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Early View

Original article

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Validation of Swedevox registry of continuous positive airway pressure (CPAP), long-term mechanical ventilator (LTMV) and long-term oxygen therapy (LTOT)

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Running head: Validation of the Swedevox registry

Keywords: long-term oxygen therapy; CPAP; sleep apnea; hypoventilation; home mechanical ventilation: long-term mechanical ventilation;

ABSTRACT

Background: The Swedish Registry of Respiratory Failure (Swedevox) collects nationwide data on patients starting continuous positive airway pressure (CPAP) treatment, long-term mechanical ventilator (LTMV) and long-term oxygen therapy (LTOT). We validated key information in Swedevox against source data from medical records.

Methods: This was a retrospective validation study of patients starting CPAP (n=175), LTMV (n=177) or LTOT (n=175) across seven centres 2013–2017. Agreement with medical record data was analyzed using differences in means (standard deviation) and proportion (%) of a selection of clinically relevant variables. Variables of interest included for CPAP: Apnea Hypopnea Index (AHI), height, weight, body mass index (BMI) and Epworth Sleepiness Scale (ESS) score; for LTMV: date of blood gas, $PaCO_2$ (breathing air), weight and diagnosis group; and for LTOT: blood gases breathing air and oxygen, spirometry and main diagnosis.

Results: Data on CPAP and LTOT had very high validity across all evaluated variables (all <5% discrepancy). For LTMV, variability was higher against source information for $PaCO_2$ (> 0.5 kPa in 25.9%), weight (> 5kg in 47.5%) and diagnosis group. Inconsistency was higher for patients starting LTMV acutely vs. electively ($PaCO_2$ difference >0.5 kPa in 36% versus 21%, $p<0.05$, respectively). However, there were no signs of systematic bias (mean differences close to zero) across the evaluated variables.

Conclusion: Validity of Swedevox data, compared with medical records, was very high for CPAP, LTMV and LTOT. The large sample size and lack of systematic differences support that Swedevox data are valid for health care quality assessment and research.

INTRODUCTION

Continuous positive airway pressure (CPAP), long-term mechanical ventilation (LTMV) and long-term oxygen therapy (LTOT) are established treatments for obstructive sleep apnea (OSA) [1], hypoventilation [2-4], and for chronic severe hypoxemia [5], respectively.

CPAP treatment [1] is established for patients with verified sleep apnea with excessive daytime sleepiness (strong recommendation), reduced sleep related quality of life (conditional recommendation), or comorbid hypertension (conditional recommendation).

LTMV is primarily used for chronic extra-pulmonary hypoventilation disorders, such as obesity hypoventilation and neurological diseases [2]. Its use for treatment of chronic hypercapnic respiratory failure in COPD has been controversial, but recent research seem to have established its role in selected patients [3].

LTOT improves survival in severe hypoxemia defined by partial pressure of arterial oxygen (PaO_2) < 7.4 kPa breathing room air at rest, or <7.8 kPa together with signs of right heart failure or secondary polycythemia [6, 7]. Evidence for benefit pertain to patients with hypoxemia that is chronic, defined as persisting ≥ 3 weeks despite optimal treatment for the underlying disease(s).

The Swedish National Registry of Respiratory Failure (Swedevox) collects nationwide data prospectively, on patients starting LTOT since 1987 (coverage about 85%) [8], LTMV since 1996 (estimated coverage 90%), and CPAP since 2010 (current coverage about 75%). Swedevox data are extensively used for assessing and informing about clinical practice across the country and in previous and ongoing research [9-16].

Validation of data entered into the Swedevox registry compared with medical records has not yet been performed. Such a validation is important to evaluate data quality, finding ways to

improve correct entry and data capture, and most importantly to ensure scientific validity. The aim of this study was to validate registered data in Swedevox against medical records for a selection of key variables in the three treatment arms CPAP, LTMV and LTOT.

MATERIAL AND METHODS

Study design and population

This was a multicenter, retrospective validation study comparing registered Swedevox data with the patients' medical records.

Inclusion criteria were: patients registered in Swedevox between 2013 and 2017, with complete data on the evaluated validation variables (listed in the next section), who were registered at any of the centres participating in the validation (pulmonary departments at hospitals in Blekinge, Gothenburg, Gävle, Halmstad, Lund/Malmö, Stockholm [Solna], Luleå [Sunderbyn] and Uppsala). The centres were selected as they represent a substantial amount of patients in the Swedevox registry due to a long period of reporting and also represent both larger and smaller regions across the entire country.

Of the patients in Swedevox during the time period at each centre, a random sample of 25 patients aged ≥18 years was selected for each treatment arm (CPAP, LTMV and LTOT). One study centre was later excluded (Solna) due to inability to provide data. In contrast, the centre Lund/Malmö included data from a larger randomized sample of LTMV (n=30), as Blekinge had only 22 eligible LTMV patients during the time period. The final validation population comprised 175 CPAP, 177 LTMV and 175 LTOT patients (Table 1).

Data entry in Swedevox

Data entered into the web-based Swedevox registry are obtained from medical records mainly by specialized nurses. Data should be obtained directly from the medical files, including the main diagnosis, and specific sources like questionnaires. Numerical data for e.g. weight, sleep apnea severity and blood gases should be representative for the situation when the decision was taken to start the treatment [8].

Current strategies to increase validity of registered Swedevox data include so called hard entry limits, such as limits on the age span that can be entered, and also so called soft validation checks that prompt the user when entering data outside the indications or physiologically unlikely (but not impossible) values, such as for blood gases.

