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Using modeling to inform patient-centered care choices at the end of life

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Abstract

Aim—Advance directives are often under-informed due to a lack of disease-specific prognostic information. Without well-informed advance directives patients may receive default care that is incongruent with their preferences. We aimed to further inform advance care planning in patients with severe chronic obstructive pulmonary disease by estimating outcomes with alternative advance directives.

Methods—We designed a Markov microsimulation model estimating outcomes for patients choosing between the Full Code advance directive (permitting invasive mechanical ventilation), and the Do Not Intubate directive (only permitting noninvasive ventilation).

Results—Our model estimates Full Code patients have marginally increased one-year survival after admission for severe respiratory failure, but are more likely to be residing in a nursing home and have frequent rehospitalizations for respiratory failure.

Conclusion—Patients with severe chronic obstructive pulmonary disease may consider these potential tradeoffs between survival, rehospitalizations and institutionalization when making informed advance care plans and end-of-life decisions. We highlight outcomes research needs for variables most influential to the model's outcomes, including the risk of complications of invasive mechanical ventilation and failing noninvasive mechanical ventilation.

Keywords

advance directives; chronic obstructive pulmonary disease decision modeling; end of life; informed decision-making; intensive care unit outcomes; prognostication

With advances in critical care, increasingly invasive treatment options are available to patients at the end of life. Often, unless patients choose to explicitly forego invasive

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Financial & competing interests disclosure

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treatments, the default is to ‘do everything’ to prolong survival. However, survivors of invasive treatments may have decreased functional capacity, may need to be placed in a nursing home and may have recurrent hospitalizations that may adversely impact upon quality of life [1–3]. Patients with severe chronic disease are at increased risk for these adverse outcomes [4]. In addition, 1-year survival after critical illness in patients with multiple chronic diseases is low, with or without invasive treatments [5–7].

Clinicians could assist patients and families in making more informed advance care plans by educating them about the potential outcomes in terms of factors that may influence quality of life and survival after hospitalization. Outcomes that are meaningful to patients when deciding between treatments include progression of their underlying disease [8], changes in functional capacity [9], and likelihood of repeat hospitalization. Patients also value the option to die comfortably outside the hospital setting [10], and many patients prefer to die at home when diagnosed with a terminal disease [11,12]. Providing patients with estimates of outcomes with alternative treatments for critical illness, such as posthospital survival, rehospitalization and institutionalization, will more fully inform advance care planning and may lead to more preference-congruent care at the end of life.

Chronic obstructive pulmonary disease (COPD) is an example of a highly prevalent chronic disease in which patients are at higher risk for adverse outcomes after invasive treatments and could, therefore, benefit from more information in their advance care planning [3,13]. Many patients with severe COPD do not have an advance directive and are at risk of defaulting to the most invasive care when hospitalized, without understanding potential trade-offs, such as ventilator dependence and needing long-term institutionalization. In this study, we use a Markov decision model to compare the outcomes of patients with severe COPD choosing between alternative advance directives about respiratory support in the event of critical illness. Specifically, we modeled outcomes after severe respiratory failure, which is the most common cause of death in patients with advanced COPD [14]. Outcomes modeled included hospital survival, number of rehospitalizations, 1-year survival and the place of residence preceding death. In addition, we explored the impact of uncertain data and different practice patterns on predicted model outcomes, which may in turn inform future research.

Methods

We designed a Markov-state transition model (TreeAge Pro 2011, TreeAge Inc., MA, USA) to compare two alternative advance directives about invasiveness of mechanical ventilation for patients with severe COPD: Full Code, permitting all forms of mechanical ventilation; and Do Not Intubate (DNI), permitting only noninvasive mechanical ventilation (NIMV) (Supplementary Figure 1, see online at www.futuremedicine.com/doi/suppl/10.2217/cer.13.53). Our hypothetical cohort included patients with severe COPD, as defined by the American Thoracic Society criteria [15], hospitalized for severe, acute respiratory failure. Severe respiratory failure (severely ill) was defined as pH <7.29, based on the parameters most commonly used in clinical studies [16–27]. The cohort age was 65 years, which is the mean age of patients included in large COPD survival studies [8,15]. We did not specify sex or race owing to lack of data. Patients could exist in one of five Markov states: baseline in community (baseline health state with COPD and no respiratory failure); hospitalized (with respiratory failure); short-term extended care facility (ECF; living in a short-term ECF for rehabilitation); nursing home (living in a long-term ECF/long-term institutionalization); or dead.

