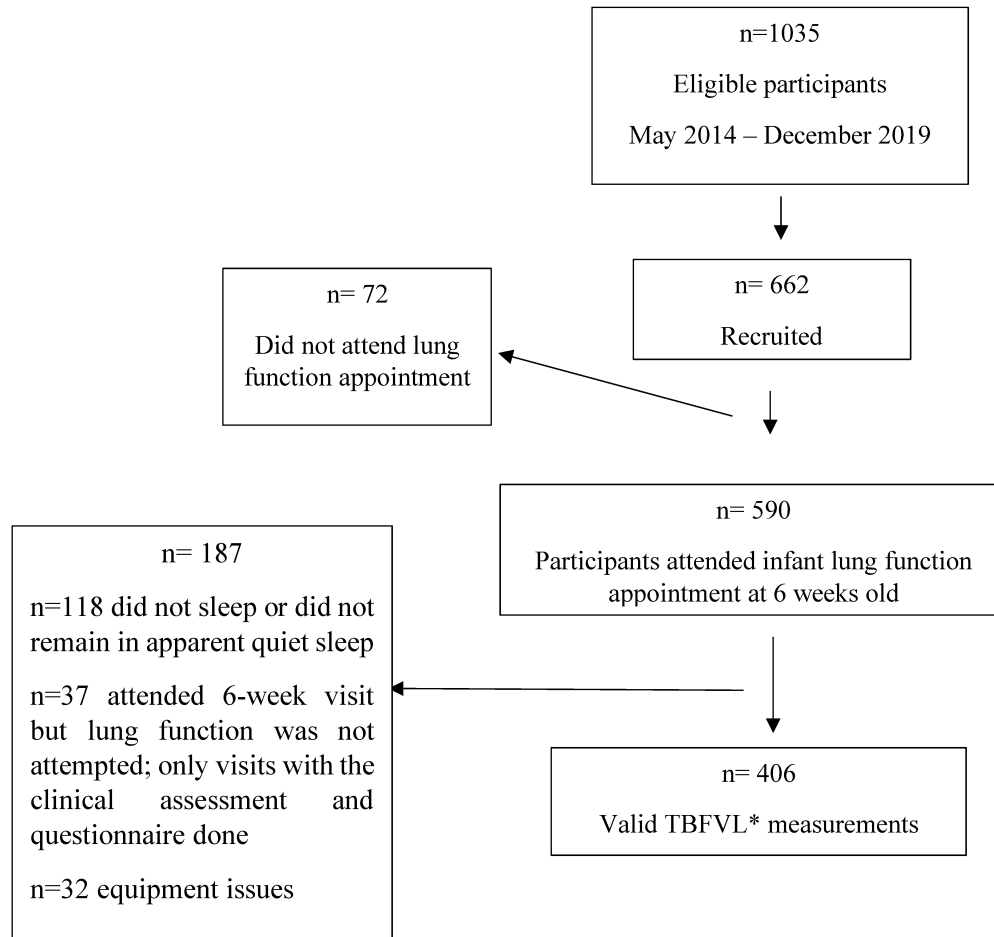


Online Data Supplement

Maternal asthma is associated with reduced lung function in male infants in a combined analysis of the BLT and BILD cohorts