Validation variables

A set of variables of interest was selected by the steering committee of the Swedevox registry in order to represent important markers for disease etiology and severity, comorbidities, and quality markers of patient management at the different centres. The following variables were validated: A) For CPAP: start date, baseline apnea hypopnea index (AHI), weight (kg), height (cm), body mass index (BMI; kg/m^2), and Epworth Sleepiness Scale (ESS) score [17]; B) for LTMV: start date, date of blood gas assessment breathing air (before starting therapy), $PaCO_2$ (air), weight (kg), and main diagnosis group (amyotrophic lateral sclerosis [ALS], other neuromuscular disease [NMD], respiratory disease, obesity hypoventilation syndrome [OHS], thoracic restriction, or other); and for LTOT: start date, PaO_2 (air), PaO_2 (oxygen), forced expired volume in one second (FEV_1), vital capacity (VC; defined as the highest value of the slow and forced VC), and the main diagnosis categorized as COPD, alpha-1-antitrypsin deficiency (AATD) with emphysema, other respiratory disease, pulmonary fibrosis (PF), sarcoidosis, other parenchymal disease, pulmonary arterial hypertension, chronic pulmonary embolism, other pulmonary vascular disease, heart disease, thoracic deformity,

hypoventilation, tumor in lung or pleura, or other. The validation was restricted to diagnoses with more than 5 patients.

Procedures of the validation

A standardized data entry sheet was used, including the patients' Swedish personal identity number (used to link the data), treatment arm (CPAP, LTMV or LTOT), date of registration in Swedevox, and entry fields for each variable to be obtained from the medical records. Data were entered by co-authors and staff at each centre and were returned to and quality checked by the principal investigator (ME). The data were then compared with the corresponding data in the Swedevox registry. Cut-off limits for differences regarded as clinically significant were defined by consensus by the Swedevox steering board and are listed in Table 2-4. The cut-off for ESS was set to its published minimal clinically important difference of 2 points for that scale [17].

Statistical analyses

Baseline patient characteristics were summarized using mean with standard deviation (SD) and median with range or interquartile range (IQR) for continuous variables with normal and skewed distribution, respectively. Categorical variables were expressed as frequencies and percentages. Representativeness of the validation sample for all patients in Swedevox was assessed by comparing the characteristics in Swedevox between patients included and not included in the validation sample during the study time period (2013-17). Differences were compared using t-tests and Wilcoxson rank sum tests for continuous variables with normal and skewed distributions, respectively, and using chi2 tests for categorical variables.

Agreement between the Swedevox registry and medical record data were evaluated as mean differences with 95% confidence intervals (CIs), and the prevalence of differences above a pre-specified cut off for each variable. Statistical analyses were conducted using the software packages Stata, version 16.0 (StataCorp LP; College Station, TX).

Ethical considerations

The study protocol was approved by the Head of Department as part of quality assessment of the registration process in Swedevox at each participating centre. According to Swedish law and research regulation, all participants were informed and had the opportunity to opt out from being registered in Swedevox, and individual consent for participation was waived.

RESULTS

A total of 527 patients were included in the validation across the seven centres (Table 1). Within each treatment arm, the age and sex distribution were similar across the centres (Table 1). Characteristics of the validation sample were overall similar to patients in the Swedevox registry who were not included in the validation during the time period, for CPAP (supplemental Table S1), LTMV (supplemental Table S2) and LTOT (supplemental Table S3).

CPAP

CPAP data validity was very high (Table 2). The mean differences (Swedevox versus medical records) for the key variables start date, AHI, BMI and ESS were close to zero; and the

proportion of differences being categorized as clinically significant was < 5% for all comparisons between Swedevox registry and medical records.

LTMV

LTMV data validity is shown in Table 3. There were none or very small systematic differences between the registry and medical records data for the key variables. There was higher variability than for CPAP: start date of LTMV differed by more than seven days in 9.1% of cases, and similar time differences were seen for 18.6% of dates of blood gas assessments. The difference in $PaCO_2$ between registry and source data exceeded > 0.5 kPa in 25.9% of patients, and a weight difference of > 5kg was detected in 47.5% of cases. However, the differences were evenly distributed leading to a mean difference near zero, indicating no systematic bias. When analyzed separately for acute and elective LTMV start, agreement was higher for patients starting LTMV in the elective setting (Table 3). This difference was also seen between acute and elective starts when analyzing by each underlying condition (Table S4 in the supplement).

Agreement for LTMV main diagnosis group in Swedevox compared with medical records was high for the main diagnosis groups of ALS (95%), respiratory disease (87%), other NMDs (80%) and slightly lower for OHS (73%), as shown in Figure 1. Nineteen patients with OHS according to Swedevox had a discrepancy in diagnoses in the comparison; of these, 16/19 had a diagnosis of respiratory disease in the medical records (supplemental Table S5).Vice versa, the majority (4/7) of patients classified as respiratory disease in Swedevox and discrepancy were classified as OHS in medical records. For most misclassified patients, the diagnosis group based on medical records was not captured by the variable for additional diagnosis group in Swedevox.

LTOT

In the LTOT arm of the registry, mean differences were very small and close to zero for all assessed variables (Table 4). Variability was low for treatment start date and PaO_2 (breathing room air), whereas the rate of substantial differences were higher for PaO2 (breathing oxygen) (14.4%) and VC (16.9%).