We simulated outcomes for hospitalized patients with severe COPD using a Markov cohort analysis, which mimics a clinical cohort and records patients’ locations and experiences

within the model at 1 month time intervals. We also performed a probabilistic sensitivity analysis to evaluate the effects of both first- and second-order uncertainty on individual patient outcomes.

We used the patients' perspective for the simulation model, specifically, patients with severe COPD who suffer a severe COPD exacerbation requiring hospitalization. This translates to the question from the patient perspective: "what happens if I have a severe breathing attack and am so ill that I need to make a decision about whether or not to receive a breathing tube and be attached to a breathing machine?"

Data inputs and plausible ranges were derived from review of published clinical trials or from expert opinion if such data were not available (Table 1). We excluded congestive heart failure as a cause of respiratory failure owing to the markedly different outcomes when compared with other causes of respiratory failure in patients with COPD. Outcome measures were hospital survival, 1-year survival, number of rehospitalizations and the place of residence preceding death.

Available treatments with alternative advance directives

The likelihood of receiving alternative treatments for respiratory failure depended on the advance directive chosen and the severity of respiratory failure (Supplementary Figure 1). We set the initial respiratory exacerbation requiring hospitalization to be a severe exacerbation requiring intensive care unit (ICU) admission. Subsequent exacerbations for survivors could be either moderate or severe. In response to a respiratory exacerbation, Full Code patients could receive either NIMV, for instance, pressurized air via a noninvasive mask (bilevel positive airway pressure ventilation or continuous positive airway pressure); or invasive mechanical ventilation, for instance, endotracheal tube (ETT) insertion and attachment to a mechanical ventilator. DNI patients, however, could not receive invasive mechanical ventilation, but could receive either NIMV or forego mechanical ventilation to receive supplemental oxygen and medications. If initial treatments failed, the probability of receiving subsequent treatments depended on the advance directive. For example, if Full Code patients failed initial NIMV, they could subsequently be intubated to receive invasive mechanical ventilation. However, if DNI patients failed initial NIMV, they could only receive palliative care (comfort measures only).

Model pathways

After hospitalization and treatment for acute COPD exacerbation, hypothetical patients could move along different pathways in the model depending on: the need for either NIMV or ETT; successful weaning from mechanical ventilation; failure to wean from mechanical ventilation; complications of mechanical ventilation; and death during hospitalization. If patients survived hospitalization, they could continue along different pathways in the model depending on: discharge to the community versus discharge to short-term ECF versus discharge to nursing home; rehospitalization owing to respiratory failure; and death after hospital discharge.

Probability estimates/variable values

Estimates were obtained by systematically reviewing the literature using the MEDLINE database for the key terms: 'COPD', 'chronic obstructive lung disease', 'respiratory exacerbation', 'mechanical ventilation', 'hospitalization', 'advance directive', 'outcomes', 'complications', 'intubation' and 'noninvasive mechanical ventilation' (Table 1). Exclusion criteria were articles that were not available in English, articles that only included patients admitted for congestive heart failure as a cause of respiratory failure and articles that were based on studies before 1990. The last two criteria are based on known differences in

outcomes compared with our population of interest. Patients with congestive heart failure often have improved outcomes with mechanical ventilation compared with patients with COPD exacerbation; and patients receiving mechanical ventilation after 1990 were more likely to be receiving lung-protective mechanical ventilation modalities. Probability estimates are informed by the proportion of patients in which the outcome of interest was observed and are bound between 0 and 1. We used decision rules to pool relevant data using the random effects method of DerSimonian and Laird, and tested for homogeneity defined as a Q-statistic of >0.10 , I-statistic of $<25\%$ and a p-value of <0.05 , with no significant outliers on the Forest plot [28]. If data were not homogeneous, the median value was used and the plausible range included the lowest and highest reported 95% CIs. For estimates unable to be obtained from the literature, we used 'expert opinion' by surveying three pulmonary and critical care physicians at an academic tertiary care center. Physicians were asked to estimate the probabilities for a given outcome. Specifically, they were asked to provide a 'best guess' estimate for the probabilities and a range corresponding to a 90% CI. We used the mean value and a wide range of plausible values, which included the lower and upper limits of all the estimates provided, to test the impact of uncertainty around these estimates in sensitivity analysis.

