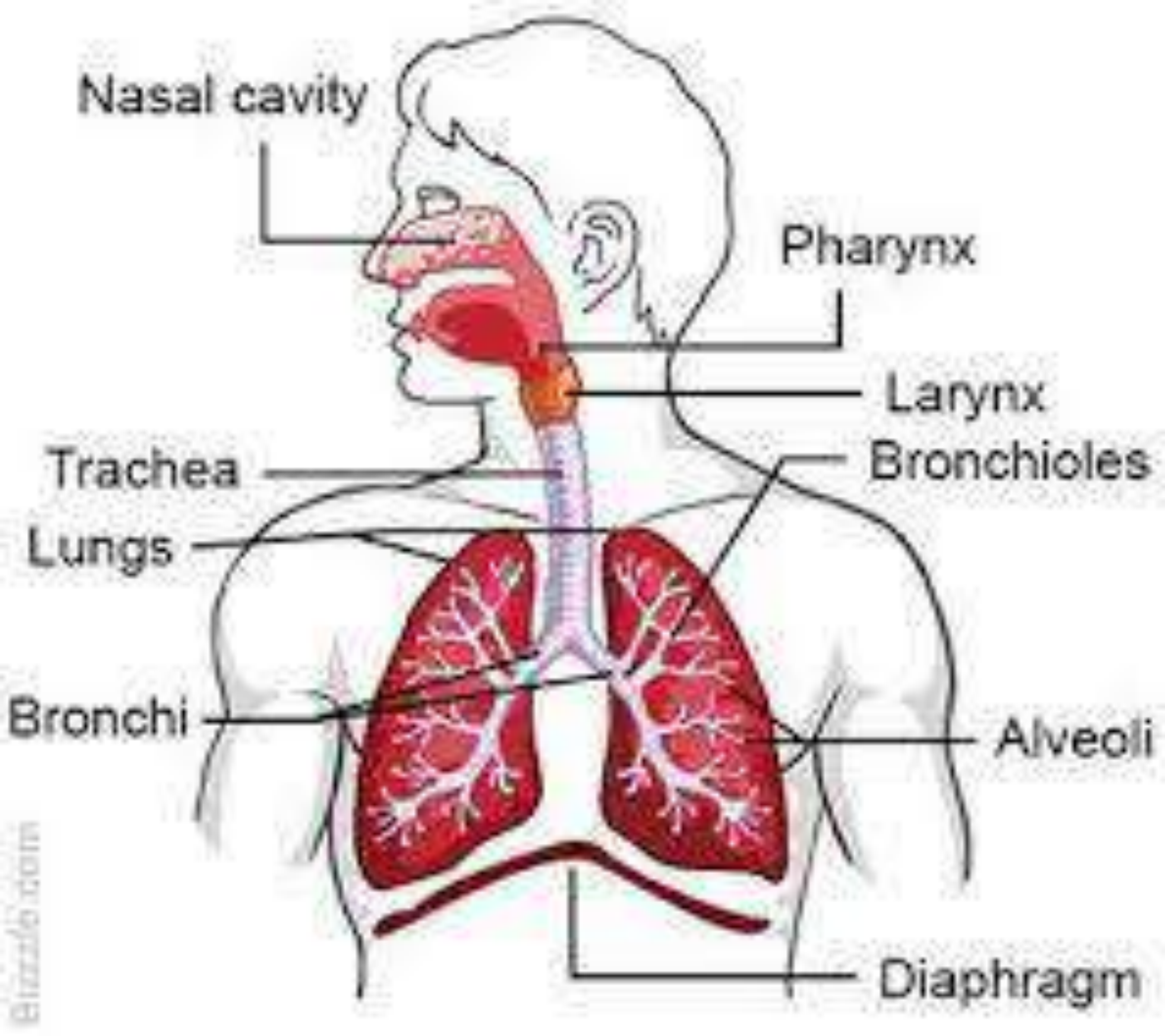
Early Life Origins of Respiratory Diseases

Rebecca Nantanda (MBChB, M. Med Paediatrics and Child Health, PhD)

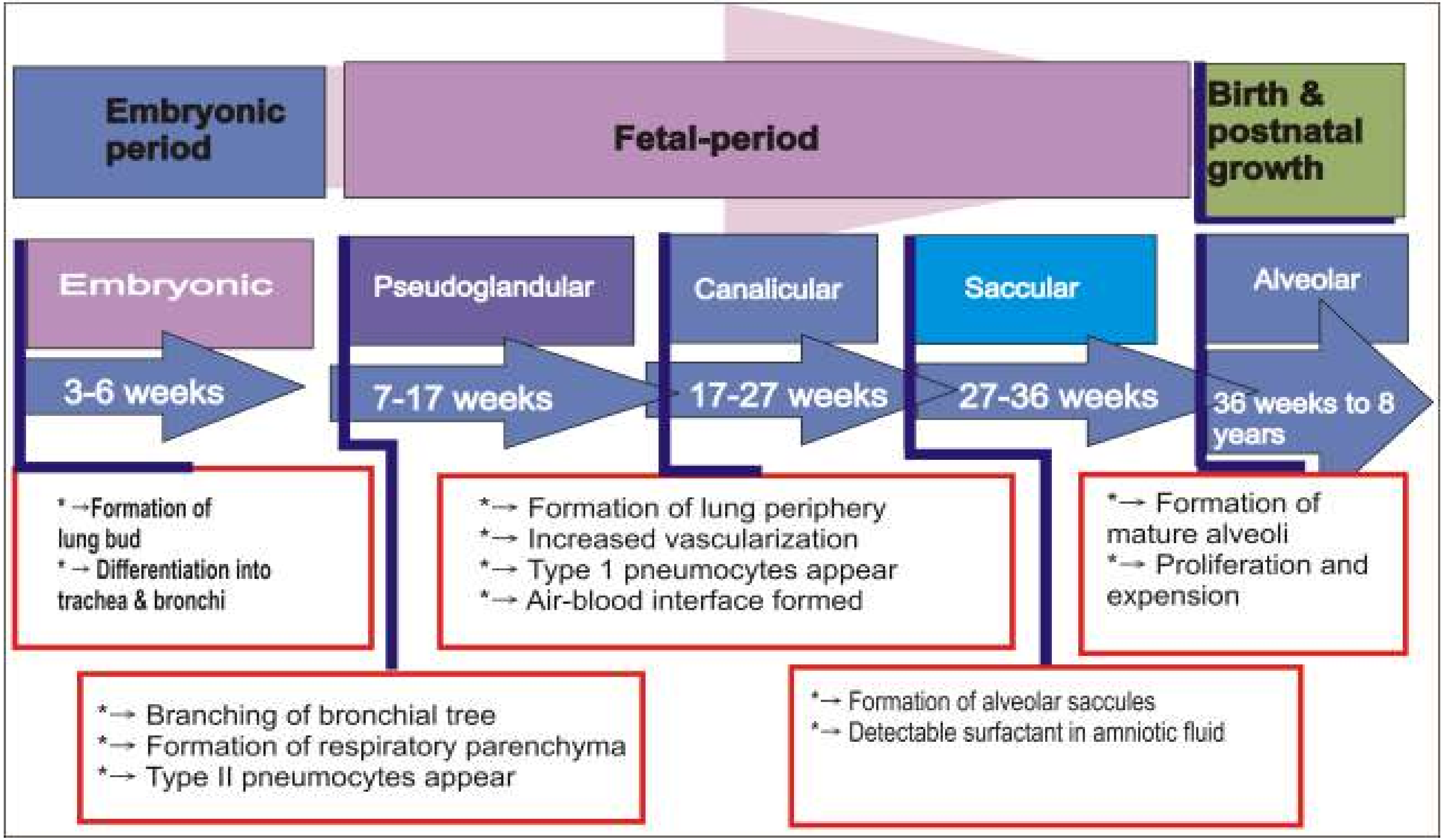
Outline of presentation

- Overview of the respiratory system
- Burden of common respiratory diseases
- Risk factors for respiratory diseases
- Prevention of respiratory diseases: Interventions
- Conclusion



