


The challenge of addressing obesity in people with poorly controlled asthma

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Abstract

Objective: There is a high prevalence of obesity in people with asthma, and obesity is associated with poorly controlled asthma. Significant weight loss might improve asthma control: the purpose of this study was to investigate patient characteristics and factors that might affect implementation of a weight loss and/or roflumilast intervention, to target both obesity and asthma.

Methods: A cross-sectional study of people with obesity and poorly controlled asthma performed at 13 sites across the United States.

Results: One hundred and two people participated in this study. Median BMI was 37 (IQR 35–42). The majority, 55%, were African American and 76% were female. Fifty two percent had very poorly controlled asthma. Most participants were quite sedentary (70% reported being inactive or participating only in light-intensity activities according to the Stanford Brief Activity Survey). Participants reported significant impairments related to physical function on the Impact of Weight on Quality of Life-Lite questionnaire (median score 67 [IQR 41–84]). Thirty-five percent of participants reported mild, and 2 % moderate, depressive symptoms as assessed by the Patient Health Questionnaire-9.

Conclusions: Poorly controlled asthma and obesity often affect minority populations and are associated with significant impairments in health related to physical function and low levels of physical activity that might complicate efforts to lose weight. Interventions targeted at poorly controlled asthma associated with obesity in the United States need to address factors complicating health in underserved communities, such as increasing opportunities for physical activity, while also managing activity limitations related to the combination of asthma and obesity.

KEYWORDS

exercise, lung function, nutrition, obesity, weight loss

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1 | INTRODUCTION

There is a very high prevalence of asthma in people with obesity: in the United States 11% of adults with obesity have asthma, compared with only 7% of lean adults.¹ Obesity is particularly common in minority people with asthma.² The combination of obesity and asthma is a major public health issue as obesity is associated with severe, difficult to control asthma and people with obesity tend not to respond as well to standard asthma medications as lean people.³ All medications currently used to treat asthma have been developed for the treatment of asthma in leaner populations, and so there is a paucity of data to guide treatment options for patients with obesity and asthma. Developing better ways to control asthma in people with obesity is an important public health issue, and yet there are few studies assessing factors that might affect response to treatments targeted at asthma and obesity.

As obesity is associated with severe, difficult to control asthma, one approach to treatment is weight loss. Although a few single center studies demonstrate improvement in asthma control with lifestyle and surgical interventions,^{4–6} little is known about feasibility of these approaches among diverse populations of people with obesity and poorly controlled asthma, a patient group that might have particular difficulty with increasing physical activity.⁷

Another approach to treating asthma in people with obesity would be to repurpose already existing medications. One such medication is roflumilast—a phosphodiesterase-4 inhibitor currently used in the treatment of chronic obstructive pulmonary disease—which promotes weight loss, though has side effects of gastrointestinal intolerance, and anxiety and depression.^{8–12}

The feasibility of implementing such interventions in diverse patient populations with asthma and obesity is not known. Implementing lifestyle interventions, which require changes in diet and increase in physical activity, can be challenging, particularly for those with a comorbidity that affects exercise tolerance.⁷ The purpose of this current study was to evaluate the characteristics of the patient population and potential feasibility of either a weight loss and/or roflumilast trial in a diverse population of people with obesity and poorly controlled asthma—specifically, understanding the socio-demographic characteristics of this study population, indicators of mental health, quality of life, physical activity, and diet. The goal of this manuscript is to describe this population to guide future interventional clinical trials.

2 | METHODS

This was a multicenter, observational study conducted at 13 sites and data-coordinating center of the American Lung Association-Airways Clinical Research Centers (ALA-ACRC, listed in acknowledgments). Participants were recruited between January 2019 and January 2020. The study was approved by the institutional review boards at all participating sites, and informed consent was obtained from all participants.

2.1 | Participants

Enrollment criteria were purposely broad to ensure that the study population reflected the diverse types of individuals with obesity and poorly controlled asthma that might be encountered in the general medical setting. Inclusion criteria were as follows: physician diagnosis of asthma and on regular daily controller therapy for at least 3 months; poorly controlled asthma (Asthma Control Test score <20,¹³ or use of rescue inhaler on average > 2 times per week for the preceding month, or nocturnal asthma awakening on average one or more times per week in the preceding month, or emergency department/hospital visit or prednisone course for asthma in the last 6 months); age ≥ 18 years; and, BMI ≥ 30 kg/m². Exclusion criteria were as follows: COPD; any condition that might put a participant at risk from weight loss (in the opinion of the site investigator); elevated risk of uncontrolled depression (Patient Health Questionnaire-9 [PHQ-9] score of ≥ 10 , and changed to 15 or greater in November 2019¹⁴); suicidal ideation; elevated risk of uncontrolled anxiety (score of 10 or more on the Generalized Anxiety Disorder-7 [GAD-7] questionnaire¹⁵); pregnancy or lactation; history of bariatric surgery; or, asthma exacerbation in the prior 4 weeks. Participants with uncontrolled anxiety, depression, and suicidal ideation were excluded because of concern such conditions may be exacerbated in a future trial of roflumilast.

