

ESM Table 1 Bacterial and Viral Infection timing and number in first 12 months of life by antibody and diabetes status

Infection Number/timing		AB+ Status			Multi-AB+ Status			T1D status		
		No AB+ N=1175	Any AB+ N=842	p- value#	Not Multi- AB+ N=1781	Multi- AB+ N=236	p- value#	Did Not develop T1D N=1883	Developed T1D N=134	p- value#
Number of Infections - % (N)	0	28.8% (338)	23.6% (199)	0.027	26.6% (474)	26.7% (63)	0.665	26.5% (498)	29.1% (39)	0.717
	1-3	47.2% (554)	49.3% (415)		48.5% (863)	44.9% (106)		48.4% (911)	43.3% (58)	
	4-6	18.5% (217)	19.2% (162)		18.5% (330)	20.8% (49)		18.6% (351)	20.9% (28)	
	6 or higher	5.6% (66)	7.8% (66)		6.4% (114)	7.6% (18)		6.5% (123)	6.7% (9)	
Number of Viral Infections - % (N)	0	38.1% (448)	34.4% (290)	0.137	36.8% (656)	34.8% (82)	0.531	36.6% (690)	35.8% (48)	0.480
	1-3	48.3% (568)	49.1% (413)		48.6% (866)	48.7% (115)		48.4% (912)	51.5% (69)	
	4-6	11.5% (135)	13.4% (113)		12.2% (218)	12.7% (30)		12.5% (236)	9.0% (12)	
	6 or higher	2.0% (24)	3.1% (26)		2.3% (41)	3.8% (9)		2.4% (45)	3.7% (5)	
Number of Bacterial Infections - % (N)	0	64.0% (752)	57.5% (484)	0.015	61.4% (1094)	60.2% (142)	0.940	61.6% (1159)	57.5% (77)	0.425
	1-3	32.3% (380)	39.1% (329)		35.1% (625)	35.6% (84)		35.0% (659)	37.3% (50)	
	4-6	3.2% (38)	3.2% (27)		3.1% (56)	3.8% (9)		3.1% (58)	5.2% (7)	
	6 or higher	0.4% (5)	0.2% (2)		0.3% (6)	0.4% (1)		0.4% (7)	0% (0)	
Number of Infections <3 mos of age - % (N)	0	72.9% (856)	67.5% (568)	0.007	71.3% (1270)	65.3% (154)	0.147	71.0% (1336)	65.7% (88)	0.354
	1-3	26.5% (311)	32.2% (271)		28.1% (500)	34.8% (82)		28.5% (536)	34.3% (46)	
	4-6	0.7% (8)	0.2% (2)		0.6% (10)	0% (0)		0.5% (10)	0% (0)	
	6 or higher	0% (0)	0.1% (1)		0.1% (6)	0% (0)		0.1% (1)	0% (0)	
Number of Infections between 3 and 6 mos of age - % (N)	0	65.3% (767)	62.6% (527)	0.633	64.3% (1145)	63.1% (149)	0.493	64.2% (1208)	64.2% (86)	0.846
	1-3	33.5% (394)	36.1% (304)		34.5% (615)	35.2% (83)		34.6% (652)	34.3% (46)	
	4-6	1.0% (12)	1.2% (10)		1.1% (19)	1.3% (3)		1.1% (20)	1.5% (2)	
	6 or higher	0.2% (2)	0.1% (1)		0.1% (2)	0.4% (1)		0.2% (3)	0% (0)	
Number of Infections	0	42.0% (494)	37.3% (314)	0.091	39.9% (711)	41.1% (97)	0.744	39.9% (751)	42.5% (57)	0.942

between 6 and 12 mos of age - % (N)	1-3	47.7% (561)	51.3% (432)		49.5% (882)	47.0% (111)		49.4% (930)	47.0% (63)	
	4-6	8.5% (100)	8.7% (73)		8.5% (152)	8.9% (21)		8.6% (162)	8.2% (11)	
	6 or higher	1.7% (20)	2.7% (23)		2.0% (36)	3.0% (7)		2.1% (40)	2.2% (3)	

p-values based on Chi- Square test or Fisher's Exact test (based on cell size)

ESM Table 2 Univariable and Multivariable (adjusted for HLA, Gender, Breastfeeding Duration and Birth Order) Cox regression results based on time to initial AB+ development. The definition other or unspecified infections, bacterial or viral, means previously not specified as eg pneumonia, sepsis etc

