Electronic Appendices

eAppendix 1: Comparison of custom programmed LCA (latent class analysis) with GBM (group based modeling) using PROC TRAJ

LCA: We determined the number of classes based on the AIC for models with 4, 5 or 6 classes. We considered at least 4 clusters to take full advantage of our relatively large dataset and to ensure we had sufficient granularity. We also used the AIC to determine whether a model with equal or unequal within cluster covariance matrices fitted better. We found that in both boys and girl models with 5 clusters and unequal within cluster covariance matrices fitted best.

GBM: We considered group based modeling in PROC TRAJ. For each sex, we first performed group-based modeling to determine the number of clusters, based on the AIC. For girls, the best clustering according to AIC (and actually BIC) was five clusters with a polynomial with order 3. For boys, the best clustering according to the AIC (and actually BIC) was four clusters with a polynomial with order 3.

The performance of LCA and GBM was compared in eTable 1 which shows that LCA performed better than Proc TRAJ due to the unrestricted assumption on variance-covariance matrices. The independent assumption for repeated observations in weight over time periods in Proc TRAJ was not valid. Based on the clustering using PROC TRAJ, the maximum of the correlation coefficients between weights at two occasions were 0.74 and 0.77 for girls and boys, respectively, both are highly significantly different from a zero correlation coefficient.

eTable 1: Comparison of latent class analysis and group based-modeling (PROC TRAJ)

Sex	Method	AIC	BIC
Boy	Latent class analysis – 5-clusters	19916	20548
	Proc TRAJ – 4-clusters, order=3	24640	24794
Girl	Latent class analysis – 5-clusters	15737	16360
	Proc TRAJ – 5-clusters, order=3	19010	19201

eAppendix 2: Latent class analysis

Growth trajectories were constructed by latent class analysis based on Vermunt's paper[18].

Weights were interpolated to exact ages (at 1m, 3m, 9m and 12m) by linear interpolation using all available weights up to 36m. This step was performed using PROC EXPAND.

Given each cluster, a vector of weights on different occasions (birth, 1m, 3m, 9m and 12m) was assumed to follow multivariate normal distribution. The prior probability of belonging to each cluster was assumed to be equal, i.e.,$1/K$, where K is the number of clusters. Thus, the likelihood function for all unknown parameters (means, variances and co-variances) was equal to $\prod_{i=1}^{n}\sum_{k} f(y_i \mid \theta_k)/K$, where y_i is a vector of weights on different occasions for the i^{th} individual, i.e., $y_i = (w_0, w_1, w_3, w_9, w_{12})$. Maximum likelihood estimators were obtained by Newton-Raphson optimization method.

We first performed maximum-likelihood hierarchical cluster analysis for mixtures of spherical multivariate normal distributions on those individuals with completed weight measures on all five occasions (birth, 1m, 3m, 9m and 12m) (1917 boys and 1801 girls). The means, variances and co-variances obtained from each cluster were then used as the starting values of unknown parameters for obtaining maximum likelihood estimators by numerical method.

For missing data, imputation is not necessary. Classification for observations with missing values works exactly the same as classification without missing values. $f(y_i \mid \theta_k)$ is simply based on the variables that are observed for the i^{th} individual. For example, if weight for 3m is missing, $f(y_i \mid \theta_k)$ still follows a multivariate normal distribution where $y_i = (w_0, w_1, w_9, w_{12})$.

The posterior probability of belonging to the k^{th} trajectory for the i^{th} individual is equal to $\frac{f_k(y_i \mid \hat{\theta}_k)}{\sum_k f_k(y_i \mid \hat{\theta}_k)}$. For each individual, the probabilities of belonging to each trajectory can be calculated. Analysis upon the probabilistic assignment of cluster trajectory was performed and similar results were obtained.

In longitudinal latent class analyses, a vector of weights on different occasions (birth, 1m, 3m, 9m and 12m) was assumed to follow a multivariate normal distribution for each sex. The mean vector was assumed to be different for each sex and each cluster and the covariance matrix was assumed to have unequal and equal covariance matrices across clusters for each

sex.

For each sex, we performed longitudinal latent class analyses for the number of clusters equal to 4, 5 & 6 and for unequal and equal within-cluster covariance matrices across clusters. Both the AIC and the BIC for five trajectories with unequal covariance matrices across clusters for each sex were smaller, as shown in eTable 2.

eTable 2: Comparison of latent class analysis models

	Model	AIC	BIC
Boys	4-cluster – unequal covariance	20312	20818
	5-cluster – unequal covariance	**19916**	**20548**
	6-cluster – unequal covariance	20480	21238
	4-cluster – equal covariance	23208	23430
	5-cluster – equal covariance	23138	23391
	6-cluster – equal covariance	23344	23628
Girls	4-cluster – unequal covariance	16019	16517
	5-cluster – unequal covariance	**15737**	**16360**
	6-cluster – unequal covariance	15865	16612
	4-cluster – equal covariance	18352	18570
	5-cluster – equal covariance	18347	18596
	6-cluster – equal covariance	18493	18773

e**Appendix 3**

eTable 3 Causes of admissions (with ICD-9CM codes) and the number of children (among 7833 included) ever hospitalised from 3 month to 8 years.