Overview of the respiratory system: Growth and Development

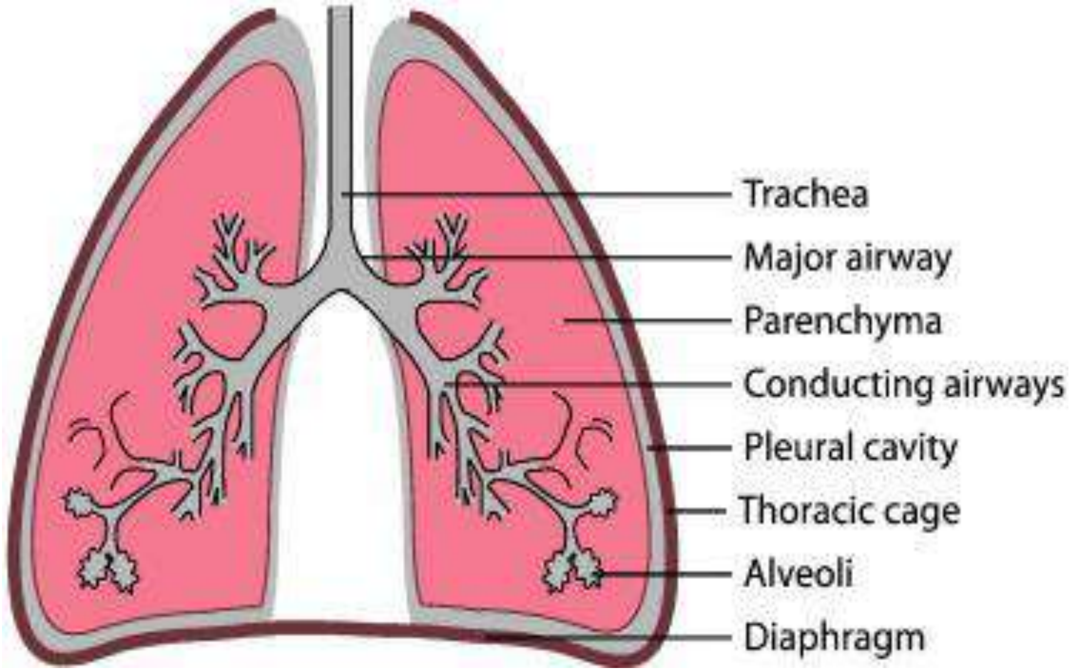
Stages of lung development



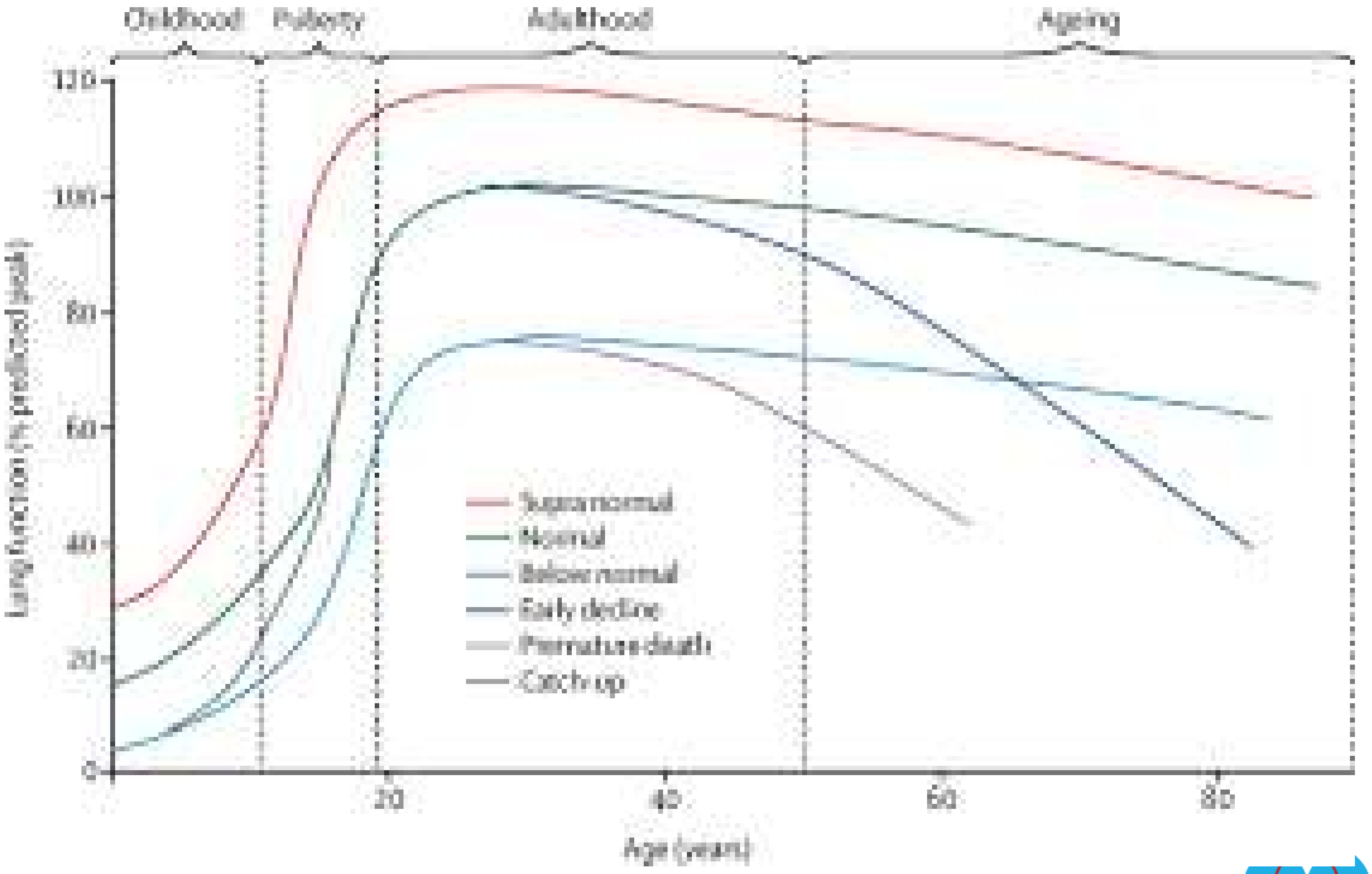
Lung development

- Normal lung development is a series of well orchestrated events
- Full lung maturation occurs at 22 years of age
- Lung function follows a predictable progression.

