

Lung and Heart-Lung Transplantation in PH

Indications and screening procedures

Laurent SAVALE

Service de Pneumologie et Soins Intensifs Respiratoires

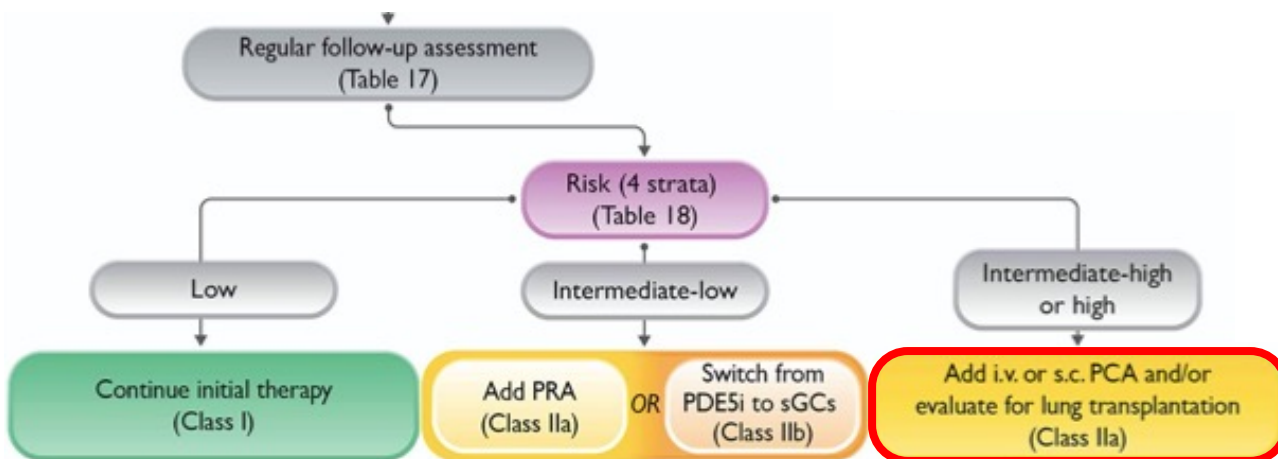
Centre de Référence de l'Hypertension Pulmonaire Sévère

Hôpital Universitaire de Bicêtre – INSERM U999

Université Paris-Saclay – Le Kremlin-Bicêtre – France

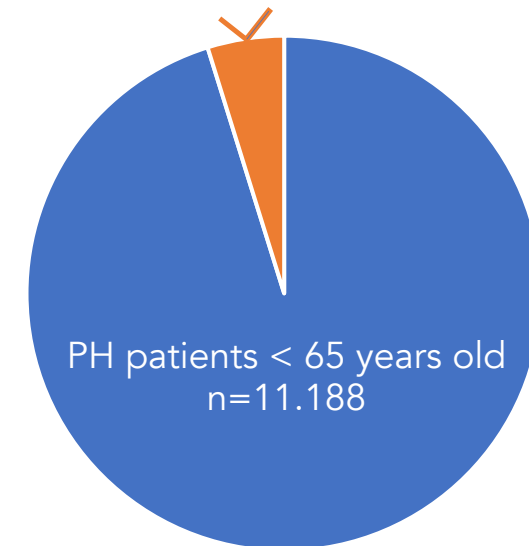
Lung transplantation in PH registries

« Lung transplantation remains an important treatment option for patients with PAH refractory to optimized medical therapy. In patients with PAH, referral to an LTx centre should be considered early ».



