Annals of the American Thoracic Society, 2026, 23(5), 711–719
https://doi.org/10.1093/annalsats/aaoaf038
Published: January 23, 2026
Original Research

thoracic.org

Economic evaluation of long-term oxygen therapy: 24 hours versus 15 hours per day in severe hypoxemia—the REDOX trial

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Abstract

Rationale: **Long-term oxygen therapy (LTOT) given for at least 15 hours/day improves survival in patients with severe chronic hypoxemia. However, the recent REDOX trial showed that LTOT prescribed for 24 hours/day was not superior to 15 hours/day in terms of death, hospitalizations, or self-reported outcomes.**

Objectives: **We aimed to examine the cost effectiveness of prescribing LTOT for 24 versus 15 hours/day.**

Methods: **A cost minimization analysis of the REDOX trial data on 241 patients with severe hypoxemic respiratory failure randomized 1:1 to either LTOT 24 hours/day ($n = 117$) or 15 hours/day ($n = 124$) and followed up to 12 months. Data on medical care consumption including prescribed medication costs, specialized outpatient care, and inpatient care were retrieved from national registries. Mean differences in healthcare consumption costs (United States dollars [$], 2024 prices) between groups were analyzed using generalized linear models. The cost analysis took a healthcare payer perspective and oxygen therapy costs are presented separately as out-of-pocket payments.**

Results: **During the 12 months of follow-up, patients prescribed LTOT for 24 hours/day had significantly lower mean costs for respiratory-specific medications (-$175 [95% CI, -$329 to -$29]) but higher oxygen therapy costs ($173 [95% CI, $80 to $268]), compared to patients prescribed LTOT 15 hours/day. There were no significant differences between the groups in mean specialized outpatient and inpatient care costs, total medication costs, or in overall total costs (-$4951 [95% CI, -$10 667 to $443]) but numerically favoring usage of LTOT 24 hours/day. A population-level projection shows substantial potential cumulative cost savings of $7.64 million if LTOT 24 hours/day is adopted.**

Conclusions: **In addition to previously shown similar treatment efficacy, overall healthcare costs did not significantly differ between LTOT prescribed 15 hours/day and LTOT 24 hours/day. However, there is an observable numerical difference in favor of usage of LTOT 24 hours/day.**

Keywords economic evaluation, cost minimization analysis, long-term oxygen therapy, direct healthcare costs, chronic severe hypoxemia

Introduction

Long-term oxygen therapy (LTOT) is standard of care in the management of patients with chronic severe hypoxemic respiratory failure, seen in diseases such as chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis.[1-4] Research on LTOT documents improvements in survival in this patient population, at least for COPD.[4-9] However, there is limited and conflicting evidence in relation to LTOT's effect in patients with severe hypoxemic respiratory failure regarding tolerance of day-to-day activities/exercise, impact on cognitive abilities, patients' health-related quality of life (HRQoL),[2,10-12] and cost effectiveness.[13]

Patients with severe chronic respiratory failure, especially those with COPD, consume a substantial portion of healthcare

Received: June 9, 2025. **Accepted:** October 21, 2025

resources,[14-17] and LTOT is one of the common recurring costs in these patients.[18,19] LTOT is cost-intensive and requires continued contact with healthcare for monitoring and supervision, together with equipment maintenance and replacement.[20] Some measures for controlling costs related to LTOT include the use of oxygen concentrators and cylinders over liquid oxygen,[21-23] portable oxygen for use outside the home, and strict prescription guidelines. However, there are still differences in prescription patterns for LTOT, such as in the prescribed daily time of oxygen use.

A recent registry-based randomized controlled trial (RCT) of treatment duration and mortality in long-term oxygen therapy (REDOX) showed that LTOT use for 24 hours per day was not superior to LTOT 15 hours per day in terms of decreasing mortality or hospitalizations, or improving patient-reported outcomes such as HRQoL.[24] The cost effectiveness of the respective prescription options has, however, not been studied.

The aim of this study was to evaluate the cost effectiveness of LTOT prescribed for 24 hours/day compared to 15 hours/day. With the background of shown similar clinical effectiveness, we hypothesized that there would be no differences in healthcare consumption costs other than in the out-of-pocket payments for LTOT. We expected the LTOT related out-of-pocket payments to be higher in the group prescribed LTOT for 24 hours/day, making the LTOT 15 hours/day option a possible cost-saving alternative.

