Astma hos barn och ungdomar – ökar det risken för kronisk sjukdom i vuxen ålder?

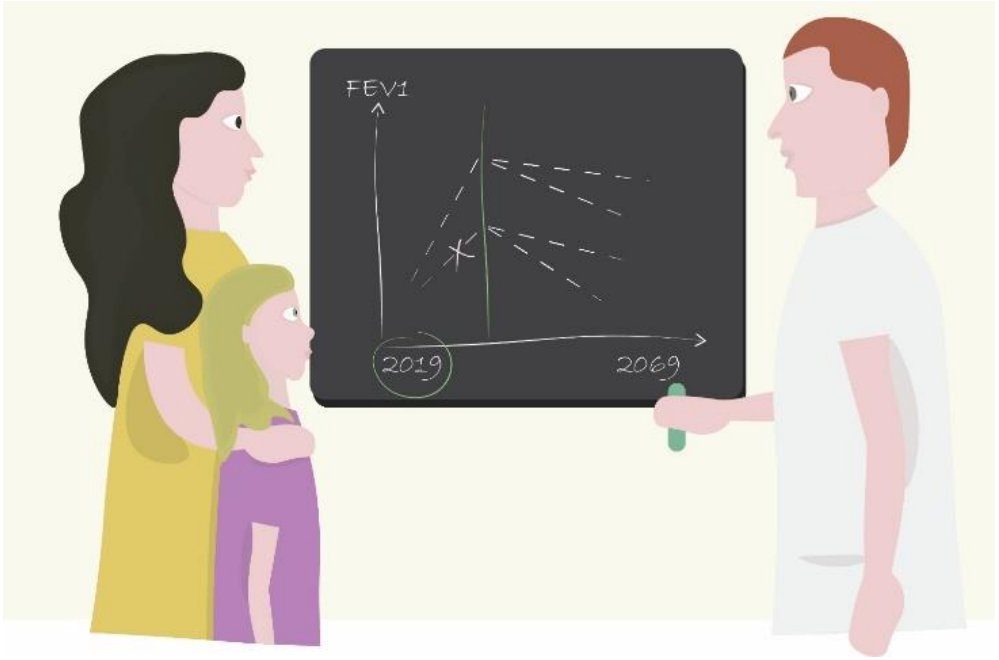
Lungan genom livet, 2023-03-29

Erik Melén
Professor, överläkare och barnallergolog
Sachsska barnsjukhuset och KI SÖS

COI:
Advisory board och/ eller föreläsningsarvode från ALK, AstraZeneca, Chiesi, Novartis och Sanofi.

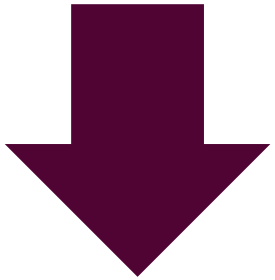
The challenge

- 10% av barn har astma
- Ingen botande behandling
- Lunghälsa genom livet?
  - barnastma: 5-30 ggr ökad risk för KOL
  - 50% av KOL-förekomst kopplad till barndomen (Lange, *NEJM* 2015)



Linking COPD epidemiology with pediatric asthma care; implications for the patient and the physician
(Melén, Guerra, Hallberg, Jarvis, Stanojevic, *Pediatr All Immunol* 2019)

Astma hos barn och ungdomar – ökar det risken för kronisk sjukdom i vuxen ålder?

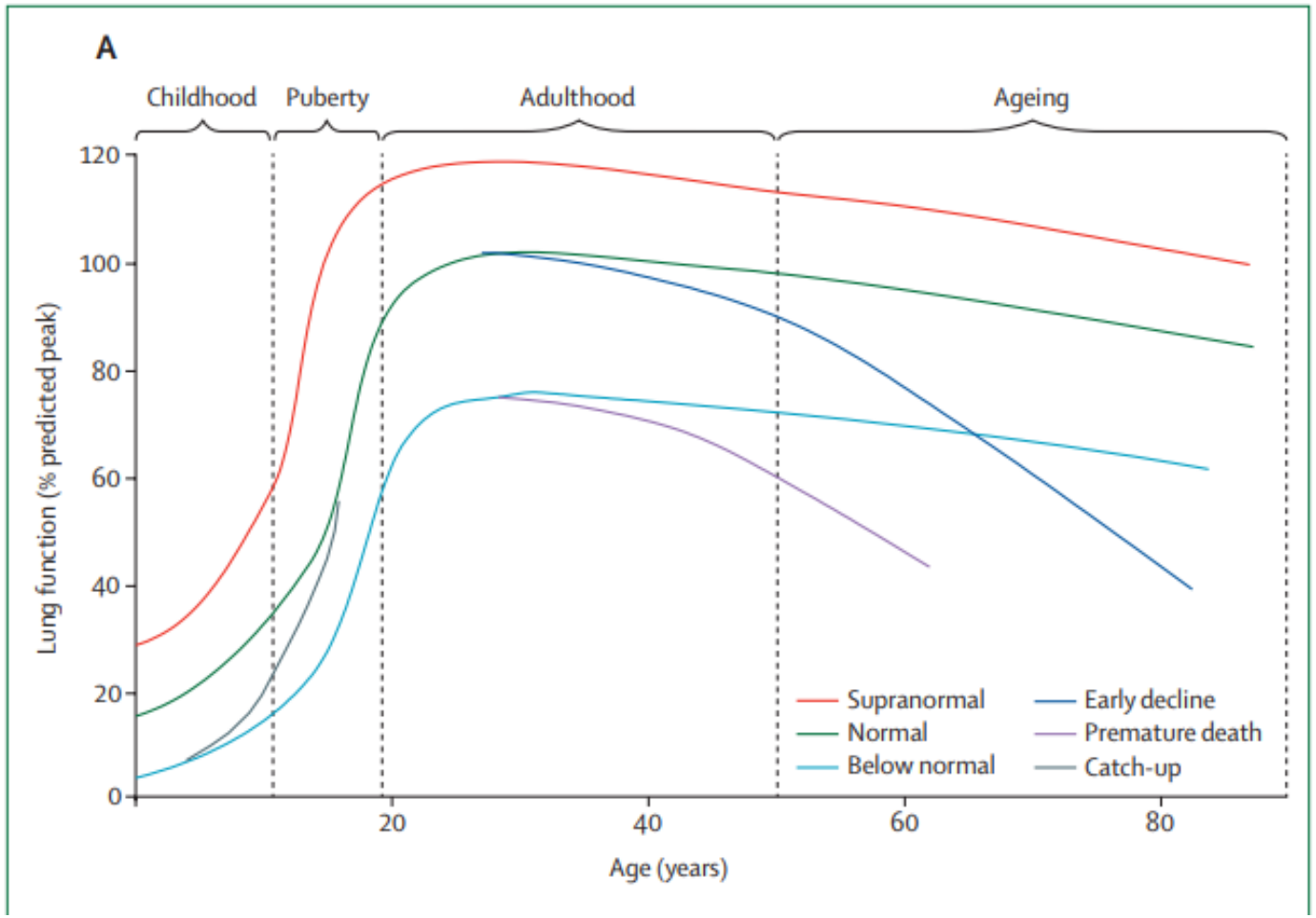


Svar ja.

Kan vi minska risken? Svar ja.

Hur? Lyssna vidare....

Lunghälsa genom hela livet

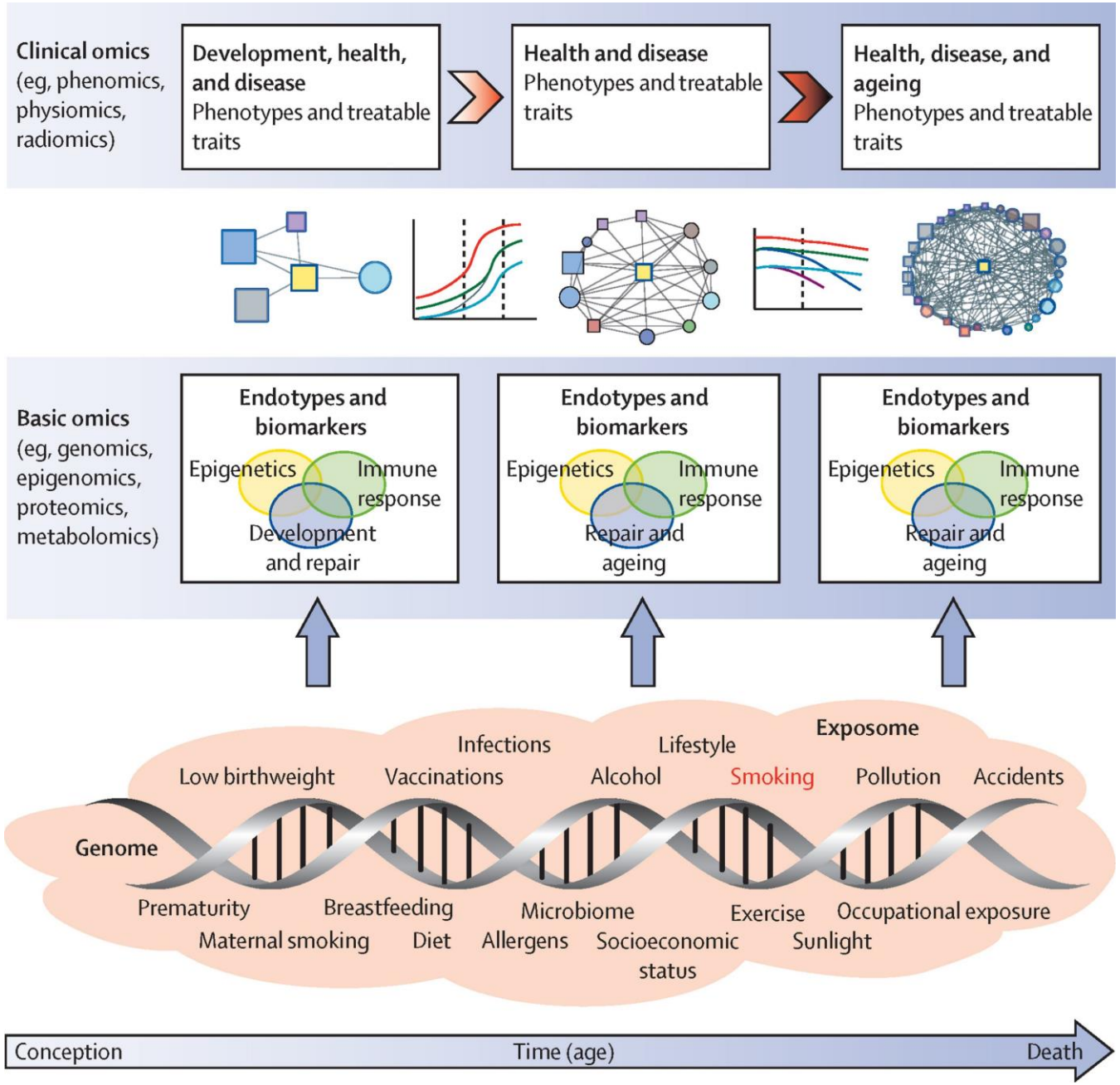


Pathogenesis of chronic obstructive pulmonary disease: understanding the contributions of gene–environment interactions across the lifespan.
Agusti, Melén et al. *Lancet Resp Med* 2022