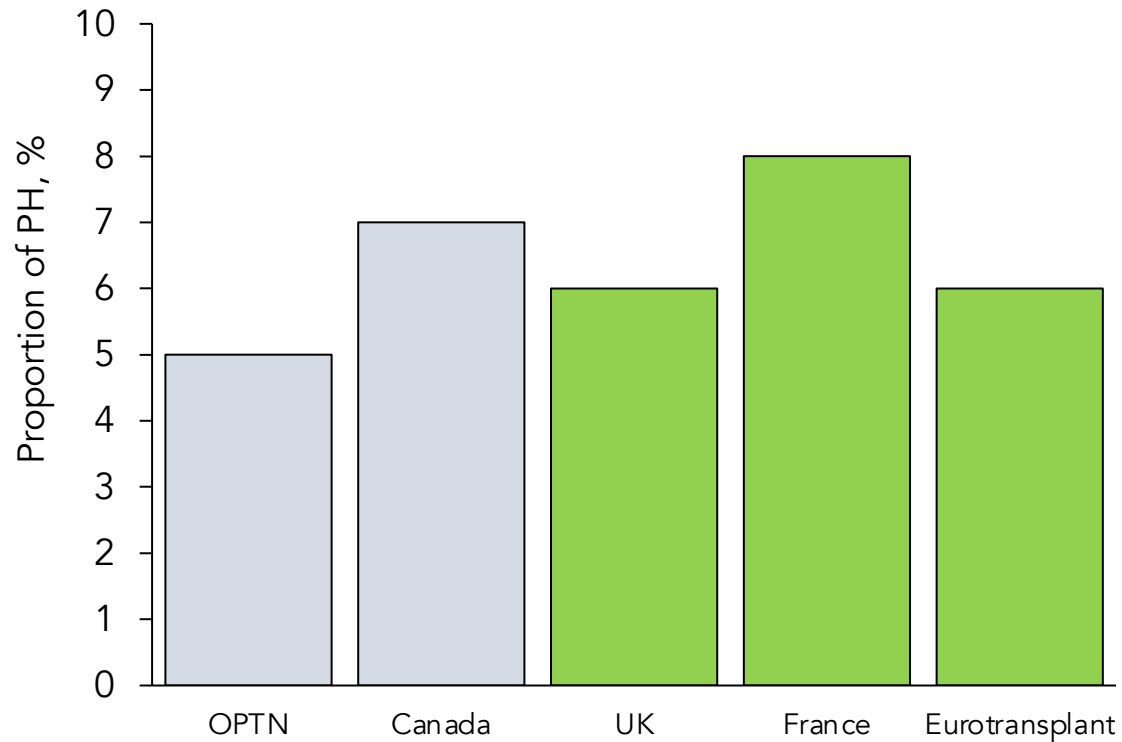
Lack of published data on the proportion of PAH or PH patients who underwent lung transplantation

Number of lung transplantation, n=558 (5%)



Ratio death:transplantation in i,h,a-PAH => 2:1

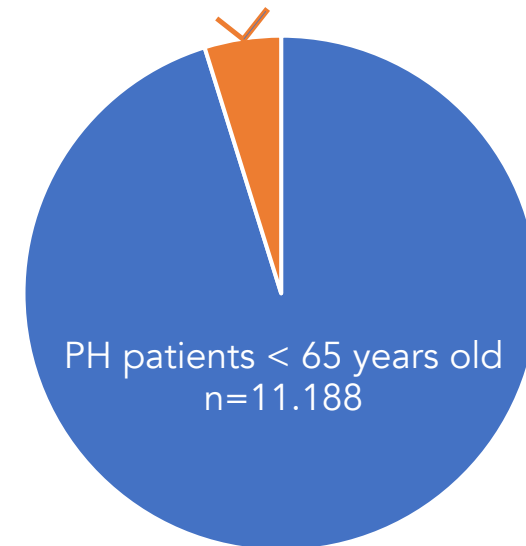
PH in Lung transplantation registries



Gottlieb J, Dtsch Arztebl Int 2017
Kolaitis, Am J Respir Crit Care Med 2023
France, data from « agence de biomedecine » 2019

Lack of published data on the proportion of PAH or PH patients transplanted

Number of lung transplantation,
n=558 (5%)



Ratio death:transplantation in i,h,a-PAH : 2:1

French PH registry, unpublished data

Why access to transplantation is challenging in PH?

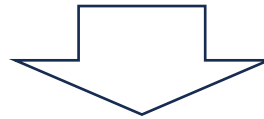
- Small proportion of patients (<8% of lung transplantations) requiring highly specific intra- and post-operative strategies in expert centres
- Specific prognostic parameters for risk assessment on list and postoperatively (inequities in the organ allocation process)
- Short-term life threatening complications (acute decompensated PH) needing priority access to transplantation
- Need for heart-lung transplantation in specific cases

Three stages for lung transplant as part of a patient's treatment plan

1. **Discussion** about transplant as a concept and potential therapy

2. Full lung transplant **assessment** to determine eligibility and timing of listing

3. **Listing** for lung transplant - includes prioritisation for transplantation and bridging options