  E.g. lower quartile at birth=lower quartile in adulthood

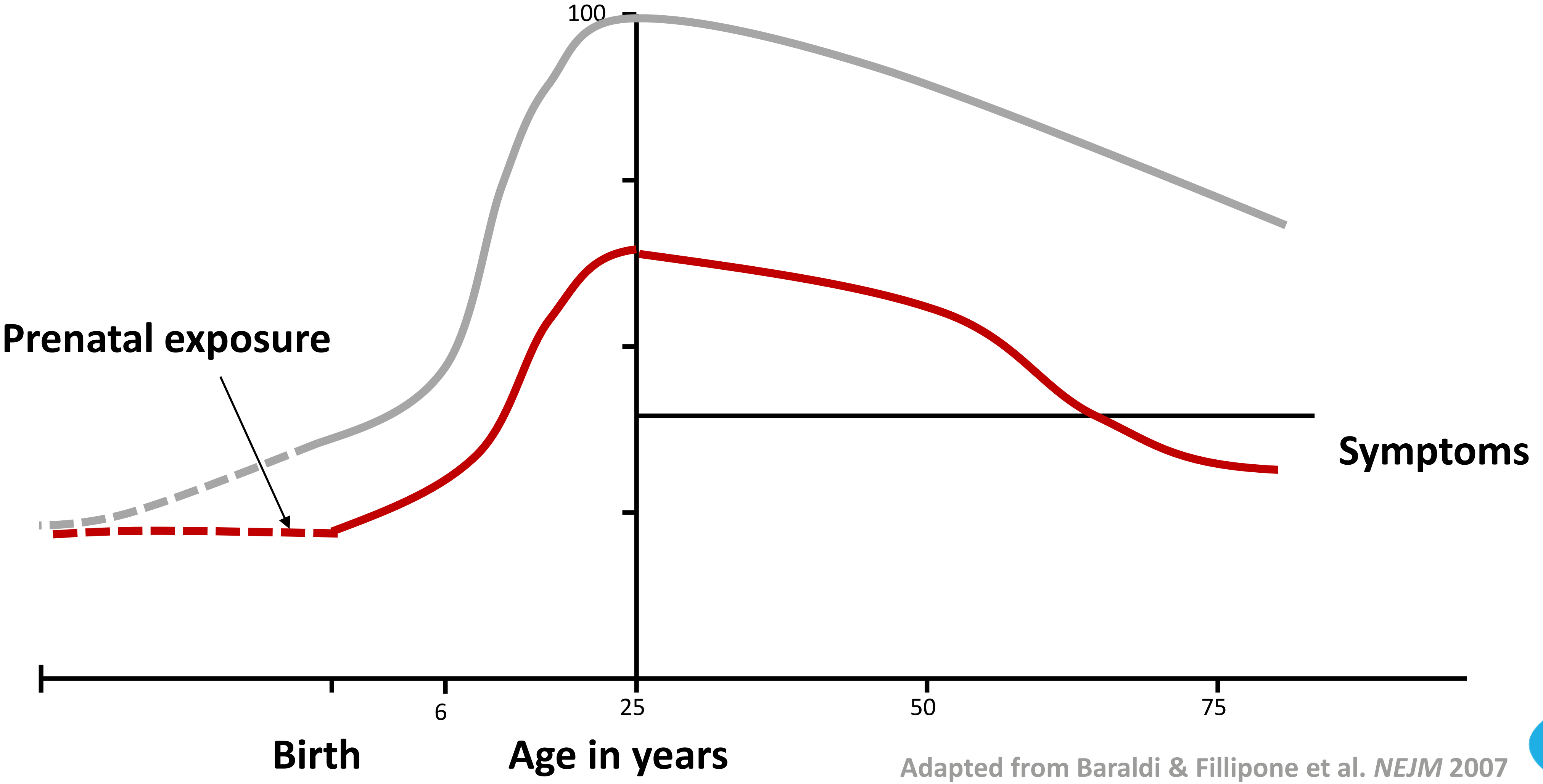


Trajectories of lung development



Agusti and Faner R, Lancet 2019 (DOI:https://doi.org/10.1016/S2213-2600(18)30529-0)

Lung development and prenatal exposure



Adapted from Baraldi & Fillipone et al. *NEJM* 2007

Common Respiratory Diseases

Childhood

- Chronic Lung Disease (CLD)
- URTIs- Otitis media, pharyngitis
- Pneumonia
- Tuberculosis
- Asthma
- Bronchiectasis
- Post-TB Lung Disease

Adulthood

- URTIs
- Pneumonia
- Tuberculosis
- Asthma
- Chronic Obstructive Pulmonary Disease (COPD)
- Post-TB Lung Disease
- Lung cancer

Burden of Respiratory Disease in Uganda

Childhood pneumonia: top three causes of child morbidity and mortality

Mortality rates of 10%-30%

Childhood asthma

Author/Year	Age group	Prevalence
Bitimwine et.al. 2010	8-14 years	13.8%
Aniku et.al 2015	9-12 years	Urban- 21% Rural -13%
Nantanda et.al 2013	2-59 months	41%

