Brief Report

Respiratory Failure, Noninvasive Ventilation, and Symptom Burden: An Observational Study

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Abstract

Background. Noninvasive ventilation (NIV) is commonly used to manage acute respiratory failure due to decompensated cardiorespiratory disease. We describe symptom burden in this population.

Measures. Fifty consecutive, consenting, English-speaking, cognitively intact patients, admitted to wards other than the intensive care unit in a tertiary teaching hospital and treated with NIV for hypercapnic respiratory failure, were recruited. The 14-item Condensed Memorial Symptom Assessment Scale was used to assess physical and psychological symptoms within 36 hours of commencing NIV. Breathlessness (using Borg score), pain location and intensity using a numerical rating scale, and four symptoms potentially prevalent in patients undergoing NIV (cough, sputum, gastric bloating, and dry eyes) were also assessed.

Outcomes. Patients reported a median of 10 symptoms (IQR 9–13). A median of five symptoms (IQR 3–7) were rated as severe. Breathlessness was the most prevalent and most distressing symptom, with participants reporting a mean maximum Borg score of 7.55 over the 24 hours before admission. Dry mouth, lack of energy, cough, sputum, difficulty sleeping, and psychological symptoms were prevalent. Pain, when reported, was of moderate intensity and contributed to distress.

Conclusions/Lessons learned. This study describes the patient-reported symptoms occurring during an episode of acute respiratory failure. Understanding the symptom profile of patients in this setting may allow clinicians to target symptom relief while simultaneously managing respiratory failure, enhancing care. J Pain Symptom Manage 2019;57:282–289.

Key Words
Dyspnea, noninvasive ventilation, palliative care, pulmonary disease, chronic obstructive, heart failure, respiratory insufficiency

Introduction

Noninvasive ventilation (NIV) is used to treat acute and acute-on-chronic respiratory failure due to decompensated cardiorespiratory disease.[1] NIV improves gas exchange and can "buy time," whereas other treatments, such as bronchodilators, corticosteroids, diuretics, and/or antibiotics, as appropriate to the underlying illness, reverse acute physiological disturbances.[1] Although life-saving measures are crucial, symptom assessment and management are also important.

Symptom burden is inherently subjective and may be assessed by validated, patient-reported outcome measures. Understanding the epidemiology of symptoms in specific populations serves to enable development of strategies to ameliorate distress and reduce suffering.[2] Patients with chronic cardiorespiratory disease assessed in stable outpatient settings report high symptom burden.[3–5]

Worsening symptoms are a common trigger for hospital presentation and are intrinsic to the diagnosis of exacerbations of chronic obstructive pulmonary disease (COPD)[6] and decompensated heart failure.[7] A recent study assessed symptom experience in an inpatient heart failure population,[8] and another explored

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Health Related Quality of Life (HRQoL) in inpatients with hypercapnic respiratory failure,[9] and a third evaluated breathlessness in patients treated with NIV.[10] However, the overall symptom burden in patients with respiratory failure requiring treatment with NIV has not been reported to our knowledge.

The aim of this study was to describe the symptom burden of patients admitted to hospital with acute hypercapnic respiratory failure who were treated with NIV.

Methods

We describe a prospective, cross-sectional study of patients with hypercapnic respiratory failure (confirmed on arterial blood gas sampling) requiring NIV. This study was undertaken in a tertiary teaching hospital in Australia. Data were collected between January 2010 and December 2011. Ethical approval for the study was obtained from the South Eastern Sydney Illawarra Area Health Service Human Research Ethic Committee—Central Network (approval number 09/STG/128). Written informed consent was obtained from all participants. The *Strengthening The Reporting of OBservational studies in Epidemiology* guidelines were used to guide development of this article.[11]

English-speaking patients were offered participation in the study in a time frame of 12—36 hours after starting NIV. Participants were excluded if they had a documented history of dementia, were unable to understand the consent process, declined consent, or were unable to communicate. In the study institution, NIV was administered in the emergency department, high dependency unit, and the respiratory ward. Participants treated in the intensive care unit (ICU) were excluded. Fifty patients completed the study. Details of enrollment and exclusions are outlined in Figure 1. Patients most often declined participation because they felt too unwell or were uninterested.

