ORIGINAL RESEARCH

Non-communicable respiratory disease in Malawi: a systematic review and meta-analysis

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Abstract

Background
Non-communicable respiratory diseases are important contributors to morbidity and mortality in sub-Saharan African countries such as Malawi.

Aim
To conduct a systematic review of the available literature relating to chronic respiratory disease in Malawi.

Methods
We conducted a systematic protocol-driven literature search of key scientific databases including Scopus and Medline. Papers were independently assessed for eligibility by two authors and included if they reported objective measures (including self-reported standard symptoms) of chronic respiratory disease and were conducted in Malawi. A meta-analysis of available estimates was then conducted. We re-analysed data from three of these studies in a secondary data analysis to allow for between-study comparisons.

Results
Our search identified 393 papers of which 17 (5 involving children and 12 involving adults) met the inclusion criteria. Wheeze was the symptom most frequently reported in children in the community (12.1%), hospital (11.2%) and HIV clinic (8.1%) settings. Cough was the symptom most frequently reported by adults in the community (3–18%). Spirometric abnormalities varied substantially between studies. For example, in adults, airflow obstruction varied between 2.3% and 20% and low forced vital capacity (FVC) varied between 2.7% and 52.8%.

Conclusion
We identified a high burden of chronic respiratory symptoms and abnormal spirometry (particularly low FVC) within paediatric and adult populations in Malawi. The estimates for country-wide burden related to this disease were limited by the heterogeneity of the methods used to assess symptoms and spirometry. There is an urgent need to develop a better understanding of the determinants and natural history of non-communicable respiratory disease across the life-course in Malawi.

Key Words: COPD, asthma, chronic lung disease, cough, non-communicable disease, Malawi

Introduction

Non-communicable diseases (NCDs) kill 41 million people globally, accounting for 71% of deaths worldwide[1]. More than three quarters (32 million) of these deaths occur in low- and middle-income countries (LMICs), including LMICs in sub-Saharan Africa, such as Malawi. Health policy has historically focussed on communicable rather than non-communicable disease in sub-Saharan African countries[2], although the need to prioritise the prevention and control of NCDs is increasingly recognised, with the Malawi National Health Research Agenda highlighting the fact that chronic lung disorders are a priority research area for the country[3-5]. Non-communicable respiratory diseases are major contributors to NCD mortality with 3.6 million attributable deaths globally in 2015[6]. Of these diseases, asthma and chronic obstructive pulmonary disease (COPD) are the most common[7-10]. The International Study of Asthma and Allergies in Childhood (ISAAC) estimated the prevalence of asthma using standardised questionnaires in 105 countries[11]. In the seven countries from sub-Saharan Africa, the prevalence of asthma varied between 9.1% in Ethiopia and 20.3% in South Africa[11]. The prevalence of COPD has been estimated from cross-sectional spirometry-based studies, including the International Burden of Obstructive Lung Disease (BOLD) initiative[12]. The highest prevalence was seen in Cape Town, South Africa where moderate to severe obstruction was present in 19.1% of the adult population whilst prevalence in Ile-Ife (Nigeria), urban Blantyre (Malawi) and rural Chikwawa (Malawi) were 7.7%, 3.6% and 8.7%, respectively[13-16]. Recently, two further studies have reported lower levels of obstruction in Uganda: 6.1% and 2% in rural populations, and 1.5% in an urban population[17,18].

We conducted a systematic review and pooled analysis of the burden of NCDs and the risk factors associated with NCDs in Malawi. This review adopted a broad approach and focused on any population, any intervention, any comparison technique, any outcome, and any study design.

Methods

Systematic review

This systematic review is registered with the Centre for Reviews and Dissemination (Registration number: CRD42018117325). The full protocol is available at http://

https://doi.org/10.4314/mmj.v32i2.3

www.crd.york.ac.uk/prospero.

Eligibility criteria

Publications were included if they described the burden of non-communicable respiratory diseases (including COPD, asthma, low forced vital capacity (FVC)/restrictive disease and bronchiectasis) in Malawian individuals of any population (any sex or age), involving any intervention and outcomes linked to non-communicable respiratory disease. We included any form of study design, including studies that defined non-communicable respiratory diseases using symptoms, self-reported diagnosis, doctor diagnosis, and spirometry.

Search strategy

The databases and grey literature listed in Box 1 were searched using the specific search terms and Boolean phrases listed in Box 2 and the search strategy set out in Box 3. Identified papers were then imported into EndNote X7. The reference lists of all selected papers were also reviewed to identify any potentially eligible titles. For studies where relevant details were not available, authors were invited to supply information if their contact details were available.

