# Position Statement from the Canadian Thoracic Society (CTS) on Clinical Triage Thresholds in Respiratory Disease Patients in the Event of a Major Surge during the COVID-19 Pandemic – UPDATED with recommendations for *pulmonary arterial hypertension*

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## UPDATE – JUNE 29, 2020

This update includes the addition of a "Pulmonary Arterial Hypertension" (PAH) section to our original CTS position statement (May 11, 2020)[1].

## BACKGROUND

With the rapid rise in cases of COVID-19 across the world, health systems face unprecedented challenges in the delivery of patient care. This includes constrained capacity for intensive care unit (ICU) beds and life saving equipment such as ventilators[1]. As a result, clinicians have been forced to make life-or-death resource allocation decisions, often without an adequate ethical or implementation framework[1]. Not only does this create the possibility of resource allocation decisions that do not align with societal preferences[2], but it also places a great deal of pressure on front line clinicians, particularly given the existing prognostic uncertainty around COVID-19.[3]

If faced with significant shortages, the rationing of healthcare resources should occur in accordance with a transparent ethical framework[4] which ideally should empirically reflect societal preferences and views.[5] It also requires a logistical framework for application in complex health settings, often with little time for allocation decisions to be made. This overarching ethical framework and specifics around operationalization of resource allocation are outside the scope of this document, and are being addressed independently by jurisdictions around the world,[6,7] including by various health authorities[8] within Canada.

Universal principles around responsible resource stewardship focus on the dual aims of both saving the most lives (generally considered the primary goal) and maximizing gains in post-treatment length of life.[2] Practically speaking, if clinicians are faced with a scenario requiring rationing of critical care resources, fulfilling these aims requires clinicians to consider each patient's age and comorbidities in order to reach comparative estimates both of their probability of surviving the acute illness and their life expectancy after an episode of critical illness with prolonged intubation. To this end, Ontario Health recently introduced the "Clinical Triage Protocol for Major Surge in COVID Pandemic,"[8] which outlines an ethical clinical framework using morbidity-related criteria for consideration should ICU access be limited. Specifically, this document proposes three levels of surge planning, with progressively more strict exclusion criteria for ICU admission (and continued ICU care in those already receiving it), as follows:



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Level 1 – Patients with > 80% expected mortality during or in the 6-12 months following critical illness will not be offered ICU intervention

Level 2 - Patients with > 50% expected mortality during or in the 6-12 months following critical illness will not be offered ICU intervention

Level 3 - Patients with > 30% expected mortality during or in the 6-12 months following critical illness will not be offered ICU intervention

Other provincial guidelines have proposed identical expected mortality cutoffs for each surge level. To guide clinicians in approximating these predicted mortalities, these guidelines provide descriptions of morbidities that might carry the corresponding prognoses. Morbidities/clinical contexts covered include severe trauma, burns, cardiac arrest, malignant disease, neurologic disease, and organ-specific conditions. In the latter category, documents focus on underlying lung conditions such as chronic obstructive pulmonary disease (COPD), pulmonary fibrosis (PF), cystic fibrosis (CF), and pulmonary arterial hypertension (PAH).

This position statement aims to provide criteria corresponding to estimated mortalities, as per the framework outlined in this statement for COPD, PF, CF, and PAH. Each disease section was prepared independently by experts from across Canada, including members of the corresponding CTS assembly where applicable. Criteria were informed by published survival data, and where possible, complimented by (mostly indirect) data to estimate the impact of critical illness. As such, these criteria are primarily based on expert opinion and should only be used as a starting point for resource allocation decisions in a pandemic environment when capacity is limited. Ultimately, any resource allocation decisions should be made in accordance with local surge planning guidance, individualized, and supplemented with clinical judgement. As well, these recommendations are subject to change as new data become available. We plan to update this guidance as new information becomes available. We recommend periodically visiting the Canadian Thoracic Society website (https://cts-sct.ca/covid-19) for updates.

As the national expert society on lung diseases, the CTS believes that it is important for our organization to provide guidance in this area. This would not only be to provide a reference for groups that may be developing similar guidance but also to reassure members of our profession and the public that the best available evidence and expert opinion has been utilized in estimating respiratory disease-specific predicted mortalities.

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## SUMMARY OF RECOMMENDATIONS

