										0.97-1.19		
12	2003	Australia	Cross-sectional	Doctor-diagnosed asthma	1601	M/F	20-44	Whole milk	No 1.00	Yes 0.73 0.54-0.99		Y
12	2003	Australia	Cross-sectional	Doctor-diagnosed asthma	1601	M/F	20-44	Ricotta cheese	No 1.00	Yes 1.45 0.93-2.26		N
12	2003	Australia	Cross-sectional	Doctor-diagnosed asthma	1601	M/F	20-44	Law-fat cheese	No 1.00	Yes 1.50 1.03-2.19		Y
12	2003	Australia	Cross-sectional	Doctor-diagnosed asthma	1601	M/F	20-44	Butter	No 1.00	Yes 0.52 0.32-0.82		Y
13	2002	Japan	Cross-sectional	Asthma at 7 M	2642	F	29.2 (mean)	Milk/milk products (during pregnancy)	per increased 80 kcal 0.99 0.81-1.21			N
14	2002	New Zealand	Cross-sectional	Asthma ever	293	M/F	7-10	Yoghurt (at <2 year) (times/week)	<1 1.00	1+ 1.1 0.6-2.4		N
14	2002	New Zealand	Cross-sectional	Asthma ever	293	M/F	7-10	Unpasteurized milk (at <2 year)	No 1.00	Yes 0.7 0.2-2.4		N
14	2002	New Zealand	Cross-sectional	Asthma ever	293	M/F	7-10	Pasteurized milk (at <2 year) (times/week)	<1 1.00	1+ 1.3 0.6-2.7		N
14	2002	New Zealand	Cross-sectional	Asthma ever	293	M/F	7-10	Cheese (at <2 year) (times/week)	<1 1.00	1+ 1.1 0.6-2.4		N
15	2001	Austria, Germany, and Switzerland	Cross-sectional	Asthma	2618	M/F	6-13	Stables and farm milk (<1 year)	Stables (-) Farm milk (-) 1.00	Stables (+) Farm milk (+) 0.14 0.04-0.48	Stables (+) Farm milk (-) 0.51 0.14-1.86	Stables (-) Farm milk (+) 0.48 0.21-1.1	N
15	2001	Austria, Germany, and Switzerland	Cross-sectional	Asthma	2618	M/F	6-13	Stables and farm milk (1+ year)	Stables (-) Farm milk (-) 1.00	Stables (+) Farm milk (+) 0.88 0.42-1.86			N

16	2001	Germany	Cross-sectional	Astham/asthmalike bronchitis	2348	M/F	5-14	Buter, margarine	Butter 1.00	Margarine 1.41 0.79-2.53	Mixed 1.42 0.73-2.76		N
17	2000	Saudi Arabia	Case-control	Asthma	Case: 114 Control: 202	M/F	12	Milk (portions/day)	>3 1.00	2-3 1.51 0.70-3.26	<2 2.4 1.21-4.75	0.04	Y
Wheeze													
5	2007	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Current wheeze	8263	M/F	5-13	Farm milk (times/week)	<1 1.00	1+ 0.74 0.58-0.96			Y
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Current wheeze	14,424	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.86 0.72-1.04			N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Current wheeze	14,424	M/F	5-13	Butter from farm milk (ever in life)	No 1.00	Yes 0.89 0.71-1.12			N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Current wheeze	14,424	M/F	5-13	Yoghurt from self produces or directly purchased on a farm (ever in life)	No 1.00	Yes 0.92 0.75-1.12			N
7	2006	The Netherlands	Cross-sectional	Current wheeze	598	M/F	8-13	Dairy products (g/day)	Low 7.5%	Medium 8.0%	High 10.1%		N
18	2006	Korea	Cross-sectional	Wheeze	24,260	M/F	6-12	Cow's milk				0.10	N
18	2006	Korea	Cross-sectional	Wheeze	24,260	M/F	6-12	Butter				0.83	N
10	2005	Sweden	Cross-sectional	Wheeze	1014	M/F	5-14	Fresh milk 0: never eaten 1: <1 time/week 2: 1 time/week 3: 1+ times/week	0.83 0.66-1.03 (change by one unit)				N

								4: daily								
10	2005	Sweden	Cross-sectional		Wheeze	1014	M/F	5-14	Butter 0: never eaten 1: <1 time/week 2: 1 time/week 3: 1+ times/week 4: daily	0.95 0.51-1.79 (change by one unit)						N
10	2005	Sweden	Cross-sectional		Wheeze	1014	M/F	5-14	Fermented milk 0: never eaten 1: <1 time/week 2: 1 time/week 3: 1+ times/week 4: daily	1.01 0.83-1.23 (change by one unit)						N
11	2003	The Netherland	Prospective	1 Y	Current wheeze	2978	M/F	2	Full cream milk (day/week)	<1 1.00	1-5 0.87 0.54-1.40	6-7 0.81 0.58-1.13				N
11	2003	The Netherland	Prospective	1 Y	Current wheeze	2978	M/F	2	Butter (day/week)	<1 1.00	1-5 1.12 0.71-1.77	6-7 0.49 0.28-0.87				Y
11	2003	The Netherland	Prospective	1 Y	Current wheeze	2978	M/F	2	Milk products (yoghurt and chocolate (day/week)	<6 1.00	6-7 0.68 0.54-0.86					Y
11	2003	The Netherland	Prospective	1 Y	Current wheeze	2978	M/F	2	Semi-skimmed milk (day/week)	<1 1.00	1-5 1.05 0.72-1.52	6-7 0.99 0.71-1.38				N
19	2003	Italy	Prospective	1 Y	Wheeze	4104	M/F	6-7	Bread and butter (times/week)	0 1.00	<1 1.20 0.79-1.81	1-2 1.04 0.62-1.73	3-4 1.64 0.57-4.72	>4 2.09 0.80-5.44	0.14	N
19	2003	Italy	Prospective	1 Y	Wheeze	4104	M/F	6-7	Milk (times/week)	0 1.00	<1 0.88 0.35-2.10	1-2 1.20 0.59-2.48	3-4 1.15 0.55-2.40	>4 0.90 0.47-1.71	0.35	N
19	2003	Italy	Prospective	1 Y	Wheeze	4104	M/F	6-7	Cheese (times/week)	0 1.00	<1 0.71 0.38-1.32	1-2 0.70 0.42-1.72	3-4 0.70 0.41-1.20	>4 0.86 0.49-1.52	0.86	N
14	2002	New Zealand	Cross-sectional		Current wheeze	293	M/F	7-10	Yoghurt (at <2 year) (times/week)	<1 1.00	1+ 1.0 0.4-2.3					N