Life expectancy

The probability of death in the model was based on COPD survival data from a prominent prospective observational study of patients with varying levels of COPD severity [8]. In particular, the Kaplan–Meier survival curves were used to estimate all-cause mortality rates in patients with severe COPD. We assumed the same life expectancy for patients living in the community or in a short-term ECF. We estimated the life expectancy for patients living in a nursing home using a study of 1-year mortality risk in nursing homes [29]. We used the declining exponential approximation of life expectancy to convert survival probabilities into life expectancy [30]. This is a validated method for patients who have mortality rates greater than 0.10 per year, and assumes a constant mortality rate [31].

Assumptions

We assumed that patients who were severely ill were admitted to the ICU. We also assumed that patients were discharged to a nursing home if they experienced complications of mechanical ventilation (both invasive and noninvasive). Both of these assumptions were tested in sensitivity analyses. In addition, we assumed that only survivors who were discharged to a nursing home had a decrease in life expectancy. However, all survivors of severe COPD exacerbation had an increased likelihood of rehospitalization for another exacerbation. Finally, our model assumes that patients' advance directives are honored during hospitalization. For example, a patient with a Full Code directive would receive invasive ventilation if needed, without consideration of whether clinicians may deem such care as potentially futile. In addition, we assume that patients do not change their minds about whether to endorse Full Code during hospitalization.

Verification & comparison of model results to published data

The model structure and associated assumptions were verified using a stepwise 'debugging' process. In prior work, we compared the baseline model's 2-year survival estimates for patients with severe COPD who are living in the community with prospective cohort study results [32]. We also compared the baseline model survival estimates with different strata of underlying disease severity, including mild and moderate COPD to clinical study results [8,15,33]. In this simulation, we compared the model's outcomes for patients with severe COPD who are hospitalized, with the 1-year survival, place of residence and rehospitalizations reported in published clinical studies.

Sensitivity analysis

To assess the effect of data uncertainty, we performed one-way and multiway sensitivity analyses, wherein each parameter estimate is varied across its plausible range (e.g., 95% CI), for 10,000 hypothetical patients. One-way sensitivity analysis varies each parameter estimate individually, whereas multiway sensitivity analysis varies all estimates simultaneously to assess the effect on outcomes. We used β distributions for all variables [34,35], except for those informed by expert opinion for which we used uniform distributions, bound by the lowest and highest estimates to account for a higher degree of data uncertainty.

Results

Comparison of model results to published data

We compared the model's estimated outcomes with published clinical study outcomes for place of residence after hospitalization, hospital readmission and 1-year survival.

Place of residence after hospitalization—In our model, 15% of Full Code patients were discharged to a long-term care facility. In comparison, 26% of patients (95% CI: 18–34%) in a retrospective cohort study of ICU patients admitted for mechanical ventilation owing to a COPD exacerbation (and admitted from the community), were discharged either to rehabilitation or long-term care facilities [23].

Hospital readmission—In our model, 7.2% of patients who were admitted for respiratory failure were readmitted for respiratory failure within 30 days of the initial admission. By comparison, a recent analysis of readmissions for COPD found that 7.1% (95% CI: 6.9–7.1%) of index admissions for patients admitted with COPD were readmitted for respiratory failure within 30 days [36].

Long-term survival—Our model estimates a 61% 6-month survival for Full Code patients and 54% for DNI patients. By comparison, a recent prospective study of COPD patients admitted to the ICU with respiratory failure measured a 62% 6-month survival for patients who were Full Code (95% CI: 58.7–65.4%) and 48% for patients who were DNI (95% CI: 40.6–55.6%) [37]. In addition, our model estimates a 46% 1-year survival for Full Code patients, compared with 51.4% 1-year survival (95% CI: 39%–63%) measured in a different cohort study [38].