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|---|
| **Level 1 (> 80% predicted mortality during or in the 6-12 months following critical illness).** ***Patients with:*** |
| **1. CYSTIC FIBROSIS** |
| • $FEV_1$ of <20% predicted when measured at the time of clinical stability. |
| **2. PULMONARY FIBROSIS** |
| • FVC <50-60%; **OR**<br>• DLCO < 30-40% predicted; **OR**<br>• Chronic supplemental oxygen at home (more than 12 hours per day); **OR**<br>• Echocardiographic evidence of pulmonary hypertension (estimated right ventricular systolic pressure >50 mmHg)[a]; **OR**<br>• Rapidly progressive disease[b]; **OR**<br>• History of Acute Exacerbation-Interstitial Lung Disease in the last 12 months. |
| **3. CHRONIC OBSTRUCTIVE PULMONARY DISEASE** |
| • Severe ($FEV_1$<50% predicted) or very severe airway obstruction ($FEV_1$<30% predicted)<br>**AND** chronic hypoxemia (PaO2 </= 55 mmHg) and/or chronic hypercapnia (PaCO2 >55 mmHg)<br>**AND** Clinical Frailty Score of >/=7. |
| **4. PULMONARY ARTERIAL HYPERTENSION** |
| • High-risk profile (REVEAL 2.0 score ≥ 9 or high-risk ESC/ERS score) while on optimal therapy[c]. |
| **Level 2 (>50% predicted mortality during or in the 6-12 months following critical illness).** ***Patients with:*** |
| **1. CYSTIC FIBROSIS** |
| • $FEV_1$ of <20% predicted when measured at the time of clinical stability. **(Same as Level 1)** |
| **2. PULMONARY FIBROSIS** |
| • FVC <50-60%; **OR**<br>• DLCO < 30-40% predicted; **OR**<br>• Chronic supplemental oxygen at home (more than 12 hours per day); **OR**<br>• Echocardiographic evidence of pulmonary hypertension (estimated right ventricular systolic pressure >50 mmHg)[a]; **OR**<br>• Rapidly progressive disease[b]; **OR**<br>• History of Acute Exacerbation-Interstitial Lung Disease in the last 12 months. **(Same as Level 1)** |
| **3. CHRONIC OBSTRUCTIVE PULMONARY DISEASE** |
| • Severe ($FEV_1$<50% predicted) or very severe airway obstruction ($FEV_1$<30% predicted)<br>**AND** Clinical Frailty Score of >/=6. |
| **4. PULMONARY ARTERIAL HYPERTENSION** |
| • An intermediate-risk profile (REVEAL 2.0 score 7-8 or Intermediate risk ESC/ERS score) while on optimal therapy<br>**AND** age ≥ 75 years old<br>**AND** either a recent hospitalization for worsening PAH/right heart failure in the past 3 months or the presence of other significant comorbidities (especially chronic renal failure) |
| **Level 3 (> 30% predicted mortality during or in the 6-12 months following critical illness).** ***Patients with:*** |
| **1. CYSTIC FIBROSIS** |
| • $FEV_1$ of <30% predicted when measured at the time of clinical stability. |
| **2. PULMONARY FIBROSIS** |
| • FVC < 75% or DLCO < 55% predicted. |
| **3. CHRONIC OBSTRUCTIVE PULMONARY DISEASE** |
| • Severe ($FEV_1$<50% predicted) or very severe airway obstruction ($FEV_1$<30% predicted)<br>**AND** >/=2 hospitalizations within the previous 12 months for treatment of an acute exacerbation of COPD<br>**AND** Clinical Frailty Score of >/=5. |
| **4. PULMONARY ARTERIAL HYPERTENSION** |
| • An intermediate-risk profile (REVEAL 2.0 score 7-8 or Intermediate risk ESC/ERS score) while on optimal therapy<br>**AND** age < 75 years old<br>**AND** either a recent hospitalization for worsening PAH/right heart failure in the past 3 months or the presence of other significant comorbidities (especially chronic renal failure) |

**a:** Presence of prominent RV dilation and hypokinesis, preceding COVID-19 infection, should be taken into account when making prognostic determinations. A conservative measure of 50 mmHg was selected, given the heterogeneous and predominantly retrospective nature of the supporting evidence and the high prevalence of risk factors for Group 2 PH in the ILD population.

**b:** >10% decline in FVC over the last 6 months associated with pronounced radiographic and clinical deterioration. Eligible patients with this phenotype are ordinarily referred for urgent lung transplant assessment.

**c:** optimal medical therapy for patients with high risk PAH includes at least 2 oral medications and should include a parenteral prostacyclin (e.g. treprostinil or epoprostenol) if they are eligible.



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## SECTION 1 - CYSTIC FIBROSIS

**Contributors: Anne L. Stephenson, Elizabeth Tullis**

**Background**

The survival for people with CF has improved markedly over the past 3 decades.[1,2,3,4] In 1990 the median survival in CF was 30 years. By 2018, the median survival for Canadians living with CF had increased to 52 years of age.[3] Lung function, specifically forced expiratory volume in 1 sec (FEV1) percent predicted, is a key prognostic marker for health outcomes such as survival in CF. There are limited published data about the impact of COVID-19 infection on the health of patients with CF.[5]

These predicted mortalities are informed by contemporary Canadian CF Registry data as well as published literature. They have been reviewed and endorsed by the Healthcare Advisory Council of Cystic Fibrosis Canada.

***Level 1 (> 80% predicted mortality during or in the 6-12 months following critical illness)***

- ***CF patients*** *with* *$FEV_1$ of < 20% predicted when measured at time of clinical stability*

The Canadian CF Registry captures demographic and clinical data annually on virtually all patients diagnosed with CF in Canada, distributed across 42 Canadian CF care centers. It is estimated that less than 1% of the Canadian CF patients have declined consent to have their data captured in the registry (personal communication with CF Canada). All individuals within the registry have provided informed consent to have their data collected.