Box 1: Databases and Grey Literature

Databases:

- Scopus (including EMBASE)
- MEDLINE (OVID)
- Web of Science
- Cochrane Central Register of Controlled Trials (CENTRAL)
- CINAHL (OVID)
- SciELO

Grey literature:

- World Health Organization Clinical Trials Registry
- www.clinicaltrials.gov
- European Association for Grey Literature Exploitation (EAGLE)

Box 2: Search terms and Boolean phrases used

Outcomes (OR): "chronic respiratory" OR "non-communicable lung" OR "chronic obstructive pulmonary disease" OR "COPD" OR "asthma" OR "obstructive lung" OR "restrictive lung" OR "obstructive respiratory" OR "restrictive respiratory" OR "obstructive airway*" OR "restrictive airway*" OR "spirometr*" OR "wheeze" OR "chronic cough" OR "shortness of breath" OR "breathlessness" OR "chronic sputum"

AND

Location: "Malawi"

Article screening

Following the removal of duplicates, the titles of all identified papers were independently reviewed for eligibility by two authors (HJ & RN). Abstracts of the selected titles, and then the full text of the selected articles, were independently reviewed for eligibility by two authors (HJ & RN), according to the selection criteria. Discordant decisions were resolved by discussion, with final arbitration by a third author.

Box 3: Example search strategy for Medline (OVID)

1. "chronic respiratory" .mp,tw.
2. "non-communicable lung" .mp,tw.
3. "chronic obstructive pulmonary disease" .mp,tw.
4. COPD.mp,tw.
5. asthma.mp,tw.
6. "obstructive lung" .mp,tw.
7. "restrictive lung" .mp,tw.
8. "obstructive respiratory" .mp,tw.
9. "restrictive respiratory" .mp,tw.
10. "obstructive airway*".mp,tw.
11. "restrictive airway*".mp,tw.
12. spirometr*.mp,tw.
13. wheeze.mp,tw.
14. "chronic cough" .mp,tw.
15. "shortness of breath.mp,tw.
16. "breathlessness" .mp,tw.
17. "chronic sputum" .mp,tw.
18. 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16 OR 17
19. Malawi.mp,tw.
20. 18 AND 19

mp is combined search field , tw is title and abstract field

Data extraction

Data were extracted by HJ and RN from the selected papers using a data extraction form (which had been pre-tested). These forms were used to create summary tables and narrative syntheses. Data extraction was independently checked by ML. We also collated information regarding exposure to household air pollution, smoking and previous TB, where available.

Methodological quality assessment

The methodological quality of the selected studies was assessed by HJ using the Newcastle-Ottawa Scale for cohort and case-control studies (scored out of 9) and a modified version of the Newcastle-Ottawa Scale for cross-sectional studies (scored out of 5) (Table 1).

Statistical analysis

Published estimates of the prevalence of symptoms, obstruction or low FVC, and mean (standard deviation [SD]) and median (interquartile range ([IQR]) carbon monoxide (CO), and fine particulate matter ($PM_{2.5}$) were extracted for meta-analysis. We then created Forest plots using the estimated proportion and 95% confidence intervals. Meta-analysis estimates of overall prevalence were stratified by age group (adult, paediatric) and estimated using the DerSimonian-Laird random effects model (R package metaviz)[19]. Estimates derived from meta-analysis were only calculated for outcomes in which the studies were deemed to be adequately homogenous. Estimates of measures of heterogeneity (I^2, tau^2) and an overall Q-test were generated using linear mixed effects models (R package metaphor) and reported. Publication bias was evaluated by visual inspection of funnel plots.

Data from three of the studies included in the meta-analysis that had been performed using the same core BOLD protocol were re-analysed in order to provide comparable estimates: the Adult Lung Health Study (ALHS), the