		Univariate Model Unadjusted Model				Multivariate Model Adjusted by HLA, Gender, Breastfeeding Duration and Birth Order			
Parameter	Level	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL
Age at First Infection (Categorical) (Ref = None reported)	0-<3 mos	0.7065	0.966	0.804	1.159	0.8889	0.987	0.820	1.187
	3-<6 mos	0.1426	0.859	0.702	1.052	0.2953	0.896	0.730	1.100
	6-12 mos	0.0882	0.842	0.690	1.026	0.1087	0.850	0.696	1.037
Age at First Viral Infection (Categorical) (Ref = None reported)	0-<3 mos	0.3126	0.909	0.756	1.093	0.4275	0.928	0.771	1.116
	3-<6 mos	0.6101	0.952	0.789	1.149	0.9521	0.994	0.823	1.201
	6-12 mos	0.0362	0.823	0.686	0.988	0.0425	0.828	0.689	0.994
Age at First Bacterial Infection (Categorical) (Ref = None reported)	0-<3 mos	0.0778	1.200	0.980	1.470	0.0683	1.210	0.986	1.484
	3-<6 mos	0.5088	0.923	0.726	1.172	0.6438	0.945	0.743	1.202
	6-12 mos	0.8429	1.018	0.853	1.215	0.7048	1.035	0.866	1.237
Number of Infections (Categorical) (Ref = 0)	1-3	0.2287	0.901	0.761	1.067	0.3085	0.915	0.772	1.085
	4-6	0.0807	0.831	0.675	1.023	0.1776	0.866	0.702	1.068
	6 or higher	0.7118	1.054	0.798	1.392	0.5550	1.089	0.821	1.445
Number of Infections (Continuous)		0.9440	0.999	0.973	1.026	0.8046	1.003	0.977	1.031
Number of Viral Infections (Categorical) (Ref = 0)	1-3	0.0546	0.863	0.743	1.003	0.0904	0.878	0.755	1.021
	4-6	0.5689	0.939	0.755	1.167	0.8159	0.974	0.783	1.213
	6 or higher	0.3738	1.200	0.803	1.792	0.2917	1.244	0.829	1.866
Number of Viral Infections (Continuous)		0.9384	1.001	0.968	1.036	0.6572	1.008	0.974	1.043
Number of Bacterial Infections (Categorical) (Ref = 0)	1-3	0.3382	1.071	0.931	1.232	0.2434	1.088	0.944	1.254
	4-6	0.4702	0.867	0.588	1.277	0.5112	0.877	0.594	1.296
	6 or higher	0.3412	0.509	0.127	2.043	0.2869	0.469	0.117	1.889
Number of Bacterial Infections (Continuous)		0.8044	0.993	0.943	1.047	0.8501	0.995	0.944	1.049
Infection Types (Categorical) (Ref = No Infections)	Bacterial Inf Only	0.0646	0.843	0.703	1.010	0.1068	0.861	0.718	1.033
	Viral Inf Only	0.8625	0.978	0.763	1.254	0.9558	0.993	0.772	1.277
	Viral and Bacterial	0.4444	0.931	0.775	1.118	0.6747	0.961	0.798	1.158
	1-3	0.2553	1.088	0.941	1.257	0.2298	1.093	0.945	1.265

		Univariate Model Unadjusted Model				Multivariate Model Adjusted by HLA, Gender, Breastfeeding Duration and Birth Order			
Parameter	Level	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL
Number of Infections before 3 mos (Categorical) (Ref = 0)	4-6	0.1680	0.377	0.094	1.510	0.1827	0.389	0.097	1.561
	6 or higher	0.0380	8.002	1.122	57.09	0.0278	9.146	1.273	65.71
Number of Infections before 3 mos (Continuous)		0.3255	1.042	0.960	1.132	0.2611	1.049	0.965	1.140
Number of Infections between 3 and 6 mos (Categorical) (Ref = 0)	1-3	0.7943	0.981	0.852	1.130	0.9093	1.008	0.874	1.163
	4-6	0.9009	0.961	0.514	1.797	0.8623	1.057	0.562	1.988
	6 or higher	0.7918	0.768	0.108	5.460	0.7708	0.747	0.105	5.325
Number of Infections between 3 and 6 mos (Continuous)		0.8145	1.009	0.939	1.084	0.4878	1.026	0.954	1.104
Number of Infections between 6 and 12 mos (Categorical) (Ref = 0)	1-3	0.1138	0.889	0.769	1.028	0.1486	0.898	0.776	1.039
	4-6	0.0559	0.780	0.605	1.006	0.0808	0.796	0.616	1.028
	6 or higher	0.2905	1.256	0.823	1.918	0.2424	1.290	0.842	1.975
Number of Infections between 6 and 12 mos (Continuous)		0.5072	0.987	0.949	1.026	0.6112	0.990	0.952	1.030
Occurrence of ANY Upper Respiratory Infection		0.3055	0.930	0.809	1.069	0.5675	0.960	0.834	1.105
Occurrence of ANY Gastroenteritis		0.5964	0.951	0.791	1.144	0.9069	0.989	0.822	1.190
Occurrence of ANY Urinary Tract Infection		0.8988	0.973	0.643	1.473	0.8991	0.974	0.643	1.474
Occurrence of ANY Middle Ear Infection		0.1497	0.887	0.754	1.044	0.1743	0.892	0.757	1.052
Occurrence of ANY Pneumonia		0.7329	1.047	0.804	1.364	0.6911	1.056	0.807	1.381
Occurrence of ANY Sepsis		0.7627	1.106	0.574	2.134	0.7266	1.125	0.582	2.172
Occurrence of ANY Other Bacterial Infection		0.0203	1.379	1.051	1.808	0.0135	1.410	1.073	1.852
Occurrence of ANY Other Viral Infection		0.8093	1.023	0.848	1.234	0.8010	1.025	0.849	1.237

		Univariate Model Unadjusted Model				Multivariate Model Adjusted by HLA, Gender, Breastfeeding Duration and Birth Order			
Parameter	Level	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL
Occurrence of ANY Other Viral Infection with Fever		0.9893	0.998	0.799	1.248	0.9567	1.006	0.805	1.258
Occurrence of ANY Antibiotic Use		0.8878	1.010	0.879	1.160	0.7466	1.023	0.889	1.178

ESM Table 3 Univariable and Multivariable (adjusted for HLA, Gender, Breastfeeding Duration and Birth Order) Cox regression results based on time to initial multiple-AB+ development. The definition other or unspecified infections, bacterial or viral, means previously not specified as eg pneumonia, sepsis etc

