

RESEARCH ARTICLE

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Effects of infant weight gain on subsequent allergic outcomes in the first 3 years of life



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Abstract

Background: The association between early weight gain and later allergic outcomes has not been well studied. We examined the relation between weight gain and the subsequent development of allergic outcomes in the first 36 months of life in a Singapore birth cohort.

Methods: In repeated visits in the first 15 months, we measured infant weight and administered questionnaires ascertaining allergic outcomes. At ages 18 and 36 months, we administered skin prick tests (SPTs) to inhalant and food allergens.

Results: At 18 months, 13.5% had a positive SPT, 3.5% had wheeze and a positive SPT, 3.9% had rhinitis and a positive SPT, and 6.1% had eczema and a positive SPT. Higher weight gain from 6 to 9 months, 9 to 12 months and 12 to 15 months were independently associated with a reduced risk of developing a positive SPT at 18 months (p -trend ≤ 0.03). At 36 months, 23.5% had a positive SPT, 11.9% had wheeze and a positive SPT, 12.2% rhinitis and a positive SPT, and 11.5% eczema and a positive SPT. Higher weight gain from 12 to 15 months was associated with a reduced risk of developing a positive SPT at 36 months (p -trend < 0.01). No significant associations were observed between weight gain in any period and wheeze, rhinitis or eczema combined with a positive SPT at 18 or 36 months.

Conclusion: Higher weight gain in the first 15 months of life was associated with a reduced risk of allergen sensitization, but not with combinations of allergic symptoms.

Trial registration: NCT01174875 Registered 1 July 2010, retrospectively registered.

Keywords: Obesity, Allergy, Allergen sensitization, Birth cohort, Early childhood

Background

Allergic diseases and childhood obesity have increased in parallel worldwide in recent decades, suggesting a potential causal link between them [1]. Obesity is also considered a state of chronic inflammation, with activation of multiple cytokines [2]. Positive associations between obesity and allergic diseases in childhood have been reported, [3–5] although studies of the association between weight gain and atopy have shown inconsistent results. [6, 7].

Most previous studies have focused on older children (≥ 3 years), [7, 8] and knowledge is limited on the impact of early weight gain on subsequent allergic sensitization and atopic conditions (e.g., eczema, asthma, and rhinitis). [9] We hypothesized that rapid weight gain during infancy would be associated with an increased risk of developing allergic outcomes later in childhood and tested this hypothesis in the Growing Up in Singapore Towards healthy Outcomes (GUSTO) birth cohort. To our knowledge, ours is the first study to examine the effect of weight gain in early life on allergic outcomes in an Asian population. This population has a dissimilar genetic constitution to Western populations, along with many differences in dietary and environmental exposures.

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Methods

The methodology of the GUSTO study has been described previously. [10, 11] Briefly, we recruited 1247 healthy pregnant mothers who agreed to enroll their offspring for future follow-up. Interviewers gathered information on demographics, family history of allergy, social data and lifestyle factors. Anthropometric measurements were carried out in the home at 3 weeks and 3, 6, 9, 12 and 15 months of age, with examination of the child at the study clinic site at 18 and 36 months. Definitions were standardized in the questionnaires administered at 3, 6, 9, 12, 15, 18, 24 and 36 months to ensure consistency during interviews and home visits. Skin prick testing (SPT) to inhalant allergens (house dust mites *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, and *Blomia tropicalis*) and to food allergens (egg, peanut and cow's milk) was carried out at the 18- and 36-month visits. All of the allergens for skin prick testing were obtained from Greer Laboratories (Lenoir, NC, USA), except for *B. tropicalis*, which was obtained from our in-house laboratory. SPTs were taken to be positive if the wheal was at least 3 mm, and a child was considered as SPT-positive if any one or more of the individual tests was positive with a positive reaction to the positive control (histamine) and a negative reaction to the negative control (saline).

Subjects were shown pictures of eczema. Physician-diagnosed atopic eczema was based on a positive answer to the written question: "Has your child ever been diagnosed with eczema?". "Wheezing" was based on a positive answer to the written question "Has your child ever wheezed?", while "rhinitis" was based on a positive response to the question "Has your child ever had sneezing, running nose, blocked or congested nose, snoring or noisy breathing during sleep or when awake that has lasted for 2 or more weeks duration?" Study team members called the subjects who reported rhinitis to collect information on the number of episodes of rhinitis and the duration of each episode. A case prior to 18 months required a single episode that lasted for at least 4 weeks or two or more episodes each lasting at least 2 weeks. New cases of rhinitis after 18 months were defined by one or more episodes lasting at least 2 weeks.

Allergic clinical outcomes until 18 months were to the above-noted written questions in the first 18 months, combined with a positive SPT at 18 months. Allergic clinical outcomes until 36 months were defined as positive responses to the above-noted written questions in the first 36 months, combined with a positive SPT at 36 months. Children were included in the analysis if they were at risk for development of new allergic outcomes, i.e., did not have the allergic outcome before the period of weight gain analyzed. The allergic outcome was classified as absent when the answers for all visits were "no."

