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Il percorso di salute respiratoria lungo tutto l'arco della vita

Enrico Lombardi
SOSD Broncopneumologia
AOU «Meyer» IRCCS, Ospedale Pediatrico, Firenze

*Per quanto concerne i moderatori, relatori, formatori, tutor, docenti è richiesta dall'Accordo Stato-Regioni vigente apposita dichiarazione esplicita dell'interessato, di trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali relativi agli **ultimi 2 anni** dalla data dell'evento.*
La documentazione deve essere disponibile presso il Provider e conservata per almeno 5 anni.

Dichiarazione sul Conflitto di Interessi

Il sottoscritto Enrico Lombardi

in qualità di relatore

dell'evento "Congresso Nazionale SIMRI 2024", Torino, 10-12 Ottobre 2024

ai sensi dell'Accordo Stato-Regione in materia di formazione continua nel settore "Salute" (Formazione ECM) vigente,

Dichiara

che negli **ultimi 3 anni** ha avuto rapporti anche di finanziamento con i seguenti soggetti portatori di interessi commerciali in campo sanitario:

- Alfa-Sigma
- Angelini
- Boehringer
- Chiesi
- Cosmed
- Deca
- GSK
- Lusofarmaco
- Novartis
- Recordati
- Restech
- Sanofi

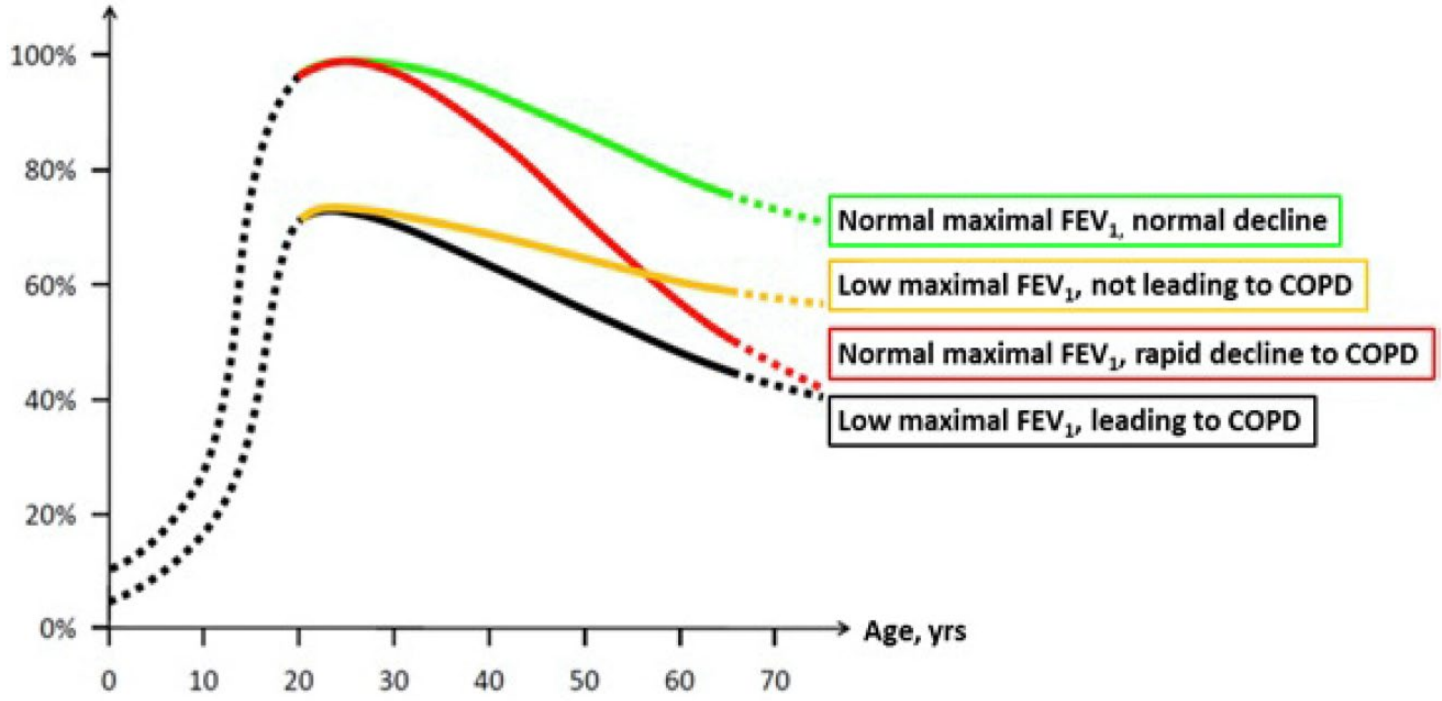
enrico.lombardi@meyer.it 12 Ott 2024

Contenuti

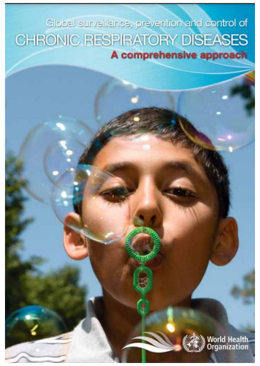
1. Traiettorie di salute respiratoria
2. Prematurità, BPD e meccanismi di malattia
3. Altri fattori di rischio (modificabili)
4. Trattamento e prevenzione

Recent advances in understanding lung function development

Melén E & Guerra S. F1000Res 2017;6:726



Lange P, et al. *N Engl J Med* 2015;373:111-22
Melén E & Guerra S. F1000Res 2017;6:726



COPD is estimated by the WHO to become the third leading cause of death worldwide by 2030

25 August 2007
ISBN: 978 92 4 156346 8

- Three trajectories contributed 75% of COPD burden and were associated with modifiable early-life exposures whose impact was aggravated by adult factors

Bui DS, et al. Lancet Respir Med. 2018;6:535-44

Plasticity of Individual Lung Function States from Childhood to Adulthood

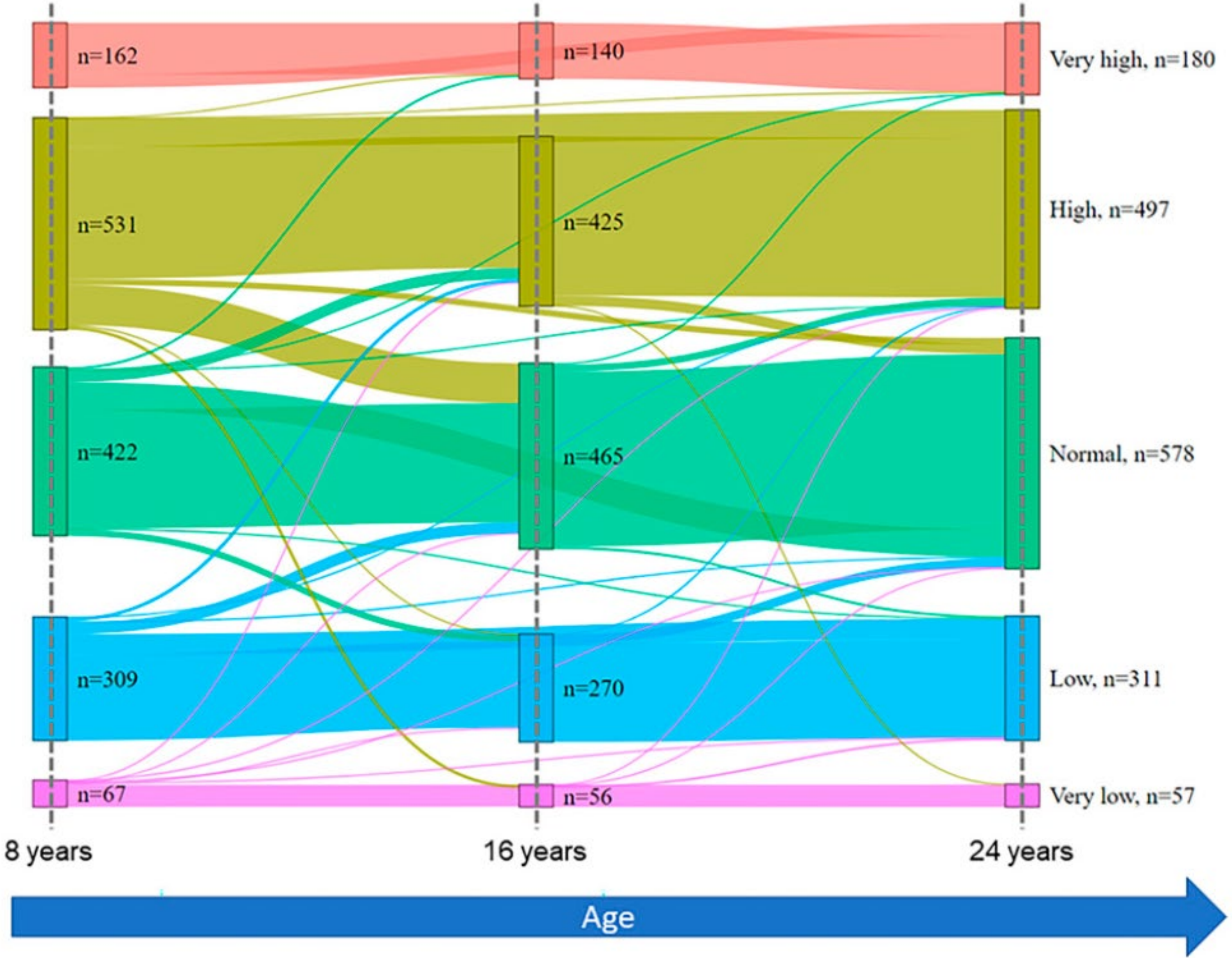
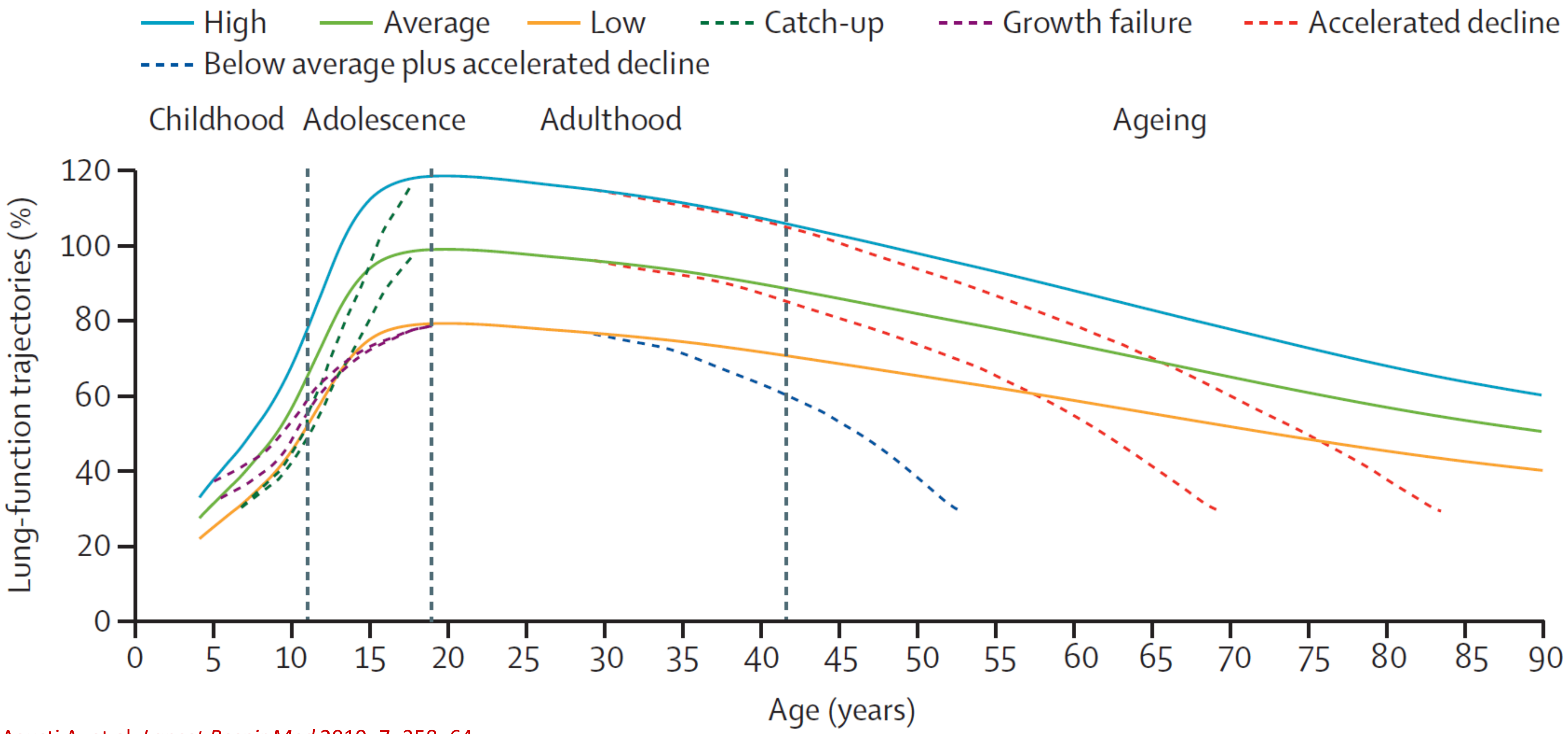


Figure 1. Alluvial plot that illustrates transition of lung function states from childhood to early adulthood. Participants with two or more lung function measures recorded were included. The width of each line is proportional to the number of participants included. The numbers behind Figure 1 are available in Table E6.