COPD in Uganda

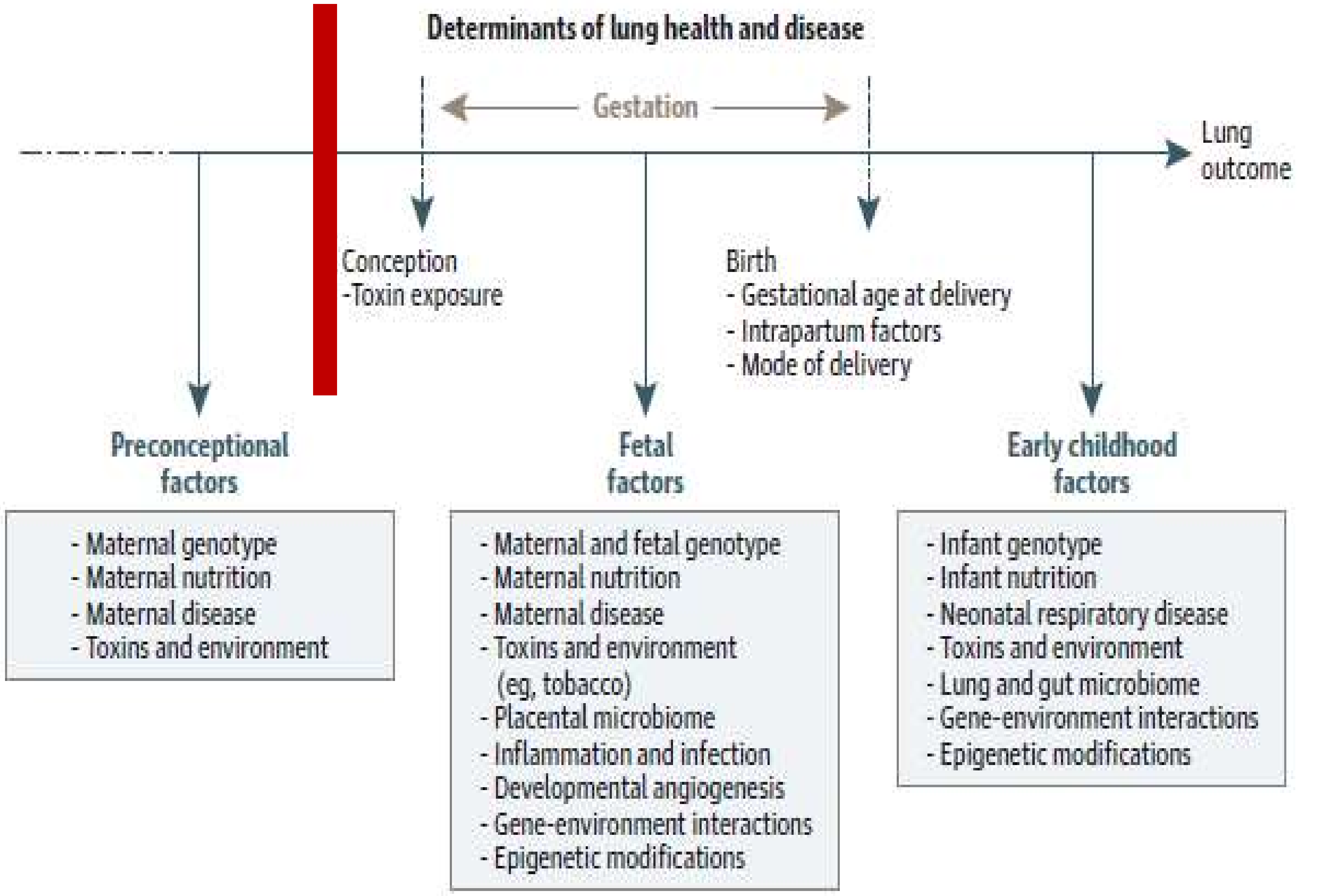
Prevalence

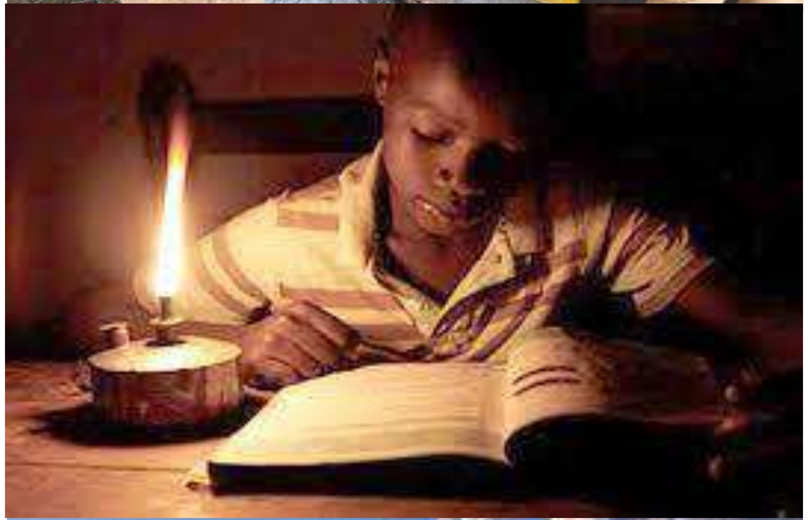
- 1.5%(urban)-16.2% (Rural)
- Prevalence higher in women
  16.8% women vs 15.4% men
- Prevalence among HIV patients 6.2%

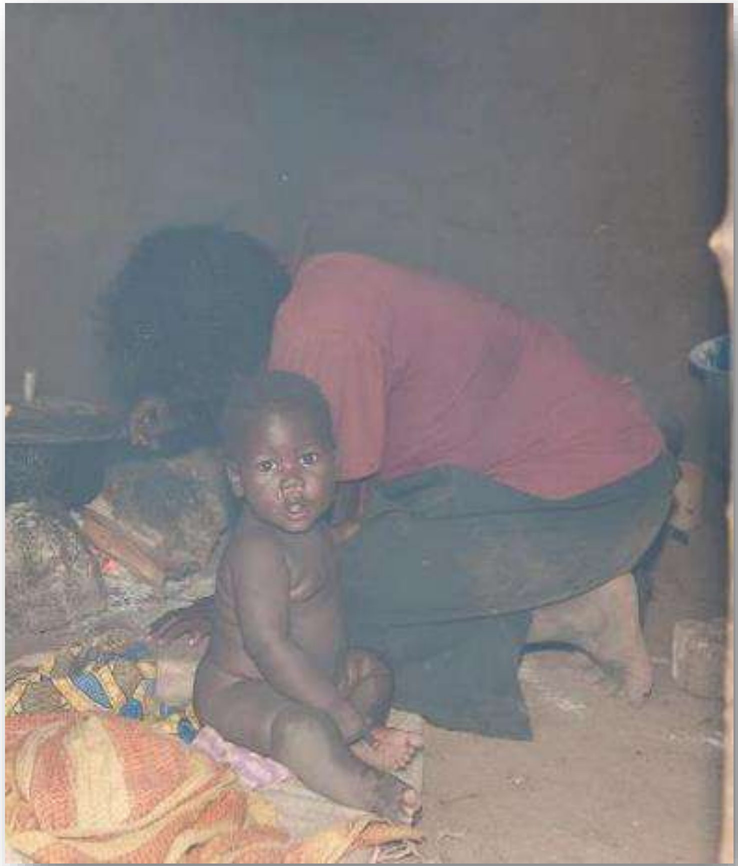
Fredrick van Gamert, Bruce et al(2017)	Masindi (Rural)	16.2%
Trishul ,grisby et al (2019)	Nakaseke	6.1%
Trishul, grisby et al (2019)	Kampala (Urban)	1.5%
Kayongo, et al (2020)	Nakaseke (Rural)	6.2% (HIV population)
Trishul et al (2022)	Nakaseke (rural)	7%

Risk factors for respiratory diseases

1. Genetics
2. Environment: air pollution, tobacco smoke
3. Nutrition
4. Disease


Determinants of lung health and disease
Gestation
Lung outcome
Conception
-Toxin exposure
Birth
- Gestational age at delivery
- Intrapartum factors
- Mode of delivery
Preconceptional factors
- Maternal genotype
- Maternal nutrition
- Maternal disease
- Toxins and environment
Fetal factors
- Maternal and fetal genotype
- Maternal nutrition
- Maternal disease
- Toxins and environment (eg, tobacco)
- Placental microbiome
- Inflammation and infection
- Developmental angiogenesis
- Gene-environment interactions
- Epigenetic modifications
Early childhood factors
- Infant genotype
- Infant nutrition
- Neonatal respiratory disease
- Toxins and environment
- Lung and gut microbiome
- Gene-environment interactions
- Epigenetic modifications