Methods

Study design, participants, and procedure

This study was a cost minimization analysis[25,26] of the REDOX trial.[24,27] Focused on a healthcare payer perspective, the costing perspective included direct care consumption costs and presented separately were the out-of-pocket payments for the electricity bills for LTOT for the participants who used concentrators. The REDOX trial is a registry-based randomized study of 241 patients with severe hypoxemic respiratory failure randomized to either receiving LTOT for 24 hours per day ($n = 117$) or 15 hours per day ($n = 124$) over a 12-month period. Recruitment and follow-up took place between May 18, 2018 and April 4, 2023. The healthcare consumption of the enrolled patients was followed up using national registries, the National Patient Register (NPR),[28] and the National Drug Register (NDR).[29] The costing of utilization of care was done for the duration the participant was in the study, that is, until either death or study completion at the end of the 12 months of follow-up. The study was approved by the Swedish Ethical Review Authority (2016/190, 2016/910, 218/286, 2018/706, 2018/983, and 2023–03354-02). All patients provided informed written consent.

Long-term oxygen therapy

All participants were prescribed a stationary oxygen device, and some also a portable device in accordance with Swedish clinical guidelines.[2,3] Both the stationary and portable oxygen devices prescribed could be concentrators, oxygen cylinders, or liquid oxygen, and the study participants could have only concentrators, only oxygen cylinders, only liquid oxygen, or a combination. The oxygen concentrators mainly use atmospheric air and electricity, while the liquid oxygen equipment contains compressed air and requires regular refills when they run out. Both forms of equipment require regular maintenance services of a technician every 3-6 months or in case of any malfunction. To deliver and use the oxygen, there are accessory parts to the equipment such as masks, nasal prongs, and tubing, which are similar irrespective of type of oxygen delivery mode. Adherence to the allocated study treatment was self-reported as high.

Baseline characteristics of the study population

Baseline information on demographic characteristics, primary diagnosis causing the respiratory failure, performance status, pulmonary function tests, and level of hypoxemia were collected from the Swedish National Quality Registry for Respiratory Failure (Swedevox)[3] (Table 1).

Cost data and unit costs for healthcare contacts

Data on frequencies of healthcare contacts for the time of follow-up for each participant in form of inpatient care and specialized outpatient care were retrieved from the NPR hosted by the Swedish National Board of Health and Welfare.[28] For this work, we retrieved information from the NPR on primary diagnosis based on ICD-10 (*International Classification of Diseases*) codes and reason for admission, hospital length of stay, and dates. Information on retrieved prescriptions for all prescribed medications that the participants received was collected using the NDR.[29] The NDR provides information on prescribed drugs, Anatomical Therapeutic Classification codes, dosage, amount, date, and retail prices. The unit costs for the different healthcare contacts were retrieved from publicly available data in the cost per patient database hosted by the Swedish Association of Local Authorities and Regions.[30]

The cost of liquid oxygen/oxygen cylinders was retrieved from the pricelist from the Dental and Pharmaceutical Benefits Agency of Sweden (TLV).[31] Prices from the prominent suppliers in the country were also retrieved from the respective supply companies and used as benchmarks. All costs were converted from Swedish krona (SEK) to United States dollars ($) in 2024 prices using purchasing power parities.[32]

Healthcare usage and related costs

Using the frequencies of healthcare contacts retrieved in the national registries mentioned above, the related healthcare consumption costs were estimated as the product of the frequencies and the unit costs presented (Table 2). From the cost data provided in the NDR, the total medication consumption was estimated directly through the summation of the values for the respective participants over time of the study. Costs related to medications commonly used for respiratory illness (as maintenance and/or exacerbation treatment) were analyzed separately. The studied respiratory medications included oral corticosteroids, inhalational medications (not nebulized), oral broad-spectrum antibiotics, and antifibrotics (Table S1).

Table 1 Descriptive statistics of the study sample at baseline.