Agreement between Swedevox and medical records for LTOT main diagnosis (Figure 2) was very high for the major categories COPD (94%) and pulmonary fibrosis (89%, with some of the other cases categorized as PH), as shown in supplemental Table S6.

DISCUSSION

This is the first validation of a representative patient sample from the national Swedevox registry against source data (medical records) for patients starting CPAP, LTMV and LTOT during a five-year period. Data quality in the registry was very high for both CPAP and LTOT across all validated variables. For LTMV, agreement was high especially for patients starting the therapy electively. As could be expected, there were some discrepancies for patients starting LTMV acutely in the hospital setting. However, variability was evenly distributed with no mean difference in registered values compared with those in medical records, indicating that there was no systematic bias. This validation study strongly supports the suitability of the data reported in the Swedevox registry for use in evaluations and research.

Data quality is essential for both data analysis and the interpretation of clinical research. According to the principles of Good Clinical Practice applied in clinical drug trials, extensive data quality management with comparison between source data and reported data are performed to ensure correct results in the evaluation process of new therapeutic entities [18].

The findings of this study are in line with reported validations of other Swedish national registries [19-21].

The higher variability in LTMV data could reflect that the treatment is often initiated in relation to an acute decompensation of chronic respiratory failure, often requiring emergency and intensive care. Selection of blood gas values to report can be difficult as several assessments are often available from admission through acute management, decision to long-term treatment, to discharge. A similar problem may be relevant for the differences in weight, where patients starting LTMV may lose several kilogram during a short period of time due to mobilization of edema. We have not had clear instructions as to report weight before initiation or after a short period of LTMV treatment. However, there was no systematic differences in the reported values on the group-level which supports that also LTMV data are valid for health care quality assessment and research.

Reporting of the underlying diagnosis requiring LTMV showed the highest agreement for ALS, which probably reflects that most of these patients come with a precise diagnosis at their first contact with the LTMV clinic. As in OHS vs respiratory disease (consisting mainly of COPD), these diseases are known to frequently overlap and have an over-additive impact on respiration, and the distinction which of the two is the main contributor is in some cases difficult or even arbitrary. Furthermore, many of these patients start their therapy in an acute setting, before a firm diagnosis is established. This validation suggests that when using Swedevox data with OHS and respiratory disease, incorporating available data on BMI and lung function is likely to be valuable.

Strengths of the present analysis include that it evaluated clinically and scientifically relevant data for each treatment across multiple centres, and that the validation cohorts were representative for the remaining patients reported into the Swedevox registry. The validated variables and response categories were unchanged throughout the study period, and the

registry has near complete geographical coverage throughout Sweden. In addition, our validation study was blinded to the registered data in Swedevox. Finally, individuals reporting data into the registry differed at least in part from those who performed the validation process which increases the generalizability of our results.

Potential limitations of our study included the fact that data were only validated at baseline, as that is the main time point of interest for the registry, and rates of missing data are higher at follow-up. As the aim was to validate the registered data, we only included patients with complete data on the evaluated variables, and the rate of missing data in Swedevox was not assessed. However, characteristics were similar between the validation sample and all registered patients in Swedevox during the study period (Table S1-S3), supporting the generalizability of the findings to Sweden and similar settings.

Implications of the present findings include that Swedevox data closely mirrors the clinical patient characteristics and trajectories documented in the medical records, which supports the validity of using Swedevox data for clinical surveillance and follow-up of the therapies, nationwide comparisons of health care quality and for recommendations and clinical guidelines.

In conclusion, the present validation support that Swedevox data are valid, of high quality and suitable for use in research. Taken together with cross-linkage to national registry data, such as diagnosed diseases, medical procedures/surgery, hospitalizations and survival, with near-complete follow-up, as well as linkage with other national disease-specific quality registries, this poses strong research opportunities. The validity of Swedevox data are of fundamental importance for ongoing large scale clinical trials [11, 16].

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TABLES

Table 1. Characteristics by centre and treatment arm

Centre	Variable	All	CPAP	LTMV	LTOT
All	N (% females)	527 (51%)	175 (29%)	177 (61%)	175 (62%)
	Age	66.0 (13.5)	57.3 (11.5)	66.1 (13.5)	74.6 (9.0)
Blekinge	N (% females)	72 (46%)	25 (45%)	22 (45%)	25 (52%)
	Age	64.4 (13.5)	56.0 (11.7)	63.5 (13.0)	73.6 (9.5)
Gävle	N (% females)	75 (56%)	25 (32%)	25 (68%)	25 (68%)
	Age	66.0 (13.3)	55.6 (11.7)	67.7 (11.7)	74.7 (8.6)
Gothenburg	N (% females)	75 (41%)	25 (20%)	25 (48%)	25 (56%)
	Age	63.6 (15.3)	53.9 (12.4)	63.6 (15.0)	73.2 (12.2)
Halmstad	N (% females)	75 (51%)	25 (28%)	25 (52%)	25 (72%)
	Age	69.9 (9.6)	62.0 (8.6)	74.3 (5.5)	73.4 (8.8)
Lund/Malmö	N (% females)	80 (48%)	25 (20%)	30 (63%)	25 (56%)
	Age	64.8 (15.8)	58.4 (13.2)	61.0 (17.3)	75.8 (10.0)
Sunderbyn	N (% females)	75 (57%)	25 (28%)	25 (84%)	25 (60%)
	Age	67.9 (11.9)	59.5 (11.0)	68.4 (12.0)	75.8 (6.0)
Uppsala	N (% females)	75 (55%)	25 (36%)	25 (60%)	25 (68%)
	Age	65.5 (13.5)	55.8 (10.8)	65.0 (13.3)	75.9 (7.4)

Age presented as mean (standard deviation).