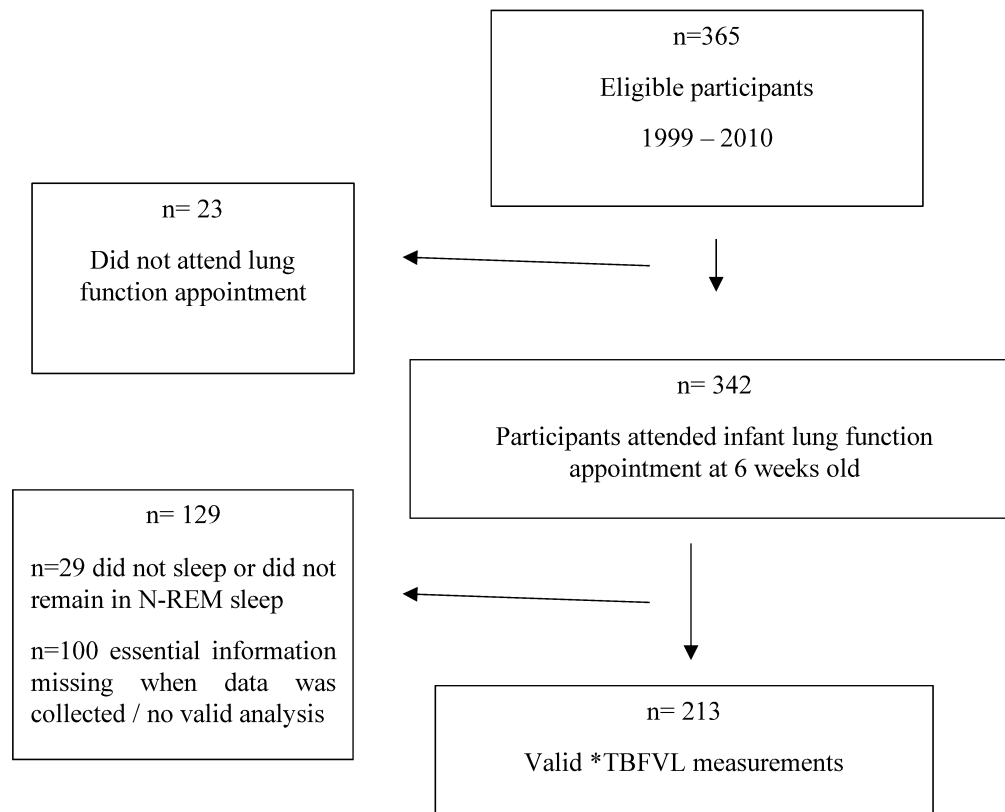
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Supplement Figure E1: Recruitment, participation and tidal breathing flow-volume loop success rate in the Breathing for Life Trial cohort



*TBFVL: tidal breathing flow-volume loop

Supplement Figure E2: Recruitment, participation and tidal breathing flow-volume loop success rate in the Bern Infant Lung Development study cohort



*TBFVL: tidal breathing flow-volume loop

Supplement Table E1: Similarities and differences between the Bern Infant Lung Development and Breathing for Life Trial studies

	BREATHING FOR LIFE TRIAL	BERN INFANT LUNG DEVELOPMENT
Type of study	Multicentre, parallel group, randomised controlled trial of asthma management guided by fractional exhaled nitric oxide (FENO), a marker of eosinophilic airway inflammation, compared to usual care, with prospective infant follow-up	Ongoing prospective birth cohort of unselected, healthy neonates recruited antenatally
Location	Newcastle and Sydney, Australia	Bern, Switzerland
Time of data collection	Between May 2014 and December 2019	Between 1999 and 2010
Inclusion criteria	Preterm and term delivery No apparent major birth defects or perinatal disease that would preclude performing unsedated infant lung function at 6 weeks of age	Term delivery (≥ 37 weeks) No known major birth defects or perinatal disease that would preclude performing unsedated infant lung function at 5 weeks of age
Lung function equipment	Tests were performed with the infant supine using an infant mask (size 0, 0/1 and 1; Homedica AG, Huenenberg, Switzerland), according to the ERS/ATS standards of infant lung function testing. Flow was measured using an ultrasonic flow meter (Spiroson®; EcoMedics AG, Duernten, Switzerland)	Tests were performed with the infant supine using an infant mask (size 1; Homedica AG, Huenenberg, Switzerland), according to the ERS/ATS standards of infant lung function testing. Flow was measured using an ultrasonic flow meter (Spiroson®; EcoMedics AG, Duernten, Switzerland)
Lung function analysis	TBFVL measures were calculated using the software version Wbreath v3.28.0. Ndd Medizintechnik, AG, Zurich, Switzerland.	TBFVL measures were calculated using the software version Wbreath v3.28.0. Ndd Medizintechnik, AG, Zurich, Switzerland.
Age at test	Mean age 6.8 weeks SD 1.9	Mean age 5.0 weeks SD 0.8
Caucasian n (%)	288 (71%)	191 (90%)
History of maternal asthma n (%)	406 (100)	20 (9)