Characteristic	LTOT 15 hours/day (*n* = 124)	LTOT 24 hours/day (*n* = 117)
Demographic data		
Age, y, mean (SD)	75.0 (7.51)	76.4 (7.26)
Female sex	67 (54)	74 (63)
Cause of respiratory failure		
COPD	92 (74.20)	80 (68.38)
Pulmonary fibrosis	14 (11.29)	20 (17.09)
Other	18 (14.52)	15 (12.82)
Missing	0	2 (1.71)
Level of hypoxia at baseline		
PaO_2 at room air, kPa, mean (SD)	6.50 (0.63)	6.54 (0.79)
PaO_2 with LTOT, kPa, mean (SD)	8.42 (1.13)	8.61 (1.30)
Level of CO_2 retention at baseline		
$PaCO_2$ at room air, kPa, mean (SD)	5.66 (1.49)	5.62 (1.38)
$PaCO_2$ with LTOT, kPa, mean (SD)	5.80 (1.29)	5.83 (1.57)
Oxygen therapy (LTOT)		
Modalities		
Stationary concentrator (yes)	122 (98.39)	115 (98.29)
Missing	0	2 (1.71)
Liquid oxygen (yes)	2 (1.61)	2 (1.71)
Missing	0	2 (1.71)
Portable modalities		
Portable concentrator (yes)	87 (70.16)	102 (87.18)
Liquid oxygen (yes)	4 (3.23)	5 (4.27)
Cylinders (yes)	2 (1.61)	1 (0.85)
Missing	1 (0.81)	0
Prescribed flow rate, L/min, mean (SD)	1.77 (1.48)	1.70 (0.94)
Self-reported used flow rate, L/min, mean (SD)	1.77 (0.86)	2.00 (1.39)
Spirometry values at baseline		
FEV_1/L, mean (SD)	1.26 (0.71)	1.15 (0.68)
VC/L (highest of FVC and SVC), mean (SD)	2.40 (0.95)	2.08 (0.81)
WHO performance status		
0 (fully active)	12 (9.68)	11 (9.40)
1 (active but restricted in strenuous activities)	58 (46.77)	44 (37.61)
2 (ambulatory and capable of self-care but not work)	14 (11.29)	22 (18.80)
3/4 (capable of only limited self-care, or disabled)	5 (4.03)	7 (5.98)
Missing	35 (28.23)	33 (28.21)

Data are presented as No. (%) unless otherwise specified.
Abbreviations: CO_2, carbon dioxide; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; LTOT, long-term oxygen therapy; $PaCO_2$, partial pressures of carbon dioxide; PaO_2, partial pressures of oxygen; SD, standard deviation; SVC, slow vital capacity; VC, vital capacity; WHO, World Health Organization.

Table 2 Unit costs (US dollars) for the healthcare contacts, by year.

Year	Outpatient contact	Inpatient contact	Day of hospitalization
2018	324	6228	1675
2019	357	6475	1724
2020	391	7173	1906
2021	429	7471	1886
2022	455	7735	1851
2023	498	8528	1912

Data obtained from the cost per patient (KPP) database hosted by the Swedish Association of Local Authorities and Regions.
Unit cost per kWh: mean, $0.44 (range, $0.22 to $0.66). Retrieved from The Swedish Consumer Energy Markets Bureau.

The cost of LTOT was estimated based on volume of oxygen used or the total amount of electricity required during the follow-up period. That is, for the individuals using liquid oxygen, total cost was the product of prescribed flow rate in hours, duration of use per day in hours, follow-up period in days, and the cost per liter of gaseous oxygen produced from the liquid oxygen. According to TLV's price list and product documents, 20 L of liquid oxygen produces 17 500 L of gaseous oxygen and costs 990 SEK ($109). This gives a cost of 1 L of liquid oxygen at $5.45 (109/20) and that of 1 L of gaseous oxygen produced at $0.006 (5.45/875). The cost for the concentrators' users was estimated based on the total duration of usage in hours, and the related kilowatts of electricity required multiplied by the cost per kilowatt hour (kWh). The cost of 1 kWh was considered to be $0.44, based on data from the Swedish Consumer Energy Markets Bureau. A concentrator was estimated to use 300 W per hour (0.3 kWh).[20] This was treated as an out-of-pocket payment. The costs of equipment, accessories, refills, and routine maintenance (done by the product suppliers) costs were considered similar in both groups and thus not included in the present analysis. No discounting of costs was done, as all the costs occurred within 12 months of follow-up.

