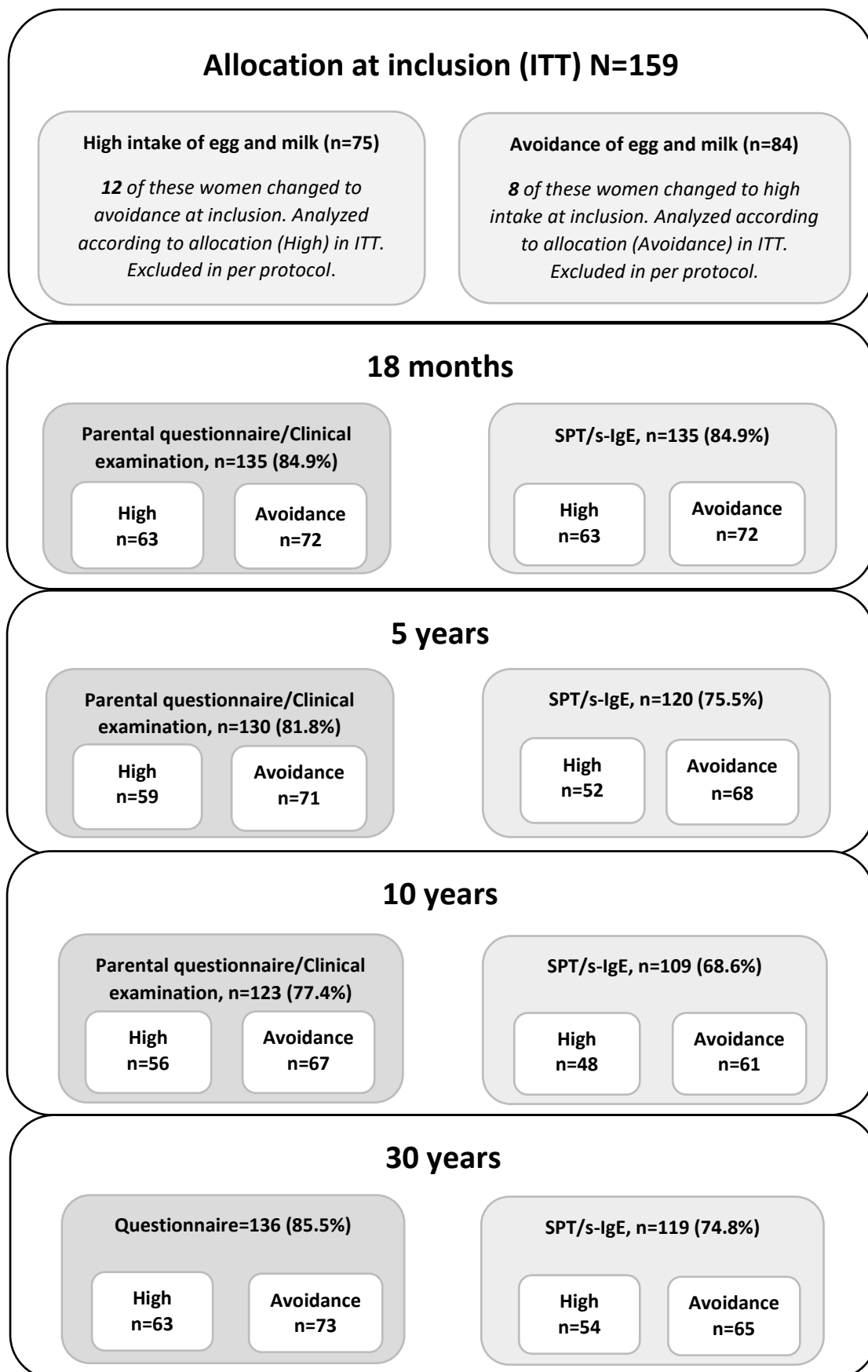


Fig S1. Flowchart of the study population according to the original allocation. Study population consists of all individuals who attended data collection at 30 years of age. For a majority of individuals data is available at all prior follow-ups at 18 months, 5 and 10 years.