Wang G, et al. *AJRCCM* 2023;207:406-15

Traiettorie di Salute Respiratoria



Agusti A, et al. *Lancet Respir Med* 2019; 7: 358–64
Melén E, et al. *Lancet* 2024; 403: 1494–503

Lung-function trajectories: relevance and implementation in clinical practice

Melén E, et al. *Lancet* 2024; 403: 1494–503

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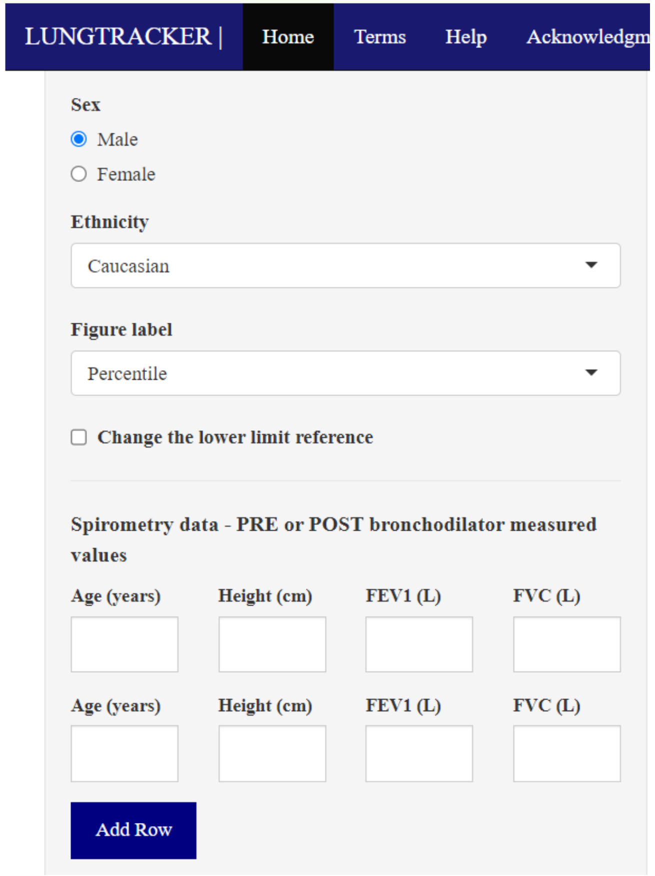
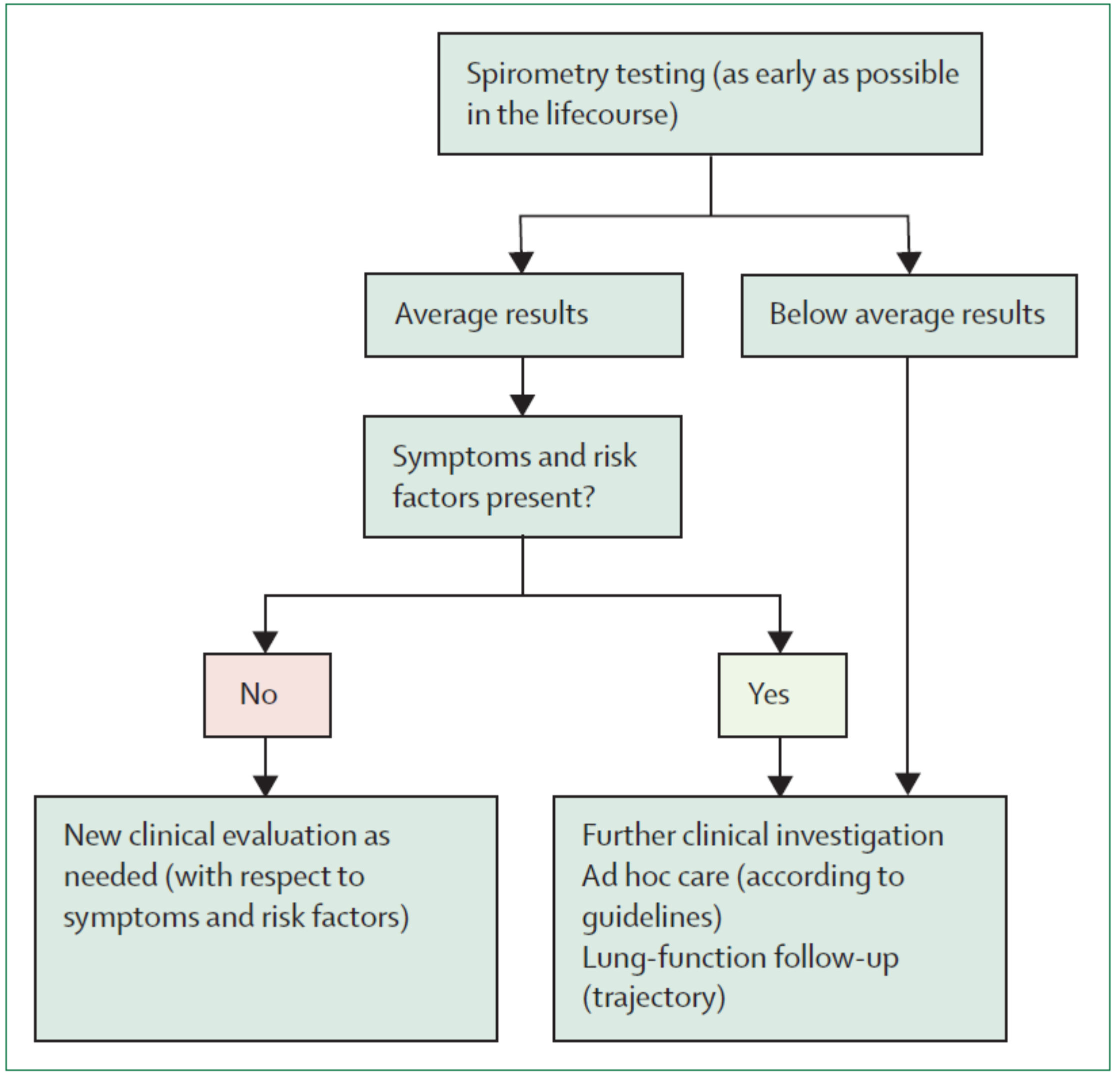
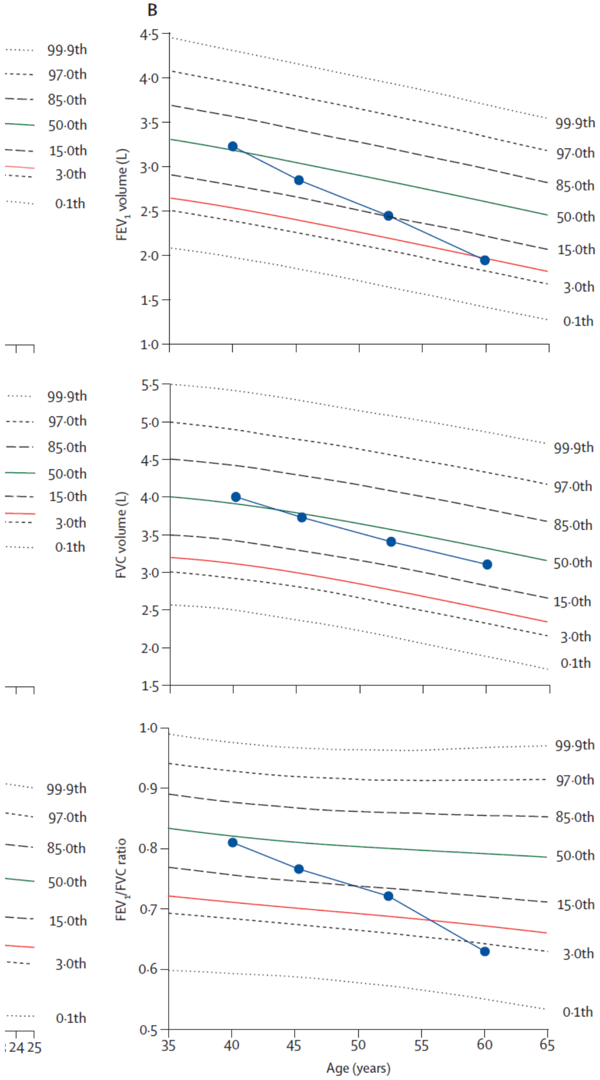
2024

Lung Function Tracker tool

https://gli-calculator. ersnet.or







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Recent advances in understanding lung function development

Melén E & Guerra S. F1000Res 2017;6:726

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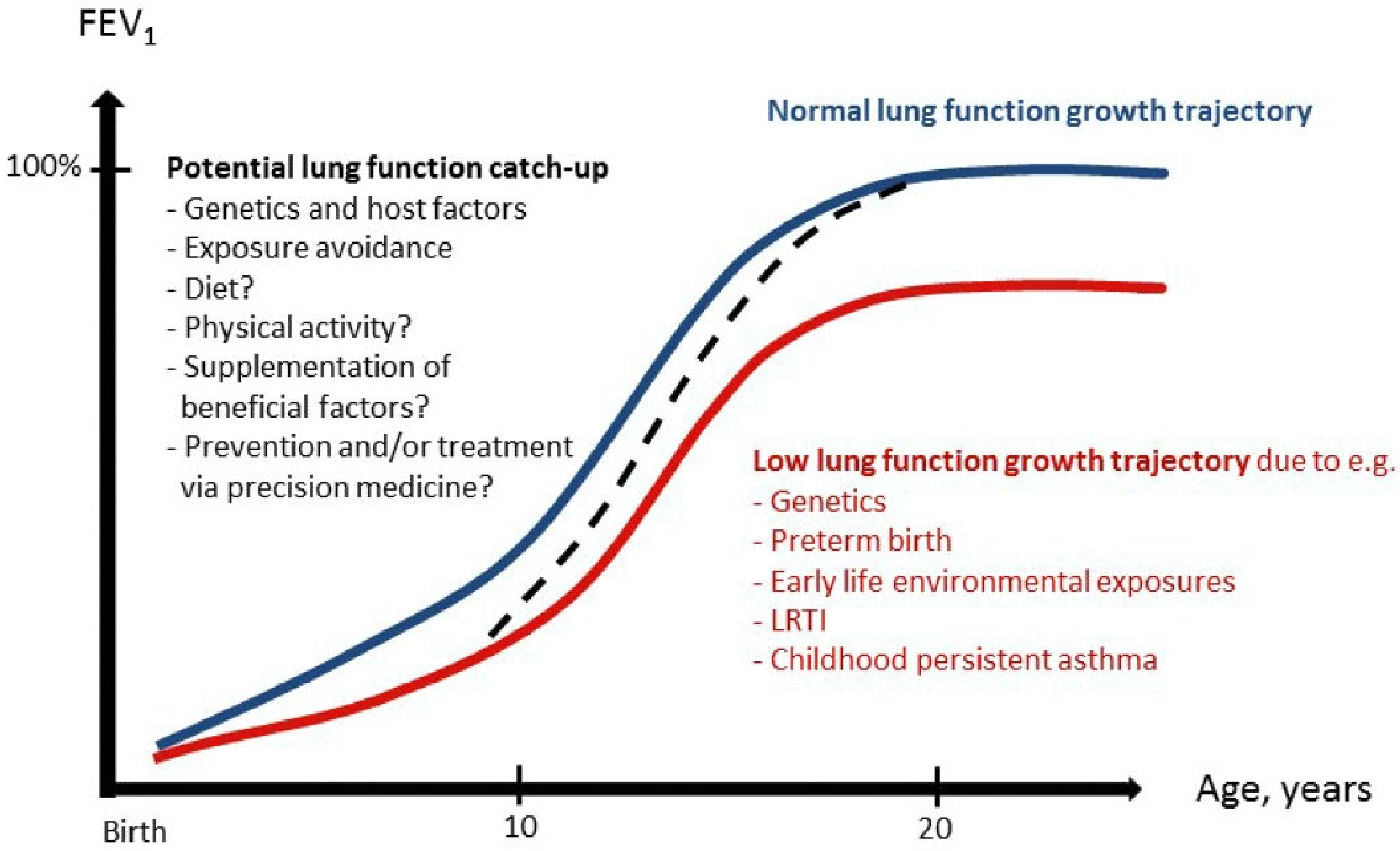
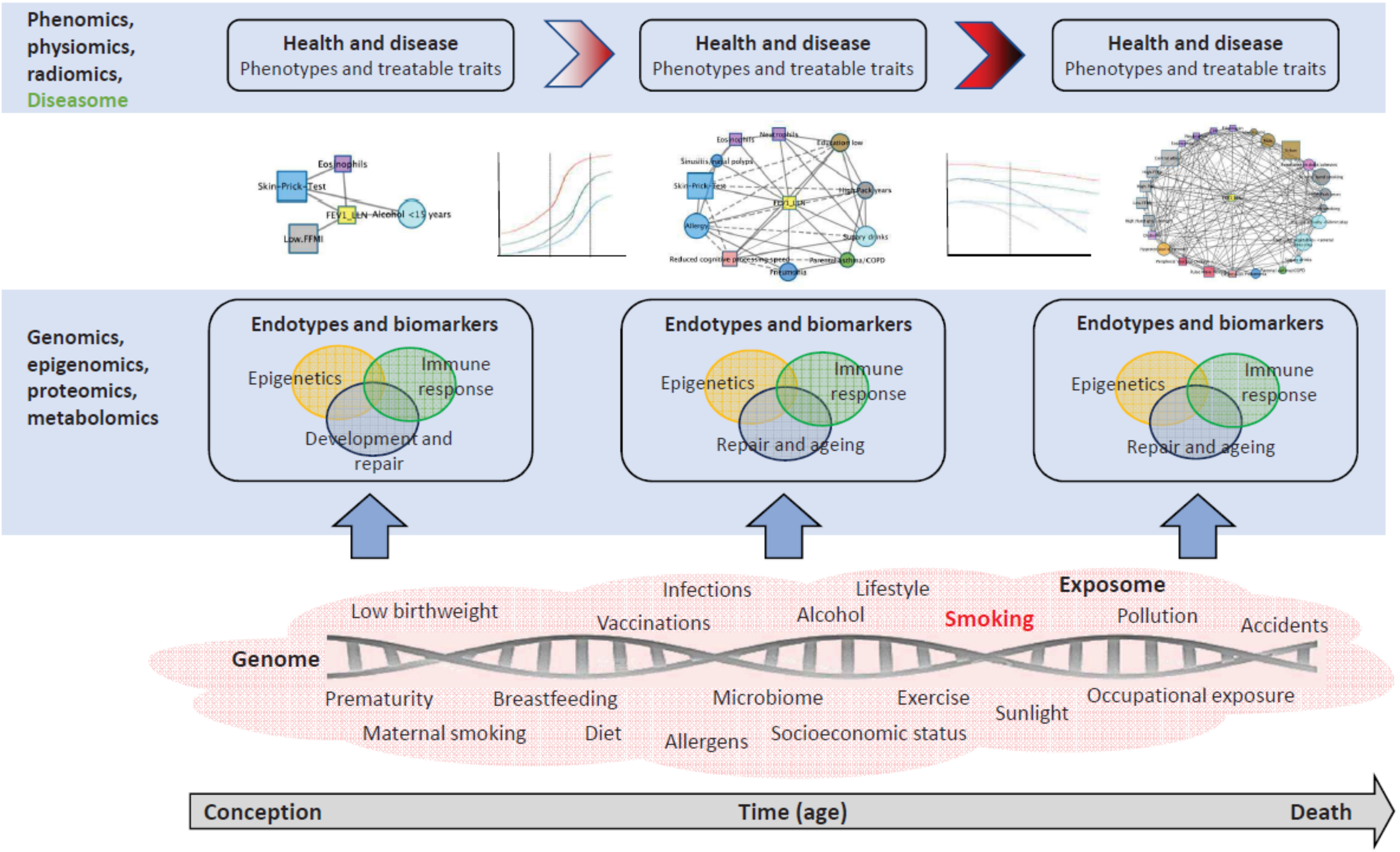