List of abbreviations: CPAP, continuous positive airway pressure; LTMV, long-term mechanical ventilation; and LTOT, long-term oxygen therapy.

Table 2. Continuous positive airway pressure (CPAP) data: agreement between Swedevox and medical records and proportion of patients with clinically significant differences

Variable	**Value**
N	175
Start date, median difference (IQR)	0.0 (0.0, 0.0)
> 7d difference, n (%)	6 (3.5%)
AHI, mean (SD)	34.7 (21.8)
Mean difference (SD)	0.0 (2.1)
> 10 points difference, n (%)	4 (2.3%)
Height (cm), mean (SD)	175.0 (8.8)
Mean difference (SD)	0.1 (0.8)
> 3cm difference, n (%)	1 (0.8%)
Weight (kg), mean (SD)	99.4 (22.5)
Mean difference (SD)	0.5 (6.1)
> 5kg difference, n (%)	4 (3.0%)
BMI, mean (SD)	32.3 (6.9)
Mean difference (SD)	-0.01 (2.2)
> 5 units difference , n (%)	3 (1.8%)
ESS, mean (SD)	10.5 (4.9)
Mean difference (SD)	0.01 (1.4)
> 2 points difference, n (%)	7 (4.3%)

Mean differences were calculated as the Swedevox value minus the value from medical records. *List of abbreviations:* AHI, apnea-hypopnea index; BMI, body mass index; ESS, Epworth Sleepiness Scale; IQR, interquartile (25%, 75%) range; SD, standard deviation.

Table 3. Long-term mechanical ventilation (LTMV) data: agreement between Swedevox and medical records and proportion of patients with clinically significant differences

Variable	**All**	**Acute start**	**Elective start**	**P-value**
N	177	66	100	
Start date, median difference (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.48
> 7d difference, n (%)	16 (9.1%)	8 (12.5%)	7 (7%)	0.23
Date of blood gas breathing air, median difference (IQR)	0.0 (-1.0, 0.0)	0.0 (-4.0, 0.0)	0.0 (0.0, 0.0)	0.35
> 7d difference, n (%)	30 (18.6%)	14 (25%)	14 (15%)	0.10
$PaCO_2$ (breathing air), mean (SD)	7.1 (1.1)	7.5 (1.1)	6.8 (1.0)	< 0.001
Mean difference (SD)	0.1 (0.8)	0.3 (0.9)	-0.0 (0.7)	0.079
> 0.5 kPa difference, n (%)	42 (25.9%)	20 (36%)	20 (21%)	0.049
Weight (kg), mean (SD)	90.3 (29.8)	91.4 (33.0)	91.6 (27.3)	0.97
Mean difference (SD)	-0.3 (9.0)	-1.6 (13.4)	0.8 (4.7)	0.13
> 5kg difference, n (%)	75 (47.5%)	34 (57%)	36 (41%)	0.068

Mean differences are the Swedevox value minus the value from medical records. The analysis by acute/elective start comprised somewhat fewer patients due to some having missing data on setting of starting LTMV. *List of abbreviations:* IQR, interquartile (25%, 75%) range; $PaCO_2$, partial pressure of arterial carbon dioxide; SD, standard deviation. P-values were calculated using t-tests for continuous and chi2-tests for the binary data.

Table 4. Long-term oxygen therapy (LTOT) data: agreement between Swedevox and medical records and proportion of patients with clinically significant differences

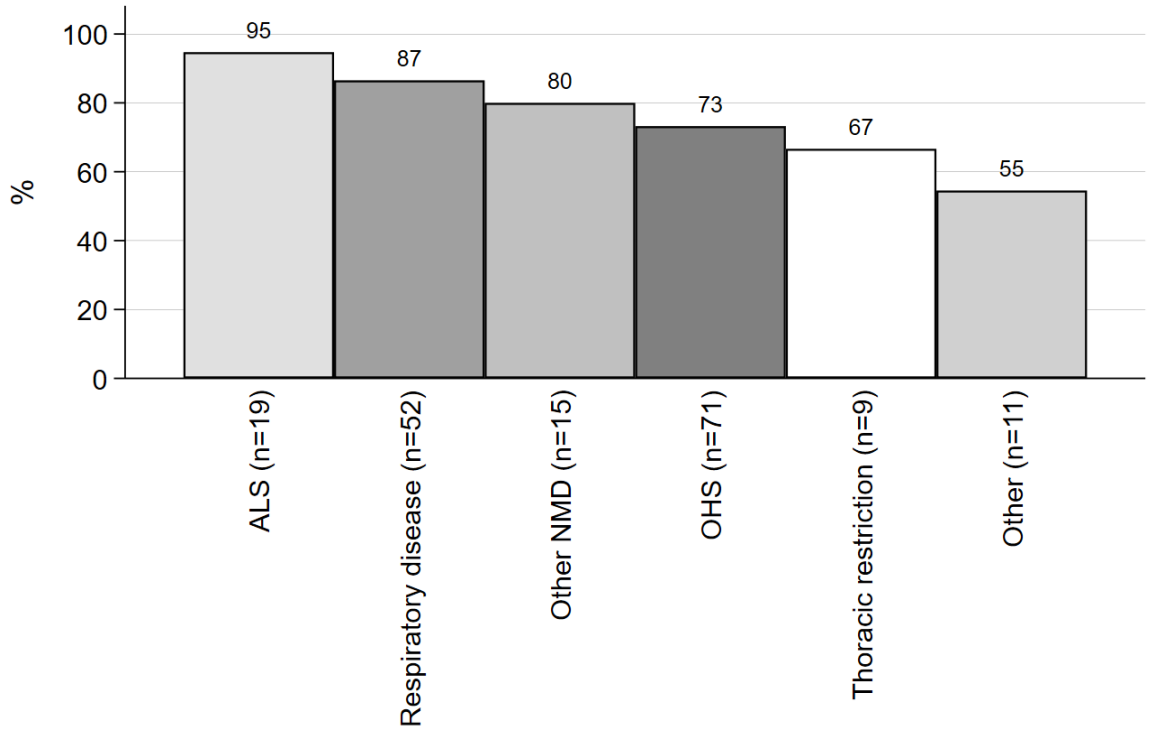
Variable	**Value**
N	175
Start date, median difference (IQR)	0.0 (0.0, 0.0)
> 7d difference, n (%)	5 (2.9%)
PaO_2 (breathing air), mean (SD)	7.1 (6.6)
Mean difference (SD)	-0.6 (6.6)
> 0.5 kPa difference, n (%)	10 (6.7%)
PaO_2 (breathing oxygen), mean (SD)	8.6 (1.0)
Mean difference (SD)	-0.0 (0.5)
> 0.5 kPa difference, n (%)	20 (14.3%)
FEV_1, mean (SD)	1.1 (0.6)
Mean difference (SD)	0.0 (0.3)
> 0.2 L difference, n (%)	14 (9.6%)
VC, mean (SD)	2.1 (0.8)
Mean difference (SD)	-0.0 (0.3)
> 0.2 L difference, n (%)	23 (16.1%)