2.2 | Study procedures

Participants underwent spirometry testing according to ATS guidelines.¹⁶ Participants answered questions pertaining to asthma control,¹³ asthma quality of life,¹⁷ asthma symptoms,¹⁸ obesity quality of life,¹⁹ general health related quality of life (Rand-36-item Health Survey 1.0),²⁰ depression,¹⁴ anxiety,¹⁵ physical activity,²¹ and gastrointestinal symptoms.²² Dietary intake was assessed with the Arizona Food Frequency Questionnaire.²³ Participants were asked about participation in previous weight loss programs, and availability of WiFi and electronic devices (for purposes of remote contact).

The presence of metabolic syndrome was based on having three of the following: self-report of diabetes, hypertension (either by self-report or measured systolic BP > 130 or diastolic > 80 mm Hg), self-report of high cholesterol and measured waist circumference >88 cm for women, and >102 cm for men.²⁴

2.3 | Statistical approach

This was a convenience sample designed to generate information on participant characteristics and variability estimates on factors that might affect the feasibility of a weight loss and/or roflumilast intervention. Descriptive statistics including medians and proportions, as appropriate, were used to describe the population.

3 | RESULTS

3.1 | Screening

Of 237 individuals screened in-person and by telephone for the study, 117 (49%) were not eligible. Sixty-seven (28%) were not interested or could not be re-contacted; twenty-five (22%) did not meet criteria related to asthma; fifteen (13%) did not meet BMI cut-off or had a history of bariatric surgery; and five (4%) were excluded based on elevated scores on depression or anxiety screening questionnaires. Of the 137 individuals who underwent in-person, screening 102 were enrolled. The most common reason for not meeting criteria at in-person screening visits was well-controlled asthma (29, 78%).

3.2 | Demographics

Baseline characteristics of the study population are shown in Table 1.

The median age of participants was 55 (IQR 40–64) years, the majority were female, and there was an overrepresentation of African American participants. Forty percent of participants reported a household income of less than \$30,000. The majority of participants reported at least some college education.

TABLE 1 Demographics of study population

Demographics, N = 102		
Age, median (IQR), yr.		55 (40–64)
BMI, median (IQR), kg/m ²		37 (35–42)
Sex, no. (%)	Female	77 (75.5)
Race, no. (%)	Black/African American	56 (55.4)
	Caucasian	36 (35.6)
Ethnicity, no. (%)	Hispanic/Latino	14 (14.0)
Smoking status, no. (%)	Current	4 (4.0)
	Former	22 (21.8)
Income, no. (%)	<30,000	41 (40.2)
	30,001–50,000	17 (16.7)
	50,001–75,000	11 (10.8)
	>75,000	17 (16.7)
	Do not know	10 (9.8)
	Declined to answer	6 (5.9)
Education, no. (%)	Eight grade or less	2 (2.0)
	Some high school	11 (10.8)
	High-school graduate or equivalent	20 (19.6)
	Some college	25 (24.5)
	2-year college or technical school	19 (18.6)
	4-year college	13 (12.7)
	Post-graduate studies	12 (11.8)

Participants were queried about use of electronic devices and WiFi access, which might be important for a remote intervention/study: 97% reported access to an electronic device, and 93% reported access to WiFi.

3.3 | Asthma characteristics

The median age of onset asthma was 19 (IQR 5–39) years, with the majority of participants (60 [59%]) reporting asthma onset at age 12 years or older. Participants were selected to have poorly controlled asthma; it was notable that 92% of participants had more than one marker of poorly controlled asthma, with 30% of participants reporting an Emergency Department visit or hospitalization for asthma in the last 6 months (Table 2).

