INT J TUBERC LUNG DIS 24(9):000–000

http://dx.doi.org/10.5588/ijtld.20.0083

Determinants of lung health across the life course in sub-Saharan Africa

S. Rylance,[1,2] R. Masekela,[3] N. P. K. Banda,[4] K. Mortimer[2]

[1]Lung Health Group, Malawi Liverpool Wellcome Trust Clinical Research Programme, Blantyre, Malawi; [2]Department of Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK; [3]Department of Paediatrics and Child Health, University of KwaZulu Natal, Durban, South Africa; [4]Department of Medicine, University of Malawi College of Medicine, University of Malawi, Blantyre, Malawi

SUMMARY

LUNG HEALTH ACROSS THE life course is influenced by factors affecting airway and alveolar development and growth during antenatal and perinatal periods, throughout childhood and adolescence, and into adulthood. Lung function trajectories are set in early life and childhood deficits may predispose to non-communicable respiratory diseases, such as asthma and chronic obstructive pulmonary disease, in later years. Potential risk factors are common in many sub-Saharan African (sSA) countries; adverse antenatal environments cause *in utero* growth restriction and prematurity; HIV and respiratory infections, including TB are common; exposure to air pollution is widespread, including household air pollution from biomass fuel use, traffic-related pollution in rapidly expanding cities, and tobacco smoke exposure. Multiple disadvantages experienced in early life require an integrated approach that addresses reproductive, maternal and child health. Public health strategies need to tackle multiple risk factors, emphasising Universal Health Coverage, to maximise lung health in the world's poorest, most vulnerable populations. This review explores potential determinants of lung health across the life course. Due to the extensive topic and wide range of related literature, we prioritised more recent citations, especially those from sSA, focusing on risk factors for which there is most information, and which are most prevalent in the region.

KEY WORDS: epidemiology; lung function; air pollution; early life; lung growth and development

LUNG GROWTH AND DEVELOPMENT in early life impacts on adult lung health, and poverty-related risk factors are commonly encountered across the sub-Saharan African (sSA) region.[1] In contrast to high-income countries (HICs), the region bears a high burden of communicable respiratory disease, including childhood pneumonia, TB and HIV-related lung infections.[2-4] Non-communicable respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD) are also increasingly prevalent in sSA, placing a burden on overstretched health care systems, which are poorly equipped to diagnose, monitor and treat long-term conditions.[5] Spirometry data from the region have identified that both child and adult lung volumes are decreased compared to Caucasian reference ranges; the prognostic significance of this finding is unclear and locally appropriate reference ranges, representing maximal lung growth in the absence of adverse factors for sSA populations are lacking.[6–8]

This review aims to highlight the issues which impact on the lung health, including both non-communicable and communicable respiratory diseases, of some of the world's poorest communities. We reviewed PubMed referenced literature, published pre-December 2019, with studies identified through combinations of MeSH and key word searches for each topic, including pregnancy, infant, child, adolescent, lung, lung function, pneumonia, nutrition, air pollution, smoke, TB, HIV, **and** a search line relating to Africa **or** individually named African countries, with subsequent cited reference searching. Research originating from sSA was prioritised, with a focus on risk factors most relevant to the region, guided by the authors' local expertise. To provide context, we begin with a brief overview of lung development and growth.

LUNG DEVELOPMENT AND GROWTH: IN UTERO, THROUGH CHILDHOOD AND ADOLESCENCE

Human foetal lung development occurs in five phases (Table), with the formation of the conducting airways and alveoli, essential components for effective *ex utero* gas exchange, by the end of a full-term pregnancy. By the start of the third trimester of

Correspondence to: Sarah Rylance, Malawi-Liverpool-Wellcome Trust Clinical Research Programme, PO Box 30096, Blantyre 3, Malawi. e-mail: sarah.rylance@lstmed.ac.uk

Article submitted 14 February 2020. Final version accepted 19 May 2020.

Table Phases of *in utero* lung development[1]

Phase (timing)	Developmental processes
Embryonic phase (4–7 weeks' gestation) Pseudoglandular phase (7–16 weeks' gestation)	• Lung buds develop • Conductive airway pattern develops • Early airway epithelium differentiation
Canalicular phase (17–26 weeks' gestation)	• Completion of airway branching • Development of gas exchange region
Saccular phase (27–36 weeks' gestation)	• Growth and maturation of peripheral airways, differentiation of alveolar epithelial cells and maturation of surfactant system
Alveolar phase (34 weeks' gestation to adolescence)	• Increase in alveolar number and subsequent increase in gas exchange area

pregnancy, airway branching is completed, the gas-exchange region is developing and surfactant production has begun. Subsequently, there is further growth of the pulmonary parenchyma and maturation of the surfactant system. From approximately 32 weeks' gestation, there is rapid expansion of alveolar numbers and resulting lung growth, which continues postnatally during the first 2 years of life. Stereological assessment of lungs from human autopsies and studies using helium-3 magnetic resonance to assess alveolar size suggest that neo-alveolarisation continues throughout childhood and adolescence.[9,10] After this point, alveolar size continues to increase with somatic growth but alveolar numbers remain constant, at around 300–600 million.[11] There is some evidence that lung growth is possible in adulthood, through expansion of alveolar numbers, under specific circumstances (e.g., post-pneumonectomy).[12] Although airway development is largely completed by birth, airway growth, with increasing airway diameter and length, continues to a plateau at 20–25 years of age, with gradual decline thereafter.[13]

Timings are approximate and there is overlap between developmental phases. Insults to the lungs at any point across the life course have potential to disrupt the normal stages of growth and development (Figure 1). Repair of damaged airways and pathological remodelling can affect various airway elements, occurring even in early childhood: bronchial reticular basement thickening has been identified in children with severe pre-school wheeze.[14 15]

The early life origins of lung function and respiratory disease have been established in several longitudinal birth cohort studies, all conducted in HIC.[1] The Tucson Children's Respiratory Study described symptom patterns in early childhood and subsequent respiratory morbidity; wheezing at age 6 years was associated with both chronic and new-onset asthma in adulthood, and lung function deficits present by age 6 years, persisted thereafter.[16] Birth cohort studies from New Zealand and Australia, also reported tracking of lung function, with lung function following centiles set in early childhood throughout later childhood and adulthood, regardless of asthma