A *GETomics** understanding of chronic airway disease

**Proposed holistic strategy that considers all gene (G) – environment (E) interactions that an individual may encounter through the life span (T) to better understand the pathogenesis of COPD and chronic respiratory disease.*

Agusti, Melén, DeMeo, Breyer-Kohansal, Faner. *Lancet RM* 2022



The BAMSE study 1994-

1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006

Baseline questionnaire
4 089 100%
PM, NO_2 , indoor environment

5 488
(75%)

1-year questionnaire
3 925 96%

2-year questionnaire
3 843 94%

4-year follow-up

Questionnaire	3 729	91%
Dust	3 610	97%
PEF	2 966	80%
Blood, DNA	2 614	70%
Urine	1 033	25%

8-year follow-up

Questionnaire	3 417	84%
Spirometry	2 613	64%
Food freq quest	2 630	64%
Blood, DNA	2 461	60%

2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 **2020-22** **2023-**

12-year follow-up
Questionnaire

Parent	3 356	82%
Children	2 795	68%
Parent or child	3 369	82%

16-year follow-up

Questionnaire	3 247	79%
Spirometry	2 312	57%
Impulse Oscil.	2 300	57%
FeNO	2 300	57%
Blood, DNA, RNA	2 547	63%
Patch test	2 285	56%

24-year follow-up

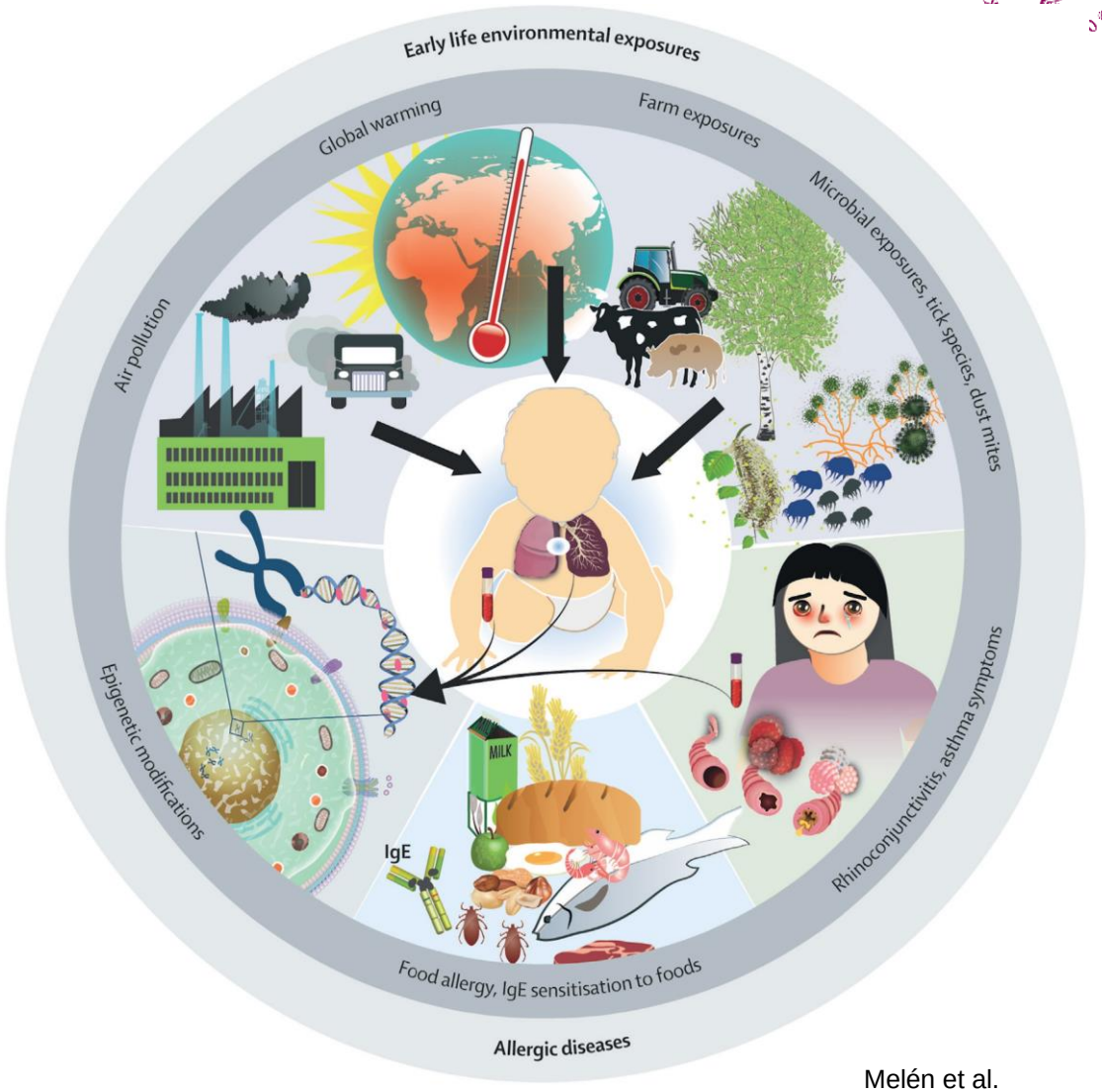
Questionnaire	3064	75%
Examination	2270	56%
Spirometry	2039	50%
N_2 washout	1660	41%
FeNO	1926	47%
Blood pressure	2268	55%
Blood	2234	55%
Nasal sample	661	16%
Urine	2235	55%
Saliva	1596	39%