1 **Data S1**

2 *Study population*

3 The intervention was conducted in 1983-85. All nine maternity clinics connected to Södersjukhuset
4 in Stockholm, Sweden were included in the study. Two of the clinics were small and considered to
5 be located in similar socioeconomic areas; they were merged in the study and seen as one clinic.
6 These eight maternity clinics were paired socioeconomically and allocated to one of two different
7 dietary interventions for pregnant women (1). Pregnant women with a history of bronchial asthma
8 and/or rhino-conjunctivitis, when exposed to animal dander and/or tree or grass pollen, were asked to
9 participate. Totally 159 participants were recruited to the study. Women attending four of the
10 maternity clinics were assigned a diet avoiding all visible intake (foods containing possible traces of
11 milk or egg protein were allowed) of cow's milk protein and hen's egg during the third trimester
12 (n=84, hereafter called the "avoidance" group). Women attending the other four maternity clinics
13 were assigned a daily intake of 0.5-1 l of cow's milk and at least one hen's egg during the third
14 trimester (n=75, hereafter called the "high" group) (Fig S1). The intervention was taking place
15 during a time when cow's milk in Sweden came from a very limited number of dairies, and when the
16 cow's milk products that people in general used were pasteurised. Hence, in this study we by cow's
17 milk mean pasteurised cow's milk and pasteurised cow's milk products.

18 All mothers in this study were given the same general recommendation from the
19 maternity clinics, given to all allergic mothers at the time, to exclusively breastfeed for at least six
20 months. When this was not feasible, these "high-risk" mothers were recommended to give soy-based
21 formula. According to the national guidelines at that time, introduction of high-risk allergens, such as
22 hen's egg and fish, was recommended to be postponed to nine to twelve months of age in both
23 groups. In the avoidance group, 21 women that exclusively breast-fed continued the elimination diet
24 during the first 2 months of breast-feeding, whereas 44 women from the same group went back to a
25 diet without any restrictions (1). In the questionnaires at age 18 months, parents reported the length
26 of breastfeeding and type of formula used.

27 At inclusion to the original study, data on background factors were obtained from a
28 parental questionnaire. The offspring have been followed prospectively from birth to adulthood.
29 Parental questionnaires were answered when the child was 18 months, 5 and 10 years of age. At age
30 26-30 years the study participants themselves answered a web-based questionnaire. Clinical
31 examinations, skin prick tests (SPT) and blood testing for IgE sensitization were performed at the
32 same ages. In addition, at the clinical examinations at 18 months, and 5 and 10 years, presence of
33 allergic disease was evaluated by a paediatrician combining the parental questionnaires and a

physical examination of the child, following a standardized protocol.

The women showed a good concordance in background characteristics compared to other pregnant allergic mothers. However, there was a moderately higher atopic burden and fewer smokers in the study population, which possibly suggests a greater awareness of allergy preventive measures in our study population than among allergic mothers in general (2).

Whether our results are dependent on the timing of intervention (third trimester), or the intervention was sufficient in amounts (avoidance or intake of 1 egg and 0.5–1 l of milk daily), is of course of interest. Edelbauer showed that ovalbumin and β -lactoglobulin were found on the fetal side of the term placenta (> 36 weeks of gestation) when pregnant women consumed 500 ml of non-processed milk per day and 2 eggs per week, in contrast to the pregnant women consuming milk- and egg-containing nutriment, where the levels were undetectable in fetal blood (3). This supports that the dietary intake of our study was sufficient. Bunyavanich et al concluded that a possible reason why many studies could not show any association between maternal diet during pregnancy and allergic disease in the offspring, was that the intervention was in the later part of the pregnancy, which suggests that timing of the intervention is an important factor. To support this hypothesis they found their strongest associations between the allergic outcomes in the offspring with the diet registered during the first trimester of the pregnancy (4). Maslova et al found that midpregnancy nut intake was inversely associated with asthma at 18 months of age (5). However there is no clear evidence on when an intervention should begin.

The study was approved by the Regional Ethics Committee, Stockholm. Parents, and the study participants themselves in the long-term follow-up, gave written informed consent to participate in the study.

IgE sensitization

SPT at 18 months and 5 years included ovalbumin, ovomucoid and β -lactoglobulin (1). At 5, 10, and 30 years, a number of other common allergens were also tested (hen's egg white, cow's milk (3% fat), *cladosporium*, *Dermatophagoides pteronyssinus*, dog, cat, birch and timothy). At 5 years, SPT also included fish, soy, hazelnut, horse and mugwort; at 10 years, horse, fish, soy, hazelnut and peanut; and at 30 years, peanut. Extracts (Soluprick SQ®; ALK-Abello, Copenhagen, Denmark) were used at the follow-up at 5, 10, and 30 years of age. At all ages, a SPT wheal reaction after 15 minutes with size ≥ 3 mm was regarded as positive.

The presence of IgE antibodies towards ovomucoid and β -lactoglobulin in serum at 18 months and 5 years of age was analysed using an extra-sensitive RAST (Termo Fischer Scientific,

Uppsala, Sweden) (cut-off ≥ 0.15 PRU/ml) (1). At 5, 10, and 30 years of age, IgE sensitization to dog, cat, birch, timothy and *Dermatophagoides Pteronyssinus* and *cladosporium* was analysed using ImmunoCAP (Termo Fischer Scientific); and at 30 years of age also towards horse, hen's egg, cow's milk, fish, soy, hazelnut and peanut (ImmunoCAP) (cut-off ≥ 0.35 kU_A/L).