Model results

On average, our model estimated that patients with severe COPD who chose the Full Code directive would have increased hospital and 1-year survival in the setting of acute respiratory failure. However, Full Code patients were, on average, more likely to be discharged to a nursing home and had increased rehospitalizations for respiratory failure.

Hospital survival & 1-year survival

Patients with severe COPD who chose the Full Code advance directive had increased hospital survival (Full Code vs DNI: 83 vs 74%). Of the patients who chose the Full Code directive, 46% were alive at the end of 1 year, compared with 43% of patients who chose the DNI directive (Figure 1).

Rehospitalizations for respiratory failure

In the 1 year after hospitalization, 48% of Full Code patients were rehospitalized at least once for respiratory failure and 6.8% of patients were rehospitalized within 1 month of the

initial hospitalization. In the 1 year after hospitalization, 38.6% of DNI patients were rehospitalized at least once for respiratory failure, but only 1.7% of patients were rehospitalized within 1 month of the initial hospitalization (Table 2).

Place of residence after hospitalization

Of the patients who chose the Full Code directive and survived 1 year after hospitalization, 15% were living in a nursing home, 2% were living in a short-term ECF and 81% were living in the community. Of the patients who chose the DNI directive and survived 1 year after hospitalization, 4% were living in a nursing home, 2% were living in a short-term ECF and 93% were living in the community.

Place of residence directly preceding death

Of the Full Code patients who died in the months after hospitalization, 64% died in the hospital due to respiratory failure (during a subsequent admission), 21% died after being discharged back into the community and 15% died after being discharged to a nursing home. Of the DNI patients who died in the months after hospitalization, 77% died in the hospital due to respiratory failure, 22% died after being discharged back into the community and 1% died after being discharged to a nursing home. Of note, in our model, patients with DNI directives who failed NIMV received comfort measures only and died in the hospital. Therefore, discharge to a nursing home was more likely in patients who were Full Code.

Sensitivity analyses

In one-way sensitivity analysis, the model was most sensitive to parameter uncertainties for four variables: failing NIMV when severely ill; complications from invasive mechanical ventilation (ETT complications); surviving uncomplicated invasive mechanical ventilation; and the probability of recurrent respiratory exacerbation. In particular, when the probability of failing NIMV increased, patients with DNI advance directives had decreased 6-month and 1-year survival. When the probability of complications from invasive mechanical ventilation increased, patients with Full Code advance directives had decreased 6-month and 1-year survival. The frequency of rehospitalization increased with increased probability of recurrent respiratory exacerbation. In multiway sensitivity analysis, Full Code patients yielded the highest estimated survival in 70% of trials.

Estimating the effect of a change in clinical practice

We tested the effect of a change in clinical practice whereby all patients would first receive a trial of NIMV (as opposed to being immediately intubated). This was based on the fact that the model's estimates of long-term institutionalization and rehospitalization depended on the incidence of complications after invasive mechanical ventilation (ETT). With this new scenario, in which all patients first received a trial of NIMV, the model estimated a 21% increase in 1-year survival (from 46% with current practice to 67% for Full Code patients). Rehospitalizations decreased marginally (from 48 to 44%) and the frequency of hospitalizations decreased (from 9 to 4%; patients hospitalized more than once). These improved outcomes are due to the decreased risk of complications with NIMV compared with invasive mechanical ventilation. Only patients with Full Code directives were affected since all patients with DNI directives received NIMV for severe respiratory failure in our model (DNI directives did not permit invasive mechanical ventilation).

Discussion

Our results demonstrate that patients with severe COPD may, on average, have increased hospital survival; however, there may be a trade-off with increased rehospitalizations and

treatment complications that may necessitate nursing home admission. Patients may place more weight on factors that could affect quality of life when considering these trade-offs. Our clinical paradigm of survival as the main clinical benchmark of treatment success should, therefore, also include more patient-centered outcomes, such as the quality of dying, particularly for chronic disease patients with marginal benefit in survival after critical illness.