At enrollment, symptom burden was measured using the Condensed Memorial Symptom Assessment Scale (CMSAS).[12] The CMSAS was administered verbally to patients as the population was frail and some were wearing NIV masks at the time making reading difficult. The patients were asked if the 11 physical symptoms listed on the CMSAS had been present in the last 72 hours. If the symptom was present, they were asked how much the symptom bothered them—"not at all," "somewhat," "quite a bit," or "very much" as per the CMSAS. Participants were then asked about the presence of three psychological symptoms and how frequently they had experienced these over the last 72 hours. The scoring process for this instrument is outlined in Table 1. As suggested by Portenoy et al.,[13] physical symptoms rated as "quite a bit" or "very" bothersome and psychological symptoms present "frequently" or "almost constantly" were rated as "severe." We also asked patients to rate the bothersomeness of four additional symptoms potentially prevalent in patients treated with NIV, namely cough, sputum production, dry eyes, and gastric bloating using the same process as other physical symptoms on the CMSAS and the same cut points to rate severity. These additional symptoms were selected by an expert panel consisting of medical, nursing, and physiotherapy staff familiar with NIV.

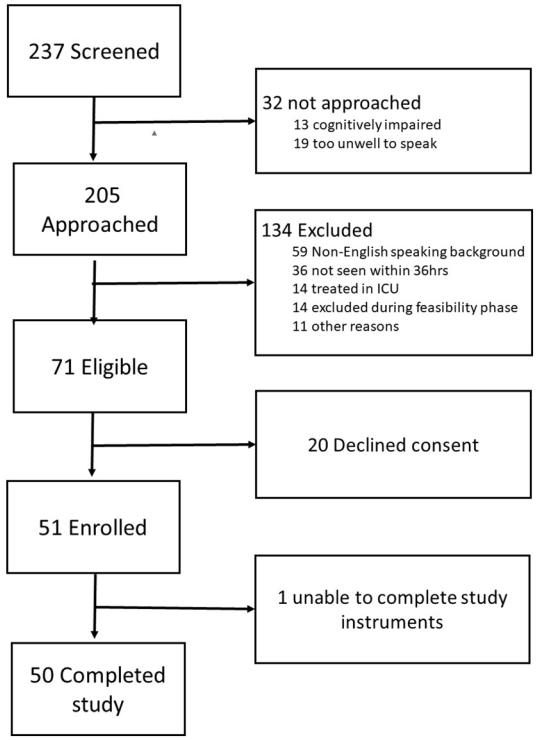

Fig. 1. Details of screening and reasons for exclusion.

The CMSAS summary score is the mean of all 14 symptom scores, whereas the physical and psychological subscale scores are the mean scores of the physical and psychological scores, respectively.[12] Only

Table 1
Scores for Patient Symptom Descriptors for the Condensed Memorial Symptom Assessment Scale (CMSAS)

Patient Response	Score
Physical symptoms	
Not present	0
Symptom present but no bother	0.8
A little bit bothersome	1.6
Somewhat bothersome	2.4
Quite a bit of a bother	3.2
Very bothersome	4.0
Psychological symptoms	
Not present	0
Rarely	1
Occasionally	2
Frequently	3
Almost constantly	4

symptoms described in the original CMSAS were used to calculate these scores, and Cronbach alpha was calculated based on these symptoms.[12]

Breathlessness and pain were further assessed. Patients were asked to rate their breathlessness using the modified Borg scale (0−10, higher score = worse breathlessness).[14] Patients were asked to report their breathlessness at the time of assessment, and their highest and lowest score over the preceding 24 hours. Patients were asked if they had chest pain, nasal bridge pain (i.e., where the NIV interface often causes irritation), or pain elsewhere. Patients responding positively were asked to rate the severity of any reported pain site on a 0−10 numerical rating scale. In addition, the bothersomeness of pain at each pain site was collected using the same scoring system as the CMSAS.