COVID-19

BAMSE-PROJEKTET
BARN • ALLERGI • MILJÖ • STOCKHOLM • EPIDEMIOLOGI
SEDAN 1994

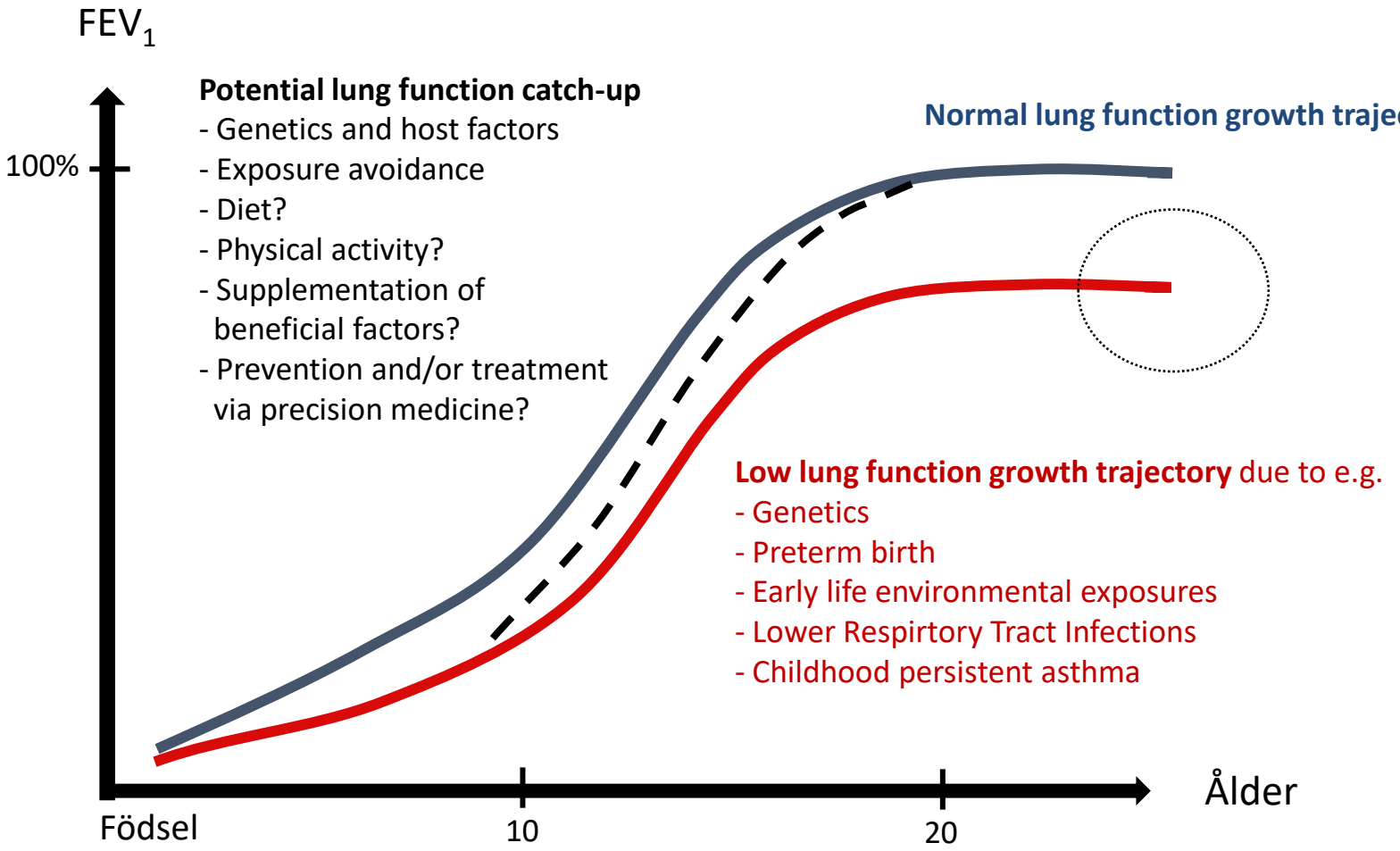
http://ki.se/bamse

BAMSE – ett translationellt forskningsprojekt



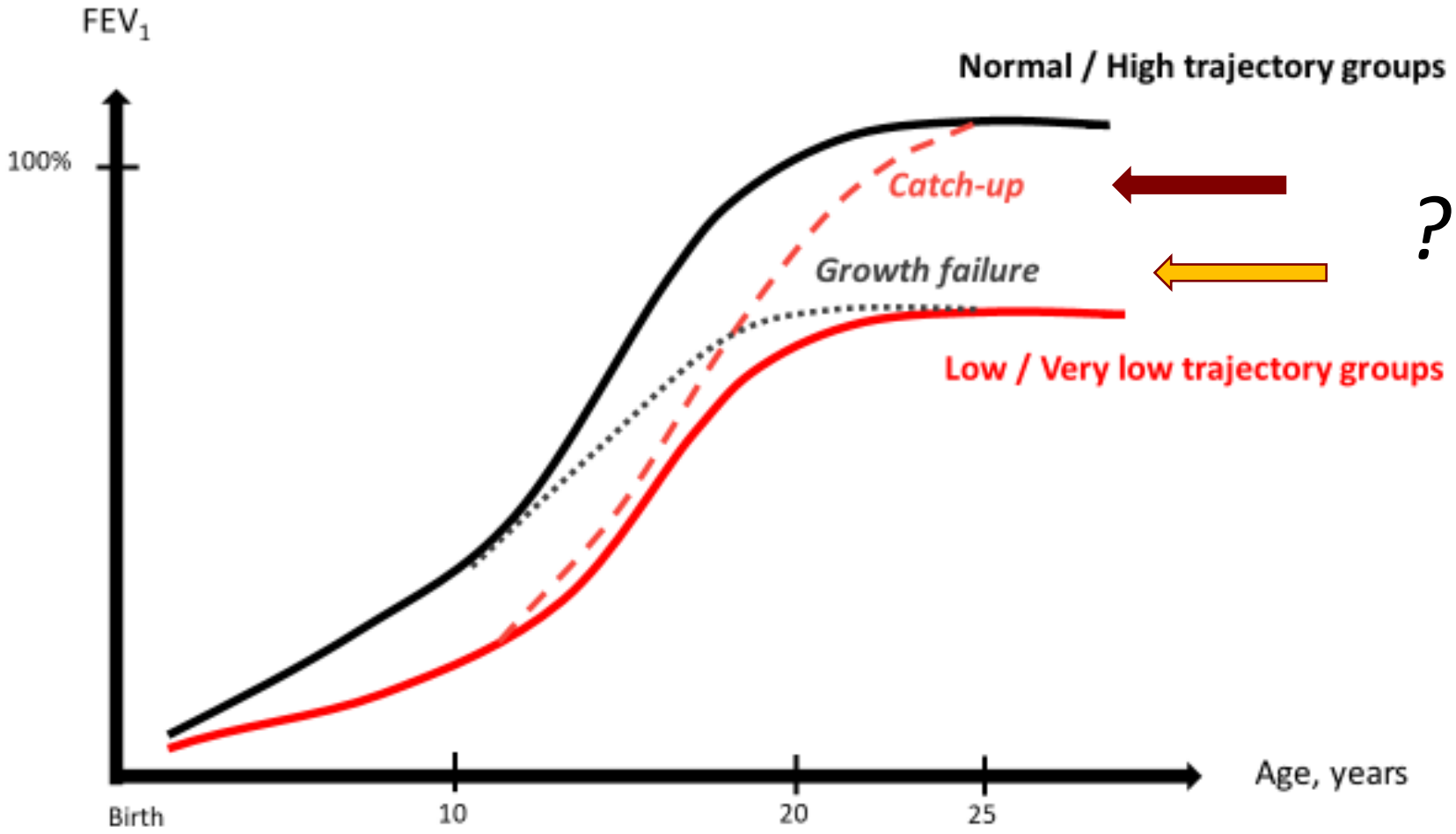
Melén et al.
Lancet Child & Adolescent Health 2022

Lung development from childhood to adulthood



Melén and Guerra, *F1000Res* 2017

Changing the trajectories – preventing COPD?



Wang et al. *AJRCCM* 2023

American Journal of Respiratory and Critical Care Medicine

Plasticity of Individual Lung Function States from Childhood to Adulthood

Gang Wang , Jenny Hallberg ; Rosa Faner , Hans-Jacob Koefoed , Simon Kebede Merid , Susanna Klevebro , Sophia Björkander , Olena Gruzieva , Göran Pershagen , Marianne van Hage , Stefano Guerra , Matteo Bottai , Antonios Georgelis , Ulrike Gehring , Anna Bergström , Judith M. Vonk , Inger Kull , Gerard H Koppelman ; Alvar Agusti , and Erik Melén ... Show less

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https://doi.org/10.1164/rccm.202203-0444OC PubMed: 36409973

Received: March 03, 2022 Accepted: November 21, 2022

Abstract PDF

Hopp för barn med svår astma

Det är viktigt att ha en bra lungfunktion som barn, eftersom det minskar risken för lungsjukdomar senare i livet. Men det går att komma upp i en normal funktion även om man som barn haft en sänkt nivå. Det visar en ny studie från det stora Bamse-projektet.

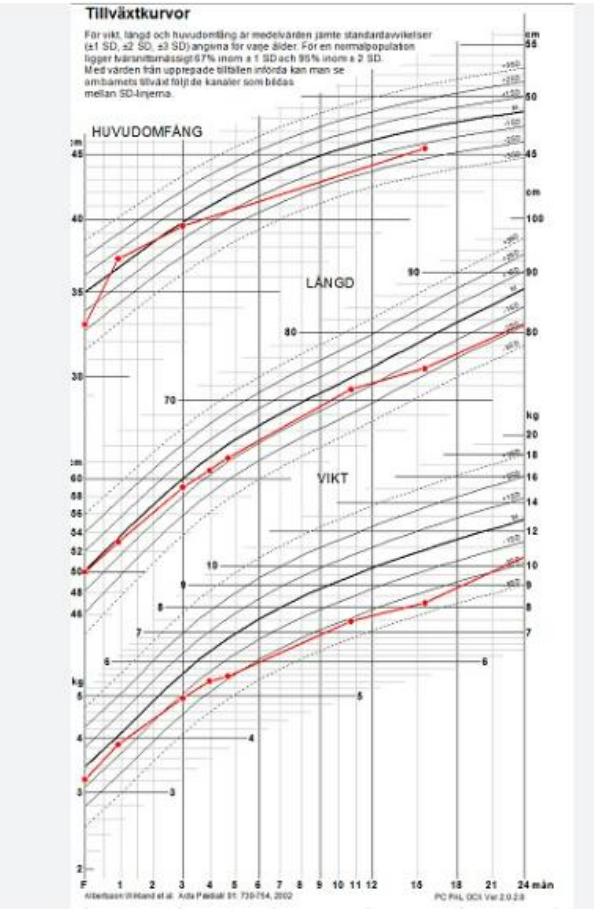
Forskning har visat att om vår lungfunktion av någon anledning inte utvecklas normalt när vi är barn till följd av till exempel infektioner, luftföroreningar, allergi eller svår astma, kan det bli svårt att ta igen det och få en normal lungfunktion som vuxen. Detta ökar i sin tur risken för att drabbas av lungsjukdom senare i livet.

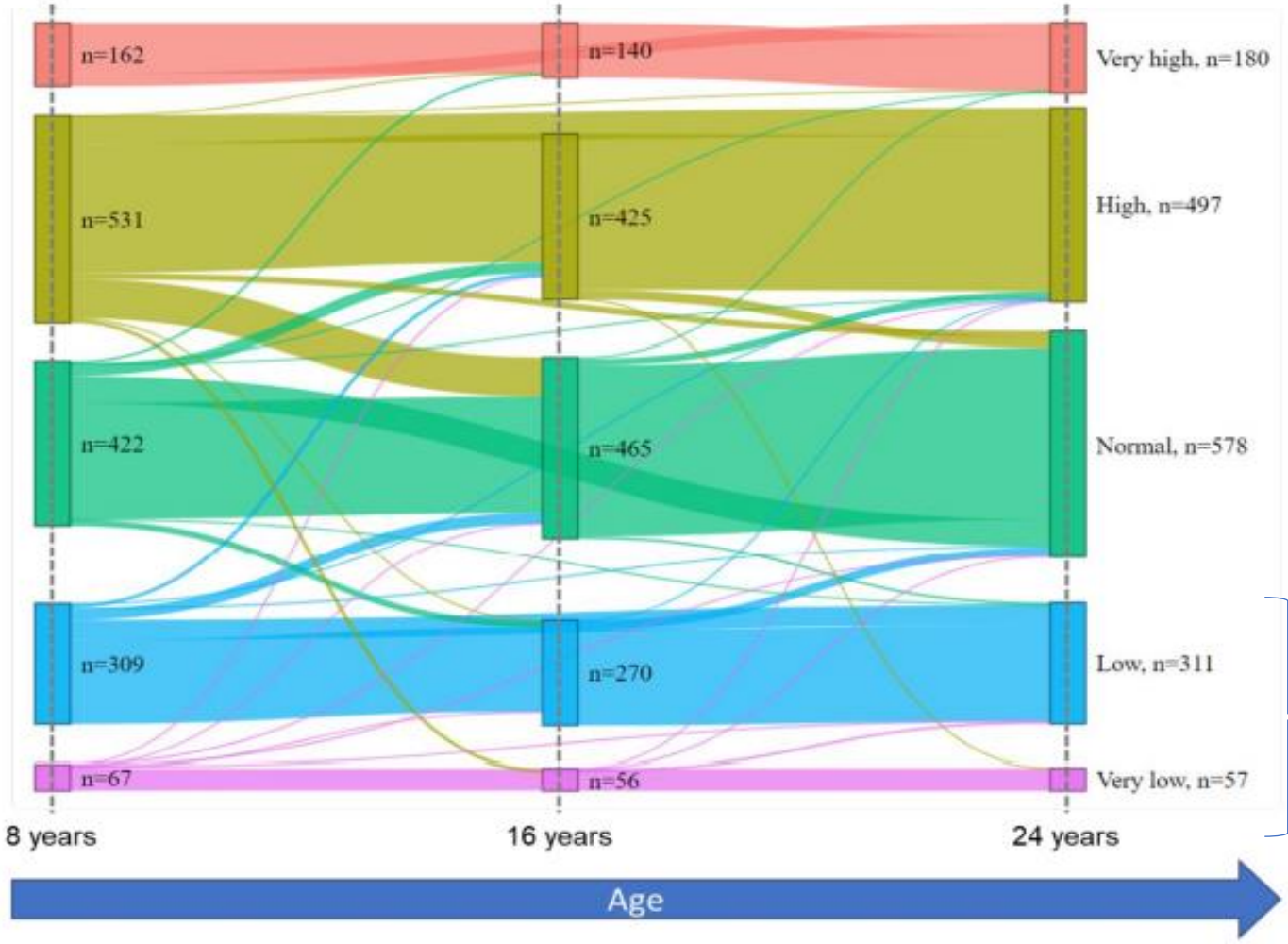
Forskarna bakom den nya studien ville undersöka vilka möjligheter det ändå finns att påverka den här utvecklingen. Mätningar av lungfunktionen gjordes på drygt 3 000 deltagare från den stora befolkningsstudien Bamse*.