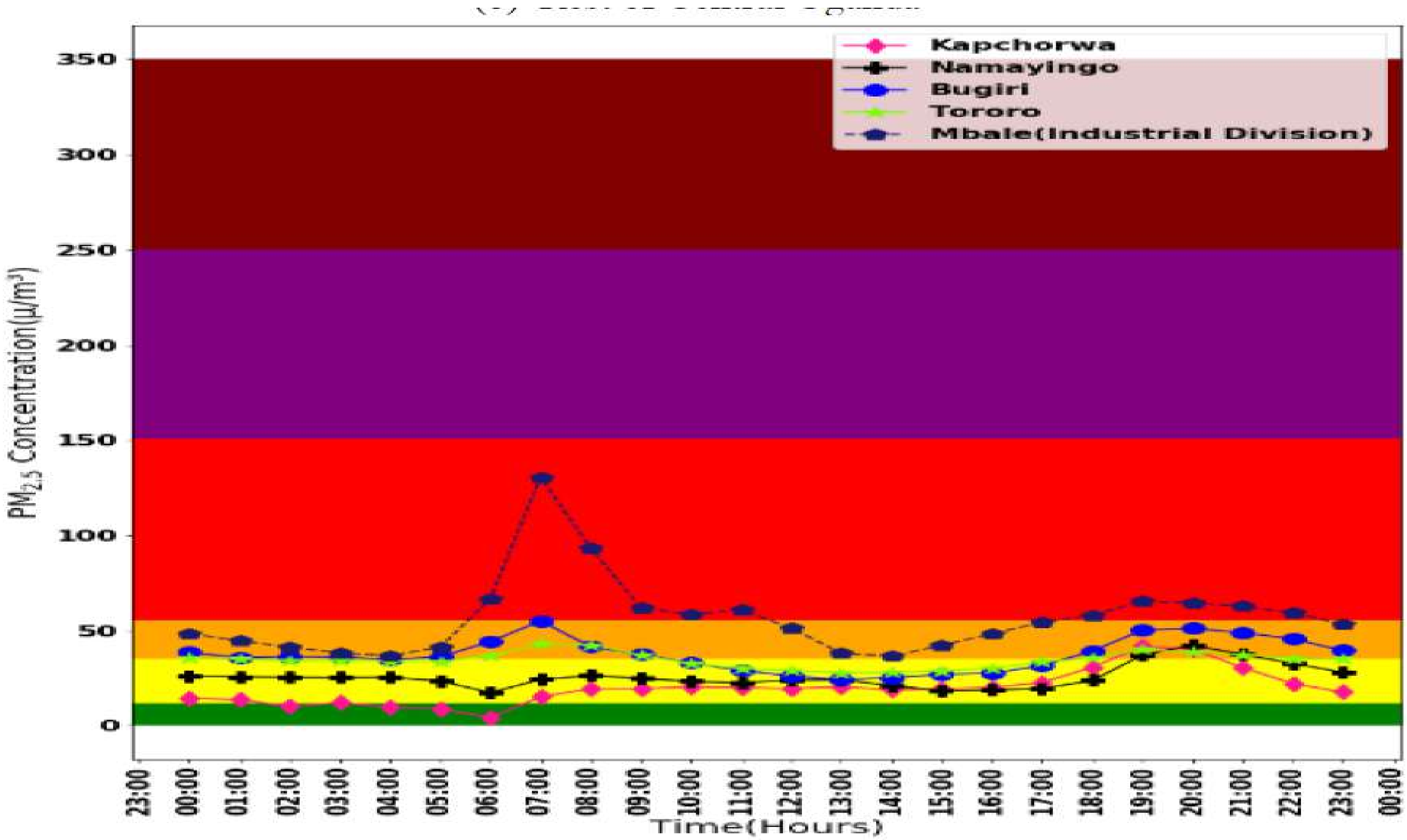




Common sources of air pollution

Ambient air pollution

AQI Category	Corresponding PM2.5 Conc./μgm^{-3}
Good	0-12.0
Moderate	12.1-35.4
Unhealthy for sensitive groups	35.5-55.4
Unhealthy	55.5-150.4
Very unhealthy	150.5-250.4
Hazardous	Above 250.5



(c) Eastern Uganda

Okure D, et.al 2021

Effects of Air pollution

Pregnancy/unborn baby: compromise placental blood flow Direct effect on the baby	• Low birth weight • Premature births • Bleeding (antepartum haemorrhage) • Poor lung function at birth
Lungs	• Increased risk of lung diseases- pneumonia, asthma, lung cancer, COPD
Heart	• Cardiovascular disease- Heart attacks
Brain	• Poor neurocognitive functioning • Stroke
Eyes	• Cataracts

mli

Maternal nutrition

Maternal malnutrition during pregnancy affects airway size and alveolar number

- Associated with poor birth outcomes-LBW, Prematurity

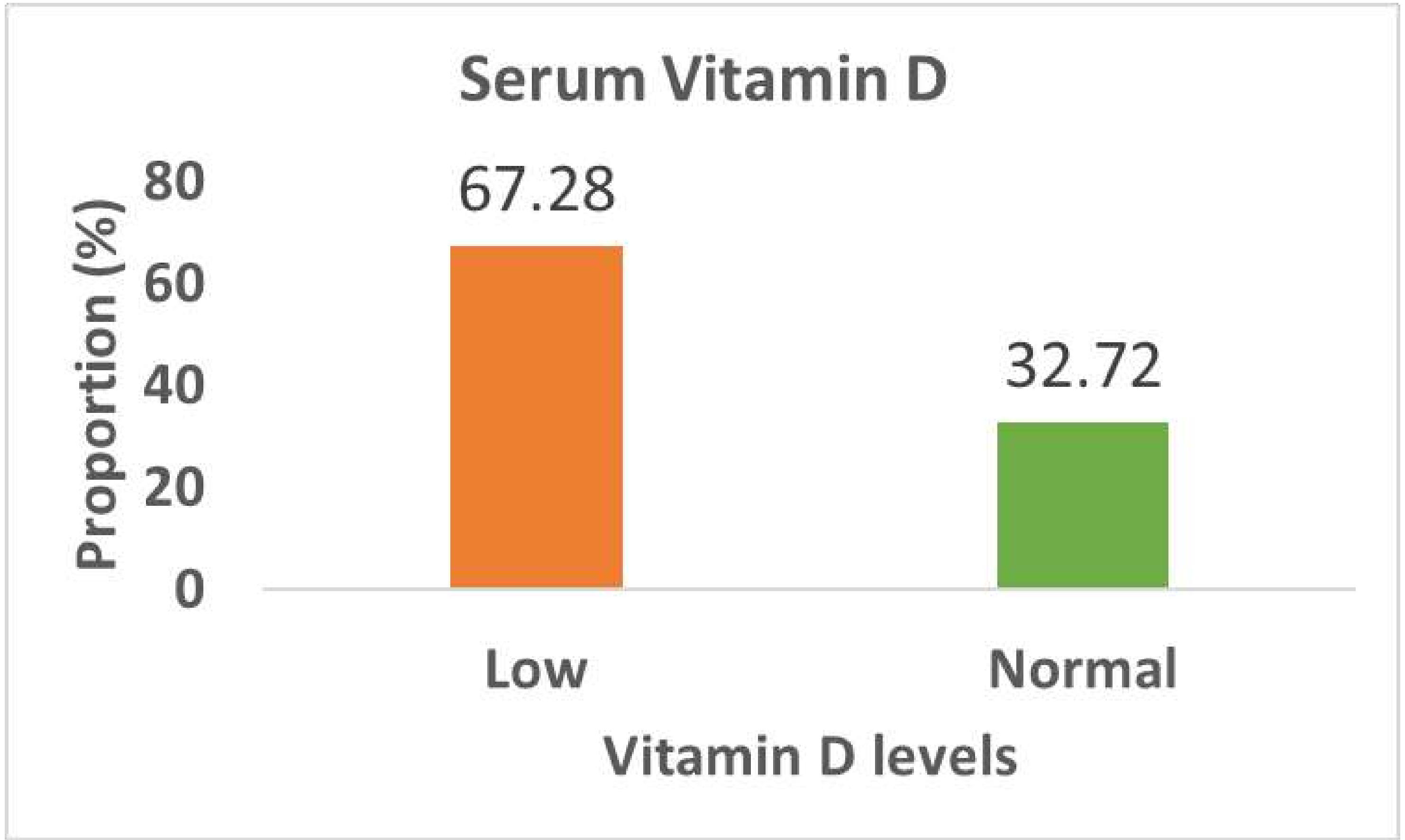
Maternal iron status during pregnancy has also been associated with childhood wheezing disease and sub-optimal lung function up to the age of 10 years

In a cohort of rural Nepali children whose mothers received vitamin A as part of a supplementation trial in pregnancy, lung function at age 9-13 years was noted to be better than for those whose mothers did not receive vitamin A