		Univariate Model Unadjusted Model				Multivariate Model Adjusted by HLA, Gender, Breastfeeding Duration and Birth Order			
Parameter	Level	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL
Age at First Infection (Categorical) (Ref = None reported)	0-<3 mos	0.7087	0.939	0.676	1.305	0.7400	0.945	0.678	1.318
	3-<6 mos	0.0787	0.709	0.484	1.040	0.1108	0.730	0.496	1.075
	6-12 mos	0.0381	0.669	0.457	0.978	0.0324	0.660	0.451	0.966
Age at First Viral Infection (Categorical) (Ref = None reported)	0-<3 mos	0.6523	0.923	0.652	1.307	0.7531	0.946	0.667	1.341
	3-<6 mos	0.9999	1.000	0.705	1.419	0.8285	1.040	0.732	1.477
	6-12 mos	0.2283	0.807	0.569	1.144	0.2079	0.798	0.562	1.133
Age at First Bacterial Infection (Categorical) (Ref = None reported)	0-<3 mos	0.1160	1.332	0.932	1.906	0.1467	1.308	0.910	1.880
	3-<6 mos	0.1929	0.722	0.442	1.179	0.1939	0.722	0.441	1.181
	6-12 mos	0.2500	0.810	0.567	1.159	0.2591	0.813	0.567	1.165
Number of Infections (Categorical) (Ref = 0)	1-3	0.0769	0.755	0.553	1.031	0.0761	0.753	0.550	1.030
	4-6	0.3450	0.835	0.575	1.214	0.4303	0.859	0.589	1.253
	6 or higher	0.6401	0.882	0.523	1.490	0.6309	0.878	0.516	1.493
Number of Infections (Continuous)		0.7214	1.009	0.961	1.060	0.6990	1.010	0.961	1.061
Number of Viral Infections (Categorical) (Ref = 0)	1-3	0.4073	0.887	0.668	1.178	0.4490	0.896	0.675	1.190
	4-6	0.5259	0.873	0.575	1.327	0.6581	0.909	0.597	1.386
	6 or higher	0.3697	1.370	0.688	2.728	0.3891	1.357	0.677	2.718
Number of Viral Infections (Continuous)		0.9423	1.002	0.940	1.069	0.8191	1.007	0.945	1.074
Number of Bacterial Infections (Categorical) (Ref = 0)	1-3	0.5848	0.928	0.708	1.215	0.5798	0.926	0.705	1.216
	4-6	0.9307	1.030	0.525	2.021	0.9857	1.006	0.510	1.984
	6 or higher	0.9577	0.948	0.133	6.779	0.7921	0.767	0.106	5.524
Number of Bacterial Infections (Continuous)		0.5544	1.028	0.937	1.128	0.6898	1.019	0.929	1.118
Infection Types (Categorical) (Ref = No Infections)	Bacterial Inf Only	0.1228	0.770	0.553	1.073	0.1391	0.778	0.558	1.085
	Viral Inf Only	0.1144	0.662	0.396	1.105	0.1000	0.647	0.386	1.087
	Viral and Bacterial	0.3409	0.850	0.608	1.188	0.3576	0.853	0.607	1.197
	1-3	0.1522	1.216	0.930	1.590	0.1493	1.219	0.931	1.597

		Univariate Model Unadjusted Model				Multivariate Model Adjusted by HLA, Gender, Breastfeeding Duration and Birth Order			
Parameter	Level	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL
Number of Infections before 3 mos (Categorical) (Ref = 0)	4-6	0.9723	0.000	0.000	2E287	0.9727	0.000	0.000	7E291
	6 or higher	0.9912	0.000	0.000	.	0.9915	0.000	0.000	.
Number of Infections before 3 mos (Continuous)		0.2214	1.094	0.947	1.263	0.1927	1.102	0.952	1.275
Number of Infections between 3 and 6 mos (Categorical) (Ref = 0)	1-3	0.6138	0.933	0.713	1.221	0.7240	0.952	0.725	1.250
	4-6	0.9912	1.006	0.321	3.157	0.9519	1.036	0.327	3.279
	6 or higher	0.2594	3.101	0.434	22.17	0.3469	2.578	0.358	18.54
Number of Infections between 3 and 6 mos (Continuous)		0.4220	1.055	0.926	1.201	0.3526	1.064	0.933	1.213
Number of Infections between 6 and 12 mos (Categorical) (Ref = 0)	1-3	0.0407	0.752	0.573	0.988	0.0379	0.749	0.570	0.984
	4-6	0.3029	0.780	0.487	1.251	0.2881	0.773	0.481	1.243
	6 or higher	0.8192	1.094	0.508	2.355	0.8416	1.082	0.501	2.337
Number of Infections between 6 and 12 mos (Continuous)		0.6493	0.983	0.913	1.058	0.6143	0.981	0.911	1.057
Occurrence of ANY Upper Respiratory Infection		0.6316	0.938	0.721	1.220	0.8162	0.969	0.743	1.263
Occurrence of ANY Gastroenteritis		0.2818	0.817	0.566	1.180	0.5163	0.885	0.611	1.281
Occurrence of ANY Urinary Tract Infection		0.1637	0.445	0.143	1.390	0.1716	0.452	0.145	1.412
Occurrence of ANY Middle Ear Infection		0.4826	0.896	0.658	1.218	0.4402	0.885	0.649	1.207
Occurrence of ANY Pneumonia		0.8284	0.944	0.559	1.592	0.6743	0.893	0.525	1.517
Occurrence of ANY Sepsis		0.8292	0.858	0.213	3.451	0.8671	0.888	0.220	3.577
Occurrence of ANY Other Bacterial Infection		0.0438	1.620	1.014	2.589	0.0379	1.649	1.028	2.644
Occurrence of ANY Other Viral Infection		0.2078	0.779	0.528	1.149	0.1933	0.772	0.523	1.140

		Univariate Model Unadjusted Model				Multivariate Model Adjusted by HLA, Gender, Breastfeeding Duration and Birth Order			
Parameter	Level	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL
Occurrence of ANY Other Viral Infection with Fever		0.4654	0.846	0.541	1.325	0.5202	0.863	0.551	1.352
Occurrence of ANY Antibiotic Use		0.5543	0.923	0.709	1.203	0.5160	0.915	0.700	1.196

ESM Table 4 Univariable and Multivariable (adjusted for HLA, Gender, Breastfeeding Duration and Birth Order) Cox regression results based on time to type-1 diabetes. The definition other or unspecified infections, bacterial or viral, means previously not specified as eg pneumonia, sepsis etc