***Level 2 (> 50% predicted mortality during or in the 6-12 months following critical illness)***

- ***CF patients with*** *$FEV_1$ of < 20% predicted when measured at time of clinical stability*

***(Same as Level 1)***

Canadian CF Registry data show that the median time to death or lung transplant after the first measurement of $FEV_1$< 20% predicted is 1 year (Figure 1). Although this corresponds to a ~50% probability of death or transplant at 1 year, because there are no data to support patient characteristics that would predict a mortality of > 80%, this criterion is recommended for Level 1 given the additional expected mortality impact of the critical illness itself. In recent years, listing for lung transplant in Ontario usually occurs when $FEV_1$ < 20% predicted.

Canadian CF Registry data show that the median time to death or lung transplant after the first measurement of $FEV_1$< 20% predicted is 1 year (i.e. a 50% probability of death or transplant after the first measurement of $FEV_1$< 20% predicted) (Figure 1).



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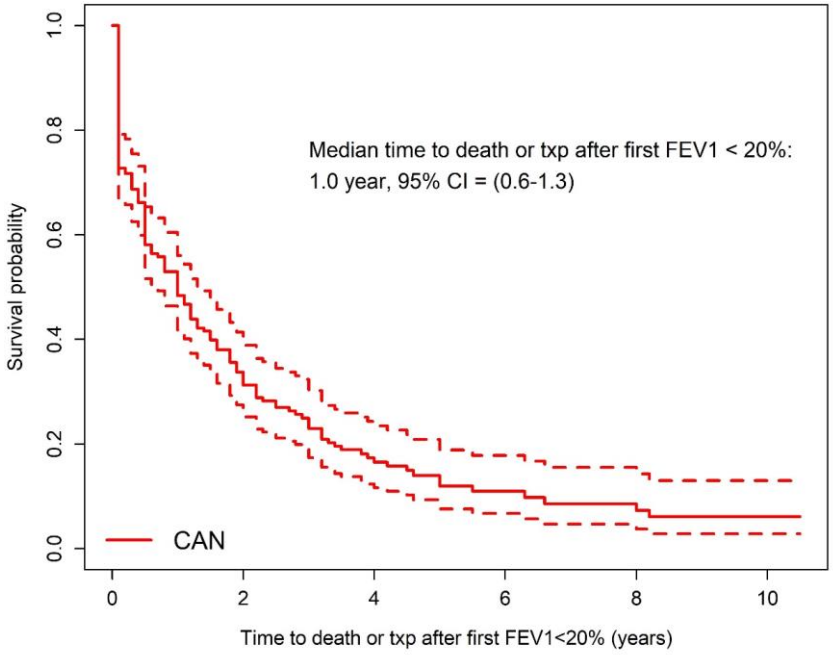


**Figure 1:** Kaplan Meier survival curve representing time to death or transplant (Txp) after lung function ($FEV_1$) falls below 20% predicted using Cystic Fibrosis Registry data (2005-2016).

***Level 3 (> 30% predicted mortality during or in the 6-12 months following critical illness)***

- ***CF patients with*** *$FEV_1$ of <30% predicted when measured at the time of clinical stability.*

Median survival of Canadians with CF with $FEV_1$ of <30% predicted is 3.5 years and 30% of patients will have died or received a transplant by 2 years (Figure 2).

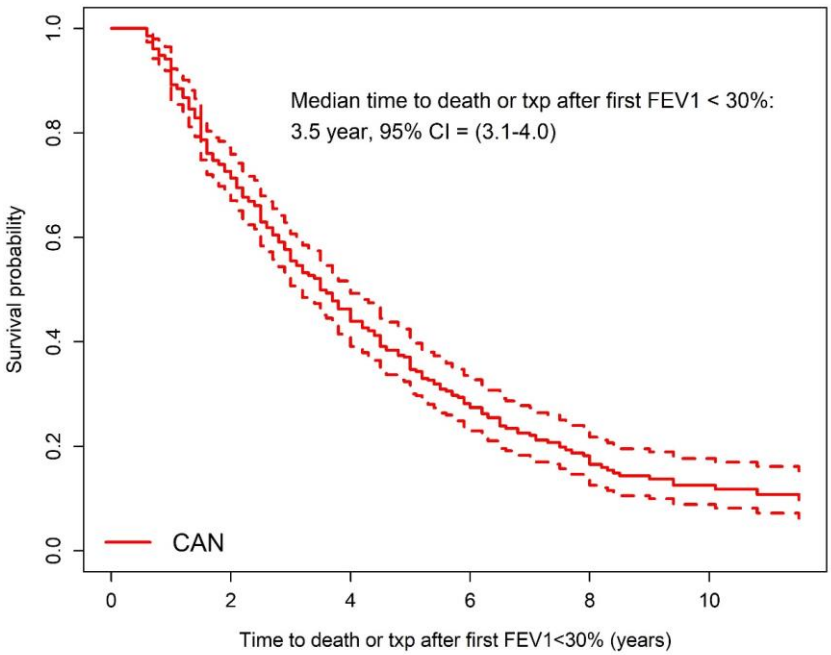


**Figure 2:** Kaplan Meier survival curve representing time to death or transplant (Txp) after lung function ($FEV_1$) falls below 30% predicted using Cystic Fibrosis Registry data (2005-2016).