Supplement Table E2: Baseline characteristics and tidal breathing flow-volume loop parameters in Breathing for Life Trial and Bern Infant Lung Development study infants stratified for term pregnancy (BLT, all born to asthmatic mothers) and asthma in pregnancy (BILD, all term)

	MATERNAL ASTHMA, TERM INFANTS (BLT cohort, n=373)	NO MATERNAL ASTHMA, TERM INFANTS (BILD cohort, n=193)		MATERNAL ASTHMA, PRETERM INFANTS (BLT cohort, n=33)	MATERNAL ASTHMA, TERM INFANTS (BILD cohort, n=20)
	Mean(SD)	Mean(SD)	P-value	Mean(SD)	Mean(SD)
Gestational age (weeks)	39.1(1.1)	39.6(1.2)	<0.0001	34.9(1.8)	39.4(1.4)
Birth weight (kg)	3.5(0.5)	3.4(0.5)	0.0213	2.5(0.6)	3.4(0.3)
Birth weight (centile)	54.5(27.8)	52.8(28.4)	0.5138	11.7(16.6)	53.6(24.7)
Birth length (cm)	51.4(2.6)	49.6(2.0)	<0.0001	46.6(6.2)	50.0(2.2)
Birth length (centile)	71.9(29.4)	52.8(28.4)	<0.0001	34.7(32.7)	55.6(30.4)
Age (weeks)	6.6(1.5)	5.0(0.8)	<0.0001	9.2(3.5)	5.2(0.9)
Age (days)	48.1(10.7)	35.8(5.2)	<0.0001	65.2(22.6)	36.9(5.6)
Weight at test (kg)	4.9(0.7)	4.4(0.6)	<0.0001	4.4(0.7)	4.3(0.6)
Weight at test (centile)	54.1(26.0)	45.4(28.1)	0.0004	36.7(30.6)	37.8(29.4)
Length at test (cm)	56.3(2.7)	54.7(2.2)	<0.0001	53.7(2.6)	54.7(1.6)
Length at test (centile)	56.5(27.5)	50.2(29.3)	0.0142	26.6(29.0)	47.2(24.3)
Weight gain (kg per day)	0.031(0.012) ^s	0.028 (0.009)	0.0703	0.030 (0.008)	0.025 (0.009)
Length gain (cm per day)	0.10(0.07)	0.14 (0.04)	<0.0001	0.098(0.06)	0.12(0.04)
Birth order	1.7(1.0)	1.7(0.8)	0.2299	1.6(0.9)	1.5(0.8)
Maternal age (years)	30.0(5.2)	32.5(4.2)	<0.0001	30.2(4.4)	32.4(2.9)
	N(%)	N(%)		N(%)	N(%)
Caesarean section	107 (29)	30 (15)	0.0004	26 (79)	9 (45)
Male sex	190 (51)	101 (52)	0.7904	19 (58)	13 (65)
Caucasians	268 (72)	173 (90)	0.0098	20 (60)	18 (90)
Tobacco exposure in pregnancy	37(10)	17(9)	0.7634	4(12)	0
Exclusive breastfeeding	220(59)	181 (94)	<0.0001	16 (48)	19 (95)
Mixed breastmilk and formula since birth	51(14)	-	-	7 (21)	-
Never breastfed	29(8)	-	-	1 (3)	-

Supplement Table E3: Baseline characteristics and tidal breathing flow-volume loop parameters stratified by study site