Causes of admissions	ICD-9CM[b]	No. of Admissions	No. of children subjects included	% of
Respiratory and related infections				
Whooping cough	33	0	0	0.0%
Streptococcal sore throat	34.0	1	1	0.01%
Otitis media	381-2	117	112	1.4%
Nasopharyngitis	460	9	9	0.1%
Sinusitis	461	2	2	0.03%
Pharyngitis	462	117	163	2.1%
Tonsillitis	463	129	122	1.6%
Laryngitis and tracheitis	464	111	103	1.3%
Upper respiratory tract infections of multiple or nonspecific sites	465	782	687	8.8%
Bronchitis and bronchiolitis	466;490	393	327	4.2%
Allergic rhinitis	477	1	1	0.01%
Pneumonia	480-6	523	445	5.7%
Influenza	487	86	86	1.1%
Asthma	493	302	207	2.6%
Any respiratory infections[a]		2633	1746	22.3%
Gastritis/gastroenteritis	535.00, 535.50, 558.9, 538, 535.40	389	362	4.6%
Non-respiratory infections				
Scarlet fever	034.1	9	9	0.1%
Infectious and parasitic disease	1-139 (≠ 33&34.0)	943	807	10.3%
Meningitis	320-1	2	2	0.03%
Keratitis	370	0	0	0.0%
Conjunctivitis	372.0-372.3	5	5	0.1%
Rheumatic fever	390-2	0	0	0.0%
Appendicitis	540-2	13	13	0.2%
Kidney infections	590	2	2	0.03%
Cystitis	595	2	2	0.03%
Urinary tract infections	599.0	96	71	0.9%
Infections of skin and subcutaneous tissue	680-6	41	38	0.5%
Infections specific to the perinatal period	771	1	1	0.01%
Convulsions	780.3	285	205	2.6%
Fever	780.6	9	9	0.1%
Diarrhea	787.91	0	0	0.0%
Any non-respiratory infections[a]		1399	1095	14.0%

(cont'd) Causes of admissions (with ICD-9CM codes) and the number of children (among 7833 included) ever hospitalised from 3 month to 8 years.

	ICD-9CM	No. of admissions	No. of children	% of subjects included
Non-infectious illnesses				
Neoplasms	140-239	114	24	0.3%
Endocrine, nutritional and metabolic diseases, and immunity disorders	240-279	22	17	0.2%
Diseases of the blood and blood-forming organs	280-289	39	31	0.4%
Mental disorders	290-319	25	17	0.2%
Diseases of the nervous system and sense organs	320-389 (≠ 320-1, 381-2, 370, 372.0-372.3)	114	69	0.9%
Diseases of the circulatory system	390-459	42	28	0.4%
Diseases of the respiratory system	460-519 (≠ 460-466, 477, 480-487, 490, 493)	50	48	0.6%
Diseases of the digestive system	520-579 (≠540-2, 535.00, 535.50, 558.9, 538, 535.40)	174	143	1.8%
Diseases of the genitourinary system	580-629 (≠ 590, 595, 599.0)	147	120	1.5%
Diseases of the skin and subcutaneous tissue	680-709 (≠ 680-6)	58	47	0.6%
Diseases of the musculoskeletal system and connective tissue	710-739	48	45	0.6%
Congenital anomalies	740-759	235	131	1.7%
Conditions originating in the perinatal period	760-779 (≠ 771)	3	3	0.04%
Symptoms, signs and ill-defined conditions	780-799 (≠ 780.3, 780.6,787.91)	259	219	2.8%
Factors influencing health status and contact with health service	V01-V85	153	115	1.5%
Any non-infection illness[a]		1483	883	11.3%
Accidents/Injuries	800-999; E800-E999	498	462	5.9%
Unknown causes	Missing	40	38	0.5%
All causes		6442	3193	40.8%

[a]Number of children is not equal to the summation of cases for individual type of illness because the same child could have been admitted for different causes