Family history of allergy was defined as positive if the mother, father or an older sibling ever had atopic eczema, asthma or allergic rhinitis.

Serial anthropometric measurements of weight at birth, 3 weeks, and 3, 6, 9, 12 and 15 months were taken by trained research staff. Infant weight was recorded to the nearest gram using a calibrated infant scale (SECA 334 Weighing Scale, SECA Corp.). All measurements were taken in duplicate and the average used for all analyses.

Classification of breastfeeding has been previously described. [12] High breastfeeding was defined by exclusive or predominant breastfeeding for at least 4 months, with subsequent partial breastfeeding to at least 6 months, while low breastfeeding was defined as exclusive formula feeding or weaning before 3 months. Intermediate breastfeeding was defined as breastfeeding to at least 3 months but without meeting the criteria for high breastfeeding.

Ethics approval was obtained from the Domain Specific Review Board of Singapore National Healthcare Group and the Centralised Institutional Review Board of SingHealth. Informed written consent was obtained from all subjects.

Statistical analysis

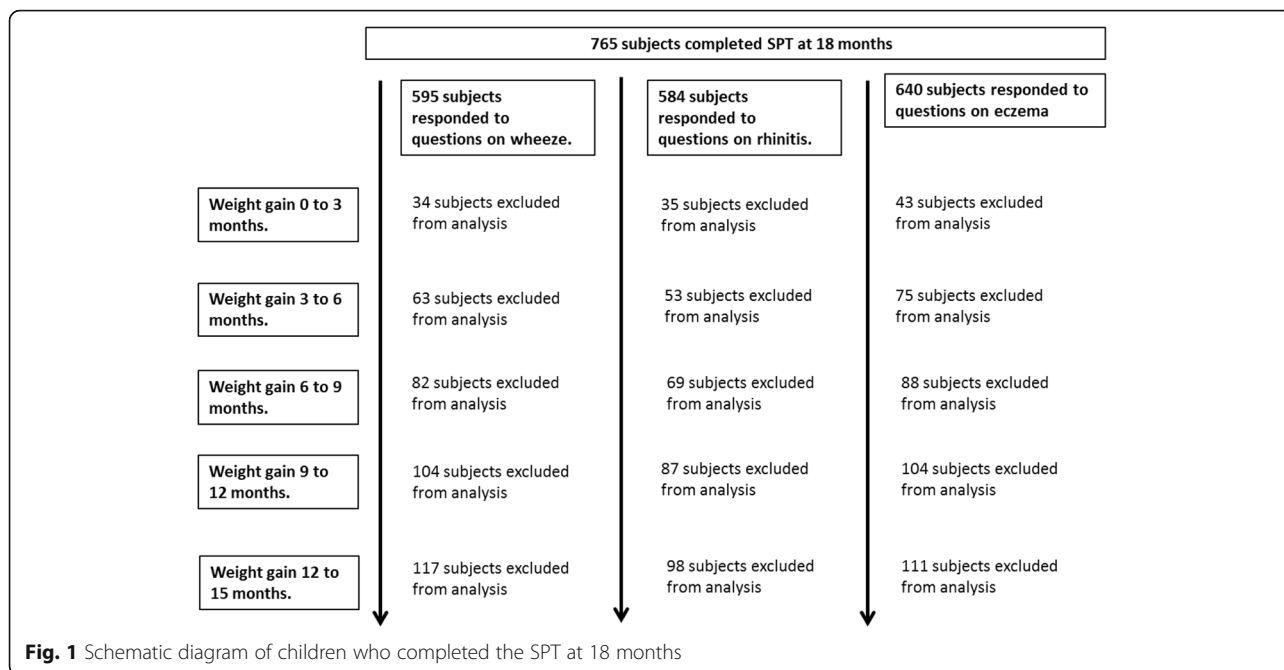
Statistical analysis was carried out using IBM SPSS version 20.0 (IBM SPSS Statistics, Armonk, NY). The weight change from the initial weight at the beginning of each period to the final weight at the end of each period was calculated in kilograms and divided into quartiles. The strength of association between quartiles of weight gain and the allergic outcomes was estimated using univariable and multivariable logistic regression (adjusting for relevant covariates). Chinese and male were used as the reference categories for ethnicity and sex, respectively.

Results

Description of the study cohort

Of the 1247 mothers recruited into GUSTO, 1059 gave birth to full-term infants (gestational age ≥ 37 weeks) and were considered eligible for this study. The response rates to questions on allergic outcomes and SPT as well as schematic diagrams of the children included in the analysis are shown in Figs. 1 and 2. The main reason for non-completion of the questionnaires was the mothers' not having been contactable and hence not having a home visit. Tables 1 and 2 compare the characteristics of those children with complete information and those with missing data. While the distribution of sex remains fairly similar between those with complete information and those with missing data, there are some differences in distribution of ethnicity and maternal education levels between them.

