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An enhanced care package to improve asthma management in Malawian children: a randomised controlled trial

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ABSTRACT

Background Shortages of clinical staff make chronic asthma care challenging in low-income countries. We evaluated an outpatient asthma care package for children, including task-shifting of asthma management roles.

Methods We conducted a non-blinded individually randomised controlled trial at a tertiary-level government hospital in Blantyre, Malawi. Children aged 6–15 years diagnosed with asthma were recruited from outpatient clinic, stratified by Childhood Asthma Control Test (cACT) score and allocated 1:1 from a concealed file, accessed during electronic questionnaire completion. The intervention, delivered by non-physicians, comprised clinical assessment, optimisation of inhaled treatment, individualised asthma education. The control group received standard care from outpatient physicians. Primary outcome for intention-to-treat analysis was change in cACT score at 3 months. Secondary outcomes included asthma exacerbations requiring emergency healthcare and school absence.

Findings Between September 2018 and December 2019, 120 children (59 intervention; 61 control) were recruited; 65.8% males, with mean (SD) age 9.8 (2.8) years, mean (SD) baseline cACT 20.3 (2.6). At 3 months, intervention children (n=56) had a greater mean (SD) change in cACT score from baseline (2.7 (2.8) vs 0.6 (2.8)) compared with standard care participants (n=59); a difference of 2.1 points (95% CI: 1.1 to 3.1, p<0.001). Fewer intervention children attended emergency healthcare (7.3% vs 25.4%, p=0.02) and missed school (20.0% vs 62.7%, p<0.001) compared with standard care children.

Interpretation The intervention resulted in decreased asthma symptoms and exacerbations. Wider scale-up could present substantial benefits for asthmatic patients in resource-limited settings.

Trial registration number PACTR201807211617031.

Key messages

What is the key question?

► Can an enhanced asthma care package, including optimisation of inhaler treatment and task-shifting of asthma education roles to non-physicians, improve asthma outcomes for children in a resource-limited setting, such as Malawi?

What is the bottom line?

► Children receiving a pragmatic enhanced asthma care package reported significantly fewer symptoms and decreased exacerbations resulting in emergency health care attendance or school absence after 3 months compared with those receiving standard care in a government hospital outpatient clinic in Blantyre, Malawi.

Why read on?

► Asthma is an increasing concern in low-income and middle-income countries, but evidence to guide long-term management in these settings is lacking—it is essential to develop, evaluate and scale-up strategies specifically tailored to resource-limited settings to improve asthma care for the world's poorest populations.

INTRODUCTION

Asthma is the most common chronic condition in childhood and is a growing concern in Africa.[1] Asthma causes an estimated 1000 deaths worldwide every day and is a major cause of morbidity in children, ranking in the top 10 causes of disability-adjusted life years.[1 2] Asthmatic adults in sub-Saharan Africa (sSA) suffer frequent acute exacerbations and have symptoms that are poorly controlled.[3 4] Limited data from asthmatic children living in sSA suggest higher rates of severe symptoms compared with high-income settings, likely due to challenges with diagnosis and quality of asthma care.[5]

The Malawi Standard Treatment Guidelines for asthma management are extrapolated from global guidelines, adopting a stepwise approach centred on inhaled corticosteroid (ICS) therapy.[6 7] These guidelines are appropriate where steroid-responsive, allergen-driven, eosinophilic asthma predominates: it is unknown whether this is true for Malawi. Limited evaluation of asthma guideline implementation in selected low-income and middle-income countries (LMICs) found that physicians often underutilise ICS treatment and that patient adherence to treatment is a challenge.[8] Reasons for poor adherence are likely to be multifactorial, including unreliable supplies of affordable medication and misconceptions regarding effective asthma treatments.[9 10]

Asthma education and the use of an asthma action plan (AAP) are considered important elements of chronic asthma management in high-income countries (HIC) and are recommended in international guidelines.[7] Studies demonstrating a beneficial impact of asthma education in HIC include a wide range of interventions, with variable content, duration and delivery methods.[11] AAPs facilitate the early detection and treatment of an exacerbation and have been shown to improve asthma health outcomes in HIC.[12] However, the provision of asthma education can be time-consuming and human resources constraints in Malawi limit the quality of care available. Task-shifting, defined as 'the transfer of a task normally performed by a more highly trained healthcare worker to another with a different, usually lower level of training,' is a possible solution, but research exploring this approach to asthma management in low-income countries (LIC) is lacking.[13 14]

We implemented a package of enhanced asthma care, appropriate for an LIC, delivered by non-physicians, which included a standardised clinical assessment, optimisation of locally available inhaled asthma treatment and personalised asthma education.

We did a non-blinded, individually randomised controlled trial (RCT) comparing the effects of the enhanced asthma care package with standard outpatient care, on asthma outcomes over a 3-month period.