14	2002	New Zealand	Cross-sectional		Current wheeze	293	M/F	7-10	Unpasteurized milk (at <2 year)	No 1.00	Yes 0.6 0.2-0.8			Y
14	2002	New Zealand	Cross-sectional		Current wheeze	293	M/F	7-10	Pasteurized milk (at <2 year) (times/week)	<1 1.00	1+ 1.1 0.5-2.5			N
14	2002	New Zealand	Cross-sectional		Current wheeze	293	M/F	7-10	Cheese (at <2 year) (times/week)	<1 1.00	1+ 1.4 0.5-3.3			N
15	2001	Austria, Germany, and Switzerland	Cross-sectional		Current wheeze	2618	M/F	6-13	Stables and farm milk (<1 year)	Stables (-) Farm milk (-) 1.00	Stables (+) Farm milk (+) 0.17 0.07-0.45	Stables (+) Farm milk (-) 0.43 0.12-1.52	Stables (-) Farm milk (+) 0.43 0.20-0.92	Y
15	2001	Austria, Germany, and Switzerland	Cross-sectional		Current wheeze	2618	M/F	6-13	Stables and farm milk (1+ year)	Stables (-) Farm milk (-) 1.00	Stables (+) Farm milk (+) 0.60 0.28-1.28			N
20	1984	Australia	Prospective	20M	Wheeze (cummulative incidence: %)	79	M/F	0	Feeding in the first 4 months	Cow's milk 31.3%	No cow's milk 21.4%			N
Eczema														
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional		Doctor-diagnosed atopic eczema	14,424	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.89 0.75-1.06			N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional		Doctor-diagnosed atopic eczema	14,424	M/F	5-13	Butter from farm milk (ever in life)	No 1.00	Yes 0.89 0.73-1.09			N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional		Doctor-diagnosed atopic eczema	14,424	M/F	5-13	Yoghurt from self produces or directly purchased on a farm (ever in life)	No 1.00	Yes 0.98 0.82-1.18			N

6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Current atopic eczema symptoms	14,424	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.89 0.76-1.05			N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Current atopic eczema symptoms	14,424	M/F	5-13	Butter from farm milk (ever in life)	No 1.00	Yes 0.94 0.77-1.14			N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Current atopic eczema symptoms	14,424	M/F	5-13	Yoghurt from self produces or directly purchased on a farm (ever in life)	No 1.00	Yes 0.91 0.76-1.08			N
8	2006	England	Cross-sectional	Current eczema symptoms	4767	M/F	Primary school children	Unpasteurized milk (times/week)	0 1.00	1-2 0.54 0.33-0.88	3+ 0.59 0.40-0.87		Y
21	2006	Germany	Cross-sectional	Eczema symptoms (incidence in 2 years)	2582	M/F	2	Buter, margarine	Mixed 1.00	Butter 1.29 0.89-1.88	Margarine 1.3 0.67-2.55		N
21	2006	Germany	Cross-sectional	Eczema symptoms (lifetime prevalence)	2582	M/F	2	Buter, margarine	Mixed 1.00	Butter 1.05 0.80-1.37	Margarine 1.71 1.12-2.61		N
21	2006	Germany	Cross-sectional	Doctor-diagnosed eczema (incidence in 2 years)	2582	M/F	2	Buter, margarine	Mixed 1.00	Butter 1.02 0.68-1.55	Margarine 1.7 0.84-3.41		N
21	2006	Germany	Cross-sectional	Doctor-diagnosed eczema (lifetime prevalence)	2582	M/F	2	Buter, margarine	Mixed 1.00	Butter 0.97 0.74-1.29	Margarine 2.10 1.36-3.25		N
9	2005	Germany	Cross-sectional	Atopic dermatitis ev	1084	M/F	18-29	Buter, margarine	Regular butter 1.00	Low-fat butter 1.07 0.53-2.15	Mixed 0.71 0.40-1.26	Margarin 1.17 0.68-2.01	N
13	2002	Japan	Cross-sectional	Atopic dermatitis	2642	M/F	0.6	Milk/milk products (during pregnancy)	per increased 80 kcal 0.79 0.66-0.96				Y
14	2002	New Zealand	Cross-sectional	Atopic eczema	293	M/F	7-10	Yoghurt (at <2 year)	<1	1+			N