https://doi.org/10.4314/mmj.v32i2.3

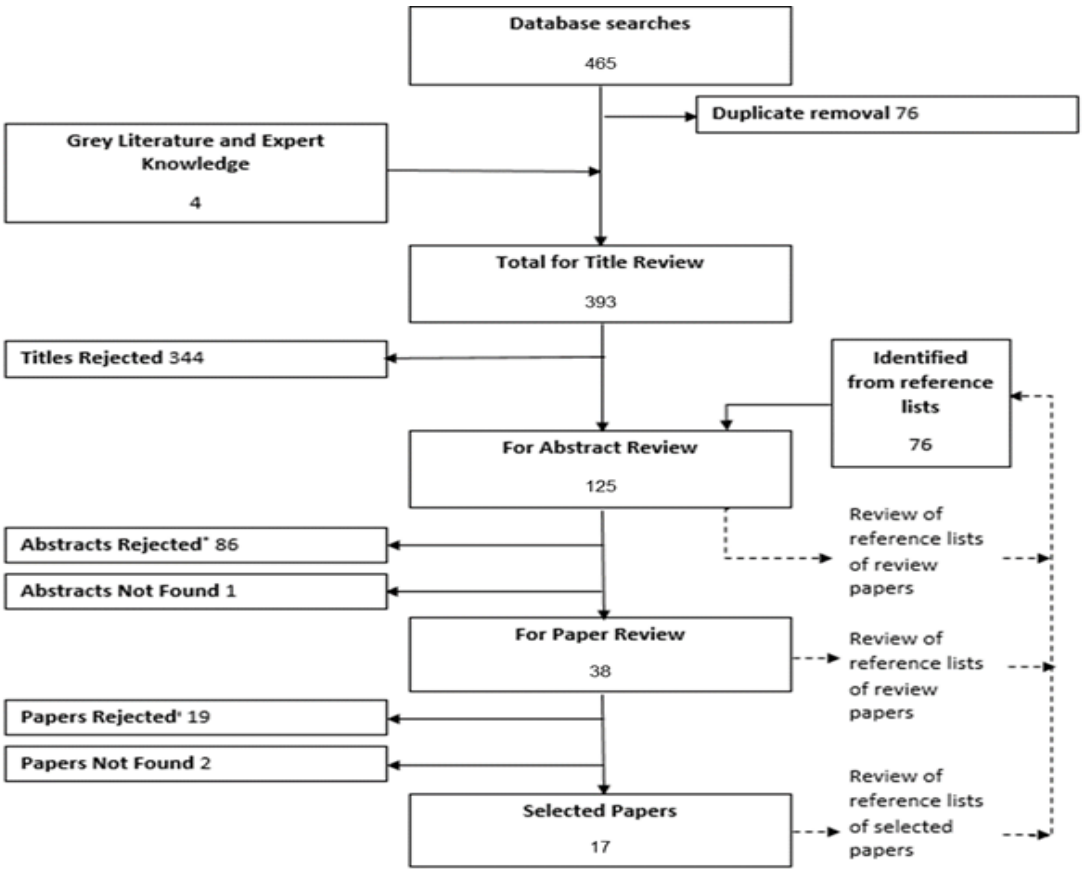

Figure 1: PRISMA Flow Chart depicting the inclusion and inclusion of studies. *Reasons for abstract rejection: no primary data (45), no Malawian data (26), no assessment of non-communicable lung disease (12), duplicate data (2), data not yet available (1). †Reasons for paper rejection: no Malawian data (9), duplicate data (6), no assessment on non-communicable lung disease (2), data not yet available (1), no primary data (1).

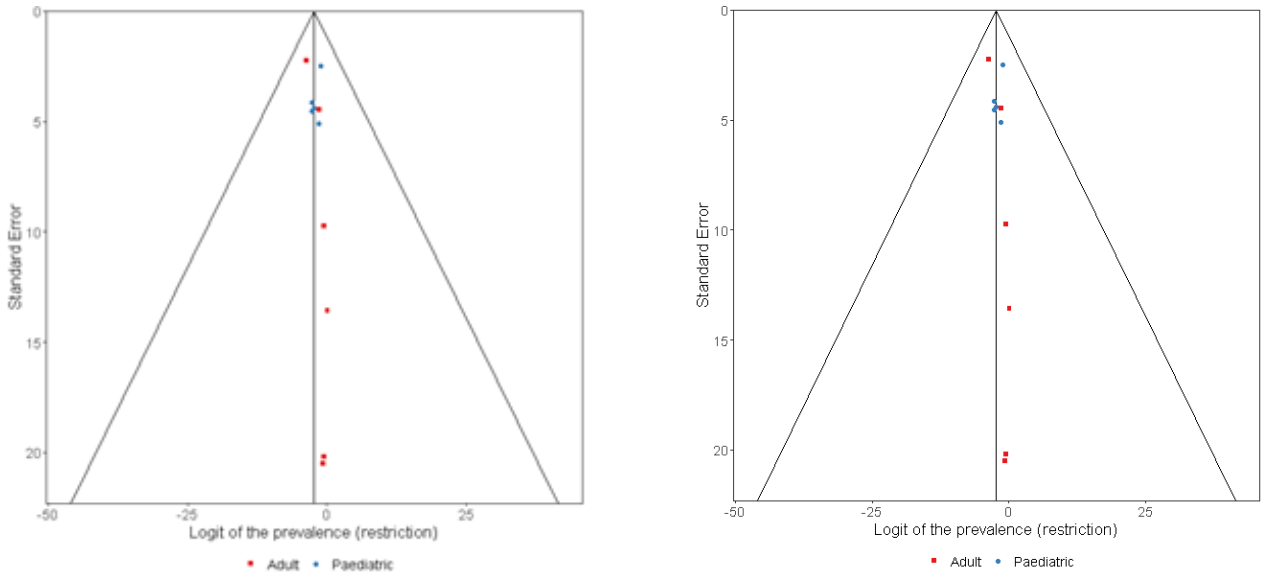

Figure 2. Funnel plots for lung function estimates in paediatric (blue) and adult (red) populations. Panel A (left): restriction, Panel B (right) obstruction.