METHODS

Setting

Queen Elizabeth Central Hospital (QECH) is a government-run, tertiary hospital located in Blantyre, Malawi's second largest city, receiving referrals from the Southern Region. Children attending the general paediatric clinic are referred from primary health centres and from within QECH following emergency department attendance or admission.

Participants

All children aged 6–15 years attending the general paediatric outpatient clinic at QECH with a doctor diagnosis of asthma recorded in their health passport were invited to participate. Children with symptoms suggestive of TB; productive cough, haemoptysis, weight loss, recurrent fevers or night sweats, were excluded.

Consent and randomisation

Study information was provided in the local language (Chichewa). Following written informed consent from the parent or guardian and assent from the child, a baseline electronic questionnaire was completed; children were stratified by their level of asthma control, as assessed by the Childhood Asthma Control Test (cACT), into two groups (cACT ≥20 or cACT ≤19).[15] Within each group, individuals were allocated 1:1 to intervention or standard care arms using pregenerated variable length, permuted block randomisation codes. Allocation information was not accessible to any staff prior to electronic questionnaire completion.

Procedures

The intervention comprised three components delivered by non-physicians; clinical assessment, optimisation of locally available inhaled asthma treatment and asthma education. The components address the common challenges we have observed in Malawi and reallocate tasks usually performed by doctors to nursing staff and lay educators (table 1).

Intervention: clinical assessment

Participants in the intervention arm attended the hospital shortly after recruitment for an assessment visit, which included clinical examination, anthropometry, exhaled nitric oxide (FeNO) measurement, and pre-bronchodilator and post-bronchodilator spirometry. All procedures were performed according to standardised operating procedures, with regular quality control monitoring by the study clinician. Asthma symptoms were assessed using Global Initiative for Asthma (GINA) and International Study of Asthma and Allergies in Childhood (ISAAC) questionnaires.[5 7] Spirometry was conducted by experienced technicians, using an Easy On-PC spirometer (ndd Medical Technologies), according to American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines.[16] Lung function was measured before and after 400 µg salbutamol administered by metered dose inhaler via a volumatic spacer. Lung function parameters; FEV_1, FVC and FEV_1/FVC ratio were interpreted with reference to the African American Global Lung Initiative 2012 equations.[17] FeNO was measured using an NObreath machine (Bedford Scientific), following ATS/ERS guidelines.[18]

Table 1 Components of enhanced care intervention; rationale for inclusion and member of staff performing each task

Factors contributing to suboptimal care	Component of intervention	Rationale	Staff*
	Assessment		
Assessment may be rushed or not systematic: symptoms often under-reported or under-recognised	Administration of cACT	Objective and repeatable measurement of symptoms	L
	Measurement of FeNO	Identify airway inflammation phenotype in this population	L
	Spirometry measurement	Objective measurement of airway obstruction	L
	Spirometry QC/interpretation		N
	Physical examination (auscultate chest, look for clubbing/lymph nodes)	Exclude comorbidity or misdiagnosis (congenital/rheumatic heart disease, TB)	N
	Treatment optimisation		
Clinicians reluctant to prescribe ICS and escalate dose if needed	Treatment increased according to protocol based on cACT and FEV_1/FVC ratio	Encourage appropriate use of ICS	L/N
	Asthma education		
Fears and misconceptions, poor understanding of asthma and inhalers	1-hour individualised asthma education session	Increase knowledge levels, improve inhaler technique and compliance	L
	6-week review: revision of asthma education		L

*Staff responsible for performing each intervention task: L, lay educator (non-clinical); N, nurse.
cACT, Childhood Asthma Control Test; FeNO, exhaled nitric oxide; ICS, inhaled corticosteroid; QC, quality control.;

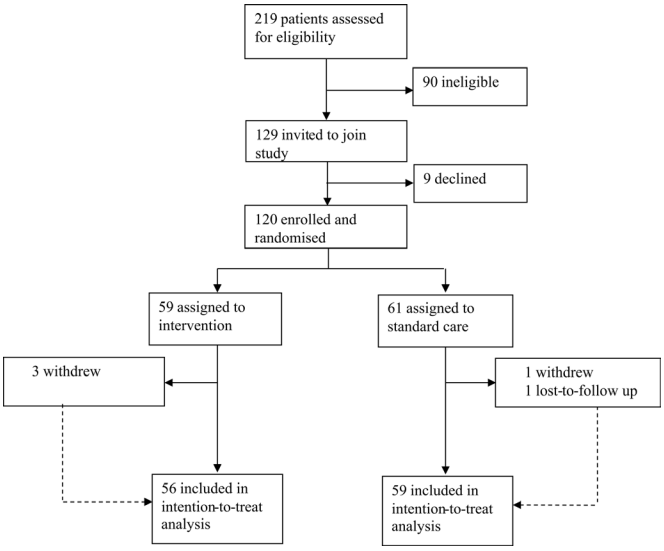

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) flow diagram.