Other data collected included the patient's usual level of breathlessness before admission, using the modified Medical Research Council scale [15] and the New York Heart Association Scale,[16] illness severity using the Acute Physiology and Chronic Health Evaluation score (APACHE II),[17] comorbidities using the Charlson Comorbidity Index,[18] and performance status using the Australia-modified Karnofsky Performance Score.[19] Clinical data, including arterial blood gas measures and respiratory rate, were collected either before or within 30 minutes of NIV initiation. Hospital length of stay was collected from hospital records. The cause of patients' respiratory failure and total time spent on NIV were assessed by the first author at the end of hospitalization using all available clinical information in patients' medical record.

Descriptive statistics of clinical and demographic data were calculated. Correlation between CMSAS summary score using either Spearman (ordinal variables) or Pearson (interval or ratio variables) with demographic and clinical variables was performed. GraphPad Prism, version 6.07, (GraphPad Software, 2016) was used for statistical calculations.

Results

The characteristics of the population are outlined in Table 2. The mean age of participants was 72.0 ± 13.1 (mean ± SD) years, and 32/50 were female. Participants were assessed a mean of 23.3 ± 8.69 hours after starting NIV. At presentation, the study population had moderate-to-severe respiratory failure (mean pH 7.29 ± 0.08; mean $PaCO_2$ 58.3 ± 12.7 mm Hg) and moderate illness severity (mean APACHE II score 17.6 ± 5.93). No patients were intubated or transferred to the ICU during the study; five were intolerant of NIV but were included as they tolerated at least one hour of NIV; and three of the cohort died during hospitalization in the time period after initial assessment.

Table 2
Patient Characteristics

Patient Characteristics	
Age, years, mean (SD)	72.0 (13.1)
Gender, n (%), female	32 (64%)
Social support	
Lives alone, n (%)	15 (30%)
Lives with informal carer, n (%)[a]	27 (54%)
Lives in aged care facility, n (%)	8 (16%)
Cause of current presentation of respiratory failure	
AECOPD	12
APO	16
Pneumonia	6
SDB ± APO	6
AECOPD and APO	4
Other	6
Preadmission mMRC breathlessness class, median (IQR)	3 (2−3)
Preadmission NYHA, median (IQR)	3 (2−3)
Australian modified Karnofsky Performance Scale, median (IQR)	60 (50−80)
Charlson Comorbidity Score, median (IQR)	2 (2−3)
Clinical values	
Pre-NIV arterial pH, mean (SD)	7.29 (0.08)
Pre-NIV $PaCO_2$ (mmHg), mean (SD)	58.3 (12.07)
Pre-NIV PaO_2, mean (SD)[b]	85.2 (48.14)
Pre-NIV SaO_2, mean (SD)	89.44 (11.15)
APACHE II Score, mean (SD)	17.6 (5.93)
Time between starting NIV and symptom assessment (hours), mean (SD)	23.3 (8.69)
Length of hospital stay (days), mean (SD)	11.3 (9.4)

AECOPD = acute exacerbation of chronic obstructive pulmonary disease; APO = acute pulmonary edema; SDB = sleep disordered breathing; mMRC = modified Medical Research Council dyspnea score; NYHA = New York Heart Association; NIV = noninvasive ventilation; APACHE II = Acute Physiology and Chronic Health Evaluation II.
[a]Most often a family member.
[b]Fraction of inspired oxygen (FiO_2) was highly variable. At the time the ABG was taken, the FiO_2 was not recorded for two patients; 22% were breathing room air; 40% were receiving an FiO_2 of greater than 40%, with the remainder receiving an FiO_2 between 21% and 40%.

Figure 2 outlines symptom prevalence. Breathlessness, dry mouth, lack of energy, difficulty sleeping, cough, and sputum were the most prevalent symptoms. Psychological symptoms were highly prevalent with half of the cohort reporting the presence of worrying, feeling sad, and feeling nervous. The mean CMSAS summary score for the population was 1.60 (SD .66), the mean CMSAS physical symptom subscale score was 1.62 (SD .64), and the CMSAS psychological symptom subscale score was 1.57 (SD 1.23). The Cronbach alpha for the CMSAS summary score was 0.72, for the CMSAS physical subscale was 0.65, and for the psychological subscale was 0.74.