Blantyre Health Study (BHS), and the Acute Infection of the Respiratory tract Study (AIR Study)[15,16,20]. This allowed for the pooled analysis of data which had not previously been performed (referred to subsequently as the "pooled analysis" to distinguish this from the "meta-analysis"). Details of the sampling and measurement procedures for these three studies have been described previously; consequently, we restricted our description of these methods to the secondary analysis presented here[12,13,15,16,20,21]. The prevalence (with SD) of symptoms, exposures, obstruction, and low FVC, were estimated using a combination of the three data sources, and is referred to as "pooled data" hereafter. We also calculated median (IQR) estimates for CO and $PM_{2.5}$ exposure.

https://doi.org/10.4314/mmj.v32i2.3

Table 1. The risk of bias, as determined by the Newcastle-Ottawa Scale

Case-control and cohort studies				
	Selection (out of 4)	Comparability (out of 2)	NCLD assessment (out of 3)	Overall score (out of 9)
Jary et al., 2017	3	2	2	7
Lelijveld et al., 2017	3	2	2	7
Descriptive cross-sectional studies				
	Selection (out of 3)	NCLD assessment (out of 2)		Overall score (out of 5)
Zverev et al., 2001	1	2		3
Fullerton et al., 2011	2	2		4
To et al., 2012	2	1		3
Cook et al., 2013	1	2		3
Jary et al., 2014	1	0		1
Manjomo et al., 2016	2	0		2
Meghji et al., 2016	2	2		4
Mwalukomo et al., 2016	1	2		3
Wang et al., 2016	0	0		0
Banda et al., 2017	2	1		3
Das et al., 2017	1	1		2
Townend et al., 2017	1	2		3
Cohen et al., 2019	1	1		2
Nightingale et al., 2019	2	2		4
Rylance et al., 2019	2	2		**4**
NCLD: non-communicable lung disease.				

Ethics

Liverpool School of Tropical Medicine provided ethical approval for all three studies which we included for secondary data analysis (Reference numbers: 12.08, 12.40 and 14.016). The ALHS and AIR were approved by the College of Medicine Research and Ethics Committee, Malawi (References: p.11/12/1308 and P.02/14/1518, respectively), and the BHS was approved by the National Research and Ethics Committee of Malawi (Reference: 12.08). All participants provided informed consent.

Results

Study selection

Database and grey literature searches on 9 October 2018 and updated on 3 June 2019 identified 393 titles for review; 17 papers met the inclusion criteria (Figure 1)[15,16,20,22-35]. Funnel plots were limited by the small number of studies but were relatively symmetrical (P=0.017 for obstruction and P=0.032 for restriction, as determined by the Eager test) (Figure 2).

Quality assessment

Analyses showed that the included studies were of variable quality. Studies that had been specifically designed to assess the burden of non-communicable respiratory disease were found to be of the highest quality (Table 1).

Study characteristics

The studies incorporated cohort (n=1)[25], case-control (n=1)[20], and cross-sectional (n=15) study designs (or included a cross-sectional description of non-communicable respiratory disease burden nested within a Randomised Control Trial or economic evaluation) (Table 2). Five studies reported paediatric populations[22-26], while 12 reported adult populations[15,16,20,27-35]; one of the studies included a population from 10 to 65 years of age (Table 2)[31]. Nine studies were from urban settings only (four healthcare or clinic-based, three community-based, and the case-control and cohort studies were performed in both community and health care settings)[16,20,22-25,30,35], five were from rural settings only (all community-based)[15,26,29,31,32,34], and three studies incorporated both rural and urban settings (all community-based)[27,28,33].

Symptoms

Thirteen studies assessed self-reported respiratory symptoms or diagnoses using questionnaires; of these, five used BOLD questionnaires[15,16,20,23,24,26-29,31-34] (Table 3).

In the paediatric population, the most commonly reported symptom in the community was wheeze, with a prevalence of 12.1%, followed by cough (prevalence 8%)[24]. In the two studies related to the prevalence of symptoms in hospital clinics, cough was more common (41.7% and 37.5%) than wheeze (11.2% and 8.1%)[23,24]. Our meta-analysis estimated that the prevalence of cough symptoms in children was 29.1±10.6 (P=0.0059, I^2=98%, Q-test P<0.0001) (Figure 3). Within the adult populations in the community, cough was the most commonly reported symptom (range: 3–18.6%), followed by shortness of breath (range: 1.6–13%). Productive cough and phlegm production were less commonly reported (range: 0.2–9% and 1.4–5.9% respectively). Our meta-analysis and pooled analysis estimates for prevalence of cough symptoms in adults were 13.3±10.6%, P<0.0001,