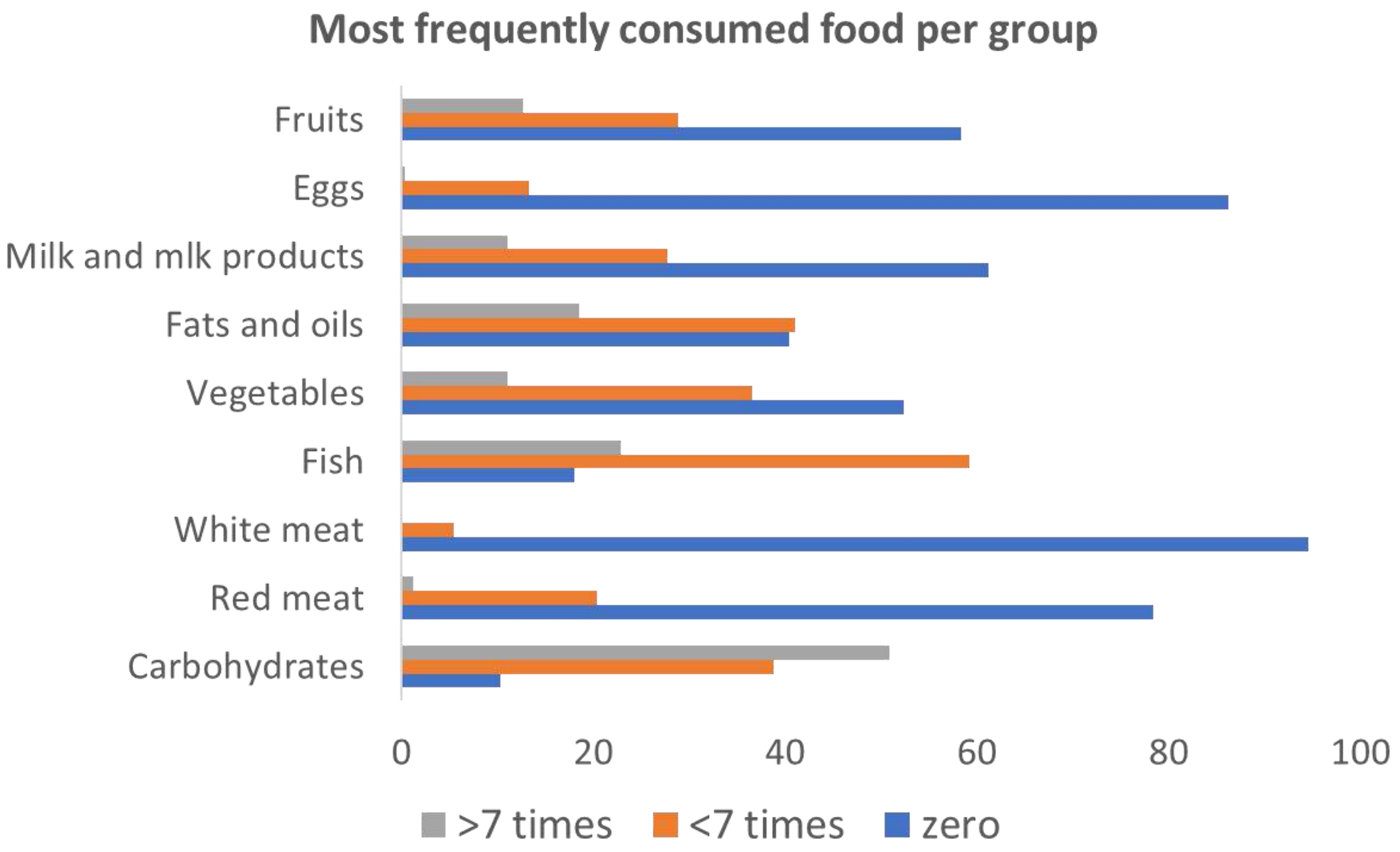
Nurmatov U, et.al. 2019, Checkley W, et.al 2010, Beckhaus AA, et.al 2017

mli

IMPALA study in Uganda: Prenatal vitamin D (N=564)



FREQUENCY OF CONSUMPTION OF FOODS



Interventions

- When?
- How?
- What works?
- How does it work?

Global Public Health

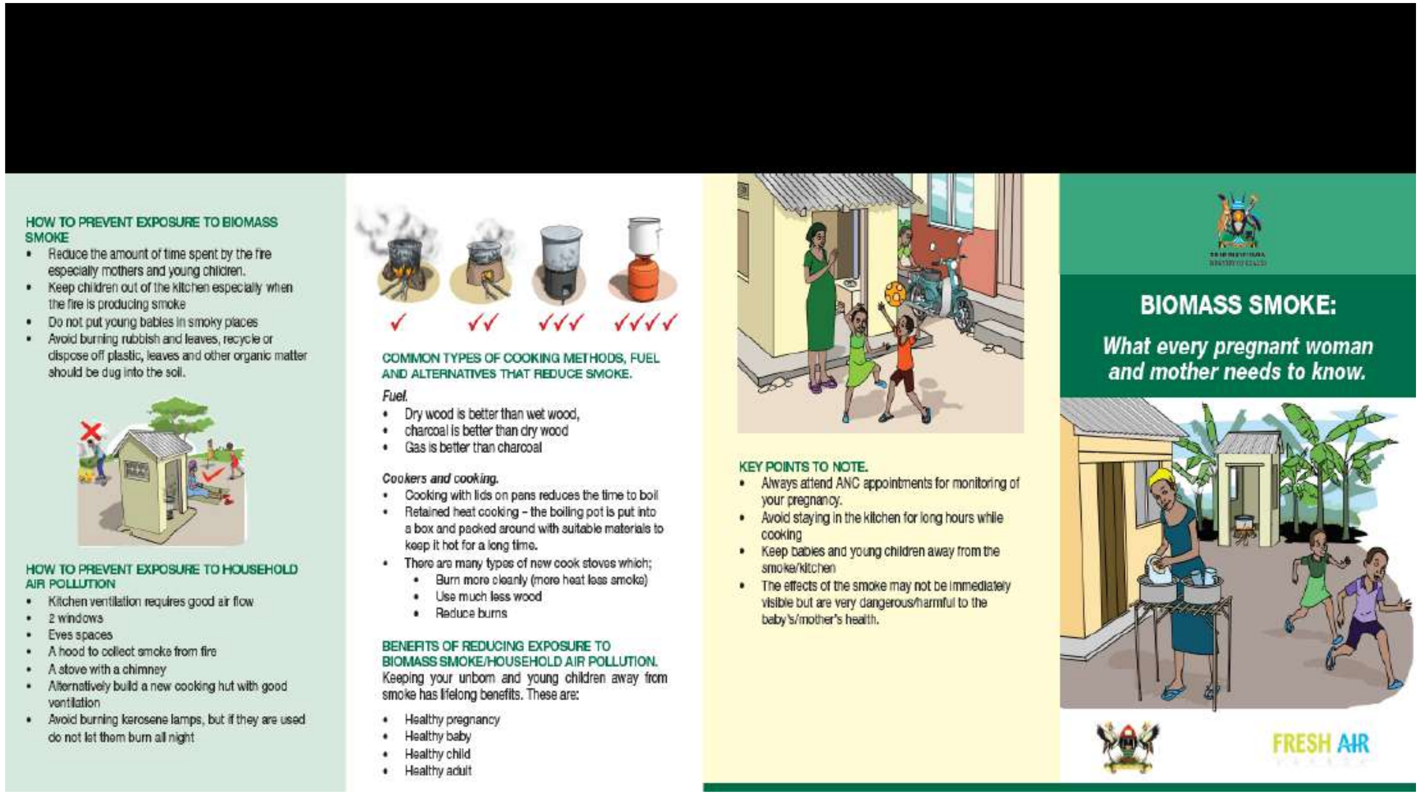
An International Journal for Research, Policy and Practice

ISSN: 1744-1692 (Print) 1744-1706 (Online) Journal homepage: https://www.tandfonline.com/loi/rgph20

Feasibility and acceptability of a midwife-led health education strategy to reduce exposure to biomass smoke among pregnant women in Uganda, A FRESH AIR project

Rebecca Nantanda, Shamim Buteme, Sanne van Kampen, Lucy Cartwright, Jill Pooler, Andy Barton, Lynne Callaghan, Jean Mirembe, Grace Ndeezi, James K. Tumwine, Bruce Kirenga & Rupert Jones

Educational interventions: Midwife-led project in Uganda



Key findings

- Improvements in knowledge about risks of biomass smoke
- Changes made- keeping away from smoke, burying refuse
- Intent to change
- Buy solar panels, clean cookstoves
- Put chimneys on the kitchen
- Major barrier -Poverty

CLEAN COOKSTOVES

<u>THE RESPIRE TRIAL: Guatemala highlands</u>

534 households with a pregnant woman or infant

randomized to receive a chimney stove or retain the open fire

Primary outcome: incidence of pneumonia in children

<u>Results</u>

- Non-significant reduction in incidence of physician-diagnosed pneumonia
- Significant reduction in physician-diagnosed severe pneumonia (RR 0.67; 95% CI 0.45 to 0.98)

Smith, K.R., et al. Lancet 2011, Heinzerling AP., et al. Thorax 2016

Cooking and Pneumonia Study (CAPS)

A cleaner burning biomass-fuelled cookstove intervention to prevent pneumonia in children under 5 years old in rural Malawi (the Cooking and Pneumonia Study): a cluster randomised controlled trial

Kevin Mortimer, Chifundo B Ndamala, Andrew W Naunje, Jullita Malava, Cynthia Katundu, William Weston, Deborah Havens, Daniel Pope, Nigel G Bruce, Moffat Nyirenda, Duolao Wang, Amelia Crampin, Jonathan Grigg, John Balmes, Stephen B Gordon

Summary

Background WHO estimates exposure to air pollution from cooking with solid fuels is associated with over 4 million premature deaths worldwide every year including half a million children under the age of 5 years from pneumonia. We hypothesised that replacing open fires with cleaner burning biomass-fuelled cookstoves would reduce pneumonia incidence in young children.