Table 3 details the number of symptoms reported and the number of severe symptoms. Participants reported a median of 10 symptoms (IQR 9−13) of the 18 symptoms assessed, of these a median of 5 (IQR 3−7) were reported as severe.

Figure 3 details the bothersomeness of physical symptoms and frequency of psychological symptoms. Symptoms with the highest mean scores (in rank

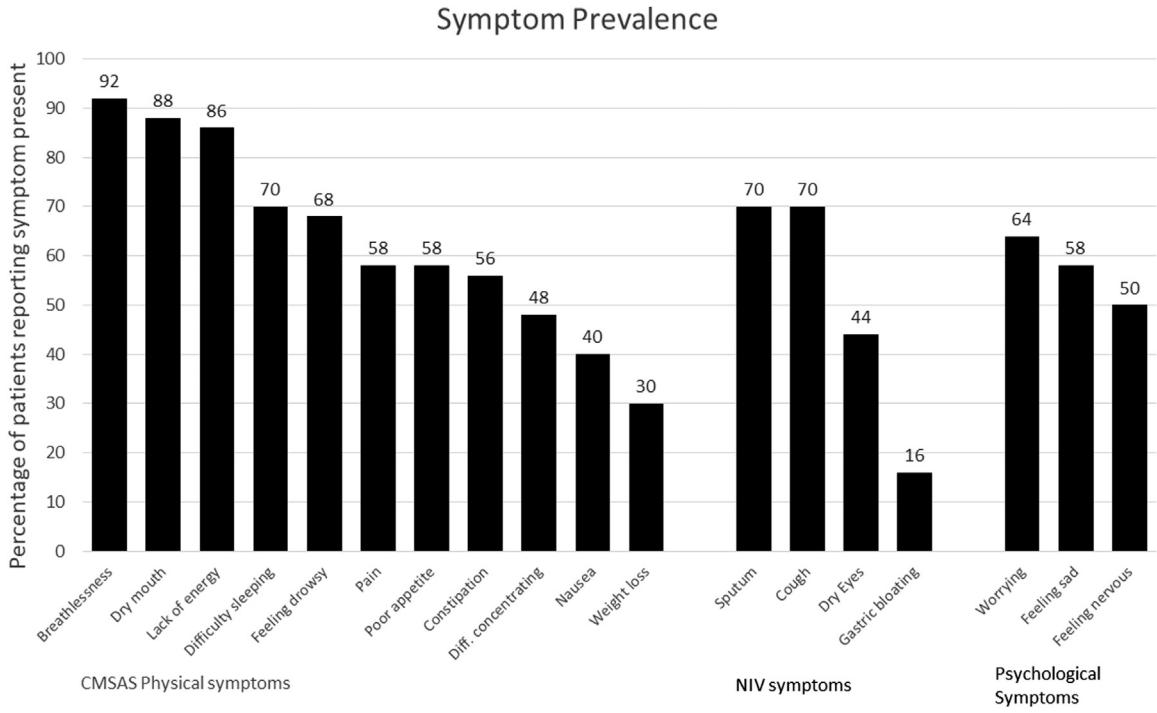

Fig. 2. Symptom prevalence. CMSAS = Condensed Memorial Symptom Assessment Scale.

order) were breathlessness, lack of energy, pain, dry mouth, difficulty sleeping, and worrying. More detail regarding mean scores for individual symptoms appears in the Supplementary Material (Table S1).

The mean Borg score at the time of assessment was 2.63 (SD 1.90). The mean worst (highest) Borg score over the previous 24 hours was 7.55 (SD 3.31), and the mean best (lowest) was 2.33 (SD 1.86). The overall prevalence of pain at any site was 58% (see Fig. 2). Detailed pain results are outlined in Table 4. Mean pain intensity ratings suggest pain was of moderate intensity, and mean bothersomeness ratings (ranging from 2.4–3.2; max score 4) suggest that pain was a significant concern to patients.