A total of 103 (13.5%) subjects had a positive SPT at 18 months, of whom 82 (7.7%) had a positive SPT to



inhalant allergens while 36 (3.4%) a positive SPT to food allergens and 15 (1.4%) a positive SPT to both. Twenty one (3.5%) subjects had wheeze and a positive SPT, 23 (3.9%) rhinitis and a positive SPT, and 39 (6.1%) eczema and a positive SPT.

A total of 184 children (23.5%) had a positive SPT at 36 months; 180 (17.0%) had a positive SPT to inhalant allergens, 15 (1.4%) had a positive SPT to food allergens and 11 (1.0%) a positive SPT to both. Seventy-seven(11.9%) subjects had wheeze and a positive SPT, 72 (12.2%)

rhinitis and a positive SPT, and 68 (11.5%) eczema and a positive SPT.

Associations between weight gain and allergic outcomes

As shown in Table 3, increasing weight gain quartile from 6 to 9 months, 9 to 12 months and 12 to 15 months was associated with a reduced risk of developing a positive SPT at 18 months (p-trend ≤0.03). Comparing extreme weight gain quartiles between 6 to 9 months, infants in the highest quartile had a reduced risk of a

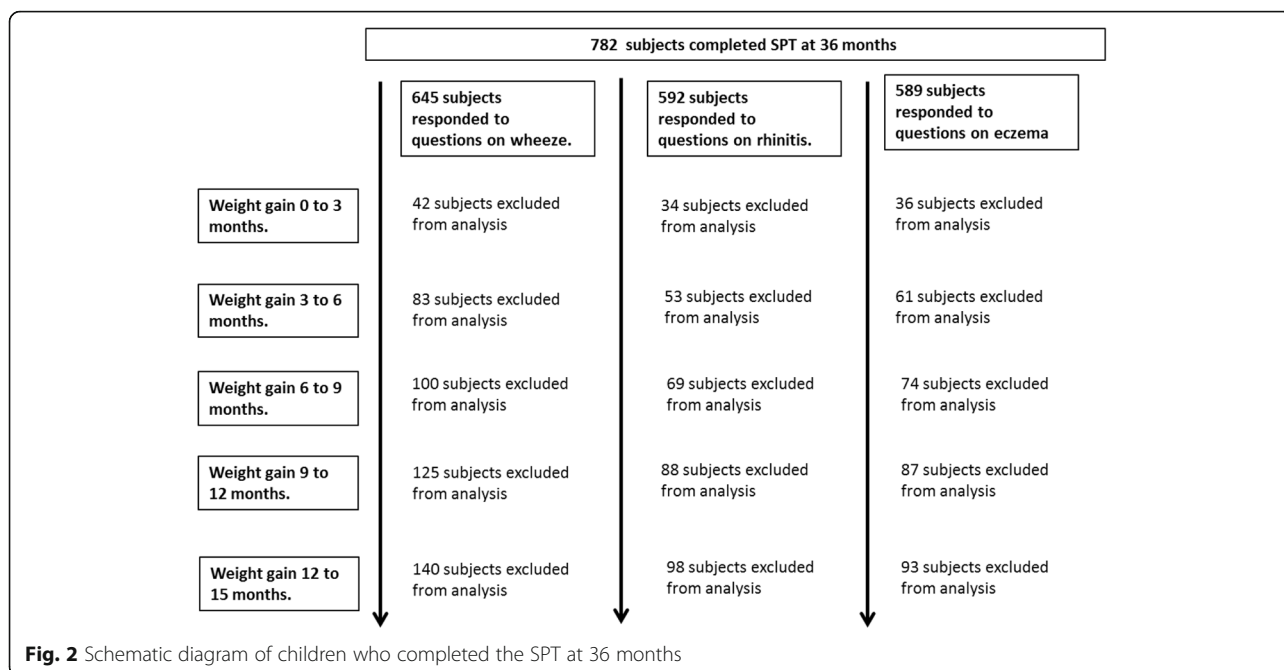


Table 1 Comparison of study children who completed questionnaires and SPT at 18 months vs other GUSTO children