				syndrome				(times/week)	1.00	0.6 0.3-1.2					
14	2002	New Zealand	Cross-sectional	Atopic eczema syndrome	293	M/F	7-10	Unpasteurized milk (at <2 year)	No 1.00	Yes 0.2 0.1-2.2					N
14	2002	New Zealand	Cross-sectional	Atopic eczema syndrome	293	M/F	7-10	Pasteurized milk (at <2 year) (times/week)	<1 1.00	1+ 1.4 0.7-3.0					N
14	2002	New Zealand	Cross-sectional	Atopic eczema syndrome	293	M/F	7-10	Cheese (at <2 year) (times/week)	<1 1.00	1+ 1.3 0.6-2.7					N
20	1984	Australia	Prospective	20M Atopic dermatitis (cumulative incidence: %)	79	M/F	0	Feeding pattern in the first 4 months	Cow's milk 43.1%	No cow's milk 57.1%					N
Allergic rhinitis															
22	2007	Japan	Cross-sectional	Allergic rhinitis	1002	F	29.8 (mean)	Dairy products (g/day)	Q1 1.00	Q2 1.34 0.80-2.26	Q3 1.06 0.62-1.81	Q4 0.64 0.35-1.13		0.10	N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Doctor-diagnosed rhinoconjunctivitis	14,424	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.56 0.43-0.73					Y
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Doctor-diagnosed rhinoconjunctivitis	14,424	M/F	5-13	Butter from farm milk (ever in life)	No 1.00	Yes 0.73 0.52-1.02					N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	Doctor-diagnosed rhinoconjunctivitis	14,424	M/F	5-13	Yoghurt from self produces or directly purchased on a farm (ever in life)	No 1.00	Yes 0.87 0.66-1.15					N
6	2006	Austria, Germany, The Netherlands, Sweden, and	Cross-sectional	Current rhinoconjunctivitis symptoms	14,424	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.70 0.57-0.85					Y

		Switzerland														
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional		Current rhinoconjunctivitis symptoms	14,424	M/F	5-13	Butter from farm milk (ever in life)	No 1.00	Yes 0.98 0.77-1.24					N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional		Current rhinoconjunctivitis symptoms	14,424	M/F	5-13	Yoghurt from self produces or directly purchased on a farm (ever in life)	No 1.00	Yes 0.95 0.77-1.17					N
8	2006	England	Cross-sectional		Current seasonal allergic rhinitis	4767	M/F	Primary school children	Unpasteurized milk (times/week)	0 1.00	1-2 1.06 0.66-1.72	3+ 0.61 0.36-1.02				N
9	2005	Germany	Cross-sectional		Hay fever ever	1084	M/F	18-29	Buter, margarine	Regular butter 1.00	Low-fat butter 0.72 0.41-1.26	Mixed 0.85 0.57-1.25	Margarin 1.15 0.77-1.71			N
19	2003	Italy	Prospective	1Y	Allergic rhinitis	4104	M/F	6-7	Bread and butter (times/week)	0 1.00	<1 0.72 0.49-1.07	1-2 0.98 0.65-1.48	3-4 1.10 0.43-2.80	>4 1.79 0.83-3.89	0.70	N
19	2003	Italy	Prospective	1Y	Allergic rhinitis	4104	M/F	6-7	Milk (times/week)	0 1.00	<1 1.11 0.59-2.08	1-2 0.62 0.36-1.09	3-4 0.56 0.31-0.99	>4 0.61 0.38-0.96	0.01	Y
19	2003	Italy	Prospective	1Y	Allergic rhinitis	4104	M/F	6-7	Cheese (times/week)	0 1.00	<1 0.77 0.46-1.28	1-2 0.77 0.50-1.19	3-4 0.74 0.47-1.16	>4 0.85 0.52-1.39	0.67	N
14	2002	New Zealand	Cross-sectional		Hayfever ever	293	M/F	7-10	Yoghurt (at <2 year) (times/week)	<1 1.00	1+ 0.3 0.1-0.7					Y
14	2002	New Zealand	Cross-sectional		Hayfever ever	293	M/F	7-10	Unpasteurized milk (at <2 year)	No 1.00	Yes 1.1 0.2-5.0					N
14	2002	New Zealand	Cross-sectional		Hayfever ever	293	M/F	7-10	Pasteurized milk (at <2 year) (times/week)	<1 1.00	1+ 1.7 0.7-4.6					N
14	2002	New Zealand	Cross-sectional		Hayfever ever	293	M/F	7-10	Cheese (at <2 year) (times/week)	<1 1.00	1+ 2.1					N

											0.8-5.6		
14	2002	New Zealand	Cross-sectional		Current allergic rhinitis	293	M/F	7-10	Yoghurt (at <2 year) (times/week)	<1 1.00	1+ 0.3 0.2-0.7		Y
14	2002	New Zealand	Cross-sectional		Current allergic rhinitis	293	M/F	7-10	Unpasteurized milk (at <2 year)	No 1.00	Yes 0.3 0.1-1.1		N
14	2002	New Zealand	Cross-sectional		Current allergic rhinitis	293	M/F	7-10	Pasteurized milk (at <2 year) (times/week)	<1 1.00	1+ 1.5 0.7-3.3		N
14	2002	New Zealand	Cross-sectional		Current allergic rhinitis	293	M/F	7-10	Cheese (at <2 year) (times/week)	<1 1.00	1+ 1.3 0.6-2.8		N
15	2001	Austria, Germany, and Switzerland	Cross-sectional		Hay fever	2618	M/F	6-13	Stables and farm milk (<1 year)	Stables (-) Farm milk (-) 1.00	Stables (+) Farm milk (+) 0.20 0.08-0.50	Stables (+) Farm milk (-) 0.25 0.05-1.13	Stables (-) Farm milk (+) 0.24 0.10-0.56	Y
15	2001	Austria, Germany, and Switzerland	Cross-sectional		Hay fever	2618	M/F	6-13	Stables and farm milk (1+ year)	Stables (-) Farm milk (-) 1.00	Stables (+) Farm milk (+) 0.88 0.44-1.74			N
16	2001	Germany	Cross-sectional		Hay fever	2348	M/F	5-14	Buter, margarine	Butter 1.00	Margarine 1.37 0.88-2.14	Mixed 1.53 0.93-2.50		N
16	2001	Germany	Cross-sectional		Rhinitis symptoms	2348	M/F	5-14	Buter, margarine	Butter 1.00	Margarine 1.41 1.01-1.97	Mixed 1.27 0.86-1.86		Y
20	1984	Australia	Prospective	20M	Rhinitis (cumulative	79	M/F	0	Feeding pattern in the first 4 months	Cow's milk 52.9%	No cow's milk 60.7%			N
Bronchial hyperreactivity														
12	2003	Australia	Cross-sectional		Bronchial hyperreactivity	1601	M/F	20-44	Milk	No 1.00	Yes 1.41 0.90-2.21			N
12	2003	Australia	Cross-sectional		Bronchial hyperreactivity	1601	M/F	20-44	Cheese, ice cream, and yogurt	No 1.00	Yes 1.01			N