- A holistic understanding of COPD pathogenesis requires the integration of a time axis (T) that considers all **gene (G) - environment (E) interactions** that the individual may encounter through the life span
- Here we use the term **GETomics** to refer to this integrated view (GxExT).



Agusti A, et al. *Lancet Respir Med* 2022;10:512-24

Prematurità

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Torino 10-12 Ott 2024

- Worldwide, about **15 million (10%)** infants are born prematurely **each year (<37 weeks' gestation)**
- More than 80% of preterm births are **moderate-to-late preterm** (32 to ≤37 weeks' gestation)
- Fewer are **very preterm** (28 to <32 weeks' gestation), even fewer are **extremely preterm** (<28 weeks' gestation)

Bronchopulmonary dysplasia (BPD)

- For the past two decades, supplemental O2 therapy for more than 28 days after birth and **respiratory support at 36 weeks' postmenstrual age** (PMA) has been used to define BPD and its severity
- More recently, other investigators have suggested using respiratory support at 36 weeks' PMA or oxygen or respiratory support at 40 weeks' PMA as alternative criteria for the diagnosis of BPD and its severity

Simpson S, et al. *Lancet Respir Med* 2024;12:167-80
Pijnenburg M, et al. Pediatr Pulmonol 2024 Oct 3 online ahead of print

Global, Regional, and National Incidence and Mortality of Neonatal Preterm Birth, 1990-2019

Figure 1. Global Trends in the Incidence of Neonatal Preterm Birth in 204 Countries and Territories

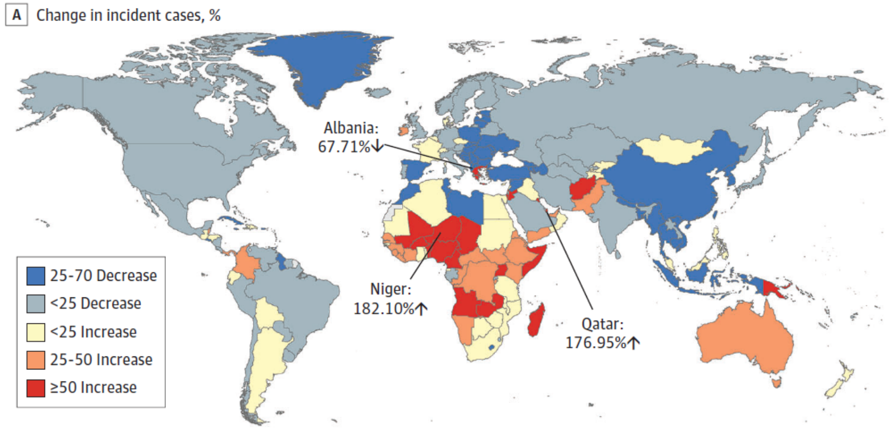
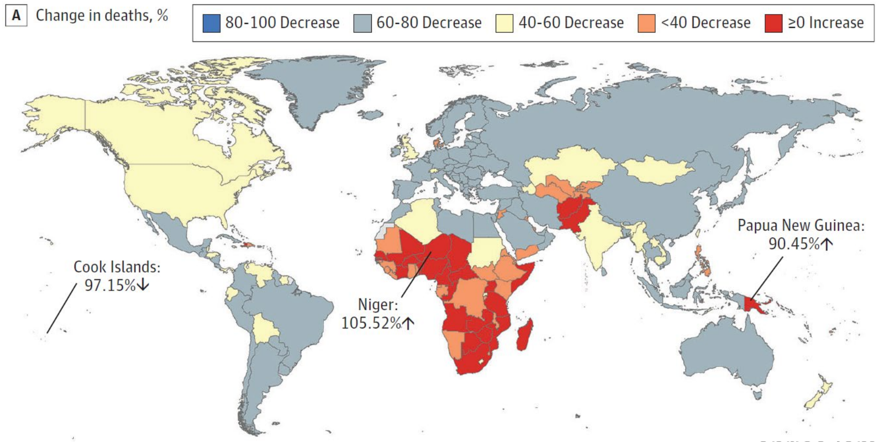


Figure 2. Global Trends in the Mortality of Neonatal Preterm Birth in 204 Countries and Territories



Simpson S, et al. *JAMA Pediatr* 2022;176:787-96

enrico.lombardi@meyer.it 12 Ott 2024

Prematurità

PELICAN
Prematurity's Effects on the Lungs
In Children and Adults Network

The PELICAN (Prematurity's Effect on the Lungs In Children and Adults Network) ERS Clinical Research Collaboration: understanding the impact of preterm birth on lung health throughout life

- PELICAN was launched in 2020 as the fourth CRC within the ERS Paediatric Assembly

Simpson SJ & Hallberg J, on behalf of the PELICAN CRC
Eur Respir J 2021;57:2004387

Unravelling the respiratory health path across the lifespan for survivors of preterm birth

Shannon J Simpson, Cassidy Du Berry, Denby J Evans, James T D Gibbons, Maria Vollsæter, Thomas Halvorsen, Karl Gruber, Enrico Lombardi, Sanja Stanojevic, John R Hurst, Petra Um-Bergström, Jenny Hallberg, Lex W Doyle, Sailesh Kotecha, on behalf of PELICAN

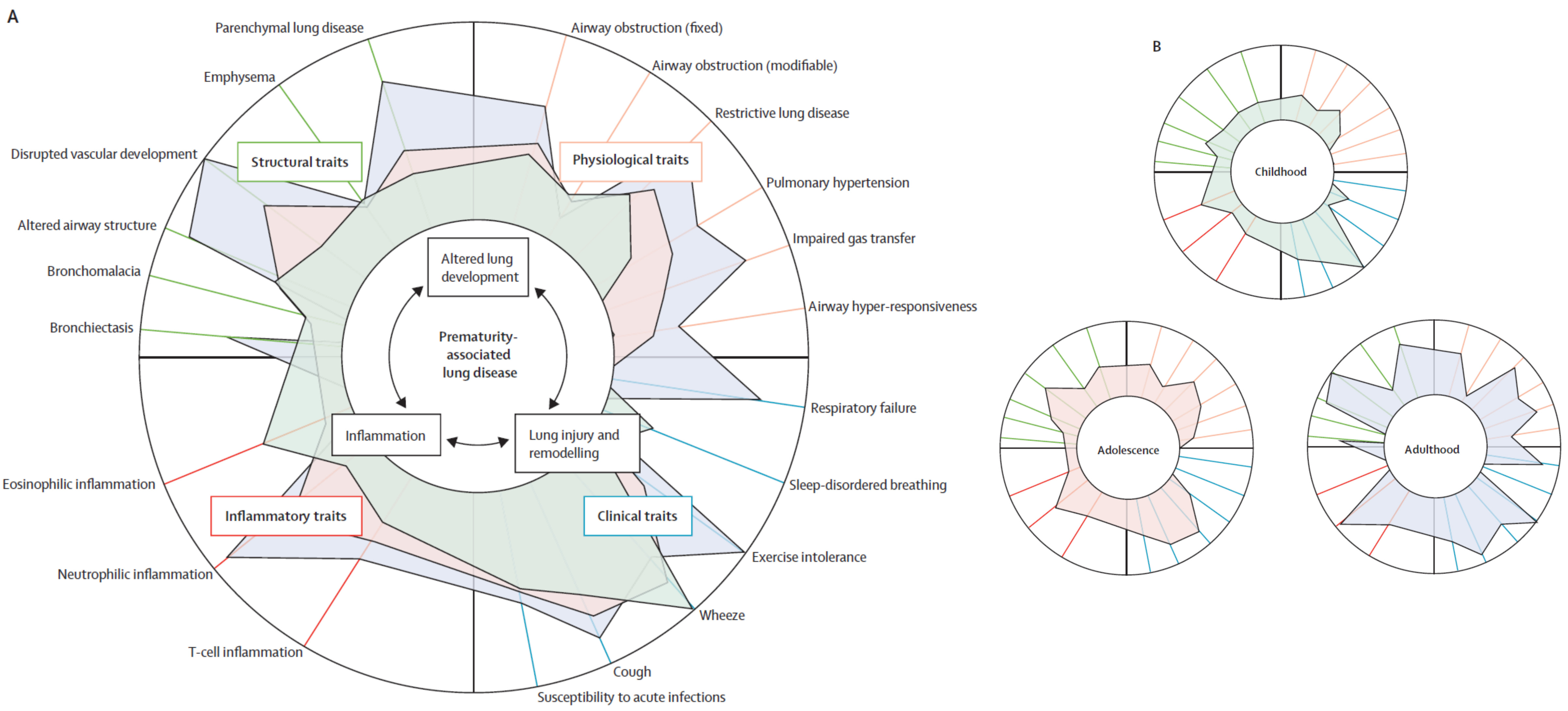
Prematurity-associated lung disease
A chronic lung disease that has occurred following preterm birth, characterised by abnormal structural, physiological, clinical, or inflammatory respiratory phenotypes; the term prematurity-associated lung disease encompasses the broad implications of preterm birth on later-life respiratory health irrespective of BPD diagnosis during infancy

Lancet Respir Med 2024;12:167-80

Unravelling the respiratory health path across the lifespan for survivors of preterm birth