	N(%)		P-value	Subjects that complete questions on wheeze and SPT		P-value	Subjects that complete questions on eczema and SPT		P-value	Subjects that complete SPT		P-value
	Subjects that complete questions on rhinitis and SPT	Excluded		Excluded	Subjects that complete questions on wheeze and SPT		Excluded	Excluded		Subjects that complete SPT		
Gender												
Male	299 (51.2)	262 (55.2)	0.2	299(50.3)	262 (56.5)	0.047	326 (50.9)	235 (56.1)	0.1	398 (52.0)	163 (55.4)	0.3
Female	285 (48.8)	213 (44.8)		296 (49.7)	202 (43.5)		314 (49.1)	184 (43.9)		367 (48.0)	131 (44.6)	
Ethnicity												
Chinese	352 (60.3)	253 (53.3)	0.1	363 (61.0)	242 (52.2)	<0.01	387 (60.5)	218 (52.0)	<0.01	438 (57.3)	167 (56.8)	0.8
Malay	138 (23.6)	127 (26.7)		147 (24.7)	118 (25.4)		156 (24.4)	109 (26.0)		194 (25.4)	71 (24.1)	
Indian	94 (16.1)	95 (20.0)		85 (14.3)	108 (22.4)		97 (15.2)	92 (22.0)		133 (17.4)	56 (19.0)	
Maternal Education ≥12 years	371 (64.0)	267 (57.3)	0.03	375 (63.5)	263 (57.8)	0.1	401 (63.1)	237 (57.7)	0.1	464 (61.3)	174 (60.2)	0.8
Maternal Education <12 years	209 (36.0)	199 (42.7)		216 (36.5)	192 (42.2)		234 (36.9)	174 (42.3)		293 (38.7)	115 (39.8)	

Table 2 Comparison of study children who completed questionnaires and SPT at 36 months vs other GUSTO children

	N(%)		P-value	Subjects that complete questions on wheeze and SPT		P-value	Subjects that complete questions on eczema and SPT		P-value	Subjects that complete SPT		P-value
	Subjects that complete questions on rhinitis and SPT	Excluded		Subjects that complete questions on wheeze and SPT	Excluded		Subjects that complete questions on eczema and SPT	Excluded		Subjects that complete SPT	Excluded	
Sex												
Male	303 (51.2)	258 (55.2)	0.2	342 (53.0)	219 (52.9)	1.00	304 (51.6)	257 (54.7)	0.3	414 (52.9)	147 (53.1)	1.00
Female	289 (48.8)	209 (44.8)		303 (47.0)	195 (47.1)		285 (48.4)	213 (45.3)		368 (47.1)	130 (46.9)	
Ethnicity												
Chinese	360 (60.8)	245 (52.5)	0.02	377 (58.4)	228 (55.1)	0.04	349 (59.3)	256 (54.5)	0.02	446 (57.0)	159 (57.4)	0.60
Malay	139 (23.5)	126 (27.0)		168 (26.0)	97 (23.4)		152 (25.8)	113 (24.0)		201 (25.7)	64 (23.1)	
Indian	93 (15.7)	96 (20.6)		100 (15.5)	89 (21.5)		88 (14.9)	101 (21.5)		135 (17.3)	54 (19.5)	
Maternal Education												
≥12 years	379 (64.2)	259 (56.8)	0.02	395 (61.5)	243 (60.1)	0.70	365 (62.4)	273 (59.2)	0.3	474 (61.1)	164 (60.7)	0.90
<12 years	211 (35.8)	197 (43.2)		247 (38.5)	161 (39.9)		220 (37.6)	188 (40.8)		302 (38.9)	106 (39.3)	

Table 3 Associations between infant weight gain and allergic outcomes by 18 months

