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Liberation and Mortality Outcomes in Pediatric Long-term Ventilation: A Qualitative Systematic Review

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Abstract

Objective: To provide a systematic review of liberation from positive pressure ventilation and mortality of children with chronic respiratory failure who used long-term invasive and noninvasive ventilation (LTV).

Methods: Papers published from 1980 to 2018 were identified using Pubmed MEDLINE, Ovid MEDLINE, Embase, and Cochrane databases. Search results were limited to English-language papers with (1) patients <22 years at initiation, (2) patients who used invasive ventilation (IV) via tracheostomy or noninvasive ventilation (NIV), and (3) data on mortality or liberation from LTV. Data were presented using descriptive statistics; changes in outcomes over time were explored using linear regression. Follow-up variability, cohort heterogeneity, and insufficient data precluded combining data to estimate incidences or rates.

Results: One hundred and thirty papers with 12,704 patients were included. The median number of patients was 37 (interquartile range [IQR] 17–74, range 6–3802). Twenty-five percent of patients were initiated on IV; 75% on NIV. The maximum follow-up ranged 0.5–31.8 years (median 8.8 years). The median proportion of patients liberated in these papers was 3% (IQR 0–21%). The median proportion of mortality was 18% (IQR 8–27%). Proportions of liberation and mortality did not significantly change over time. Progression of underlying disease (44%), respiratory illness (19%), and LTV accident (11%) were the most common causes of death.

Conclusions: These papers collectively show most patients survive for many years using LTV; in many subgroups, death is a more common outcome than liberation. However, the limitations of these papers preclude robust prognostication.

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Keywords

Respiration; Artificial; Child

Introduction

For decades, children and young adults with chronic respiratory failure have used long-term positive pressure ventilation outside of intensive care settings.¹ Such long-term ventilation (LTV), whether delivered invasively via a tracheostomy or noninvasively via a facial interface, has prolonged and benefited the lives of countless children with a wide variety of diagnoses.²³

Some children can be successfully liberated from LTV⁴; some must use LTV for the rest of their lives.⁵ Many have life-limiting or complex chronic conditions that cannot be mitigated by LTV and that put them at risk for early or unexpected death. In addition, dependency on positive pressure ventilation and/or tracheostomies carry their own life-threatening risks.⁶⁷ Therefore, robust outcomes data are imperative for setting realistic expectations regarding the benefits and limitations of LTV and make informed decisions around LTV.

However, the majority of published papers of children using LTV are retrospective, reflect small numbers of patients, and/or are from single institutions. Furthermore, because of small study cohorts and their heterogeneity, papers commonly pool patients with various diagnoses and who use different LTV modalities. For these reasons, we conducted a systematic review of published outcomes of mortality and of liberation from LTV in children, focusing on those with life-limiting or complex chronic conditions. Our goal is to provide a synopsis of current knowledge and a resource for caregivers to easily identify those papers that are most applicable to their patients. In doing so, we also highlight how far we remain from robust outcome data.

Materials and Methods

Data Sources and Study Selection

Systematic searches were performed using Pubmed MEDLINE, Ovid MEDLINE, Embase, and Cochrane databases with the assistance of a professional research librarian. The protocol for this review was developed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines⁸, and the full protocol with search terms was registered in the PROSPERO database.⁹ Deviations from the original protocol can be found in the E-appendix.

English-language peer-reviewed papers published between January 1980 and December 2018 were considered. Inclusion criteria were longitudinal studies with (1) patients less than 22 years of age at initiation of LTV, (2) patients with full- or part-time use of positive pressure ventilation via tracheostomy or noninvasive interface, and (3) data on mortality or liberation from LTV. We chose to study both invasive LTV (IV) and noninvasive LTV (NIV) as many studies followed cohorts that used both modalities. Modality choice for particular patient populations can be multi-factorial and fluid, and patients sometimes transition from