Statistical analysis

Descriptive statistics

Baseline characteristics and differences for the study sample are presented as means and standard deviations or minimum to maximum values for numerical variables and counts and percentages for categorical variables. Differences were assessed using *t*-tests or Mann–Whitney tests based on the distribution for the numerical variables and χ^2 tests for the categorical variables.

Analysis of cost and outcome data

The differences in the frequency variables, that is, outpatient visits, hospitalizations, and hospital length of stay, were analyzed using generalized linear models. A quasi-Poisson distribution and a logit link function were chosen to accommodate the distributional properties of count data. The effect measure was an incidence rate ratio (IRR) obtained as exponentials of the model coefficients.

The cost differences between the 2 study arms were assessed using generalized linear models. Due to the skewed nature of cost data, we used a gamma distribution with an identity link function in the analysis.

Where significant findings were noted, the analyses were further adjusted for potential confounders including age at baseline, sex, World Health Organization performance status, and primary diagnosis causing the respiratory failure, as these were deemed to affect the relationship between duration of LTOT use and healthcare consumption. The unadjusted estimates of mean cost differences are presented as the primary outcome of interest in the tables. Given the low number of participants prescribed liquid oxygen only ($n=2$, and both in the 15-hour arm), the LTOT cost results were calculated and presented separately for the liquid oxygen group.

In the base case analysis, due to the missing values in the daily duration of use for LTOT, an assumption was made to use the patient-reported values at 3-month follow-up, to apply for the whole of the follow-up period. This variable had 32% missing values and was imputed using multiple imputations using predictive mean matching done employing the MICE package in R.

The final results from the regression model estimates were bootstrapped using nonparametric bootstrapping with 5000 iterations to generate the mean cost difference and the confidence limits. All analyses were conducted in R version 4.1.3 statistical software, and statistical significance was set at $P<.05$.

Sensitivity analysis

As a sensitivity analysis, the same analysis was conducted using a set of one-way deterministic sensitivity analyses—first, varying the price of electricity (cost of 1 kWh) over the reported price range of $0.22 to $0.66.

Second, we examined the unimputed data. Third, we examined the work again with all variables imputed and not only the daily duration of LTOT use as in the base case analysis. Fourth, we analyzed the data without overt outliers, that is, there were 3 patients with extreme values: 1 individual who was admitted 12 times in 1 year because of COPD exacerbations, another individual who had dialysis visits 1 to 3 times per week, and finally a patient taking a costly selective prostacyclin receptor agonist, selexipag. Additionally, we conducted the analysis using inpatient care costs determined as the product of number of inpatient care episodes and the hospital length of stay. Furthermore, we examined the data for all cost items considering only the participants that were prescribed only concentrators (a stationary and/or a portable concentrator) and removing overt outliers, $n=221$, to assess if this would impact the direction of results and conclusions. Last, we analyzed only the COPD patient population.

Budget impact analysis

We also performed a budget impact analysis (BIA) to project the population level healthcare consumption costs and LTOT costs. The analysis is based on the prevalence of patients on LTOT in Sweden which is estimated as 21 per 100 000 individuals.[33] The prevalence is further corrected for the percentage population coverage of the Swedish National Quality Registry for Respiratory Failure estimated at 85% as well as the proportion of patients on LTOT due to airway disease estimated at 62%.[33] We incorporate a phased uptake of LTOT for 24 hours/day while phasing out LTOT 15 hours/day in increments of 20% to 100%.

Results

Descriptives

The study sample of 241 participants (58.5% female; mean age, 75.7 years) was balanced in terms of baseline characteristics except for vital capacity (Table 1). The mean follow-up duration was 273 (interquartile range [IQR], 180-365) days in the LTOT 24 hours/day group and 302 (IQR, 299-365) days in the LTOT 15 hours/day group.

Analysis of outcomes and cost data

Healthcare usage data

Outpatient care visits

The LTOT 24 hours/day group had statistically significant fewer outpatient visits compared to the LTOT 15 hours/day group (IRR, 0.67 [95% CI, 0.45-0.97]; $P=.039$).