Möjligt komma ifatt senare

Resultatet visar att även om lungfunktionen vanligtvis följer sin tillväxtkurva, kan barn med sänkt lungfunktion ändå komma upp i en normal lungfunktion på sikt.

Lungfunktionsnivå från barn till vuxen

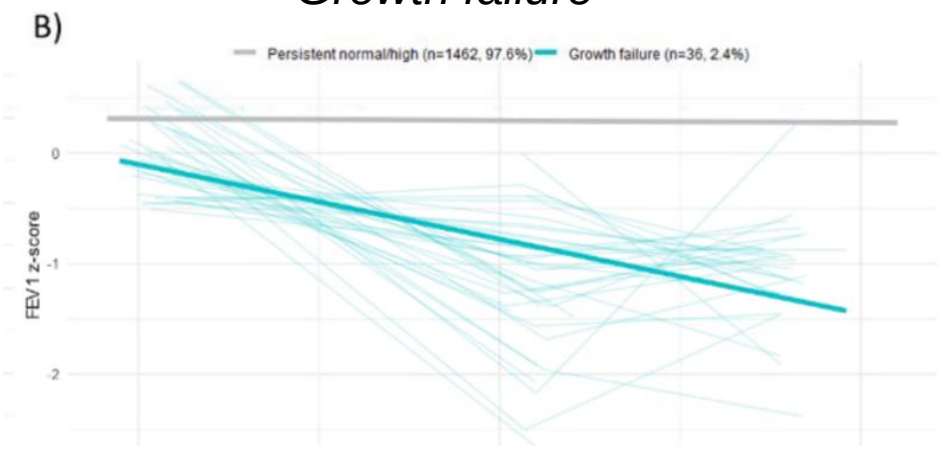




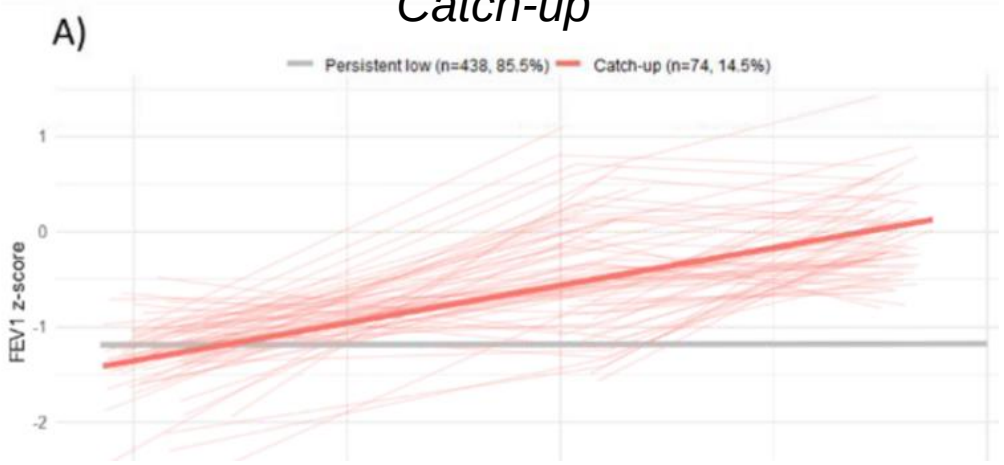
- Astma ↑
- FEV1 ↓
- 40% < LLN
- Små luftvägar affekterade

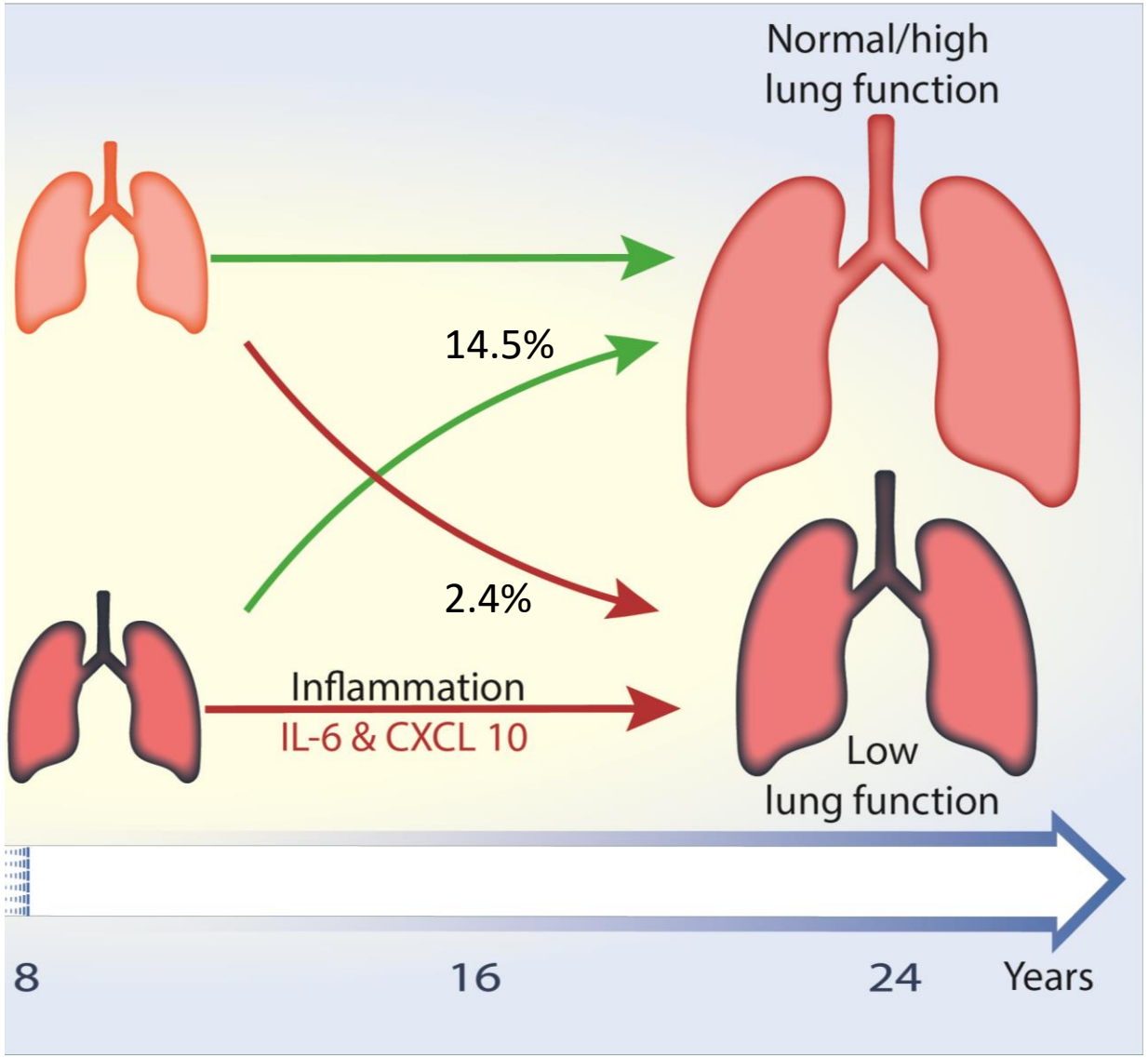
Lung function catch-up and growth failure