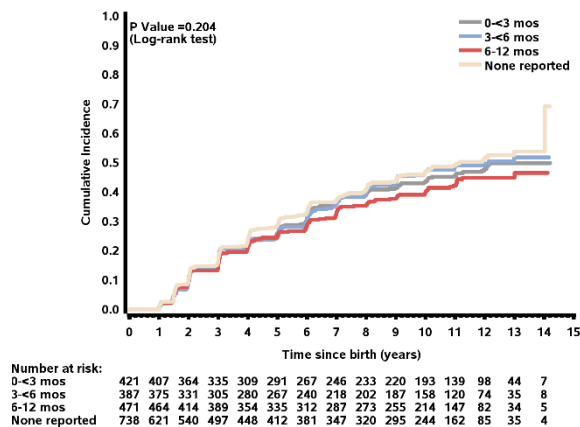
		Univariate Model Unadjusted Model				Multivariate Model Adjusted by HLA, Gender, Breastfeeding Duration and Birth Order			
Parameter	Level	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL
Age at First Infection (Categorical) (Ref = None reported)	0-<3 mos	0.9152	0.977	0.638	1.497	0.9856	0.996	0.645	1.538
	3-<6 mos	0.0898	0.636	0.377	1.073	0.1159	0.654	0.385	1.110
	6-12 mos	0.2713	0.759	0.465	1.240	0.2639	0.755	0.461	1.236
Age at First Viral Infection (Categorical) (Ref = None reported)	0-<3 mos	0.7865	0.938	0.588	1.495	0.9277	0.978	0.611	1.566
	3-<6 mos	0.9645	0.989	0.617	1.586	0.8946	1.033	0.642	1.660
	6-12 mos	0.8871	0.968	0.616	1.521	0.9568	0.988	0.628	1.553
Age at First Bacterial Infection (Categorical) (Ref = None reported)	0-<3 mos	0.0576	1.570	0.986	2.502	0.0627	1.565	0.976	2.510
	3-<6 mos	0.1443	0.562	0.259	1.218	0.1661	0.578	0.266	1.256
	6-12 mos	0.4465	1.186	0.765	1.838	0.4191	1.200	0.771	1.869
Number of Infections (Categorical) (Ref = 0)	1-3	0.1923	0.763	0.509	1.146	0.2069	0.768	0.510	1.157
	4-6	0.7386	0.921	0.566	1.496	0.8630	0.958	0.585	1.568
	6 or higher	0.6167	0.831	0.402	1.716	0.6295	0.834	0.400	1.742
Number of Infections (Continuous)		0.8001	0.991	0.926	1.061	0.8792	0.995	0.928	1.066
Number of Viral Infections (Categorical) (Ref = 0)	1-3	0.9190	1.019	0.705	1.474	0.8043	1.048	0.724	1.516
	4-6	0.2141	0.670	0.356	1.261	0.2929	0.710	0.376	1.343
	6 or higher	0.4742	1.400	0.557	3.518	0.4449	1.438	0.567	3.648

		Univariate Model Unadjusted Model				Multivariate Model Adjusted by HLA, Gender, Breastfeeding Duration and Birth Order			
Parameter	Level	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL
Number of Viral Infections (Continuous)		0.4299	0.964	0.880	1.056	0.5545	0.973	0.888	1.066
Number of Bacterial Infections (Categorical) (Ref = 0)	1-3	0.5729	1.108	0.776	1.582	0.5255	1.124	0.784	1.612
	4-6	0.2050	1.650	0.761	3.577	0.2176	1.635	0.748	3.573
	6 or higher	0.9745	0.000	0.000	2E287	0.9740	0.000	0.000	3E289
Number of Bacterial Infections (Continuous)		0.4612	1.047	0.927	1.183	0.5479	1.038	0.919	1.172
Infection Types (Categorical) (Ref = No Infections)	Bacterial Inf Only	0.0918	0.681	0.435	1.064	0.1096	0.693	0.442	1.086
	Viral Inf Only	0.1348	0.575	0.279	1.187	0.1138	0.554	0.266	1.152
	Viral and Bacterial	0.8230	1.049	0.688	1.602	0.7167	1.083	0.704	1.666
Number of Infections before 3 mos (Categorical) (Ref = 0)	1-3	0.2428	1.237	0.866	1.767	0.2123	1.257	0.877	1.802
	4-6	0.9798	0.000	0.000	.	0.9801	0.000	0.000	.
	6 or higher	0.9939	0.000	0.000	.	0.9943	0.000	0.000	.
Number of Infections before 3 mos (Continuous)		0.3293	1.100	0.908	1.334	0.2749	1.115	0.917	1.355
Number of Infections between 3 and 6 mos (Categorical) (Ref = 0)	1-3	0.7090	0.934	0.653	1.336	0.8110	0.957	0.665	1.376
	4-6	0.7892	1.211	0.298	4.923	0.6881	1.336	0.324	5.508
	6 or higher	0.9765	0.000	0.000	9E285	0.9766	0.000	0.000	2E292
Number of Infections between 3 and 6 mos (Continuous)		0.9628	1.004	0.835	1.207	0.8275	1.021	0.848	1.229
Number of Infections between 6 and 12 mos (Categorical) (Ref = 0)	1-3	0.3330	0.838	0.585	1.199	0.3443	0.841	0.586	1.205
	4-6	0.5738	0.831	0.436	1.585	0.6161	0.847	0.442	1.623
	6 or higher	0.9260	0.946	0.296	3.023	0.9617	0.972	0.303	3.117
Number of Infections between 6 and 12 mos (Continuous)		0.4074	0.957	0.863	1.062	0.4135	0.957	0.862	1.063
Occurrence of ANY Upper Respiratory Infection		0.8999	0.978	0.692	1.383	0.8616	1.032	0.727	1.465
Occurrence of ANY Gastroenteritis		0.3809	0.797	0.479	1.325	0.5979	0.871	0.522	1.454
Occurrence of ANY Urinary Tract Infection		0.9702	0.000	0.000	3E291	0.9706	0.000	0.000	7E294