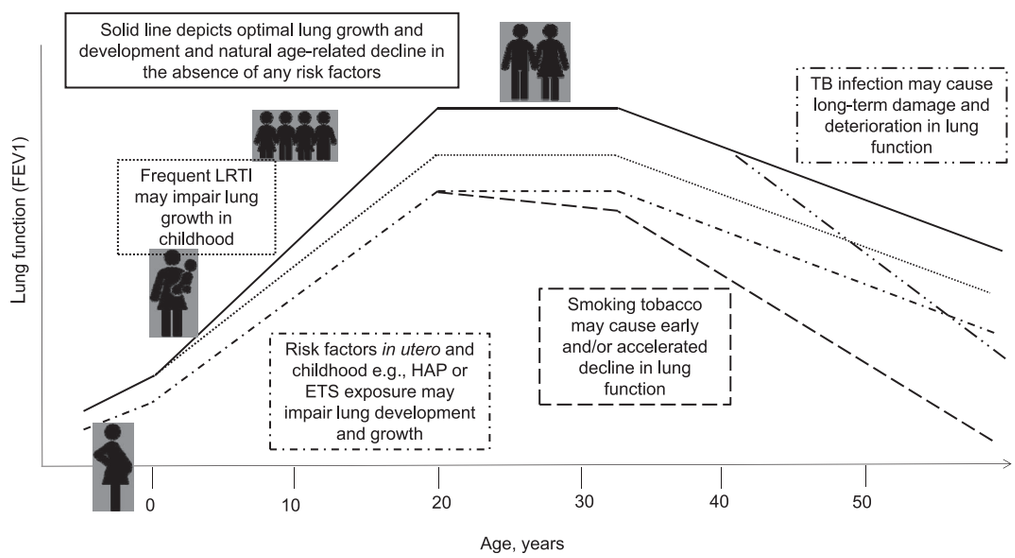

Figure 1 The impact of common risk factors encountered in sub-Saharan Africa on lung function trajectories across the life course. Trajectories shown (not to scale) demonstrate possible impact of adverse factors acting in childhood (dotted), *in utero* and childhood (dot-dash), in early adulthood (long dash) and later adulthood (long dash-dot-dot), compared to optimal lung growth (solid line). FEV_1 = forced expiratory volume in 1 sec; TB = tuberculosis; LRTI = lower respiratory tract infection; HAP = household air pollution; ETS = environmental tobacco smoke.

severity.[17,18] The Drakenstein Child Health Study (DCHS) in South Africa, will provide data of greater relevance to populations in sSA, as this cohort ages.[19–21] Potential risk factors for adverse lung health outcomes vary between high- and low-income settings: risk factors of particular relevance to low- and middle-income countries (LMICs) in sSA are discussed in subsequent sections, divided into antenatal, perinatal, childhood and adulthood life stages.

MATERNAL EXPOSURE TO INHALED POLLUTANTS DURING PREGNANCY: TOBACCO SMOKE, HOUSEHOLD AND AMBIENT AIR POLLUTION

There is strong evidence from HICs that *in utero* exposure to tobacco smoke is associated with reduced respiratory function in the early neonatal period, and increased prevalence of respiratory infections and asthma.[22] The South African DCHS reported altered lung function at age 6–10 weeks in infants of maternal smokers, and increased wheeze and lower respiratory tract infection (LRTI) at age 1 year.[19,21] Nicotine exposure is thought to be a key mediator of altered pulmonary function: this is not currently a major problem in sSA, where rates of maternal smoking are low, but impaired lung development may also result from hypoxaemia secondary to carbon monoxide (CO) exposure. High CO levels are found in cigarette smokers and also in those using biomass fuels to cook in low-income settings.[7] The effect of *in utero* household air pollution from incomplete combustion of biomass fuels on foetal lung development is largely unknown. Recent work from Ghana described an association between *in utero* household air pollution exposure and impaired infant lung function at 30 days of age.[23] In South Africa, antenatal exposure to the volatile organic compound toluene was associated with severe LRTI in infants; further research on this kind of exposure in early life is needed.[21]

A few studies from high-income settings have explored the impact of air pollution exposure during pregnancy, reporting associations between maternal exposure to pollutants and altered lung function in early infancy and at pre-school age.[24] A population-based nested case-control study reported an increased risk of asthma diagnosis with increased exposure to pollutants *in utero* and during the first year of life, with the strongest effects noted for traffic-related air pollutants.[25]

MATERNAL NUTRITION DURING PREGNANCY

Modification of maternal nutrition has been suggested as a potential strategy in the primary prevention of asthma, with particular interest in maternal intake of vitamins D, E and omega-3 polyunsaturated fatty acids (PUFAs) during pregnancy.[26] A large UK-based birth cohort study reported a beneficial effect of maternal zinc intake during pregnancy on lung function at age 7–9 years but no effect on asthma diagnosis, and found no association between other antioxidants, including vitamin E, and asthma or lung function.[27] Although randomised controlled trials (RCTs) from Denmark and United States suggested that high dose vitamin D_3 supplementation during the second and third trimester of pregnancy might protect against wheeze at age 3 years, but neither trial found an effect on asthma diagnosis at age 6 years.[28,29]

The COPSAC group also conducted an RCT of n-3 long-chain PUFA supplementation during the third trimester of pregnancy. A 31% risk reduction for persistent wheeze at age 3–5 years was seen in children of mothers receiving supplementation, with the greatest effect seen in mothers with the lowest blood levels of long-chain PUFAs at randomisation.[30]

There has been no research to date on maternal micronutrient status and respiratory outcomes in LICs. Considering maternal nutritional intake more broadly, maternal undernutrition and subsequent foetal undernutrition leads to intrauterine growth restriction (IUGR). The effects on lung structure depend on the gestational timing and severity of IUGR; potential mechanisms include impaired alveolarisation, thickening of inter-alveolar septa due to increased extracellular matrix deposition, and thickening of the alveolar blood-air barrier due to increased basement membrane thickness.[31]

LOW BIRTH WEIGHT AND PREMATURITY

Low birth weight (LBW; defined as a birth weight of <2500 g) may be due to IUGR, premature delivery (before 37 weeks' gestation) or both. Premature delivery and IUGR are more common in LICs; in sSA, approximately one in eight infants are born early.[32] Young maternal age and short inter-pregnancy intervals are common risk factors contributing to premature delivery and IUGR. Poor maternal nutrition, intrauterine and systemic infection (e.g., malaria and syphilis), and physical labour during pregnancy may precipitate early labour, while low maternal weight, hypertensive disorders of pregnancy, and congenital infections (e.g., cytomegalovirus [CMV], HIV, syphilis and malaria) are associated with IUGR.[33,34] Meta-analysis of studies from HICs found a strong association between birth weight and adult forced vital capacity (FVC); with 60 ml higher FVC in adulthood per kg increase in birth weight (95% confidence interval [CI] 43–76), but weaker evidence for airflow obstruction.[35]

A recent meta-analysis of 11 studies conducted in HICs found that infants born <32 weeks' gestation or with a birth weight of <1500 g had decreased

airflow in late adolescence and early adulthood, with a mean difference in forced expiratory volume in 1 sec (FEV_1) *Z*-score of –0.78 (95% CI –0.96 to –0.61) compared to infants born at term or with normal birthweight.[36] The infants included in these studies were born before the early 1990s, when surfactant therapy was not available, as is currently the case in many countries in sSA. However, there is increasing availability and use of non-invasive continuous positive airways pressure (CPAP) in LMIC hospitals.[37] With advances in neonatal care and improved outcomes, increasing numbers of survivors may reach adulthood with sub-maximal lung volumes and airflow deficits.