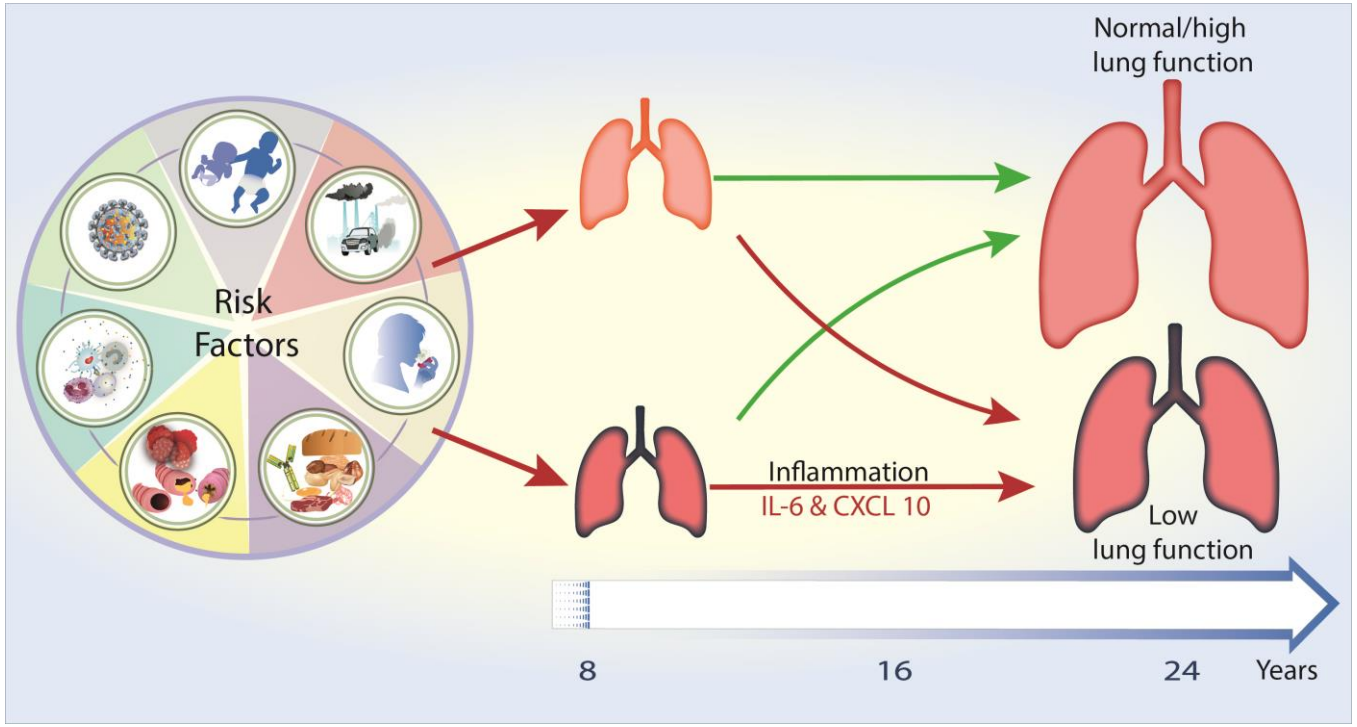
Growth failure

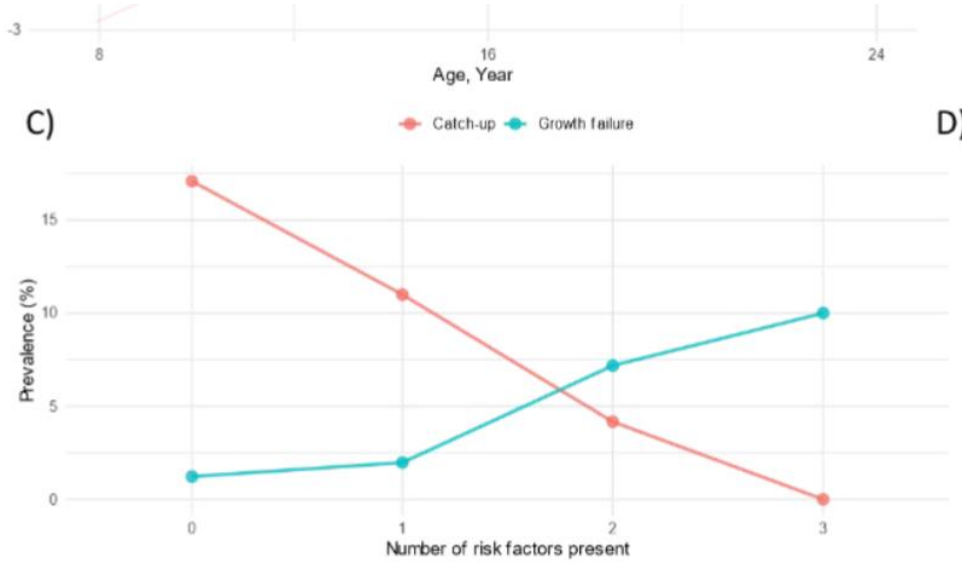


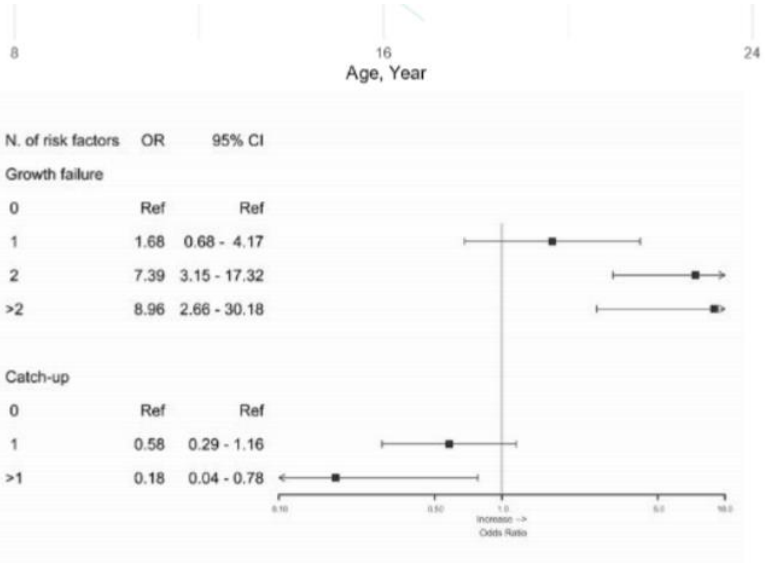
Catch-up






Normal/high
lung function
Risk
Factors
Inflammation
IL-6 & CXCL 10
Low
lung function
8
16
24
Years


-3
8
16
24
Age, Year
C)
Catch-up
Growth failure
Prevalence (%)
15
10
5
0
0
1
2
3
Number of risk factors present


8
16
24
Age, Year
D)
N. of risk factors OR 95% CI
Growth failure
0 Ref Ref
1 1.68 0.68 - 4.17
2 7.39 3.15 - 17.32
>2 8.96 2.66 - 30.18
Catch-up
0 Ref Ref
1 0.58 0.29 - 1.16
>1 0.18 0.04 - 0.78

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Barns lungkapacitet förbättrades när luften blev renare

Publikation

Publicerad: 2023-02-23 15:59 | Uppdaterad: 2023-02-23 20:19

Barns lungkapacitet förbättrades när luften blev renare

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
Z. YU ET AL.

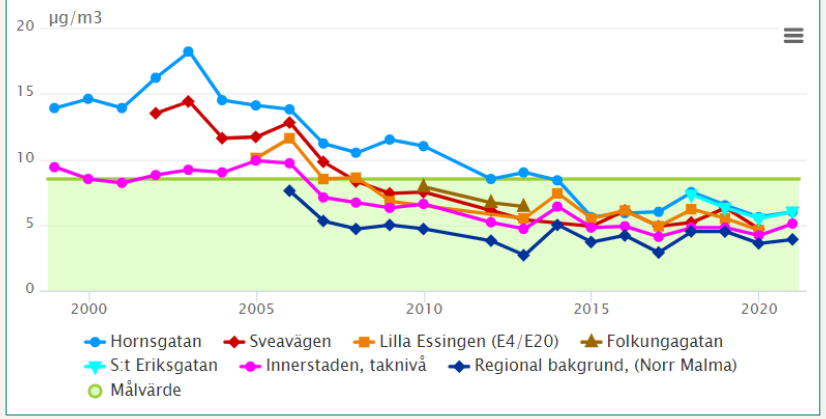
Associations of improved air quality with lung function growth from childhood to adulthood: the BAMSE study

Zhebin Yu[1], Simon Kebede Merid[2], Tom Bellander[1,3], Anna Bergström[1,3], Kristina Eneroth[4], Antonios Georgelis[1,3], Jenny Hallberg[2,5], Inger Kull[2,5], Petter Ljungman[1,6], Susanna Klevebro[2,5], Massimo Stafoggia[1,7], Gang Wang[1,2], Göran Pershagen[1,3], Olena Gruzieva[1,3] and Erik Melén[2,5]

Halterna av PM2,5 i luft, årsmedelvärden.

Välj mätstation: Alla mätområden

Välj tidsperiod: Hela mätserien



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Air pollution

Cutting air pollution improves children's lung development, study shows

Conclusions from long-term survey in Sweden come days after 10th anniversary of Ella Kissi-Debrah's death in London

Nicola Davis *Science correspondent*

@NicolaKSDavis

Thu 23 Feb 2023 16.51 GMT

The researchers said the results sent 'a strong message to policymakers and city planners'. Photograph: Fabrizio Bensch/Reuters

TABLE 4 Association between improvement of air quality and differences in lung function growth from age 8 to 24 years

	Unit of improvement in exposure	Raw value		GLI z-score	
		Difference in FEV_1 growth, mL per year (95% CI)[#]	Difference in FVC growth, mL per year (95% CI)[#]	Difference in FEV_1 growth, SD per year (95% CI)	Difference in FVC growth, SD per year (95% CI)
$PM_{2.5}$	2.19 $\mu g \cdot m^{-3}$	4.63 (1.64–7.61)	9.38 (4.76–14.00)	0.03 (0.02–0.04)	0.04 (0.03–0.05)
PM_{10}	1.00 $\mu g \cdot m^{-3}$	0.72 (−0.91–2.35)	2.77 (0.19–5.35)	0.01 (0.00–0.02)	0.01 (0.01–0.02)
BC	0.28 $\mu g \cdot m^{-3}$	2.80 (0.66–4.93)	5.59 (2.30–8.87)	0.02 (0.01–0.03)	0.02 (0.01–0.03)
NO_x	6.17 $\mu g \cdot m^{-3}$	1.70 (−0.16–3.57)	3.29 (0.35–6.23)	0.01 (0.01–0.02)	0.01 (0.01–0.02)

Från barn till vuxen

JOURNAL OF ASTHMA
2020, VOL. 57, NO. 10, 1119–1127
https://doi.org/10.1080/02770903.2019.1640726

Taylor & Francis
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MANAGEMENT

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Lost in the transition from pediatric to adult healthcare? Experiences of young adults with severe asthma

Maria Ödling, MA[a], Marina Jonsson, PhD[b], Christer Jan
Anna Bergström, PhD[b,d], and Inger Kull, PhD[a,e]

Original Article

A Gap Between Asthma Guidelines and Management for Adolescents and Young Adults

Maria Ödling, MSc[a], Niklas Andersson, MSc[b], Jenny Hallberg, PhD[a,c], Catarina Almqvist, MD, PhD[d,e], Christer Janson, MD, PhD[f], Anna Bergström, PhD[b,g], Erik Melén, MD, PhD[a,b,c], and Inger Kull
Uppsala, Sweden

What is already known about this topic? Clinical guidelines for management of asthma exist, b
generally low. For adolescents, asthma management can be challenging during the transition to

What does this article add to our knowledge? Asthma-related health care consultations were fe
in guidelines and decreased after the transition to adult health care. Almost no one had regular
dispensed during the transition process.

How does this study impact current management guidelines? There is a gap between asthr
management. Increased adherence to current guidelines is required when planning for optimal
young adults, and their process of transition.