										0.91-1.12	
12	2003	Australia	Cross-sectional	Bronchial hyperreactivity	1601	M/F	20-44	Whole milk	No 1.00	Yes 0.68 0.48-0.92	Y
12	2003	Australia	Cross-sectional	Bronchial hyperreactivity	1601	M/F	20-44	Ricotta cheese	No 1.00	Yes 1.62 1.04-2.55	Y
12	2003	Australia	Cross-sectional	Bronchial hyperreactivity	1601	M/F	20-44	Low-fat cheese	No 1.00	Yes 1.72 1.16-2.53	Y
12	2003	Australia	Cross-sectional	Bronchial hyperreactivity	1601	M/F	20-44	Butter	No 1.00	Yes 0.61 0.38-0.98	Y
Atopy											
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	IgE (Phadiatop) ≧3.5 kU/L	3818	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.93 0.71-1.22	N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	IgE (egg white, milk, fish, wheat, peanut, soya bean) ≧3.5 kU/L	3818	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.42 0.19-0.92	Y
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	IgE (pollen) ≧3.5 kU/L	3818	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.67 0.47-0.96	Y
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	IgE (house dust mit ≧3.5 kU/L	3818	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 1.35 0.98-1.87	N
6	2006	Austria, Germany, The Netherlands,	Cross-sectional	IgE (storage mite) ≧0.35 kU/L	3818	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 1.22 0.78-1.92	N

		Sweden, and Switzerland											
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	IgE (cat dander) ≧0.35 kU/L	3818	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.86 0.59-1.25			N
6	2006	Austria, Germany, The Netherlands, Sweden, and Switzerland	Cross-sectional	IgE (horse dander) ≧0.35 kU/L	3818	M/F	5-13	Farm milk (ever in life)	No 1.00	Yes 0.50 0.28-0.87			Y
8	2006	England	Cross-sectional	Positive skin prick test (any response)	944	M/F	Primary school children	Unpasteurized milk (times/week)	0 1.00	1-2 0.10 0.03-0.28	3+ 0.34 0.17-0.69		Y
8	2006	England	Cross-sectional	Positive skin prick test (3+ mm mean respose)	944	M/F	Primary school children	Unpasteurized milk (times/week)	0 1.00	1-2 0.01 0.03-0.37	3+ 0.24 0.10-0.53		Y
8	2006	England	Cross-sectional	Positive house dust mite (3+ mm mean respose)	944	M/F	Primary school children	Unpasteurized milk (times/week)	0 1.00	1-2 0.32 0.08-1.24	3+ 0.23 0.06-0.85		Y
8	2006	England	Cross-sectional	Positive grass pollen (3+ mm mean respose)	944	M/F	Primary school children	Unpasteurized milk (times/week)	0 1.00	1-2 0.13 0.01-1.09	3+ 0.30 0.10-0.86		Y
23	2006	Italy	Retrospective	Atopy (positive skin prick test to food allergens)	277 (with allergic mothers)	M/F	5 (mean)	Butter (during pregnancy)	<1time/month 1.00	1 time/week 0.49 0.16-1.43	2+ times/week 0.84 0.26-2.71	0.80	N
23	2006	Italy	Retrospective	Atopy (positive skin prick test to food allergens)	627 (without allergic mothers)	M/F	5 (mean)	Butter (during pregnancy)	<1time/month 1.00	1 time/week 0.91 0.37-2.25	2+ times/week 0.92 0.27-3.13	0.46	N
23	2006	Italy	Retrospective	Atopy (positive skin prick test to inhalant allergens)	277 (with allergic mothers)	M/F	5 (mean)	Butter (during pregnancy)	<1time/month 1.00	1 time/week 0.27 0.10-0.73	2+ times/week 1.59 0.51-4.97	0.77	N
23	2006	Italy	Retrospective	Atopy (positive skin prick	627 (without allergic mothers)	M/F	5 (mean)	Butter (during pregnancy)	<1time/month 1.00	1 time/week 1.73	2+ times/week 0.81	0.15	N

			test to inhalant allergens)							1.00-2.99	0.38-1.70		
21	2006	Germany	Cross-sectional	Allergic sensitizatio (food or inhalant allergens)	2582	M/F	2	Buter, margarine	Mixed 1.00	Butter 0.98 0.68-1.39	Margarine 1.52 0.89-2.58		N
21	2006	Germany	Cross-sectional	Allergic sensitizatio (food allergens)	2582	M/F	2	Buter, margarine	Mixed 1.00	Butter 1.03 0.69-1.55	Margarine 1.58 0.87-2.86		N
21	2006	Germany	Cross-sectional	Allergic sensitizatio (inhalant allergens)	2582	M/F	2	Buter, margarine	Mixed 1.00	Butter 1.00 0.57-1.72	Margarine 2.10 1.01-4.41		-
10	2005	Sweden	Cross-sectional	Atopic sensitization (self-reported)	1014	M/F	5-14	Fresh milk 0: never eaten 1: <1 time/week 2: 1 time/week 3: 1+ times/week 4: daily	0.94 0.76-1.15 (change by one unit)				N
10	2005	Sweden	Cross-sectional	Atopic sensitization (self-reported)	1014	M/F	5-14	Fermented milk 0: never eaten 1: <1 time/week 2: 1 time/week 3: 1+ times/week 4: daily	0.97 0.83-1.13 (change by one unit)				N
10	2005	Sweden	Cross-sectional	Atopic sensitization (self-reported)	1014	M/F	5-14	Butter 0: never eaten 1: <1 time/week 2: 1 time/week 3: 1+ times/week 4: daily	1.20 0.73-1.96 (change by one unit)				N
9	2005	Germany	Cross-sectional	Sensitization	1084	M/F	18-29	Buter, margarine	Regular butter 1.00	Low-fat butter 0.71 0.46-1.10	Mixed 0.76 0.55-1.05	Margarin 0.83 0.59-1.17	N
24	2004	German	Cross-sectional	Atopy (IgE 0.70+ kU/L)	321	M/F	18-44	Raw milk consumption	No 1.00	Yes 0.65 0.36-1.18			N
12	2003	Australia	Cross-sectional	Atopy (positive skin prick test 3+ mm)	1601	M/F	20-44	Milk	No 1.00	Yes 1.25 0.81-1.92			N