https://doi.org/10.4314/mmj.v32i2.3

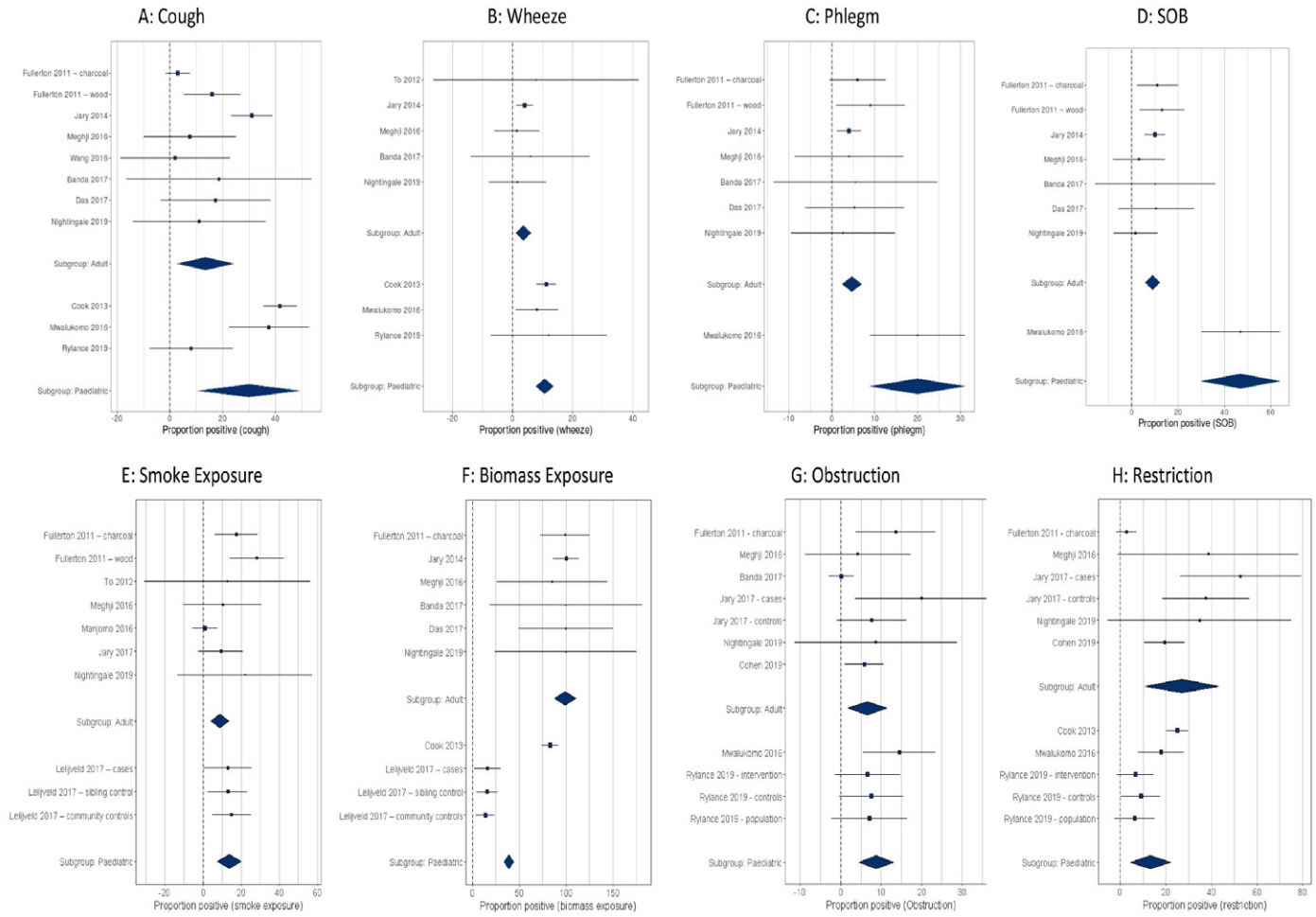

Figure 3. Forest plots and meta-analysis estimates for symptoms (A–D), exposure (E, F) and respiratory outcomes (G, H). SOB: shortness of breath.

I^2=93%, Q-test *P*<0.0001) and 10.7%, respectively (Figure 3).

Lung function

Eight of the nine studies (four paediatric and four adult) that performed spirometry reported data that were collected in accordance with standards reported by the American Thoracic Society (ATS)/European Respiratory Society (ERS). However, five different ranges were used and a mix of raw values, proportional (%) predicted values and Z-scores were used in analysis[20,23-27,33-35] (Table 4).

One study, a community-based cross-sectional study, focused on peak expiratory flow rate (PEFR) in stunted children, reported that PEFR was reduced in those with poor growth[20]. In paediatric community populations, 6.6–9.0% of the population had obstruction while 6.6–7.5% had low FVC. In those with sickle cell disease and HIV infection, obstructive spirometry was identified in 0 and 18% of cases while low FVC was detected in 25% and 17% of cases, when using local reference ranges (58% and 20% if using international reference ranges), respectively[23,24]. The cohort study that assessed lung function in malnourished children reported a reduced FEV_1 (forced expiratory volume in the first second) and FVC in all study groups, but with no significant difference between paediatric survivors of severe acute malnutrition and healthy controls[25]. The diagnosis of asthma in children, based on spirometry and questionnaires, was reported in 3.9% of the community or 12.1% if wheeze was used as the definition; asthma was also reported in 4.2% of children with sickle cell anaemia[23,26]. None of the studies used the same definition for asthma in the same way.

The range of obstruction reported in adults where spirometry had been completed was 2.3–20% with low FVC varying from 2.7% to 52.8%[20,27]. The use of different ranges within the same population resulted in a prevalence of obstruction of 2.3–4.2%, and low FVC of 9–38.6%, using local and NHANES (National Health and Nutrition Examination Survey) Caucasian ranges, respectively[15,16]. The prevalence of asthma in adults ranged from 0% to 12.2% with a mixture of diagnostic types: doctor diagnosis (7.6–12.2%), self-reported (4.7–8%) and diagnoses involving spirometry (0–4.2%)[16,18,25,26,28,30-32]. In our meta-analysis, the prevalence of obstruction in adults was 8.3±2.4%, *P*=0.0007, I^2 = 89%, Q-test *P*<0.0001), and low FVC 31±7.2%, *P*<0.0001, I^2=97%, Q-test *P*<0.0001 (Figure 2). Pooled analysis estimated overall FEV_1 of 2.64 L (0.69), FVC of 3.28 L (0.77) and FEV1/FVC of 80.5% (8.48). The pooled prevalence of obstruction was 8.4% and low FVC was 37.5% (NHANES) or 16.3% (using the local range).