Ödling *et al. BMC Pulmonary Medicine* (2023) 23:34
https://doi.org/10.1186/s12890-022-02259-6

BMC Pulmonary Medicine

RESEARCH Open Access

Check for updates

Health-related quality of life decreases in young people with asthma during the transition from adolescence to young adulthood: a birth cohort study

Maria Ödling[1*], Niklas Andersson[2], Christer Janson[3], Erik Melén[1,2,4], Anna Bergström[2,5] and Inger Kull[1,4]

Lessons from birth cohorts and longitudinal studies

Persistent asthma from childhood to adulthood is associated with:

- Frequency and severity of asthma symptoms
- Atopy, especially early in life
- Poly-sensitisation
- Eosinophilia
- Allergic comorbidities (e.g. rhinitis, eczema)
- Other comorbidities (e.g. obesity)
- Repeated airway / lung infections (e.g. HRV)
- Impaired lung function
- Bronchial hyperresponsiveness

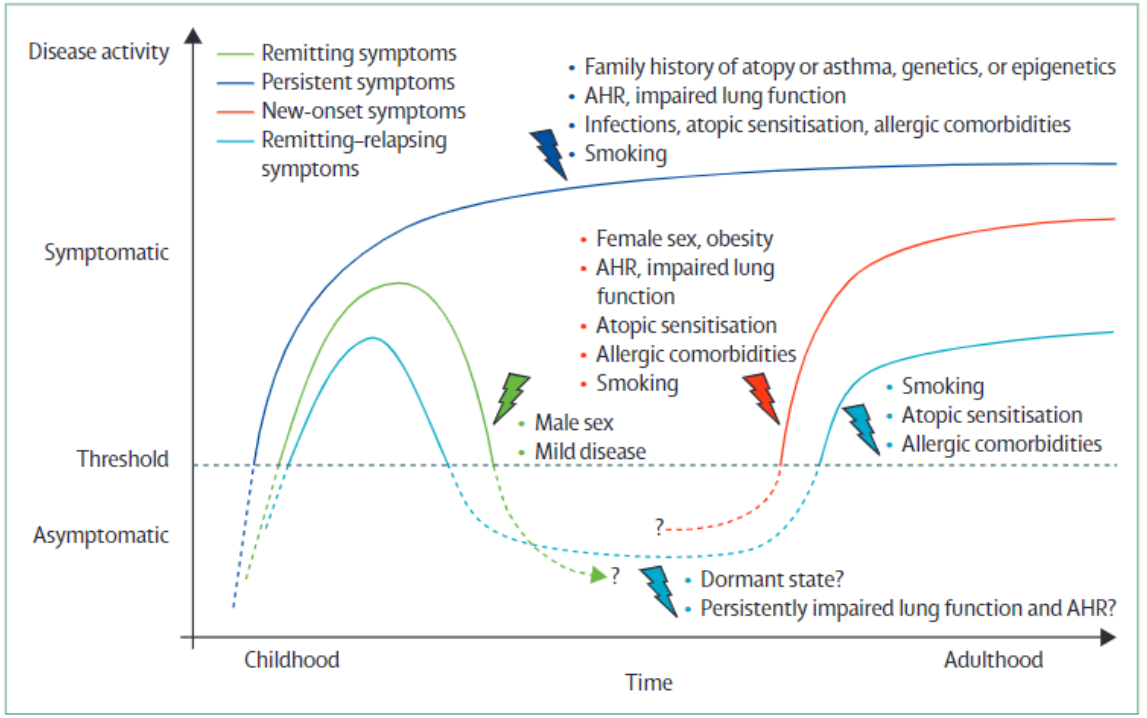

Figure 2: **Determinants of disease course across asthma transition and ages**

Fuchs et al, *Lancet RM* 2017

Thorax 2014

Chronic obstructive pulmonary disease

ORIGINAL ARTICLE

The association between childhood asthma and adult chronic obstructive pulmonary disease

Andrew Tai,[1] Haily Tran,[2] Mary Roberts,[3] Nadeene Clarke,[2] John Wilson,[4] Colin F Robertson[2,5]

Editor's choice
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1. Svårighetsgrad

Table 2 Outcome at the age of 50 by recruitment groups

	Asthma remission (n=57)	Current asthma (n=65)	COPD (n=27)
MWB	11/23 (48%)	11/23 (48%)	1/23 (4%)
WB	24/43 (56%)	16/43 (37%)	3/43 (7%)
A	17/49 (35%)	24/49 (49%)	8/49 (16%)
SA	5/34 (15%)	14/34 (41%)	15/34 (44%)

1/48 of the control group had COPD at the age of 50.

Table 3 The childhood predictors of adult COPD

	OR (95% CI) (univariate)	OR (95% CI) (multivariate)
Severe asthma	37.1 (4.6 to 301)	31.9 (3.4 to 269)
Asthma	9.1 (1.1 to 76.4)	9.6 (1.0 to 77)
Wheezy bronchitis	3.5 (0.4 to 35.2)	
Mild wheezy bronchitis	2.1 (0.1 to 35.8)	
Male sex	2.4 (0.9 to 6.3)	
Ever smoker	1.0 (0.5 to 2.3)	
Current smoker	1.1 (0.5 to 2.4)	
Childhood hay fever	1.0 (0.3 to 3.8)	

MWB = Mild wheezy bronchitis, WB = Wheezy bronchitis
A = Asthma, SA = Severe asthma

2. Astmakontroll

ERJ OPEN RESEARCH
ORIGINAL RESEARCH ARTICLE
I. MOGENSEN ET AL.

Uncontrolled asthma from childhood to young adulthood associates with airflow obstruction

Ida Mogensen [1], Jenny Hallberg [1,2], Sandra Ekström [3,4], Anna Bergström [3], Erik Melén [1,2] and Inger Kull [1,2]

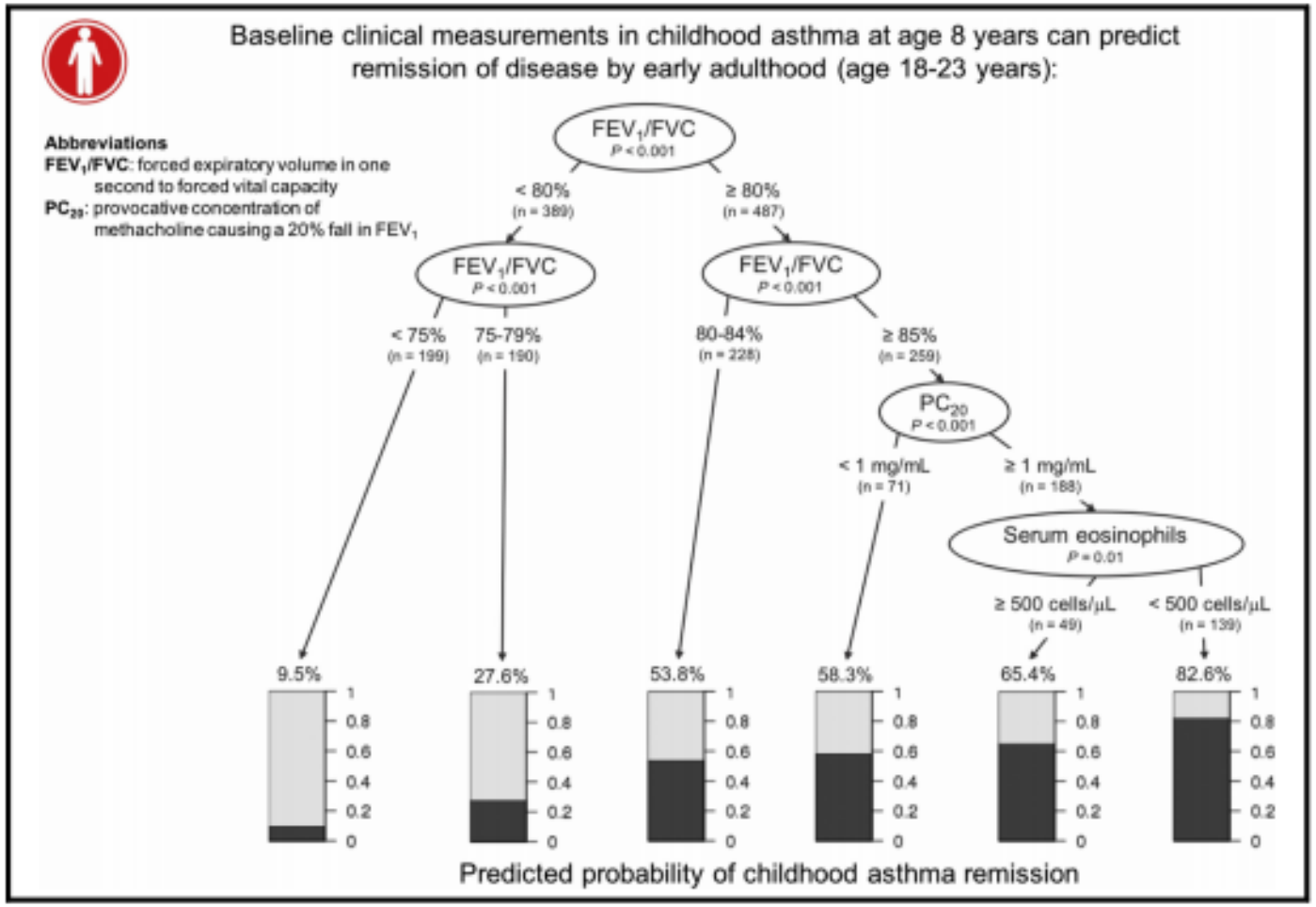
[1]Dept of Clinical Science and Education Södersjukhuset, Karolinska Institute, Stockholm, Sweden. [2]Sachs' Children and Youth Hospital, Södersjukhuset, Stockholm, Sweden. [3]Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden. [4]Center for Occupational and Environmental Medicine, Region Stockholm, Stockholm, Sweden.

Corresponding author: Ida Mogensen (ida.mogensen@ki.se)

Remission of persistent childhood asthma: Early predictors of adult outcomes

Alberta L. Wang, MD,[a,b] Soma Datta, MS,[a] Scott T. Weiss, MD,[a] and Kelan G. Tantisira, MD[a,c] *Boston, Mass*

