Adverse Effects, Smoking, Alcohol Consumption, and Quality of Life during Long-Term Oxygen Therapy

A Nationwide Study

Filip Björklund[1] and Magnus Ekström[1,2]

[1]Respiratory Medicine and Allergology, Department of Clinical Sciences Lund, Faculty of Medicine, Lund University, Lund, Sweden; and
[2]Department of Medicine, Blekinge Hospital, Karlskrona, Sweden

ORCID IDs: 0000-0002-5199-3570 (F.B.); 0000-0002-7227-5113 (M.E.).

Abstract

Rationale: Long-term oxygen therapy (LTOT) is prescribed for at least 15 hours per day and often used by patients for several years, but knowledge is limited regarding adverse effects, risk exposures, and health-related quality of life (HrQoL) among those treated.

Objectives: To determine the prevalence of adverse effects, smoking, and alcohol consumption and their relations to HrQoL among patients treated with LTOT.

Methods: This was a cross-sectional survey of a randomized sample of adults with ongoing LTOT in the Swedish National Registry for Respiratory Failure (Swedevox). Patient characteristics and the prevalence of 26 prespecified adverse effects, smoking, and alcohol consumption, were compared between respondents with better and worse HrQoL on the chronic obstructive pulmonary disease assessment test.

Results: A total of 151 respondents were included (mean age, 74.7 yr [standard deviation, 8.6 yr]; 58.9% women; median LTOT duration, 2.2 yr [interquartile range, 1.0–3.8 yr]). Characteristics upon starting LTOT were similar between respondents and nonrespondents. Active smoking was very rare ($n = 4$, 2.6%). For alcohol use, 67.2% of participants reported no consumption during an average week, whereas risk use was reported by 25.8% of men and 16.9% of women. The most prevalent adverse effects were reduced mobility or physical activity (70.9%), dry mouth (69.5%), congestion or nasal drip (61.6%), increased tiredness (57.0%), and dry nose (53.0%). Patients with higher numbers of total and systemic adverse effects experienced worse HrQoL, whereas no associations were found for smoking status or alcohol consumption. The majority (54.8%) of adverse effects were untreated and unreported to health professionals.

Conclusions: Adverse effects are common among patients with LTOT and are associated with worse HrQoL. As the majority of adverse effects had not been discussed or treated, structured assessment and management of risk exposures and adverse effects is warranted.

Keywords: adverse effects; alcohol consumption; HrQoL; LTOT; smoking

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Correspondence and requests for reprints should be addressed to Magnus Ekström, M.D., Ph.D., Department of Medicine, Blekinge Hospital, Lasarettsvägen, SE-37185, Karlskrona, Sweden. E-mail: pmekstrom@gmail.com.

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Long-term oxygen therapy (LTOT) prescribed for at least 15 hours per day improves survival in patients with severe chronic resting hypoxemia (1, 2). Evidence for the use of LTOT pertains to two randomized controlled trials from the late 1970s in patients with chronic obstructive pulmonary disease (COPD), but in clinical practice, LTOT is also commonly prescribed for patients with other diagnoses, such as interstitial lung disease or pulmonary arterial hypertension using the same criteria as for COPD (1–4). As patients are normally initiated on LTOT as a consequence of severe illness and poor health status, they may also be likely to experience high degrees of symptoms and adverse effects related to underlying disease and treatment, be more sensitive to related risk exposures such as smoking and alcohol use, and be prone to impairments in health-related quality of life (HrQoL) (5). However, knowledge regarding adverse effects, smoking, alcohol use, and HrQoL among these patients is limited.

The largest study to date of adverse effects related to LTOT was performed by Kampelmacher and colleagues in the early 1990s and included 528 patients in the Netherlands (6). It reported a high prevalence of adverse effects, most commonly related to restricted autonomy and local symptoms from the mouth and nose. The study was, however, limited to patients being provided oxygen by a single company and located within a relatively small geographic area, and in addition, the study population differed from a modern patient group in regards of age, sex, LTOT duration, equipment used, and reason for oxygen prescription (6, 7). Since then, qualitative studies have further suggested that practical problems related to equipment, reductions in mobility, and social stigmatization are common among patients treated with LTOT, but no additional quantitative studies have, to our knowledge, been performed (8–10).

Active smoking during oxygen treatment is known to pose a risk of burn injury or fire, and although most guidelines consider active smoking a contraindication for LTOT, studies from some regions have previously estimated that more than 20% of patients smoke at initiation of therapy (1, 2, 11–16). Heavy alcohol use is, like smoking, known to be a potential cause of negative long-term health effects and could negatively affect the ability of patients to manage their oxygen equipment in a safe and beneficial manner (17).

The HrQoL experienced by patients with LTOT has previously been reported by a small number of studies, which have generally presented poor scores (18–22). To our knowledge, no study has investigated the potential associations between HrQoL and modifiable factors such as adverse effects, alcohol consumption or smoking. Elucidating the prevalence of adverse effects, alcohol consumption, and smoking in patients treated with LTOT could contribute to improvements in care for those affected and could potentially contribute to enhancing patient adherence, which is currently known to be suboptimal among many patients (23, 24).

The objective of this study was to determine the prevalence of adverse effects, smoking, and alcohol consumption and their relations to HrQoL among patients treated with LTOT.