3.4 | Weight and metabolic history

The majority of participants reported gaining weight as an adult. Nearly all participants reported previous participation in weight loss programs (the most common, reported by 22 participants, was WW, formerly Weight Watchers). The majority reported fluctuating weight in the

TABLE 2 Asthma characteristics

Lung function median (IQR)	
Pre-BD FEV, liters	2.0 (1.6–2.4)
Pre-BD FVC, liters	2.7 (2.2–3.3)
Pre-BD FEV ₁ % predicted	76 (64–88)
Post-BD % reversibility	5 (2–12)
Asthma exacerbations in prior 6 months no. (%)	
ED/Hospital visit	30 (29.7)
Prednisone course 6 months	48 (47.5)
Asthma control test category^a, no. (%)	
Very poorly controlled asthma	54 (52.4)
Poorly controlled asthma	42 (40.8)
Well-controlled asthma	7 (6.8)
Marks AQOL median (IQR)	
Sum ^b	24 (13–36)
Breathlessness ^c	1 (1–2)
Mood disturbance ^c	1 (0–2)
Social disruption ^c	1 (0–2)
Concerns for health ^c	1 (0–2)

Abbreviations; AQOL, asthma quality of life; BD, bronchodilator; ED, emergency department; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

^aAsthma control test Score ≤ 15 indicative of very poorly controlled, 16–19 poorly controlled asthma, and ≥ 20 well-controlled asthma.

^bRange 0–80, lower score indicative of better health.

^cRange 0–4, lower score indicative of better health.

prior 12 months, with 21 participants reporting both weight loss and weight gain. The presence of metabolic syndrome was common in this cohort, present in 39% of participants (Table 3).

3.5 | Diet and physical activity

Participants were asked how many days they had exercised (including walking or more vigorous activity) in the last 4 weeks; the median reported was 3 days of exercising 5–30 min in the last 4 weeks. According to the Stanford Activity Scale, only 30% of the population participated in moderate or more intense activity (Table 3). Thirty-six participants (35%) reported they had used an activity monitor, and 29 participants (28%) reported they had a current gym/health club membership.

Median caloric intake was 2033 (IQR 1205–3802) kCal, with 25% of participants reporting more than 3802 kCal per day. Participants reported their total calories from protein (15.8%) was at the low range of current recommendations (10%–35%), whereas calories from fat (33.5%) was at the high end of current recommendations (25%–35%).²⁵

TABLE 3 Weight, exercise, and dietary history

Weight history	
BMI (kg/m ²) median (IQR)	37 (35–42)
Height (cm) median (IQR)	164 (158–172)
Weight (kg/m ²) median (IQR)	103 (93–116)
BMI at 18 years, median (IQR)	23 (20–28)
Prior weight loss program, no. (%)	101 (99.0)
Weight loss in last 6 months, no. (%)	42 (41.2)
Weight gain in last 6 months, no. (%)	52 (51.0)
Metabolic dysfunction, no. (%)	40 (39.2)
Days with exercise in past 4 weeks, median (IQR)	
5–30 min	3 (0–8)
31–60 min	0 (0–8)
>60 min	0 (0–3)
Stanford brief activity survey category, no. (%)	
Inactive	36 (35.3)
Light intensity	35 (34.3)
Moderate intensity	16 (15.7)
Hard intensity	8 (7.8)
Very hard intensity	7 (6.9)
Energy intake, median (IQR)	
Total energy (kCal)	2033 (1205–3802)
Protein (percentage of total energy)	15.8 (13.6–18.0)
Fat (percentage of total energy)	33.5 (29.7–37.9)
Carbohydrate (percentage of total energy)	51.0 (44.6–58.1)

3.6 | Quality of life

The Impact of weight on quality of life questionnaire-Lite was administered (Table 4): the most severely affected domain related to physical functioning, with a median score of 67 (IQR 41–84; scale 0–100, higher score indicative of better health). When evaluating overall quality of life, assessed by the Rand-36, the lowest scoring domains were energy/fatigue (median score 50, IQR 40–65) and role limitations due to physical functioning (median score 50, IQR 0–100, Table 4) (scale 0–100, higher score indicative of better health).

3.7 | Markers of general health

3.7.1 | Gastrointestinal symptoms

Gastrointestinal (GI) symptoms were assessed because of the potential for this to be a barrier to taking roflumilast (Table 5). Overall score was low with a median score of 2 (IQR 1–2; scale 1–7, lower score indicative of better health).