Hospitalizations and hospital length of stay

There were no statistically significant differences noted in the rate of hospitalizations between the groups (IRR, 0.86 [95% CI, 0.62-1.20]; $P=.380$). The participants in the LTOT 24 hours/day group did have shorter hospital stays when admitted compared to the LTOT 15 hours/day group (IRR, 0.79 [95% CI, 0.53-1.17]; $P=.253$). However, this difference did not meet the set statistical significance level required.

Healthcare consumption costs

Medication costs

The LTOT 24 hours/day group had a statistically significant lower cost for respiratory illness–specific medications compared to the LTOT 15 hours/day group (-$175 [95% CI, -$329 to -$29]; $P=.021$). However, in terms of total medication costs, no significant differences were noted between the arms (-$2319 [95% CI, -$5445 to -$134]; $P=.056$).

Inpatient care costs

No statistically significant differences were noted in the inpatient care costs between the study groups (-$1780 [95% CI, -$6261 to $2563]; $P=.414$).

Outpatient care costs
There was a statistically significant difference in the mean outpatient care costs between the study groups (-$1012 [95% CI, -$2036 to -$105]; $P = .034$), with the LTOT 24 hours/day group consuming less than the LTOT 15 hours/day group.

LTOT costs
Considering the out-of-pocket payments for electricity bills for the participants using oxygen concentrators, the LTOT 24 hours/day group had statistically significant higher mean oxygen therapy–related costs than their LTOT 15 hours/day counterparts ($173 [95% CI, $80-$268]; $P < .001$). The mean cost for the 2 participants with liquid oxygen was estimated as $3417 (Table 3).

Total costs
Overall, the mean total healthcare consumption costs between the 2 study arms were numerically in favor of the LTOT 24 hours/day group compared to the 15 hours/day group. However, this difference did not reach the set statistical significance (-$5111 [95% CI, -$10 850 to $269]; $P = .066$). A similar direction of results was noted with the total costs, including out-of-pocket LTOT costs (-$4951 [95% CI, -$10 667 to $443]; $P = .075$; Figure 1 and Table 4).

Cost effectiveness

Base case analysis
In the base case analysis, the mean healthcare consumption cost was $21 824 (minimum, 0 to maximum, $177 139) for the LTOT 15 hours/day group and $16 871 (minimum, 0 to maximum, $112 452) for the LTOT 24 hours/day group. The major cost driver for both groups was inpatient care consumption costs. There was no statistically significant difference in the total mean cost estimates.

Sensitivity analysis
The sensitivity analyses did not change the overall direction of the findings. However, removal of the overt outliers (3 observations) changed the difference in outpatient care visits and related consumption costs to a statistically nonsignificant finding (-$697 [95% CI, -$1478 to $25]; $P = .063$; Tables S2–S9). The rest of the observations remained similar with the differences in respiratory-specific medication and oxygen therapy (LTOT) costs being statistically significant, while the overall cost difference was not (Tables S2–S9).

Budget impact analysis
The BIA showed that the projected overall mean cost at a national level for LTOT 15 hours/day (assuming 100% uptake) was approximately $33.78 million compared to $26.14 million for LTOT 24 hours/day. Uptake of LTOT 24 hours/day compared to LTOT 15 hours/day results in approximately $7.64 million in cumulative cost savings (Table 5).

Discussion

Summary of results

The main finding of this study is that there was no statistically significant difference in the overall healthcare utilization costs between patients using LTOT for 24 or 15 hours per day. As expected, the LTOT 24 hours/day group had higher costs for the oxygen therapy (including increased electricity costs), whereas costs for other respiratory-specific medications were numerically lower. The observed benefit here does cancel out with the increased LTOT costs.

As for the difference in respiratory-specific medications, despite the absence of a statistically significant difference in the likelihood of being hospitalized, the LTOT 15 hours/day group had a numerically higher likelihood to be admitted compared with the LTOT 24 hours/day group. After a hospitalization episode, patients usually receive an extended treatment in terms of oral steroids and antibiotics above and beyond their maintenance treatments, thus a possible explanation for the higher costs.