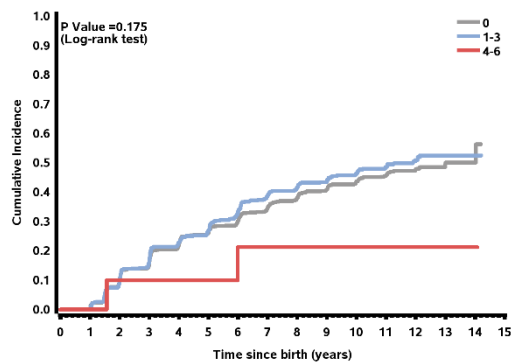
		Univariate Model Unadjusted Model				Multivariate Model Adjusted by HLA, Gender, Breastfeeding Duration and Birth Order			
Parameter	Level	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL	p-value	Hazard Ratio	Lower 95% CL	Upper 95% CL
Occurrence of ANY Middle Ear Infection		0.8357	0.957	0.634	1.445	0.8815	0.969	0.640	1.468
Occurrence of ANY Pneumonia		0.5329	1.228	0.644	2.339	0.5166	1.241	0.646	2.386
Occurrence of ANY Sepsis		0.4506	1.712	0.424	6.917	0.4668	1.682	0.415	6.818
Occurrence of ANY Other Bacterial Infection		0.0054	2.193	1.261	3.814	0.0107	2.069	1.184	3.616
Occurrence of ANY Other Viral Infection		0.0472	0.536	0.289	0.992	0.0355	0.515	0.277	0.956
Occurrence of ANY Other Viral Infection with Fever		0.0928	0.521	0.243	1.115	0.0951	0.522	0.244	1.120
Occurrence of ANY Antibiotic Use		0.7118	1.068	0.753	1.514	0.6264	1.092	0.766	1.556

ESM Figure 1 Kaplan-Meier curve of time from birth to development of any positive antibody by A) Age at first viral infection, B) Number of infections before 3 mos, C) Occurrence of any unspecified bacterial infection

A.



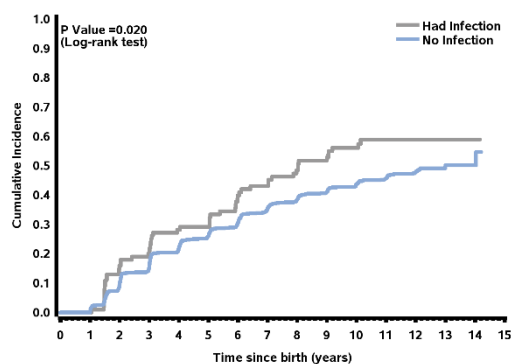
B.



Number at risk:

0	1424	1291	1140	1055	961	899	836	766	713	661	558	386	215	95	16
1-3	582	565	499	462	421	398	357	325	308	289	245	178	120	50	7
4-6	10	10	9	9	9	8	7	7	7	7	6	4	4	3	1

C.

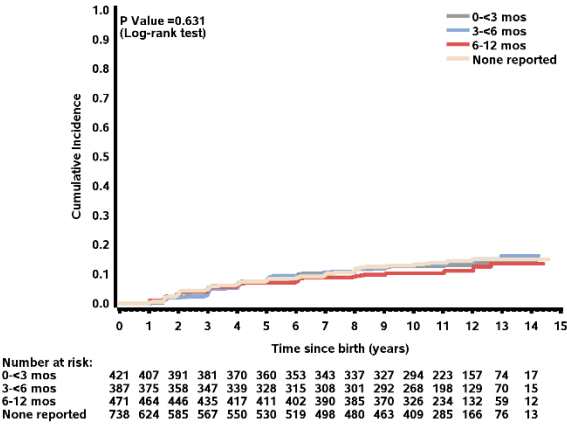


Number at risk:

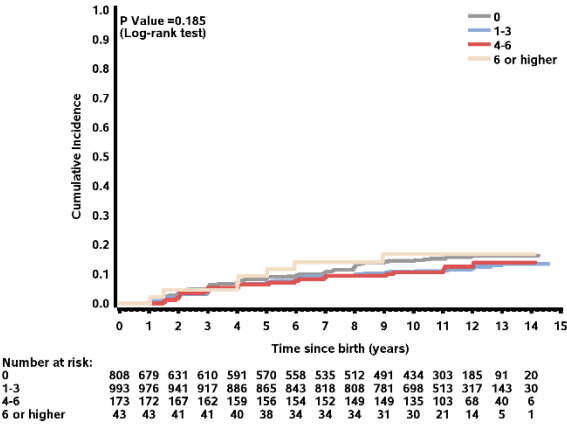
Had Infection	102	100	84	78	70	67	56	53	48	43	33	21	12	6	2
No Infection	1915	1767	1565	1448	1321	1238	1144	1045	980	914	776	547	327	142	22

ESM Figure 2 Kaplan-Meier curve of time from birth to development of multi-positive antibody by A) Age at first viral infection, B) Number of infections between 6 and 12 mos, C) Occurrence of any unspecified bacterial infection

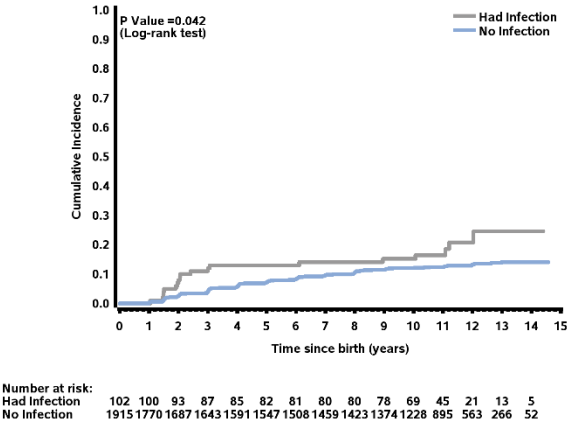
A.



B.