Methods

This was a cross-sectional, survey-based study of patients with ongoing LTOT in the Swedish National Registry for Respiratory Failure (Swedevox), a quality register containing prospective data on ∼85% of all patients having started LTOT in Sweden since 1987 (5, 7). From Swedevox, a randomized sample of patients ($N = 650$) aged 18 years or older and with ongoing LTOT as of January 12, 2021, was obtained (from a total of 2,327 patients with ongoing LTOT in the registry). For the random sample, data were obtained from Swedevox on age, sex, body mass index, treatment duration, and underlying cause for starting LTOT, along with the arterial blood gas values, spirometry values, oxygen prescription, World Health Organization performance status and COPD assessment test (CAT) score reported at the start of their treatment with LTOT. No data regarding patient comorbidities such as sleep disordered breathing were available for analysis. At the time of the survey, sampled patients in this study had used LTOT for between 0.2 and 28.1 years (median, 2.4 yr; interquartile range, 1.1–4.4 yr).

The study is reported in accordance with the Strengthening the Reporting of Observational studies in Epidemiology guidelines (25). Ethical approval was granted by the Swedish Ethical Review Agency (Identifier: 2020–04528).

Survey

Each patient in the sample was sent a postal survey and was asked to return it in an enclosed envelope after completion. The survey (provided in an English translation in the online supplement) contained questions regarding physiological and social data, oxygen prescription and usage, sleep, adverse effects, smoking, alcohol consumption, and the standardized instruments CAT, Short Form-12 (SF-12), and the Euro-QoL-5D Visual Analogue Scale (EQ-VAS). In total, 26 specified adverse effects selected from previous qualitative studies and from clinical experience of patients treated with short- or long-term oxygen were provided (6, 8, 10, 26). For each adverse effect, patients were asked to indicate the experienced frequency since initiating LTOT (never, yearly or more rarely, several times per year, monthly, weekly, or daily), and whether (yes, no, or not applicable) each experienced adverse effect had been treated or discussed with healthcare personnel. For smoking, patients were asked to indicate smoking status (never, former, current occasional, or current daily), smoking duration, average daily amount of tobacco smoked, and whether they ceased smoking before or after starting their oxygen treatment. Patients who reported smoking after initiating treatment were asked to indicate whether they had disclosed this information to healthcare personnel and the average daily amount of tobacco smoked since initiating treatment. All patients were also asked to indicate any eventual exposure to secondhand smoke (never, occasionally, or daily). For alcohol consumption, patients were asked to indicate their average weekly consumption of beer (cans or bottles), wine (bottles), and spirits (cl).

Patients who did not return their survey and did not otherwise contact the researchers regarding their participation within 2 weeks obtained a postal reminder. Nonresponders were defined as patients who either did not return their survey within a further 2 weeks from obtaining a reminder, or patients who did return their survey without fully

completing the CAT or indicating the frequency of any adverse effect, as these variables were used to calculate main outcomes.

Statistical Analyses

Patient characteristics reported to Swedevox upon initiation of LTOT were compared between respondents and nonrespondents using Student's *t* tests (for continuous variables with normal distributions), Mann-Whitney *U* tests (for ordinal data and continuous variables with nonnormal distributions) and χ^2-tests (for categorical variables). Nonrespondents were not included in further analysis.

Using survey data, respondents were then dichotomized based on HrQoL using a cutoff at the median CAT score as having better HrQoL (CAT $\leq$ 24), or worse HrQoL (CAT $>$ 24). The CAT was chosen for dichotomization as previous research supports its use as an HrQoL instrument among patients with both COPD and ILD, who together make up the absolute majority of LTOT users in Sweden. (7, 27–32) Sensitivity analyses of HrQoL dichotomization were performed by *1*) analyzing the correlation between CAT scores and EQ-VAS and SF-12 scores using Spearman's rank correlation; and *2*) recategorizing HrQoL using the median EQ-VAS score as better (EQ-VAS $\geq$ 40) and worse (EQ-VAS $<$ 40).

Characteristics, smoking status (ever-smoker or never-smoker), and average weekly alcohol consumption were tabulated for all respondents and both HrQoL groups individually. Risk use of alcohol was defined as an average weekly consumption of at least 14 standardized units/wk for men and at least 7 standardized units/wk for women.

Statistical comparisons between the groups were performed using Student's *t* tests (for continuous variables with normal distributions), Mann-Whitney *U* tests (for ordinal data and continuous variables with nonnormal distributions), and Fisher exact tests (categorical variables).

Adverse effects were evaluated in terms of their prevalence, frequency, and proportion that had been discussed with or treated by a health professional. For descriptive purposes, prevalent adverse effects were defined as those reported to occur monthly or more often. For each patient, the number of prevalent adverse effects was summed by four categories, local, systemic, practical, and social, as well as in a total sum. To avoid a compound effect of missing values upon summing, adverse effects without an indicated frequency were categorized as nonprevalent in this stage.