3.7.2 | Anxiety

Overall score on the anxiety (GAD-7) questionnaire was low, with 21% of participants having symptoms of mild anxiety; five potential participants with scores ≥ 10 (moderate anxiety) were excluded

TABLE 4 Quality of life

Impact of weight on quality of life-lite median (IQR) ^a	
Total score	79 (60–90)
Physical function	67 (41–84)
Self-esteem	82 (54–96)
Sexual life	94 (69–100)
Public distress	100 (85–100)
Work	94 (75–100)
RAND 36-item health survey median (IQR) ^a	
RAND-36 score	60 (41–75)
Physical functioning	55 (35–75)
Role limitations due to physical health	50 (0–100)
Role limitations due to emotional problems	100 (67–100)
Energy/fatigue	50 (40–65)
Emotional well-being	80 (68–92)
Social functioning	75 (50–100)
Pain	68 (45–78)
General health	50 (25–60)

^aScales 0–100, higher score indicative of better health.

TABLE 5 General health questionnaires

Gastrointestinal Symptom Rating Scale ^a (median, IQR)	
2 (1–2)	
Anxiety questionnaire, GAD-7 ^b	
Category	n (%)
Minimal/none (0–4)	81 (79.4)
Mild (5–9)	21 (20.6)
Depression questionnaire, PHQ-9 ^c	
Category	n (%)
Minimal/none (0–4)	65 (63.7)
Mild (5–9)	35 (34.3)
Moderate (10–14)	2 (2.0)

^aScale 1–7, higher scores indicative of more severe gastrointestinal symptoms.

^bScale 0–21, higher score indicative of more severe anxiety symptoms, thresholds as indicated.

^cScale 0–27, higher score indicative of more severe symptoms of depression, thresholds as indicated.

(Table 5). The score changed minimally over the two study visits (median score of 2 [IQR 0–4] and 1 [IQR 0–3] at baseline and follow-up), which is less than the minimal clinically important difference of 4.²⁶

3.7.3 | Depression

Many participants had symptoms of mild to moderate depression on the PHQ-9 (Table 5); we had initially used a threshold of less than or equal to 10 (moderate depression), but increased this to less than or equal to 15 because of a concern that some of the somatic symptoms of depression overlapped with symptoms related to obesity. Twenty-three potential participants were ineligible because of scores of 10 or greater, nine of whom had scores of 15 or greater. The scores changed minimally over the two study visits (3.5 [IQR 1.0–6.0] and 3.0 [IQR 2.0–5.0] at baseline and follow-up), and less than the minimal clinically important difference of 5.²⁷

4 | DISCUSSION

This is the first study to assess patient population characteristics and potential feasibility of lifestyle and medical interventions to treat poorly controlled asthma in people with obesity, in a diverse patient population across the United States. Our study has important findings to guide future trials. Nearly all participants had previously participated in weight loss programs, suggesting that participants were interested in weight-loss interventions. There may be barriers to incorporating exercise into lifestyle interventions: many participants reported significantly impaired physical health and were quite

sedentary. Many participants had elevated scores on a depression questionnaire (though some of these symptoms may overlap with those of obesity). Our data reflect the fact that obesity and asthma reflect a health burden particularly afflicting minorities and those of lower socioeconomic status (SES): interventions targeting obesity are likely important to address health disparities related to asthma in the United States.

The population in this study were predominantly African American, and predominantly female. This differs from the typical population recruited into prior ALA-ACRC studies: prior studies have included 4462 participants with asthma, 36% have been African Americans, compared to 55% in the current study. Prior ALA-ACRC studies in adults with asthma also recruited predominantly females. Forty percent of participants in the current study reported a household income under \$30,000 per year, which is a higher percentage of low income than in the general US population; data from the US census for 2018 reported 27% of households with incomes less than \$30,000 per year.²⁸ This is likely related both to the demographics of our study population in terms of race and sex, and also to the presence of obesity, which is increased in lower SES populations.²⁹ Overall, educational attainment appeared similar to the US population as a whole; in 2019, 90.5% of women and 89.6% of men had graduated high school (compared with 87% of participants in this study). While this was not a population based study, when comparing to prior studies completed by the same centers and US population data, the current study population included a higher number of African American and lower SES participants, reflecting the fact that obesity associated with asthma contributes to disparities in health.²