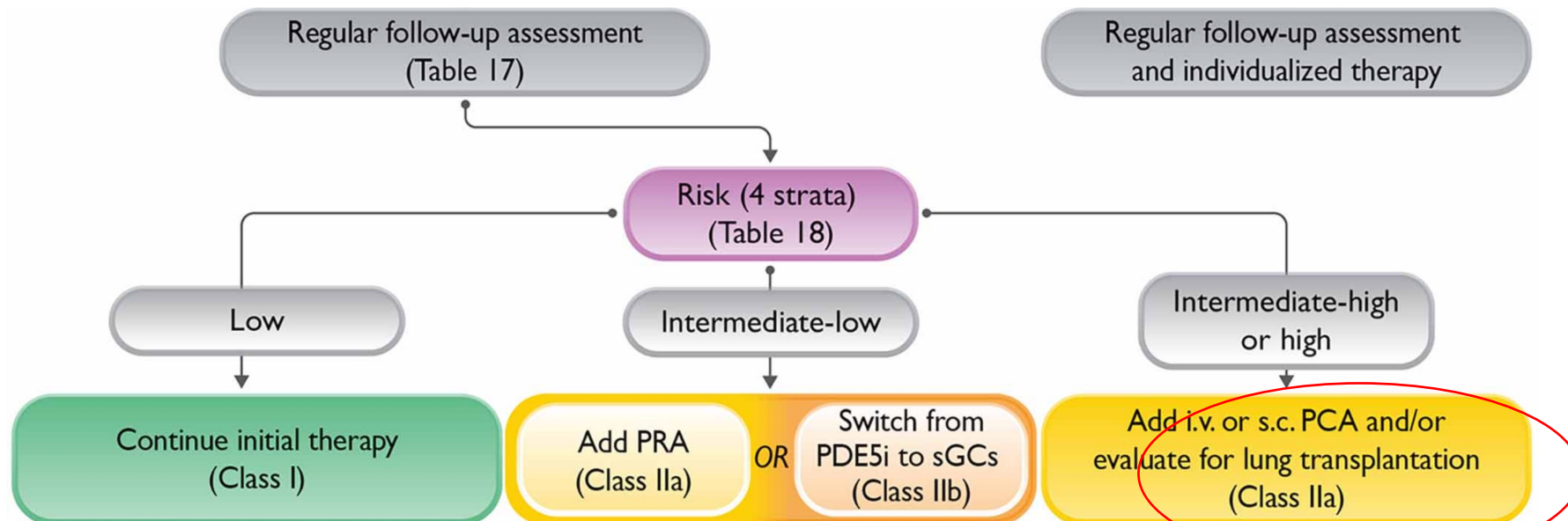


Lung or Heart-Lung transplantation under optimal conditions

Treatment decisions based on risk stratification

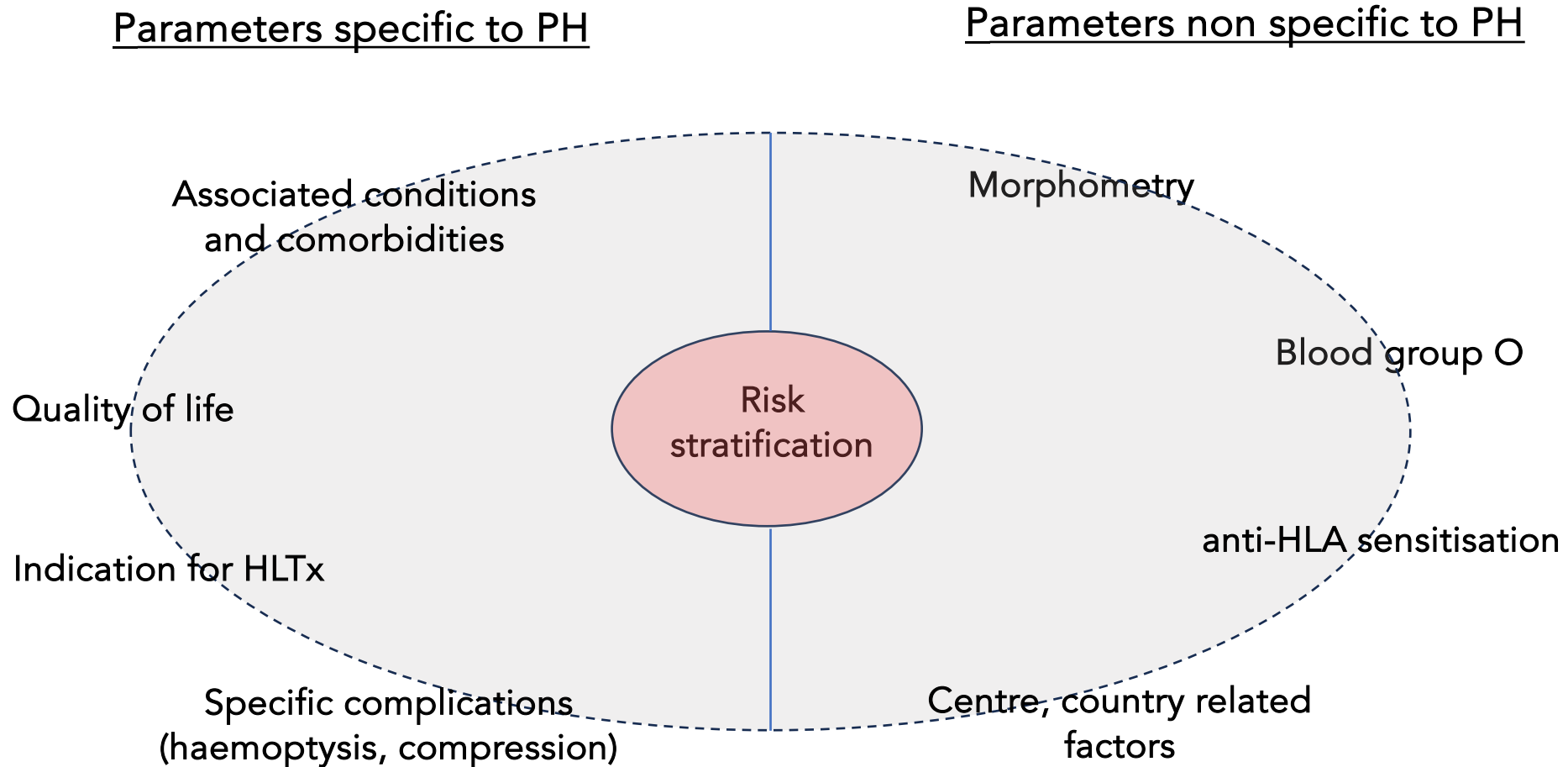
| Determinants of prognosis | Low risk | Intermediate-low risk | Intermediate-high risk | High risk |
|---------------------------|-------------|-----------------------|------------------------|---------------|
| Points assigned | 1 | 2 | 3 | 4 |
| WHO-FC | I or II | - | III | IV |
| 6MWD, m | >440 | 320–440 | 165–319 | <165 |
| BNP or NT-proBNP, ng/L | <50 <300 | 50–199 300–649 | 200–800 650–1100 | >800 >1100 |

- Right heart catheterization
- MRI
- Echocardiography
- CPET...



Timing for transplantation : what criteria should be used?

Risk stratification tools should not be used in isolation to inform when to refer patients for transplant assessment



When should we talk about transplantation as a concept and potential therapy?

1. **Discussion** about transplant as a concept and potential therapy

When should we talk about transplantation as a concept and potential therapy?


No clear consensus

- For potential candidates who present with high-risk features at the time of diagnosis, notion of transplant as a potential treatment option should be introduced to the patient.
- For patients with low or intermediate-risk feature at time of diagnosis, notion of transplant as a potential treatment option can be introduced in a second step after failure of a first-line therapy