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**Additional factors to consider at all surge levels:**
Comorbidities that may be associated with an increased mortality would include infection with *Burkholderia cepacia* complex (specifically, *B. cenocepacia* ET12 strain)[1] or severe liver disease[6] (specifically, cirrhosis with portal hypertension or synthetic liver dysfunction) and should be considered by clinicians at all surge levels.

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## SECTION 2 - PULMONARY FIBROSIS


**Contributors: Nathan Hambly, Martin Kolb**


**Background**
Interstitial lung disease (ILD) refers to a group of heterogenous conditions characterized by diffuse fibrotic and/or inflammatory infiltration of the alveolar space and septa. Disease course and prognosis varies substantially, with the relative burden of fibrosis being associated with poor long-term outcome. Progressive-fibrosing ILD (PF-ILD) is a term recently coined to describe these patients.[1] Idiopathic pulmonary fibrosis (IPF) is regarded as the prototypical PF-ILD; however, progressive fibrosis can occur in other ILDs albeit at a lower frequency than encountered in IPF.[2] Given the prognostic relevance of this disease phenotype, consideration of expected survival in PF-ILD is highly relevant to any standardized approach to the rationing of critical care resources in the setting of a major COVID-19 surge.

Survival in the setting of fibrotic lung disease is variable, with the majority of prognostic estimates derived from the placebo arm of IPF treatment studies. Whether these results are generalizable across the spectrum of pulmonary fibrosis patients is uncertain. Median survival in IPF has been reported to range from 2-5 years.[3] Despite these grim numbers, published reports suggest that 20-25% of patients survive greater than 10 years from the time of diagnosis.[4] The GAP prediction model represents the most widely validated prognostic tool used in clinical practice.[5] The model incorporates gender, age, FVC, and DLCO into a simple scoring tool to predict 1-,2-, and 3-year mortality. Clinical course is also a strong predictor of outcome, as a 10% or greater reduction in FVC over 6-12 months predicts the onset of an acute exacerbation, hospitalization, and death.

Although no robust data exist regarding the natural history of COVID-19 infection in the pulmonary fibrosis population, estimations of prognosis in patients with pulmonary fibrosis facing critical illness from severe lung injury can be informed by: 1) outcomes of acute exacerbation of ILD; and 2) outcomes following diagnostic surgical lung biopsy (SLB).

Acute exacerbations of IPF (AE-IPF) lead to widespread acute lung injury, characterized by diffuse alveolar damage with hyaline membrane formation and interstitial edema; similar features are encountered in the setting of acute respiratory distress syndrome.[6] The prognostic implications of an AE-IPF are profound. Acute exacerbation in the non-IPF fibrotic ILD population has also been well-described.[7] Available data suggest that up to 46% of deaths in IPF are preceded by an acute exacerbation.[8,9] Median survival following an acute exacerbation is 3-4 months.[10,11] In-hospital mortality rates in the setting of an acute exacerbation are roughly 50%.[10,12,13] Data from retrospective

case series suggest a 3-month mortality rate of over 90% for those critically ill patients undergoing intubation and mechanical ventilation in the setting of an acute exacerbation.[14] Given these dismal outcomes, international guidelines make a weak recommendation against the use of mechanical ventilation to treat respiratory failure in IPF.[3] With the knowledge that respiratory viral infection has been proposed as a putative triggering factor for AE-IPF and that prognosis following idiopathic AE-IPF and infection-related acute exacerbations are similar, it is reasonable to expect a comparably poor prognosis in PF-ILD patients experiencing severe COVID-19 infection.[13,15]

Exacerbations have an annual incidence of 4–20%, with those patients with physiologically advanced disease at greatest risk for acute deterioration. Low FVC has proven the most consistent risk factor for AE-IPF. Other variables associated with increased risk include low DLCO, reduced 6-minute walk distance (6MWD), pulmonary hypertension, resting hypoxia, and a prior history of acute exacerbation.[6] In the INPULSIS trial, a FVC < 70% was clearly identified as a risk factor for AE-IPF. In the placebo arm of this trial, rates of acute exacerbation were 14.9% versus 3.3% in patients with FVC below and above 70% respectively.[16] This rate is further reduced to 2.8% in those patients with FVC >90%.[17] As such, our knowledge of the natural history of AE-IPF is biased by those patients with advanced disease. In the setting of preserved FVC, and a potentially reversible insult, the natural history of acute respiratory failure is unknown.