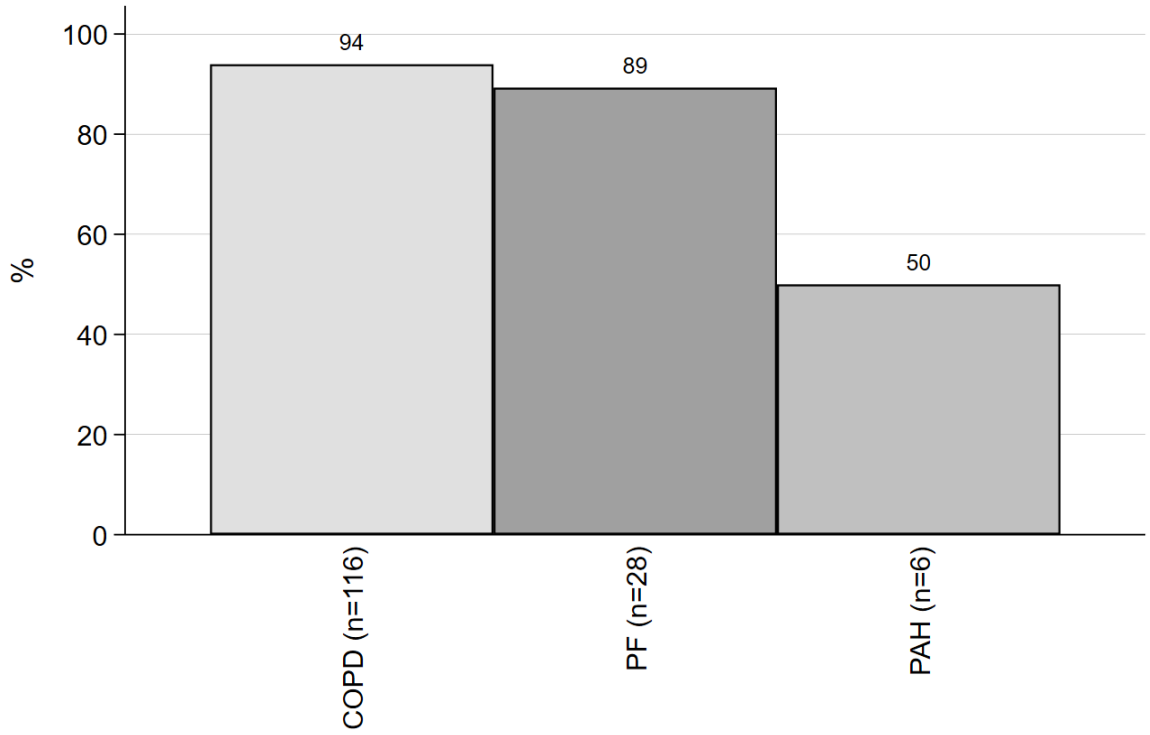
Mean differences are the Swedevox value minus the value from medical records. *List of abbreviations:* FEV_1, forced expired volume in one second; IQR, interquartile (25%, 75%) range; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; SD, standard deviation; VC, vital capacity.

FIGURE LEGENDS

Figure 1. Agreement (%) for patients with long-term mechanical ventilation (LTMV) of the main diagnosis group between Swedevox and medical records. *Abbreviations:* ALS, amyotrophic lateral sclerosis; NMD, neuromuscular disease; and OHS, obesity hypoventilation syndrome.

Figure 2. Agreement (%) for patients with long-term oxygen therapy (LTOT) of the main diagnosis between Swedevox and medical records, shown for diagnoses with n>5. Abbreviations: COPD, chronic obstructive pulmonary disease; PF, pulmonary fibrosis; and PAH, pulmonary arterial hypertension.