- Allows the patient to prepare for this therapeutic eventuality
- Provide time to help the patient address modifiable factors that may initially preclude eligibility such as financial resources, elevated BMI, vaccinations, deconditioning and social supports or substance misuse disorders (e.g. smoking)

Time for referral for transplantation



1. **Discussion** about transplant as a concept and potential therapy

2. Full lung transplant **assessment** to determine eligibility and timing of listing

Time for referral for transplantation

- **At time of diagnosis (disease variant that poorly responds to medical therapy) :**
 - PVOD
 - PAH due to scleroderma with venular involvement and/or associated extensive pulmonary fibrosis
 - Severe PH group 3
- **During follow-up according to the risk status :**
 - Patients at intermediate-high risk or high risk after a first line oral therapy needing parenteral PGI2 analogs initiation
 - Patients who doesn't reach low-risk status after a first line triple therapy including parenteral PGI2 analogs
 - Significant RV dysfunction despite optimal medical therapy,
- **Specific at risk conditions :**
 - Episode of acute decompensated PH requiring hospitalization
 - Onset of new atrial arrhythmia
 - Recurrent non severe hemoptysis

Screening procedures

1. Meet the transplant team in charge of the lung transplant process



- Surgeons
- Medical doctors
- Anaesthetists
- Psychologists
- Transplant coordinator
- Social workers