The impact of obesity on quality of life in our study population was investigated. Obesity is often associated with low self-esteem and public distress as measured by the “Impact of Weight on Quality of Life” questionnaire, a validated questionnaire assessing quality of life related to weight.³⁰ This low self-esteem might relate to the social stigmatization often encountered by people with obesity.^{31–33} However, obesity had a more marked effect on quality of life related to physical health than these other domains: median score for physical function was 67 and for self-esteem was 82 in our study. By comparison, mean scores of 65 for physical functioning and 58 for self-esteem were reported in a weight loss trial that enrolled a diverse population with a similar BMI range.³⁴ A minimal clinical important difference for overall score on this questionnaire ranges from 7.7–12 (depending on baseline severity), so the higher self-esteem scores in our current study are in the range likely to be clinically significant.³⁵ A general health related quality of life questionnaire (RAND 36-item health survey) was used to ascertain the effects of obesity coupled with asthma on overall health related quality of life and found that scores related to physical health were lower in our study population versus studies in people with a similar BMI: a recent study found much higher scores (means 75–80 for physical functioning and 76–85 for role limitations in different study groups) than in our population (50 and 55, respectively).³⁶ Our study suggests that people with obesity and poorly controlled asthma have

worse quality of life related to physical function compared to others with similar BMI.

Impaired physical function may decrease the ability to participate in physical exercise. Our study suggests that 35% of this population were sedentary (both at work and during leisure time), and another 34% only took part only in light-intensity activity. This appears to be more sedentary than that reported for the US population, 27% of whom report no physical activity and an additional 18% report low or moderate physical activity.³⁷ A recent meta-analysis reported that people with asthma were less physically active than those without asthma,³⁸ and some studies reporting this was independent of obesity status.³⁹ In the current study, the low rates of physical activity might also be related to the demographic composition of our participants since there are significant racial and socioeconomic disparities in physical activity, which relate to neighborhood factors (such as having a safe place and time to exercise).⁴⁰

Both asthma and demographics are likely to be a significant factor impairing exercise in our participants. In a study to identify barriers to physical activity in an urban African American population with asthma and obesity, Nyenhuis et al. noted that all participants reported asthma was limiting their activity and they were uncertain how to better manage their asthma to increase physical activity.⁷ Having a safe place to walk was also a significant concern for many participants.⁷ Interventions to target weight reduction in obese people with asthma need to tailor interventions that take into account this population may have particular difficulties with physical activity.

The median caloric intake reported appeared appropriate for weight maintenance, though many participants were likely taking excess to their requirements.²⁵ Participants reported consuming relatively low protein and high fat compared to recommendations,²⁵ suggesting there may be opportunities to improve dietary quality in this population.

A significant proportion of the study population had mild-moderate symptoms of depression as assessed by the PHQ-9. Anxiety disorder and depression are common in people with severe obesity, thought related to social stigma, isolation, impairments in health,⁴³ and possibly also to shared biological mechanisms.⁴⁴ However, somatic symptoms on the PHQ-9 screening questionnaire overlap with symptoms related to obesity (symptoms related to sleep, energy level, and appetite). Increasing the eligibility cut-off score from mild to moderate (PHQ-9 less than or equal to 10 to less than or equal to 15) increased the pool of interested, eligible individuals and lessened the potential effect of conflating symptoms. Future studies, including a more detailed evaluation than a screening questionnaire, will be valuable to delineate the prevalence of depression among people with asthma and obesity. Few participants reported elevated anxiety or GI symptoms, suggesting that these factors would not interfere with recruitment to future trials involving medications that might worsen such symptoms.

In conclusion, when attempting to assess the participants characteristics and feasibility of interventions to treat poorly controlled asthma in people with obesity, we found a very high proportion of

African American and lower income participants. Our study highlighted important factors to be considered when designing interventions for this population: obesity associated with asthma is associated with significant decrements in quality of life related to physical health and low levels of physical activity. While standard weight loss interventions targeting reduced caloric intake are likely to be appropriate for this population, specific interventions targeting increasing physical activity will be needed. African American, low-income participants require exercise interventions targeted to their specific needs,⁷ and increasing physical activity will need include strategies to control respiratory symptoms related to asthma.⁴⁵

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CONFLICT OF INTEREST

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Anne E. Dixon conceived study, assisted with recruitment, and preparation of the manuscript. Kathryn V. Blake assisted with study design, patient recruitment and revision of manuscript. Emily A. DiMango assisted with study design, patient recruitment, and revision of manuscript. Mark T. Dransfield assisted with study design, patient recruitment, and revision of manuscript. Laura C. Feemster assisted with study design, patient recruitment, and revision of manuscript. Olivia Johnson assisted with implementation of the study, patient recruitment, and revision of manuscript. Gem Roy assisted with implementation of the study, patient recruitment, and revision of manuscript. Heather Hazucha assisted with implementation of the study, patient recruitment, and revision of manuscript. Jean Harvey assisted with study interpretation and revision of the manuscript. Meredith C. McCormack assisted with study

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