[b]Congenital conditions include Cancers [ICD9-CM: 140-208.9], chronic rheumatic heart disease [393-398], congenital anomalies of heart or circulatory system [745 – 745.9, 746 – 746.9, 747 – 747.9], congenital anomalies of respiratory system [748 – 748.9], ischemic heart disease [410-414], diseases of pulmonary circulation [415-417], diabetes mellitus [250], thalassemia [282.4], congenital pneumonia [770.0], severe mental retardation [318.1], hypothyroidism [243, 244.9], disorders of amino-acid transport and metabolism [270], disorders of carbohydrate transport and metabolism [271], disorders of lipid metabolism [272], Hirschsprung's disease [751.3], spina bifida [741], Encephaloceles [742.0] and Down syndrome [758.0]

eAppendix 4: AIC tables

eTable 4 **Akaike Information Criterion for growth trajectory models.**

	Adjusted model† includes		Adjusted model† includes	
	Main effects	Interaction with sex	Main effects and birth weight z-score	Interaction with birth weight z-score
Respiratory infections	9252	9260	9253	9260
Gastritis/gastroenteritis	2800	2806	2800	2806
Any infection	14358	14365	14352	14358
Non infectious illnesses	6112	6117	6100	6107
Any illness	15075	15081	15066	15072
Accidents	3357	3362	3359	3364

†Adjusted for gestational age, highest parental education, type of birth hospital, health status (congenital conditions) and sex.

eTable 5 **Akaike Information Criterion for 0-3 month growth rate models.**

	Adjusted model† includes		Adjusted model† includes	
	Main effects	Interaction with sex	Main effects and birth weight z-score	Interaction with birth weight z-score
Respiratory infections	10571	10573	10572	10574
Gastritis/gastroenteritis	2911	2913	2913	2915
Any infection	14434	14436	14432	14434
Non infectious illnesses	6639	6641	6582	6578
Any illness	16685	16687	16764	16772
Accidents	3496	3498	3498	3498

†Adjusted for gestational age, highest parental education, type of birth hospital, health status (congenital conditions) and sex.

eTable 6 **Akaike Information Criterion for 3-12 month growth rate models.**

	Adjusted model† includes		Adjusted model† includes	
	Main effects	Interaction with sex	Main effects and 3 month weight z-score	Interaction with 3 month weight z-score
Respiratory infections	8325	8327	8327	8328
Gastritis/gastroenteritis	2544	2544	2546	2548
Any infection	12923	12925	12925	12926
Non infectious illnesses	5633	5633	5613	5716
Any illness	13596	13597	15388	13590
Accidents	3038	3038	3040	3041

†Adjusted for gestational age, highest parental education, type of birth hospital, health status (congenital conditions) and sex.

eAppendix 5: Analyses results after excluding children without recent contacts or with congenital diseases

eTable 7 **Association of growth trajectory at 0-12 months with number of hospital admissions until 8 years of age, after excluding children without recent contacts or with congenital diseases.**

		Model 1[a]		Model 2[b]		Model 3[c]	
		IRR	95% CI	IRR	95% CI	IRR	95% CI
Respiratory infections	Trajectory I	1.00	Ref	1.00	Ref	1.00	Ref
	Trajectory II	1.04	0.86 , 1.26	1.04	0.86 , 1.25	1.05	0.87 , 1.27
	Trajectory III	1.11	0.92 , 1.35	1.14	0.94 , 1.37	1.16	0.96 , 1.41
	Trajectory IV	1.01	0.83 , 1.23	1.05	0.86 , 1.27	1.09	0.89 , 1.35
	Trajectory V	0.91	0.75 , 1.12	0.93	0.76 , 1.14	0.98	0.78 , 1.23
Gastritis/gastroenteritis	Trajectory I	1.00	Ref	1.00	Ref	1.00	Ref
	Trajectory II	0.98	0.69 , 1.38	0.98	0.69 , 1.39	0.97	0.68 , 1.37
	Trajectory III	0.84	0.58 , 1.21	0.85	0.59 , 1.23	0.82	0.56 , 1.20
	Trajectory IV	0.84	0.58 , 1.21	0.85	0.58 , 1.23	0.79	0.53 , 1.18
	Trajectory V	0.79	0.53 , 1.16	0.78	0.53 , 1.16	0.72	0.47 , 1.11
Any infection	Trajectory I	1.00	Ref	1.00	Ref	1.00	Ref
	Trajectory II	0.91	0.79 , 1.05	0.91	0.79 , 1.04	0.92	0.81 , 1.06
	Trajectory III	0.94	0.81 , 1.08	0.95	0.83 , 1.09	0.98	0.85 , 1.14
	Trajectory IV	0.84	0.73 , 0.97	0.86	0.75 , 1.00	0.92	0.79 , 1.07
	Trajectory V	0.86	0.74 , 1.00	0.87	0.75 , 1.01	0.94	0.80 1.10
Non infectious illnesses	Trajectory I	1.00	Ref	1.00	Ref	1.00	Ref
	Trajectory II	0.61	0.47 , 0.78	0.60	0.47 , 0.78	0.64	0.49 , 0.82
	Trajectory III	0.70	0.54 , 0.91	0.69	0.54 , 0.89	0.78	0.60 , 1.01
	Trajectory IV	0.55	0.43 , 0.72	0.56	0.43 , 0.74	0.69	0.52 , 0.91
	Trajectory V	0.53	0.41 , 0.70	0.54	0.41 , 0.71	0.68	0.50 , 0.92
Any illness	Trajectory I	1.00	Ref	1.00	Ref	1.00	Ref
	Trajectory II	0.83	0.72 , 0.95	0.83	0.72 , 0.95	0.85	0.74 , 0.97
	Trajectory III	0.88	0.77 , 1.01	0.89	0.78 , 1.02	0.94	0.81 , 1.08
	Trajectory IV	0.79	0.68 , 0.91	0.81	0.70 , 0.93	0.89	0.76 , 1.03
	Trajectory V	0.75	0.65 , 0.86	0.75	0.65 , 0.87	0.85	0.72 0.99
Accidents	Trajectory I	1.00	Ref	1.00	Ref	1.00	Ref
	Trajectory II	0.74	0.54 , 1.00	0.75	0.55 , 1.02	0.74	0.54 , 1.01
	Trajectory III	0.77	0.56 , 1.06	0.81	0.59 , 1.10	0.79	0.58 , 1.10
	Trajectory IV	0.80	0.58 , 1.09	0.82	0.60 , 1.13	0.80	0.57 , 1.13
	Trajectory V	0.87	0.63 , 1.19	0.90	0.65 , 1.24	0.87	0.61 1.24