More informed advance care planning can facilitate preference-congruent care at the end of life including treatments focused on a 'good death' [39]. A good death has been described as "a death free from distressing symptoms, with psychosocial and spiritual needs addressed, and the chance for patients and family to face the inevitable without additional fear or misinformation" [40]. This is an important goal of end-of-life care for many patients [41,42], and healthcare providers can assist with advance care planning for a good death by discussing alternative treatment options and likely outcomes, including those affecting the quality of life and of dying.

Physicians could use our model to inform patients not only about their choices in the event of critical illness, but also what the likely outcomes would be. A patient may decide that nursing home placement is acceptable if there is a personally meaningful increase in survival and, therefore, choose to endorse the Full Code advance directive. On the other hand, patients may decide that, if there is a marginal increase in survival, at the cost of increased rehospitalizations and probable nursing home placement, they would rather not receive invasive mechanical ventilation. Instead, they may be willing to accept a trial of NIMV and initiate palliative care. These patients would, therefore, endorse the DNI advance directive.

Importantly, our model also helps to highlight outcomes research needs for patients with severe COPD who receive mechanical ventilation. In particular, data that have a significant impact on the model's projected outcomes with alternative advance directives should be prioritized. These include the probability of: failing NIMV for patients suffering severe COPD exacerbations; complications from invasive mechanical ventilation; surviving uncomplicated invasive mechanical ventilation; and the probability of recurrent severe respiratory exacerbation. There may also be variation in practice and outcomes between institutions both nationally and internationally, which in turn may affect longer term outcomes of ICU care. Until further evidence is generated, a decision model such as ours may be a useful approach to synthesize the best available data and begin to provide patients and clinicians with the information they need to make a joint decision about advance care planning.

Several limitations deserve particular attention. First, our model does not directly estimate where patients will actually die. As a proxy, we model where patients live directly preceding their death. However, we believe that it is valid to assume (in the USA) that most deaths occur after a period of illness requiring hospitalization or other form of acute medical care, unless the patient has made their refusal to be hospitalized explicit and/or is in hospice care. However, we do not include discharge to a hospice owing to insufficient data in patients with COPD. Furthermore, our model does not consider seasonal variation in mortality since it is designed to reflect mean outcomes over longer time periods (over 1 year).

Second, our model only simulates hospitalization for acute respiratory failure. However, patients with COPD die of other illness including cardiac arrest and cancer. We intentionally limited our modeling to patients with severe COPD hospitalized for acute respiratory failure as advance directives have been criticized for being too vague and hard to apply to specific disease states [43]. Our projection of patients living in a nursing home at 1 year after initial hospitalization does not take into account admission to ECF after hospitalizations for

nonrespiratory illness, or admission from the community due to general deterioration in health and inability to care for themselves. In addition, we do not explicitly consider the possibility of being discharged to a hospice from the hospital. Instead, patients who receive comfort measures are only discharged to a nursing home in our model.

Third, the model overestimates 6-month survival for patients with DNI but underestimates 1-year survival in patients with Full Code directives. This may be explained by an underestimation of the probability of NIMV failure in patients with DNI directives, and an overestimation of the probability of ETT complications in patients with Full Code directives, as demonstrated in sensitivity analysis. Furthermore, the model may underestimate the likelihood of discharge to a nursing home (model estimate 15% vs study report of 26%); however, the study used for comparison included patients discharged to rehabilitation facilities.

Fourth, we did not simulate quality-adjusted life years since available utilities are population-based and would not account for the individual heterogeneity level that is particularly important for end-of-life decision-making. In addition, as supported by a recent comparative effectiveness research review [44], there is very little research on functional status or health-related quality of life after NIMV. Instead, we believe that presentation of the likely outcomes for patients choosing between alternative advance directives will allow patients to implicitly weigh the potential tradeoffs. Furthermore, we have focused on 1-year survival rather than life expectancy or quality-adjusted life expectancy as our clinical experience led us to assume that patients would find 1-year survival to be very concrete and, therefore, particularly useful for decision-making. However, we have not yet investigated whether this assumption is correct and since our model simultaneously predicts life expectancy, we will be able to test whether patients prefer to see outcomes in terms of 1-year survival or life expectancy.