%
100
80
60
40
20
0
95
87
80
73
67
55
ALS (n=19)
Respiratory disease (n=52)
Other NMD (n=15)
OHS (n=71)
Thoracic restriction (n=9)
Other (n=11)


100
80
60
40
20
0
%
94
89
50
COPD (n=116)
PF (n=28)
PAH (n=6)

SUPPLEMENTAL MATERIAL

Validation of Swedevox registry of continuous positive airway pressure (CPAP), long-term mechanical ventilator (LTMV) and long-term oxygen therapy (LTOT)

Table S1. CPAP: comparison of characteristics between patients in the validation sample and all patients in the Swedevox CPAP arm, during the time period 2013-2017

Factor	**Not included in the validation**	**Included in the validation**
N	46,600	175
Age, mean (SD)	57.3 (12.7)	57.3 (11.5)
Gender		
Male	32,600 (70.0%)	124 (70.9%)
Female	14,000 (30.0%)	51 (29.1%)
Days from referral to sleep evaluation, median (IQR)	87.0 (41.0, 140.0)	96.0 (55.0, 128.0)
Days from sleep evaluation to CPAP start, median (IQR)	67.0 (33.0, 118.0)	83.5 (42.0, 133.0)
AHI, mean (SD)	35.4 (22.0)	34.5 (21.6)
ODI, mean (SD)	32.6 (21.8)	34.1 (21.0)
Height (cm), mean (SD)	174.6 (9.5)	175.3 (9.3)
Weight (kg), mean (SD)	97.4 (20.8)	98.7 (22.4)
Body mass index, mean (SD)	31.9 (6.1)	32.0 (6.6)
ESS, mean (SD)	10.2 (5.0)	10.5 (4.9)

Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; CPAP, continuous positive airway pressure; ESS, Epworth Sleepiness Scale; IQR, interquartile (25%, 75%) range; ODI, oxygen desaturation index; SD, standard deviation.

Table S2. LTMV: comparison of characteristics between patients in the validation sample and all patients in the Swedevox LTMV arm, during the time period 2013-2017.

Factor	**Not included in the validation**	**Included in the validation**
N	2,610	177
Age at therapy start, mean (SD)	63.7 (14.6)	66.1 (13.5)
Female	1333 (51.1%)	107 (60.5%)
Height (cm), mean (SD)	168.8 (11.0)	166.1 (11.6)
Weight (kg), mean (SD)	94.3 (33.5)	89.3 (29.2)
Body mass index, mean (SD)	33.1 (10.9)	32.4 (9.9)
Grouped main diagnosis		
Amyotrophic lateral sclerosis	430 (16.5%)	19 (10.7%)
Lung disease	618 (23.7%)	52 (29.4%)
Neuromuscular disease	242 (9.3%)	15 (8.5%)
Restrictive thoracic disease	108 (4.1%)	9 (5.1%)
OHS	938 (35.9%)	71 (40.1%)
Other	238 (9.1%)	11 (6.2%)
Missing	36 (1.4%)	0 (0.0%)
Start Situation at initiation of LTMV		
Continuation from ICU	292 (11.2%)	19 (10.7%)
Acute	853 (32.7%)	47 (26.6%)
Elective	1318 (50.5%)	100 (56.5%)
Missing	147 (5.6%)	11 (6.2%)
Start concomitant O_2		
None	1,865 (71.5%)	139 (78.5%)
During spontaneous and assisted breathing	407 (15.6%)	15 (8.5%)
During assisted breathing	44 (1.7%)	1 (0.6%)
During spontaneous breathing	27 (1.0%)	2 (1.1%)
Missing	267 (10.2%)	20 (11.3%)
PCO_2 (kPa), mean (SD)	7.0 (1.4)	7.3 (1.2)
Base excess (mmol/l), mean (SD)	6.7 (4.5)	7.2 (4.1)
FEV_1 (litres), mean (SD)	1.3 (0.8)	1.1 (0.7)
VC sitting (litres), mean (SD)	2.0 (0.9)	1.7 (0.9)
VC supine (litres), mean (SD)	1.7 (0.9)	1.5 (0.8)

Abbreviations: FEV_1, forced expired volume in one second; IQR, interquartile (25%, 75%) range; $PaCO_2$, partial pressure of arterial carbon dioxide; SD, standard deviation; VC, vital capacity.

Table S3. LTOT: comparison of baseline characteristics between patients in the validation sample and all patients in the Swedevox LTOT arm, during the time period 2013-2017.