EFFECT OF BREASTFEEDING ON LUNG HEALTH

Human breast milk contains many immunological components, including antimicrobial, anti-inflammatory and immunomodulatory agents.[38] It is widely accepted that breastfeeding reduces morbidity and mortality related to LRTIs.[38] A meta-analysis of 18 studies estimated that breastfeeding reduces the risk of LRTI by 32%, LRTI-related hospital admissions by 57% and LRTI-related deaths by 70%.[39]

However, the effect of breastfeeding on the development of wheeze and asthma is less clear. Results are conflicting, there is heterogeneity of methodology and definitions used, and the ethical problem of conducting RCTs with breastfeeding mothers limits the quality of evidence available. Human milk composition varies within and between mothers, which may also explain conflicting data, particularly relating to breastfeeding and the development of allergic sensitisation and allergic disease.[38] Furthermore, the research largely represents populations from HICs: a systematic review of 117 studies included only one study from Africa and none from LICs.[40] The findings of this systematic review suggested that breastfeeding protects against the development of childhood asthma, with the strongest association seen in children aged 0–2 years.[40] Another meta-analysis reported decreased asthma at age 5–18 years in breastfed children, with a greater effect seen in LMICs; however, the quality of the studies included was suboptimal.[41] The International Study of Asthma and Allergies in Childhood (ISAAC) reported decreased non-atopic wheeze in children who had been breastfed, with a stronger effect in those from LMICs: adjusted odds ratio (aOR) 0.69 vs. 0.87 for LMICs and HICs, respectively.[42] It seems likely that the major effect of breastfeeding is on viral-induced wheezing, rather than atopic wheeze. In addition, the reduction in early life respiratory infections associated with breastfeeding may reduce the subsequent development of asthma.[41]

MALNUTRITION DURING CHILDHOOD

The recent ChroSAM study from Malawi found that survivors of severe acute malnutrition (SAM) during early childhood had comparable lung function to control groups (siblings and community controls) at 7-years post-treatment; however 46% of the SAM cases had died before follow-up: these children are likely to have had more severe disease and possibly poorer lung function had they survived.[43] Stunting of somatic growth, with preserved torso height and shorter legs, is seen in survivors of malnutrition and might suggest that lung function could also be preserved.

A cross-sectional study of school-aged children from Angola, Democratic Republic of Congo and Madagascar found reduced FEV_1 and FVC *Z*-scores, but normal FEV_1/FVC ratios, comparing undernourished (body mass index *Z*-score <–2) to normally grown children, suggesting decreased lung growth without evidence of airway obstruction.[44]

EXPOSURE TO INHALED POLLUTANTS DURING CHILDHOOD: TOBACCO SMOKE, HOUSEHOLD AND AMBIENT AIR POLLUTION

Over 90% of the world's population breathe air that fails to meet WHO Air Quality Guidelines, with those from least developed countries worst affected.[45] Inhaled pollutants come from various sources: exposure levels depend on many factors, including social habits, domestic fuel use, urbanisation, traffic and transport, power plants and industry, policy and legislation.

There is strong evidence from across the globe that children exposed to tobacco smoke from either parent have an increased risk of asthma.[46] This risk is greatest for children exposed to maternal smoking in the first year of life, highlighting the importance of exposures during early childhood.

Large cohort studies from high-income settings following children in later childhood have explored the impact of both regional air quality and local traffic exposure on lung development. Diminished lung function, most notably FEV_1, was found in children exposed to higher levels of air pollution (particularly nitrogen dioxide [NO_2], particulate matter <2.5 μm [$PM_{2.5}$], acid vapour and elemental carbon), and conversely, long-term improvements in air quality have been associated with positive effects on lung function growth in older children.[47]

Although it is well established that outdoor air pollution contributes to exacerbations of pre-existing asthma, the association with new-onset asthma is less clear.[48] There is accumulating evidence that ambient air pollution, particularly traffic-related, is associated with incident asthma in children.[25,49] However, a meta-analysis of cross-sectional studies comparing

communities with different air pollution levels found no effect of long-term exposure to pollution on asthma diagnoses at community level.[50]

Research has tended to focus on individual pollutants, reflecting air quality regulation methodology. However, the health effects of the pollutant mixture may be more relevant.[48] Traffic-related air pollution (TRAP) is a complex pollution mixture containing particulate matter (PM) and primary gaseous emissions, including nitrogen oxides; these emissions generate secondary pollutants such as ozone, nitrates and organic aerosols. Health risks are greatest for those living nearest to roadways, particularly roads carrying heavy vehicles.[51]

Exposure to household air pollution (HAP) is a major concern in LMICs, where the use of inefficiently burned, highly polluting biomass fuel is common. Incomplete combustion using traditional "open-fire" cooking methods produces high levels of pollutants such as CO and PM.[52]

Exposure to solid fuel use assessed using questionnaires and interviews is associated with increased pneumonia risk in children aged <5 years.[53] However, the few studies that assessed exposure through objective measurements of CO and $PM_{2.5}$ have not confirmed this association, raising the possibility that this association is at least partly explained by confounding by other poverty-related exposures.[54]

The effect of HAP on wheezing and asthma is unclear. ISAAC reported an association between the use of open fires for cooking and increased wheeze (OR 2.17, 95% CI 1.64–2.87).[55] However, a previously published meta-analysis of four small asthma studies in children exposed to biomass fuels was inconclusive, reporting a pooled OR of 0.5 (95% CI 0.12–1.98).[53] Young children are susceptible to high concentrations of particle deposition in lung tissue due to physiological and anatomical factors.[56] Environmental exposures, including inhaled pollutants, during critical periods of lung growth and development may lead to irreversible long-term deficits in adult lung function.[57]

RESPIRATORY INFECTIONS IN EARLY LIFE

The importance of childhood respiratory infections on mortality in childhood and adult lung function is well recognised.[2,58] Acute respiratory infections are the leading cause of death in children aged <5 years worldwide, and may lead to long-term sequelae in survivors, particularly in populations with significant comorbidity, such as HIV and malnutrition.[2,59] A meta-analysis evaluating long-term pneumonia outcomes in children under 5 years reported the risk of serious sequelae (e.g., restrictive or obstructive lung disease, bronchiectasis) at respectively 13.6% and 5.5% in hospitalised and non-hospitalised children, with the highest risk in children from Africa.[60]

Wheezing illnesses in infancy due to respiratory syncytial virus (RSV) and rhinovirus (RV) are associated with increased risk of childhood asthma in later childhood.[61] Adenovirus infection is associated with the highest rates of long-term sequelae, including development of bronchiolitis obliterans in LMICs.[60,62] Globally, RSV is the most common cause of childhood respiratory infection, with the highest incidence seen in LICs.[63]

Children from a high-risk birth cohort (with parental allergy or asthma) showed an increased risk of asthma at age 6 years, following wheezing RSV and RV infections in the first 3 years of life (OR 2.6, 9.8 and 10.0 with respectively RSV, RV, and RSV/RV co-infection); this increased asthma risk persisted at age 13 years following early life RV infection (OR 3.3) but not RSV infection.[64]