Simpson S, et al. *Lancet Respir Med* 2024;12:167-80

Torino
10-12 Ott
2024



Chronic Lung Disease after Premature Birth

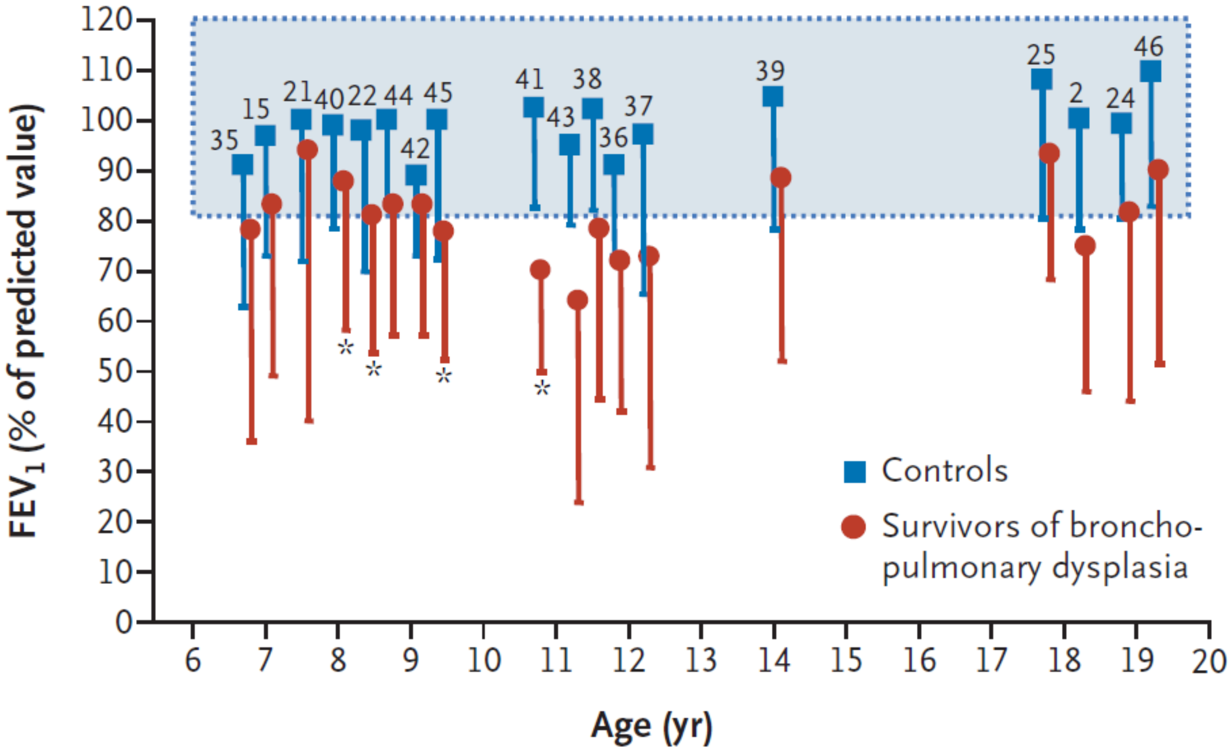


Figure 3. FEV_1 Values in Children, Adolescents, and Young Adults Who Were Born Prematurely and Had Bronchopulmonary Dysplasia, as Compared with Controls Born at Term.

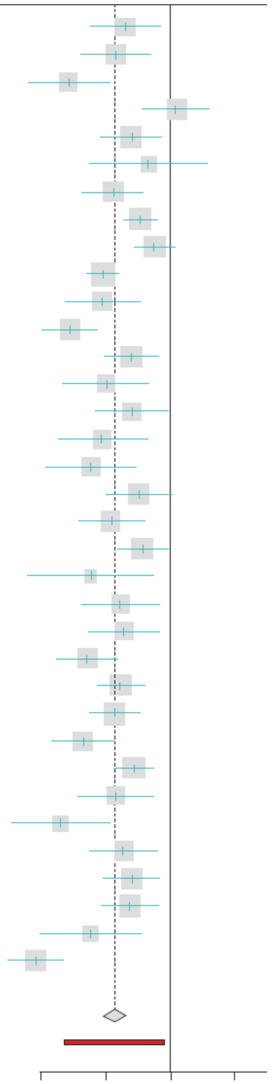
Data (presented as means −2 SD) are from 18 studies, reported since 1990, in which survivors of bronchopulmonary dysplasia who were 6 to 19 years of age were compared with a reference population born at term. In all but two studies, the mean forced expiratory volume in 1 second (FEV_1) was significantly lower in the patients with bronchopulmonary dysplasia than in the healthy controls. Eighty percent of the predicted FEV_1 value is the accepted lower limit of the normal range. An asterisk indicates that the study was performed after the introduction of surfactant therapy. The studies were conducted in the United States,[2,15,35-37] Australia,[22,24,38,39] Finland,[21,40,41] Canada,[42,43] Italy,[44,45] Norway,[25] and the Netherlands.[46] The numbers within the graph refer to the reference numbers of the studies.

Baraldi E & Filippone M. N Engl J Med 2007;357:1946-55

Increasing airway obstruction through life following bronchopulmonary dysplasia: a meta-analysis

	BPD			Term			Standardised mean difference (SMD)
	Total	Mean	SD	Total	Mean	SD	
Arigliani 2020 [23]	17	−0.41	0.92	60	0.09	0.64	
Baraldi 2005 [25]	31	81.80	11.14	31	89.40	5.57	
Bozzetto 2016 [28]	27	−1.35	1.40	27	0.60	1.00	
Cazzato 2013 [31]	22	0.12	1.23	46	0.03	0.78	
Chang 2020 [32]	55	−0.32	1.29	29	0.39	0.85	
Di Filippo 2021 [37]	5	0.40	0.60	55	0.70	0.90	
Doyle 2001 (1977–1982 cohort) [39]	39	78.60	11.10	39	87.00	7.00	
Doyle 2006 (1981–1992 cohort) [40]	89	87.90	9.40	208	91.40	6.60	
Doyle 2017 (1997 cohort) [38]	56	−0.31	1.39	149	0.01	1.27	
Fawke 2010 [43]	129	−1.40	1.30	161	−0.20	1.00	
Fortuna 2016 [45]	28	−0.40	0.95	27	0.57	0.85	
Gough 2014 [50]	56	−0.68	0.22	55	0.34	0.89	
Hadchouel 2018 [53]	49	−0.60	1.40	44	0.20	1.20	
Hakulinen 1996 [55]	20	95.50	7.60	20	102.90	6.71	
Kaplan 2012 [63]	28	88.00	10.00	23	93.00	5.00	
Karila 2008 [64]	20	72.30	16.30	18	86.40	4.10	
Kilbride 2003 [68]	16	81.00	8.00	25	89.00	5.00	
Korhonen 2004 [70]	29	88.00	9.00	33	92.00	7.00	
Landry 2016 [75]	31	70.00	12.00	35	79.00	7.00	
MacLean 2016 [76]	47	−1.14	1.50	64	−0.57	1.14	
Mitchell 1998 [79]	10	77.00	11.00	10	88.00	5.00	
Molgat-Seon 2019 [80]	25	−1.62	1.30	20	−0.76	0.72	
Praprotnik 2015 [92]	23	78.30	18.60	33	87.50	5.00	
Prenzel 2020 [93]	39	−0.63	1.24	40	0.98	1.22	
Ronkainen 2015 [94]	49	92.90	8.50	88	98.90	7.30	
Simpson 2017 [5]	70	−1.14	1.04	48	−0.27	0.92	
Sorensen 2018 [99]	42	−1.33	1.08	38	0.02	0.86	
Thunqvist 2018 [102]	82	−0.45	1.17	98	0.20	1.14	
Um-Bergstrom 2019 [103]	26	−0.79	1.60	24	0.34	0.91	
Vardar-Yagli 2015 [105]	18	73.70	13.10	20	91.10	5.90	
Vollsaeter 2013 (1991–1992 cohort) [106]	26	−0.72	1.05	35	0.01	0.95	
Vollsaeter 2013 (1982–1985 cohort) [106]	37	−0.12	1.04	46	0.53	1.08	
Vollsaeter 2015 (1999–2000 cohort) [107]	31	−0.90	1.05	54	−0.30	0.90	
Vrijlandt 2006 [110]	8	78.80	8.10	48	87.40	6.60	
Yang 2020 [114]	46	−1.67	1.28	100	0.65	1.01	
Random effects model	**1326**			**1851**			
Prediction interval							

Heterogeneity: I^2=72%, τ^2=0.1379, p<0.01



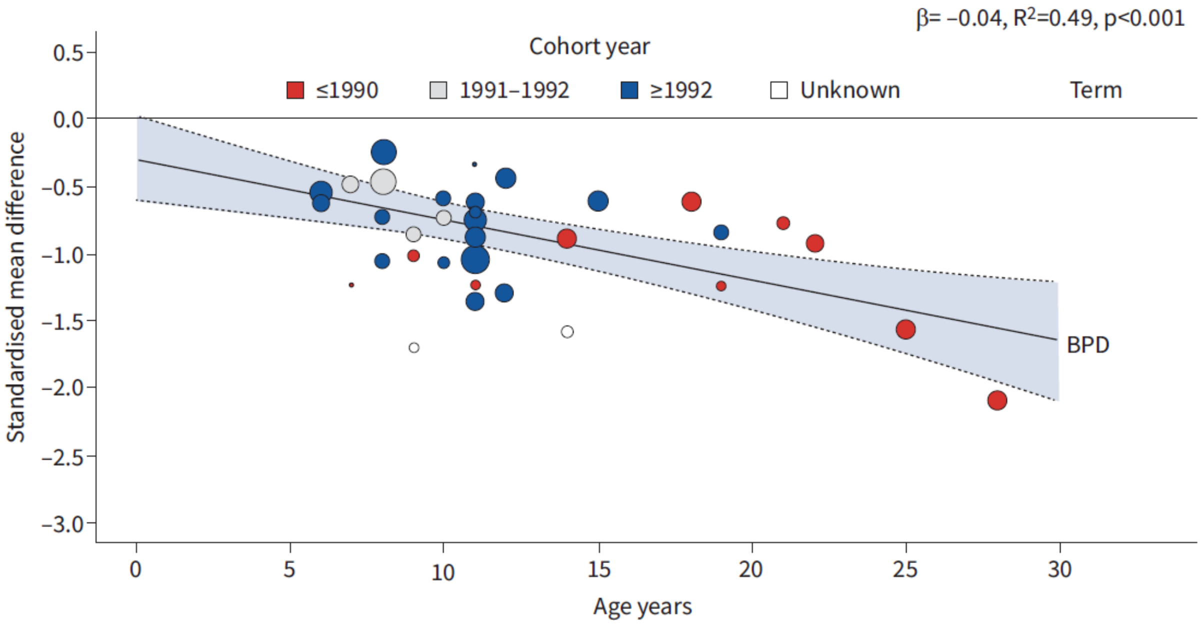
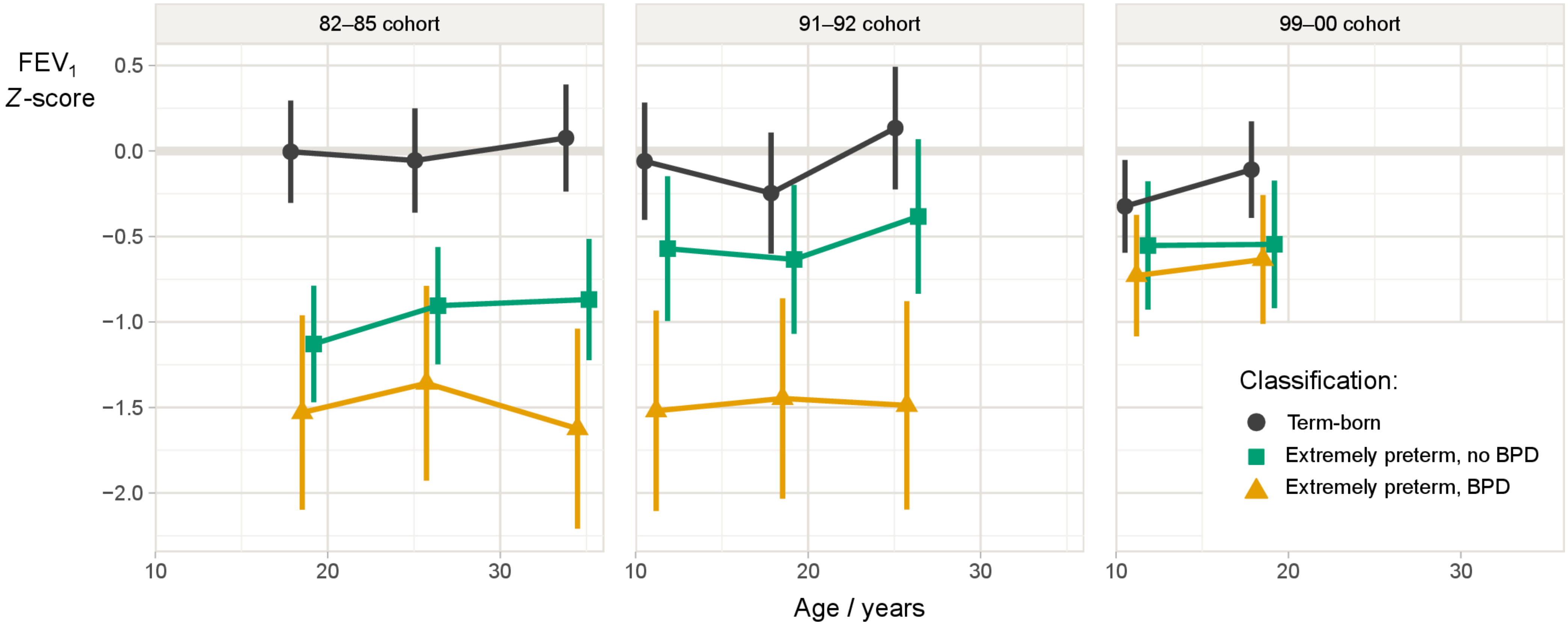


FIGURE 2 Meta-regression of forced expiratory volume in 1 s/forced vital capacity moderating for age: bronchopulmonary dysplasia (BPD) *versus* Term.