Factor	**Not included in the validation**	**Included in the validation**
N	5,782	175
Age at therapy start, mean (SD)	75.4 (9.5)	74.6 (9.0)
Female	3,329 (57.6%)	108 (61.7%)
Height (cm), mean (SD)	166.6 (9.8)	166.0 (9.3)
Weight (kg), mean (SD)	71.4 (21.1)	67.8 (18.8)
Body mass index, mean (SD)	25.7 (7.0)	24.6 (6.3)
Main diagnosis		
COPD	3,354 (58.0%)	116 (66.3%)
Sarcoidosis	37 (0.6%)	1 (0.6%)
Lung fibrosis	955 (16.5%)	28 (16.0%)
Primary pulmonary hypertension	191 (3.3%)	6 (3.4%)
Chronic pulmonary embolism	80 (1.4%)	1 (0.6%)
Emphysema AAT-deficiency	63 (1.1%)	1 (0.6%)
Other airways disease	258 (4.5%)	5 (2.9%)
Other parenchymal disease	93 (1.6%)	6 (3.4%)
Other pulmonary vascular disease	81 (1.4%)	2 (1.1%)
Heart disease	244 (4.2%)	5 (2.9%)
Other	200 (3.5%)	1 (0.6%)
Hypoventilation	138 (2.4%)	1 (0.6%)
Thoracic deformities	29 (0.5%)	1 (0.6%)
Tumour in lungs or pleura	44 (0.8%)	1 (0.6%)
Missing	15 (0.3%)	0 (0.0%)
Grouped main diagnosis		
Airways disease	3,675 (63.6%)	122 (69.7%)
Parenchymal disease	1,085 (18.8%)	35 (20.0%)
Thoracic deformities	29 (0.5%)	1 (0.6%)
Hypoventilation	138 (2.4%)	1 (0.6%)
Pulmonary vascular disease	352 (6.1%)	9 (5.1%)
Tumour in lungs or pleura	44 (0.8%)	1 (0.6%)

Other	200 (3.5%)	1 (0.6%)
Heart disease	244 (4.2%)	5 (2.9%)
Missing	15 (0.3%)	0 (0.0%)
FEV_1 (litres), mean (SD)	1.2 (0.7)	1.1 (0.7)
VC (litres), mean (SD)	2.1 (0.9)	2.1 (1.0)
PO_2 (kPa), mean (SD)	6.5 (0.9)	6.6 (0.8)
PCO_2 (kPa), mean (SD)	5.8 (1.3)	5.7 (1.2)
PaO_2 oxygen (kPa), mean (SD)	8.6 (1.2)	8.6 (1.1)
$PaCO_2$ oxygen (kPa), mean (SD)	6.1 (1.4)	5.9 (1.2)
Prescribed O_2 dose (L/min), median (IQR)	1.5 (1.0, 2.0)	1.5 (1.0, 2.0)
Prescribed daily O_2 duration (h/day), median (IQR)	18.0 (16.0, 24.0)	18.0 (16.0, 24.0)
WHO performance status, median (IQR)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)

Mean differences are the Swedevox value minus the value from medical records. *List of abbreviations:* FEV_1, forced expired volume in one second; IQR, interquartile (25%, 75%) range; $PaCO_2$, partial pressure of arterial carbon dioxide; PaO_2, partial pressure of arterial oxygen; SD, standard deviation; VC, vital capacity; WHO, World Health Organization.

Table S4. Long-term mechanical ventilation (LTMV) data validity for acute and elective start separately by underlying condition

Factor	ALS	Other NMD	Respiratory disease	OHS	Thoracic deformity	Other	P-value
ACUTE START							
N	6	3	30	21	3	3	
Start date, median difference (IQR)	0.0 (0.0, 0.0)	0.0 (-12.0, 3.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	1.0 (0.0, 31.0)	0.0 (0.0, 0.0)	0.35
> 7d difference, n (%)	1 (17%)	1 (33%)	2 (7%)	3 (15%)	1 (33%)	0 (0%)	0.57
Date of blood gas breathing air, median difference (IQR)	0.0 (0.0, 0.0)	1.0 (1.0, 1.0)	0.0 (0.0, 0.0)	-5.0 (-16.0, 0.0)	0.0 (-1.0, 30.0)	0.0 (-3.0, 0.0)	0.007
> 7d difference, n (%)	0 (0%)	0 (0%)	8 (32%)	5 (28%)	1 (33%)	0 (0%)	0.58
$PaCO_2$ (breathing air), mean (SD)	7.1 (2.0)	7.0 (.)	7.5 (1.1)	7.6 (1.0)	7.6 (0.5)	7.9 (0.7)	0.96
Mean difference (SD)	-0.3 (1.3)	0.0 (.)	0.2 (0.8)	0.5 (1.1)	0.4 (0.4)	0.3 (0.5)	0.64
> 0.5 kPa difference, n (%)	2 (40%)	0 (0%)	8 (31%)	7 (39%)	2 (67%)	1 (33%)	0.82
Weight (kg), mean (SD)	82.7 (43.1)	81.5 (47.4)	83.2 (21.6)	115.4 (34.5)	67.6 (22.6)	61.8 (15.3)	0.003
Mean difference (SD)	-14.5 (41.1)	-8.5 (12.0)	-0.3 (3.3)	1.4 (3.9)	-5.3 (4.9)	1.5 (3.5)	0.17
> 5kg difference, n (%)	3 (50%)	1 (50%)	14 (52%)	11 (58%)	2 (67%)	3 (100%)	0.73
ELECTIVE START							
N	14	11	29	34	6	6	
Start date, median difference (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.25
> 7d difference, n (%)	0 (0%)	0 (0%)	4 (14%)	3 (9%)	0 (0%)	0 (0%)	0.41
Date of blood gas breathing air, median difference (IQR)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 1.0)	0.0 (-1.0, 0.0)	0.0 (0.0, 0.0)	0.0 (-1.0, 0.0)	0.25
> 7d difference, n (%)	2 (14%)	3 (27%)	6 (23%)	3 (9%)	0 (0%)	0 (0%)	0.35
$PaCO_2$ (breathing air), mean (SD)	6.2 (1.2)	6.8 (1.2)	7.1 (1.0)	7.0 (0.8)	7.1 (0.8)	6.2 (0.7)	0.067
Mean difference (SD)	0.3 (0.9)	-0.2 (0.3)	-0.1 (1.0)	0.1 (0.4)	-0.2 (0.6)	0.5 (0.7)	0.21