Screening procedures

1. Meet the transplant team in charge of the lung transplant process

2. To screen absolute or relative contraindication for lung transplantation

- Lack of patient willingness or acceptance of transplant
- Malignancy with high risk of recurrence or death related to cancer
- Severe extrathoracic organ failure (Stroke, liver cirrhosis, severe renal failure)
- Active infection
- Progressive cognitive impairment
- Repeated episodes of non-adherence without evidence of improvement
- Active substance use or dependence including current tobacco use, vaping, marijuana smoking, or IV drug use.
- Other severe uncontrolled medical condition

Screening procedures

1. Meet the transplant team in charge of the lung transplant process

2. To screen absolute or relative contraindication for lung transplantation

3. To decide the type of transplantation
BLT vs HLT

Type of transplantation

- Bilateral lung transplantation (BLT) is the preferred option.
- Heart-Lung transplantation (HLT) only in specific cases :
 - non-correctable cardiac conditions
 - Coexisting left sided heart disease
 - PA aneurysm or massive cardiomegaly
- In some patients with interstitial lung disease and COPD/ emphysema and mild PH, single lung transplantation may be sufficient

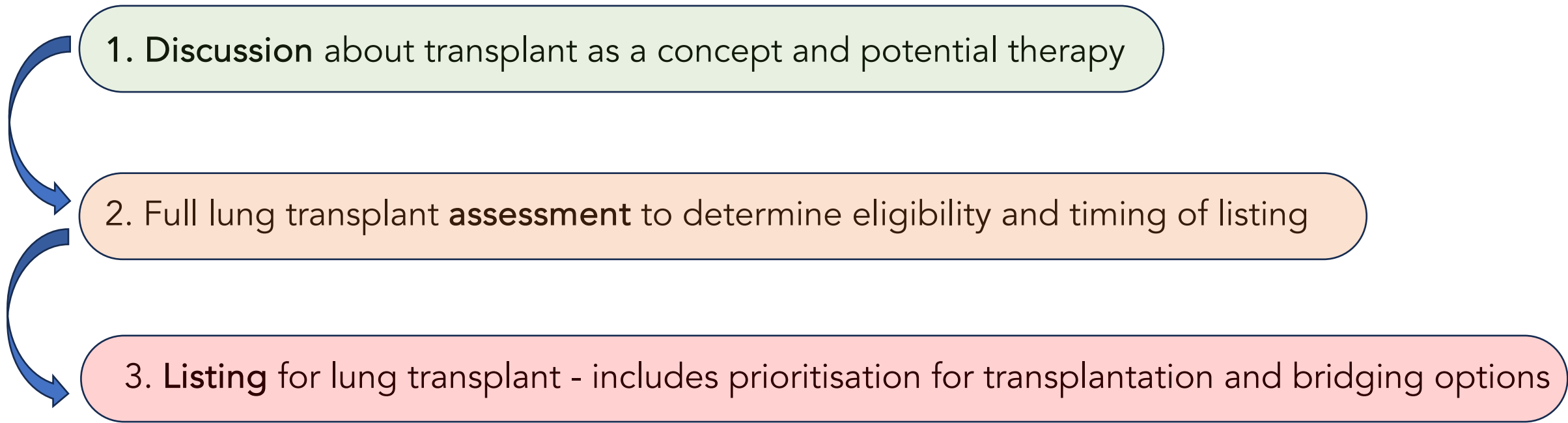
Screening procedures

1. Meet the transplant team in charge of the lung transplant process
2. To screen absolute or relative contraindication for lung transplantation
3. To decide the type of transplantation
BLT vs HLT
4. To determine eligibility and timing for transplant

"The patient and their next of kin should be fully engaged in the transplant assessment process and informed of the risks and benefits, and the final decision should be jointly made between the patient and medical team"

Humbert et al, Eur Respir J 2022.