12	2003	Australia	Cross-sectional	Atopy (positive skin prick test 3+ mm)	1601	M/F	20-44	Cheese, ice cream, and yogurt	No 1.00	Yes 0.97 0.88-1.07			N
12	2003	Australia	Cross-sectional	Atopy (positive skin prick test 3+ mm)	1601	M/F	20-44	Whole milk	No 1.00	Yes 0.71 0.54-0.94			Y
12	2003	Australia	Cross-sectional	Atopy (positive skin prick test 3+ mm)	1601	M/F	20-44	Ricotta cheese	No 1.00	Yes 1.20 0.78-1.84			N
12	2003	Australia	Cross-sectional	Atopy (positive skin prick test 3+ mm)	1601	M/F	20-44	Low-fat cheese	No 1.00	Yes 1.02 0.70-1.48			N
12	2003	Australia	Cross-sectional	Atopy (positive skin prick test 3+ mm)	1601	M/F	20-44	Butter	No 1.00	Yes 0.77 0.54-1.11			N
14	2002	New Zealand	Cross-sectional	Positive skin prick test (any response)	275	M/F	7-10	Yoghurt (at <2 year) (times/week)	<1 1.00	1+ 0.8 0.4-1.7			N
14	2002	New Zealand	Cross-sectional	Positive skin prick test (any response)	275	M/F	7-10	Unpasteurized milk (at <2 year)	No 1.00	Yes 0.6 0.2-1.9			N
14	2002	New Zealand	Cross-sectional	Positive skin prick test (any response)	275	M/F	7-10	Pasteurized milk (at <2 year) (times/week)	<1 1.00	1+ 0.8 0.4-1.7			N
14	2002	New Zealand	Cross-sectional	Positive skin prick test (any response)	275	M/F	7-10	Cheese (at <2 year) (times/week)	<1 1.00	1+ 0.7 0.3-1.4			N
25	2001	Crete	Cross-sectional	Atopy (positive skin prick test)	997	M/F	11-19	Farm animal contact (any) and unpasteurized milk (<	Farm (-) Milk (-) 1.00	Farm (+) Milk (-) 0.56 0.35-0.88	Farm (-) Milk (+) 0.32 0.13-0.78	Farm (+) Milk (+) 0.58 0.34-0.98	Y
15	2001	Austria, Germany, and Switzerland	Cross-sectional	Atopic sensitisation (positive 1+ IgE)	901	M/F	6-13	Stables and farm milk (<1 year)	Stables (-) Farm milk (-) 1.00	Stables (+) Farm milk (+) 0.32 0.17-0.62	Stables (+) Farm milk (-) 0.56 0.25-1.27	Stables (-) Farm milk (+) 0.43 0.24-0.77	Y
15	2001	Austria, Germany, and	Cross-sectional	Atopic sensitisation (positive 1+ IgE)	901	M/F	6-13	Stables and farm milk (1+ year)	Stables (-) Farm milk (-)	Stables (+) Farm milk (+)			N

	Switzerland								1.00	0.99 0.58-1.69		
16	2001 Germany	Cross-sectional	Sensitized (RAST class≧1, IgE≧0.35kU/L)	2348	M/F	5-14	Buter, margarine	Butter 1.00	Margarine 1.30 1.01-1.67	Mixed 1.30 0.97-1.75		Y

Y: significant association
N: not statistically siginificant

Ⅲ. 研究成果の刊行一覧・別冊

研究成果の刊行に関する一覧表

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
Miyake Y, Sasaki S, Tanaka K, Ohya Y, Miyamoto S, Matsunaga I, Yoshida T, Hirota Y, Oda H, The Osaka Maternal and Child Health Study Group.	Fish and fat intake and prevalence of allergic rhinitis in Japanese females: the Osaka Maternal and Child Health Study.	J Am Coll Nutr.	26 (3)	279-287	2007
Miyake Y, Ohya Y, Tanaka K, Yokoyama T, Sasaki S, Fukushima W, Ohfuji S, Saito K, Kiyohara C, Hirota Y, The Osaka Maternal and Child Health Study Group.	Home environment and suspected atopic eczema in Japanese infants: The Osaka Maternal and Child Health Study.	Pediatr Allergy Immunol.	18 (5)	425-432.	2007
Miyake Y, Arakawa M, Tanaka K, Sasaki S, Ohya Y.	Cross-sectional study of allergic disorders associated with breastfeeding in Japan: The Ryukyus Child Health Study.	Pediatr Allergy Immunol.	18 (5)	433-440.	2007
Tanaka K, Miyake Y, Arakawa M, Sasaki S, Ohya Y.	Prevalence of asthma and wheeze in relation to passive smoking in Japanese children.	Ann Epidemiol.	17 (12)	1004-1010.	2007
Tanaka K, Miyake Y, Sasaki S, Ohya Y, Matsunaga I, Yoshida T, Hirota Y, Oda H, The Osaka Maternal and Child Health Study Group.	Relationship between intake of vegetables, fruit, and grains and the prevalence of tooth loss in Japanese women.	J Nutr Sci Vitaminol.	53 (6)	522-528.	2007
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Miyake Y, Tanaka K, Sasaki S, Kiyohara C, Ohya Y, Fukushima W, Yokoyama T, Hirota Y.	Breastfeeding and the risk of wheeze and asthma in Japanese infants: The Osaka Maternal and Child Health Study.	Pediatr Allergy Immunol.		in press.	
田中景子、三宅吉博.	アレルギー疾患の発症関連要因.	公衆衛生.	72 (3)	184-189	2008

Original Research

Fish and Fat Intake and Prevalence of Allergic Rhinitis in Japanese Females: the Osaka Maternal and Child Health Study

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Key words: allergic rhinitis; cross-sectional study; fat; fish; Japanese females

Objective: It remains uncertain whether intake of fish or n-3 polyunsaturated fatty acids is preventive against allergic disorders. This cross-sectional study investigated the association of intake of selected high-fat foods and specific types of fatty acids with the prevalence of allergic rhinitis in Japan where intake of fish is high.