The absence of a statistically significant difference in overall healthcare costs but with a numerical difference favoring the LTOT 24 hours/day arm could be multifactorial. For example, even though no statistically significant difference was noted in the frequencies of healthcare contacts and usage, the numerical differences observed favored the LTOT 24 hours/day group. Therefore, it is possible that the LTOT 24 hours/day group had reduced exacerbations, if we use hospitalizations as a proxy for an exacerbation, despite not reaching statistical significance in our material.

Furthermore, in case of a hospitalization, our results show that the LTOT 15 hours/day group did have numerically longer hospital stays compared to LTOT for 24 hours/day per day. This translates into higher costs to the LTOT 15 hours/day group. However, the possible clinical and physiological explanations were not possible to explore in this work.

Table 3 Outcome variables and liquid oxygen costs.

Variable	LTOT 15 h/day ($n = 124$), mean (min-max)	LTOT 24 h/day ($n = 117$), mean (min-max)	IRR or mean difference (95% CI)	*P* value
Outpatient visits	6.51 (0-91)	4.34 (0-16)	0.67[a] (0.45-0.97)	**.039**
Admissions	1.68 (0-9)	1.44 (0-12)	0.86[a] (0.62-1.20)	.380
Admission duration, days	9.92 (0-81)	7.88 (0-55)	0.79[a] (0.53-1.17)	.253
Oxygen consumption (LTOT)				
Reported mean usage h/day[b]	16.22 (0-24)	21.72 (9-24)	5.50[c] (-6.57 to -4.44)	**<.001**
Daily oxygen use, L	1702 (0-13 500)	2251 (540-6750)	549[c] (189-909)	**.003**
Liquid LTOT costs, US dollars	$3417 ($0-$3942)	_	_	_

The bold values represent significant findings.
Abbreviations: CI, confidence interval; IRR, incidence rate ratio; LTOT, long-term oxygen therapy.
[a]IRR.
[b]Imputed values are reported. The unimputed estimates were 15.99 hours/day versus 21.72 hours/day.
[c]Mean difference.

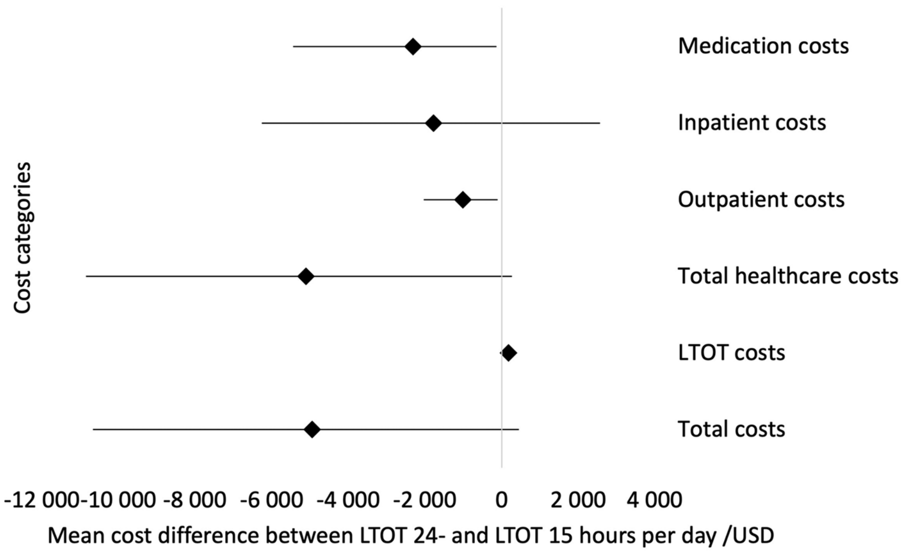

Figure 1 Group mean healthcare consumption cost differences and 95% confidence intervals. All costs are reported in 2024 prices (United States dollars). Medication costs pertain to all prescribed medications. Abbreviation: LTOT, long-term oxygen therapy.

Table 4 Mean healthcare care consumption costs in US dollars for the entire trial sample.