Risk factors

The most commonly reported risk factors for non-communicable respiratory disease were the use of biomass fuel and smoking. Exposure to biomass fuel was assessed in a variety of different ways in different studies. In paediatric studies, 14–83% of the study populations were exposed to biomass fuels[23,25] (Table 3). In adult studies, self-reported exposure to biomass fuel was reported in

https://doi.org/10.4314/mmj.v32i2.3

Table 2. Summary of the main findings from literature searches (date order)

Author (year)	Year	Rural/Urban	Mean Age (years)	Setting and study design	Sample size	Assessment methods
Paediatric						
Zverev	2001	Urban		Children in primary school, children from each class were randomly selected	539	Peak expiratory flow only. No symptoms questionnaires. No spirometry
Cook	2013	Urban clinic	11.5	Consecutive recruitment from paediatric Sickle Cell Anaemia Clinic	25	Self-reported respiratory symptoms (ISAAC questionnaire) and spirometry.
Mwalukomo	2016	Urban clinic	11.1	First 3 eligible patients at paediatric HIV clinic per day were recruited	160	Self-reported respiratory symptoms and clinical observation and spirometry
Lelijveld	2017	Urban hospital		Cases: consecutive patients admitted with severe acute malnutrition in 2006–2007. Sibling controls: closest in age to case. Community controls: random direction selected from case home then door-to-door recruitment (age- & sex-matched).	320 cases (of 477 alive 1 year after original discharge); 217 sibling controls; 184 community controls	Spirometry
Rylance	2019	Rural	7.1	Population sampling with control and intervention arm	804 including 476 (260 intervention and 216 control) from CAPS households	Self-reported respiratory symptoms (BOLD questionnaire) and spirometry
Adult						
Fullerton	2011	Rural/urban	39	Cross-sectional survey. Rural: first household semi-randomly selected, then snowballing sampling strategy. Urban: randomly selected from 360 research volunteers, then snowballing sampling strategy. Biased selection toward women	374	Self-reported respiratory symptoms and diagnoses and spirometry.
To	2012	Rural/urban		Multi-stage cluster design: random	3890	Self-reported respiratory symptoms and diagnoses and self-reported doctor diagnosed.
Jary	2014	Rural	35	Community based survey of women wishing to purchase a cookstove – not randomly selected.	51	Self-reported respiratory symptoms.
Meghji[a]	2016	Urban	42	Random sample from enumerated population – age- and sex-stratified population-representative sample.	1059 (of 1240 eligible)	Self-reported respiratory symptoms (BOLD questionnaire) and spirometry.
Manjomo	2016	Urban		All patients registered with NCDs attending a chronic care clinic at a primary health care centre.	1135	Diagnosis of asthma at clinic
Wang	2016	Rural		Cross sectional survey, from three districts. Sampling method unclear. Paediatric adult overlap with participant 10–65 years old.	5643 individuals from 1199 households	Self-reported chronic respiratory symptoms reported as a group
Banda	2017	Rural	36	Population proportional sampling using electronic satellite maps: 30 villages randomly selected from each cluster (27 health centre catchment population), 7 households randomly selected from each village.	15795 individuals from 6304 households with 1728 who had health passports checked for symptoms	Self-reported respiratory symptoms / health passport assessment of symptoms.
Das	2017	Rural/peri-urban	37.3	Random sample of households from representative villages.	655 households (382 rural, 273 peri-urban).	Self-reported respiratory symptoms.

[a]From the same study population.

51–100% of the study populations[29,34]. The self-reported prevalence of smoking ("ever smoked") ranged from 1% to 28.2% in the adult population[27,30]. Previous TB and low BMI were considered as possible risk factors in the BOLD studies. Meta-analysis and pooled analysis of associations between risk factors and lung function was not possible due to the incomplete nature of reporting across different studies[15,16,20,34].

Table 3. Extracted proportions (%) of cases showing symptoms and specific exposures (where reported). Empty cells indicate not reported.

Author (year)	Symptoms (%)				Exposures (%)		
	Cough	Wheeze	Phlegm	SOB	Previous TB	Ever Smoked	Biomass
Paediatric							
Zverev at al., 2001							
Cook 2013	41.7	11.2					83
Mwalukomo 2016	37.5	8.1	20	46.9			
Lelijveld 2017					5	13[d]	16[d]
					0.6	13[d]	16[d]
					0.8	15[d]	14[d]
Rylance 2019	8	12.1			0.4		
Adult							
Fullerton 2011	3		6	11		17.5	99
	16		9	13		28.2	
To 2012		7.8				12.7[b]	
Jary 2014	31	4	4	10			100
Meghji 2016[d]	7.5	1.4	4.0	3.1	2.9	10.4	85.2
Manjomo 2016						1	
Wang et al., 2016	2.0[c]						
Banda 2017	18.6	5.9	5.5	10.1			100
Das 2017	17.3		5.3	10.5			100
Jary 2017						9.3	
Townend 2017					5	17	51[a]
Cohen 2019							
Nightingale 2019	11.1	1.6	2.6	1.6	3.2	22.1	99.8
Secondary analysis from Malawi (pooled data 2019)	10.7	2.2	4.0	3.2	4.1	17.7	92.8

[a]Open fire for >20 years. [b]Africa region estimate. [c]Chronic symptoms combined. [d]Indoor tobacco/biofuel use. SOB: shortness of breath.