There was no statistically significant correlation between the CMSAS summary score and a range of clinical or demographic variables including age, APACHE II score, breathlessness measures, length of hospital stay, Charlson score, or Karnofsky score as detailed in the Supplementary Material (Table S2).

Discussion

The wide array of symptoms described by patients with hypercapnic respiratory failure highlights the importance of symptom assessment. Breathlessness was, unsurprisingly, highly prevalent (although not universal) and was often reported as severe and distressing. Dry mouth, perhaps related to anticholinergic medication, diuretics, and/or NIV itself, has a high prevalence and bothersomeness, suggesting the need for ameliorating strategies. Lack of energy, while clinically explicable, was reported as bothersome and may be linked to other prevalent, bothersome symptoms, including poor sleep and feeling drowsy. Pain was both prevalent and bothersome. More than half

Table 3
Number of Symptoms and Number of Severe Symptoms Reported

Symptom Type	Mean Number of Symptoms (±SD)	Mean Number of Severe Symptoms (±SD)	Median Number of Symptoms (IQR)	Median Number of Severe Symptoms (IQR)
Total CMSAS symptoms	8.7 ± 2.3	4.4 ± 2.7	8 (7–10)	4 (3–6)
CMSAS physical symptoms[a]	6.9 ± 1.9	3.4 ± 2.1	7 (6–8)	3 (2–4.75)
CMSAS psychological symptoms[a]	1.7 ± 0.8	1.0 ± 1.0	1 (0.25–2)	1 (0–2)
Other physical symptoms[b]	2.0 ± 1.1	0.7 ± 1.0	2 (1–3)	0 (0–1.75)
Total symptoms	10.7 ± 3.0	5.1 ± 3.0	10 (9–13)	5 (3–7)

CMSAS = Condensed Memorial Symptom Assessment Scale; NIV = noninvasive ventilation.
For detailed description of CMSAS scoring, see *Table S1* in *Supplementary Material*.
[a]The CMSAS includes assessment of 11 physical and three psychological symptoms.
[b]Symptoms assessed were cough, sputum, gastric bloating, and dry eyes.