Gibbons JTD, et al. *ERJ Open Res* 2023;9:00046-2023

Tracking of lung function from 10 to 35 years after being born extremely preterm or with extremely low birth weight



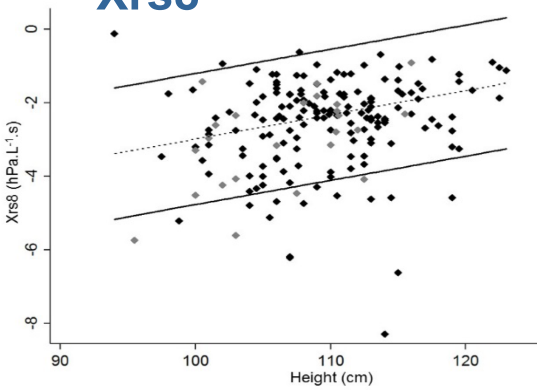
Bardsen T, et al. *Thorax* 2022;77:790-8

Lung function in a cohort of 5-year-old children born very preterm

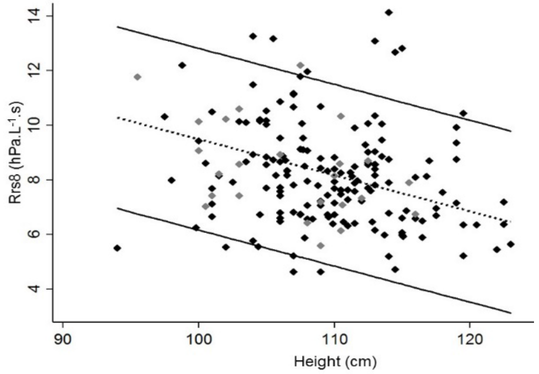
Enrico Lombardi MD[1] | Valentina Fainardi PhD[2] | Claudia Calogero MD[1] | Monia Puglia MSc[3] | Fabio Voller MSc[3] | Marina Cuttini PhD[4] | Franca Rusconi MD[5]

- A cohort of infants born **22-31 weeks of gestational age** in Tuscany (Italy)
- A total of **194 children** tested at **mean age 5.2 yr**

Xrs8



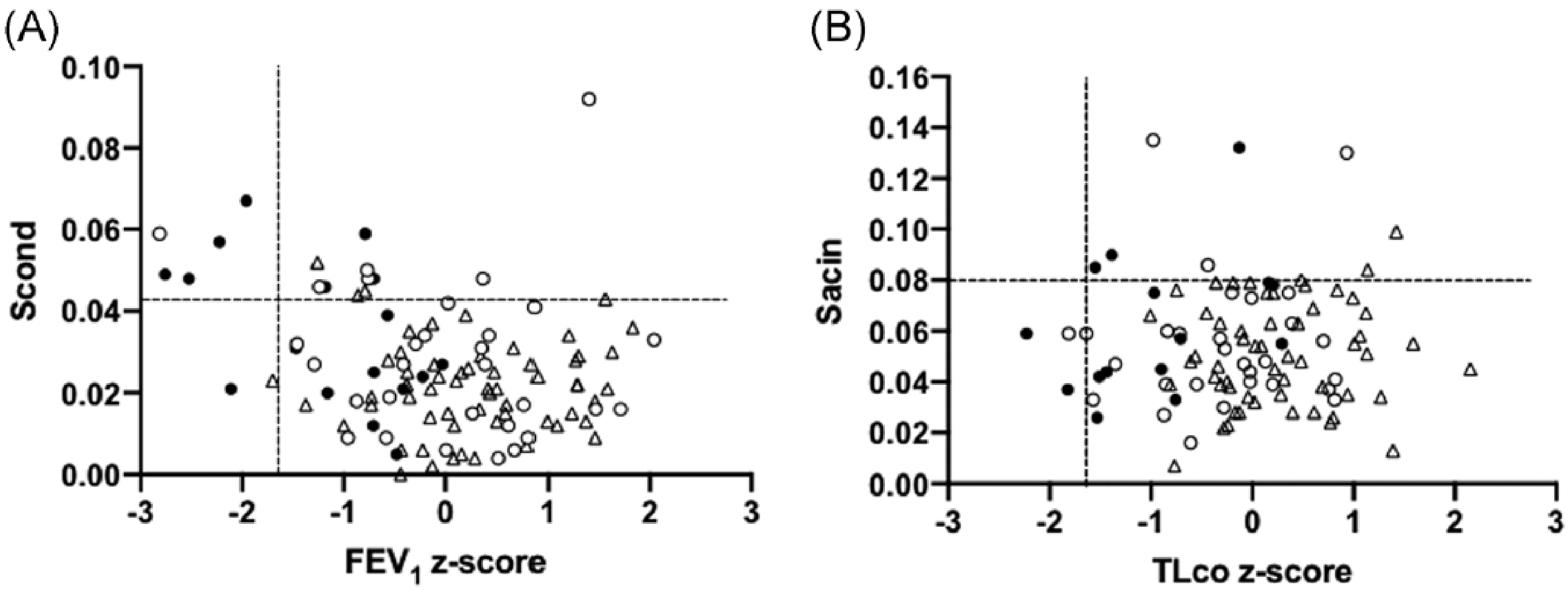
Rrs8



	Measured values baseline	Predicted values	P[a]
Rint	n = 194		
$kPa.L^{-1}.s$	0.90 (0.23)	0.76 (0.07)	<0.001
Z-score	0.72 (1.13)		
Rrs8	n = 185		
$hPa.L^{-1}.s$	8.20 (1.85)	8.26 (0.73)	0.663
Z-score	−0.03 (1.08)		
Xrs8	n = 185		
$hPa.L^{-1}.s$	−2.62 (1.25)	−2.37 (0.36)	0.005
Z-score	−0.28 (1.34)		
AX	n = 185		
$hPa.L^{-1}$	41.41 (27.81)	32.49 (0.14)	<0.001
Z-score	0.29 (1.41)		

Lombardi E & Fainardi V, et al. *Pediatr Pulmonol* 2018;53:1633-9

Regional ventilation inhomogeneity in survivors of extremely preterm birth



Conclusion: Almost a third of extremely preterm children at school age showed Scond alterations that affected also children without BPD. Longitudinal studies should clarify the prognostic meaning of Scond abnormalities in this group.

Arigliani M, et al. *Pediatr Pulmonol* 2020;55:1366-74

Long-term expiratory airflow of infants born moderate-late preterm: A systematic review and meta-analysis

Study	N	SD	Mean $zFEV_1$ with 95% CI	Weight (%)
2012 Kotecha	317	0.98	-0.12 (-0.23, -0.01)	9.51
2013 Narayanan	21	0.92	-0.16 (-0.64, 0.32)	4.67
2016 Carbonell-Estrany	243	1.2	-0.32 (-0.45, -0.19)	9.25
2016 Gonçalves	46	1.08	-0.44 (-0.76, -0.12)	6.67
2016 Landry	12	0.9	-1.07 (-1.66, -0.48)	3.67
2016 Thunqvist	99	0.84	0.22 (0.03, 0.41)	8.56
2016 Yammine	12	0.99	-0.11 (-0.65, 0.43)	4.10
2017 Kaczmarczyk	12	1.17	-0.36 (-1.06, 0.34)	2.92
2018 Nasanen-Gilmore	320	0.91	-0.19 (-0.30, -0.08)	9.45
2018 Scheltema	335	0.8	-0.24 (-0.33, -0.15)	9.71
2018 Vrijlandt	37	1.2	-0.60 (-0.92, -0.28)	6.61
2019 Yaacoby-Bianu	29	0.45	0.03 (-0.14, 0.20)	8.72
2020 Arroyas	74	1.18	-0.43 (-0.70, -0.16)	7.41
2021 Aoyama	7	1.96	-1.06 (-2.55, 0.43)	0.83
2021 Pérez-Tarazona	102	1.21	-0.29 (-0.52, -0.06)	7.93
Overall			**-0.26 (-0.40, -0.11)**	**100.0**

Heterogeneity: $I^2 = 85.16\%$

Test of overall effect: $z = -3.54$, $p < 0.001$

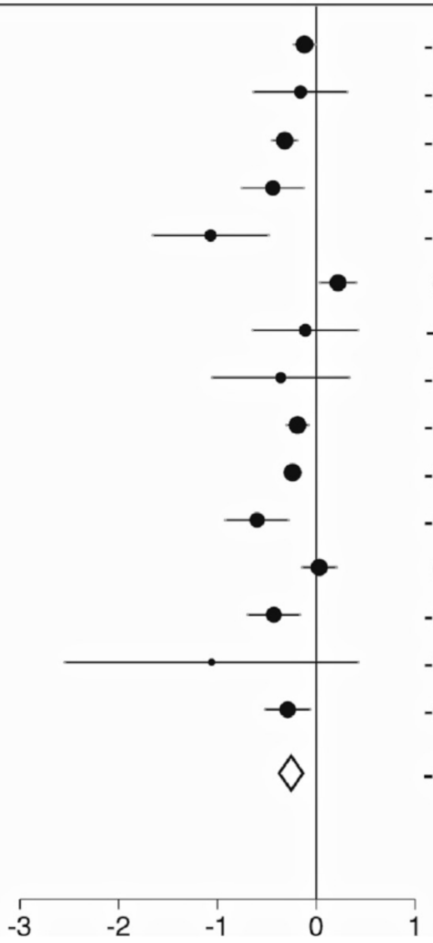
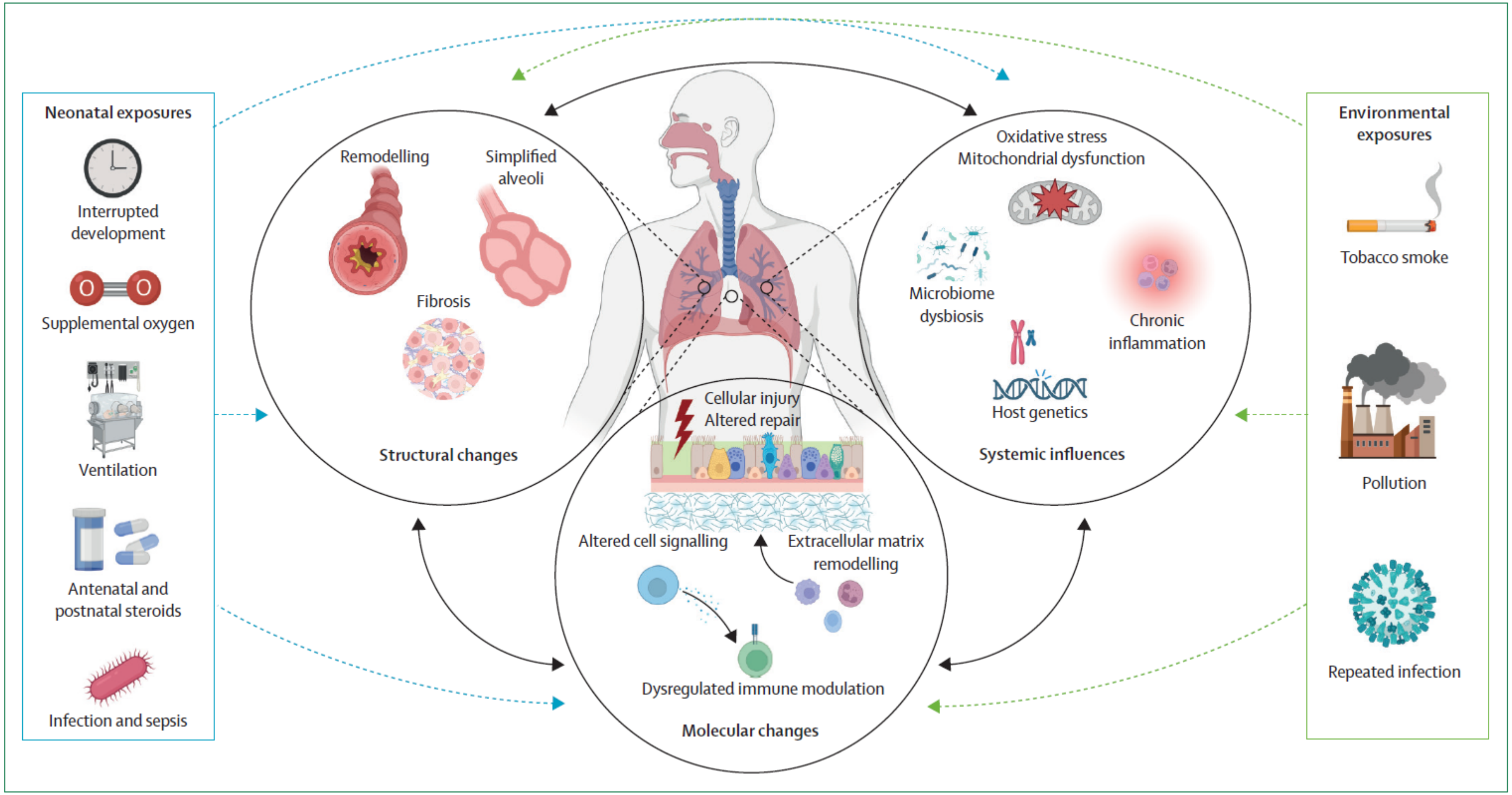