Intervention: optimisation of inhaled asthma treatment

Following clinical assessment, ICS treatment was started or escalated to a maximum daily dose of 400 µg of beclometasone dipropionate, for children with poor control or obstructive spirometry (defined as cACT ≤19 or FEV_1/FVC ratio below the lower limit of normal (LLN), respectively). These participants were reviewed after 6 weeks to assess their response and encourage treatment adherence. Participants with cACT ≥20 and FEV_1/FVC above the LLN continued their previous medication.

Intervention: asthma education delivered lay educators

Non-clinical 'lay educators' delivered a 1-hour asthma education session to the child and carer, including discussion of a personalised AAP, with clinical support available if required. Educators were secondary school graduates, with no previous experience in medical education. Before study initiation, educators completed a structured training programme and were required to pass a formal assessment of their knowledge and skills. Each asthma education session followed a structured approach, with checklist, to ensure consistency within and between educators. Details of the educators' background, training programme and education session checklist are included in the online supplemental text S1 and tables S1 and S2.

Standard care

Participants in standard care continued with their asthma treatment and follow-up schedule prescribed by the QECH clinic staff (paediatric specialist of registrar or consultant level).

All participants received their medication from QECH pharmacy: salbutamol and beclometasone dipropionate inhalers are included in the Malawi Standard Treatment Guidelines, and usually available, free of charge. When inhalers were out of stock, children received their inhalers from a private supply, purchased by the paediatric department.

Outcomes

All participants were invited for review at 3 months to assess primary and secondary outcomes. The primary outcome, asthma symptom control, was measured by the cACT, a 7-item questionnaire, translated into Chichewa according to linguistic validation guidelines, with forward and back translation and local piloting. Secondary outcomes were; asthma exacerbations requiring hospitalisation, emergency healthcare use or treatment with oral corticosteroid; school absence; lung function; FeNO. Serious adverse events were reported within 72 hours to a Data Safety and Monitoring Board, which also met at regular intervals.

Follow-on care

At the end of the 3-month RCT period, participants receiving standard care were offered the intervention package. At the end of the intervention, all participants returned to QECH general clinic for ongoing care, with review after 3 months or sooner if clinically indicated.

Statistical analysis

We planned to enrol 120 participants, aiming for at least 90 children with complete data, after loss-to-follow-up and technical difficulty with clinical procedures. Using two-tailed Student's t-test, 45 children in each arm will detect a 3-point difference in cACT; an effect size of 0.6, given SD 5, with 80% power at a 5% significance level.

Intention-to-treat analysis compared primary and secondary outcomes between the two arms using two-tailed Student's t-test and Wilcoxon signed-rank test for normally distributed and skewed continuous data, respectively, with the primary outcome subanalysed, stratified by baseline cACT . Pearson's χ^2 tests were used to compare proportions. Analyses were conducted using R V.3.4.1 statistical software.

The trial was registered with the Pan African Clinical Trials Registry; the trial protocol is publicly available.[19]

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation or writing of this report. The corresponding author had full access to all the data in the study and final responsibility for the decision to submit for publication.

Table 2 Baseline characteristics of study population (n=120)

	Intervention n=59	Standard care n=61
Age, mean (SD) years	10.1 (2.8)	9.4 (2.9)
Sex: female, n (%)	18 (30.5)	23 (37.7)
Hospital admission ever, n (%)	47 (79.7)	49 (80.3)
Hospital admission in past 3 months, n (%)	14 (23.7)	14 (23.0)
Health facility attendance in past 3 months, n (%)	18 (30.5)	21 (34.4)
School absence in past 3 months, n (%)	40 (67.8)	39 (63.9)
School absence in past 3 months, median days (IQR)	3 (2–5)	3 (2–5)
Reported using salbutamol inhaler	45 (76.3)	51 (83.6)
Reported using steroid inhaler regularly	21 (35.6)	28 (45.9)
Daily dose beclometasone	238 µg (n=21)	273 µg (n=28)
GINA: well controlled (score* 0)	12 (20.3)	7 (11.5)
GINA: partly controlled (score* 1–2)	20 (33.9)	21 (34.4)
GINA: uncontrolled (score* 3–4)	27 (45.8)	33 (54.1)
cACT, mean (SD)	20.4 (2.9)	20.3 (2.3)
cACT ≥20 (well controlled)	37 (62.7)	40 (65.6)
cACT ≤19 (poor control)	22 (37.3)	21 (34.4)

*Score 1 for each positive response to: in the past 4 weeks, has the patient had: (1) daytime asthma symptoms more than twice/week? (2) any night waking due to asthma? (3) reliever needed for symptoms more than twice/week? (4) Any activity limitation due to asthma?
cACT, Childhood Asthma Control Test; GINA, Global Initiative for Asthma.