> 0.5 kPa difference, n (%)	2 (14%)	2 (18%)	8 (31%)	5 (15%)	1 (17%)	2 (40%)	0.58
Weight (kg), mean (SD)	74.4 (13.6)	72.3 (21.6)	83.3 (27.8)	112.2 (19.4)	65.7 (17.4)	97.2 (21.6)	<0.001
Mean difference (SD)	0.2 (7.7)	0.8 (3.9)	2.1 (5.1)	0.3 (3.5)	0.5 (1.4)	-1.2 (4.0)	0.64
> 5kg difference, n (%)	5 (45%)	5 (63%)	9 (35%)	12 (38%)	1 (20%)	4 (80%)	0.28

Table S5. LTMV main diagnosis group in Swedevox vs. medical records

		Swedevox registry					
		ALS	**Respiratory disease**	**Other NMD**	**OHS**	**Thoracic restriction**	**Other**
Medical records	**ALS**	18	0	2	0	0	0
		(94.7)	(0.0)	(13.3)	(0.0)	(0.0)	(0.0)
	Respiratory disease	1	45	0	16	3	0
		(5.3)	**(86.5)**	(0.0)	(22.5)	(33.3)	(0.0)
	Other NMD	0	0	12	0	0	3
		(0.0)	(0.0)	**(80.0)**	(0.0)	(0.0)	(27.3)
	OHS	0	4	0	52	0	1
		(0.0)	(7.7)	(0.0)	**(73.2)**	(0.0)	(9.1)
	Thoracic restriction	0	2	0	1	6	1
		(0.0)	(3.9)	(0.0)	(1.4)	**(66.7)**	(9.1)
	Other	0	1	1	2	0	6
		(0.0)	(1.9)	(6.7)	(2.8)	(0.0)	**(54.6)**

Accordance between Swedevox (columns) and medical records (rows) diagnosis groups for patients starting LTMV. Data presented as frequency (percentage of Swedevox cases). *Abbreviations:* ALS, amyotrophic lateral sclerosis; LTMV, long-term mechanical ventilation; NMD, neuromuscular disease (other than ALS); OHS, obesity hypoventilation syndrome.

Table S6. LTOT main diagnosis in Swedevox *vs.* medical records

		Swedevox												
		COPD	**AATD**	**Other airway disease**	**Pulmonary fibrosis (PF)**	**Sarcoidosis**	**Other LD**	**PAH**	**Chronic pulmonary embolism**	**Other pulmonary vasc dis**	**Heart disease**	**Thoracic deformity**	**Hypoventilation**	**Other**
Medical records	**COPD**	109	0	2	1	0	0	1	1	0	0	0	1	2
		(94.0)	(0.0)	(40.0)	(3.6)	(0.0)	(0.0)	(16.7)	(100.0)	(0.0)	(0.0)	(0.0)	(100.0)	(66.7)
	AATD	1	1	0	0	0	0	0	0	0	0	0	0	0
		(0.9)	**(100.0)**	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
	Other AD	0	0	2	0	0	0	0	0	0	0	0	0	1
		(0.0)	(0.0)	**(40.0)**	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(33.3)
	PF	2	0	1	25	0	1	1	0	0	0	0	0	0
		(1.7)	(0.0)	(20.0)	**(89.3)**	(0.0)	(16.7)	(16.7)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
	Sarcoidosis	0	0	0	0	1	0	0	0	0	0	0	0	0
		(0.0)	(0.0)	(0.0)	(0.0)	**(100.0)**	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
	Other LD	1	0	0	1	0	3	0	0	0	1	0	0	0
		(0.9)	(0.0)	(0.0)	(3.6)	(0.0)	**(50.0)**	(0.0)	(0.0)	(0.0)	(20.0)	(0.0)	(0.0)	(0.0)
	PAH	1	0	0	0	0	1	3	0	1	0	0	0	0
		(0.9)	(0.0)	(0.0)	(0.0)	(0.0)	(16.7)	**(50.0)**	(0.0)	(50.0)	(0.0)	(0.0)	(0.0)	(0.0)
	Other PVD	0	0	0	0	0	1	0	0	0	0	0	0	0
		(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(16.7)	(0.0)	(0.0)	**(0.0)**	(0.0)	(0.0)	(0.0)	(0.0)
	HD	0	0	0	0	0	0	1	0	0	3	0	0	0
		(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(16.7)	(0.0)	(0.0)	**(60.0)**	(0.0)	(0.0)	(0.0)
	Thor. def.	2	0	0	0	0	0	0	0	0	0	1	0	0
		(1.7)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	**(100.0)**	(0.0)	(0.0)
	Other	0	0	0	0	0	0	0	0	1	1	0	0	0
		(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(50.0)	(20.0)	(0.0)	(0.0)	**(0.0)**
	Missing	0	0	0	1	0	0	0	0	0	0	0	0	0
		(0.0)	(0.0)	(0.0)	(3.6)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)

Agreement between Swedevox (columns) and medical records (rows) diagnosis groups for patients starting LTOT. Data presented as frequency with percentage. *Abbreviations:* AATD, severe alpha-1-antitrypsin deficiency; AD, airway disease; COPD, chronic obstructive pulmonary disease; HD, heart disease; LD, lung disease; LTOT, long-term oxygen therapy; PAH, pulmonary arterial hypertension; PF, pulmonary fibrosis; and PVD, pulmonary vascular disease.