SLB is considered appropriate when a definitive ILD diagnosis cannot be established using non-invasive measures. Meta-analysis data suggests a 90-day post-operative mortality rate of 3.4%, with the risk being as high as 16% in emergent situations.[18] It is thought that many of these deaths are related to acute exacerbations, triggered by the insult of the operative procedure.[19] As such, a recent Canadian Thoracic Society position statement provided a list of relative contraindications to SLB including: age > 75, pre-operative resting hypoxemia, mechanical ventilation, FVC <55% predicted, DLCO < 35% predicted, pulmonary hypertension, immunocompromised state, clinically significant medical comorbidity, or rapidly progressive disease.[20] These risk factors are also associated with ILD mortality, independent of the operative procedure. It is, therefore, reasonable to expect that ILD patients with similar features would be at high risk of poor long-term outcome following severe COVID-19 infection.

***Level 1 (> 80% predicted mortality during or in the 6-12 months following critical illness)****

***PF patients with:***

- *FVC <50-60%;* ***OR***
- *DLCO < 30-40% predicted;* ***OR***
- *Chronic supplemental oxygen at home (more than 12 hours per day);* ***OR***
- *Echocardiographic evidence of pulmonary hypertension (estimated right ventricular systolic pressure >50 mmHg)[a];* ***OR***
- *Rapidly progressive disease[b];* ***OR***
- *History of AE-ILD in the last 12 months.*

There is no single standard method or set of clinical criteria to predict long-term outcome in pulmonary fibrosis. This uncertainty is further magnified by the fact that predictors of survival tend to be poor predictors of disease progression.[21] As such, given the heterogeneous nature of the pulmonary fibrosis population, the indirect nature of the supporting evidence, and the variety of patient specific factors that determine individual risk, a range of lung function parameters have been outlined to provide physicians with both guidance and flexibility in making treatment decisions. These criteria were derived from the published literature describing long-term outcomes in IPF, the predisposing factors and clinical course of AE-IPF, and the risk of poor outcomes following SLB.[5,6,7,20]

***Level 2 (> 50% predicted mortality during or in the 6-12 months following critical illness)****

***PF patients with:***

- *FVC <50-60%;* ***OR***
- *DLCO < 30-40% predicted;* ***OR***
- *Chronic supplemental oxygen at home (more than 12 hours per day);* ***OR***
- *Echocardiographic evidence of pulmonary hypertension (estimated right ventricular systolic pressure >50 mmHg)[a];* ***OR***
- *Rapidly progressive disease[b];* ***OR***
- *History of AE-ILD in the last 12 months.*

***(Same as Level 1)***

a: Presence of prominent RV dilation and hypokinesis, preceding COVID-19 infection, should be taken into account when making prognostic determinations. A conservative measure of 50 mmHg was selected, given the heterogeneous and predominantly retrospective nature of the supporting evidence and the high prevalence of risk factors for Group 2 PH in the ILD population.

b: >10% decline in FVC over the last 6 months associated with pronounced radiographic and clinical deterioration. Eligible patients with this phenotype are ordinarily referred for urgent lung transplant assessment.

***** Because we could not identify clear criteria for a predicted >50% mortality, we have chosen to re-iterate the criteria for a predicted >80% mortality in Level 1, above. This is in keeping with the poor prognosis normally encountered in patients experiencing an AE-ILD.[6]

***Level 3 (> 30% predicted mortality during or in the 6-12 months following critical illness)***

- ***PF patients with*** *FVC <75% or DLCO <55% predicted.*

These criteria have been validated in the GAP risk assessment system to predict a low probability of 1-year mortality.[5]

**Additional factors to consider at all surge levels:**

Comorbidities that may be associated with an increased mortality include radiographic evidence of moderate/severe emphysema, life-threatening malignancy including lung cancer, and/or advanced coronary artery disease/congestive heart failure. These factors should be considered by clinicians at all surge levels.[22]

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## SECTION 3 – CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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### Background

Patients with COPD are at an increased risk of developing severe complications of a SARS-CoV-2 infection[1]. Reports suggest that COPD patients admitted to hospital with a SARS-CoV-2 infection are more likely to require ICU support and to have increased mortality as compared to non-COPD patients.[2,3] For a clinician attempting to triage a patient with a history of COPD, classifying them into one of the three levels proposed in this document is challenging and fraught with uncertainty. There are many factors contributing to the complexity of this clinical decision when it involves COPD patients.

Simply put, there is significant variability in the outpatient management of COPD. Gaps in care exist from confirmation of diagnosis to planning of end-of-life care. A large proportion of patients being treated for COPD may not have the disease, as it has not been confirmed by spirometry.[4] This overdiagnosis is accompanied by under diagnosis in patients at risk of having COPD.[5] Access to proven, beneficial non-pharmacological interventions such as pulmonary rehabilitation (PR) is limited in Canada. In 2015, a national survey conducted by the CTS COPD Clinical Assembly found that only 0.4% of COPD patients had access to PR[6], an intervention demonstrated to reduce exacerbations and improve quality of life. Lastly, despite well developed and disseminated pharmacological guidelines,[7] there is great variability in the inhaled maintenance therapies prescribed for patients. This is influenced by many factors including provincial reimbursement policies, physician prescribing habits and patient behaviors. Thus, a patient with COPD may not be optimized in their outpatient management, thereby impacting the frequency and severity of their acute exacerbations. A clinician involved in

the decision-making of a COPD patient's triage level  resource limited setting must be aware of these potential clinical care gaps and factor them into their assessment.