Finally, many of the data estimates for which we use expert opinion owing to a lack of published evidence are ‘process’ issues in the clinical pathway, such as the chance of being admitted to the ICU if a patient has severe respiratory failure, or the chance of the patient receiving a trial of NIMV before ETT. Many of these issues will be subject to variation across centers depending on local resources and practices. In fact, our model can be adapted to local settings by incorporating setting-specific parameters, allowing local hospitals to tailor results to their own patients based on their own data.

The limitations pertinent to decision modeling in general, including the effect of parameter uncertainty for the variables used in the model, apply to our model. To address this concern, we have used several validation and verification techniques, including the use of the Monte Carlo simulation to include the effect of first- and second- order uncertainty.

Conclusion

In conclusion, our model identifies specific areas for further clinical studies to refine prognostic estimates for patients with severe COPD who suffer acute respiratory failure. Our model may also inform end-of-life shared decision-making for patients with severe chronic diseases, and their families and could potentially address important communication barriers to advance care planning and to a good death. Future studies must explore both effective methods of communicating estimated outcomes and trade-offs as well as patients’ attitudes toward using these estimates to inform advance care planning.

Future perspective

We anticipate that our work will stimulate further investigation of outcomes of critical care beyond in-hospital survival, to include outcomes that are equally important to patients in their informed decision-making about end-of-life care. Effectively communicating comparative effectiveness research results such as ours will allow patients to consider pertinent tradeoffs in their decision-making about whether or not to receive invasive care when critically ill and will lead to more preference-congruent care at the end of life.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Executive summary

- The authors designed a Markov decision model comparing outcomes over time for severe chronic obstructive pulmonary disease (e.g., emphysema) patients choosing between Full Code vs Do Not Intubate (DNI) advance directives.
- Hypothetical patients who endorsed the Full Code advance directive had marginally increased 1-year survival: Full Code vs DNI, 46 vs 43%, respectively.
- Full Code patients were more likely to be residing in a nursing home 1 year after initial hospitalization for acute, severe respiratory failure: Full Code vs DNI, 15 vs 4% residing in a nursing home.
- Full Code patients were also more likely to be rehospitalized for respiratory failure: Full Code vs DNI, 48 vs 39% rehospitalized during the 1 year after initial hospitalization, respectively.
- Full Code patients were more likely to die while living in a nursing home (Full Code vs DNI, 14 vs 1%, respectively).
- If all patients first received a trial of noninvasive mechanical ventilation, as opposed to being immediately intubated, 1-year survival for Full Code patients increased from 46 to 67%.
- Model outcomes were most sensitive to: the probability of complications from invasive mechanical ventilation and the probability of failing noninvasive mechanical ventilation; an increase in these probabilities led to lower survival, increased admission to nursing homes and increased rehospitalizations.
- Overall, choosing a Full Code directive for patients with severe chronic obstructive pulmonary disease may result in a marginally increased likelihood of survival but increased likelihood of recurrent hospitalization and institutionalization when compared with DNI.
- Our model highlights outcomes research needs for patients with severe chronic obstructive pulmonary disease who receive mechanical ventilation to include more refined estimates of the likelihood of failing noninvasive mechanical ventilation and the likelihood of suffering complications from invasive mechanical ventilation.
- Future work will include collaboration with patients and clinicians on how to most effectively communicate these research results.

Figure 1.
Estimated probabilities of 1-year survival for Full Code versus Do Not Intubate advance directives after hospitalization for respiratory failure.
DNI: Do Not Intubate.

Table 1

Parameter values used for model and ranges examined in sensitivity analysis.