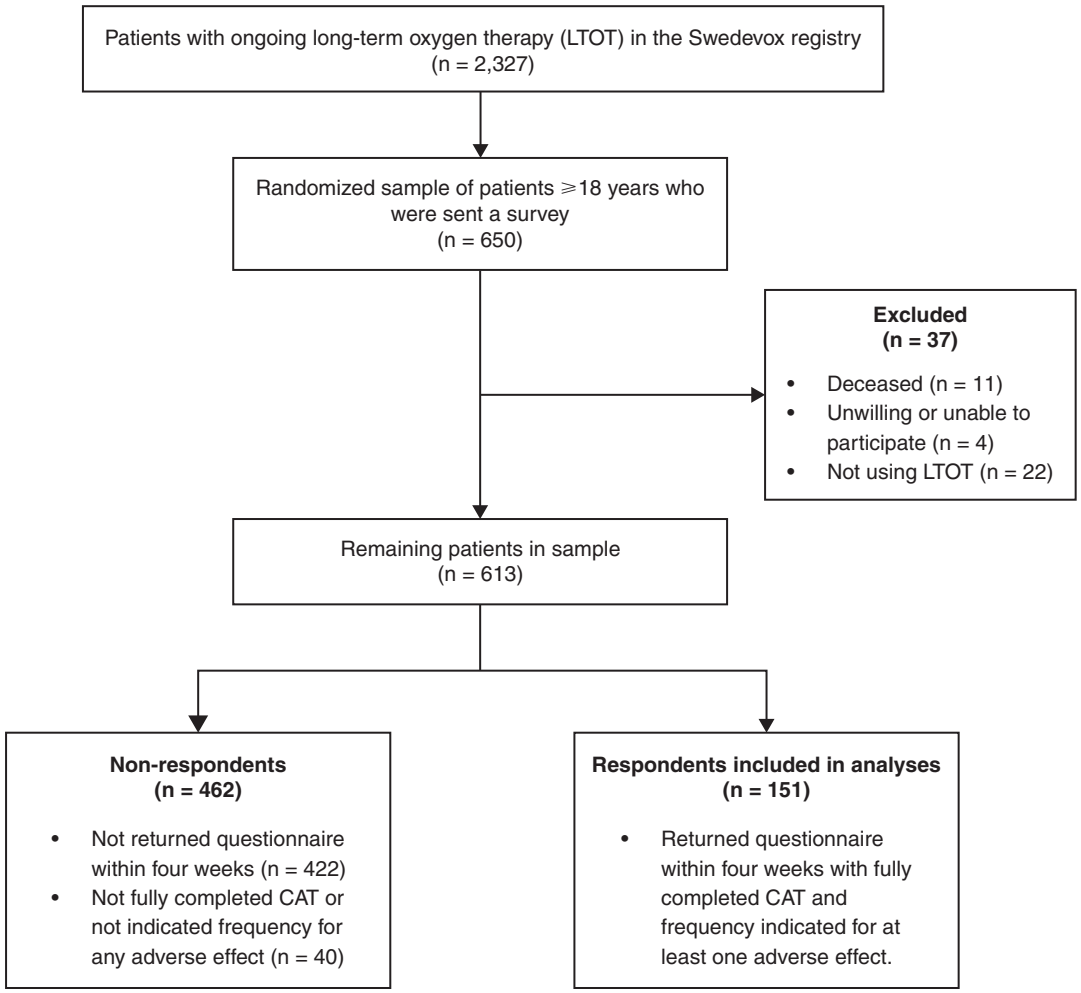

Figure 1. Flowchart of study recruitment. CAT = chronic obstructive pulmonary disease assessment test.