Figure 4. Forced expiratory volume in 1 second z-score (zFEV1) of the moderate-late preterm group compared with a z-score of 0. A mean $zFEV_1$ less than 0 indicates individuals born MLP are performing worse than population norms, as derived from relevant reference equations, on average.

Du Berry C, et al.
EClinicalMedicine 2022;52:101597

Meccanismi di Malattia



Simpson S, et al. *Lancet Respir Med* 2024;12:167-80

The role of growth and nutrition in the early origins of spirometric restriction in adult life: a longitudinal, multicohort, population-based study

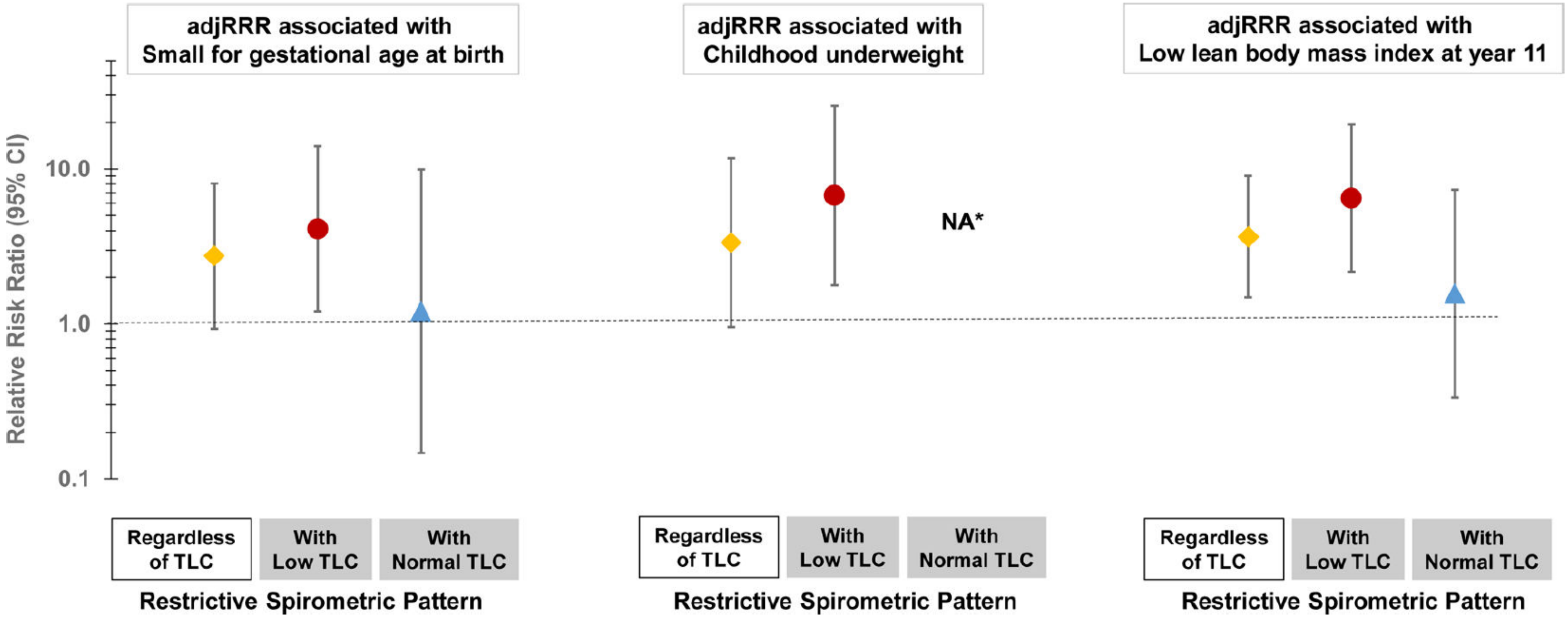
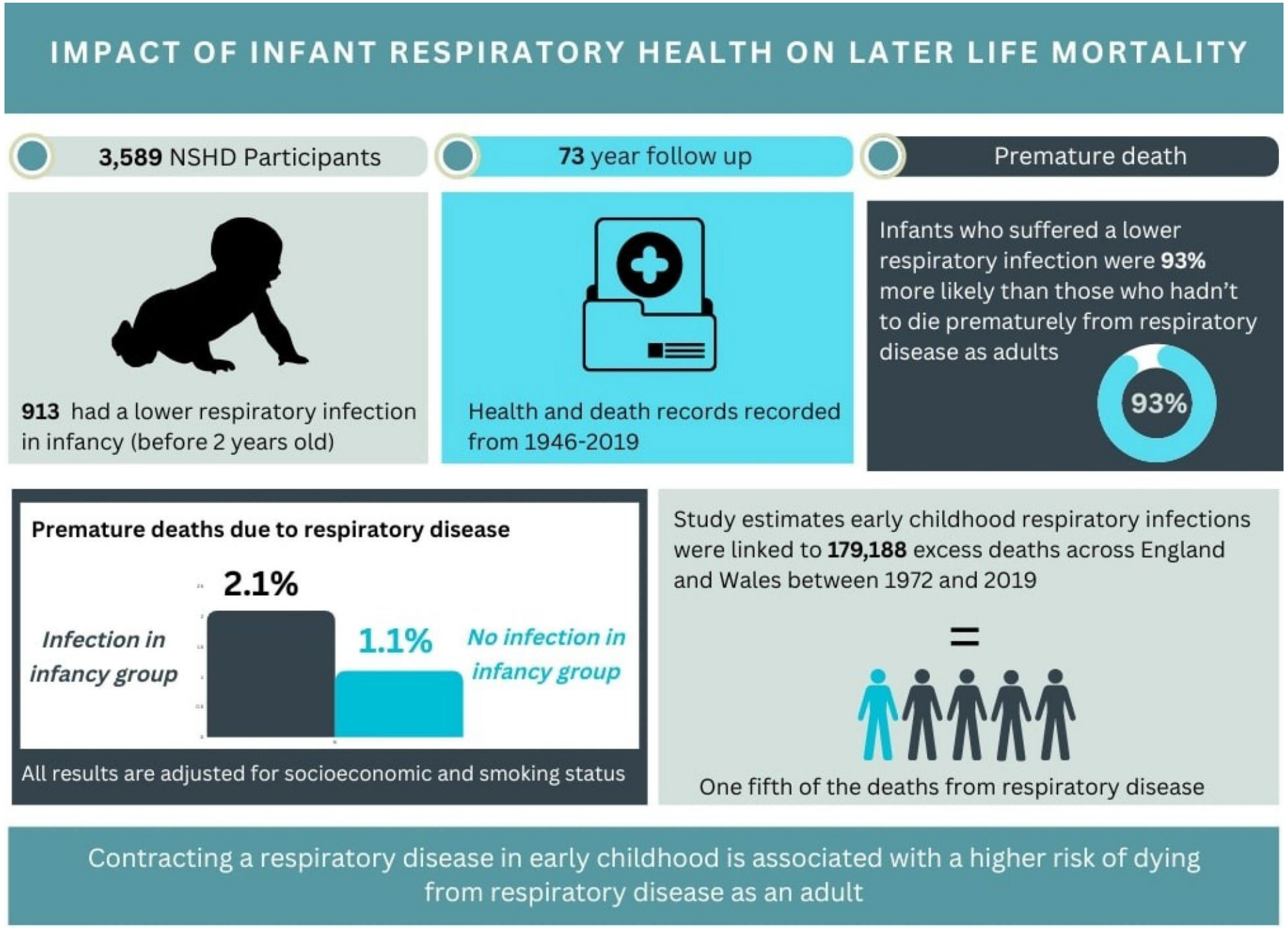


Figure 4: Associations of small for gestational age at birth, childhood underweight, and low lean body mass index at year 11 with spirometric restriction with and without low total lung capacity (TLC) at year 18 in MAAS

Voraphani N, et al. *Lancet Respir Med* 2022;10:59–71

Early childhood lower respiratory tract infection and premature adult death from respiratory disease in Great Britain: a national birth cohort study

Allinson JP, et al.
Lancet 2023;401:1183-93



Credit: UCL

https://doi.org/10.1016/S0140-6736(23)00131-9

Early-life respiratory tract infections and the risk of school-age lower lung function and asthma: a meta-analysis of 150 000 European children

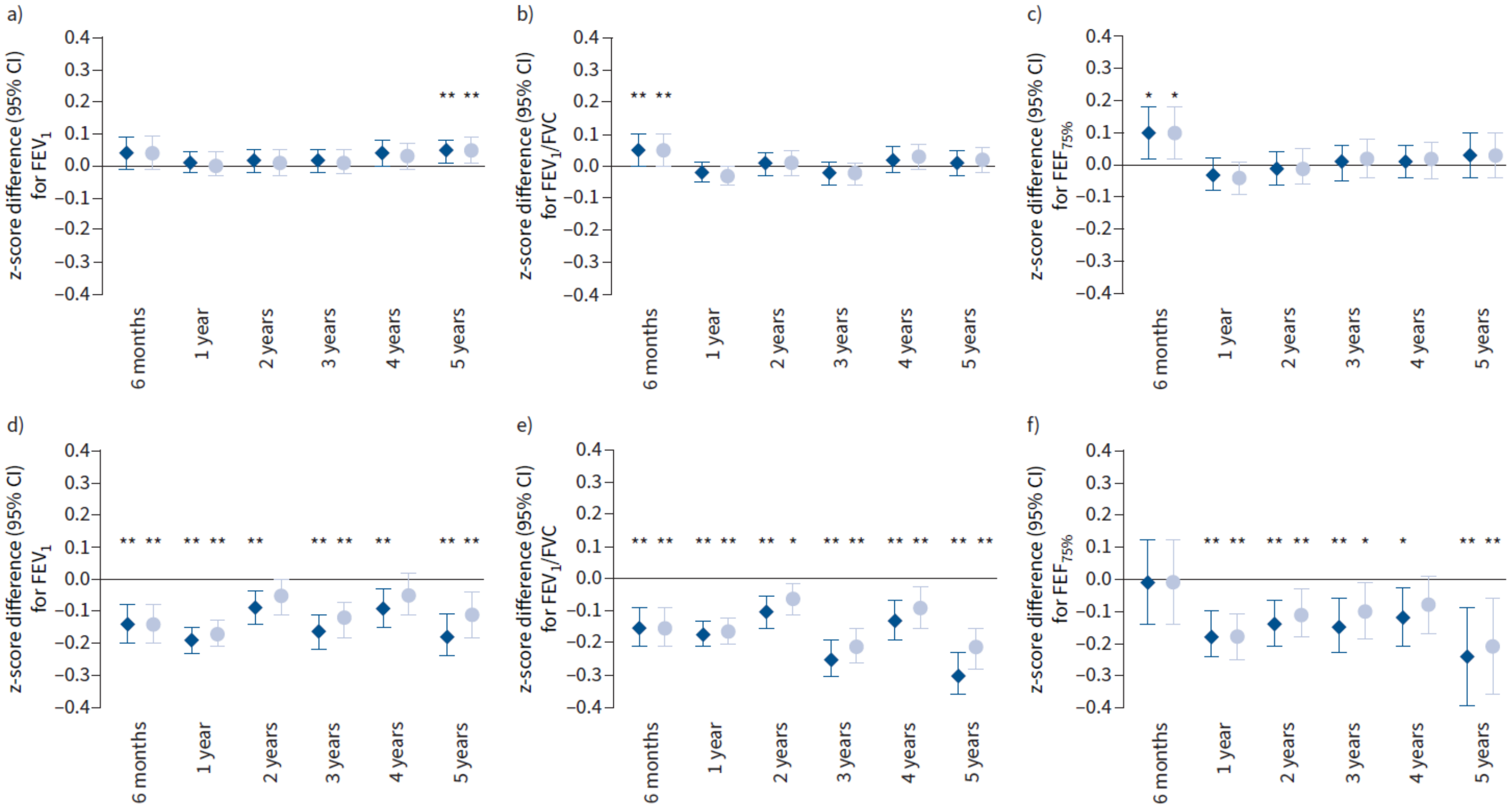


FIGURE 1 Associations of early-life a–c) upper and d–f) lower respiratory tract infections with school age: a, d) forced expiratory volume in 1 s (FEV_1), b, e) FEV_1/forced vital capacity (FVC) and c, f) forced expiratory flow at 75% of FVC ($FEF_{75\%}$). Data are presented as change in z-score (95% confidence interval), derived from multilevel linear regression models. The dark blue diamonds represent models adjusted for maternal history of asthma and atopy, ethnicity, education level, smoking during pregnancy, parity and pet keeping, and child's sex, gestational age at birth, birthweight, season of birth, breastfeeding, and daycare attendance. The light blue circles represent models additionally adjusted for preceding a–c) upper or d–f) lower respiratory tract infections. *: $p<0.05$; **: $p<0.01$.