Table 4. Summary extracted spirometry (FEV1, FVC) or obstruction/low FVC where available. Blank cells indicate data that were not reported.

Author (year)	Group/subgroup	Asthma (%)	Low FVC (%)	Obstruction (%)	Reference range	FEV1, L Mean (SD)	FVC, L Mean (SD)	FEV1/FVC % Mean (SD)
Paediatric								
Zverev et al 2001	School children							
Cook 2013	Clinic		25	0	Local	1.45 (0.54)	1.68 (0.58)	86 (2.09)
			58	0	Wang	−1.64[a]	−1.49[a]	−0.39[a]
Mwalukomo 2016	Clinic – HIV infected		20	17.9	GLI	−1.31[a]	−0.89[a]	−0.27[a]
			17.2	12.4	Local	92.2[b]	93.9[b]	87.9[b]
Lelijveld 2017	Cases – clinic				GLI	−0.47 (1.1)[a]	−0.32 (1.0)[a]	−0.21 (0.9)[a]
	Controls – siblings				GLI	−0.48 (1.0)[a]	−0.38 (1.1)[a]	−0.15 (0.9)[a]
	Controls – population				GLI	−0.34 (1.1)[a]	−0.15 (1.1)[a]	0.16 (1.0)[a]
Rylance 2019	Intervention	4.2	6.6	6.6	GLI	−0.41 (0.92)[a]	−0.22 (0.77)[a]	−0.4 (0.91)[a]
	Controls	4.6	9.0	7.5	GLI	−0.60 (0.97)	−0.44 (0.98)[a]	−0.34 (0.93)[a]
	Population	3.9	6.3	7.1	GLI	−0.48 (0.93)	−0.30 (0.96)	−.038 (0.90)

https://doi.org/10.4314/mmj.v32i2.3

Table 4 Cont...

Adult								
Fullerton 2011	Charcoal users	7	2.7	13.6	Knudsen & asthma self-reported	2.78 (0.68)	3.49 (0.87)	79.8 (7.5)
To 2012	Population	4.7						
Jary 2014	Women cooking on cookstoves							
Meghji 2016	Population	4.2	38.6	4.2	NHANES			
			9	2.3^	Local			
Manjomo 2016	Clinic	12.2						
Wang et al 2016	Population							
Banda 2017	Population reporting respiratory symptoms	7.6		0.15	Medical Diagnosis only			
Das 2017	Women cooking on biomass							
	Wood users	8				2.43 (0.67)	3.19 (0.83)	76.5 (9.1)
Jary 2017	Cases – clinic	0	52.8	20	NHANES	2.73 (0.69)		
	Controls	0	37.5	7.6	NHANES	2.48 (0.68)		
Townend 2017	Population	5			NHANES			78 (8)
Cohen 2019^	TB re-treatment patients at hospital		19.4	5.83	NHANES			
Nightingale 2019	Population		34.8	8.7	NHANES			
Secondary analysis from Malawi pooled data 2019	Population		16.3 (Local) 37.5 (NHANES)	8.4	NHANES	2.64 (0.69)	3.28 (0.77)	80.5 (8.48)

Discussion

We conducted a systematic review, secondary data analysis, and meta-analysis, of studies relating to non-communicable respiratory disease in Malawi. We identified 17 papers of variable quality with scores on the Newcastle-Ottawa scale ranging from 0 to 7[15,16,20,22-34]. Five of these studies related to children while 12 of the studies involved adult populations. In children we found that the main symptom was wheeze, with low FVC being reported in 6.3–20% of the population; obstruction was reported in 7.1–17.9% of the study population[22-26]. In adults, we identified a high burden of lung disease, with cough being the most reported symptom. In studies that used spirometry as an outcome measure, over 40% of the population showed abnormal spirometry results[15,16,20,27]. Low FVC was the most common abnormal spirometry finding, with a pooled population estimate of 37.5% using NHANES Caucasian reference ranges. We also identified a high prevalence of exposure to biomass fuel (50–100%) and a smoking prevalence of 1–21%[27,29,30,34].