Description	Baseline estimates (range)	Method used for baseline estimation (method used for range)	Distribution: uniform (low–high values) or β distribution (mean, SD)	Ref.
Change to CMO if failed NIMV when DNI	1.00 (0.90–1.00)	Expert opinion (lowest–highest estimates)	Uniform (0.90–1.00)	N/A
Change to CMO if failed NIMV when Full Code	0.04 (0.00–0.20)	Published estimates and expert opinion (lowest–highest estimates)	Uniform (0.0–0.20)	[45,46]
ETT complications	0.42 (0.19–0.77)	Published estimates (median, lowest–highest estimates)	β (0.42, 0.145)	[16,17,47]
Discharge to community from nursing home	0.05 (0.00–0.10)	Expert opinion (lowest–highest estimates)	Uniform (0.0–0.10)	N/A
Discharge to community from short-term ECF	0.70 (0.50–1.00)	Expert opinion (lowest–highest estimates)	Uniform (0.50–1.00)	N/A
Death in community	0.02 (0.01–0.04)	Single study (95% CI) ^{†‡}	β (0.017, 0.03)	[8]
Death in nursing home	0.05 (0.02–0.10)	Published estimates (median, lowest–highest estimates)	β (0.05, 0.01)	[29,48,49]
Death in short-term ECF	0.02 (0.01–0.04)	Single study (95% CI)	β (0.02, 0.03)	[8]
Discharge to nursing home if CMO	0.99 (0.80–1.00)	Expert opinion (lowest–highest estimates)	Uniform (0.80–1.00)	N/A
Discharge to short-term ECF after uncomplicated ETT	0.30 (0.22–0.40)	Single study (95% CI)	β (0.30, 0.04)	[23]
Discharge to nursing home after complicated ETT	0.76 (0.55–0.91)	Single study (95% CI)	β (0.76, 0.09)	[23]
Discharge to short-term ECF after successful NIMV	0.10 (0.01–0.15)	Expert opinion (lowest–highest estimates)	Uniform (0.01–0.15)	N/A
Discharge to short-term ECF after no NIMV (no mechanical ventilation used)	0.05 (0.00–0.10)	Expert opinion (lowest–highest estimates)	Uniform (0.00–0.10)	N/A
ETT if DNI when moderately ill	0.00 (0.00–0.02)	Model assumption (N/A)	Uniform (0.00–0.02)	N/A
ETT if Full Code when moderately ill	0.21 (0.06–0.36)	Published estimates (median, lowest–highest estimates)	β (0.21, 0.07)	[50,51]
ICU admission if moderately ill	0.20 (0.10–0.30)	Expert opinion (lowest–highest estimates)	Uniform (0.10–0.30)	N/A
ICU admission if severely ill	1.00 (N/A)	Model assumption (N/A)	N/A	[23]
Mechanical ventilation (NIMV) in ICU when moderately ill if DNI	1.0 (0.50–1.00)	Expert opinion (lowest–highest estimates)	N/A	N/A
Mechanical ventilation (NIMV or ETT) in ICU when moderately ill if Full Code	0.99 (0.80–1.00)	Expert opinion (lowest–highest estimates)	N/A (0.80–1.00)	N/A
Mechanical ventilation (NIMV) in ICU when severely ill if DNI	0.99 (0.50–1.00)	Expert opinion (lowest–highest estimates)	Uniform (0.50–1.00)	N/A
Mechanical ventilation (NIMV or ETT) in ICU when severely ill if Full Code	0.99 (0.90–1.00)	Expert opinion (lowest–highest estimates)	N/A (0.90–1.00)	N/A
NIMV in the ICU when severely ill if Full Code	0.16 (0.00–0.54)	Published estimates (median, range)	β (0.16, 0.19)	[23,25–27]