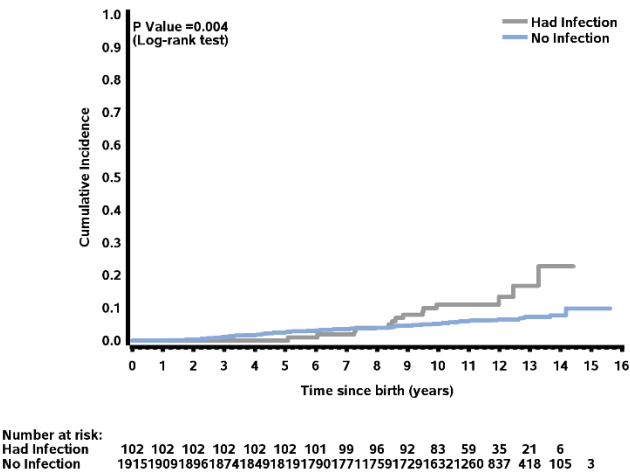


C.

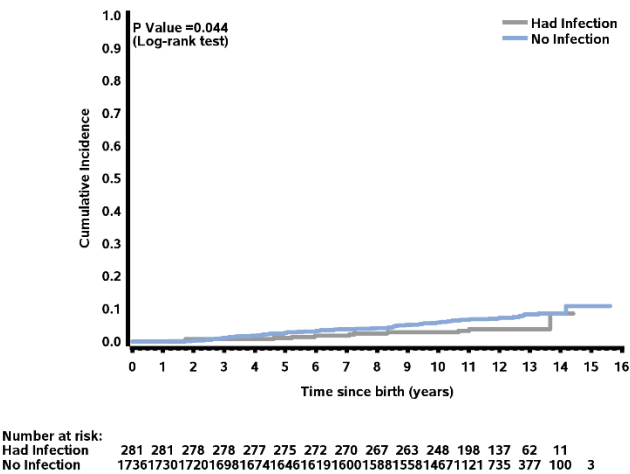


ESM Figure 3 Kaplan-Meier curve of time from birth to development of type-1 diabetes by A) Occurrence of any unspecified bacterial infection, B) Occurrence of any unspecified viral infection

A.



B.



LIST OF TRIGR INVESTIGATORS

<u>Administration/ Country</u>	<u>Study center</u>	<u>Last name</u>	<u>First name</u>	<u>Position</u>
Data Safety Monitoring Board		Mandrup- Poulsen,	Thomas	Chair University of Copenhagen, Copenhagen, Denmark
		Arjas	Elias	Member, University of Helsinki, Helsinki, Finland
		Läärä	Esa	Member, University of Oulu, Oulu, Finland
		Lernmark	Åke	Member, University of Lund, Malmö, Sweden
		Schmidt	Barbara	Member, University of Pennsylvania, Philadelphia, PA, USA
		Krischer	Jeffrey P.	Observer, University of South Florida. Tampa FL, USA
International Coordinating Center (ICC), University of Helsinki, Helsinki, Finland		Åkerblom	Hans K. † *	PI of the Study until 30.6.08, Deputy PI from 1.7.2008
		Hyytinen Knip	Mila Mikael	European Study Monitor Deputy PI until 30.6.2008, PI of the Study from 1.7.2008, National Investigator
		Koski	Katriina	European Study Monitor
		Koski	Matti	IT Specialist
		Pajakkala Salonen	Eeva Marja	European Study Monitor Study Coordinator
Data Management Unit (DMU), University of South Florida, Tampa, Florida, USA		Cuthbertson	David	Biostatistician
		Krischer	Jeffrey P.	PI of the DMU
		Shanker	Linda	Coordinator

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Canadian Coordinating Center, University of Western Ontario, London, and University of Ottawa, Ontario		Bradley	Brenda	National Coordinator
		Dosch	Hans-Michael	Co-Investigator for Canada
		Dupré	John † *	Co-PI for North America and National Investigator until 08/12/2015, Executive Committee
		Fraser	William	Co-Investigator for Canada Executive Committee
		Lawson	Margaret	Co-Investigator for Canada Executive Committee
		Mahon	Jeffrey L.	Co-PI for North America and National Investigator after 08/12/2015, Executive Committee
		Sermer	Mathew	Co-Investigator for Canada, Executive Committee
USA Coordinating Center, University of Pittsburgh, Pennsylvania and University of Washington, Seattle, Washington		Taback	Shayne P.	Co-Investigator for Canada, Executive Committee
		Becker	Dorothy	Co-PI for North America, National Investigator, Executive Committee
		Franciscus Nucci	Margaret Anita	National Coordinator National Coordinator, Nutrition Coordinator of North America
		Palmer	Jerry	Executive Committee

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Nutritional Epidemiology Unit, National Institute for Health and Welfare, Helsinki, Finland		Virtanen	Suvi M.	Head of Nutritional Epidemiology Unit
Australia	AUS01 – Westmead, New South Wales - Children’s Hospital	Catteau Howard	Jacki Neville	National Coordinator National Investigator
	AUS02 – Newcastle, New South Wales - John Hunter Children’s Hospital	Crock	Patricia	Local Investigator
	AUS03 – Sydney, New South Wales - Sydney Children’s Hospital	Craig	Maria	Local Investigator
Canada	CAN01 – London, Ontario - St. Joseph's Health Care Centre	Clarson Bere	Cheril L. Lynda	Local Investigator Coordinator
	CAN02 – Vancouver, British Columbia - Children's and Women's Health Centre of British Columbia	Thompson	David	Local Investigator
		Metzger	Daniel	Local Investigator
		Marshall	Colleen	Coordinator (In Transition)
		Kwan	Jennifer	Coordinator (In Transition)
	CAN03 – Calgary, Alberta - Alberta Children’s Hospital	Stephure Pacaud Schwarz	David K. Daniele Wendy	Local Investigator Co-Investigator Coordinator