Period of weight gain	Allergic outcomes	Quartile 1		Quartile 2		Quartile 3		Quartile 4		Reference group	Quartile 2		Quartile 3		Quartile 4		p-trend
		N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)	N(%)		Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)		
0 to 3 months	Wheeze with a positive skin prick test	1 (0.6)	5 (3.0)	2 (1.3)	11 (7.6)	1.00	1.4 (0.1–17.9)	1.3 (0.1–18.6)	4.5 (0.4–53.4)	0.2							
	Prolonged rhinitis with a positive skin prick test	3 (1.9)	1 (0.7)	2 (1.4)	7 (5.2)	1.00	0.2 (0.0–3.0)	0.2 (0.0–3.4)	1.7 (0.2–14.5)	0.2							
	Atopic eczema with a positive skin prick test	5 (3.0)	4 (2.4)	2 (1.3)	9 (6.2)	1.00	0.4 (0.1–2.4)	0.3 (0.0–2.2)	0.8 (0.1–4.9)	0.8							
3 to 6 months	Positive skin prick test	28 (14.1)	25 (14.0)	12 (6.7)	34 (19.3)	1.00	1.1 (0.5–2.4)	0.6 (0.2–1.4)	1.7 (0.7–3.9)	0.5							
	Wheeze with a positive skin prick test	5 (3.2)	4 (2.5)	2 (1.3)	3 (1.9)	1.00	1.1 (0.1–8.5)	0.5 (0.0–6.5)	1.8 (0.3–12.4)	0.7							
	Prolonged rhinitis with a positive skin prick test	0 (0)	4 (2.8)	4 (2.9)	4 (2.9)	1.00	#	#	#	#							
6 to 9 months	Atopic eczema with a positive skin prick test	5 (3.1)	3 (1.8)	1 (0.7)	3 (2.0)	1.00	1.6 (0.2–10.6)	#	1.0 (0.1–8.7)	0.6							
	Positive skin prick test	31 (17.6)	30 (16.8)	21 (12.4)	14 (8.3)	1.00	1.4 (0.7–3.0)	0.9 (0.4–2.0)	0.6 (0.2–1.4)	0.1							
	Wheeze with a positive skin prick test	3 (1.9)	2 (1.2)	5 (3.1)	3 (2.0)	1.00	0.3 (0.0–3.6)	1.6 (0.3–9.7)	0.6 (0.1–7.9)	0.9							
9 to 12 months	Prolonged rhinitis with a positive skin prick test	2 (1.4)	1 (0.7)	3 (2.1)	1 (0.8)	1.00	1.0 (0.1–12.6)	0.7 (0.1–9.6)	0.7 (0.0–11.4)	0.8							
	Atopic eczema with a positive skin prick test	5 (3.2)	4 (2.6)	1 (0.7)	1 (0.7)	1.00	2.4 (0.3–16.7)	0.6 (0.0–7.0)	#	0.3							
	Positive skin prick test	30 (17.9)	26 (15.4)	22 (13.2)	16 (9.7)	1.00	0.5 (0.2–1.1)	0.5 (0.2–1.0)	0.3 (0.1–0.7)	<0.01							
12 to 15 months	Wheeze with a positive skin prick test	3 (1.9)	1 (0.6)	3 (1.9)	0 (0)	1.00	0.7 (0.1–9.6)	1.8 (0.2–16.1)	#	0.5							
	Prolonged rhinitis with a positive skin prick test	1 (0.7)	0 (0)	0 (0)	2 (1.3)	1.00	#	#	#	#							
	Atopic eczema with a positive skin prick test	3 (2.0)	2 (1.3)	1 (0.7)	3 (2.0)	1.00	0.6 (0.0–7.0)	0.4 (0.0–4.9)	#	0.2							
18 months	Positive skin prick test	34 (20.0)	26 (15.8)	12 (7.3)	20 (11.3)	1.00	0.9 (0.4–1.8)	0.4 (0.2–0.96)	0.5 (0.2–1.2)	0.03							
	Wheeze with a positive skin prick test	0 (0)	3 (1.7)	0 (0)	1 (0.6)	1.00	#	#	#	#							
	Prolonged rhinitis with a positive skin prick test	0 (0)	0 (0)	0 (0)	0 (0)	1.00	#	#	#	#							
18 months	Atopic eczema with a positive skin prick test	1 (0.6)	0 (0)	0 (0)	2 (1.2)	1.00	#	#	#	#							
	Positive skin prick test	32 (17.7)	25 (14.3)	19 (11.2)	20 (11.3)	1.00	0.7 (0.3–1.4)	0.5 (0.2–1.0)	0.4 (0.2–0.8)	<0.01							

Weight gain at 0–3 months adjusted for birthweight for gestational age and sex, family history of allergy, ethnicity, sex, gestational age, breastfeeding, maternal education levels, maternal height and maternal BMI
 Weight gain (Kg) at 3–6 months, 6–9 months, 9–12 months and 12–15 months were adjusted for the baseline weight at the beginning of the period, family history of allergy, ethnicity, sex, breastfeeding, maternal education levels, maternal height and maternal BMI

#Not estimable, owing to insufficient number of children with studied outcomes Effects of infant weight gain on allergic outcomes

Values in italics have reached statistical significance with p-value <0.05

positive SPT at 18 months [adjusted odds ratio 0.3 (0.1–0.7)] compared with the lowest quartile, after adjustment for baseline weight at the beginning of the period, family history of allergy, ethnicity, sex, maternal education levels, breastfeeding, maternal height and maternal BMI. Similarly, the highest quartile of weight gain between 12 to 15 months was associated with a reduced risk of a positive SPT at 18 months vs the lowest quartile [adjusted odds ratio 0.4 (0.2–0.8)]. A similar but nonsignificant association was observed for weight gain from 9 to 12 months.

Further sub-analysis of the associations between increasing weight gain and positive SPT to inhalant allergens and to food allergens showed a similar trend. Increasing weight gain from 6 to 9 months was associated with a reduced risk of developing positive SPT to inhalant allergens, in particular to *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae* (p-trend <0.05 Additional file 1: Tables S1 and S2). Increasing weight gain from 9 to 12 months was associated with a reduced risk of developing positive SPT to food allergens (p-trend =0.03, Additional file 1: Table S1).

No significant associations were observed between weight gain in any period and wheeze, allergic rhinitis or atopic eczema.