RESULTS

We recruited 120 children between 12 September 2018 to 11 December 2019; 59 and 61 were randomised to receive the intervention and standard care, respectively. Mean age (SD) of participants was 9.8 (2.8) years with 65.8% males. One hundred and fifteen participants were reviewed at 3 months (figure 1): 114 children attempted spirometry, of these 86.8% (99/114) and 80.7% (92/114) produced acceptable FEV_1 and FEV_1/FVC measurements, respectively. Primary outcome questionnaire data was missing for one participant, and FeNO results for three participants due to technical issues. Mean (SD) duration of follow-up was 96.6 (12.0) days and 91.0 (10.1) days for intervention and standard care participants, respectively.

Eighty per cent of participants reported previous hospital admission with asthma symptoms. In the preceding 3 months, 28/120 (23.3%) were admitted to hospital, 39/120 (32.5%) attended a health facility, but did not require admission, and 79/120 (65.8%) missed school due to asthma symptoms. Median (IQR) school absence was 3 (2–5) days, with 58.2% (46/79) of absentees seeking medical review. Baseline clinical characteristics were similar for both study arms (table 2).

Most children (106/120, 88.3%) reported wheezing in the past year; overall, 68.3% (82/120) experienced ISAAC-defined severe asthma symptoms, with at least one of; ≥4 attacks (64/106, 60.4%), wheeze-related sleep disturbance more than once per week (34/106, 32.1%) or wheeze affecting speech (38/106, 35.8%), in the past year. By GINA criteria, asthma symptoms were well controlled in 19 (15.8%), partly controlled in one-third (41/120) and uncontrolled in half (60/120) of the participants. The baseline mean (SD) cACT score was 20.3 (2.6), with 43 (35.8%) participants stratified as having poor control (cACT ≤19) and 77 (64.2%) with good control (cACT ≥20) (online supplemental table S3).

At enrolment, 96/120 (80.0%) participants reported using a salbutamol inhaler, with 67/96 (69.8%) using a spacer; 41/120 (34.1%) participants reported using a beclometasone inhaler (plus spacer) regularly, with a mean daily dose of 258 µg and self-reported adherence of 89.6%.

None of the participants had been previously treated for TB. Of 105/120 participants who had been tested for HIV, all were HIV-negative. Half of the participants (62/120, 51.7%) reported a family history of asthma, including 47/120 (39.2%) with asthma in a first-degree relative. The majority of participants experienced wheezing in early childhood; 52/120 (43.3%) reported wheeze onset before age 3 years, 41/120 (34.2%) aged 3–6 years and 27/120 (22.5%) after age 6 years. Atopic symptoms were common, with self-reported rhinitis, hay fever and eczema in 72/120 (60.0%), 37/120 (30.8%) and 31/120 (25.8%), respectively.

At 3 months, children in the intervention arm had a mean (SD) cACT of 22.9 (2.3), compared with 20.8 (3.0) in standard care (p<0.001). Children receiving the intervention had a greater mean (SD) change in cACT score from baseline; 2.7 (2.8) compared with 0.6 (2.8) for standard care participants, a difference of 2.1 points (95% CI: 1.1 to 3.1, p<0.001) (table 3). On stratified analysis, overall those with baseline ACT ≤19 showed greater change in mean (SD) cACT than those with baseline ACT ≥20 (2.9 (3.3) vs 0.9 (2.5), p<0.001): this was true for both intervention and standard care groups (table 3). Participants receiving the intervention reported improvement in symptoms

Table 3 Asthma outcomes at 3 months for 114 participants

	Intervention n=55	Standard care n=59	Comparison
Primary outcome: cACT score			
cACT score, mean (SD)	22.9 (2.3)	20.8 (3.0)	p<0.001
Change in cACT score from baseline, mean (SD)	2.7 (2.8)	0.6 (2.8)	p<0.001
Stratified: baseline cACT ≤19	4.7 (2.6) n=21	1.1 (3.0) n=21	p<0.001
Stratified: baseline cACT ≥20	1.5 (2.2) n=34	0.3 (2.7) n=38	p=0.046
Secondary outcomes			
Healthcare use			
Exacerbations with hospitalisation, n (%)	2 (3.6)	6 (10.2)	p=0.32
Exacerbations with health facility attendance but not admission, n (%)	3 (5.5)	11 (18.6)	p=0.06
Exacerbations with any emergency healthcare use, n (%)	4 (7.3)	15 (25.4)	p=0.019
School absence			
School absence, n (%)	11 (20.0)	37 (62.7)	p<0.001
Pre-bronchodilator lung function			
Mean (SD) % predicted FEV_1*	86.9 (18.0)	92.0 (17.5)	p=0.15
Mean (SD) % predicted FEV_1/FVC ratio†	90.9 (12.5)	92.8 (10.3)	p=0.42
FEV_1/FVC ratio below LLN, n (%)†	15/47 (31.9)	13/45 (28.9)	p=0.93
Fractional concentration of exhaled nitric oxide (FeNO)			
Median (IQR) FeNO, ppb ‡	41.8 (23.4–68.0)	39.8 (22.9–57.9)	p=0.64
High (>35 ppb), n (%)	33 (58.9)	31 (55.4)	p=0.85
Intermediate (20–35 ppb), n (%)	11 (19.6)	15 (26.8)	p=0.50
Low (<20 ppb), n (%)	12 (21.4)	10 (17.9)	p=0.81

*Technically acceptable FEV_1 data available for 99 participants.
†Technically acceptable FEV_1/FVC data available for 92 participants.
‡FeNO data available for 112 participants.
cACT, Childhood Asthma Control Test; LLN, lower limit of normal.