Cost item	LTOT 15 h/day, mean (min-max)	LTOT 24 h/day, mean (min-max)	Mean difference (95% CI)	*P* value
Respiratory medication, *n* = 241	747 (0-2336)	572 (0-2039)	-175 (-329 to -29)	**.021**
All medication, *n* = 241	4477 (0-170 578)	2158 (0-22 379)	-2319 (-5445 to -134)	.056
Inpatient care, *n* = 241	13 690 (0-74 349)	11 910 (0-100 912)	-1780 (-6261 to 2563)	.414
Outpatient care, *n* = 241	3029 (0-44 810)	2017 (0-7835)	-1012 (-2036 to -105)	**.034**
Total healthcare costs, *n* = 241	21 195 (0-176 416)	16 084 (0-111 861)	-5111 (-10 850 to 269)	.066
LTOT (concentrators), *n* = 239	628 (0-1156)	801 (0-1156)	173 (80-268)	**<.001**
Total cost, *n* = 241	21 824 (0-177 187)	16 871 (0-112 452)	-4951 (-10 667 to 443)	.075
Bootstrapped totals	21 870 (13 525-33 356)	16 885 (11 478-23 535)	-4985 (-10 668 to 600)	_

All costs are reported in 2024 prices (United States dollars). Respiratory medications; oral and inhalational treatment for mild exacerbations managed as outpatients; extended treatment after hospital discharge; and maintenance treatment.
Abbreviations: CI, confidence interval; LTOT, long-term oxygen therapy.

A budget impact analysis projecting the population level estimates showed rather numerically substantial cost savings despite the non–statistically significant findings in the study sample. This finding paints a picture of the financial impact of adopting LTOT 24 hours/day compared to LTOT 15 hours/day.

Comparison with other studies

There are no previous studies comparing costs for LTOT 15 hours/day versus LTOT 24 hours/day. Yet, the observed cost data are comparable to figures reported in other studies exploring the health economics aspects of LTOT.[13,22] Oba and colleagues[13] reported a mean LTOT cost per month of about $198, which would be higher when extrapolated to a yearly cost, than our findings of a mean cost for the 12-month follow-up period of $801 in the LTOT 24 hours/day group and $628 in the LTOT 15 hours/day group. This difference may be due to a number of factors ranging from the patient population studied to country-level differences in healthcare delivery and electricity prices. The same applies to values reported in a study by Andersson and colleagues,[22] who reported the average cost for a 6-month follow-up for LTOT with a concentrator of about $1310, which is higher than our findings even when annualized. This could be due to the small sample size and different patient populations.

Previous studies find inpatient care costs/hospitalizations to be the largest proportion of the total costs for this patient population, in line with the present observation.[15,21]

Strengths and limitations

This study was a cost minimization analysis alongside an RCT complemented with register-based care consumption data. This creates a solid ground portraying both day-to-day routine care practice as well as capturing data without recall bias. The registers are also representative of the general population, given their reported good coverage of 100% of all inpatient care, 80% for private specialist outpatient care, and 100% for public specialist outpatient care consumption nationwide.[28]

However, the study has some shortcomings. First, it uses a limited costing perspective where only healthcare-related costs and patient out-of-pocket payments for electricity. However, this patient population is severely ill and will have high informal care costs; thus, a societal costing perspective would have been preferred to capture that component.

Table 5 Projections of population level costs with varying uptake of LTOT 15 hours/day versus LTOT 24 hours/day.

Year	LTOT uptake	Population		Costs, 2024 prices (United States dollars)						
				Medications	Inpatient care	Outpatient care	Total healthcare	LTOT	Overall total	Cumulative savings
0	0 (100% LTOT 15 h/day)	0	1548	6 930 396	21 192 120	4 688 892	32 811 408	972 144	33 783 552	0
1	20%	310	1238	6 212 434	20 641 032	4 375 577	31 229 042	1 025 705	32 254 747	-1 528 805
2	40%	619	929	5 494 471	20 089 944	4 062 262	29 646 677	1 079 266	30 725 942	-3 057 610
3	60%	929	619	4 776 509	19 538 856	3 748 946	28 064 311	1 132 826	29 197 138	-4 586 414
4	80%	1238	310	4 058 546	18 987 768	3 435 631	26 481 946	1 186 387	27 668 333	-6 115 219
5	100% LTOT 24 h/day	1548	0	3 340 584	18 436 680	3 122 316	24 899 580	1 239 948	26 139 528	-7 644 024

Note: Under the column population, the first subdivision refers to the population taking up LTOT for 24 h/day and the second column to the 15 h/day group.
Abbreviation: LTOT, long-term oxygen therapy.