Methods: Study subjects were 1002 Japanese pregnant females. Allergic rhinitis (including cedar pollinosis) was defined as present if subjects had received drug treatment at some point during the previous 12 months. Information on dietary factors was collected using a validated self-administered diet history questionnaire. Adjustment was made for age, gestation, parity, cigarette smoking, passive smoking at home and at work, indoor domestic pets, family history of asthma, atopic eczema, and allergic rhinitis, family income, education, mite antigen level in house dust, changes in diet in the previous month, season when data were collected, and body mass index.

Results: There was a tendency for an inverse dose-response association between fish intake and allergic rhinitis although the adjusted odds ratio for comparison of the highest with the lowest quartile was not statistically significant (p for trend = 0.09). Intake of eicosapentaenoic and docosahexaenoic acids was independently associated with a decreased prevalence of allergic rhinitis: the multivariate odds ratio for the highest quartile was 0.56 (95% confidence interval: 0.32–0.96, p for trend = 0.03). Intake of n-6 polyunsaturated fatty acids in the third quartile but not the second and fourth quartiles showed a tendency for an inverse association with the prevalence of allergic rhinitis. No measurable relationship was found between consumption of meat, eggs, dairy products, total fat, saturated, monounsaturated, and n-3 polyunsaturated fatty acids, and cholesterol or the ratio of n-3 to n-6 polyunsaturated fatty acids and allergic rhinitis.

Conclusion: Our findings suggest that the intake of eicosapentaenoic and docosahexaenoic acids may be associated with a reduced prevalence of allergic rhinitis.

INTRODUCTION

The etiology of allergic rhinitis is though to be largely environmental. Japanese cedar pollinosis is a common allergic disorder in Japan caused by inhalation of the pollen of the Japanese cedar. The age-adjusted prevalence value of Japanese cedar pollinosis was 19.4% throughout Japan [1]. The prevalence of allergic rhinitis in urban areas is higher than that in rural areas [1–3]. Therefore, factors associated with the traditional Japanese, but not Western, lifestyle may be protective

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*Other members of the Study Group are listed in the Appendix.

There is no conflict of interest.

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against allergic rhinitis. In particular, Japanese people consume a much larger quantity of fish than Western populations.

Epidemiological evidence is inconclusive regarding the association of intake of fish or n-3 polyunsaturated fatty acids with allergic disorders. A significant inverse relationship between eating fish more than once a week and the prevalence of bronchial hyperresponsiveness and that between oily fish intake and current asthma were reported in 2 cross-sectional studies in Australian children, respectively [4,5]. A case-referent study in Norway showed that among female adults with moderate to severe atopic dermatitis, intake of docosahexaenoic and eicosapentaenoic acids was lower than in the reference group [6]. The Oslo Birth Cohort Study found that fish consumption in the first year of life was related to a reduced risk of allergic rhinitis, but not asthma, at the age of 4 years [7]. An intervention study in Australian high-risk infants demonstrated that supplementation with n-3 fatty acids resulted in a 9.8% reduction in the prevalence of any wheeze during the first 18 months of life [8]. In contrast, a significant positive association of oily fish intake with the prevalence of asthma but not allergic rhinitis among adolescents was found in a cross-sectional study in Taiwan [9]. A significantly higher prevalence of asthma was noted among Japanese children who ate fish 1 to 2 times a week than among those who ate fish 1 to 2 times a month [10]. Several epidemiological studies reported no association of fish intake with any allergic disorders [11–15]. An association of the ratio of n-3 to n-6 polyunsaturated fatty acids with allergic rhinitis among German adults was shown in 2 epidemiological studies, but the results were inconsistent [16,17]. There is limited epidemiological information regarding the relationship of the intake of total fat, saturated fatty acids, monounsaturated fatty acids, and n-6 polyunsaturated fatty acids with allergic rhinitis [16–18].

Therefore, we wished to investigate the association of intake of selected high-fat foods and specific types of fatty acids with the prevalence of allergic rhinitis in Japan. We examined these issues in a cross-sectional study among Japanese pregnant females using baseline data from the Osaka Maternal and Child Health Study (OMCHS).

SUBJECTS AND METHODS

Study Population

The OMCHS is an ongoing prospective cohort study that assesses preventive and risk factors for maternal and child health problems such as allergic disorders and postpartum depression. Details of the OMCHS have been described elsewhere [19]. In brief, the OMCHS is composed of a baseline survey completed by pregnant females and several post-natal follow-up surveys. Eligible females were those who became pregnant in Neyagawa City, which is 1 of the 44 municipalities in Osaka Prefecture, a metropolis in Japan with a total population of approximately 8.8 million. Of the 3639 eligible females in Neyagawa City, 627 (17.2%) participated in this study between November 2001 and March 2003. Eight pregnant females who did not live in Neyagawa City but who had become aware of the present study at an obstetric clinic before August 2002 decided by themselves to participate in this study. Also, there were 77 participants who received explanations regarding the OMCHS from public health nurses in 6 other municipalities between August 2002 and March 2003. From October 2002 to March 2003, 290 participants were recruited from a university hospital and three obstetric hospitals in 3 other municipalities; these women were recommended for participation in the OMCHS by an obstetrician. Finally, a total of 1002 pregnant women gave their fully informed consent in writing and completed the baseline survey. The ethics committees of the Osaka City University School of Medicine and the Osaka Prefectural Institute of Public Health approved the OMCHS.