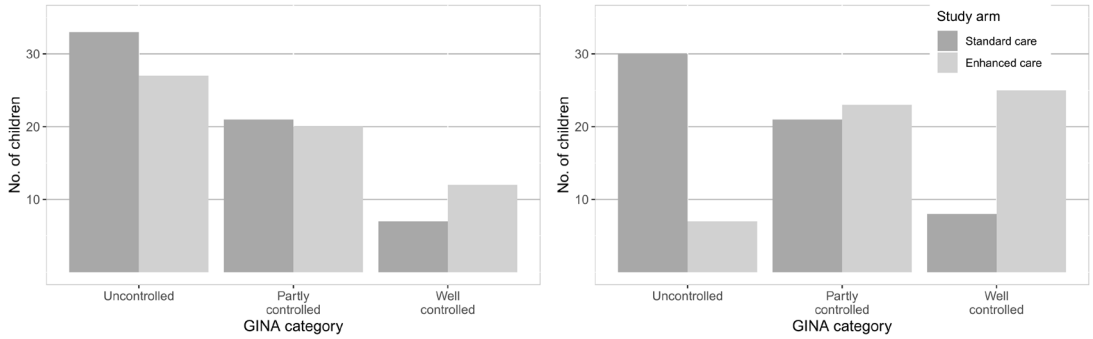

Figure 2 Comparison of Global Initiative for Asthma (GINA) categories at baseline (n=120) (left) and at 3-month follow-up (n=114) (right). Standard care is shown in dark grey and intervention in light grey.

and GINA score, with little change for those receiving standard care (figure 2).

Hospital admission and health facility attendance fell in both arms compared with baseline. Compared with standard care, the intervention arm reported lower rates of admission (3.6% vs 10.2%, p=0.32), overall emergency health facility attendance (7.3% vs 25.4%, p=0.02) and school absence (20.0% vs 62.7%, p<0.001) (table 3). Oral prednisolone was given during 8/30 (26.7%) exacerbations requiring emergency healthcare use.

FeNO levels and spirometry results were similar for both study arms at 3 months (table 3). There were no significant differences in age, sex, study arm and baseline cACT between those with and without spirometry results (online supplemental table S4).

At 3 months, 98.1% (54/55) children in the intervention group were using a salbutamol inhaler with a spacer compared with 83.1% (49/59) receiving standard care (p=0.02). Daily ICS use was more common in the intervention group (47/55, 85.5% participants) compared with standard care (41/59, 69.5% participants) (p=0.07), with intervention participants prescribed a higher mean (SD) daily beclometasone dose: 331 (121) µg vs 266 (99) µg (p=0.007). Self-reported adherence was 85.4% and 85.5% among intervention and standard care participants, respectively. Four carers (three from intervention, one from standard care) reported non-availability of inhalers at QECH during the trial period.

Overall mean percentage predicted (SD) FEV_1 was 89.4 (17.8) and mean percentage predicted FEV_1/FVC ratio 91.9 (11.5), with one-third (28/92, 30.4%) of participants having an FEV_1/FVC ratio below the LLN (figure 3). Ten participants had an FEV_1/FVC ratio below 0.7; of these, seven reported 'good control' with a cACT ≥20.

FeNO levels were generally high with a median (IQR) value of 41.5 (23.0–66.3) ppb and over half of the participants (64/112, 57.1%) recording an FeNO level greater than 35 ppb (figure 4).

No adverse events were reported except for asthma-related hospital admissions, which were not attributed to study procedures.

After RCT completion, 58 children in standard care received the intervention; 48 were reviewed again after 3 months (the remaining reviews were cancelled due to COVID-19). FeNO levels and lung function were similar, before and after the intervention (table 4).

DISCUSSION

To our knowledge, this is the first RCT of a task-shifting intervention using nurses and lay educators to deliver asthma management in sSA. The key finding was a clinically and statistically significant improvement in asthma control in the intervention versus standard care group, with a difference in mean cACT change from baseline of 2.1 points (95% CI: 1.1 to 3.1) between groups. Greatest benefit was seen in those with poorer asthma control at baseline.