van Meel ER, et al. Eur Respir J Open Res 2022;60:2102395

Associations of improved air quality with lung function growth from childhood to adulthood: the BAMSE study

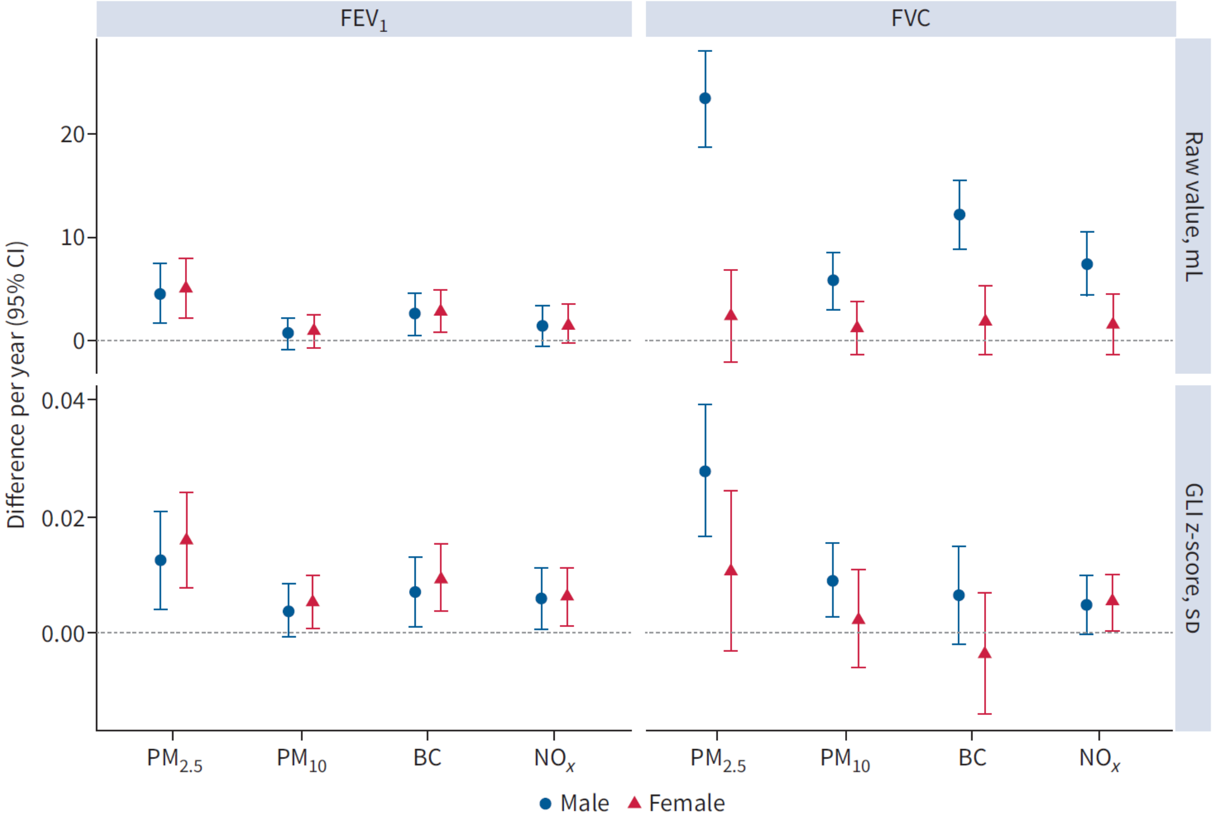


FIGURE 1 Sex-specific associations between improvement of air quality and differences in forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) growth from age 8 to 24 years. Results were adjusted for age, height, body mass index (BMI) at age 8 years, municipality at birth, parental education level at birth, parental occupation at birth, maternal smoking during pregnancy, environmental tobacco smoke at 8 years, air pollution exposure during the first year of life, BMI at 16 and 24 years, active smoking at 16 and 24 years, and education level at 24 years. Estimates were interpreted as the difference in 1-year growth (95% CI) in FEV_1 and FVC for per unit improvement of air pollution concentrations, with positive values indicating positive associations between improved air quality and increased rate of FEV_1 or FVC growth. GLI: Global Lung Initiative; $PM_{2.5}$: particulate matter with diameter ⩽2.5 µm; PM_{10}: particulate matter with diameter ⩽10 µm; BC: black carbon; NO_x: nitrogen oxides.

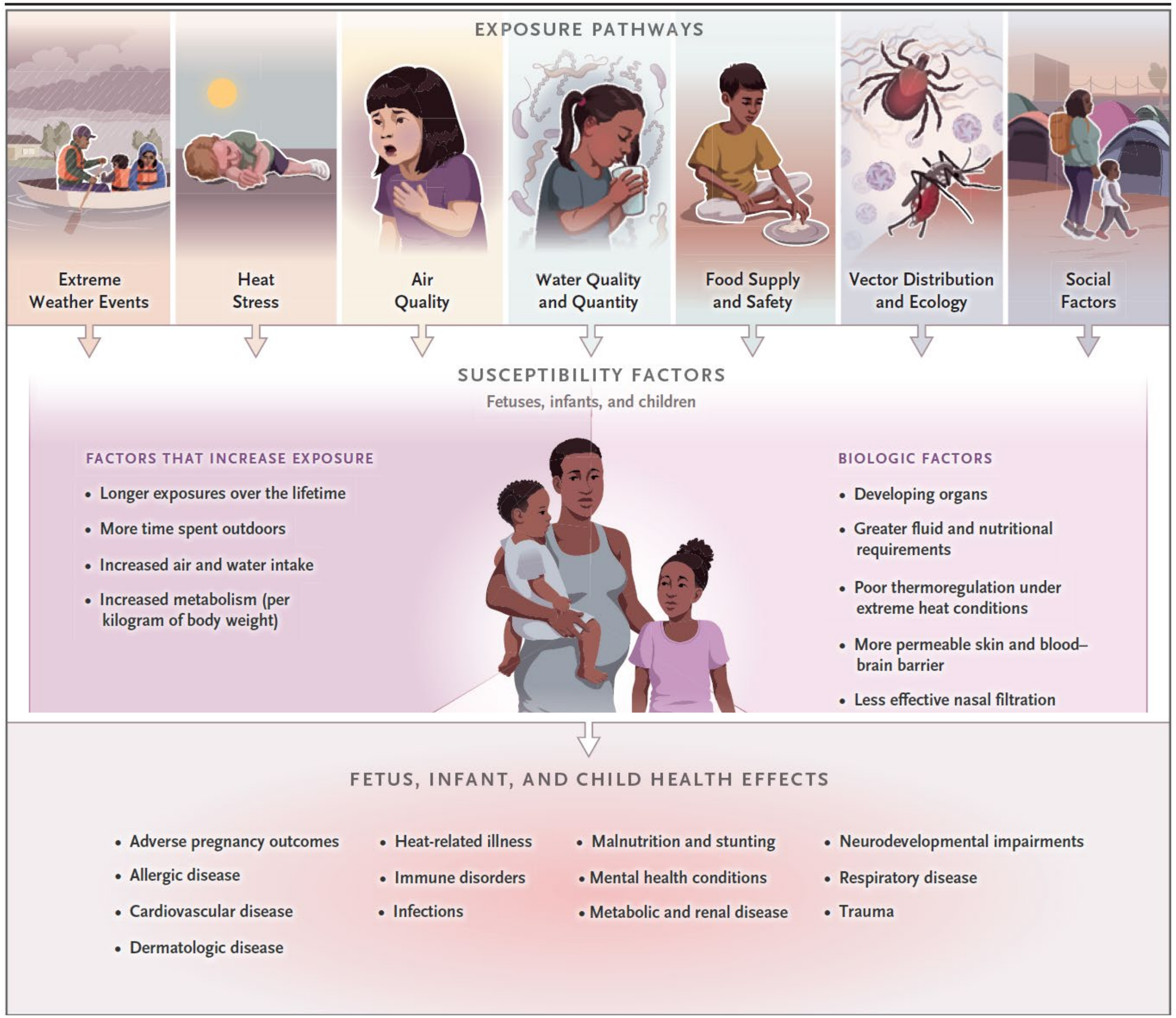
Yu Z, et al. *Eur Respir J* 2023; 61: 2201783

Predictors of lung function trajectories in population-based studies: A systematic review

Risk factors/age (years)	Studies investigated	Evidence of adverse association	Associated lung function trajectory	Timepoint of lung function measurement (years)
Childhood and adolescent environmental characteristics				
SHS exposure (infants 3, 7)	TAHS[3]	✓	Persistently low FEV_1 trajectories	7–53
	MAAS[18]	✓	Persistently low FEV_1 trajectories	5–16
	ALSPAC[18]	✓	Below average FEV_1 trajectories	8–24
	IOW[19]	×		10–26
	Pelotas 1993 birth cohort[21]	×		15–22

Okyere DO, et al. Respirology 2021;26:938-59

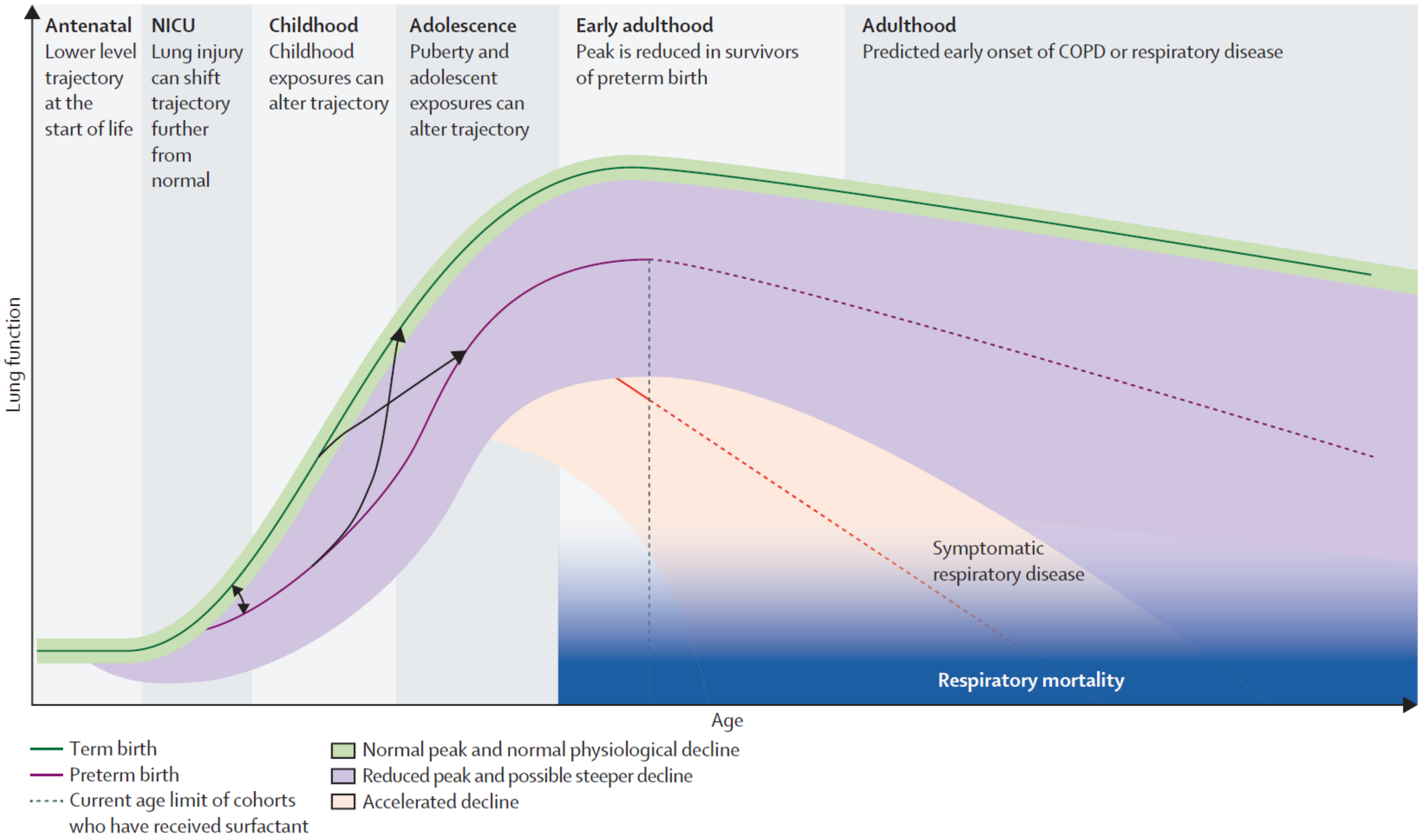
Climate Change, Fossil-Fuel Pollution, and Children's Health



Perera F, et al.
N Engl J Med 2022;386:2303-14

Unravelling the respiratory health path across the lifespan for survivors of preterm birth

Simpson S, et al. *Lancet Respir Med* 2024;12:167-80



enrico.lombardi@meyer.it 12 Ott 2024

Cosa possiamo fare?