Measurements

In the baseline survey, each participant filled out a set of 2 self-administered questionnaires and collected 2 dust samples from a 1 m^2 area of bedclothes and flooring for 1 minute using a vacuum cleaner fitted with a collection apparatus. Participants then mailed these materials to the data management center. Research technicians completed missing or illogical data by telephone interview.

A validated self-administered diet history questionnaire was used to assess dietary habits over a period of 1 month. The structure and validity of the questionnaire were described in detail elsewhere [20,21]. In this instrument, intake of 147 food items was calculated using an ad-hoc computer algorithm developed to analyze the questionnaire. Because composition values for dietary fatty acids were not available in the standard Japanese food composition table, they were obtained from the fatty acid food composition table of Japanese foods developed for Japanese populations [22]. Energy-adjusted intake by the residual approach was used for the analyses [23].

A second self-administered questionnaire inquired about age, gestation, parity, smoking habits, passive smoking exposure, personal history of allergic rhinitis, family history of asthma, atopic eczema, and allergic rhinitis, indoor domestic pets, family income, education, weight, height, and changes in diet in the previous 1 month. Allergic rhinitis (including Japanese cedar pollinosis) was defined as present when subjects had been treated with medications at some time in the previous 12 months. A family history of asthma, atopic eczema, and allergic rhinitis (including Japanese cedar pollinosis) was considered to be present if 1 or more parents or siblings of the study subject had manifested any of these allergic disorders. Body mass index was calculated by dividing self-reported body weight (kg) by the square of self-reported height (m).

Antigen levels from extracts of fine dust fractions were measured by a double-antibody sandwich enzyme-linked immunosorbent assay using a soluble antigen prepared from

whole *Dermatophagoides farinae* mite bodies as a reference standard and were expressed as antigen equivalent in $\mu g/m^2$ of surface area (Mitey checker®, Shinto Fine Co., Ltd., Osaka, Japan) [24,25]. Antigen levels were semi-quantitatively classified with scores of− (<2 $\mu g/m^2$), ± (5 $\mu g/m^2$), + (10 to 15 $\mu g/m^2$), and ++ (> 35 $\mu g/m^2$). In the present study, we used only antigen levels in the sample collected from bedclothes because the correlation between antigen levels from bedclothes and flooring was almost collinear (Spearman correlation coefficient = 0.54, $p < 0.0001$).

Statistical Analysis

Intake of selected foods rich in fat and specific types of fatty acids was categorized at quartile points based on the distribution of all study subjects. Age was divided into 3 categories (< 29, 29–31, and 32+ years); gestation into 3 (< 15, 15–20, and 21+ weeks); parity into 2 (0 and 1+); cigarette smoking into 3 (never, former, and current); passive smoking at home into 3 (never, former, and current); passive smoking at work into 3 (never, former, and current); family income into 3 (JPY < 4,000,000, 4,000,000–5,999,999, and 6,000,000+/year); education into 3 (< 13, 13–14, and 15+ years); dust mite antigen levels into 4 (−, ±, +, and ++); changes in diet in the previous 1 month into 3 (none or seldom, slight, and substantial); and season when data were collected into 4 (spring, summer, fall, and winter). Body mass index was used as a continuous variable.

Logistic regression analysis was used to estimate crude odds ratios (ORs) and 95% confidence intervals (CIs) and to control for the potential confounding effects of selected factors. Trend of association was assessed by a logistic regression model assigning scores to the levels of the independent variable. A p value < 0.05 was considered to indicate statistical significance. All computations were performed using the SAS software package version 8.2 (SAS Institute, Inc., Cary, NC).

RESULTS

Among 1002 pregnant females, 141 participants (14.1%) had used medications for allergic rhinitis (including Japanese cedar pollinosis) at some time in the previous 12 months. The mean age was 29.8 years and 30% of subjects were from 29 to 31 years of age (Table 1). About 70% of the women took part in this study by the 20th week of gestation. About half had a parity of 1 or more. Many more participants had a family history of allergic rhinitis than a family history of asthma or atopic eczema. Slight or substantial changes in diet in the previous 1 month were reported by 702 pregnant females due to nausea gravidarum (585 females), maternal and fetal health (107 females), and other reasons (10 females). Mean daily total energy and energy-adjusted fish consumption were 6815 kJ and 48.3 g, respectively (Table 2).

Table 1. Distribution of Selected Characteristics in 1002 Pregnant Females, OMCHS, Japan

Variable	*n* (%) or mean (SD)
Age (% years)	
<29	380 (37.9)
29–31	299 (29.8)
32+	323 (32.2)
Gestation (% weeks)	
<15	357 (35.6)
15–20	329 (32.8)
21+	316 (31.5)
Parity of 1 or more (%)	513 (51.2)
Cigarette smoking (%)	
Never	697 (69.6)
Former	121 (12.1)
Current	184 (18.4)
Passive smoking at home (%)	
Never	284 (28.3)
Former	224 (22.4)
Current	494 (49.3)
Passive smoking at work (%)	
Never	344 (34.3)
Former	538 (53.7)
Current	120 (12.0)
Family history of asthma (%)	101 (10.1)
Family history of atopic eczema (%)	138 (13.8)
Family history of allergic rhinitis (%)	429 (42.8)
Indoor domestic pets (cats, dogs, birds, or hamsters) (%)	114 (11.4)
Family income (% JPY/year)	
<4 000 000	301 (30.0)
4 000 000–5 999 999	403 (40.2)
6 000 000+	298 (29.7)
Education (% years)	
<13	323 (32.2)
13–14	413 (41.2)
15+	266 (26.6)
Mite antigen level in house dust (%)[1]	
−	436 (43.5)
±	297 (29.6)
+	196 (19.6)
++	73 (7.3)
Body mass index (kg/m^2)	21.4 (2.8)
Changes in diet in the previous 1 month (%)	
None or seldom	300 (29.9)
Slight	435 (43.4)
Substantial	267 (26.7)
Season when data were collected (%)	
Spring	318 (31.7)
Summer	162 (16.2)
Fall	223 (22.3)
Winter	299 (29.8)

[1] Antigen levels were semi-quantitatively classified with scores of − (<2 $\mu g/m^2$), ± (5 $\mu g/m^2$), + (10 to 15 $\mu g/m^2$), and ++ (>35 $\mu g/m^2$).