	Newcastle (n=296)	Sydney (n=110)	Bern (n=213)		
	Mean (SD)	Mean (SD)	Mean (SD)	P value	
Gestational age (weeks)	38.54 (1.7)	39.36 (1.2)	39.61 (1.2)	<0.0001	*!
Birth weight (kg)	3.36 (0.57)	3.41 (0.46)	3.35 (0.44)	0.5756	
Birth weight (centile)	48.79 (30.01)	56.92 (27.09)	52.87 (28.05)	0.0318	*
Birth length (cm)	51.6 (3.29)	50.29 (2.46)	49.60 (2.02)	<0.0001	*!
Birth length (centile)	73.08 (29.83)	61.34 (31.66)	50.02 (29.38)	<0.0001	*!@
Age (weeks)	6.67 (1.87)	7.08 (1.88)	5.04 (0.78)	<0.0001	!@
Age (days)	48.5 (12.9)	52.2 (12.9)	35.9 (5.2)	<0.0001	*!@
Weight at test (kg)	4.79 (0.72)	5.06 (0.68)	4.37 (0.56)	<0.0001	*!@
Weight at test (centile)	50.41 (27.27)	58.70 (24.40)	44.69 (28.27)	<0.0001	*@
Length at test (cm)	55.67 (2.73)	57.24 (2.67)	54.68 (2.14)	<0.0001	*!@
Length at test (centile)	50.24 (28.94)	64.33 (25.99)	49.87 (28.87)	<0.0001	* @
Weight gain (kg per day)	0.029 (0.010)	0.033 (0.014)	0.028 (0.009)	0.0091	*@
Length gain (cm per day)	0.090 (0.059)	0.143 (0.073)	0.142 (0.045)	<0.0001	*!
Birth order	1.7 (1.1)	1.4 (0.7)	1.6 (0.8)	0.0074	*
Maternal age (years)	29.6 (5.1)	30.9 (5.0)	32.5 (4.1)	<0.0001	!@
RR (ipm)	45.04 (10.8)	44.8 (8.8)	42.7 (9.0)	0.0249	
V _T /kg	7.17 (1.3)	6.30 (1.0)	7.61 (1.3)	<0.0001	*!@
V'E/kg	312.8 (58.8)	275.4 (40.7)	319.1 (57.4)	<0.0001	*@
tPTEF/tE%	31.6 (9.8)	32.1 (9.6)	35.0 (10.3)	0.0010	!@
	n (%)	n (%)	n (%)		
First born	165 (56)	78 (71)	114 (54)	0.0073	*@
Second born	76 (26)	21 (19)	67 (31)	0.0526	
Third born or later	55 (19)	11 (10)	32 (15)	0.1007	

	Newcastle (n=296)	Sydney (n=110)	Bern (n=213)		
	Mean (SD)	Mean (SD)	Mean (SD)	P value	
Caesarean section	110 (37)	23 (21)	39 (18)	<0.0001	*!
Male sex	154 (52)	55 (50)	114 (54)	0.8328	
Caucasians	210 (71)	78 (71)	191 (90)	<0.0001	!@
Tobacco exposure in pregnancy	40 (14)	1 (1)	17 (8)	0.0004	*@
Prematurity	31 (10)	2 (2)	-	0.0046	-
Maternal asthma	296 (100)	110 (100)	20 (9)	<0.0001	!@
Exclusive breastfeeding	160 (54.1)	81 (74)	200 (95)	<0.0001	*!@
Mixed breastmilk and formula since birth	43 (15)	4 (4)	-	-	-
Never breastfed	26 (9)	4 (4)	-	-	-

*Significant between Newcastle and Sydney; ! Significant between Newcastle and Bern; @ Significant between Sydney and Bern

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2. Frey U, Stocks J, Coates A, Sly P, Bates J. Specifications for equipment used for infant pulmonary function testing. ERS/ATS Task Force on Standards for Infant Respiratory Function Testing. European Respiratory Society/ American Thoracic Society. *Eur Respir J.* 2000;16(4):731-40.