As shown in Table 4, increasing weight gain quartile from 12 to 15 months was associated with a reduced risk of developing a positive SPT at age 36 months (p-trend <0.01). Comparing extreme weight gain quartiles between 12 to 15 months, infants in the highest quartile had a reduced risk of a positive SPT at 18 months [adjusted odds ratio 0.4 (0.2–0.8)] compared with the lowest quartile. Further sub-analysis of the association between increasing weight gain and positive SPT to inhalant allergens showed a similar trend. Increasing weight gain from 12 to 15 months was associated with a reduced risk of developing positive SPT to inhalant allergens, in particular to *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae* (p-trend <0.05, Additional file 1: Tables S3 and S4). Increasing weight gain from 3 to 6 months and 9 to 12 months was associated with a reduced risk of developing a positive SPT to food allergens at 36 months (p-trend <0.05, Additional file 1: Table S3).

No significant associations were obtained between weight gain in any period and allergic wheeze, allergic rhinitis or atopic eczema by 36 months.

Discussion

Rapid weight gain in the first year of life among GUSTO children was associated with a reduced risk of allergen sensitization at age 18 months. Weight gain from 12 to 15 months of life reduced the risk of allergen sensitization at both 18 and 36 months. Findings from previous studies have been mixed. The PROBIT study from Belarus found

no consistent associations between infant weight gain and SPT results at 6.5 years but observed an inverse association of weight gain velocity from 12 to 34 months and from 34 to 60 months. [7] In the United Kingdom, 1548 children were followed up with SPTs at 3 years; no significant associations were observed with postnatal weight gain velocity. [9] Similarly, the PIAMA birth cohort study from the Netherlands followed a subgroup ($n = 1554$) to 8 years and found no associations between BMI changes from 1 to 2 years and allergen-specific IgE at 8 years. [8] Finally, the SCAALA cohort study from Brazil reported a lower mean z-score for growth rate in the first 2 years of life among non-sensitized (SPT-negative) children aged 4–11 years. [6].

A possible reason for the inconsistent results of these studies is the earlier age at which SPTs were obtained in the GUSTO cohort: 18 and 36 months in our study vs 3–11 years in other cohorts. Allergen sensitization patterns are known to change with age. [13, 14] The association we observed between increased weight gain and reduced subsequent allergen sensitization may be a chance finding, however, and requires confirmation in other studies. While our observations are in agreement with studies reporting an increased sensitization to food allergens in underweight individuals, [15] other studies have reported increased food allergen sensitization in overweight individuals vs those of normal weight. [16, 17] If confirmed, one possible mechanism for the associations we observed is increased leptin secretion from adipose tissue, which could skew the immune response towards a T-helper type 1 (Th1) response, with subsequent production of pro-Th1 cytokines such as IFN- γ and IL-2 and suppressed production of pro-T-helper 2 (Th2) cytokines such as IL-4, [18–20] thereby reducing allergen sensitization.

We observed a nonsignificant positive association between weight gain from 0 to 3 months and allergic wheeze (i.e., wheeze with a positive SPT) by 18 months, which is limited by the small number of subjects with allergic wheeze. An association between increasing weight gain in the first 3 months and risk of wheeze has been reported in several previous studies. [7, 21] The PROBIT study from Belarus reported that weight gain velocity between 0 to 3 months was positively associated with ever having wheezed by 6.5 years. [7] Similarly, a study from the United Kingdom found a 1-SD increase in weight gain from birth to 6 months to be associated with a statistically significant 22% increase in risk of atopic wheeze (defined as ever having wheezed by 3 years and a positive SPT at 3 years). [9].

An important strength of our study is its prospective collection of outcome data at multiple time points. A limitation, however, is that allergic symptoms were all reported by the parent (usually the mother). We therefore used the SPT as an objective assessment of allergic

Table 4 Associations between infant weight gain and allergic outcomes by 36 months