We found a high burden of symptoms among asthmatic children attending an outpatient clinic at baseline; in the preceding 3 months, one-quarter of participants had been admitted to hospital, a further one-third had attended a health facility, without overnight admission, and two-thirds had missed school due to acute asthma symptoms. The overall mean (SD) cACT was 20.3 (2.6), with 85% of participants reporting suboptimal asthma control, by GINA criteria. Despite a high burden of symptoms and previous engagement with the healthcare system,

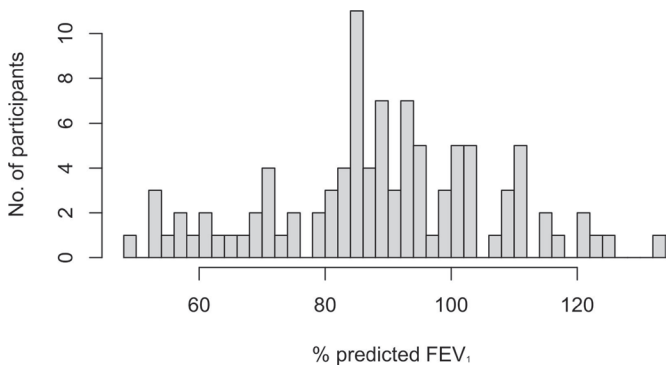

Figure 3 Distribution of percentage predicted FEV_1 measurements at 3 months (n=99).

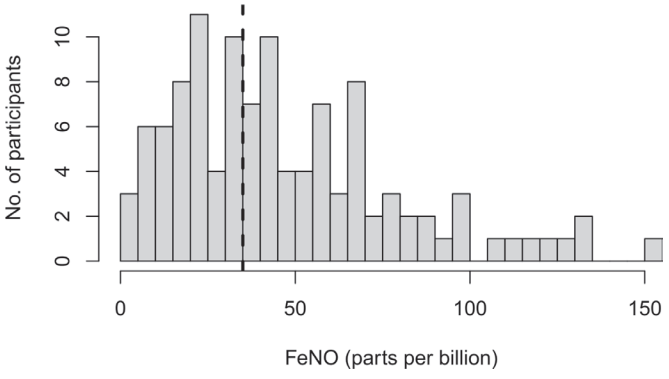

Figure 4 Distribution of FeNO levels measured at 3 months (n=112). Dashed line shows threshold for high FeNO (>35 ppb).

Table 4 Preintervention and postintervention FeNO levels and lung function, split by initial allocation groups*

Initial allocation	Preintervention	Postintervention	Pre–post comparison†
	Median (IQR) FeNO, ppb		
Enhanced care	44.5 (27.5–66.5) n=57	41.8 (23.4–68.0) n=56	p=0.98
Standard care	39.8 (22.9–57.9) n=56	35.0 (22.8–58.4) n=48	p=0.11
	Mean (SD) % predicted FEV_1		
Enhanced care	88.5 (17.8) n=48	86.9 (18.0) n=50	p=0.47
Standard care	92.0 (17.5) n=49	88.1 (14.3) n=44	p=0.12
	Mean (SD) % predicted FEV_1/FVC ratio		
Enhanced care	88.9 (9.8) n=43	90.9 (12.5) n=47	p=0.29
Standard care	92.8 (10.3) n=45	89.9 (9.1) n=39	p=0.30

*A total of 117 children received the intervention (initial allocations: 59 enhanced care, 58 standard care), with 104 children reviewed 3 months postintervention (56 enhanced, 48 standard).
†Preintervention and postintervention results compared using Wilcoxon-signed rank tests for paired data (for FeNO) and paired t-tests (for spirometry).

one-fifth had no salbutamol inhaler and less than half had received ICS treatment, with relatively low daily doses.

In addition to improved asthma control, significantly fewer children in the intervention group experienced asthma exacerbations requiring emergency health facility attendance and school absence.

Participants demonstrated raised FeNO levels, confirming that ICS treatment is highly appropriate in this population. Self-reported ICS use was greater in the intervention group, with more children taking daily beclometasone, and participants prescribed a significantly higher daily dose. However, preintervention and postintervention FeNO levels were similar, suggesting unchanged levels of airway inflammation, possibly due to non-compliance with ICS treatment or lack of response in this population. Self-reported adherence rates were high (>85%); however, there are often discrepancies when objective measures of adherence are compared with self-reports.[20] Improved outcomes maybe due to increased confidence to intervene early in an attack, with self-management of symptoms at home, through effective use of inhaled salbutamol.

Current GINA guidance (for those ≥12 years) advises against salbutamol monotherapy, recommending using ICS either regularly or whenever salbutamol is taken.[7] Compliance with daily ICS is a challenge in countries across the world; further research is required in LMICs to explore the clinical and cost-effectiveness of combination inhalers, which are becoming widely used in HICs.[7] This is particularly important in children, where detrimental effects of airway inflammation during lung growth and development may have longer-term impact.

Participants were generally able to collect inhalers, free of charge, from our tertiary-level hospital pharmacy; however, this does not reflect availability of inhalers more widely in Malawi: a recent survey reported that <5% of health facilities, including district hospitals, have resources to treat chronic asthma.[21] The reliable and affordable supply of inhaled medication, across all levels of health facilities, is a major challenge which must be addressed in many LICs.[2]

We found relatively high levels of reported asthma control (64.2%), defined by cACT ≥20, compared with other studies in sSA, although most published data relate to adult patients.[3 4] Among paediatric patients attending a tertiary clinic in South Africa, 55.7% had controlled asthma (ACT/cACT >19) with mean (SD) cACT score 19.9 (5.5).[22] However, despite the baseline cACT for our participants suggesting reasonable symptom control, the burden of exacerbations requiring health facility attendance and school absence was high.