The Tucson Children's Respiratory Study Group reported an increased prevalence of wheeze until age 11, following relatively mild RSV LRTI during the first 3 years of life, although by age 13 years this risk was no longer significant.[65] In contrast, children with severe RSV LRTI in the first year of life demonstrated increased rates of allergic asthma and decreased lung function compared to controls at age 18 years.[66]

The question remains as to whether respiratory virus infections in early life are a causal factor in the development of asthma, or whether the association represents a vulnerability to viral infections in children with pre-existing airway abnormalities.[67] The DCHS identified LRTI as an independent risk factor for reduced lung function at age 1 year, independent of baseline lung function.[20] There are biologically plausible mechanisms for a causal relationship: inflammatory mediators induced by viral infection in early life may alter adaptive and innate immune responses, leading to remodelling of the developing alveoli and airways.[68]

HIV-infected children are at increased risk of infection from common childhood respiratory pathogens (viral and bacterial), and opportunistic pathogens such as *Pneumocystis jirovecii*, CMV and *Mycobacterium tuberculosis*.[59] Adolescents from sSA with perinatally acquired HIV infection have high rates of chronic respiratory symptoms, abnormal spirometry and chest radiographic abnormalities, with increased burden among those with delayed diagnosis.[69] HIV-exposed, non-infected children show altered lung function in early life, with greatest risk for children of mothers with more severe disease.[70]

Both immunocompetent and HIV-infected children are at risk of TB infection in high-burden countries.[3] Late diagnosis or inadequate treatment, may lead to long-term lung complications, including scarring and bronchiectasis.[59]

EXPOSURE TO INHALED POLLUTANTS IN ADULTHOOD: TOBACCO SMOKE, HOUSEHOLD AIR POLLUTION AND OCCUPATIONAL EXPOSURES

The detrimental effect of active tobacco smoking has been long established, with longitudinal studies documenting accelerated decline in FEV_1 among smokers compared to non-smokers.[71] Active smoking during adolescence impairs lung growth, indicating that lung function in young adults starts to decline from a lower peak FEV_1.[72]

Accelerated FEV_1 decline is one route by which patients may reach a lung function threshold in keeping with COPD; as discussed previously, impaired lung function in earlier life may lead to a lower peak FEV_1 in adulthood and COPD may occur with "normal" rates of age-related FEV_1 decline.[73] Recent data from six US population-based cohorts reported FEV_1 decline at the median age (57 years) of 31.0 ml/year in never smokers, 35.0 ml/year in former smokers and 39.9 ml/year in current smokers, suggesting that the ongoing process of progressive lung damage continues even after smoking cessation.[74] Of particular relevance to sSA, active smokers are at increased risk of TB infection, with potential long-term respiratory sequelae.[75] Compared to high-income settings, the incidence of lung cancer is relatively low in sSA, although data are unreliable due to challenges in diagnosis and reporting; tobacco smoking is an important risk factor and explains the higher burden of lung cancer reported in men throughout the region.[76]

The effects of HAP on adult lung health are likely to be most pronounced among women due to greater involvement in domestic activities, including daily cooking.[77] Studies have demonstrated increased respiratory symptoms (cough and sputum production), chronic bronchitis and obstructive airways disease among women who cook with biomass fuels.[53] The WHO identifies HAP arising from solid fuel use for cooking, as a major risk factor for COPD worldwide.[77] However, the studies informing this conclusion have largely included self-reported biomass fuel use, rather than objective measurement of pollution and heterogeneous outcome variables, rarely including post-bronchodilator spirometry to diagnose COPD. Recent meta-analyses report conflicting results—a meta-analysis of 25 BOLD (Burden of Obstructive Lung Disease) study sites found no association between airflow obstruction and self-reported use of solid fuels for cooking or heating in LMICs and HICs, while a pooled analysis from 13 LMIC sites reported increased COPD in those with self-reported HAP exposure (aOR 1.41, 95% CI 1.18–1.68].[78,79] The challenges in relying on self-reported exposure data, which is subject to recall bias and misclassification, and inadequate adjustment for confounding factors are potential explanations for the conflicting results; furthermore, all included data were from cross-sectional surveys and therefore suboptimal for assessing a causal relationship. Intervention studies aiming to reduce HAP exposure and improve respiratory outcomes for adults have also yielded inconclusive results.[80] Recent studies from rural Malawi suggest that natural age-related lung function decline is not accelerated by exposure to biomass smoke, and that lung function deficits in adults are similar to those seen in children from the same communities, highlighting the importance of early life influences on lung growth and development.[7,8]

Occupational lung disease is a considerable problem among miners (of gold, platinum and diamonds) in mineral-rich sSA countries.[81] Inhalation of silica dust by South African gold miners causes inflammation and irreversible nodular fibrosis of the lungs known as silicosis, with lung function decline proportional to the degree of pulmonary changes.[82] As strong risk factors for pulmonary TB, silica dust exposure and silicosis have additional negative impacts on lung health.[81]

HUMAN IMMUNODEFICIENCY VIRUS AND TUBERCULOSIS IN ADULTHOOD

Despite advances in screening and access to treatment, sSA continues to face the greatest global burden of both HIV and TB infection.[3,4] In sSA in 2017, an estimated 723 000 people were diagnosed with new HIV infection and 712 000 people died from HIV.[4] Many HIV-infected people living in LMIC experience serious or fatal lung complications; impaired host defences increase the frequency and severity of bacterial, mycobacterial, fungal, viral and parasite infections. Furthermore, non-infectious lung disorders—lung cancer, pulmonary arterial hypertension and COPD—are more common in HIV-infected individuals.[83] Among those living with HIV/AIDS, TB is the major cause of mortality worldwide.[83] However, although HIV and TB are common co-infections in sSA, the majority of new TB cases and deaths worldwide occurred in HIV-negative individuals in 2016.[3]

TB is associated with considerable morbidity, with increasing recognition of the long-term consequences of infection. Up to half of TB survivors have persistent respiratory dysfunction despite microbiological cure, with a wide range of structural abnormalities and consequent symptoms.[84] Cavitation, bronchiectasis and fibrosis are the main features seen on chest X-ray, and nodules, consolidation and emphysema on computed tomography imaging.[85] Resulting lung function impairment may include both obstructive and restrictive patterns, with increasing evidence that TB plays a role in the development of COPD.[84]