Methods We did a community-level open cluster randomised controlled trial to compare the effects of a cleaner burning biomass-fuelled cookstove intervention to continuation of open fire cooking on pneumonia in children living in two rural districts, Chikhwawa and Karonga, of Malawi. Clusters were randomly allocated to intervention and control groups using a computer-generated randomisation schedule with stratification by site, distance from health centre, and size of cluster. Within clusters, households with a child under the age of 4·5 years were eligible. Intervention households received two biomass-fuelled cookstoves and a solar panel. The primary outcome was WHO Integrated Management of Childhood Illness (IMCI)-defined pneumonia episodes in children under 5 years of age. Efficacy and safety analyses were by intention to treat. The trial is registered with ISRCTN, number ISRCTN59448623.

Findings We enrolled 10 750 children from 8626 households across 150 clusters between Dec 9, 2013, and Feb 28, 2016. 10 543 children from 8470 households contributed 15 991 child-years of follow-up data to the intention-to-treat analysis. The IMCI pneumonia incidence rate in the intervention group was 15·76 (95% CI 14·89–16·63) per 100 child-years and in the control group 15·58 (95% CI 14·72–16·45) per 100 child-years, with an intervention versus control incidence rate ratio (IRR) of 1·01 (95% CI 0·91–1·13; p=0·80). Cooking-related serious adverse events (burns) were seen in 19 children; nine in the intervention and ten (one death) in the control group (IRR 0·91 [95% CI 0·37–2·23]; p=0·83).

Interpretation We found no evidence that an intervention comprising cleaner burning biomass-fuelled cookstoves reduced the risk of pneumonia in young children in rural Malawi. Effective strategies to reduce the adverse health effects of household air pollution are needed.

Funding Medical Research Council, UK Department for International Development, and Wellcome Trust.

Lancet 2017; 389: 167–75

Published Online December 6, 2016 http://dx.doi.org/10.1016/S0140-6736(16)32507-7

See Comment page 130

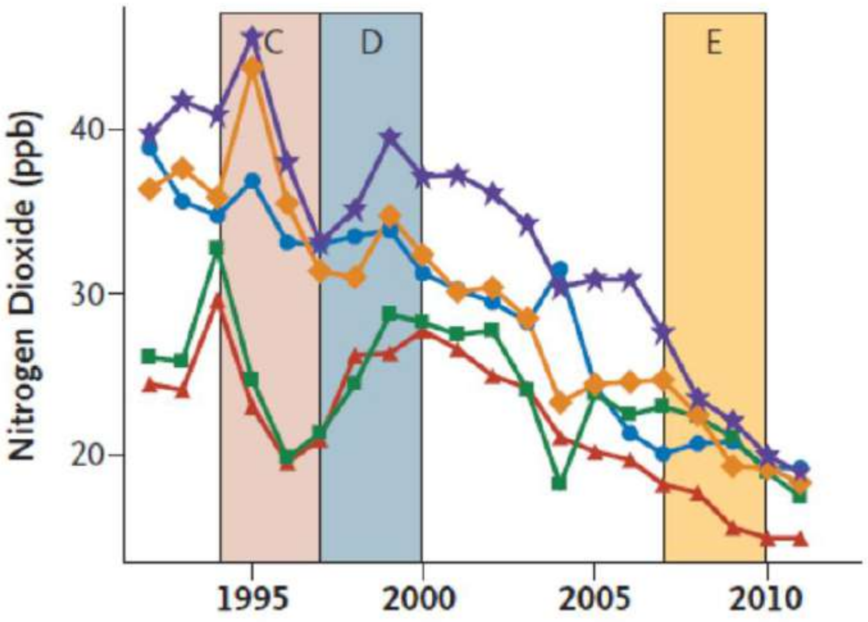
Malawi Liverpool Wellcome Trust Programme, Blantyre, Malawi (K Mortimer PhD, C B Ndamala Dip, A W Naunje, W Weston MBChB, Prof S B Gordon MD); **Liverpool School of Tropical Medicine, Liverpool, UK** (K Mortimer, W Weston, D Havens DO, Prof D Wang PhD, Prof S B Gordon); **Malawi Epidemiology and Intervention Research Unit, Chilumba, Malawi** (J Malava MPH, C Katundu Dip, Prof M Nyirenda PhD, A Crampin MPH); **University of Liverpool, Liverpool, UK** (D Pope PhD, Prof N G Bruce PhD); **London School of Hygiene & Tropical Medicine, London, UK** (Prof M Nyirenda, A Crampin); **Queen Mary University of London, London, UK** (Prof J Grigg MD); **University of**