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	CAN04 – Edmonton, Alberta - Walter MacKenzie Health Sciences	Girgis Thompson	Rose Marilyn	Local Investigator Coordinator
	CAN05 – Winnipeg, Manitoba - Health Sciences Centre	Taback Catte	Shayne P Daniel	Local Investigator Coordinator
	CAN06 – Ottawa, Ontario - Children's Hospital of Eastern Ontario and The Ottawa Hospital	Lawson Bradley	Margaret L Brenda	Local Investigator Coordinator
	CAN07 – Toronto, Ontario - Mount Sinai Hospital/Hospital for Sick Children	Daneman Sermer Martin	Denis Mathew Mary-Jean	Local Investigator Co-Investigator Coordinator
	CAN08 – Quebec, Quebec - CHUQ	Morin Frenette Ferland	Valérie Line Suzanne	Local Investigator Co-Investigator Coordinator
	CAN09 - Saint John, New Brunswick – Regional Hospital	Sanderson Heath	Susan Kathy	Local Investigator Coordinator
	CAN10 – Montreal, Quebec - L' Hôpital Sainte-Justine	Huot Gonthier Thibeault	Céline	Local Investigator Co-Investigator Coordinator
	CAN11 – Montreal, Quebec - Children's	Legault Laforte	Laurent Diane	Local Investigator Coordinator

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	Hospital			
	CAN12 – Halifax, Nova Scotia - IWK Health Centre/Dalhousie	Cummings Scott	Elizabeth A Karen	Local Investigator Coordinator
	CAN13 - St. John's, Newfoundland and Labrador - Janeway Child Health Center	Bridger Crummell	Tracey Cheryl	Local Investigator Coordinator
	CAN14 – Kingston, Ontario - Kingston General Hospital/ Queen's University	Houlden Breen	Robyn Adriana	Local Investigator Coordinator
	CAN15 – Regina, Saskatchewan - Regina Qu'Appelle	Carson Kelly	George Sheila	Local Investigator Coordinator
	CAN16 – Saskatoon, Saskatchewan - Royal University Hospital	Sankaran Penner	Koravangattu Marie	Local Investigator Coordinator
	CAN17 – Peterborough, Ontario - Peterborough Regional Health Centre	White King	Richard A Nancy	Local Investigator Coordinator
	CAN18 – Victoria, British Columbia - Vancouver Island Health Research Centre	Popkin Robson	James Laurie	Local Investigator Coordinator

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Czech Republic	CZE01 - Prague - Faculty Hospital Kralovske Vinohrady	Al Taji	Eva	National Investigator/Coordinator
		Mendlova	Pavla	National Coordinator
		Romanova	Martina	Co-Investigator
		Vavrinec	Jan † *	National Investigator
		Vosahlo	Jan	Co-Investigator
	CZE02 - Brno - Hospital Milosrdnych Bratri	Brazdova	Ludmila	Local Investigator
	CZE03- Olomouc - Faculty Hospital Olomouc	Venhacova	Jitrenka	Local Investigator
		Venhacova	Petra	Co-Investigator
	CZE04 - Usti nad Labem - Hospital of Masryk	Cipra	Adam	Local Investigator
	CZE05 - Ceske Budejovice - Hospital Ceske Budejovice	Tomsikova	Zdenka	Local Investigator
	CZE06 - Plzen - Faculty Hospital Plzen	Paterová	Petra	Local Investigator
	CZE07 - Zlin - Hospital of Bata	Gogelova	Pavla	Local Investigator
Estonia	EST01 - Tallinn - Tallinn Children's Hospital	Einberg	Ülle	Co-Investigator
		Riikjärv	Mall-Anne	Local Investigator
	EST02 - Tartu - Tartu	Ormisson	Anne	National Investigator

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	University Children's Hospital	Tillmann	Vallo	Co-Investigator

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Finland	FIN01 - Helsinki – Children’s Hospital, University of Helsinki	Johansson	Susanne	National Coordinator
		Kleemola	Päivi	National Coordinator
		Parkkola	Anna	Local Investigator
	FIN02 - Helsinki - Department of Obstetrics and Gynecology, University of Helsinki	Järvenpää	Anna-Liisa	Local Investigator
	FIN03 - Espoo - Jorvi Hospital	Hämäläinen Kiiveri	Anu-Maaria	Local Investigator
			Sanne	Local Investigator
	FIN04 - Kotka - Kymenlaakso Central Hospital	Salonen Tenhola	Maria Sirpa	Local Investigator Local Investigator
	FIN05 - Lahti - Päijät- Häme Central Hospital	Salonen	Pia	Local Investigator
	FIN06 - Tampere - Department of Pediatrics, Tampere University Hospital	Jason	Eeva	Local Investigator
		Selvenius	Jenni	Local Investigator
		Siljander	Heli	Co-Investigator
	FIN07 - Pori - Satakunta Central Hospital	Ylitalo	Samuli	Local Investigator
	FIN08 - Jyväskylä - Central Finland Central Hospital	Paajanen	Ilkka	Local Investigator

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	FIN09 - Seinäjoki - South Ostrobothnia Central Hospital	Talvitie	Timo	Local Investigator
	FIN10 - Hyvinkää - Hyvinkää Hospital	Lindström	Kaija	Local Investigator
	FIN11 - Kuopio - Department of Pediatrics, Kuopio University Hospital	Huopio Pesola	Hanna Jouni	Local investigator Co-Investigator
	FIN12 - Oulu - Department of Pediatrics, Oulu University Hospital	Veijola Tapanainen	Riitta Päivi	Local Investigator Co-Investigator
	FIN13 - Hämeenlinna - Kanta-Häme Central Hospital	Alar	Abram	Local Investigator
	FIN14 - Vaasa - Vaasa Central Hospital	Popov	Erik	Local Investigator
	FIN15 - Lappeenranta - South Carelian Central Hospital	Virransalo	Ritva	Local Investigator
	FIN16 - Mikkeli - Mikkeli Central Hospital	Nykänen	Päivi	Local Investigator