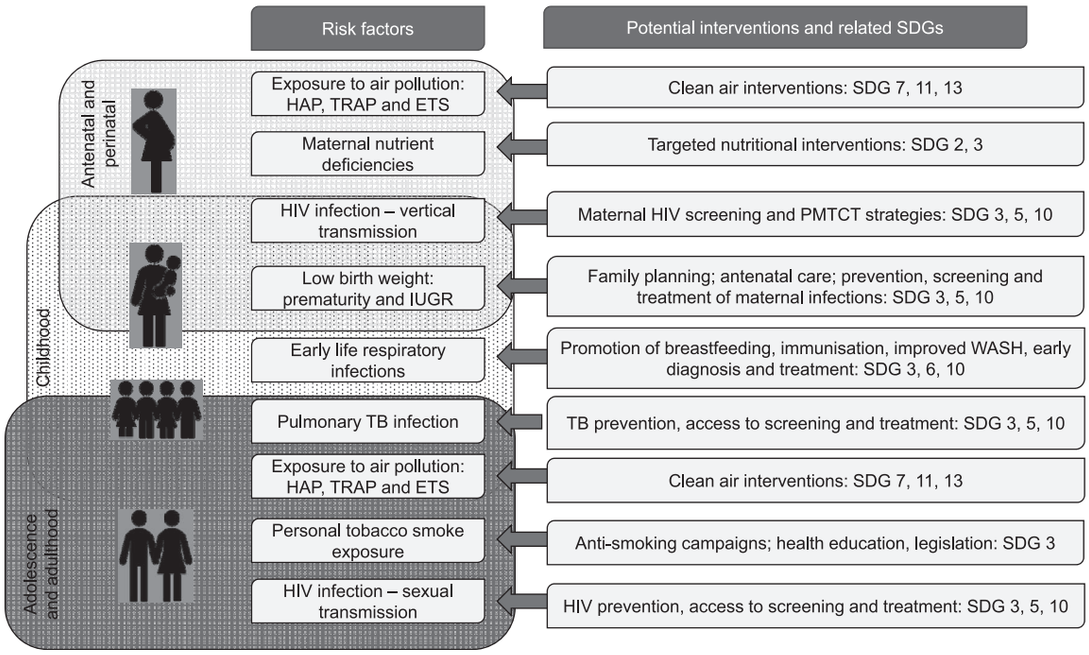

Figure 2 Risk factors for poor lung health in sub-Saharan Africa and potential interventions. SDG = Sustainable Development Goal; HAP = household air pollution; TRAP = traffic-related air pollution; ETS = environmental tobacco smoke; HIV = human immunodeficiency virus; PMTCT = prevention of mother-to-child transmission; IUGR = intrauterine growth restriction; WASH = water, sanitation and hygiene; TB = tuberculosis.

EMERGING THREATS

Research from HICs suggests that obesity increases an individual's risk of developing asthma and may lead to more severe disease and resistance to asthma treatment.[86] Although previously considered a problem in HICs, childhood obesity is now a growing concern across the globe, including LMICs.[87] Childhood obesity rates are generally low in sSA; however, southern Africa had the largest proportional rise in obesity among 5–19-year olds between 1975 and 2016 globally.[87] In southern Africa, 13.7% children under 5 years are overweight, compared to <5% in eastern, middle and west Africa.[88] This increasing public health problem is likely to have a major impact on the prevalence of non-communicable diseases, including chronic respiratory conditions, across sSA. Further research is needed to explore obesity prevention interventions in LMICs to impact on dietary behaviours and physical activity levels.[88]

Another emerging global public health concern is the use of electronic cigarettes (e-cigarettes), particularly among young people. Lack of long-term safety data means that the effect of chronic exposure to e-cigarette emissions, containing nicotine, volatile carbonyls, reactive oxygen species, furans and metals on respiratory health is unknown.[89] However, increased respiratory symptoms are recognised among adolescent e-cigarette users and proteomic studies suggest that chronic vaping exerts biological effects on the pulmonary epithelia, which may have long-term consequences.[90,91]As discussed earlier, *in utero* exposure to nicotine may adversely affect lung development, and maternal e-cigarette use in pregnancy is therefore worrying. At present e-cigarette use is low in sSA; data from the 2016 South African Demographic Health Survey reported the prevalence of e-cigarette use as respectively 2% and 3% in women and men, compared to cigarette smoking rates of 7% and 36%.

The global impact of the COVID-19 pandemic has highlighted the fragility of overstretched health care systems, particularly in LMICs where even basic medical supplies and equipment are lacking. The long-term respiratory effects of novel pathogens, such as coronavirus SARS-CoV-2, are unknown. Longitudinal study of cohorts of infected individuals from diverse populations across the world, with differing co-existing risk factors, would be helpful here.[92]

LOOKING AHEAD

In health care systems which are already under-resourced and overburdened, policy makers must focus their efforts on public health strategies which are likely to have the maximum impact. Approaches optimising lung development *in utero* and early childhood have potential to show the greatest cumulative effect; improved antenatal care will promote foetal and neonatal lung health by reducing rates of prematurity, IUGR and vertical HIV transmission, and stronger postnatal support networks

should promote exclusive breastfeeding, immunisation and improved hygiene practices to prevent early life respiratory infections (Figure 2).[30,38,39] Careful consideration of the mother-infant dyad is essential; factors affecting all aspects of maternal health—physical, mental and social—may impact the health of their child.

Beyond early childhood, prevention, screening and early diagnosis, and appropriate treatment of respiratory infections, HIV and TB are critical and need strengthening in poorly resourced settings.[59] Clean air interventions have the potential to benefit lung health across the life course and should be multisectoral, considering diverse pollution sources, and most importantly, supported by policy and legislation.[52,77]

By investing in integrative approaches which act across reproductive, maternal and child health and emphasise health education, promotion and disease prevention, we have the opportunity to improve lung health in the world's poorest populations and enable progress towards the achievement of Universal Health Coverage and many of the United Nations Sustainable Development Goals.

?1 *Conflicts of interest:* none declared.