- Changes in BPD pathology were brought about by substantial improvements in clinical practice during the 1980s and 1990s, including **antenatal maternal administration of corticosteroids**, the introduction of **exogenous surfactant after birth** to treat respiratory distress, and use of **gentler forms of mechanical ventilation**
- A recent ***Lancet* Series on small vulnerable newborns** puts forward approaches to prevent preterm birth in low-income and middle-income countries
- Preventing BPD through the use of **gentler techniques of respiratory support**, such as reduced duration of invasive mechanical ventilation, for infants born prematurely is a priority for neonatal paediatricians. However, so far, there is **little evidence of success**.
- Several treatments given soon after birth, including **caffeine** and **postnatal corticosteroids** have been shown to prevent BPD and also improve expiratory airflow in later childhood. However, **studies** of expiratory airflow **into adulthood** to determine the longevity of these benefits are **not available**. Moreover, other complications, such as **neurodevelopmental impairment**, have been associated with the use of postnatal corticosteroids to prevent BPD, thus limiting their applicability.
- Both the ERS and ATS guidelines recommend the use of **inhaled short-acting bronchodilators or inhaled steroids only in the subgroup of patients with asthma-like symptoms, recurrent hospital visits, or both**

Simpson S, et al. *Lancet Respir Med* 2024;12:167-80

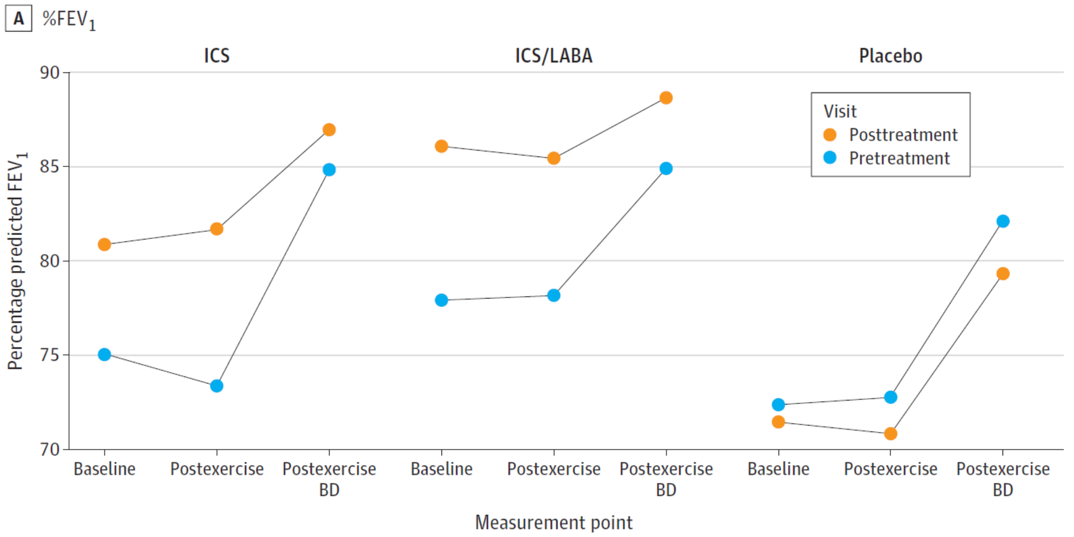
Inhaled Corticosteroids Alone and in Combination With Long-Acting β_2 Receptor Agonists to Treat Reduced Lung Function in Preterm-Born Children

A Randomized Clinical Trial

eTable 4: Results of ANCOVA of spirometry measures

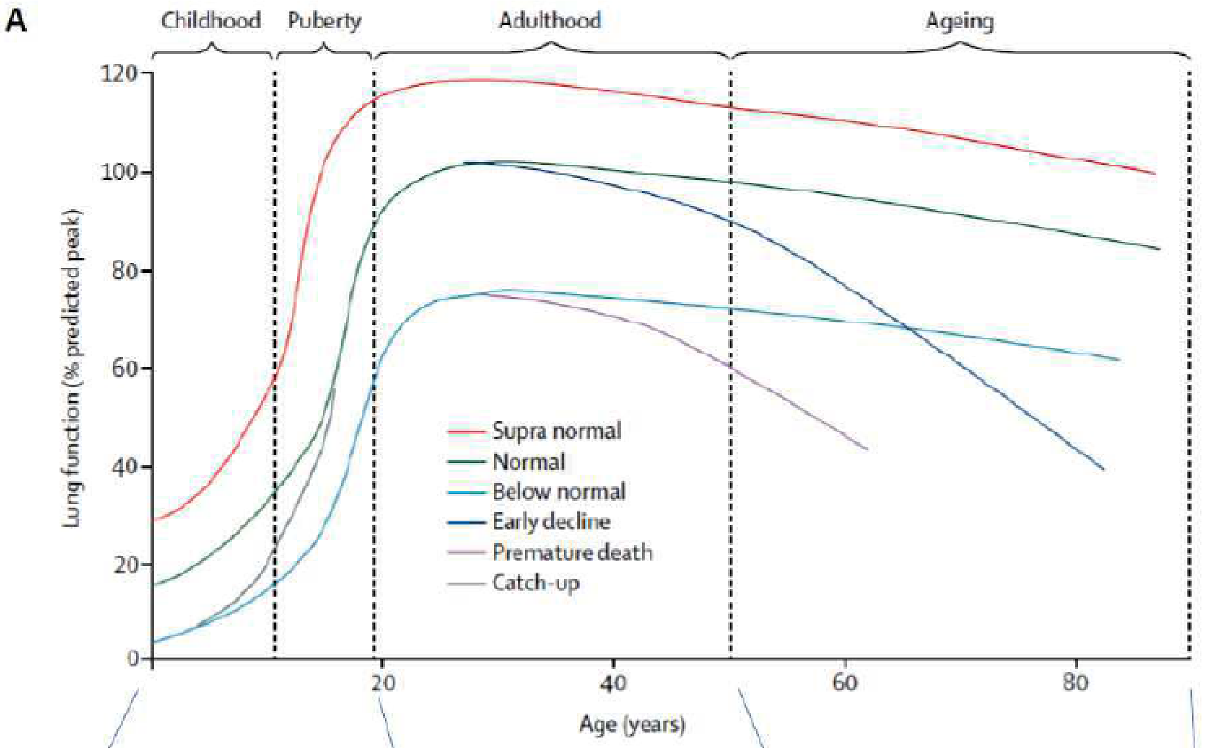
		Coefficient	SE	t	P	95% CI	
						Lower	Upper
Percentage Predicted FEV_1	Group (placebo vs ICS)	5.98	43.44	0.14	0.89	-82.10	94.07
	Group (placebo vs ICS/LABA)	159.02	48.78	3.26	**0.002**	60.13	257.91
	Corticosteroids (Not weaned vs weaned)	3.79	3.88	0.98	0.34	-4.07	11.66
	Sex (Female vs Male)	1.62	3.12	0.52	0.61	-4.72	7.96
	BPD (None vs BPD28 days)	2.04	5.62	0.36	0.72	-9.41	13.49
	BPD (None vs BPD36 weeks)	4.10	4.51	0.91	0.37	-5.07	13.27
	IUGR (No IUGR vs IUGR)	-1.76	3.90	-0.45	0.65	-9.74	6.21
	Pre-treatment value	0.61	0.26	2.37	**0.02**	0.09	1.14
	Gestation	0.22	0.15	1.46	0.15	-0.09	0.54
	Group (ICS vs placebo) * Pre value	-0.02	0.39	-0.05	0.96	-0.81	0.77
	Group (ICS/LABA vs placebo) * Pre value	-0.97	0.40	-2.40	**0.02**	-1.78	-0.15
	Group (ICS vs placebo) * gestation	0.02	0.18	0.09	0.93	-0.35	0.38
	Group (ICS/LABA vs placebo) * gestation	-0.34	0.18	-1.89	0.07	-0.71	0.02

Figure 2. Percent Predicted Forced Expiratory Volume in 1 Second ($\%FEV_1$) Spirometry Data



 Goulden N, et al. *JAMA Pediatr* 2022;176:133-41

Cosa possiamo fare?



Agusti A, et al.
Lancet Respir Med 2022;10:512-24

B

Childhood and puberty

- Spirometry check-up
- Avoid smoking exposure
- Avoiding infections (i.e. RSV vaccination)
- Understanding and treating catchup (i.e. vitamin supplementation)

Adulthood

- Spirometry check-up
- Avoid active smoking
- Reduce detrimental exposures
- Regular exercise
- Adequate nutrition

Ageing

- Spirometry check-up
- Avoid active smoking
- Reduce detrimental exposures
- Regular exercise
- Adequate nutrition

Indirizzi futuri

	Challenges, uncertainties, and considerations
Prevention of prematurity-associated lung disease	
Prevention of preterm birth Long-term evaluation of of interventions to prevent BPD	Preterm birth rates have not fallen in high-income countries in the past three decades Current studies have outcomes that are too short, with primary endpoints sometimes assessed only minutes, hours, or days after birth Not only pulmonary outcomes, but also non-pulmonary outcomes such as adverse effects on neurological, cardiovascular, or metabolic function, need to be included to enable evaluation of the long-term benefits versus risks of such treatments
Surveillance of prematurity-associated lung disease	
Establishment of respiratory (or multidisciplinary) clinics for routine and coordinated surveillance or follow-up of survivors of preterm birth across the lifespan	New clinics would be expensive and resource-intensive for the health sector; if a lung function deficit is identified, optimal treatment options in this patient population are uncertain Adequate transitions and handover to paediatric and then to adult services are mostly non-existent currently Current regulations make international data sharing challenging
Establishment of respiratory (or multidisciplinary) clinics for routine and coordinated surveillance or follow-up of survivors of preterm birth across the lifespan expiratory airflow	Funding needs to be obtained for extant cohort studies Maintenance of sufficiently high follow-up rates for extant cohorts is challenging
Assessment of other aspects of pulmonary health, such as gas diffusion, oscillometry, lung volumes, ventilation inhomogeneity, exercise capacity, pulmonary vascular abnormalities, lung structure (advanced lung imaging), or lung-related quality of life	Some techniques are invasive, or involve radiation exposure, and are hence hard to justify for research; the techniques that are of particular benefit or predict long-term pulmonary outcomes in this population are not yet known
Management of prematurity-associated lung disease	
Use of randomised controlled trials to assess various treatments and non-pharmaceutical interventions (eg, exercise) pharmaceutical interventions (eg, exercise training or other interventions to increase overall physical activity)	Sufficient sample sizes of different phenotypes need to be obtained to address research questions The potentially treatable traits that are important in the long-term prognosis and management of prematurity-associated lung disease are yet to be determined Funding needs to be obtained for studies large enough to provide clear answers; multicentre studies are needed to provide adequate sample sizes; clinical trials networks are not yet established; the choice of treatment regimens might need to be based on the phenotype or underlying mechanisms of prematurity-associated lung disease

Table: **Future directions for research, policy, and clinical practice**

SUSTAINABLE DEVELOPMENT GOALS

United Nations Development Programme

https://www.who.int/publications/i/item/978924151177

2024

24

La salute (respiratoria) dei **bambini** è il nostro **futuro**

Pubblicità