Table 1. Characteristics of 151 survey respondents with long-term oxygen therapy

Characteristic	All Respondents (*n* = 151)	Worse Quality of Life (*n* = 72)	Better Quality of Life (*n* = 79)
Age, mean (SD), yr	74.7 (8.6)	74.5 (9.0)	74.8 (8.4)
Women, *n* (%)	89 (58.9%)	41 (57.0%)	48 (60.8%)
BMI, mean (SD), kg/m^2	26.9 (7.2)	25.7 (7.1)	27.9 (7.2)
Cause for starting LTOT (grouped), *n* (%)			
Airway disease	113 (74.8%)	53 (73.6%)	60 (75.9%)
Parenchymal lung disease	20 (13.2%)	14 (19.4%)	6 (7.6%)
Other	17 (11.3%)	5 (6.9%)	12 (15.2%)
Missing	1 (0.67%)	0 (0%)	1 (1.3%)
Living situation, *n* (%)			
House	65 (43.0%)	27 (37.5%)	38 (48.1%)
Apartment	76 (50.3%)	38 (52.8%)	38 (48.1%)
Assisted care facility	10 (6.6%)	7 (9.7%)	3 (3.8%)
Missing	0 (0%)	0 (0%)	0 (0%)
Social situation, *n* (%)			
Cohabitating partner	91 (60.7%)	44 (61.1%)	47 (59.5%)
Non-cohabitating partner	8 (5.3%)	2 (2.8%)	6 (7.6%)
No partner	51 (34.0%)	25 (34.7%)	26 (32.9%)
Missing	1 (0.67%)	1 (1.4%)	0 (0%)
Oxygen equipment, *n* (%)			
Stationary oxygen concentrator	140 (92.7%)	68 (94.4%)	72 (91.1%)
Portable oxygen concentrator	111 (73.5%)	53 (73.6%)	58 (73.4%)
Compressed gas cylinders	10 (6.6%)	4 (5.6%)	6 (7.6%)
Liquid oxygen	9 (6.0%)	1 (1.4%)	8 (10.1%)
Nasal cannula	147 (97.4%)	72 (100.0%)	75 (94.9%)
Oxygen mask	24 (15.9%)	7 (9.7%)	17 (21.5%)
High flow cannula	7 (4.6%)	2 (2.8%)	5 (6.3%)
Years since LTOT start, median (IQR)	2.2 (1.0–3.8)	2.4 (1.2–3.5)	1.7 (0.9–4.4)
Reported oxygen prescription, median (IQR)			
Time (h/d)	24 (16–24)	24 (16–24)	21.5 (16–24)
Flow rate (l/min)	2 (1.1–3)	2 (1.5–3)	2 (1–2.75)
Variable flow, daytime, L/min	2 (1.5–3)	2 (1.5–3)	2 (1.5–3)
Variable flow, nighttime, L/min	2 (1.5–2.75)	2 (1.5–2.5)	2 (1.5–3)
Variable flow, effort, L/min	3 (2–4)	2.25 (1.75–3.5)	3 (2.5–4)
Reported oxygen use, median (IQR)			
Time, h/d	24 (17–24)	24 (20–24)	23 (16–24)
Flow rate, L/min	2 (1.35–3)	2 (1.5–3)	2 (1–3)
Variable flow, daytime, L/min	2 (1.3–2.875)	2 (1.5–3)	2 (1–2.5)
Variable flow, nighttime, L/min	2 (1.5–2.75)	2 (1.5–3)	2 (1–2.5)
Variable flow, effort, L/min	3 (2–4)	2.5 (2–4)	3 (2–4)
Oxygen use during nighttime	145 (96.0%)	68 (94.4%)	77 (97.5%)
Sleep quality, *n* (%)			
Very good	22 (14.6%)	8 (11.1%)	14 (17.7%)
Good	51 (33.8%)	20 (27.7%)	31 (39.2%)
Fairly good	57 (37.7%)	27 (37.5%)	30 (38.0%)
Poor	17 (11.3%)	14 (19.4%)	3 (3.8%)
Very poor	4 (2.6%)	3 (4.2%)	1 (1.3%)
Missing	0 (0%)	0 (0%)	0 (0%)
Sleep time, median (IQR), h	7 (6–8)	7 (6–8)	7 (6–8)
Smoking status, *n* (%)			
Never-smoker	23 (15.5%)	11 (15.3%)	12 (15.2%)
Ever-Smoker	124 (82.1%)	60 (83.3%)	65 (82.3%)
Missing	4 (2.6%)	1 (1.4%)	3 (3.8%)
Alcohol, median (IQR), weekly standard units	0 (0–1.8)	0 (0–0.25)	0 (0–3)
HrQoL, mean (SD)			
CAT	24.0 (6.7)	29.6 (3.4)	18.9 (4.5)
EQ-VAS	40.0 (19.8)	32.2 (16.4)	48.4 (19.7)
SF-12 MCS	40.9 (13.2)	34.5 (12.7)	46.9 (10.7)
SF-12 PCS	27.0 (8.5)	25.0 (7.4)	28.8 (9.0)

Definition of abbreviations: BMI = body mass index; CAT = chronic obstructive pulmonary disease assessment test; EQ-VAS = EuroQoL visual analogue scale; HrQoL = health-related quality of life; IQR = interquartile range; LTOT = long-term oxygen therapy; MCS = mental component summary; PCS = physical component summary; SD = standard deviation; SF-12 = short form-12.
Characteristics of patients with better and worse HrQoL were compared using Student's *t* test (continuous variables with normal distributions), the Mann-Whitney *U* test (ordinal and continuous variables with nonnormal distributions), and Fisher exact test (categorical variables).

The prevalence of adverse effects was compared between patients with better and worse HrQoL using Mann-Whitney *U* tests. A secondary analysis of the correlation between continuous CAT score and the number of prevalent adverse effects in total and in each group was also performed using Spearman's rank correlation. Adverse effect frequencies are reported without imputation of missing items. No other imputations of missing variables were made. Statistical analyses were conducted using Stata version 16.0 (StataCorp).

Results

From the initial random sample of 650 patients, 206 (31.7%) surveys were returned (Figure 1). Of these, 151 (23.2%) contained sufficient data to be included in the analysis as respondents (Table 1). Thirty-seven (5.7%) sampled patients were deceased, unwilling to participate, or reported no current use of LTOT and were excluded from all analyses. The remaining 462 (71.1%) patients in the sample who did not return their survey or returned a survey that could not be analyzed for main outcomes were categorized as nonrespondents (Figure 1). Characteristics were similar between respondents and nonrespondents, including age, sex, and LTOT duration at the time of the survey, as well as physiological measures, WHO performance status, and CAT score at the start of treatment (Table 2).

Characteristics of the 151 respondents are shown in Table 1. The mean age was 74.7 (standard deviation [SD], 8.6) years, 89 (58.9%) were women, and the mean body mass index was 26.9 (SD, 7.2) kg/m^2. The main underlying causes for LTOT treatment were airway disease (75.3%) and parenchymal lung disease (13.3%). The median LTOT duration was 2.2 (interquartile range [IQR], 1.0–3.8) years. Most respondents reported living outside of an assisted care facility and with a partner. The most common types of oxygen equipment used were stationary and/or portable oxygen concentrators, whereas compressed and liquid oxygen were used by a minority. For oxygen delivery, a majority of patients used nasal cannulae. More than half of all respondents (55.6%) had been prescribed oxygen for 24 hours per day, with a mean prescribed oxygen flow rate of 2.2 (SD, 1.2) L/min. Twenty (13.2%) respondents reported using oxygen for fewer hours than they had been prescribed, with a median difference of 3.5 (IQR, 1.75–5.5) hours. Eighteen (11.9%) respondents used oxygen for less than 15 hours per day.