one modality to another as their clinical conditions progress or regress. Because there is no established definition of LTV, we did not impose a length of time that patients needed to use positive pressure ventilation, as long as they had a condition associated with chronic respiratory failure. Positive pressure ventilation included mechanical ventilation, bilevel positive airway pressure (BPAP), and continuous positive airway pressure (CPAP), and thus did not include negative pressure ventilation or diaphragmatic pacing. Studies of patients with uncomplicated obstructive sleep apnea who used CPAP were excluded¹⁰, as our focus was on patients with life-limiting and complex chronic conditions. Papers about and patients with postpolio respiratory failure were excluded¹¹, as this disease is basically eradicated in developed countries. Case studies with 5 or fewer patients, grey literature, conference abstracts, commentaries, editorials, letters, and reviews were excluded.

Exceptions to these exclusions included the following: Papers of adult patients with childhood-onset chronic conditions associated with onset of chronic respiratory failure at various ages (eg, Duchenne muscular dystrophy, cystic fibrosis) were included because such data can be useful to pediatricians. When papers included a few patients that met our exclusion criteria (eg, patients older than 22 years, patients who only used tracheostomies, patients with uncomplicated obstructive sleep apnea, and patients that used a non-positive pressure modality), these patients' data were not included in our results. When extraction was not possible because a study did not provide granular enough data, these papers and their patients were retained if there was only a small proportion of such patients. These exceptions were noted when possible and relevant.

At least two authors independently assessed papers for eligibility. Reference lists of included articles were reviewed to identify additional relevant papers. The quality of included articles was assessed using the Newcastle-Ottawa Scale—a 9-star scale to rate case-control or cohort studies' selection, comparability, and outcome qualities.¹² Explanations of the specifics and modifications needed to apply this scale to these included papers can be found in the E-appendix.

Data Extraction, Synthesis, and Analysis

Data extracted included year published, study period, duration of follow-up, number of patients, primary diagnoses, type of ventilation at initiation, age at initiation, number and proportion liberated from LTV, number and proportion that died, causes/circumstances of death, and other germane information. In order to examine the trends over time, the total numbers of patients that used LTV from included papers were presented by decade of publication and by country/region. Duration of follow-up was reported as the longest duration a patient was followed and/or the median/mean follow-up. When a study investigated patients with various diagnoses, we categorized them as having ventilatory muscle weakness, central hypoventilation, chronic pulmonary disease, airway abnormalities, cardiac/congenital heart disease, genetic/metabolic syndromes, and other/combined. Type of ventilation could be IV via tracheostomy or NIV, which was further categorized into BPAP and CPAP, when possible. Causes of death were categorized as progression of underlying condition (eg, cardiomyopathy in patients with Duchenne muscular dystrophy), respiratory illness (eg, pneumonia, aspiration), cardiac disease, infection (other than pneumonia), LTV

accident, other, and unknown. LTV accident included obstructed natural or artificial airway (eg, mucus plug), disconnection from ventilator or interface, tracheostomy decannulation, false track placement of a tracheostomy tube, and tracheal erosion. We also reported the number of deaths described as sudden/unexpected and as occurring at home. Criteria used to define these categories of circumstances/causes of death are presented in the E-appendix. Other information included study country site (if other than U.S.), person-years as a measure of the time-at-risk that patients contributed to the study, outcome rates, factors associated with outcomes, number of patients that transitioned from one LTV modality to another, number of patients that did not tolerate NIV, and other information pertinent to interpreting the study's liberation and mortality data. At least two authors independently abstracted data, using a standardized form. Differences were resolved by consensus among the three authors.

Data were presented using descriptive statistics. Key data were organized by modality of ventilation (IV or NIV) or by decade. Scatterplots with weighted markers for the sample size were created to display the proportions of patients that were liberated or died by the paper's year of publication. To explore whether outcomes (liberation, mortality, and circumstances of death) varied significantly by decade, a series of linear regressions were fitted with the papers' proportions of the outcome as the dependent variable and decade as the independent variable. These analyses were repeated for proportions of mortality from papers focused on spinal muscular atrophy and Duchenne muscular dystrophy. STATA version 16 (StataCorp LLC, College Station, Texas) was used for all statistical analysis and figures. A P value of < 0.05 was considered statistically significant.