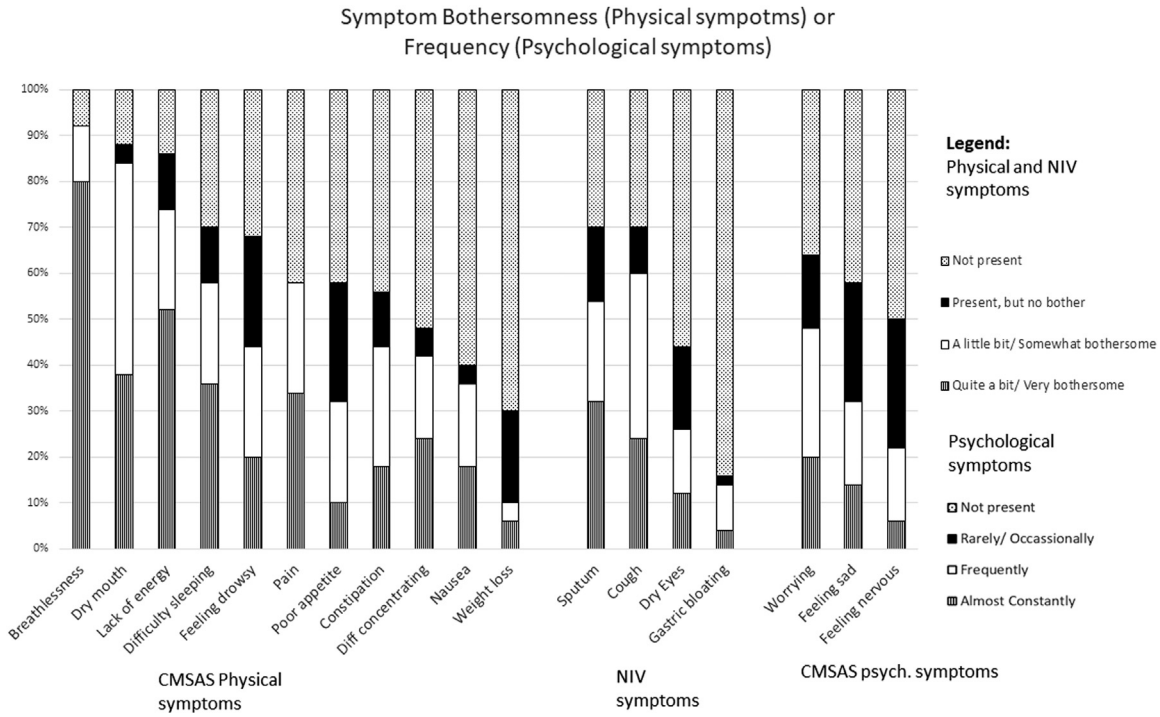

Fig. 3. Symptom bothersomeness or frequency. CMSAS = Condensed Memorial Symptom Assessment Scale; psych. = psychological.

the cohort reported constipation. Psychological symptoms were highly prevalent with half of the cohort reporting *all three* psychological symptoms assessed.

To our knowledge, this is the first study to assess a wide breadth of symptoms using a validated symptom assessment instrument in inpatients with respiratory failure requiring treatment with NIV, although another study has described the related concept of HRQoL in this population.[9] Symptoms reported in this study are similar to other studies conducted in patients with COPD or heart failure in both the inpatient and outpatient setting.[3–5,8,20] The CMSAS summary and subscale scores in our population are higher than those had been found in two predominantly outpatient cancer populations[12,21] and lower than those reported in a tracheotomized ICU stepdown population[22] and in an underserved Chinese-American cancer population.[23]

Table 4
Detailed Pain Assessment

Pain Location	Prevalence,[a] n (%)	Severity,[b] mean ± SD	Bothersomeness,[c] mean ± SD
Nasal bridge	8 (17)	4.4 ± 2.6	2.4 ± 1.1
Chest	11 (24)	6.4 ± 2.4	3.2 ± 1.0
Elsewhere	22 (48)	6.4 ± 2.8	2.9 ± 1.1

For detailed description of CMSAS scoring, see *Table S1* in *Supplementary Material*.
[a]The total number of patients able to complete reporting of detailed pain data is 46—four patients declined to answer this part of the assessment as they were feeling too fatigued. NB: patients may report pain in more than one location.
[b]Severity is rated on a 0–10 numerical rating scale. Mean score for patients reporting pain.
[c]Bothersomeness rated as per the CMSAS, range 0–4. (0 = not present; 4 = very bothersome).

As expected, breathlessness was found to be a high burden symptom with a mean maximum Borg score of 7.55. Although clinicians routinely ask about breathlessness, it is not commonly quantified objectively in the inpatient setting. Structured and comprehensive assessment of breathlessness may lead to improved clinical management.[24]

Pain was also found to be prevalent, with pain "elsewhere" reported most often. Pain is common in both COPD and heart failure.[25,26] Similar to our findings, patients with cardiorespiratory disease describe pain in a variety of bodily locations.[5,25,27] NIV mask-associated nasal bridge pain was less prevalent than estimated by an older review article.[28] Improvements in mask technology may account for some of this difference. Given the interaction between pain, breathlessness, and quality of life, treatment interventions targeting one symptom might lead to improvement in overall in quality of life and diminish patient distress.[25,26]

When assessed in the stable outpatient context, psychological symptoms are common in patients with COPD and heart failure.[4,5] Given the stress associated with hospitalization, the high prevalence reported in this study is unsurprising. Understanding the epidemiology of these phenomena is a starting point for developing effective management strategies.