Description	Baseline estimates (range)	Method used for baseline estimation (method used for range)	Distribution: uniform (low–high values) or β distribution (mean, SD)	Ref.
Mechanical ventilation (NIMV) on ward when moderately ill if DNI	0.72 (0.64–0.82)	Expert opinion (model assumption to be the same as for Full Code)	β (0.72, 0.05)	[21,52]
NIMV on ward when moderately ill if Full Code	0.72 (0.64–0.82)	Published estimates (median, range)	β (0.72, 0.05)	[21,52]
Failing NIMV when moderately ill	0.14 (0.10–0.18)	Random effects pooling, five studies (95% CI)	β (0.14, 0.02)	[18,45,53,54]
Failing NIMV when severely ill	0.28 (0.12–0.73)	Published estimates (median, range)	β (0.28, 0.23)	[16–22,24]
NIMV if failed a trial of no mechanical ventilation	0.99 (0.90–1.00)	Expert opinion (lowest–highest)	Uniform (0.90–1.00)	N/A
Recurrent respiratory exacerbation (requiring hospitalization)	0.19 (0.16–0.22)	Single study (95% CI)	β (0.19, 0.04)	[55]
Severe respiratory exacerbation (recurrent respiratory exacerbation that is severe; severely ill)	0.37 (0.29–0.46)	Single study (95% CI)	β (0.37, 0.05)	[51]
Successful treatment without mechanical ventilation if moderately ill	0.73 (0.64–0.81)	Single study (95% CI)	β (0.73, 0.04)	[53]
Successful treatment without mechanical ventilation if moderately ill if admitted from a nursing home	0.44 (0.31–0.81)	Expert opinion and single study [‡] (lowest–highest estimates)	Uniform (0.00–0.81)	[53,55]
Successful treatment without mechanical ventilation if severely ill	0.10 (0.00–0.30)	Expert opinion (lowest–highest estimates)	Uniform (0.00–0.30)	N/A
Successful treatment without mechanical ventilation if severely ill if admitted from a nursing home	0.00 (0.00–0.30)	Expert opinion and single study [‡] (lowest–highest estimates)	Uniform (0.00–0.02)	[55]
Surviving after becoming CMO	0.01 (0.00–0.10)	Random effects pooling, two studies (95% CI)	β (0.00, 0.05)	[22,56]
Surviving complicated ETT	0.62 (0.49–0.75)	Random effects pooling, two studies (95% CI)	β (0.62, 0.07)	[16,17,47,55]
Surviving complicated ETT if admitted from a nursing home	0.27 (0.00–0.75)	Random effects (two studies) plus single study (95% CI)	β (0.27, 0.25)	[16,17,55]
Surviving uncomplicated ETT	1.00 (0.72–1.00)	Single study (95% CI)	β (1.00, 0.18)	[16]
Surviving uncomplicated ETT if admitted from nursing home	0.95 (0.72–1.00)	Expert opinion and single study [§] (lowest–highest estimates)	Uniform (0.70–1.00)	N/A

[‡] The baseline estimate of survival for patients with severe chronic obstructive pulmonary disease is drawn from results of a 52-month prospective cohort analysis [8]. We chose to estimate survival using the average of three different time points (36, 40 and 52 months) because the curve was not exponential and there were large drops in incremental survival on the Kaplan–Meier curve. We included a broad range of estimates using 52-month survival in sensitivity analysis.

[§] Patients admitted from the nursing home with chronic obstructive pulmonary disease exacerbation had a 2.7 relative risk (95% CI: 1.4–5.1) of death when compared with patients admitted from home with chronic obstructive pulmonary disease exacerbation. To estimate the probabilities of death if admitted from the nursing home, we multiplied this 2.7 relative risk of death by the probabilities of death (converted to rates) if admitted from home. We used a wide range of estimates in sensitivity analysis (including the upper limit of probabilities if admitted from the community) to account for error within these estimates.

[§]We assumed that the probability of success when not receiving any mechanical ventilation for patients admitted from nursing home was lower than for patients admitted from the community. This assumption of lower survival is based on the lower baseline survival for patients admitted from the nursing home. We tested this assumption using a wide range of estimates of survival in sensitivity analysis.

CMO: Comfort measures only; DNI: Do Not Intubate; ECF: Extended care facility; ETT: Endotracheal tube insertion; ICU: Intensive care unit; N/A: Not applicable; NIMV: Noninvasive mechanical ventilation; SD Standard deviation.

Table 2

Frequency of rehospitalizations in the first year after initial hospitalization for respiratory failure, Full Code versus Do Not Intubate.

Advance directive	Rehospitalized at least once (%)	Rehospitalized at least twice (%)	Rehospitalized at least three times (%)	Rehospitalized within 1 month (%)
Full Code	48.0	8.9	0.9	6.8
Do Not Intubate	38.6	2.9	0.3	1.7