Results

The initial database searches identified 6315 papers after duplicates were removed (see Figure 1). The majority of articles were not included due to irrelevance. After initial screening, the full-texts of 568 papers were reviewed. As with the screening, most of these (328) were not applicable. The remaining 131 papers were excluded because they did not have the requisite mortality or liberation data, they were a review, commentary, letter, or abstract, or they were written in a language other than English. Twenty-one papers were identified from the references of eligible papers or other sources and were included. A summary of the review of these included papers is found in Table 1.

A total of 130 papers with 12,704 patients were included in this review (an E-table with all the data of these papers is available online; an Excel spreadsheet with ongoing data collection beyond 2018 is also available upon request from the corresponding author). A small number of these patients are likely double-counted, as investigators likely included some of them in other larger study cohorts.¹³¹⁴¹⁵¹⁶¹⁷¹⁸¹⁹²⁰ Using the Newcastle-Ottawa Scale, the included papers were of low to moderate quality with 5–8 stars (out of a possible 9). No papers had a non-exposed cohort for comparison, and only 19 controlled for or explored associations between liberation and/or mortality and other clinically meaningful factors.²⁴⁵¹⁵¹⁷¹⁹²⁰²¹²²²³²⁴²⁵²⁶²⁷²⁸²⁹³⁰³¹³² The ratings of individual papers can be found in the E-table/spreadsheet. Twelve (9%) of these papers were published between 1980 and 1989; 19 (15%) between 1990 and 1999; 38 (29%) between 2000 and 2009; and 61 (47%) between 2010 and 2018. Eighty-four (65%) studied patients outside of the U.S., most

prominently France (13), United Kingdom (13), Canada (9), and Italy (6). The numbers of reported patients from different countries/regions increased substantially over the decades (see E-table 1). Forty-two (32%) papers studied patients who were initiated solely on IV; 45 (35%) papers studied patients who were initiated solely on NIV.

The number of patients studied varied among the papers. The median number of patients was 37 (IQR 17–74, range 6–3802). Only 24 papers studied more than 100 patients. 245202932333435363738394041424344454647484950 Of the 12,704 patients, 37% could be categorized as having ventilatory muscle weakness, 14% with chronic pulmonary disease, 10% with central hypoventilation, 9% with airway abnormalities, 6% with genetic/metabolic syndromes, 1% with cardiac/congenital heart disease, and 3% other/combined. Twenty percent of patients did not have a diagnosis reported. Twenty-two papers focused on patients with Duchenne muscular dystrophy⁵⁶¹⁴¹⁵²⁵²⁶³⁷³⁹⁴⁸⁵¹⁵²⁵³⁵⁴⁵⁵⁵⁶⁵⁷⁵⁸⁵⁹⁶⁰⁶¹⁶²⁶³; 12 spinal muscular atrophy¹³¹⁶¹⁸²⁴²⁸⁶⁴⁶⁵⁶⁶⁶⁷⁶⁸⁶⁹⁷⁰; 6 chronic lung disease of prematurity⁴¹⁹²¹³¹⁷¹⁷²; and 5 congenital central hypoventilation syndrome.⁷³⁷⁴⁷⁵⁷⁶⁷⁷

Twenty-five percent of all patients were initiated on IV; 75% on NIV. For those patients for whom modality of NIV was reported, 52% used CPAP; 48% used BPAP.

The duration of follow-up likewise varied. Eighty-eight papers reported a maximum duration, the median of which was 8.8 years (IQR 5.5–14 years, range 0.5–31.8 years). Papers that studied patients initiated solely on IV seemingly had longer maximum follow-up periods (median 10 years, range 1.9–31.8) than those that focused on patients initiated on NIV (median 6.5 years, range 0.5–22). Twenty-five papers reported a median duration, which ranged from 0.2–6.3 years; 35 papers reported a mean duration, which ranged from 0.4 to 12 years. Eight papers reported person-years of follow-up (range 49–8628). 232495961627879 Twenty-three (17%) papers provided no measure of duration of follow-up.