[a] Model 1 unadjusted

[b] Model 2 adjusted for gestational age (as categorical variables), highest parental education (≤ 9th, 10th –

11th, ≥ 12th grades), type of birth hospital (private or public) and health status (presence or absence of congenital conditions) and sex.
[c]Model 3 additionally adjusted for z-score for birth weight.

eTable 8 **Associations of growth rate (change of weight-for-age z-score) at 0-3 months and 3-12 months and birth weight z-score with number of hospital admissions until 8 years of age, after excluding children without recent contacts or with congenital diseases.**

		Model 1[a]		Model 2[b]		Model 3[c]	
		IRR	95% CI	IRR	95% CI	IRR	95% CI
Change of weight for age z-score from birth to 3 months	Respiratory infections	1.01	0.95 , 1.08	1.04	0.98 , 1.11	1.03	0.96 , 1.11
	Gastritis/gastroenteritis	0.96	0.84 , 1.09	0.98	0.85 , 1.12	0.96	0.83 , 1.12
	Any infection	0.99	0.94 , 1.04	1.02	0.97 , 1.07	1.00	0.94 , 1.05
	Non-infectious illnesses	0.90	0.81 , 0.98	0.90	0.82 , 0.99	0.79	0.71 , 0.87
	Any illness	0.96	0.92 , 1.01	0.99	0.94 , 1.04	0.94	0.89 , 0.99
	Accidents/injuries	1.00	0.89 , 1.12	1.02	0.91 , 1.15	1.05	0.92 , 1.20
Change of weight for age z-score from 3 to 12 months	Respiratory infections	1.03	0.94 , 1.14	1.06	0.96 , 1.16	1.06	0.97 , 1.17
	Gastritis/gastroenteritis	0.95	0.79 , 1.14	0.97	0.80 , 1.16	0.95	0.78 , 1.15
	Any infection	0.98	0.91 , 1.05	1.01	0.94 , 1.09	1.01	0.93 , 1.08
	Non-infectious illnesses	1.18	1.03 , 1.33	1.19	1.04 , 1.35	1.06	0.92 , 1.21
	Any illness	1.04	0.98 , 1.12	1.07	1.00 , 1.15	1.03	0.96 , 1.11
	Accidents/injuries	0.85	0.72 , 1.00	0.88	0.75 , 1.03	0.89	0.75 , 1.06
Birth weight z-score	Respiratory infections	0.95	0.89 , 1.00	0.94	0.88 , 1.00	-	
	Gastritis/gastroenteritis	1.00	0.88 , 1.14	0.99	0.87 , 1.14	-	
	Any infection	0.95	0.90 , 1.00	0.93	0.89 , 0.98	-	
	Non-infectious illnesses	0.74	0.67 , 0.81	0.72	0.66 , 0.80	-	
	Any illness	0.90	0.86 , 0.94	0.88	0.84 , 0.92	-	
	Accidents/injuries	1.03	0.92 , 1.15	1.04	0.93 , 1.17	-	

[a]Model 1 unadjusted

[b]Model 2 adjusted for gestational age (as categorical variables), highest parental education (≤ 9th, 10th – 11th, ≥ 12th grades), type of birth hospital (private or public) and health status (presence or absence of congenital conditions which might affect growth or risk of infections) and sex.

[c]Model 3 additionally adjusted for birth weight for age z-score (or baseline weight for the model looking at growth at 3-12 months).