Ever-smoking was reported by 125 (82.8%) respondents, with a mean smoking duration of 37.7 (SD, 13.8) years and a previous median daily consumption of 20 (IQR 12.25–20) cigarettes per day. Current active smoking was reported by four (2.6%) respondents, all of whom reported smoking four or fewer cigarettes per day. Secondhand smoke exposure was reported by 15 (9.9%) respondents. Average weekly alcohol consumption was reported as none by 67.2% of respondents, whereas risk use of alcohol was reported by 25.8% of male respondents (⩾14 standardized units/wk) and 16.9% of female respondents (⩾7 standardized units/wk).

Adverse effects in terms of prevalence and frequency are shown in Table 3 and Figure 2. Out of the 26 prespecified adverse effects, the total number of prevalent adverse effects was a median 8 (IQR, 4–12) per respondent. The individual adverse effects

Table 2. Comparison of survey respondents and nonrespondents based on baseline data reported to Swedevox

Characteristic at Starting LTOT	Nonrespondents (*n* = 462)	Respondents (*n* = 151)
Age, mean (SD), yr	75.0 (10.6)	74.7 (8.6)
Women, *n* (%)	321 (69.5%)	89 (58.9%)
BMI, mean (SD), kg/m^2	27.8 (8.34)	28.1 (7.63)
Cause for starting LTOT (grouped), *n* (%)		
Airway disease	321 (69.9%)	113 (75.3%)
Parenchymal lung disease	41 (8.9%)	20 (13.3%)
Other	97 (21.1%)	17 (11.3%)
Missing	3 (0.65%)	1 (0.67%)
Years since LTOT start, median (IQR)	2.5 (1.2–4.7)	2.2 (1.0–3.8)
Arterial blood gas values, median (IQR)		
Pa_{O_2} air	6.7kPa (6.1–7.1) 50.3mm Hg (45.8–53.3)	6.9kPa (6.3–7.2) 51.8 mm Hg (47.3–54.0)
Pa_{O_2} oxygen	8.5kPa (7.9–9.1) 63.8 mm Hg (59.3–68.3)	8.7kPa (8.0–9.4) 65.3 mm Hg (60.0–70.5)
Pa_{CO_2} air	5.8 kPa (5.0–6.6) 43.5 mm Hg (37.5–49.5)	5.6 kPa (4.7–6.4) 42.0 mm Hg (35.3–48.0)
Pa_{CO_2} oxygen	6.0 kPa (5.1–6.9) 45.0 mm Hg (38.3–51.8)	5.9 kPa (4.9–6.6) 44.3 mm Hg (36.8–49.5)
Spirometry, median (IQR)		
FEV_1, L	0.9 (0.6–1.5)	1.1 (0.7–1.5)
FEV_1, % of predicted	41.7 (28.2–62.1)	42.0 (31.4–55.6)
Oxygen prescription at treatment initiation, median (IQR)		
Time, h/d	16 (16–24)	16 (16–20)
Flow rate, L/min	1.5 (1–2)	1.5 (1–2)
CAT score, mean (SD)	20.9 (6.6)	20.0 (7.5)
WHO performance status, median (IQR)	1 (1–3)	1 (1–2)

Definition of abbreviations: BMI = body mass index; CAT = chronic obstructive pulmonary disease assessment test; FEV_1 = forced expiratory volume in 1 second; IQR = interquartile range; LTOT = long-term oxygen therapy; Pa_{CO_2} = partial pressure of carbon dioxide in arterial blood; Pa_{O_2} = partial pressure of oxygen in arterial blood; SD = standard deviation; Swedevox = Swedish National Registry for Respiratory Failure; WHO = World Health Organization.
Characteristics of respondents and nonrespondents were compared using Student's *t* test (continuous variables with normal distributions), the Mann-Whitney *U* test (ordinal and continuous variables with non-normal distributions), and Pearson's chi^2 test (categorical variables).

Table 3. Prevalence of adverse effects overall and by health-related quality of life

Adverse Effects	All Respondents (*n* = 151)	Worse Quality of life (*n* = 72)	Better Quality of Life (*n* = 79)	*P* Value
Local, median (IQR)	**4 (2–6)**	**4 (2–6)**	**3 (2–6)**	**0.24**
Dry mouth	69.5%	76.4%	63.3%	
Nasal congestion or drip	61.6%	63.9%	59.5%	
Dry nose	53.0%	52.8%	53.2%	
Hoarseness	36.4%	41.7%	31.6%	
Nasal bleeding	31.8%	27.8%	35.4%	
Pain or soreness in nose	27.2%	26.4%	27.8%	
Worsened or changed sense of smell	21.9%	25.0%	19.0%	
Worsened or changed sense of taste	19.9%	23.6%	16.5%	
Irritated skin or chafing	19.2%	22.2%	16.5%	
Pain or soreness in throat	15.2%	19.4%	11.4%	
Dental issues	13.9%	20.8%	7.6%	
Pain or soreness in mouth	11.3%	11.1%	11.4%	
Systemic, median (IQR)	**3 (1–5)**	**4 (2–6)**	**3 (1–4)**	**<0.001**
Increased tiredness	57.0%	62.5%	51.8%	
Increased amount of phlegm	50.3%	66.7%	35.4%	
Increased thirst	47.0%	48.6%	45.6%	
Cough	45.7%	63.9%	29.1%	
Difficulty sleeping	34.4%	40.3%	29.1%	
Dizziness	28.5%	36.1%	21.5%	
Reduced appetite	27.2%	37.5%	17.7%	
Headache during other parts of the day	20.0%	26.4%	13.9%	
Morning Headache	18.5%	25.0%	12.7%	
Practical, median (IQR)	**1 (0–1)**	**1 (1–1)**	**1 (0–1)**	**0.55**
Reduced mobility or physical activity	70.9%	73.6%	68.4%	
Trip or fall due to oxygen equipment	11.9%	12.5%	11.4%	
Burn injury or fire	0.6%	0.0%	1.3%	
Social, median (IQR)	**0 (0–1)**	**0 (0–1)**	**0 (0–1)**	**0.21**
Sense of loneliness or social isolation	35.1%	41.7%	29.1%	
Sense of shame	14.7%	15.3%	13.9%	
Total number of adverse effects, median (IQR)	**8 (4–12)**	**9 (5–13)**	**7 (3–11)**	**0.011**