In addition to these "real life" gaps in the management of COPD, there are very few clinical variables that accurately predict long term survival in individual patients with COPD. We recognize that the frequency and severity of acute exacerbations of COPD (AECOPD) are major drivers of the morbidity and mortality associated with COPD[8,9,10]. However, if a patient's chronic management is not optimal (as discussed above), patients may report a history of preventable events. Clinical tools such as lung function tests and scores of dyspnea severity (e.g. mMRC) are not reliable predictors of individual morbidity and mortality[8] and we recommend against relying solely upon these measures to make a significant clinical decision regarding triage level. Patients with COPD who have documented chronic hypoxemia and hypercapnia are a group of patients that are recognized to have higher 1-year mortality[11,12]. The BODE Index[13] is a validated scoring system predicting 3-year survival; however, it requires the measurement of a 6MWD, which is often not done and/or documented, and therefore is not measurable in most patients. Even so, a history of frequent AECOPD has been demonstrated to be a stronger predictor of respiratory morbidity and mortality than the BODE Index.[8,9]

In order to satisfy the terms of this document, we convened a group of respirologists from across Canada who have a research interest in COPD and a clinical expertise in managing severe and very severe COPD patients. Given the current variability of outpatient clinical management and the lack of guidance from our literature review of predictors of survival, our group recommends that for COPD patients, the Clinical Frailty Score (CFS) be included as part of the triage criteria. The CFS is a validated[14] tool that has been shown to assist clinicians in understanding the impact frailty has on clinical care and outcomes[15]. A prospective study of admissions to the ICU demonstrated that frailty was common among older patients and that a higher CFS score on admission was predictive of increased morbidity and mortality in the year following the ICU admission.[16] Hence, the addition of a CFS score will improve the prognostication of COPD patient outcomes.

Thus, based on our review of available evidence, our group reached a consensus on the following definitions:

***Level 1 (> 80% predicted mortality during or in the 6-12 months following critical illness)***

- ***COPD patients with*** *severe ($FEV_1$<50% predicted) or very severe airway obstruction ($FEV_1$<30% predicted)*
  ***AND*** *chronic hypoxemia (PaO2 </= 55 mmHg) and/or chronic hypercapnia (PaCO2 >55 mmHg)*
  ***AND*** *Clinical Frailty Score of >/=7*

***Level 2 (> 50% predicted mortality during or in the 6-12 months following critical illness)***

- ***COPD patients with*** *severe ($FEV_1$<50% predicted) or very severe airway obstruction ($FEV_1$<30% predicted)*
  ***AND*** *Clinical Frailty Score of >/=6*

***Level 3 (> 30% predicted mortality during or in the 6-12 months following critical illness)***

- ***COPD patients with*** *severe ($FEV_1$<50% predicted) or very severe airway obstruction ($FEV_1$<30% predicted)*
  ***AND*** *>/=2 hospitalizations within the previous 12 months for treatment of an acute exacerbation of COPD*
  ***AND*** *Clinical Frailty Score of >/=5*

These definitions were informed by a combination of best scientific evidence, expert opinion and consensus. We recognize the need for more research into the natural history of patients with COPD and factors that influence and predict their outcomes, including COVID-19 infection.  We will update this document if the medical literature provides further information to guide decision-making in this circumstance.

Our group's recommendations are intended to help optimally guide health care professionals during the exceptional and challenging circumstances of resource triaging in the setting of a pandemic and should be considered as complimentary to the treating physician's global clinical judgement of the patient under his or her care.

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## SECTION 4 – PULMONARY ARTERIAL HYPERTENSION


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### Background

PAH is an obliterative vasculopathy that results in elevated pulmonary vascular resistance and pulmonary arterial pressure, which increases the load on the right ventricle (RV) and can lead to RV failure. PAH (Group 1 pulmonary hypertension[PH]) must be distinguished from other causes of pulmonary hypertension such as left heart disease (Group 2 PH), lung diseases and/or chronic hypoxemia (Group 3 PH), chronic thromboembolic pulmonary hypertension (CTEPH, Group 4 PH) and diseases with unclear or multifactorial causes (e.g. sarcoidosis, sickle cell disease, Group 5 PH).[1] PAH is a progressive, fatal disease. However, the survival for patients with PAH has improved markedly since the 1980s when the median survival after diagnosis was only 2.8 years.[2] More recent European and American registries report a median survival from diagnosis of more than 7 years.[3,4] The optimal management strategy for most PAH patients includes treatment with two or three medications targeting the nitric oxide, endothelin, and prostacyclin pathways.[5]

The key factors consistently associated with a poor prognosis in PAH are: systemic sclerosis etiology of PAH, older age, male sex, severe symptoms (New York Heart Association Class III-IV), reduced exercise capacity, comorbidities, severe right ventricular dysfunction, and hospitalizations for right heart failure.[6–10] There are currently no data regarding the incidence or outcomes of PAH patients with COVID-19. Therefore, baseline risk status, knowledge of outcomes for PAH patients admitted to the intensive care unit (ICU), and the anticipated consequences of COVID-19 on the pulmonary circulation and right ventricle must be considered.