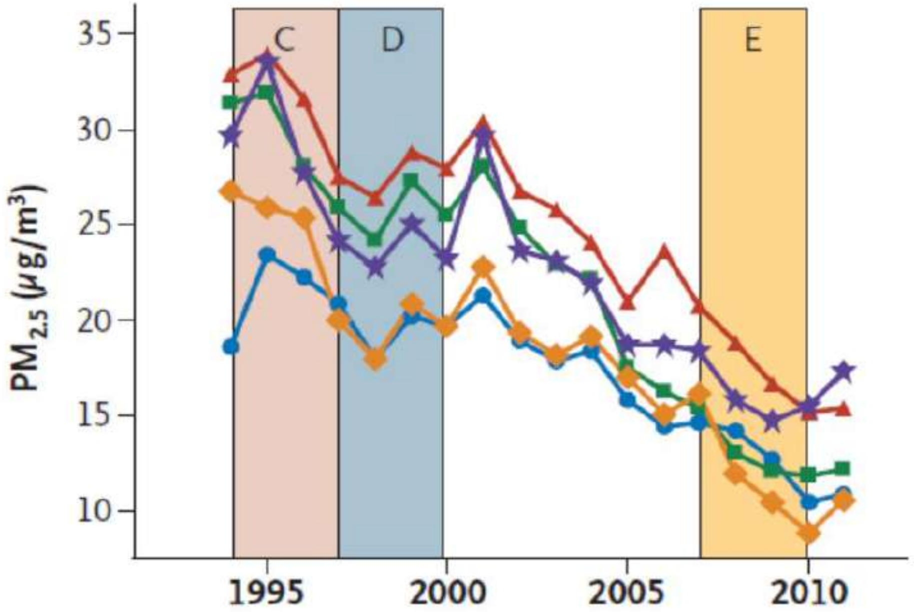
The NEW ENGLAND JOURNAL of MEDICINE

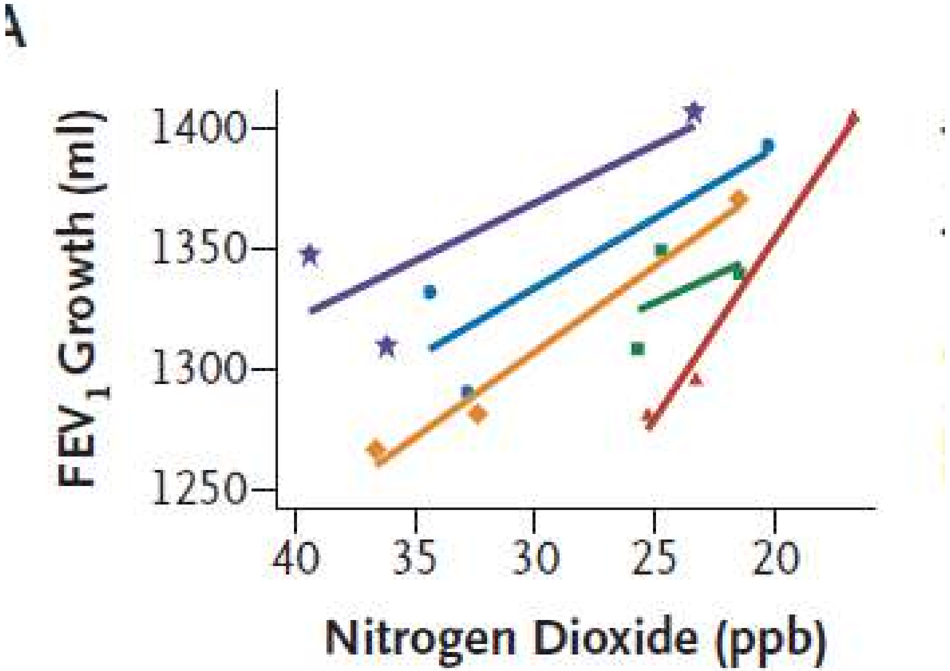
ESTABLISHED IN 1812 MARCH 5, 2015 VOL. 372 NO. 10

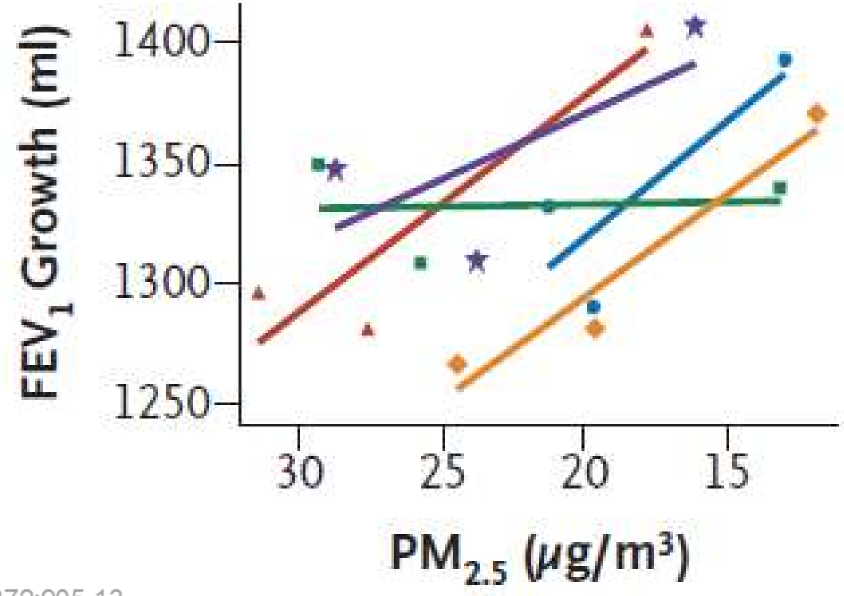
Association of Improved Air Quality with Lung Development in Children

W. James Gauderman, Ph.D., Robert Urman, M.S., Edward Avol, M.S., Kiros Berhane, Ph.D., Rob McConnell, M.D., Edward Rappaport, M.S., Roger Chang, Ph.D., Fred Lurmann, M.S., and Frank Gilliland, M.D., Ph.D.









Gauderman et al. NEJM 2015;372:905-13

Nutritional interventions

Single nutrient interventions –not helpful

Dietary approaches proposed:

- Feeding is a behaviour and therefore the required nutrients are likely to be obtained from an optimal diet,
- The interrelations between constituents in foods are significant and the health benefits appear stronger when put together in a synergistic dietary pattern than for individual foods or food constituents

Other interventions

Interventions in early childhood (1000 days)

- Healthy pregnancy, healthy newborn, health child
- Immunization
- PMTCT
- Infant feeding

Secondary prevention

Early screening and optimal management of respiratory illnesses

- Pneumonia →Bronchiectasis
- Asthma→ COPD
- Tuberculosis →Post-TB Lung Disease

Journal of Tropical Pediatrics, 2021, 00, 1–10
doi: 10.1093/tropej/fmab042
Original Paper

OXFORD

Health Workers' Practices in Assessment and Management of Children with Respiratory Symptoms in Primary Care Facilities in Uganda: A FRESH AIR Descriptive Study

Rebecca Nantanda PhD,[1,*] Joakim Bloch MD,[2,*] Marianne Stubbe Østergaard PhD,[3] Bruce J. Kirenga PhD,[1,4] James K. Tumwine PhD,[5] Grace Ndeezi PhD,[5] Susanne Reventlow D.M.Sc,[2,3] Anja Poulsen PhD,[2] *and* Jesper Kjærgaard PhD[2]

Table 2. Health workers' practices in eliciting history and signs of respiratory illnesses in children with cough and/or difficult breathing (N = 218)

Characteristics	Frequency asked by health worker [missing]	Percentage (%)
Core symptoms		
Fever	75 [5]	34.4
Recurrent cough	13 [8]	6.0
Difficult breathing during this illness	16 [6]	7.3
Recurrent difficult breathing	5 [6]	2.3
Noisy breathing	8 [5]	3.7
Wheezing during this illness	5 [6]	2.3
Night or early morning cough	15 [6]	6.9
At least one of the above except fever	36 [3]	16.5
History of asthma triggers asked, $n = 7$ (3.2) [4][a]		
Upper respiratory tract infections	0	0.0
Dusty environment	0	0.0
Biomass smoke	2	29.0
Cigarette smoke	1	14.0
Aerosols	0	0.0
Changes in temperature (cold)	1	14.0
Keeping animals at home	0	0.0
Exercise-induced symptoms (incl. crying/laughing)	1	14.0
Other relevant history, $n = 17$ (7.8) [2][a]		
History of allergy in child	3	18.0
Family history of allergy	4	24.0
Family history of asthma	3	18.0
Previous medications asked, $n = 44$ (20.2) [3]		
Salbutamol	2	5.0
Steroids	2	5.0
Clinical examination ($n = 218$)	Frequency assessed by health worker [missing]	
Expose the child's chest	47 [8]	21.8
Respiratory rate taken	23 [8]	10.6
Checked for chest in-drawing	22 [15]	10.1
Listen for audible wheeze	8 [8]	3.7
Listen for auscultatory wheeze	30	13.8
Checked throat/oropharynx	23	10.6

[a]27 of the 218 children (12.4%) included in the study had symptoms of asthma.

mli

Under-diagnosis of asthma

OPEN ACCESS Freely available online

PLOS ONE

Asthma and Pneumonia among Children Less Than Five Years with Acute Respiratory Symptoms in Mulago Hospital, Uganda: Evidence of Under-Diagnosis of Asthma

Rebecca Nantanda[1*], James K. Tumwine[2], Grace Ndeezi[2], Marianne S. Ostergaard[3]

1 Child Health and Development Centre, Makerere University College of Health Sciences, Kampala, Uganda, 2 Department of Paediatrics and Child Health, Makerere University College of Health Sciences, Kampala, Uganda, 3 The Research Unit for General Practice and Section of General Practice, Department of Public Health, University of Copenhagen, Copenhagen, Denmark

41.2% (253/614) under-fives had asthma syndrome

Only 9.5% of them had a diagnosis of asthma

95.3% of them had been diagnosed as pneumonia and prescribed antibiotics

mli

Key messages

- Early life (prenatal) events affect lung growth and development, and lung function

- Sub-optimal lung function at birth is a risk factor for respiratory diseases throughout the life course

- A life course approach to prevention of lung diseases –the way to go

- Environment and nutrition are modifiable risk factors and if addressed, can lead to improvements in lung health and prevention of lung diseases