Table 3 shows crude and adjusted ORs and 95% CIs for the prevalence of allergic rhinitis according to dietary intake of selected foods high in fatty acids. Neither an inverse dose-response relationship between fish intake and the crude prevalence of allergic rhinitis nor the crude OR for comparison of

Table 2. Distribution of Daily Food and Nutrient Intake in 1002 Pregnant Females, OMCHS, Japan[1]

Variable	Mean (SD)
Daily intake	
Total energy (kJ)	6815.3 (1793.7)
Fish (g)	48.3 (27.4)
Meat (g)	59.8 (29.2)
Eggs (g)	28.3 (20.3)
Dairy products (g)	192.5 (123.1)
Daily nutrient intake	
Total fat (g)	54.3 (10.3)
Saturated fatty acids (g)	16.6 (3.5)
Monounsaturated fatty acids (g)	19.0 (4.2)
n-3 Polyunsaturated fatty acids (g)	2.3 (0.8)
Eicosapentaenoic acid (g)	0.2 (0.2)
Docosahexaenoic acid (g)	0.3 (0.2)
n-6 Polyunsaturated fatty acids (g)	11.0 (2.8)
Cholesterol (mg)	265.2 (105.3)

[1] Food and nutrient intake were adjusted for total energy intake using the residual method.

the highest with the lowest quartile reached statistical significance (p for trend = 0.09). There was no evident association of consumption of meat, eggs, and dairy products with the crude prevalence of allergic rhinitis. Adjustment for age, gestation, parity, cigarette smoking, passive smoking at home and at work, indoor domestic pets, family history of asthma, atopic eczema, and allergic rhinitis, family income, education, mite antigen level in house dust, changes in diet in the past 1 month, the season when data were collected, and body mass index did not appreciably change these results.

Crude and adjusted ORs and 95% CIs for associations with specific types of fatty acids and cholesterol are presented in Table 4. For the sum of dietary intake of eicosapentaenoic and docosahexaenoic acids, the crude ORs for comparison of the fourth with the first quartile were statistically significant, showing a clear inverse dose-response relationship. After adjustment for the confounders under investigation, the inverse relationship remained significant, albeit slightly attenuated: the multivariate ORs for comparison of the third and fourth with the first quartile were 0.56 and 0.56 (95% CI = 0.33–0.94 and 0.32–0.96, respectively). Significant inverse dose-response associations were observed between individual intake of eicosapentaenoic and docosahexaenoic acids and the prevalence of allergic rhinitis in the multivariate model (p for trend = 0.05 and 0.04, respectively). Compared with n-6 polyunsaturated fatty acid intake in the first quartile, its consumption in the third quartile but not the second and fourth quartiles was marginally significantly related to a decreased prevalence of allergic rhinitis although the linear trend was not statistically significant in the multivariate model (p for trend = 0.47). Consumption of

Table 3. Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Allergic Rhinitis by Quartiles of Intake of Selected Foods High in Fat, OMCHS, Japan

Variable[1]	Prevalence	Crude OR (95% CI)	Adjusted OR (95% CI)[2]
Fish			
Q1 (23.1)	42/250 (16.8%)	1.00	1.00
Q2 (38.7)	37/251 (14.7%)	0.86 (0.53–1.39)	0.78 (0.46–1.29)
Q3 (51.8)	32/250 (12.8%)	0.73 (0.44–1.19)	0.63 (0.37–1.07)
Q4 (72.8)	30/251 (12.0%)	0.67 (0.40–1.11)	0.67 (0.39–1.14)
p for trend		0.09	0.09
Meat			
Q1 (33.0)	35/250 (14.0%)	1.00	1.00
Q2 (48.7)	37/251 (14.7%)	1.06 (0.64–1.75)	1.16 (0.68–1.97)
Q3 (63.3)	31/250 (12.4%)	0.87 (0.52–1.46)	0.86 (0.50–1.49)
Q4 (90.6)	38/251 (15.1%)	1.10 (0.67–1.81)	1.33 (0.78–2.27)
p for trend		0.91	0.52
Eggs			
Q1 (7.8)	40/250 (16.0%)	1.00	1.00
Q2 (19.2)	32/251 (12.8%)	0.77 (0.46–1.27)	0.74 (0.43–1.25)
Q3 (34.4)	34/250 (13.6%)	0.83 (0.50–1.36)	0.87 (0.51–1.46)
Q4 (52.0)	35/251 (13.9%)	0.85 (0.52–1.39)	0.81 (0.48–1.37)
p for trend		0.59	0.56
Dairy products			
Q1 (64.7)	37/250 (14.8%)	1.00	1.00
Q2 (142.9)	40/251 (15.9%)	1.09 (0.67–1.78)	1.34 (0.80–2.26)
Q3 (210.3)	38/250 (15.2%)	1.03 (0.63–1.69)	1.06 (0.62–1.81)
Q4 (313.7)	26/251 (10.4%)	0.67 (0.39–1.13)	0.64 (0.35–1.13)
p for trend		0.15	0.10

[1] Quartile medians in g/day adjusted energy intake using the residual method are given in parentheses.

[2] Adjustment for age, gestation, parity, cigarette smoking, passive smoking at home and at work, indoor domestic pets, family history of asthma, atopic eczema, and allergic rhinitis, family income, education, mite antigen level in house dust, changes in diet in the previous 1 month, season when data were collected, and body bass index (continuous).