References

1 Stocks J, Hislop A, Sonnappa S. Early lung development: lifelong effect on respiratory health and disease. Lancet Respir Med 2013; 1(9): 728–742.
2 Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of under-5 mortality in 2000-15: an updated systematic analysis with implications for the Sustainable Development Goals. Lancet 2016; 388(10063): 3027–3035.
3 GBD Tuberculosis Collaborators. The global burden of tuberculosis: results from the Global Burden of Disease Study 2015. Lancet Infect Dis 2018; 18(3): 261–284.
4 GBD HIV Collaborators. Global, regional, and national incidence, prevalence, and mortality of HIV, 1980-2017, and forecasts to 2030, for 195 countries and territories: a systematic analysis for the Global Burden of Diseases, Injuries, and Risk Factors Study 2017. Lancet HIV 2019; 6(12): e831–e859.
5 Adeloye D, Chan K Y, Rudan I, Campbell H. An estimate of asthma prevalence in Africa: a systematic analysis. Croat Med J 2013; 54(6): 519–531.
6 Rylance S, Mortimer K. Galloping hooves in Africa: horse, zebra, or wildebeest? Ann Am Thorac Soc 2017; 14(5): 624–625.
7 Rylance S, Jewell C, Naunje A, et al. Non-communicable respiratory disease and air pollution exposure in Malawi: a prospective cohort study. Thorax 2020; 75(3): 220–226.
8 Rylance S, Nightingale R, Naunje A, et al. Lung health and exposure to air pollution in Malawian children (CAPS): a cross-sectional study. Thorax 2019; 74(11): 1070–1077.
9 Herring M J, Putney L F, Wyatt G, Finkbeiner W E, Hyde D M. Growth of alveoli during postnatal development in humans based on stereological estimation. Am J Physiol Lung Cell Mol Physiol 2014; 307(4): L338–344.
10 Narayanan M, Owers-Bradley J, Beardsmore CS, et al. Alveolarization continues during childhood and adolescence: new evidence from helium-3 magnetic resonance. Am J Respir Crit Care Med 2012; 185(2): 186–191.
11 Stocks J, Sonnappa S. Early life influences on the development of chronic obstructive pulmonary disease. Ther Adv Respir Dis 2013; 7(3): 161–173.
12 Butler J P, Loring S H, Patz S, Tsuda A, Yablonskiy D A, Mentzer S J. Evidence for adult lung growth in humans. N Engl J Med 2012; 367(3): 244–247.
13 Quanjer P H, Stanojevic S, Cole TJ, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. Eur Respir J 2012; 40(6): 1324–1343.
14 Fehrenbach H, Wagner C, Wegmann M. Airway remodeling in asthma: what really matters. Cell Tissue Res 2017; 367(3): 551–569.
15 Saglani S, Payne D N, Zhu J, et al. Early detection of airway wall remodeling and eosinophilic inflammation in preschool wheezers. Am J Respir Crit Care Med 2007; 176(9): 858–864.
16 Stern D A, Morgan W J, Halonen M, Wright A L, Martinez F D. Wheezing and bronchial hyper-responsiveness in early childhood as predictors of newly diagnosed asthma in early adulthood: a longitudinal birth-cohort study. Lancet 2008; 372(9643): 1058–1064.
17 Sears M R, Greene J M, Willan A R, et al. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. N Engl J Med 2003; 349(15): 1414–1422.
18 Phelan P D, Robertson C F, Olinsky A. The Melbourne Asthma Study: 1964-1999. J Allergy Clin Immunol 2002; 109(2): 189–194.
19 Gray D, Willemse L, Visagie A, et al. Determinants of early-life lung function in African infants. Thorax 2017; 72(5): 445–450.
20 Gray D M, Turkovic L, Willemse L, et al. Lung function in African infants in the Drakenstein Child Health Study. Impact of lower respiratory tract illness. Am J Respir Crit Care Med 2017; 195(2): 212–220.
21 Vanker A, Barnett W, Workman L, et al. Early-life exposure to indoor air pollution or tobacco smoke and lower respiratory tract illness and wheezing in African infants: a longitudinal birth cohort study. Lancet Planet Health 2017; 1(8): e328–e336.
22 McEvoy C T, Spindel E R. Pulmonary effects of maternal smoking on the fetus and child: effects on lung development, respiratory morbidities, and life long lung health. Paediatr Respir Rev 2017; 21: 27–33.
23 Lee A G, Kaali S, Quinn A, et al. Prenatal household air pollution is associated with impaired infant lung function with sex-specific effects: evidence from GRAPHS, a cluster randomized cookstove intervention trial. Am J Respir Crit Care Med 2019; 199: 738–746
24 Korten I, Ramsey K, Latzin P. Air pollution during pregnancy and lung development in the child. Paediatr Respir Rev 2017; 21: 38–46.
25 Clark N A, Demers P A, Karr C J, et al. Effect of early life exposure to air pollution on development of childhood asthma. Environ Health Perspect 2010; 118(2): 284–290.
26 Nurmatov U, Devereux G, Sheikh A. Nutrients and foods for the primary prevention of asthma and allergy: systematic review and meta-analysis. J Allergy Clin Immunol 2011; 127(3): 724-33 e1-30.
27 Bedard A, Northstone K, Holloway J W, Henderson A J, Shaheen SO. Maternal dietary antioxidant intake in pregnancy and childhood respiratory and atopic outcomes: birth cohort study. Eur Respir J 2018; 52(2): 1800507.
28 Litonjua A A, Carey V J, Laranjo N, et al. Six-year follow-up of a trial of antenatal vitamin D for asthma reduction. N Engl J Med 2020; 382(6): 525–533.
29 Brustad N, Eliasen A U, Stokholm J, Bonnelykke K, Bisgaard H, Chawes B L. High-dose vitamin D supplementation during pregnancy and asthma in offspring at the age of 6 years. JAMA 2019; 321(10): 1003–1005.
30 Bisgaard H, Stokholm J, Chawes B L, et al. Fish oil-derived fatty acids in pregnancy and wheeze and asthma in offspring. N Engl J Med 2016; 375(26): 2530–2539.