Few studies in the published literature have reported chronic respiratory symptoms and spirometry data from sub-Saharan African populations. However, the findings from our present systematic review and meta-analysis, which focussed on Malawi, are consistent with data arising from other sub-Saharan African countries. Data from the ISAAC study sites indicated that wheeze occurs in 5–16% of children in sub-Saharan Africa, with nearly a half of these children exhibiting severe symptoms[11]. On a global basis, wheeze has been reported to occur in 0.8–32.6% of young children (aged 6–7 years and 2.4–37.6% in older children (age 13–14 years)[11]. In adults, cough was the most common symptom described in studies from sub-Saharan Africa; BOLD studies in Nigeria reported a prevalence of cough that was 9.7%[36]. The prevalence of obstruction was lower in Malawi than that found in both Cape Town (19.1%) and in rural Uganda (16.2%), although tobacco smoking was more common in both these populations than in Malawi[13,37]. Two recent studies from Uganda found that the prevalence of obstruction was 2–6.1% and 2% in a rural setting and 1.5% in an urban setting; these figures are more in line with the data highlighted in the present review[18,17].The high prevalence of low FVC that was evident in Malawi was similar to that seen in Nigeria and other resource-poor settings. However, there is limited a limited body of literature relating to the possible causes of low FVC in adults residing in sub-Saharan Africa[36]. The major strength of this study is that it is the first systematic review and meta-analysis of chronic non-communicable respiratory disease in Malawi and provides a significant enhancement to the growing body of evidence highlighting the high burden of lung disease seen within Malawi and the wider sub-Saharan African region. Our work brings together studies of both paediatric and adult populations from diverse settings in Malawi and includes a secondary analysis of data in order to provide new estimates for the pooled burden of disease. The estimates given within this paper

are, however, limited by inconsistent methodologies. The studies we reported herein were carried out across a range of populations, from the community setting to subgroups within an acute clinic. The paediatric data described herein are particularly limited because only one paediatric study reported lung function in community settings; the other studies related to specific populations, such as children with sickle cell disease. Furthermore, symptoms were not reported in a consistent or standardised manner. Cough, wheeze, exertional dyspnoea, and the production of sputum, were the most common symptoms reported although there was widespread inconsistency in the definitions used for these symptoms. All symptoms were self-reported; in studies without other diagnostic tools, this inevitably reduced the specificity of diagnosis. Diagnosis of COPD and asthma were made using a combination of clinical or self-reported diagnoses and spirometry. This is likely to explain the wide variation seen in categorising the burden of disease in Malawi. All spirometry data were reported in accordance with ATS standards. However, studies used different interpretative strategies with raw FEV1 and FVC being the most common parameters provided for adult populations and Z-scores the most common parameter for the paediatric population. This lack of standardised reporting also created uncertainty with regards to the estimation of disease burden in Malawi and resulted in high heterogeneity with regards to the meta-analysis estimates. As there is no validated reference range for spirometry in sub-Saharan African populations, a variety of reference ranges were used in the studies reported here. The majority of paediatric studies used the Global Lung Function Initiative (GLI) reference ranges while the majority of adult studies used the NHANES Caucasian reference ranges. However, the NHANES Caucasian reference ranges are also known to be associated with limitations, including the potential overestimation of the prevalence of low FVC; however, this reference range does allow for comparison with other studies, including BOLD studies (the largest, multi-national study of spirometry findings thus far). Previous studies have also published results that were interpreted with local (unvalidated) reference ranges.

Conclusion

In conclusion, we identified a high burden of chronic respiratory symptoms and abnormal spirometry data (particularly low FVC) in children and adults in Malawi. Estimates for the country-wide burden of disease were limited by the heterogeneity of the methods used to assess symptoms and spirometry. Little is known about the determinants and natural history of non-communicable respiratory disease across the life course in Malawi. We strongly recommend that non-communicable respiratory disease should be a priority for future research in Malawi and that this would benefit from the use of methodologies standardised across studies. For example, it would be particularly useful to standardise diagnostic definitions and report all spirometry data to ATS/ERS standards. A specific consensus on the spirometry reference ranges used, or the development of locally appropriate specific reference ranges, is also needed. The substantial burden of chronic respiratory symptoms and abnormal spirometry data in Malawian children and adults is highly evident in our findings. Consequently, it is vital that we provide high quality, accessible and affordable care to this population, This has implications for Malawian policy- and decision-makers and our efforts to develop universal health coverage in Malawi. Although our systematic review and meta-analysis deliberately focused on Malawi, our findings are of generalisable relevance to the wider sub-Saharan African region.

Authors' contributions

Design: RN, HJ, JR, KM, ML

Acquisition of data: RN, HJ, ML

Analysis of data: RN, HJ, JM, SR, JR, KM, ML

Interpretation of data: RN, HJ, JM, SR, JM, HC, JR, KM, ML

All of the authors helped to write the manuscript and agreed for the final version to be published. All authors agree to be held accountable for all aspects of the research described herein

Funding

RN was funded by the Medical Research Council Doctoral Training Programme.

Acknowledgements

We thank the NIHR Global Health Research Unit on Lung Health and TB in Africa at LSTM - "IMPALA" for helping to make this work possible. IMPALA (Grant number 16/136/35) was commissioned by the National Institute for Health Research (NIHR) Global Health Research (GHR) using aid from the UK Government. The views expressed in this publication are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care

Conflict of Interests

There are no other conflicts to declare from the authors.

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