

## Online data supplement

### Development of lung function from 10 to 35 years of age after extremely preterm birth

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## Definitions

Gestational age was determined by the mothers' last menstruation for the 82–85 cohort, and by ultrasound scans at GA 17–18 weeks for the 91-92 and 99–00 cohort. Birthweight z-scores were extracted from Norwegian growth curves <sup>1</sup>, and small for gestational age (SGA) was defined as BW < 10<sup>th</sup> percentile for GA. BPD was defined as the need for supplemental oxygen or respiratory support at postmenstrual age  $\geq$  36 weeks according to the definition proposed by Shennan et al <sup>2</sup>. Further classification into mild, moderate and severe BPD according to the NICHD statement was not possible, as oxygen was delivered as "low flow oxygen" on a nasal cannula and quantified in litres, not in FiO<sub>2</sub> <sup>3</sup>. Atopy was defined as sensitisation to at least one common allergen by either skin prick or specific serum IgE tests. Current asthma was defined as a combination of reported wheeze during the previous 3 months and either use of asthma medication during the previous 3 months, or having reported 'asthma ever'. Self-reported smoking was defined as any current use of cigarettes.

## Subject inclusion

The region was served by two neonatal intensive care units (NICU) during the inclusion period, and follow-up was performed according to place of birth; Haukeland University Hospital for the 82-85 and 91-92 cohorts, and additionally Stavanger University Hospital for the 99-00 cohort. The 99-00 cohort was a regional part of a larger, national cohort<sup>4</sup>. All but three participants were Caucasian.

**Figure legends:**

**Figure E1:** Measured FEV<sub>1</sub>/expected peak FEV<sub>1</sub> with 95% confidence intervals For EP born with or without BPD and term-born controls.

**Figure Captions:**

**Figure E1:** Mean measured FEV<sub>1</sub> as fraction of expected peak FEV<sub>1</sub> (with 95% confidence intervals) in three population based cohorts born extremely preterm with or without BPD during three different decades and individually matched term-born controls (black line), based on mixed-effects longitudinal model. Expected peak FEV<sub>1</sub> was calculated for each individual using GLI reference equation. EP, subjects born extremely preterm (gestational age  $\leq 28$  weeks or birth weight  $\leq 1000$ g); FEV<sub>1</sub>, forced expiratory volume in 1 second; BPD, bronchopulmonary dysplasia: oxygen dependent at 36 weeks gestational age.

**Table E1: Neonatal data for extremely preterm study participants and non-participants in the 99–00 cohort**

Variable	Participants (n = 64)	Non participants (n = 24)	P-value
Female gender, n (%)	31 (48%)	8 (33%)	0.20
Region Bergen, n (%)	39 (61%)	9 (38%)	0.05
Birthweight in grams, mean (SD)	844 (168)	847 (143)	0.93
Birthweight z-score, mean (SD)	-0.8 (1.3)	-0.9 (1.2)	0.61
Gestational age in weeks, mean (SD)	26.7 (1.6)	26.9 (1.7)	0.70
Postnatal days w/oxygen treatment*, median (quartiles)§	61 (40–78)	46 (39–71)	0.23
Days on CPAP, median (quartiles)	29 (19–42)	24 (4–41)	0.14
Ventilator days*, median (quartiles)	5 (2–9)	3 (0–6)	0.72
EP BPD, n (%)	33 (52%)	12 (50%)	0.90
Antenatal steroids, n (%)	52 (81%)	20 (83%)	0.82
Surfactant, n (%)	54 (84%)	16 (67%)	0.07
Postnatal steroids, n (%)	20 (31%)	4 (17%)	0.17
PDA closure, medical or surgical (%)	14 (22%)	1 (4%)	0.05
Maternal smoking during pregnancy*, n (%)	15 (25%)	13 (56%)	< 0.01

Categorical data were compared using Pearson's  $\chi^2$  test and continuous data using Welch's *t*-test. §Data compared using the Wilcoxon–Mann–Whitney test, due to skewed data.

\* Some missing data. The number of participants and non-participants was 60 and 21 for postnatal days with oxygen treatment, 64 and 23 for ventilator days, and 59 and 23 for maternal smoking.

Abbreviations: BPD: bronchopulmonary dysplasia (supplemental oxygen or respiratory support at postmenstrual age  $\geq 36$  weeks). BW: Birthweight. EP: extremely preterm (gestational age  $\leq 28$  weeks or birthweight  $\leq 1000$  g). PDA: Persistent ductus arteriosus.