GRAPHICAL ABSTRACT



3. Lungfunktion

4. Eosinofili

5. Astma-trajectories

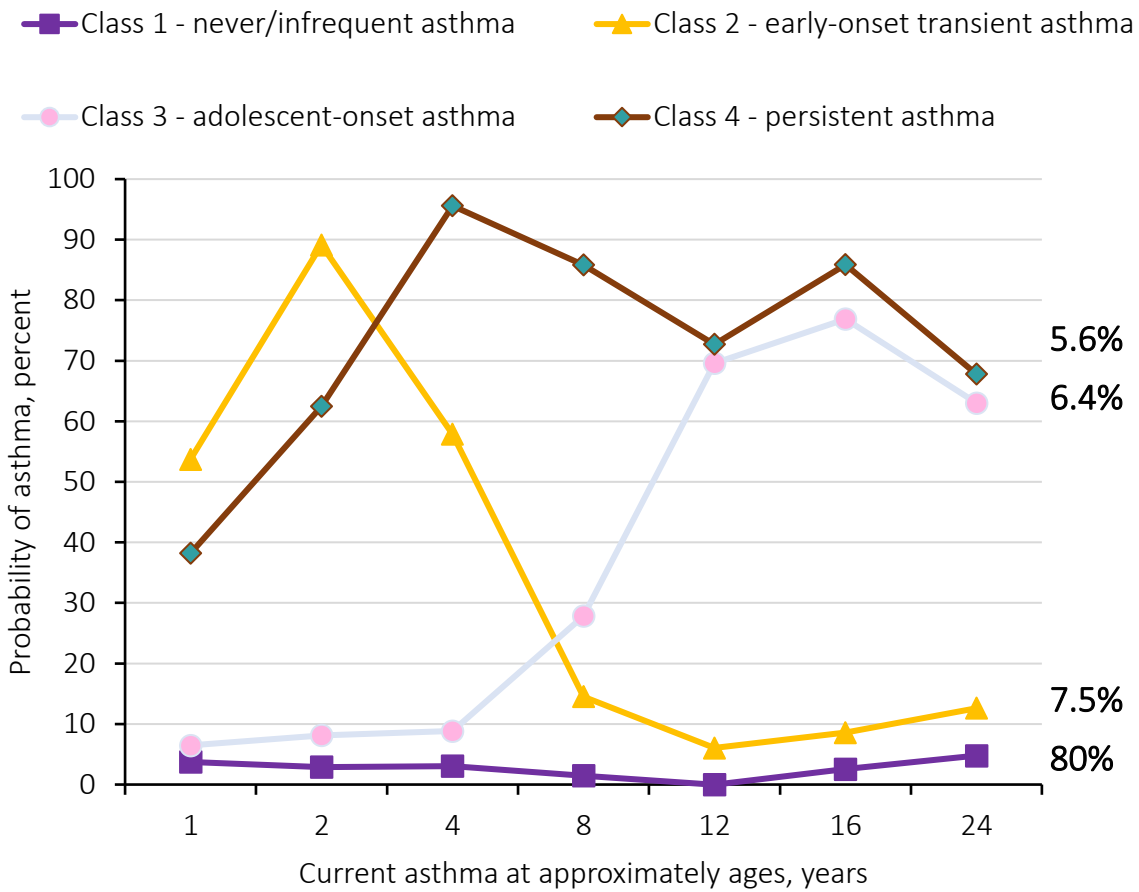
The Journal of Allergy and Clinical Immunology: In Practice

ORIGINAL ARTICLE | ARTICLES IN PRESS

Characterization of asthma trajectories from infancy to young adulthood

Maria Ödling, M.Sc. • Gang Wang, M.D. • Niklas Andersson, M.Sc. • ... Anna Bergström, Ph.D. • Erik Melén, M.D., Ph.D. • Inger Kull, Ph.D. • Show all authors

Open Access • Published: February 15, 2021 • DOI: https://doi.org/10.1016/j.jaip.2021.02.007



What is already known about this topic? Asthma has many underlying biological pathways that lead to different disease trajectories.

What does this article add to our knowledge? Subjects in the adolescent-onset and persistent asthma trajectory groups have equal burdens of asthma control and severity in adolescence and young adulthood.

How does this study impact current management guidelines? Through the defined and characterized asthma trajectories, we found that the adolescent-onset and persistent asthma trajectory groups are vulnerable groups that health care professionals need to identify, to optimize care.

6. Kostfaktorer

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
M. TALAEI ET AL.

Intake of *n*-3 polyunsaturated fatty acids in childhood, *FADS* genotype and incident asthma

Mohammad Talaei [1], Emmanouela Sdona [2], Philip C. Calder [3,4], Louise R. Jones [5], Pauline M. Emmett [5], Raquel Granell [6], Anna Bergström [2,7], Erik Melén [2,8,9] and Seif O. Shaheen [1]

[1]Institute of Population Health Sciences, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London, UK. [2]Institute of Environmental Medicine, Karolinska Institute, Stockholm, Sweden. [3]Human Development and Health, Faculty of Medicine, University of Southampton, Southampton, UK. [4]NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust and University of Southampton, Southampton, UK. [5]Centre for Academic Child Health, Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK. [6]MRC Integrative Epidemiology Unit, Population Health Sciences, Bristol Medical School, University of Bristol, Bristol, UK. [7]Centre for Occupational and Environmental Medicine, Region Stockholm, Stockholm, Sweden. [8]Dept of Clinical Science and Education, Södersjukhuset, Karolinska Institute, Stockholm, Sweden. [9]Sachs' Children and Youth Hospital, Södersjukhuset, Stockholm, Sweden.

ORIGINAL ARTICLE

WILEY

Fruit, vegetable and dietary antioxidant intake in school age, respiratory health up to young adulthood

Emmanouela Sdona[1] | Sandra Ekström[1,2] | Niklas Andersson[1] | Jenny Hallberg[3,4] | Susanne Rautiainen[5,6,7] | Niclas Håkansson[1] | Alicja Wolk[1,8] | Inger Kull[3,4] | Erik Melén[1,3,4] | Anna Bergström[1,2]

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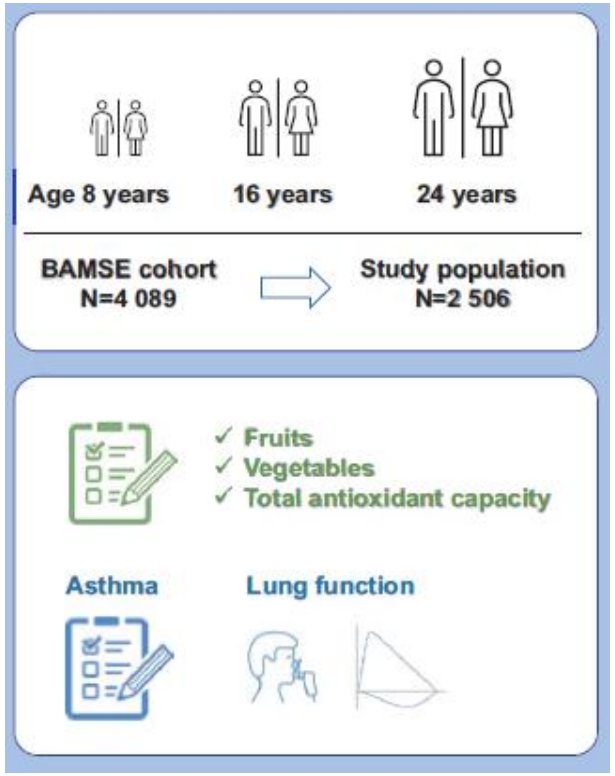
Eating oily fish could halve the risk of asthma in children

Rhys Blakely, Science Correspondent

Thursday January 28 2021, 12.01am GMT, The Times

A diet that contains plenty of fish may reduce inflammation of the airway, scientists say

PEOPLEIMAGES/GETTY IMAGES



7. KOL?

ORIGINAL ARTICLE

Patterns of Growth and Decline in Lung Function in Persistent Childhood Asthma

M.J. McGeachie, K.P. Yates, X. Zhou, F. Guo, A.L. Sternberg, M.L. Van Natta, R.A. Wise, S.J. Szefler, S. Sharma, A.T. Kho, M.H. Cho, D.C. Croteau-Chonka, P.J. Castaldi, G. Jain, A. Sanyal, Y. Zhan, B.R. Lajoie, J. Dekker, J. Stamatoyannopoulos, R.A. Covar, R.S. Zeiger, N.F. Adkinson, P.V. Williams, H.W. Kelly, H. Grasemann, J.M. Vonk, G.H. Koppelman, D.S. Postma, B.A. Raby, I. Houston, Q. Lu, A.L. Fuhlbrigge, K.G. Tantisira, E.K. Silverman, J. Tonascia, S.T. Weiss, and R.C. Strunk, for the CAMP Research Group*

"Of the 684 study participants, 170 (25%) had a normal pattern of lung-function growth without early decline, and 514 (75%) had abnormal patterns: 176 (26%) had reduced growth and an early decline, 160 (23%) had reduced growth only, and 178 (26%) had normal growth and an early decline."

11% COPD according to spirometry

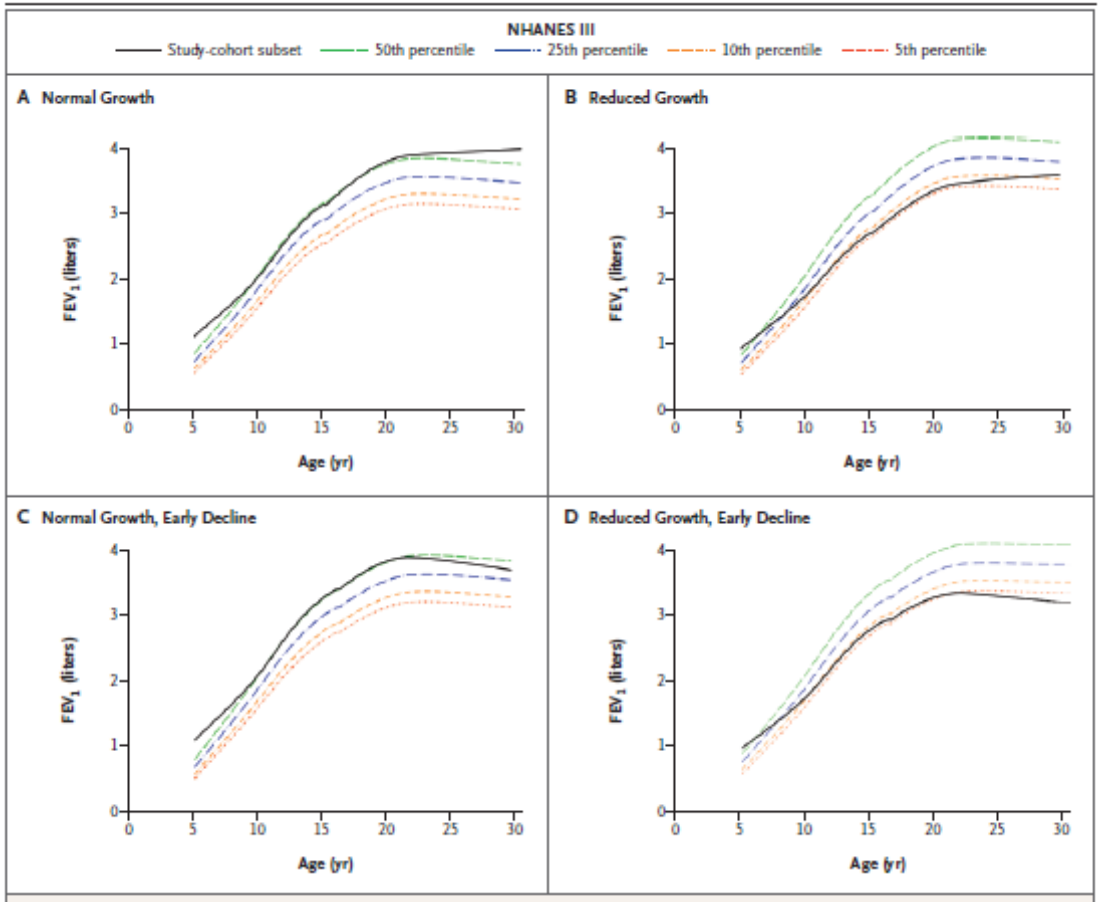


Figure 2. Average Prebronchodilator FEV_1 Trajectories for 684 Study Participants According to Pattern Classification, as Compared with FEV_1 in Persons without Asthma.