Definition of abbreviation: IQR = interquartile range.
Bold numbers denote the median number of experienced adverse effects in each category. Median number of adverse effects were compared between patients with better and worse health-related quality of life using Mann-Whitney *U* tests.

with the highest reported prevalence were reduced mobility or physical activity (70.9%), dry mouth (69.5%), congestion or nasal drip (61.6%), increased tiredness (57.0%), and dry nose (53.0%).

HrQoL was moderately to severely impaired in most respondents, median CAT score 24 (IQR 20–29). Although characteristics were overall similar between respondents reporting better and worse quality of life, patients experiencing worse HrQoL reported significantly worse sleep quality than those with better HrQoL (Table 1). Worse HrQoL was associated with a higher total number of experienced adverse effects, median 9 (IQR, 5–13) versus 7 (IQR, 3–11), $P = 0.011$, which was largely driven by higher numbers of systemic adverse effects, median 4 (IQR, 2–6) versus 3 (IQR, 1–4), $P < 0.001$ (Table 3). No significant associations with HrQoL were found for other adverse effect categories, nor for smoking status or average weekly alcohol consumption. Secondary analysis showed a significant correlation between continuous CAT score and total number of experienced adverse effects (Spearman's rho = 0.36; $P < 0.001$), as well as between CAT score and the individual number of experienced local (Spearman's rho = 0.22; $P = 0.009$), systemic (Spearman's rho = 0.44; $P < 0.001$), and social adverse effects (Spearman's rho = 0.21; $P < 0.011$).

More than half of all prevalent adverse effects (54.8%) were reported to have been untreated and not discussed with a health professional. The adverse effects that were most commonly untreated and unreported were headache during other parts of the day [than the morning] (79.2%), trip or fall due to oxygen equipment (75.0%) and morning headache (75.0%). Excluding a singular reported case of burn injury, the adverse effects that were most commonly discussed or treated were increased amount of phlegm (63.6%), dry nose (62.8%) and nasal congestion or drip (59.5%) (Figure 3).

In sensitivity analyses of HrQoL, statistically significant correlations were found between CAT scores and the EQ-VAS (Spearman's rho = −0.49; $P < 0.001$), SF-12 physical component summary (Spearman's rho = −0.25; $P = 0.003$), and SF-12 mental component summary (Spearman's rho = −0.54; $P < 0.001$), respectively. When quality-of-life groups were redefined by EQ-VAS scores, findings were similar with the exception that significant associations were seen between worse HrQoL and higher numbers of prevalent social adverse effects, median 1 (IQR, 0 to 1) versus 0 (IQR, 0 to 1), $P = 0.003$ and local adverse effects, median 5 (IQR, 2 to 6) versus 3 (IQR, 1 to 5), $P = 0.006$.