Period of weight gain	Allergic outcomes	Quartile 1		Quartile 2		Quartile 3		Quartile 4		Reference group	Quartile 1		Quartile 2		Quartile 3		Quartile 4		p-trend
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)		N (%)	N (%)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	Adjusted OR (95% CI)	
0 to 3 months	Wheeze with a positive skin prick test	11 (6.7)	15 (9.3)	19 (11.8)	19 (13.1)	1.00	1.6 (0.6–4.5)	1.8 (0.6–5.4)	1.3 (0.4–4.0)	0.7									
	Rhinitis with a positive skin prick test	10 (6.7)	9 (6.3)	16 (10.6)	24 (17.6)	1.00	0.9 (0.3–3.1)	1.3 (0.4–4.3)	1.7 (0.5–6.0)	0.3									
	Atopic eczema with a positive skin prick test	5 (3.4)	10 (6.7)	9 (6.6)	10 (7.3)	1.00	1.9 (0.5–7.1)	1.4 (0.3–5.8)	1.1 (0.3–4.9)	0.9									
3 to 6 months	Positive skin prick test	34 (17.4)	36 (20.0)	45 (24.7)	59 (31.7)	1.00	1.3 (0.7–2.6)	1.6 (0.8–3.3)	1.6 (0.8–3.3)	0.2									
	Wheeze with a positive skin prick test	12 (7.6)	14 (8.4)	7 (4.5)	16 (11.0)	1.00	1.3 (0.4–3.9)	0.3 (0.1–1.5)	2.6 (0.9–7.3)	0.2									
	Rhinitis with a positive skin prick test	9 (6.3)	22 (14.7)	10 (7.0)	13 (10.3)	1.00	6.7 (1.4–31.8)	3.2 (0.6–16.4)	4.5 (0.9–22.2)	0.3									
6 to 9 months	Atopic eczema with a positive skin prick test	7 (4.9)	6 (4.0)	2 (1.4)	7 (5.3)	1.00	0.8 (0.2–3.1)	0.2 (0.0–1.6)	1.0 (0.3–3.8)	0.8									
	Positive skin prick test	43 (23.8)	41 (22.7)	46 (25.8)	35 (21.1)	1.00	1.1 (0.6–2.2)	1.1 (0.6–2.1)	0.9 (0.5–1.8)	0.8									
	Wheeze with a positive skin prick test	12 (7.6)	11 (6.7)	13 (8.5)	8 (5.3)	1.00	0.4 (0.1–1.4)	0.7 (0.2–2.0)	1.1 (0.3–3.5)	0.9									
9 to 12 months	Rhinitis with a positive skin prick test	12 (8.3)	13 (9.2)	12 (8.6)	9 (7.1)	1.00	0.5 (0.1–1.8)	0.6 (0.2–2.0)	0.5 (0.1–1.9)	0.3									
	Atopic eczema with a positive skin prick test	6 (4.2)	7 (5.1)	4 (3.0)	2 (1.6)	1.00	1.4 (0.4–5.8)	0.8 (0.2–3.6)	0.7 (0.1–4.3)	0.6									
	Positive skin prick test	40 (23.3)	45 (25.9)	37 (22.2)	34 (20.4)	1.00	0.5 (0.3–0.96)	0.5 (0.3–1.0)	0.5 (0.3–1.0)	0.06									
12 to 15 months	Wheeze with a positive skin prick test	14 (8.9)	7 (4.5)	8 (4.9)	9 (5.5)	1.00	0.5 (0.1–1.6)	0.7 (0.2–2.1)	0.2 (0.0–0.8)	0.04									
	Rhinitis with a positive skin prick test	11 (8.2)	8 (6.0)	9 (6.1)	17 (11.7)	1.00	0.5 (0.1–2.3)	0.7 (0.2–2.7)	1.2 (0.3–4.2)	0.7									
	Atopic eczema with a positive skin prick test	4 (2.9)	1 (0.7)	6 (4.6)	4 (2.9)	1.00	#	1.3 (0.3–5.7)	0.5 (0.1–3.1)	0.9									
12 to 15 months	Positive skin prick test	43 (24.9)	39 (23.8)	37 (21.4)	39 (22.9)	1.00	0.9 (0.5–1.6)	0.8 (0.4–1.5)	0.5 (0.3–1.1)	0.1									
	Wheeze with a positive skin prick test	6 (3.6)	10 (6.0)	8 (4.8)	8 (4.6)	1.00	1.7 (0.5–5.5)	0.5 (0.1–2.1)	1.1 (0.3–4.0)	0.6									
	Rhinitis with a positive skin prick test	8 (6.1)	15 (10.7)	11 (7.6)	9 (6.0)	1.00	1.3 (0.3–5.2)	1.3 (0.3–5.1)	0.8 (0.2–3.3)	0.7									
12 to 15 months	Atopic eczema with a positive skin prick test	4 (2.7)	5 (3.3)	2 (1.4)	3 (1.9)	1.00	1.3 (0.3–6.3)	#	0.8 (0.1–5.4)	0.3									
	Positive skin prick test	49 (27.8)	40 (23.1)	37 (20.9)	37 (20.6)	1.00	0.6 (0.3–1.0)	0.4 (0.2–0.8)	0.4 (0.2–0.8)	<0.01									

Weight gain at 0–3 months adjusted for birthweight for gestational age and sex, family history of allergy, ethnicity, gestational age, sex, breastfeeding, maternal education levels, maternal height and maternal BMI. Weight gain (kg) at 3–6 months, 6–9 months, 9–12 months and 12–15 months were adjusted for the baseline weight at the beginning of the period, family history of allergy, ethnicity, sex, breastfeeding, maternal education levels, maternal height and maternal BMI
 #Not estimable, owing to insufficient number of children with studied outcomes
 Values in italics have reached statistical significance with *p*-value <0.5

sensitization, both alone and in combination with common symptoms and diagnoses that may have an allergic etiology. Another limitation is low statistical power, owing to missing data from non-completion of questionnaires. It will be important to track the future development of allergic diseases and immune phenotypes in our cohort to assess whether the associations we observed persist, and whether new ones emerge at later ages.