31 Harding R, Maritz G. Maternal and fetal origins of lung disease in adulthood. Semin Fetal Neonatal Med 2012; 17(2): 67–72.
32 March of Dimes, Partnership for Maternal, Newborn & Child Health, Save the Children, World Health Organization. Born too soon: the global action report on preterm birth. Geneva, Switzerland: WHO, 2012.
33 Suhag A, Berghella V. Intrauterine growth restriction (IUGR): etiology and diagnosis. Curr Obst Gynecol Rep 2013; 2(2): 102–111.
34 Goldenberg R L, Culhane J F, Iams J D, Romero R. Epidemiology and causes of preterm birth. Lancet 2008; 371(9606): 75–84.
35 Saad N J, Patel J, Burney P, Minelli C. Birth weight and lung function in adulthood: a systematic review and meta-analysis. Ann Am Thorac Soc 2017; 14(6): 994–1004.
36 Doyle L W, Andersson S, Bush A, et al. Expiratory airflow in late adolescence and early adulthood in individuals born very preterm or with very low birthweight compared with controls born at term or with normal birthweight: a meta-analysis of individual participant data. Lancet Respir Med 2019; 7(8): 677–686.
37 Martin S, Duke T, Davis P. Efficacy and safety of bubble CPAP in neonatal care in low and middle income countries: a systematic review. Arch Dis Child Fetal Neonatal Ed 2014; 99(6): F495–504.
38 Victora C G, Bahl R, Barros A J, et al. Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect. Lancet 2016; 387(10017): 475–490.
39 Horta B L, Victora C G. Short-term effects of breastfeeding: a systematic review of the benefits of breastfeeding on diarrhoea and pneumonia mortality. Geneva, Switzerland: World Health Organization, 2013.
40 Dogaru C M, Nyffenegger D, Pescatore A M, Spycher B D, Kuehni C E. Breastfeeding and childhood asthma: systematic review and meta-analysis. Am J Epidemiol 2014; 179(10): 1153–1167.
41 Lodge C J, Tan D J, Lau M X, et al. Breastfeeding and asthma and allergies: a systematic review and meta-analysis. Acta Paediatr 2015; 104(467): 38–53.
42 Nagel G, Buchele G, Weinmayr G, et al. Effect of breastfeeding on asthma, lung function and bronchial hyperreactivity in ISAAC Phase II. Eur Respir J 2009; 33(5): 993–1002.
43 Lelijveld N, Kerac M, Seal A, et al. Long-term effects of severe acute malnutrition on lung function in Malawian children: a cohort study. Eur Respir J 2017; 49(4): 1601301.
44 Arigliani M, Canciani M C, Mottini G, et al. Evaluation of the Global Lung Initiative 2012 reference values for spirometry in African children. Am J Respir Crit Care Med 2017; 195(2): 229–236.
45 Health Effects Institute. State of global air 2019. Special Report. Boston, MA, USA: Health Effects Institute, 2019.
46 Mitchell E A, Beasley R, Keil U, Montefort S, Odhiambo J, and the ISAAC Phase Three Study Group. The association between tobacco and the risk of asthma, rhinoconjunctivitis and eczema in children and adolescents: analyses from Phase Three of the ISAAC programme. Thorax 2012; 67(11): 941–949.
47 Gauderman W J, Urman R, Avol E, et al. Association of improved air quality with lung development in children. N Engl J Med 2015; 372(10): 905–913.
48 Guarnieri M, Balmes J R. Outdoor air pollution and asthma. Lancet 2014; 383(9928): 1581–1592.
49 Garcia E, Berhane K T, Islam T, et al. Association of changes in air quality with incident asthma in children in California, 1993–2014. JAMA 2019; 321(19): 1906–1915.
50 Anderson H R, Favarato G, Atkinson R W. Long-term exposure to outdoor air pollution and the prevalence of asthma: a meta-analysis of cohort studies. Air Qual Atmos Health 2013; 6(1): 57–68.
51 Brunekreef B, Stewart A W, Anderson H R, et al. Self-reported truck traffic on the street of residence and symptoms of asthma and allergic disease: a global relationship in ISAAC phase 3. Environ Health Perspect 2009; 117(11): 1791–1798.
52 Gordon S B, Bruce N G, Grigg J, et al. Respiratory risks from household air pollution in low and middle income countries. Lancet Respir Med 2014; 2(10): 823–860.
53 Po J Y, FitzGerald J M, Carlsten C. Respiratory disease associated with solid biomass fuel exposure in rural women and children: systematic review and meta-analysis. Thorax 2011; 66(3): 232–239.
54 Adaji E E, Ekezie W, Clifford M, Phalkey R. Understanding the effect of indoor air pollution on pneumonia in children under 5 in low- and middle-income countries: a systematic review of evidence. Environ Sci Pollut Res Int 2019; 26(4): 3208–3225.
55 Wong G W, Brunekreef B, Ellwood P, et al. Cooking fuels and prevalence of asthma: a global analysis of phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). Lancet Respir Med 2013; 1(5): 386–394.
56 Sturm R. Theoretical models of carcinogenic particle deposition and clearance in children's lungs. J Thorac Dis 2012; 4(4): 368–376.
57 Gauderman W J, Vora H, McConnell R, et al. Effect of exposure to traffic on lung development from 10 to 18 years of age: a cohort study. Lancet 2007; 369(9561): 571–577.
58 Barker D J, Godfrey K M, Fall C, Osmond C, Winter P D, Shaheen S O. Relation of birth weight and childhood respiratory infection to adult lung function and death from chronic obstructive airways disease. BMJ 1991; 303(6804): 671–675.
59 Rabie H, Goussard P. Tuberculosis and pneumonia in HIV-infected children: an overview. Pneumonia (Nathan) 2016; 8: 19.
60 Edmond K, Scott S, Korczak V, et al. Long term sequelae from childhood pneumonia; systematic review and meta-analysis. PLoS One 2012; 7(2): e31239.
61 Beasley R, Semprini A, Mitchell E A. Risk factors for asthma: is prevention possible? Lancet 2015; 386(9998): 1075–1085.
62 Zampoli M, Mukuddem-Sablay Z. Adenovirus-associated pneumonia in South African children: presentation, clinical course and outcome. S Afr Med J 2017; 107(2): 123–126.
63 Nair H, Nokes D J, Gessner B D, et al. Global burden of acute lower respiratory infections due to respiratory syncytial virus in young children: a systematic review and meta-analysis. Lancet 2010; 375(9725): 1545–1555.
64 Rubner F J, Jackson D J, Evans M D, et al. Early life rhinovirus wheezing, allergic sensitization, and asthma risk at adolescence. J Allergy Clin Immunol 2017; 139(2): 501–507.
65 Stein R T, Sherrill D, Morgan W J, et al. Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years. Lancet 1999; 354(9178): 541–545.
66 Sigurs N, Aljassim F, Kjellman B, et al. Asthma and allergy patterns over 18 years after severe RSV bronchiolitis in the first year of life. Thorax 2010; 65(12): 1045–1052.
67 Kieninger E, Fuchs O, Latzin P, Frey U, Regamey N. Rhinovirus infections in infancy and early childhood. Eur Respir J 2013; 41(2): 443–452.
68 Gern J E, Rosenthal L A, Sorkness R L, Lemanske R F, Jr. Effects of viral respiratory infections on lung development and childhood asthma. J Allergy Clin Immunol 2005; 115(4): 668–674; quiz 75.
69 Attia E F, Miller R F, Ferrand R A. Bronchiectasis and other chronic lung diseases in adolescents living with HIV. Curr Opin Infect Dis 2017; 30(1): 21–30.
70 Gray D M, Wedderburn C J, MacGinty R P, et al. Impact of HIV and antiretroviral drug exposure on lung growth and function over 2 years in an African Birth Cohort. AIDS 2020; 34(4): 549–558. >