Considering the 125 papers that provided proportions of liberation from LTV, the median proportion of patients liberated was 3% (IQR 0–21%, range 0–100%). Of those papers that studied only patients initiated on NIV, the median proportion of liberation was 0% (IQR 0–16%, range 0–100%). Of those papers with patients only initiated on IV, the median proportion of liberation was 17% (IQR 0–25%, range 0–75%). Of the papers that studied patients initiated on both NIV and IV, the median proportion of liberation was 3% (IQR 0–18%, range 0–83%). Table 2 presents the median and ranges of all of the papers' proportions of liberation (and mortality) by the decade they were published. Linear regression demonstrated that reported proportions of liberation did not significantly change over the decades ($\beta = -0.16$ [95% confidence interval $-4 - 3.69$], $p = 0.94$). Figure 2 presents a scatterplot of each study's proportion of patients liberated by the year the study was published; a seeming majority of the data points lie under the 20% threshold. Ten papers reported liberation rate, time to liberation, or related analyses. 241719294043798081 Reported 5-year IV liberation rates were 25% in cohorts with diverse diagnoses²²⁷ and 85% in a cohort with bronchopulmonary dysplasia.¹⁹

Considering the 125 papers that provided proportions of mortality, the median proportion of patients who died was 18% (IQR 8–27%, range 0–65%). Of those papers that studied only

patients initiated on NIV, the median proportion of mortality was 11% (IQR 1–26%, range 0–65%). Of those papers with patients only initiated on IV, the median proportion of mortality was 21% (IQR 15.5–33.5%, range 0–57%). Of the papers that studied patients initiated on both NIV and IV, the median proportion of mortality was 18% (IQR 8.5–23.5%, range 0–43%). Less than a third of the papers with mortalities that studied patients initiated on both NIV and IV reported how many deaths were among which modality. Linear regression showed that included papers' proportions of mortality did not significantly change over the decades ($\beta = -0.58$ [95% confidence interval $-3.2 - 2.04$], $p = 0.66$). Figure 3 presents a scatterplot of each study's proportion of patients that died by the year the study was published and suggests a wider distribution of proportions of mortality compared to proportions of liberation in Figure 2. E-tables 2 and 3 presents the median and ranges of proportions of mortality across the decades in papers focused on spinal muscular atrophy and Duchenne muscular dystrophy, respectively. Proportions of mortality did not significantly change over the decades for these subgroups. Thirty-four papers reported survival rate, time to death, or related analyses.

24561417192125272829313237394142465154555759607078828384858687888Reported 5-year survival rates for cohorts with diverse diagnoses that used IV were 76–94%.²²⁷⁴² Five-year survival rates for cohorts with diverse diagnoses that combined patients that used IV and NIV were 53–94%.²⁹⁴⁶ Diagnosis-specific LTV survival rates are available for bronchopulmonary dysplasia⁴, spinal muscular atrophy²⁸, Duchenne muscular dystrophy⁶¹⁴⁵⁴⁵⁵⁵⁷⁵⁹ (presented in E-table 4), and congenital heart disease.¹⁷

Fourteen papers reported factors associated or not associated with liberation or mortality. 25172022232429303132899091 Multiple papers found that patients with chronic pulmonary disease or airway abnormalities were more likely to be liberated than patients with other diseases.²²³⁸⁰⁹⁰ One study found that younger age and CPAP use (compared to BPAP) were associated with liberation from NIV.²⁰ The same paper found that that more comorbidities and technologies were associated with mortality while using NIV. Another study found no association between LTV modality and survival in patients with Duchenne muscular dystrophy.⁵ Some papers reported a survival difference in patients with spinal muscular atrophy using different modalities.²⁸ Some papers demonstrated differences in mortality between disease groups, for example patients with central hypoventilation or cardiac disease had higher mortality than other groups.³²⁷⁸ Other papers found no difference in mortality between disease groups.²²⁷ Similarly, three papers showed no association between age of initiation and mortality.²²²³⁰ One study found that initiation in more recent years was associated with longer survival.²