Conclusion

Higher weight gain in the first 15 months of life was associated with a reduced risk of allergen sensitization, but not with combinations of allergic symptoms. The dissociation between SPT and clinical symptoms could be due to the less specific nature of clinical symptoms of rash, rhinitis and wheezing which could be of non-atopic origins such as viral induced.

Additional file

Additional file 1: Table S1. Associations between infant weight gain and positive skin prick test to inhalant and food allergens by 18 months. **Table S2.** Associations between infant weight gain and positive skin prick test to individual allergens by 18 months. **Table S3.** Associations between infant weight gain and positive skin prick test to inhalant and food allergens by 36 months. **Table S4.** Associations between infant weight gain and positive skin prick test to individual allergens by 36 months. (DOCX 63 kb)

Abbreviations

CI: Confidence interval; OR: Odds ratio; SPT: Skin prick test

Acknowledgements

The co-authors acknowledge the contribution of Wei Wei Pang who classified the breastfeeding data and the rest of the GUSTO study group which includes Kenneth Kwek, Pratibha Agarwal, Dennis Bier, Arijit Biswas, Shirong Cai, Jerry Kok Yen Chan, Cornelia Yin Ing Chee, Helen Y. H Chen, Audrey Chia, Amutha Chinnadurai, Chai Kiat Chng, Mary Foong-Fong Chong, Shang Chee Chong, Mei Chien Chua, Chun Ming Ding, Eric Andrew Finkelstein, Doris Fok, Marielle Fortier, Yam Thiam Daniel Goh, Joshua J. Gooley, Wee Meng Han, Mark Hanson, Christiani Jeyakumar Henry, Joanna D Holbrook, Chin-Ying Hsu, Hazel Inskip, Jeevesh Kapur, Birit Leutscher-Broekman, Sok Bee Lim, Seong Feei Loh, Yen-Ling Low, Iliana Magiati, Lourdes Mary Daniel, Michael Meaney, Susan Morton, Cheryl Ngo, Krishnamoorthy Niduvaje, Anqi Qiu, Boon Long Quah, Victor Samuel Rajadurai, Mary Rauff, Jenny L. Richmond, Anne Rifkin-Graboi, Allan Sheppard, Borys Shuter, Leher Singh, Wing Chee So, Walter Stunkel, Lin Lin Su, Kok Hian Tan, Soek Hui Tan, Rob M. van Dam, Sudhakar K. Venkatesh, Inez Bik Yun Wong, P. C. Wong, George Seow Heong Yeo.

Funding

This research is supported by the Singapore National Research Foundation under its Translational and Clinical Research (TCR) Flagship Programme and administered by the Singapore Ministry of Health's National Medical Research Council (NMRC), Singapore- NMRC/TCR/004-NUS/2008; NMRC/TCR/012-NUHS/2014. This work is also supported by the National Medical Research Council, NMRC/CSA/022/2010 and NRF370062-HUJ-NUS (Project 10). Additional funding is provided by the Singapore Institute for Clinical Sciences, Agency for Science Technology and Research (A*STAR), Singapore. KMG is funded by the NIHR through the NIHR Southampton Biomedical Research Centre. The funders are not involved in the design and conduct of the study, data analysis and preparation of manuscript.

Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Authors contributions

LEX was involved in the study design, acquisition of data, analysis of the data and writing of the manuscript. AIM, GA, TOH, VBHP, LBW, TMT, SSE, YF contributed to the study design, acquisition of data and writing of the manuscript. CYH provided statistical advice for the analysis of the data, was involved in the study design and contributed to the writing of the manuscript. KK, GPD, GKM, SSM and CYC contributed to the design and conceptualization of the study, acquisition of data and to the writing of the manuscript. KMS was involved in the study design, analysis of the data and critical revision of the manuscript for intellectual content. LYS supervised the research and was involved in the study design, acquisition of data, analysis of data and critical revision of the manuscript for intellectual content. All authors read and approved the final manuscript.

Competing interests

Chong YS has received reimbursement for speaking at conferences sponsored by Abbott Nutrition, Nestle, and Danone. Godfrey KM has received reimbursement for speaking at conferences sponsored by Nestle and Shek LP has received reimbursement for speaking at conferences sponsored by Danone and Nestle and consulting for Mead Johnson and Nestle. Godfrey KM, Chong YS are part of an academic consortium that has received research funding from Abbot Nutrition, Nestle and Danone. Shek LP has received research funding from Danone.

Consent for publication

Not applicable.

Ethics approval and consent to participate

Ethical approval was obtained from the Centralized Institutional Review Board (CIRB) of SingHealth (reference 2009/280/D) and Domain Specific Review Board (DSRB) of Singapore National Healthcare Group (reference D/09/021). Conduct of this study was based on the guidelines in the Declaration of Helsinki. Written consent was obtained from the participants.

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Received: 2 November 2016 Accepted: 23 May 2017

Published online: 02 June 2017

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