Without a locally validated assessment tool, the choice of outcome measurement for this study was challenging; neither ACT nor cACT have been validated within sSA. The cACT is designed for children aged 4–11 years with four questions for the child, using a pictorial scale of Western children's faces to rate symptoms, and three questions for their accompanying adult (total score: 0–27).[15 23] The ACT is for those aged ≥12 years, with five questions (total score: 5–25).[23] We chose to use the cACT for all participants, given the younger ages of most children attending clinic, rather than two separate tools, to avoid confusion for the study team and to avoid combining different scoring systems. However, obtaining responses which truly reflect the child's clinical condition is difficult; younger children may struggle to recognise and articulate symptoms and have a poor perception of time, and children may be reluctant to answer, deferring to their elders in a culture which promotes hierarchical respect. Changing caregivers meant that adults were sometimes unsure of the child's symptoms over the preceding month, particularly at night or during the school day. To date, a clinically meaningful difference in cACT has not been established; in adults, the minimally important difference in ACT is three points.[23]

We identified several children with severe airway obstruction but normal cACT scores; symptom perception may be impaired in children with chronic airflow obstruction and the poor correlation between self-reported symptoms and spirometry is well-recognised.[24] Additionally, we recognise a cultural tendency among Malawians to under-report symptoms. Spirometry has limited availability outside of the research setting in most LICs, but peak flow metres can provide a useful alternative and may be a more appropriate component of future interventions to provide an objective assessment of airway obstruction.[7]

Given the lack of other studies using non-clinical staff for task-shifting, we deliberately set a short follow-up period for this study to minimise loss to follow-up and maximise the chances of identifying a benefit or harm from this novel approach. Overall completeness of data collection was good, including acceptable and repeatable spirometry data for over 80% of participants.

We relied on self-report of symptoms, exacerbations and inhaler use: recall bias is a potential limitation. We tried to quantify medication use by weighing inhalers but abandoned this as very few participants brought their inhaler canisters despite reminders. Our study recruited patients attending outpatient follow-up at a tertiary hospital—we would expect a high rate of previous hospital admissions and attendances, since many patients are referred to this clinic from paediatric wards and the emergency department: this may explain why both groups to showed clinical improvement during the study and means our findings represent more severely affected asthmatic children in Malawi. Despite these limitations, our findings suggest that optimisation of inhaled treatment, supported by asthma education delivered by non-physicians, can have a beneficial effect on asthma outcomes.

Malawi suffers from a shortage of trained medical staff with 2 physicians and 28 nurses per 100 000 population, well below the WHO 'critical shortage' threshold of 2.5 health professionals (including doctors, nurses and midwives) per 1000 population.[25] This huge deficit in workforce requires an alternative approach to healthcare delivery: task-shifting has been successfully employed in the community case management of childhood illnesses and to improve access to HIV services in Malawi.[26 27] Considering

asthma management specifically, a study from Cameroon reported decreased asthma attacks among mostly adult patients attending a nurse-led asthma clinic, although loss to follow-up was high.[14] Task-shifting asthma education to non-medical cadres has been explored in high-income settings, with comparable outcomes reported for asthma education delivered by lay people and nurses to adult patients.[28] The use of lay educators has not previously been evaluated in LMICs: we propose that the potential impact may be greater than in HICs, due to lower baseline education and health literacy levels among poorer populations.

These promising data require further exploration of task-shifting in low-income settings. Scale-up of similar interventions across a wider range of healthcare settings, including both children and adults, could present substantial benefits to asthmatic patients and their families; assessment of health economic and longer-term clinical outcomes is required.

Together we can, and must, do better: building networks of clinicians and researchers from across sSA is essential to raise asthma awareness among local communities, healthcare providers and policy makers, to deliver LMIC-relevant research to inform clinical guidelines and address the deplorable global disparities in access to inhaled medication.[29] Effective asthma treatment should be available to all who need it, regardless of where they live.[30]