Table E2: Background variables on all visits

Age, mean (range)		82-85						91-92						99-00			
		18 (15-20)	25 (22-27)	34 (32-38)	11 (10-12)	18 (17-19)	27 (26-28)	12 (10-14)	20 (18-21)								
Total n (eligible N)	Term-born	46 (46)	40 (46)	34 (46)	35 (35)	28 (35)	26 (34)	54 (57)	43 (57)								
	EP	46 (51)	45 (51)	36 (48)	35 (35)	31 (35)	24 (35)	58 (88)	50 (88)								
Female sex, n (%)	Term-born	21 (46%)	19 (48%)	19 (56%)	22 (63%)	20 (71%)	18 (69%)	25 (46%)	18 (42%)								
	EP	21 (46%)	19 (42%)	16 (44%)	22 (63%)	18 (58%)	14 (58%)	28 (48%)	25 (50%)								
Height in cm, female, mean (SD)	Term-born	168 (6)	168 (6)	169 (7)	144 (6)	166 (5)	167 (5)	150 (9)	168 (8)								
	EP	163 (5)	163 (4)	163 (4)	141 (9)	162 (7)	162 (6)	147 (7)	161 (6)								
Height in cm, male, mean (SD)	Term-born	177 (6)	177 (6)	178 (6)	146 (7)	178 (8)	180 (8)	153 (8)	183 (5)								
	EP	175 (6)	175 (6)	174 (7)	139 (6)	174 (5)	175 (6)	147 (8)	175 (7)								
Weight in kg, female, mean (SD)	Term-born	67 (14)	69 (16)	75 (17)	39 (7)	64 (12)	70 (13)	41 (10)	66 (14)								
	EP	60 (15)	66 (19)	67 (15)	35 (13)	61 (22)	62 (11)	38 (7)	59 (12)								
Weight in kg, male, mean (SD)	Term-born	68 (8)	76 (11)	85 (14)	38 (6)	75 (12)	80 (16)	41 (8)	79 (12)								
	EP	66 (16)	80 (15)	78 (18)	35 (12)	73 (17)	79 (12)	39 (9)	73 (14)								
Participant response to questionnaire	Term-born	46 (100)	40 (100)	31 (91)	35 (100)	28 (100)	26 (100)	54 (100)	15 (35)								
	EP	46 (100)	45 (100)	33 (92)	35 (100)	31 (100)	24 (100)	58 (100)	33 (66)								
Self-reported smoking, n (%)	Term-born	14 (30%)	8 (20%)	5 (17%)	.. ..	5 (18%)	3 (12%)	.. ..	0 (0%)								
	EP	15 (33%)	17 (40%)	3 (9%)	.. ..	1 (3%)	1 (4%)	.. ..	2 (6%)								
Wheeze last 12 months, n (%)	Term-born	12 (27%)	8 (31%)	3 (10%)	2 (6%)	10 (53%)	7 (27%)	5 (9%)	3 (20%)								
	EP	16 (35%)	18 (46%)	8 (26%)	11 (31%)	12 (55%)	7 (29%)	8 (14%)	8 (24%)								
Asthma med. last 12 months, n (%)	Term-born	1 (2%)	3 (8%)	3 (10%)	1 (7%)	1 (4%)	2 (8%)	3 (6%)	0 (0%)								
	EP	7 (15%)	5 (12%)	4 (12%)	5 (23%)	7 (23%)	4 (17%)	4 (7%)	4 (12%)								
Current asthma, n (%)	Term-born	3 (7%)	3 (8%)	1 (3%)	1 (3%)	5 (18%)	5 (19%)	4 (7%)	1 (7%)								
	EP	8 (17%)	8 (18%)	5 (15%)	10 (29%)	6 (19%)	2 (8%)	5 (9%)	4 (12%)								

Abbreviations: Asthma med: asthma medication, EP: extremely preterm (gestational age  $\leq 28$  weeks or birth weight  $\leq 1000$  g). 'Current asthma' refers to a combination of wheeze in the last 12 months plus a positive response to the questions 'asthma ever' or 'asthma medication last 12 months'. % is percentage of all subjects that were evaluated at that time-point

**Table E3: Predictors for low FEV<sub>1</sub> z-score at 18 years in EP subjects, based on multiple regression analysis (n = 121)**

	Estimate	95% CI	P-value
Cohort			0.03
82–85 (ref.)	0	– – –	–
91–92	0.6	0.0 to 1.2	0.07
99–00	1.0	0.3 to 1.8	0.008
EP BPD	–0.2	–0.6 to 0.3	0.45
Gestational age, weeks	0.2	0.0 to 0.3	0.07
Birth weight z-score	0.3	0.1 to 0.5	0.006
Prenatal steroids	0.3	–0.2 to 0.8	0.22
Surfactant	–0.3	–1.0 to 0.3	0.30
Maternal smoking	–0.1	–0.5 to 0.3	0.67

Abbreviations: BPD: bronchopulmonary dysplasia (supplemental oxygen or respiratory support at postmenstrual age  $\geq 36$  weeks). EP: extremely preterm (gestational age  $\leq 28$  weeks or birth weight  $\leq 1000$  g). ref: reference level. CI: confidence interval

## References

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