One hundred and three papers discussed the circumstances/causes of death of 992 patients (63% of all 1580 deaths). The most common cause was progression of underlying disease (44%), followed by respiratory (19%), LTV accident (11%), infection (8%), cardiac (4%), and other causes (5%). Nine percent died for unknown reasons. Eighteen percent of deaths were reported as occurring at home (some of which may have been expected), and 11% were described as sudden/unexpected, though these proportions may be underestimated as not all of these 103 papers discussed such specifics. Table 3 groups the proportions of circumstances of deaths by decade. As with other outcomes, these circumstances of death did not change significantly over the decades.

Discussion

This review is the first to gather published information on mortality and liberation outcomes in children that used LTV. By applying systematic review methodology, focusing on two outcomes of interest, and including patients that used IV and NIV, it differs from and goes beyond previous reviews that failed to do a systematic search², focused on a single modality²³, focused on one age group³ or population⁹², or sought to scan the scope of all noninvasive LTV research.⁹³

We found that the number of papers increased over time, likely reflecting the increasing number of LTV patients and the spread of LTV beyond North America and Europe. The majority of these papers included less than 100 patients from single-centers outside of the U.S. The variability of their duration of follow-up, the heterogeneity of their cohorts, and the relative lack of granular data precluded combining their data to estimate incidences or rates of liberation or death among children that use LTV.

While we felt it unjustifiable to make meta-analytic inferences, it is reasonable to conclude that these papers collectively show that most patients with chronic respiratory failure and a life-limiting illness or medical complexity survive for many years using LTV. Given that the cohorts of these papers were children and young adults with life-limiting or complex chronic conditions, death was a more common outcome than liberation from LTV in many papers, with the probable exception of patients with chronic pulmonary disease and airway abnormalities. The mortality of patients that used IV may be greater than those that used NIV, though this may reflect patient population and disease severity, more than efficacy of modality. Those patients that die commonly do so for reasons other than progression of their underlying disease, though their underlying diseases likely make them more susceptible to other causes of death. A notable proportion die from a LTV accident. Intriguingly, proportions of patients liberated, expired, and their circumstances of death did not statistically change over the decades, possibly because advances in care and technology were counter-balanced by increased variation and complexity of patients. Considering these trends in patients and care will likely continue, it is probable that contemporary and future patients that use LTV will have similar outcomes.

Along these lines, this review of approximately four decades of outcome data highlighted four other overarching points. First, for all but perhaps a few subgroups, the data available are suboptimal to provide truly useful prognostic information beyond nonspecific statements about risks for early death or a chance for liberation. The heterogeneity of pediatric conditions that lead to chronic respiratory failure, the variation of clinical severity of these conditions and chronic respiratory failure, and, perhaps even, differences in management style continue to put meaningful prognostication out of reach. Immense efforts in collaborative research with standardized reporting and either standardized management or robust statistical adjustment of confounders will be needed to make real progress in this endeavor. Second, commentators have historically raised reservations about the use of LTV for children with life-limiting or complex chronic conditions, whether for predicted brief survival, poor quality-of-life, or great burden on families.⁹⁴⁹⁵ Yet, over the years, experience and evidence have repudiated many of those reservations and will likely continue to do so.