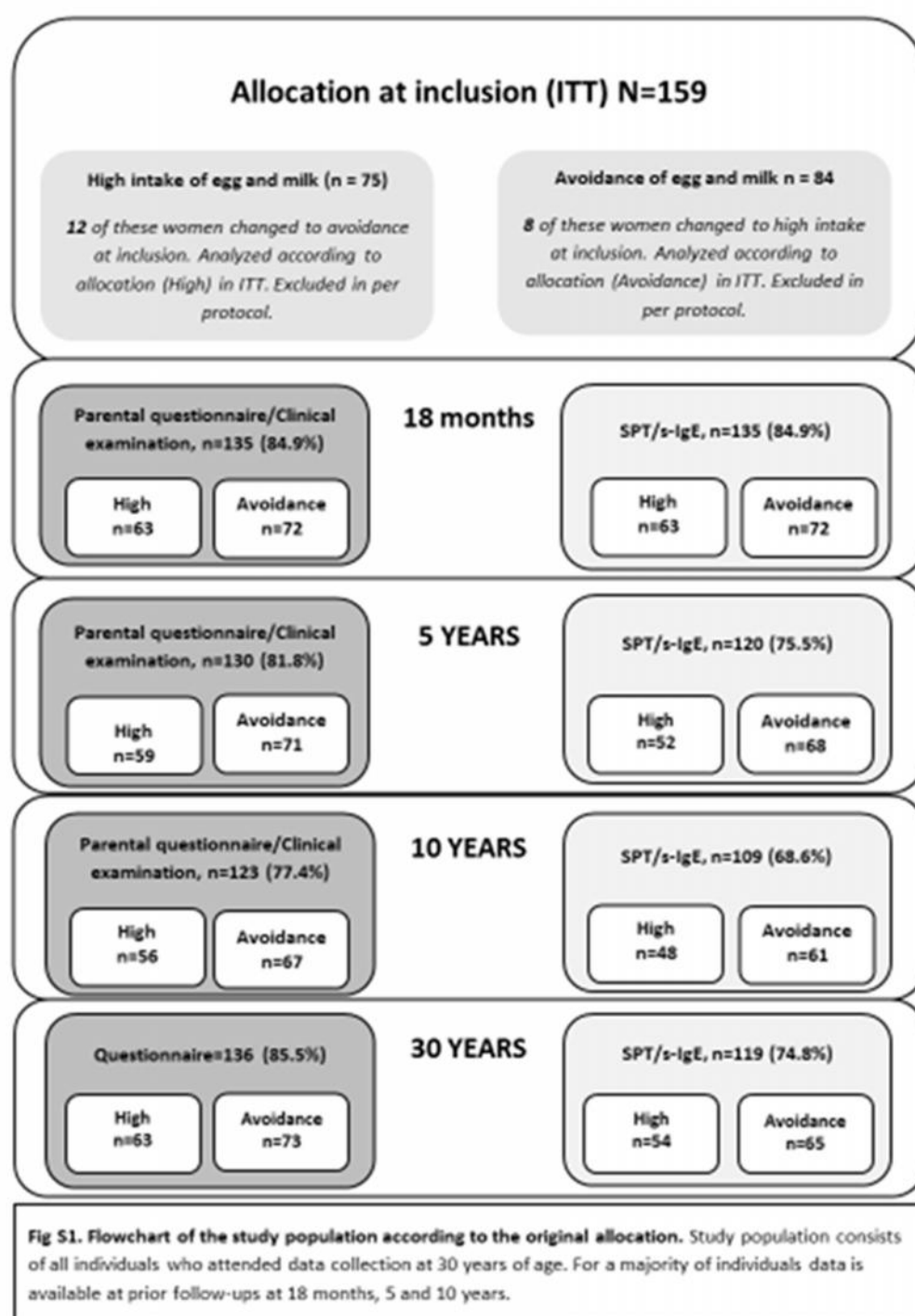
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86 National Birth Cohort. J Allergy Clin Immunol. 2012;130(3):724-32.