Second, the sample size in this work could be too small to examine the economic differences between the treatment arms. Thus, the findings must be interpreted with that in mind, where the observed results could be driven by small proportions of participants consuming more or less healthcare. Future research should aim to assess this question further in a sufficiently powered study or through health economics modeling.

Third, the assumption of clinical effect equivalence is based on 1 RCT, the REDOX trial. Ideally, a couple of studies or a meta-analysis would be a good ground to take that standpoint. However, there are no other trials and the REDOX trial was well conducted; thus, the presented results are useful as a starting point to investigate this important aspect.

Further, the distribution and use of concentrators versus liquid oxygen may vary in different parts of the world and clinical settings, hence could subsequently decrease the external validity of our findings.

There is also a possibility of recall bias regarding the self-reported duration of oxygen use. This was a key variable in the work with missing values in up to 32% of the cases. The shortcoming was addressed using multiple imputations and examined in the sensitivity analyses but does not completely eliminate the possibility of biased findings.

Last, the NPR does not capture primary healthcare consumption and thus our cost estimates may be an underestimate of the actual consumption.

Implications for clinical practice and decision making

Healthcare consumption costs related to prescribing LTOT for 24 hours/day compared to 15 hours/day in patients with severe hypoxemic respiratory failure did not differ statistically despite showing a numerical difference in favor of LTOT 24 hours/day. Therefore, it is safe to restrain from routinely prescribing LTOT for 24 hours per day while awaiting further clinical and health economics evidence. Clinicians could, for example, consider prescribing LTOT 24 hours/day to patients that are able to tolerate it; however, a full-scale rollout should only be done when further clinical and economic evidence is obtained.

Conclusions

In addition to previously shown similar treatment efficacy, the overall healthcare costs did not significantly differ between LTOT prescribed 15 hours/day versus 24 hours/day. However, there was a (statistically nonsignificant) numerical cost difference in favor of prescribing LTOT 24 hours/day.

Acknowledgments

The authors thank the participants and staff at the respective pulmonary medicine clinics at the different hospitals involved who made this study possible.

Author contributions

Data collection: M.E., J.S., A.A., A.P., A.B., E.L., C.J., and the staff at the different clinics. Conceptualization: R.S., A.P., M.E., F.B., and J.S. Data curation and formal analysis: R.S. Interpretation: All authors. Project administration: M.E., A.P., and J.S. Writing—original draft: R.S. Review and editing: All authors.

Supplementary material

Supplementary material is available at *Annals of the American Thoracic Society* online.

Conflicts of interest

Please see the ICMJE disclosure forms, which have been provided as supplementary material. The authors declare no conflicts of interest related to this study. However, J.S. has received personal fees from AstraZeneca, Boehringer Ingelheim, and Chiesi. A.A. has received personal fees from Astra-Zeneca, Boehringer Ingelheim, and Chiesi for lectures in pulmonary medicine and for production of educational materials in pulmonary medicine. F.B. is a member of the steering committee of the Swedevox registry. C.J. has received personal fees from AstraZeneca, Chiesi, GSK, Orion, and Sanofi. A.P. has received personal fees from ResMed. M.E. has received personal fees from AstraZeneca, Boehringer Ingelheim, Novartis, and Roche. M.E. has also received a research grant from ResMed.

Funding

The work was supported by grants from the Crafoord Foundation (2016-1065 and 2018-0563); the Swedish Heart Lung Foundation

(2014-0572 and 2016-0414); the Swedish Research Council (Dnr 2019–02081); the Swedish Society for Medical Research, Swedish Society of Medicine (SLS-589671 and SLS-693941); and the Örebro Research Committee (OLL-715231).

Data availability

The study data underlying this article is not publicly available due to ethical concerns. However, the data can be shared on reasonable request to the project administration supervisor Magnus Ekström.

Artificial intelligence disclaimer

No artificial intelligence tools were used in writing this manuscript.

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 Annals of the American Thoracic Society 2026 23(5) 711–719
https://doi.org/10.1093/annalsats/aaoaf038
Original Research Adult Pulmonary