71 Kerstjens H A, Rijcken B, Schouten J P, Postma D S. Decline of FEV1 by age and smoking status: facts, figures, and fallacies. Thorax 1997; 52(9): 820–827.
72 Postma D S, Bush A, van den Berge M. Risk factors and early origins of chronic obstructive pulmonary disease. Lancet 2015; 385(9971): 899-909.
73 Lange P, Celli B, Agusti A, et al. Lung-Function trajectories leading to chronic obstructive pulmonary disease. N Engl J Med 2015; 373(2): 111–122.
74 Oelsner E C, Balte P P, Bhatt S P, et al. Lung function decline in former smokers and low-intensity current smokers: a secondary data analysis of the NHLBI Pooled Cohorts Study. Lancet Respir Med 2020; 8(1): 34–44.
75 Lin H H, Ezzati M, Murray M. Tobacco smoke, indoor air pollution and tuberculosis: a systematic review and meta-analysis. PLoS Med 2007; 4(1): e20.
76 Urman A, Joysula S, Rosenburg A, Lounsbury D, Rohan T, Hosgood H D. Burden of lung cancer and associated risk factors in Africa by region. J Pulm Respir Med 2016; 6(3): 340.
77 World Health Organization. Burning opportunity: clean household energy for health, sustainable development, and wellbeing of women and children. Geneva, Switzerland: WHO, 2016.
78 Amaral A F S, Patel J, Kato B S, et al. Airflow obstruction and use of solid fuels for cooking or heating: BOLD results. Am J Respir Crit Care Med 2018; 197(5): 595–610.
79 Siddharthan T, Grigsby M R, Goodman D, et al. Association between household air pollution exposure and chronic obstructive pulmonary disease outcomes in 13 low- and middle-income country settings. Am J Respir Crit Care Med 2018; 197(5): 611–620.
80 Quansah R, Semple S, Ochieng C A, et al. Effectiveness of interventions to reduce household air pollution and/or improve health in homes using solid fuel in low-and-middle income countries: a systematic review and meta-analysis. Environ Int 2017; 103: 73–90.
81 Nelson G. Occupational respiratory diseases in the South African mining industry. Glob Health Action 2013; 6: 19520.
82 Ehrlich R I, Myers J E, te Water Naude J M, Thompson M L, Churchyard G J. Lung function loss in relation to silica dust exposure in South African gold miners. Occup Environ Med 2011; 68(2): 96–101.
83 Crothers K, Thompson B W, Burkhardt K, et al. HIV-associated lung infections and complications in the era of combination antiretroviral therapy. Proc Am Thorac Soc 2011; 8(3): 275–281.
84 Ravimohan S, Kornfeld H, Weissman D, Bisson G P. Tuberculosis and lung damage: from epidemiology to pathophysiology. Eur Respir Rev 2018; 27(147): 170077.
85 Meghji J, Simpson H, Squire SB, Mortimer K. A Systematic review of the prevalence and pattern of imaging defined post-TB lung disease. PLoS One 2016; 11(8): e0161176.
86 Peters U, Dixon A E, Forno E. Obesity and asthma. J Allergy Clin Immunol 2018; 141(4): 1169–1179.
87 NCD Risk Factor Collaboration. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. Lancet 2017; 390(10113): 2627–2642.
88 Klingberg S, Draper C E, Micklesfield L K, Benjamin-Neelon S E, van Sluijs E M F. Childhood obesity prevention in Africa: a systematic review of intervention effectiveness and implementation. Int J Environ Res Public Health 2019; 16(7): 1212.
89 Gotts J E, Jordt S E, McConnell R, Tarran R. What are the respiratory effects of e-cigarettes? BMJ 2019; 366: l5275.
90 McConnell R, Barrington-Trimis J L, Wang K, et al. Electronic cigarette use and respiratory symptoms in adolescents. Am J Respir Crit Care Med 2017; 195(8): 1043–1049.
91 Ghosh A, Coakley R C, Mascenik T, et al. Chronic E-Cigarette Exposure Alters the Human Bronchial Epithelial Proteome. Am J Respir Crit Care Med 2018; 198(1): 67–76.
92 World Health Organization. Coronavirus disease (COVID-19) pandemic. Geneva, Switzerland: WHO, 2019. https://www.who.int/emergencies/diseases/novel-coronavirus-2019

RÉSUMÉ

La santé pulmonaire est influencée tout au long de la vie par des facteurs affectant le développement des voies aériennes et des alvéoles et la croissance pendant les périodes anténatales et périnatales, tout au long de l'enfance et de l'adolescence et pendant la vie adulte. Les trajectoires de la fonction pulmonaire sont établies au début de la vie et des déficits dans l'enfance peuvent prédisposer à des maladies respiratoires non transmissibles comme l'asthme et les bronchopneumopathies chroniques obstructives par la suite. Les facteurs de risque potentiels sont fréquents dans de nombreux pays d'Afrique sub-Saharienne ; un environnement anténatal défavorable cause un retard de croissance *in utero* et une prématurité ; le VIH et les infections respiratoires, dont la tuberculose, sont fréquentes ; l'exposition à la pollution de l'air est répandue, notamment celle des foyers en raison de l'utilisation de la biomasse comme combustible, ainsi que la pollution liée à la circulation automobile dans des villes qui s'agrandissent rapidement et enfin l'exposition à la fumée de tabac. De multiples préjudices, vécus au début de la vie, requièrent une approche intégrée comprenant la santé reproductive, maternelle et enfantine. Les stratégies de santé publique doivent s'attaquer à de multiples facteurs de risque, mettant l'accent sur la couverture santé universelle, pour maximiser la santé respiratoire dans les populations les plus pauvres et vulnérables du monde. Cette revue explore les déterminants potentiels de la santé pulmonaire tout au long de la vie. En raison de l'ampleur du sujet et de la vaste littérature existante, nous avons priorisé les citations les plus récentes, surtout celles émanant d'Afrique sub-Saharienne, en nous focalisant sur les facteurs de risque pour lesquels on dispose du maximum d'information et qui sont les plus prévalents dans la région.

RESUMEN

La salud respiratoria a lo largo del ciclo de la vida está determinada por factores que interfieren con el desarrollo y el crecimiento de las vías aéreas y los alvéolos en el período prenatal y perinatal, durante la toda la infancia, la adolescencia y hasta la edad adulta. La trayectoria de la función pulmonar se define temprano en la vida y las deficiencias durante la infancia pueden predisponer a enfermedades respiratorias no transmisibles como el asma o la enfermedad pulmonar obstructiva crónica en los años futuros. Los factores de riesgo son comunes en muchos países de África subsahariana; los entornos prenatales adversos provocan restricción del crecimiento intrauterino y prematuridad; la infección por el virus de la inmunodeficiencia humana (VIH) y las infecciones respiratorias como la tuberculosis son frecuentes; la exposición a la contaminación ambiental es generalizada e incluye la contaminación de interiores por utilización de combustibles de biomasa, la contaminación asociada con el tránsito en las ciudades de crecimiento rápido y la exposición al humo de tabaco. Las desventajas múltiples impuestas en etapas tempranas de la vida exigen un enfoque integrado que aborde la salud reproductiva y maternoinfantil. Es necesario que las estrategias de salud pública afronten los factores de riesgo múltiples, con hincapié en la cobertura universal de salud, a fin de fomentar al máximo la salud respiratoria de las poblaciones más pobres y vulnerables del mundo. En la presente revisión se examinan los posibles determinantes de la salud respiratoria a lo largo del ciclo de la vida. Dada la extensión del tema y la gran diversidad de las publicaciones pertinentes, se dio prioridad a los artículos más recientes, en especial a los provenientes de África subsahariana, con un interés central en los factores de riesgo sobre los cuales existe más información y que predominan en la región.

Queries for jtld-24-09-17

This article has been typeset from the submitted materials. Check proofs carefully for conversion or other inadvertent errors. Please follow the Allen Press Guide to PDF Annotation when marking revisions. Do not edit the PDF directly.

If present, queries will be listed below with corresponding numbers in the margins or may appear as PDF comments addressed to the author or editor. If a correction is desired in response to a query, mark the necessary changes directly in the proof using the appropriate annotation tool. If no change is desired, no action is necessary in response.

1. Author: conflicts statement added per journal style. Please confirm. AP Stylemarker