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REFERENCES

1 Asher I, Pearce N. Global burden of asthma among children. *Int J Tuberc Lung Dis* 2014;18:1269–78.
2 Global Asthma Network. *The global asthma report 2018*. Auckland, New Zealand, 2018.
3 Kirenga BJ, de Jong C, Mugenyi L, *et al*. Rates of asthma exacerbations and mortality and associated factors in Uganda: a 2-year prospective cohort study. *Thorax* 2018;73:983–5.
4 Ozoh OB, Okubadejo NU, Chukwu CC, *et al*. The ACT and the ATAQ are useful surrogates for asthma control in resource-poor countries with inadequate spirometric facilities. *J Asthma* 2012;49:1086–91.
5 Lai CKW, Beasley R, Crane J, *et al*. Global variation in the prevalence and severity of asthma symptoms: phase three of the International study of asthma and allergies in childhood (Isaac). *Thorax* 2009;64:476–83.
6 Ministry of Health. *Malawi standard treatment guidelines*. 5th edn, 2015. https://extranet.who.int/ncdccs/Data/MWI_D1_Malawi-Standard-Treatment-Guidelines-Essential-Medicines-List-2015.pdf
7 Global Initiative for Asthma. Global strategy for asthma management and prevention, 2020. Available: https://ginasthma.org/
8 Aït-Khaled N, Enarson DA, Bencharif N, *et al*. Implementation of asthma guidelines in health centres of several developing countries. *Int J Tuberc Lung Dis* 2006;10:104–9.
9 Ait-Khaled N, Enarson DA, Bissell K, *et al*. Access to inhaled corticosteroids is key to improving quality of care for asthma in developing countries. *Allergy* 2007;62:230–6.
10 Jumbe Marsden E, Wa Somwe S, Chabala C, *et al*. Knowledge and perceptions of asthma in Zambia: a cross-sectional survey. *BMC Pulm Med* 2016;16:33.
11 Boyd M, Lasserson TJ, McKean MC, *et al*. Interventions for educating children who are at risk of asthma-related emergency department attendance. *Cochrane Database Syst Rev* 2009;2:CD001290.
12 Gibson PG, Powell H. Written action plans for asthma: an evidence-based review of the key components. *Thorax* 2004;59:94–9.
13 World Health Organization. *Task shifting: rational redistribution of tasks among health workforce teams: global recommendations and guidelines*. Geneva, Switzerland, 2007. https://apps.who.int/iris/handle/10665/43821
14 Kengne AP, Sobngwi E, Fezeu LL, *et al*. Nurse-led care for asthma at primary level in rural sub-Saharan Africa: the experience of Bafut in Cameroon. *J Asthma* 2008;45:437–43.
15 Liu AH, Zeiger R, Sorkness C, *et al*. Development and cross-sectional validation of the childhood asthma control test. *J Allergy Clin Immunol* 2007;119:817–25.
16 Miller MR, Hankinson J, Brusasco V, *et al*. Standardisation of spirometry. *Eur Respir J* 2005;26:319–38.
17 Quanjer PH, 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;40:1324–43.
18 American Thoracic Society, European Respiratory Society. ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. *Am J Respir Crit Care Med* 2005;171:912–30.
19 Rylance S, Phiri J, Grigg J. Enhanced versus standard outpatient care of asthmatic children in Malawi: study protocol for a pilot randomised controlled trial. *medRxiv* 2020.
20 Morton RW, Everard ML, Elphick HE. Adherence in childhood asthma: the elephant in the room. *Arch Dis Child* 2014;99:949–53.
21 Republic of Malawi Ministry of Health. The Malawi noncommunicable diseases and injuries poverty Commission report, 2018. Available: http://www.ncdipoverty.org/malawi-report
22 Garba B, Ballot D, White D. Home circumstances and asthma control in Johannesburg children. *Curr Allergy Clin Immunol* 2014;27:182–9.
23 Schatz M, Kosinski M, Yarlas AS, *et al*. The minimally important difference of the asthma control test. *J Allergy Clin Immunol* 2009;124:719–23.
24 Bacharier LB, Strunk RC, Mauger D, *et al*. Classifying asthma severity in children: mismatch between symptoms, medication use, and lung function. *Am J Respir Crit Care Med* 2004;170:426–32.
25 The Global Fund. *Global fund grants to the Republic of Malawi: audit report*. Geneva, Switzerland, 2016. https://www.theglobalfund.org/media/2665/oig_gf-oig-16-024_report_en.pdf
26 Callaghan-Koru JA, Gilroy K, Hyder AA, *et al*. Health systems supports for community case management of childhood illness: lessons from an assessment of early implementation in Malawi. *BMC Health Serv Res* 2013;13:55.
27 Bemelmans M, van den Akker T, Ford N, *et al*. Providing universal access to antiretroviral therapy in Thyolo, Malawi through task shifting and decentralization of HIV/AIDS care. *Trop Med Int Health* 2010;15:1413–20.
28 Partridge MR, Caress A-L, Brown C, *et al*. Can lay people deliver asthma self-management education as effectively as primary care based practice nurses? *Thorax* 2008;63:778–83.
29 Mosler G, Oyenuga V, Addo-Yobo E, *et al*. Achieving control of asthma in children in Africa (Acacia): protocol of an observational study of children's lung health in six sub-Saharan African countries. *BMJ Open* 2020;10:e035885.
30 Szefler SJ, Fitzgerald DA, Adachi Y, *et al*. A worldwide charter for all children with asthma. *Pediatr Pulmonol* 2020;55:1282–92.