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Germany	GER01 - Hannover - Kinder- und Jugendkrankenhaus – Auf der Bult	Aschemeier	Bärbel	National Coordinator
		Danne	Thomas	National Investigator
		Kordonouri	Olga	Co-Investigator
Hungary	HUN01 - Budapest - Sемmelweis Medical University	Krikovszky	Dóra	Co-Investigator
		Madácsy	László	National Investigator
Italy	ITA01 - Rome - University Campus Bio-Medico of Rome	Khazrai	Yeganeh Manon	Local Coordinator
		Maddaloni	Ernesto	Local Coordinator
		Pozzilli	Paolo	National Investigator
	SAR01 - Cagliari - St. Michele Hospital	Mannu Songini	Carla Marco	Local Coordinator National Investigator
Luxembourg	LUX01 - Luxembourg - Centre Hospitalier de Luxembourg	de Beaufort Schierloh	Carine Ulrike	National Investigator Co-Investigator
The Netherlands	NET01 - Rotterdam - Sophia Children's Hospital	Bruining Bisschoff	Jan † * Margriet	National Investigator National Coordinator
Poland	POL01 - Wroclaw - Medical University of Wroclaw	Basiak	Aleksander	Co-Investigator
		Wasikowa	Renata	National Investigator
	POL02 - Krakow - Polish-American Children's Hospital	Ciechanowska	Marta	Local Investigator
	POL03 - Katowice - Medical University of	Deja Jarosz-Chobot	Grazyna Przemyslaw	Co-Investigator Local Investigator

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	Silesia			
	POL04 - Lodz - Medical University of Lodz	Szadkowska	Agnieszka	Co-Investigator
	POL05 - Lodz - Polish Mother's Memorial Hospital (I.C.Z.M.P)	Cypryk Zawodniak-Szalapska	Katarzyna Malgorzata	Local Investigator Co-Investigator
Spain	SPA01 - Cruces University Hospital- UPV/EHU- CIBERDEM/CIBERER, Barakaldo, Spain	Castano Chueca Gonzalez Frutos	Luis Maria Teba	National Investigator Co-Investigator Local Coordinator
	SPA02 - Madrid - Hospital Clinico San Carlos	Serrano-Ríos Martínez-Larrad Hawkins	Manuel † * María Teresa Federico Gustavo	National Investigator Local Coordinator Co-Investigator
	SPA03 - Madrid - Hospital Gregorio Marañon	Rodriguez Arnau	Dolores	Co-Investigator
Sweden	SWE01 - Linköping - University of Linköping	Ludvigsson Smolinska Konefal	Johnny Malgorzata	National Investigator National Coordinator
	SWE02 - Uddevalla - Uddevalla Hospital	Hanas	Ragnar	Local Investigator
	SWE03 - Göteborg - GothenburgThe Queen Silvia Children's Hospital	Lindblad	Bengt	Local Investigator

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	SWE05 - Halmstad - Halmstad Hospital	Nilsson	Nils-Östen	Local Investigator
	SWE06 - Trollhättan - Trollhättan Hospital	Fors	Hans	Local Investigator
	SWE07 - Norrköping - Vrinnevi Hospital	Nordwall	Maria	Local Investigator
	SWE08 - Borås - Borås Hospital	Lindh	Agne	Local Investigator
	SWE09 - Karskrona - Karlskrona Hospital	Edenwall	Hans	Local Investigator
	SWE10 - Örebro - University Hospital	Åman	Jan	Local Investigator
	SWE11 - Jönköping - Ryhovs Hospital	Johansson	Calle	Local Investigator
Switzerland	SWT01 - Zürich - University Children's Hospital	Gadient	Margrit	Local Coordinator
		Konrad	Daniel	National Investigator
		Schoenle	Eugen	National Investigator
USA	USA01 – Pittsburgh, Pennsylvania - Children's Hospital of Pittsburgh	Becker	Dorothy	USA National Investigator / Pittsburgh Local Investigator
		Daftary Klein	Ashi Mary Beth	Co-Investigator Pittsburgh Coordinator
		Gilmour	Carol	Co-Investigator

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	USA02 – Seattle, Washington - VA Puget Sound Health Care System and University of Washington	Palmer	Jerry	Local Investigator
		Palmer	Patty	Local Investigator
		Malone	Patty	Coordinator
	USA03 - St. Louis, Missouri - Washington University	Tanner-Blaslar	Marilyn	Coordinator
		White	Neil	Local Investigator
	USA04 - Los Angeles, California - Mattel Children's Hospital of UCLA	Devaskar	Uday	Local Investigator
		Horowitz	Heather	Coordinator/dietitian
		Rogers	Lisa	Coordinator/dietitian
	USA05 – Ponce, Puerto Rico - Ponce School of Medicine	Colon	Roxana	Coordinator
		Frazer	Teresa	Co-Investigator
		Torres	Jose	Local Investigator
	USA06 - New York, New York - Naomie Berrie Diabetes Center	Goland	Robin	Local Investigator
		Greenberg	Ellen	Coordinator
		Schachner	Holly	Co-Investigator
		Softness	Barney	Co-Investigator
Laboratories	HLA-typing Laboratory – University of Turku, Turku – Finland	Ilonen	Jorma	Head of HLA-typing Laboratory
	HLA-typing Laboratory – University of Pittsburgh, Pennsylvania - USA	Trucco	Massimo	Head of HLA-typing Laboratory
		Nichol	Lynn	Chief Technician

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	Cow's Milk Antibody Laboratory – University of Helsinki, Helsinki – Finland	Savilahti	Erkki	Head of Cow's Milk Antibody Laboratory
	Autoantibody Laboratory – University of Helsinki, Helsinki – Finland	Härkönen	Taina	Co-Investigator
		Knip	Mikael	Head of Antibody Laboratory
	T-Cell Laboratory – Helsinki, Helsinki – Finland	Vaarala	Outi	Head of T-cell Laboratory
		Luopajarvi	Kristiina	Co-Investigator
	T-Cell Laboratory – Hospital for Sick Children, Toronto, Ontario - Canada	Dosch	Hans-Michael	Head of T-Cell Laboratory

† * Deceased