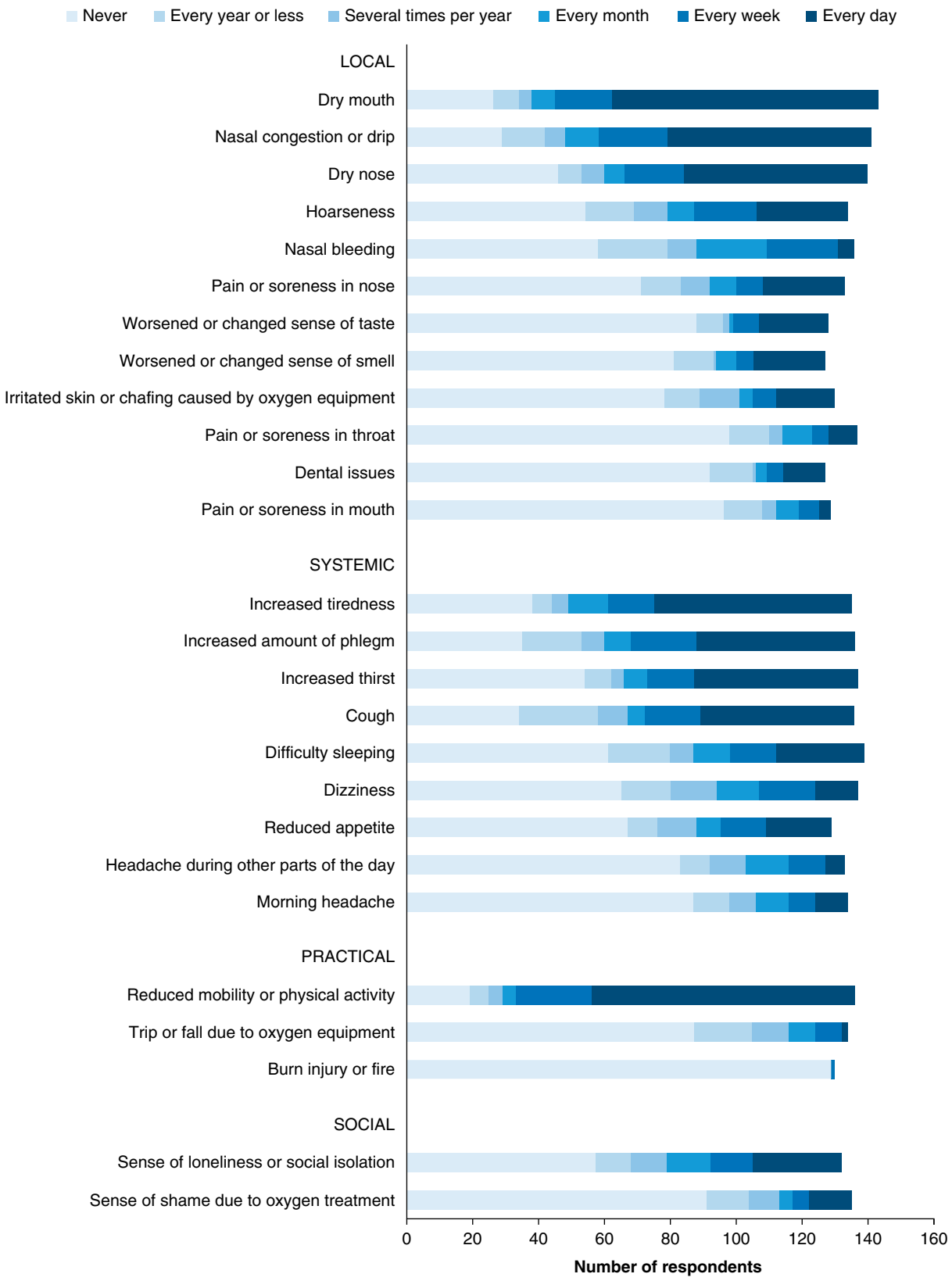

Figure 2. Reported frequencies of adverse effects among all respondents (n=151) with long-term oxygen therapy.