Third, the benefits of LTV notwithstanding, LTV has limits and risks. Examples of patients unexpectedly dying shortly after initiation of LTV are easy to find.⁶⁹⁶ Thus, patients and their families should be given measured anticipatory guidance on both. Fourth, all familial and professional providers need to remain diligent in their efforts to prevent LTV accidents.⁷

This review also permitted reflection on the optimal data elements and analyses that LTV outcome papers should have in order to provide more meaningful, robust evidence that can be more readily compared and combined. In our opinion, these include granular information on underlying diagnoses and severity. When patients with diverse diagnoses are pooled, they should be categorized in a clinically meaningful way (as we have attempted here). The field would benefit if one categorization scheme was agreed upon and used by researchers. Details on LTV modality and on full- or part-time use should be provided. Follow-up should be standardized with an agreed upon starting point (eg, tracheotomy or initial discharge for IV) and with person-years reported as a comparable measure of follow-up/time-at-risk, in addition to mean/median follow-up. Given that LTV outcome studies are inherently longitudinal, analyses should go beyond providing the proportion of patients that had an outcome and perform time-to-event analyses (eg, survival analysis) that provide estimates of rates. Given that complex pediatric patients are increasingly surviving into adulthood, patients should not be censored when they reach adulthood but should continue to be followed, if possible. Because liberation potentially include being ventilator-free, decannulation, and transition from IV to NIV or to supplemental oxygen, clear and detailed reporting is important. Finally, regression analysis is necessary to examine associations between outcomes and patient-level or other characteristics. Such associations are needed to address confounders of outcomes of interest, as well as tailor anticipatory guidance and identify modifiable factors worthy of intervention, especially when associations are corroborated in multiple studies.

Potential biases at several levels may have impacted this systematic review and our conclusions. The lack of randomization or comparison groups in almost all studies and their mainly descriptive nature means the available studies are of limited evidence/quality and are at risk for bias.⁹⁷ While we felt that the deviations from the original search protocol were justifiable to improve the reliability and feasibility of the review, these changes may have introduced reporting bias. Like other reviews, there was a possibility of publication bias, meaning that the studies published focused on certain results or cohorts and may not accurately represent the population of children who use LTV. For example, cohorts that do not experience many deaths or liberation from LTV may not get published on as often as cohorts that do. The small number of papers with redundant cohorts¹³¹⁴¹⁵¹⁶¹⁷¹⁸¹⁹²⁰ likely introduced a small amount of duplicate publication bias. While publication of data on cohorts from less-developed countries is seemingly rising, the disproportional number of papers from developed countries and our exclusion of non-English papers in this review likely contributed location and language biases.⁹⁸⁹⁹ Reviewing reference lists for additional articles may have resulted in citation bias and a subjective sample of papers.¹⁰⁰ There are several other limitations of this systematic review. First, the variability of included papers' duration of follow-up, the heterogeneity of their cohorts, and their relative lack of granular data allowed for only qualitative conclusions. Second, most papers followed a relatively small cohort at a single site. This limits the generalizability and completeness of their

results, as some patients could have died or been liberated from LTV at a different site. Third, even though earlier papers of children using LTV can be found¹, we chose 1980 (ie, the decade when reporting of these patients started in earnest) to begin our literature search. Conversely, advances in care and increased variation and complexity of patients, raise questions about the value of including papers from these early decades. However, we did not want discount potentially useful information that provide perspective on contemporaneous and future outcome data. Also, many of the more robust papers that followed larger cohorts over many years included patients from these earlier decades that could not be excluded. Fourth, a few papers had pediatric patients that could not be extracted.¹⁶¹⁰¹ Fifth, assigning Newcastle-Ottawa Scale ratings to these sorts of descriptive studies with such heterogeneous cohorts, especially regarding their cohort's representativeness and length/adequacy of follow-up, can be highly subjective.¹⁰² Sixth, our categorization of events of death also involved some subjective decisions (eg, designating deaths from cardiomyopathy in patients with Duchenne muscular dystrophy as "progression" as opposed to "cardiac"). Finally, this review did not address other important outcomes (eg, lung function, readmission¹⁰³, transition of NIV to IV⁴⁹¹⁰⁴, decannulation¹⁰⁵).