Difficulty sleeping was reported by 70% of patients in this study. A recent qualitative study reported patients perceive the ability to sleep once NIV is initiated as, of itself, therapeutic.[29] Poor sleep has been associated with both late NIV failure and delirium.[30,31] More research is needed to determine if improving sleep can reduce delirium.

Systematic assessment of symptoms increases the detection of clinically important symptoms.[32] It remains unclear which instrument should be used for routine assessment. Although the COPD Assessment Test has been predominantly used in outpatient settings, it has also been used to assess hospital inpatients[33] and is a measure of overall COPD-related health status rather than a symptom measure per se.[34] Items in the COPD Assessment Test would capture some prevalent symptoms (e.g. cough, mucus/sputum and sleep), but some high burden symptoms (particularly dry mouth and psychological symptoms) would be missed. The data contained in this study, if replicated, might inform the development of a symptom assessment instrument for inpatients. Given the importance of the inpatient care, both in terms of patient outcomes and health economics, instruments specifically assessing this may serve to inform, develop, and assess effective models of care.

The broad range of symptoms reported in this study suggests that clinicians who deliver NIV should be skilled in detecting and managing symptoms concurrently with delivering NIV. The range and intensity of symptoms reported here suggests that patients may have complex symptom needs and expert input from palliative care teams may be additive. In end-stage renal failure, palliative care clinicians are increasingly being embedded within the renal care teams.[35] This study raises a question of whether similar strategies might be effective for patients with respiratory failure.

Optimal symptom assessment and management, including both physical and psychological symptoms, has many implications that go beyond the individual patient experience. For example, these may influence discharge readiness and readmission rates, which may have a significant patient and health economic impact. Understanding longitudinal changes in symptoms, from admission through to postdischarge follow-up, may allow clinicians to provide reassurance that some symptoms resolve with time, while prioritizing management of symptoms which appear most persistent and/or troublesome.

To our knowledge, this study is the first to look at the broad symptom experience of a population treated with NIV from a subjective perspective. We assessed patients within 36 hours of hospitalization giving an insight into symptomatology close to the beginning of admission, but the study does not provide longitudinal data, and this would be an important area for follow-up research. The choice of the CMSAS to assess symptom burden deserves some comment. This tool has only been validated in a cancer population[12] though has been used in a stepdown ICU population.[22] Two potentially relevant modifications of the original Memorial Symptom Assessment Scale (from which the CMSAS is derived) have been undertaken—one in a population with heart failure and the other in a population with COPD—with both reporting good validity and reliability.[27,36] Both these instruments were thought to be too long for patients with acute respiratory failure to complete. In developing the Memorial Symptom Assessment Scale—Short form, Chang et al. demonstrated that correlation between symptom scores and HRQoL remained strong when only the bothersomeness of physical symptoms and the frequency of psychological symptoms are assessed.[37] Thus, to minimize respondent burden in this very ill inpatient population, the CMSAS was chosen.

There are other symptom assessment tools available, which are short and could be potentially useful in this context. For example, the Edmonton Symptom Assessment Scale assesses the intensity of 8–10 symptoms depending on the version used[38] and the Symptom Distress Scale[39,40] assesses a combination of intensity, frequency, and distress but does not include psychological symptoms that were thought to be important in this population. Based on Chang et al.'s work, we conclude that bothersomeness is more informative than intensity.[12] As we were interested in a broad range of symptoms, tools that focus predominantly on respiratory symptoms, such as the Chronic Bronchitis Symptom Assessment scale[41] or the Breathing Problems Questionnaire,[42] were thought to be too narrow in scope. We should acknowledge differences between our administration of the CMSAS and the method reported. First, we administered this instrument verbally for this very ill population. Second, the wording of the physical symptom question in our study varied slightly from the original CMSAS instrument. The original CMSAS asks "How much did *the (*symptom*) bother or distress* you?"[12] and in this study, patients were simply asked, "How much did the (symptom) *bother* you?" In addition, the time frame about which the symptom enquiry was "in the last 72 hours" was different from the original instrument which is "in the last 7 days."