Values for prebronchodilator FEV_1 in the study participants are group averages and are based on robust, locally weighted scatterplot smoothing regression. Also shown are percentiles of FEV_1 in persons without asthma who were participants in the third National Health and Nutrition Examination Survey (NHANES III)[18] and were matched to our study participants for sex, race or ethnic group, age, and height at each spirometric session. Panel A shows the average FEV_1 trajectory for participants classified as having normal lung-function growth without an early decline (170 participants), Panel B shows the trajectory for participants who had reduced growth without an early decline (160 participants), Panel C shows the trajectory for participants with normal growth and an early decline (178 participants), and Panel D shows the trajectory for participants who had reduced growth and an early decline (176 participants).

Riskfaktorer och “treatable traits”

• Svårighetsgrad av astma	→	**Astmakontroll, optimal behandling**
• Atopi, poly-sensibilisering	→	**Primärprevention sensibilisering**
• Eosinofili	→	**Farmakologisk behandling**
• Allergisk samsjuklighet	→	**Allergen immunterapi**
• Annan samsjuklighet (tex fetma)	→	**Rådgivning, viktkontroll, kost**
• Lung- / luftvägsinfektioner	→	**Lunghälsa! (vaccinationer, profylax etc)**
• Nedsatt lungfunktion	→	**Optimal lungutveckling**
• Bronkiell hyperreaktivitet	→	**Farmakologisk behandling**

Seminar

Asthma

Celeste Porsbjerg, Erik Melén, Lauri Lehtimäki, Dominick Shaw

Asthma is one of the most common chronic non-communicable diseases worldwide and is characterised by variable airflow obstruction, causing dyspnoea and wheezing. Highly effective therapies are available; asthma morbidity and mortality have vastly improved in the past 15 years, and most patients can attain good asthma control. However, undertreatment is still common, and improving patient and health-care provider understanding of when and how to adjust treatment is crucial. Asthma management consists of a cycle of assessment of asthma control and risk factors and adjustment of medications accordingly. With the introduction of biological therapies, management of severe asthma has entered the precision medicine era—a shift that is driving clinical ambitions towards disease remission. Patients with severe asthma often have co-existing conditions contributing to their symptoms, mandating a multidimensional management approach. In this Seminar, we provide a clinically focused overview of asthma; epidemiology, pathophysiology, diagnosis, and management in children and adults.

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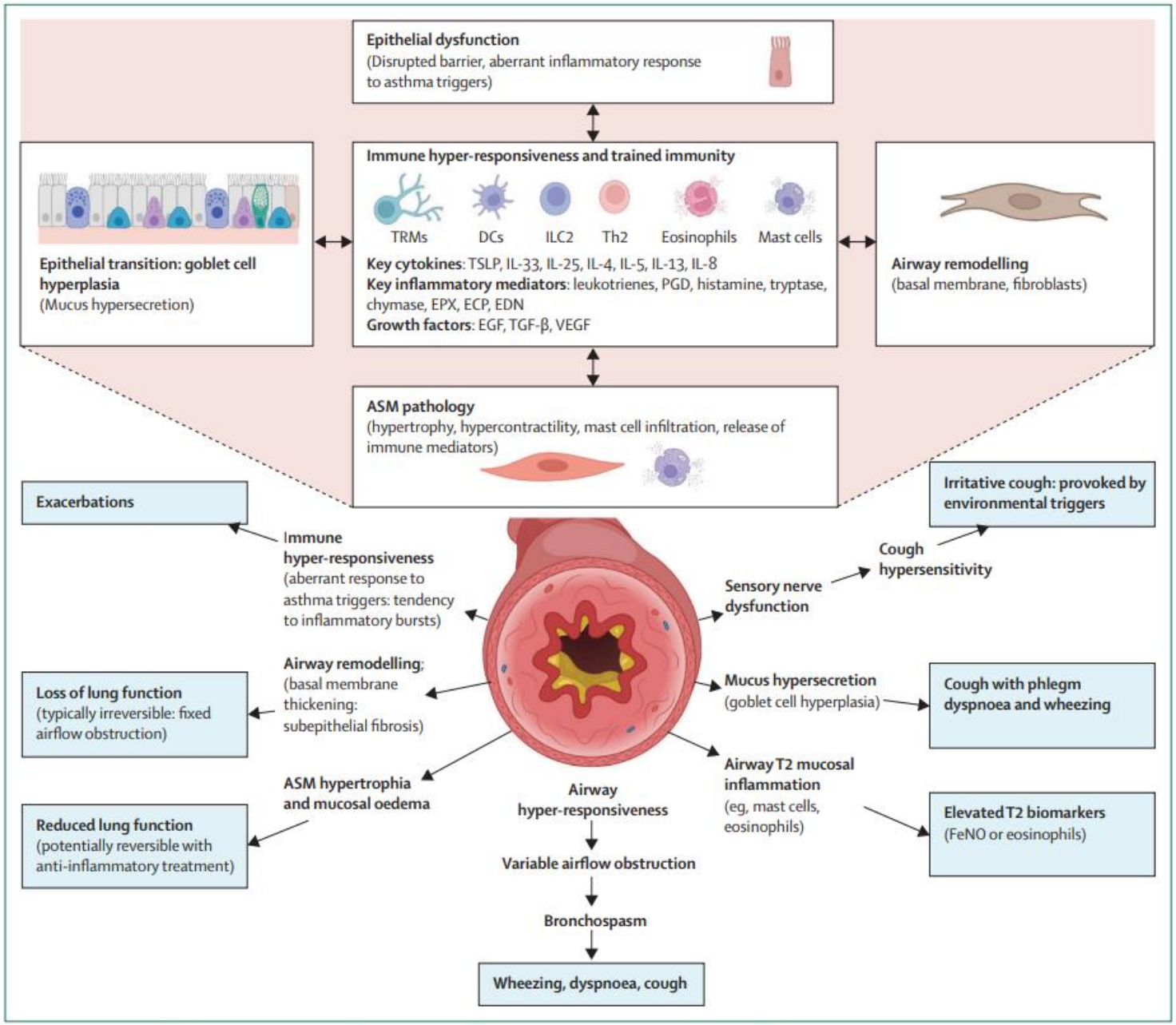

Figure 1: Key pathophysiological mechanisms of asthma and resulting disease components and clinical features

Porsbjerg et al *Lancet* 2023

EUROPEAN RESPIRATORY REVIEW
REVIEW
W.W. BUSSE ET AL.

Holy Grail: the journey towards disease modification in asthma

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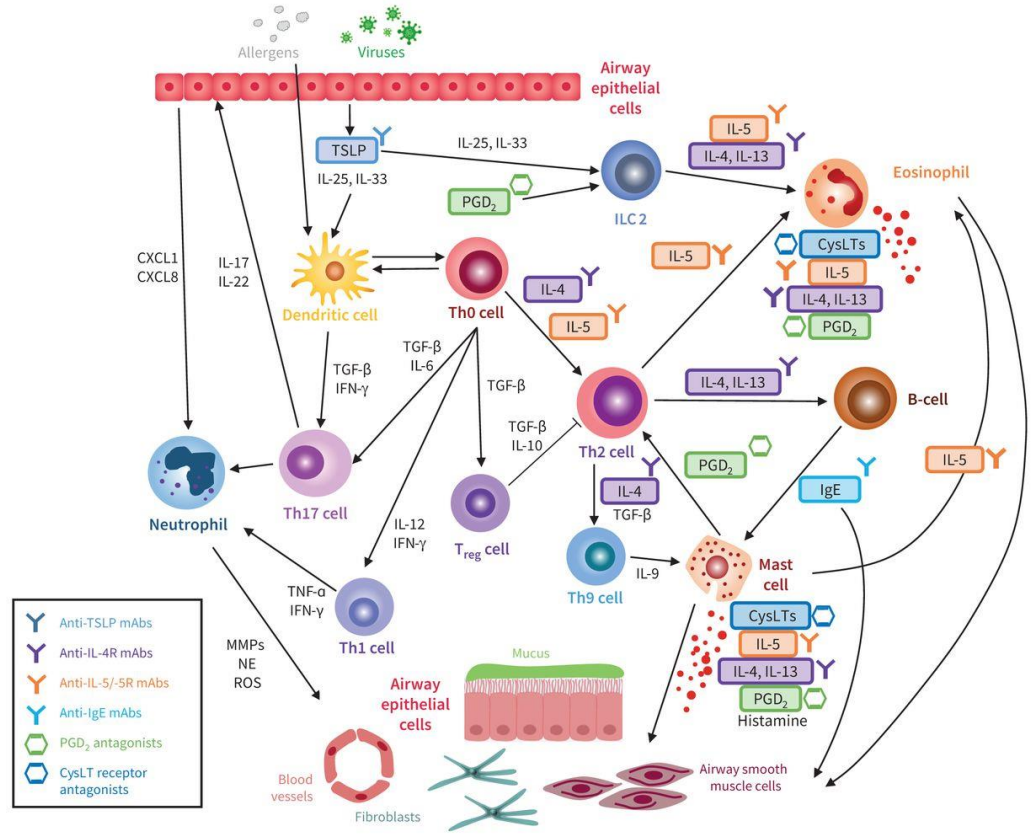

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

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Biologic Therapies for Severe Asthma

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How to Choose the Correct Drug in Severe Pediatric Asthma

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SYSTEMATIC REVIEW

WILEY

Real-world efficacy of treatment with benralizumab, dupilumab, mepolizumab and reslizumab for severe asthma: A systematic review and meta-analysis

David Charles[1] | Jemma Shanley[2] | Sasha-Nicole Temple[3] | Anna Rattu[4] | Ekaterina Khaleva[4] | Graham Roberts[5]

Sammanfattning

- Lunghälsa börjar tidigt i livet!
- Astma i barndomen viktig riskfaktor för senare kronisk sjukdom
- Flera kliniska markörer (treatable traits) för kvarstående astma identifierade
- Undersök, karaktärisera, utvärdera → personalized medicine → **remission**
- Förebygga KOL? Börja tidigt.

Tack!

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