Several risk prediction tools are available in PAH, including the U.S. Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL) 2.0 risk score[6] and the European Society of Cardiology/European Respiratory Society (ESC/ERS) risk assessment table (Appendix 1).[11] A recent study validated these risk assessment tools in a Canadian population, in which the REVEAL 2.0 score discriminated long-term survival better than the ESC/ERS methods.[12] In that study, the presence or absence of renal dysfunction (eGFR < 60 ml/min/1.73 m2) at diagnosis or deteriorating renal function during follow-up (>10% decrease in eGFR) helped re-stratify intermediate risk patients as high-risk or low risk, respectively. An online REVEAL score calculator to estimate 1-year mortality is also available.

Outcomes are also poor for PAH patients hospitalized for right heart failure or other critical illnesses. Hospitalization for right heart failure is associated with an in-hospital mortality of approximately 15% and a 30-40% mortality in the subsequent 12 months after hospital discharge.[10,13–16] In systemic sclerosis patients with PAH, the 12-month mortality after hospitalization approached 50%.[13] The in-hospital mortality for patients with PAH admitted to an intensive care unit is even higher at 30-52%[14,16–19], especially if they are admitted to the ICU because of infection (e.g. pneumonia, sepsis) rather than isolated right heart failure.[16,18] Furthermore, patients who need mechanical ventilation for hypoxemic respiratory failure or require dialysis have an ICU mortality of approximately 70%.[18] Additionally, critically ill patients with COVID-19 appear to have a high risk of pulmonary thromboembolism[20,21], which is unlikely to be tolerated by patients with PAH with limited RV reserve.

***Level 1 (> 80% expected mortality in the 6-12 months following critical illness)***

- ***PAH patients with*** *a high-risk profile (REVEAL 2.0 score ≥ 9 or High-risk ESC/ERS score) while on optimal therapy[a]*

***Level 2 (> 50% expected mortality in the 6-12 months following critical illness)***

- ***PAH patients with*** *an intermediate-risk profile (REVEAL 2.0 score 7-8 or Intermediate risk ESC/ERS score) while on optimal therapy*
  ***AND*** *age ≥ 75 years old*
  ***AND*** *either a recent hospitalization for worsening PAH/right heart failure in the past 3 months or the presence of other significant comorbidities (especially chronic renal failure)*

***Level 3 (> 30% expected mortality in the 6-12 months following critical illness)***

- ***PAH patients with*** *an intermediate-risk profile (REVEAL 2.0 score 7-8 or Intermediate risk ESC/ERS score) while on optimal therapy*
  ***AND*** *age < 75 years old*
  ***AND*** *either a recent hospitalization for worsening PAH/right heart failure in the past 3 months or the presence of other significant comorbidities (especially chronic renal failure)*

**a:** optimal medical therapy for patients with high risk PAH includes at least 2 oral medications and should include a parenteral prostacyclin (e.g. treprostinil or epoprostenol) if they are eligible.



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**Additional factors to consider at all surge levels:**
Advanced age and comorbidities must also be considered in resource allocation at surge levels, as PAH patients ≥75 years old and those with multiple comorbidities (especially chronic renal failure) have poor responses to PAH therapies and poor long term prognosis.[8,22,23]

These definitions were based upon expert opinion and consideration of the best available evidence regarding the prognosis of PAH patients with critical illness. Importantly, these definitions apply to patients with established PAH by right heart catheterization and do not apply to other types of pulmonary hypertension (i.e. left heart disease, chronic lung disease). PH in the context of left heart disease is a poor prognostic factor. However, group 2 PH requires treatment of the underlying cardiac condition and PAH therapies should not be used in this context.[24] PH is also a poor prognostic factor in patients with underlying lung disease.[25] Patients with Group 3 PH due to lung disease and/or chronic hypoxemia should be considered according to the recommendations specific to the underlying condition (e.g. COPD or PF). Patients with CTEPH who have been assessed for surgical operability and deemed operable should be managed in consultation with CTEPH surgical centres that perform pulmonary endarterectomy in Montreal, Ottawa, or Toronto. Patients with non-operable CTEPH may be treated similarly to PAH and have a similar poor prognosis. The definitions above could be applied to CTEPH patients who have been deemed surgically inoperable or to those who are medically inoperable due to advanced age or comorbidities.

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## ADDITIONAL CONSIDERATION ACROSS CONDITIONS:

### LUNG TRANSPLANTATION AND ADVANCE CARE PLANNING

Clinicians should continue to consider these factors in patients who are listed for lung transplantation, as the consequences of extended intubation and ICU stay in such patients may render them too deconditioned to receive lung transplantation, even if they survive the acute episode. Moreover, transplant services may be significantly limited during and immediately after a surge. However, it is recommended that each patient be discussed directly with transplant physicians in order to determine whether the patient remains eligible for transplantation while receiving ventilatory or extracorporeal support, and the expected likelihood of survival to transplantation. This should also be used as an opportunity to obtain any available information about prior advance care planning discussions.