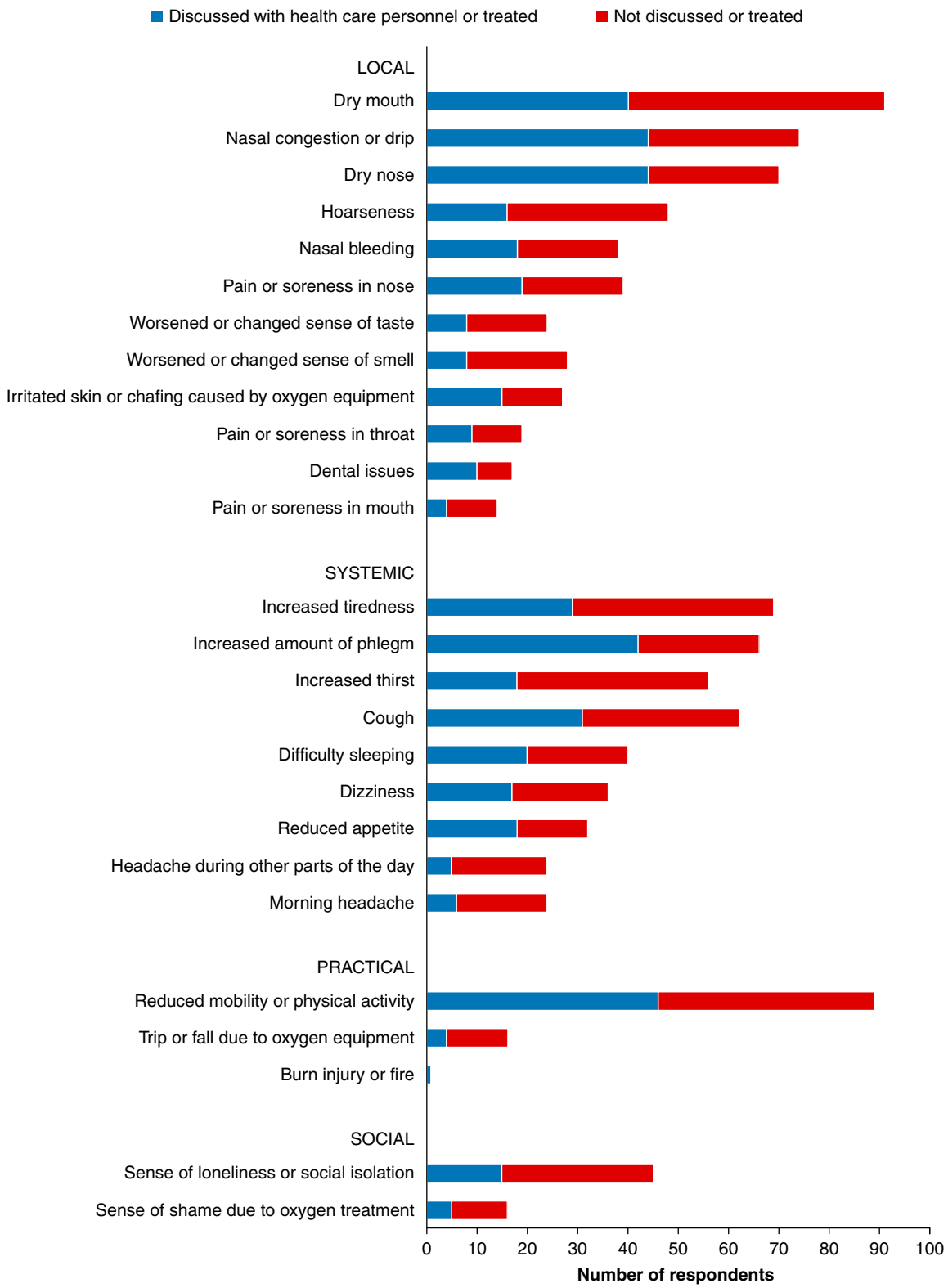

Figure 3. Proportion of prevalent adverse effects that had been discussed with a healthcare professional or treated. Prevalent adverse effects were defined as occurring monthly or more frequently.

Discussion

The main findings of this study are that adverse effects were common among patients with LTOT and most commonly related to reduced mobility, local symptoms from the mouth and nose, and increased tiredness. Other common and debilitating adverse effects were loneliness and sense of shame. It is notable that a majority of respondents used portable oxygen concentrators, and that use of oxygen canisters or other larger equipment common in some settings could likely further exacerbate complaints related to reduced mobility, which was reported as the most common adverse effect. HrQoL was generally reported as poor, with a significant association between worse quality of life and a greater total number of prevalent adverse effects. Adverse effects experienced by patients were often untreated and not discussed with health professionals, including those signifying potential hazard, such as trips or falls and morning headaches (which could indicate nocturnal hypoventilation) (1). These findings, to our knowledge, constitute the first systematic evaluation of adverse effects among modern patients with LTOT and provide novel as well as clinically relevant information regarding their frequency and the proportion of patients choosing to discuss them with healthcare personnel. This study is also the first, to our knowledge, to evaluate the relationship between adverse effects and worse HrQoL in LTOT.

Where comparison is possible, our findings are generally in accordance with earlier studies, which have indicated high numbers of adverse effects related to oxygen therapy and similarly impaired HrQoL (6, 18–20, 33). The number and type of adverse effects were similar to those presented in 1998 by Kampelmacher and colleagues despite large differences in patient populations with respect to age, equipment types, and underlying diagnoses, possibly indicating a degree of independence from these factors and wider external validity of the findings.

The low prevalence of current smoking contrasts with higher reported smoking rates from other countries (e.g., Denmark and Scotland) but was similar to those previously reported in a Swedish population and in accordance with our experience from clinical practice (14, 15, 34). That active smoking is rare likely reflects and supports adherence to the national treatment guidelines where smoking in most situations is considered a contraindication for LTOT, as well as the effects of structured management and follow-up of patients with LTOT in Sweden (5). This finding is also supported by a low prevalence of burn injuries among Swedish patients with LTOT when compared with countries such as Denmark (15, 16).

Strengths and Limitations

Strengths of this study include the population-based sample of patients with ongoing LTOT in Sweden. Characteristics at starting LTOT were similar between respondents and nonrespondents, supporting the representativeness of the sample and findings. The selection of adverse effects was based on clinical experience and previous literature, and HrQoL was assessed using established and validated instruments. Sensitivity analysis supports the chosen method of defining quality-of-life groups. Limitations of this study include first the risk of uncontrollable nonresponse bias related to current health status and the individual experience of treatment. For example, poor health status may prevent patients from completing or submitting the survey, which, given the association between HrQoL and adverse effects, may contribute to an underestimation of adverse effect prevalence. Unknown factors such as socioeconomic status may also have influenced the rate and nature of responses. Second, it is not certain that adverse effects reported by respondents were a direct consequence of their treatment with LTOT, as many adverse effects provided in the questionnaire, such as headaches, may be related to a variety of factors.

Our findings have several important implications. For clinical practice, the high prevalence of adverse effects, their association with worse HrQoL, and the fact that the majority had not been treated or discussed with a healthcare professional strongly indicate the importance of implementing structured information and assessment and follow-up of adverse effects and risk factors (including smoking and alcohol) in patients with LTOT. By identifying underreported adverse effects that may indicate future risk, such as trips or falls or morning headaches (which may indicate nocturnal hypoventilation), and assessing affected patients for targeted interventions, morbidity and mortality outcomes could potentially be improved. Although no conclusions regarding causality can be drawn from the observational data, many commonly reported adverse effects, such as dry mouth, are accessible for treatment, which could lead to a potential positive effect on HrQoL, as well as reduce the risk of poor treatment adherence reported by around one-tenth of respondents in this study. For research, further exploration of factors such as equipment type or oxygen flow rate could help provide more accurate information regarding patients' experiences of LTOT. Interventional studies aimed at identifying ways to avoid and manage adverse effects could provide opportunities to improve treatment perception, adherence, and HrQoL among those affected. Results from the current study could also provide a base for future analysis of associations between HrQoL, adverse effects, and markers such as hospital admissions and mortality.

Conclusions

Patients treated with LTOT generally report a high prevalence of adverse effects, whereas active smoking and alcohol consumption were reported as rare. HrQoL was generally reported as poor, and a statistical association was seen between greater numbers of reported systemic and total adverse effects and worse HrQoL. No association was seen for other groups of adverse effects, smoking status, or average weekly alcohol consumption. More than half of all experienced adverse effects had not been discussed with healthcare personnel or treated. Considering these factors, adverse effects should be systematically assessed and treated throughout LTOT. ■

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