The clinical heterogeneity of this population reflects the real-world experience of patients with respiratory failure. Generalizability may be limited by the large number of potential participants excluded and the inclusion of only English-speaking participants who underwent arterial blood gas sampling before initiating NIV. The symptoms of those who

do not speak English and/or did not undergo arterial blood gas assessment before commencing NIV may be different, and exploring these would be important future work. In addition, the examined cohort included a disproportionately high number of women, again limiting generalizability. No correlation between symptom burden and other clinical demographics was found, perhaps partially explained by the relatively small number of participants. We did not specifically assess "anxiety," although we did assess "feeling nervous" and "worrying" and found they were common. Future studies might explore differences in these emotional states from the patient perspective. The Cronbach alpha for the CMSAS summary score and CMSAS psychological score are acceptable (0.72 and 0.74, respectively). The relatively low Cronbach alpha for the CMSAS physical subscale (0.65) may suggest that the bothersomeness of some physical symptoms are relatively independent of each other, perhaps due to our combination of high and low prevalence symptoms. Future studies enrolling a larger cohort would be necessary to undertake valid statistical analysis to establish this.

Conclusions

These patients with acute respiratory failure requiring NIV reported a high prevalence of a wide range of physical and psychological symptoms, reporting a median of 10 symptoms, five of which were severe. The breadth and prevalence of symptoms reported suggests an opportunity to develop treatment strategies that address the total patient experience, laying the foundation for developing clinically useful tools for quantifying symptom burden in inpatients with respiratory failure. Such work is crucial to developing a truly person-centered approach to addressing the needs of people treated with NIV.

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Data statement: Original data are available from the authors on application.

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Supplementary Material

Mean symptom score for people with hypercapnic respiratory failure treated with NIV, all symptoms assessed using the Condensed Memorial Symptom Assessment Scale.

Table S1
Individual Symptom Mean Scores

	Mean	SD
Bothersomeness of CMSAS physical symptoms		
SOB	3.25	1.246
Lack of energy	2.38	1.441
Dry mouth	2.37	1.262
Pain	1.84	1.699
Difficulty sleeping	1.82	1.567
Feeling drowsy	1.33	1.358
Difficulty concentrating	1.25	1.492
Constipation	1.20	1.316
Lack of appetite	1.04	1.224
Nausea	0.99	1.39
Weight loss	0.42	.828
Frequency of psychological symptoms		
Worrying	1.96	1.607
Feeling sad	1.57	1.528
Feeling nervous	1.27	1.381
Bothersomeness of other symptoms potentially prevalent in patients treated with NIV		
Sputum	1.71	1.451
Cough	1.70	1.401
Dry eyes	0.87	1.244
Gastric bloating	0.34	.849

CMSAS = Condensed Memorial Symptom Assessment Score; NIV = noninvasive ventilation.
See *Table 1* of main manuscript for description of the CMSAS scoring system and Methods for rationale for additional symptoms.

Details of correlation between Condensed Memorial Symptom Assessment Scale (CMSAS) summary score and other variables.

Table S2
CMSAS Total Score Correlation With Other Variables

Variable	Correlation Coefficient	*P* Value
Age	−0.19	0.19
pH[a]	0.07	0.62
$PaCO_2$[a]	−0.06	0.66
Borg score at assessment	0.092	0.53
Best Borg	0.05	0.71
Worst Borg	0.10	0.51
Total hours on NIV	−0.081	0.58
Initial respiratory rate	−0.131	0.53
APACHE II	−0.087	0.55
NYHA	−0.078	0.59
mMRC	−0.093	0.52
Charlson	0.038	0.79
Karnofsky	0.227	0.11
Length of hospitalization (days)	0.095	0.529

CMSAS-SUM = Condensed Memorial Symptom Assessment Scale—Summary score; NIV = noninvasive ventilation; APACHE = Acute Physiology and Chronic Health Evaluation; NYHA = New York Heart Association breathlessness score; mMRC = modified Medical Research Council breathlessness score.
[a]pH and PaCO2—as assessed on arterial blood gas analysis either before initiation of NIV or within 30 minutes of NIV initiation.