## Appendix 1 - The REVEAL and ESC/ERS Risk Assessment Tools for PAH

| REVEAL 2.0* | | | |
|---|---|---|---|
| Group 1 Subgroup | CTD-PAH | PoPH | Heritable |
| | +1 | +3 | +2 |
| Demographics | Males Age > 60 | | |
| | +2 | | |
| Comorbidities | Renal Insufficiency or eGFR < 60 mL/min/1.73 m2 | | |
| | +1 | | |
| NYHA Functional Class | I | III | IV |
| | -1 | +1 | +2 |
| Vital Signs | SBP < 110 mmHg | HR > 96 BPM | |
| | +1 | +1 | |
| Hospitalization | All-cause hospitalization ≤ 6 mo | | |
| | +1 | | |
| 6-minute walk distance | ≥ 440 m | 320-440 m | <165 m |
| | -2 | -1 | +1 |
| BNP | BNP < 50 ng/L or NT-proBNP <300 ng/L | 200 to < 800 ng/L | ≥800 ng/L or NT-proBNP ≥1100 ng/L |
| | -2 | +1 | +2 |
| Echocardiogram | Pericardial Effusion | | |
| | +1 | | |
| PFT | DLCO < 40% predicted | | |
| | +1 | | |
| RHC | RAP > 20 mmHg in past year | PVR< 5 Wood units | |
| | +1 | -1 | |
| | **TOTAL SCORE = SUM OF ABOVE + 6** | | |
| **REVEAL 2.0 SCORE** | **Low Risk (≤ 6)** | **Intermediate Risk (7-8)** | **High Risk (≥ 9)** |

| ESC/ERS** | | | |
|---|---|---|---|
| | **Low Risk** | **Intermediate Risk** | **High Risk** |
| Clinical Signs of Heart Failure | Absent | Absent | Present |
| Progression of Symptoms | No | Slow | Rapid |
| Syncope | No | Occasional | Repeated syncope |
| NYHA Functional Class | I-II | III | IV |
| 6-minute walk distance | > 440 m | 165-440 m | < 165 m |
| Biomarkers | NT-proBNP < 300 ng/L | NT-proBNP 300-1400 ng/L | NT-proBNP > 1400 ng/L |
| | BNP <50 ng/L | BNP 50-300 ng/L | BNP > 300 ng/L |
| Cardiopulmonary exercise test | $VO_2$ > 15mL/min/kg | $VO_2$ 11-15 mL/min/kg | $VO_2$ < 11 mL/min/kg |
| | $V_E/VCO_2$ slope <36 | $V_E/VCO_2$ slope 36-44.9 | $V_E/VCO_2$ slope > 45 |
| Imaging (Echo or MRI) | RA area < 18 $cm^2$ | RA area 18-26 $cm^2$ | RA area >26 $cm^2$ |
| | No pericardial effusion | Minimal pericardial effusion | Pericardial Effusion |
| Hemodynamics | RAP < 8 mmHg | RAP 8-14 mmHg | RAP > 14 mmHg |
| | CI ≥ 2.5 L/min/$m^2$ | CI 2.0-2.4 L/min/$m^2$ | CI < 2.0 L/min/$m^2$ |
| | $SvO_2$ >65% | $SvO_2$ 60-65% | $SvO_2$ < 60% |
| **ESC/ERS Score 1-Year Mortality** | **1 = Low (<5%)** | **2 = Intermediate (5-10%)** | **3 = High (>10%)** |

**Abbreviations:** REVEAL - Registry to Evaluate Early And Long-term PAH Disease Management; ESC - European Society of Cardiology; ERS - European Respiratory Society; CTD - connective tissue disease; PoPH - portopulmonary hypertension; NYHA - New York Heart Association; SBP - systolic blood pressure; HR - heart rate; BNP - brain natriuretic peptide; PFT - pulmonary function test; DLCO - diffusion capacity for carbon monoxide; RHC - right heart catheterization; RAP - right atrial pressure; PVR - pulmonary vascular resistance; 6MWD - 6-minute walk distance; NT-proBNP - N-terminal pro-brain natriuretic peptide; RA - right atrium; CI - cardiac index; $SvO_2$ - mixed venous oxygen saturation

***** The REVEAL 2.0 Score uses the most recent recorded value for each variable. REVEAL 2.0 does not require that every variable is available, but at least 7 variables should be considered.

****** Approach to ESC/ERS Risk score is to give 1 point for each available clinical variable in the low-risk category, 2 points for each available variable in the intermediate risk category and 3 points to each available variable in the high-risk category. The total score = sum of points / number of variables counted, rounded to the nearest integer. Total score of 1 = Low risk, 2 = Intermediate risk, 3 = High risk.



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