Table S1. Definitions of health outcomes

Variables	Definitions
Sensitization	A positive s-IgE (≥ 0.35 kU _A /L) and/or pos SPT (>3 mm) to that specific allergen. For egg and milk at 18 months and 5 years the cut-off for a positive test was ≥ 0.15 PRU/ml.
Food allergy at 18 months, 5, 10 and 26-30 years of age	At least two episodes of deteriorated eczema and/or urticarial and/or vomiting and/or wheezing after exposure to a defined allergen, in combination with a positive sensitization to that specific allergen. Lack of symptoms exclude food allergy, even when no blood sample or SPT available. Information from questionnaires at all ages. At 18 months, 5 and 10 years also from clinical examination.
Asthma at 18 months, 5 and 10 years of age	Three or more episodes of <i>wheezing</i> , signs of <i>bronchial hyper-reactivity</i> (wheezing or severe coughing at exertation and/or exposure to exercise or cold weather) without ongoing upper respiratory infection and/or any episode of <i>wheezing</i> if relaxed to exposure to pollen and/or animal dander, <i>in combination with anti-asthmatic medication</i> (B2-agonist, theophyllamin, inhalation steroids) and <i>doctor's diagnosis of asthma</i> . Information from questionnaires and clinical examination.
Asthma at 26-30 years of age	Diagnostic criteria for asthma used by GA2LEN: <i>At least two of the following: 1) Episode of breathing difficulties and/or coughing without current infection during last 12 months 2) Doctor's diagnosis ever 3) Asthma medication any time during last 12 months /B2-agonist, steroids, leukotriene antagonists</i> Information from questionnaire. Doctor's diagnosis also from prior follow-ups.
Eczema at 18 months, 5 and 10 years of age	Defined according to Hanifin and Rajka and doctors diagnosis at clinical examination.
Eczema at 26-30 years of age	Defined as dry skin with itchy rashes and specific location of rash (flexures of arms/legs, wrists/fronts of ankles or neck) and/or hand eczema during last 12 months and/or doctor's diagnosis of eczema since 10 years of age. Information from questionnaire.
Rhinoconjunctivitis at 18 months, 5 and 10 years of age	Sneezing, running or blocked nose and/or itchy eyes at least twice after exposure to a particular allergen and/or seasonal exposure and unrelated to an infection. Information from questionnaires and clinical examination.
Rhinoconjunctivitis at 26-30 years of age	Symptoms from eyes/nose (suspected/evident) after exposure to furred pets and/or pollen and unrelated to an infection and/or doctors diagnosis of allergic rhinitis since 10 years of age. Information from questionnaire.



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Table S2. Prevalence of sensitization or allergy to hen's egg or cow's milk at follow-ups at 18 months, 5, 10 and 30 years.

		Intention to treat			Per protocol			
	Number of individuals at each follow-up	"High" n (%)	"Avoidance" n (%)	p-value	Number of individuals at each follow-up	"High" n (%)	"Avoidance" n (%)	p-value
Cow's milk								
<i>Sensitization</i>								
18 months	n=136	2 (3.2)	1 (1.4)	ns	n=116	1 (2.0)	1 (1.5)	ns
5 years	n=120	0	1 (1.5)	ns	n=106	0	1 (1.6)	ns
10 years	n=107	1 (2.1)	4 (6.8)	ns	n=93	1 (2.5)	3 (5.7)	ns
30 years	n=119	2 (3.7)	1 (1.5)	ns	n=101	2 (4.6)	0	ns
<i>Allergy</i>								
18 months	n=136	1 (1.6)	1 (1.4)	ns	n=116	1 (2.0)	1 (1.5)	ns
5 years	n=130	0	1 (1.4)	ns	n=113	0	1 (1.6)	ns
10 years	n=123	0	0	ns	n=106	0	0	ns
30 years	n=135	0	0	ns	n=115	0	0	ns
Hen's egg								
<i>Sensitization</i>								
18 months	n=136	11 (17.5)	10 (13.7)	ns	n=136	10 (19.6)	10 (15.4)	ns
5 years	n=120	0	1 (1.5)	ns	n=120	0	1 (1.6)	ns
10 years	n=107	1 (2.1)	3 (5.1)	ns	n=107	1 (2.5)	3 (5.7)	ns
30 years	n=119	2 (3.7)	3 (4.6)	ns	n=119	2 (4.6)	3 (5.3)	ns
<i>Allergy</i>								
18 months	n=136	1 (1.6)	2 (2.7)	ns	n=136	1 (2.0)	2 (3.1)	ns
5 years	n=130	0	1 (1.4)	ns	n=130	0	1 (1.6)	ns
10 years	n=123	0	1 (1.5)	ns	n=123	0	1 (1.7)	ns
30 years	n=135	0	1 (1.4)	ns	n=136	0	1 (1.6)	ns

Allergy = symptoms + sensitization (positive s-IgE ($\geq 0.35 \text{ kU}_A/\text{L}$) and/or pos SPT ($> 3 \text{ mm}$)).

If no symptoms registered in questionnaire, there is no allergy regardless of uncertain sensitization (no SPT or s-IgE available). This explains more individuals registered for allergies than for sensitization. P-value calculated with Fishers exact test.