Robust data on outcomes of LTV are imperative to counsel patients and families and to assess our clinical effectiveness. However, obtaining generalizable data is a challenge when the majority of studies are retrospective, reflect small numbers of heterogeneous patients that continue to grow in diversity and complexity, and/or are from single institutions with potentially different management strategies. In all likelihood, all of these factors will continue to complicate pooling of outcome data. While labor intensive, standardization of reporting, confounders, and management, was well as a national registry of patients that use LTV, would go far to mitigate these limitations. Until such goals are achieved, we hope that this systematic review and others like it provide a synopsis and resource of LTV outcomes and raise awareness of the need for more robust, uniform reporting of outcome data.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

BPAP	bilevel positive airway pressure
CPAP	continuous positive airway pressure
IQR	interquartile range

IV	invasive ventilation
LTV	long-term ventilation
NIV	noninvasive ventilation

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Figure 1.
PRISMA study flowchart

Figure 2.

Scatterplot of the proportions of patients liberated from long-term ventilation in 125 papers by the year the paper was published and what modality patients were initiated on in each paper. Area of the symbols are proportional to the number of patients in the studies.

Figure 3.

Scatterplot of the proportions of patients that died in 125 papers by the year the paper was published and what modality patients were initiated on in each paper. Area of the symbols are proportional to the number of patients in the studies.

Table 1.

Summary of findings of qualitative systematic review of liberation and mortality outcomes in children who used LTV

Findings
<ul style="list-style-type: none">• 130 papers studied 12,704 children and young adults with chronic respiratory failure and other life-limiting or complex chronic conditions who used invasive and noninvasive LTV.• These papers were of low to moderate quality due to relatively small sample sizes, lack of comparison groups, few analyses to explore associations with outcomes• The IQR of reported proportions of patients that were liberated from LTV among these study cohorts was 0–21%.• The IQR of proportions of patients that died among these study cohorts was 8–27%.• The proportions of liberation and mortality were higher in patients who used IV, compared to patients that used NIV.• Progression of underlying disease was the most common cause of death, followed by respiratory illness, then LTV accident.• The proportions of liberation, mortality, and circumstances of death did not change significantly over time.

IQR, interquartile range; IV, invasive ventilation (via tracheostomy); LTV, long-term ventilation; NIV, noninvasive ventilation

Table 2.

Proportions of liberation and mortality in longitudinal studies of LTV patients by decade

%	1980s (12 papers, 269 patients)	1990s (19 papers, 737 patients)	2000s (37 papers, 1403 patients)	2010s (61 papers, 10295 patients)
Proportions of liberation				
Median	8.5	6	0	6.5
IQR	0–32.5	0–36	0–20	0–20
Range	0–53	0–71	0–44	0–100
Proportions of mortality				
Median	26.5	17	17	18
IQR	7–34	7–23	7–32	8–26
Range	0–57	0–43	0–65	0–56

IQR, interquartile range; LTV, long-term ventilation

Table 3.

Circumstances of death of patients that used LTV by decade of study publication

Circumstance of death, n (%)	1980s n=65 (100%)	1990s n=82 (100%)	2000s n=262 (100%)	2010s n=583 (100%)	P value ^a
Progression of underlying disease	16 (25)	38 (46)	138 (53)	242 (42)	0.37
Respiratory	31 (48)	14 (17)	52 (20)	95 (16)	0.21
Infection	2 (3)	2 (2)	11 (4)	59 (10)	0.17
Cardiac	–	3 (4)	9 (3)	37 (6)	0.55
LTV accident	12 (18)	17 (21)	13 (5)	65 (11)	0.36
Other cause	3 (5)	5 (6)	13 (5)	29 (5)	0.55
Unknown cause	1 (2)	3 (4)	26 (10)	56 (10)	0.06
Died at home	5 (8)	12 (15)	19 (7)	146 (25)	0.33
Sudden death	5 (8)	16 (20)	28 (11)	62 (11)	1.0

LTV, long-term ventilation

^aDenotes the p value of β coefficient of decade in linear regression models where the proportions of the respective circumstance of death was the dependent variable (ie, slope of change in proportions over the decades).