Listing for lung transplant



1. **Discussion** about transplant as a concept and potential therapy

2. Full lung transplant **assessment** to determine eligibility and timing of listing

3. **Listing** for lung transplant - includes prioritisation for transplantation and bridging options

Timing for listing

- **During follow-up according to the risk status :**
 - High risk category despite optimal medical therapy.
 - Persistent intermediate high risk with significant RV dysfunction, recurrent hospitalization for RV failure despite optimal medical therapy.
 - Liver or kidney dysfunction
- **Specific high-risk conditions :**
 - Worsening in hypoxemia or hemodynamics in PVOD patients
 - Diagnosis of PVOD or PCH that has failed a trial of conventional PAH therapy.
 - Diagnosis of underlying ILD, COPD, or CPFE.
 - Anticipated program wait list times

Lung allocation rules in Europe

Euro-transplant – ET Lung allocation score

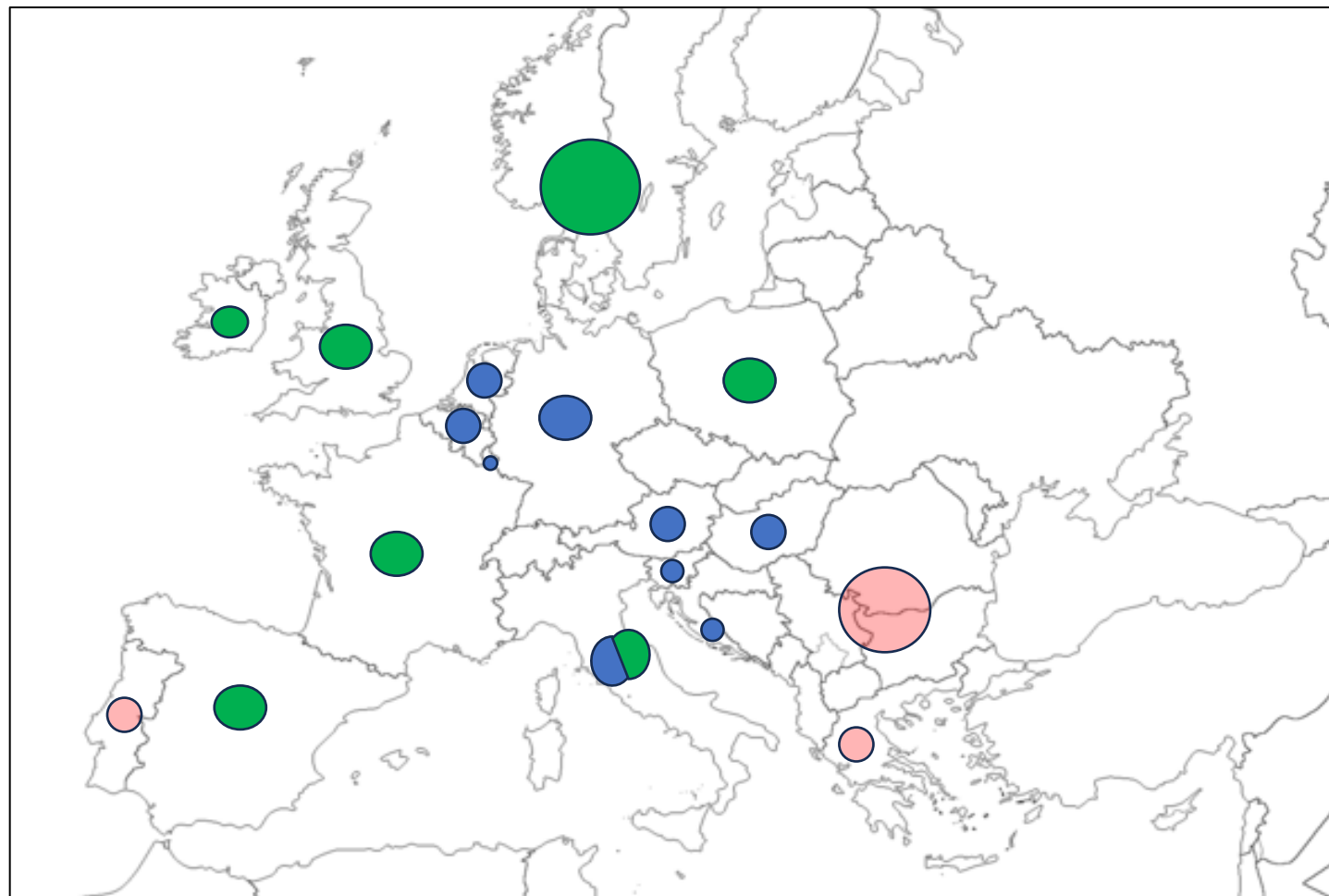
Germany, The Netherlands, Belgium, Austria, Slovenia, Luxembourg, Hungary, Croatia

Countries w/o LAS

France, UK, Spain, Switzerland, Ireland, Scandi-transplant

Emergent lung transplantation programs

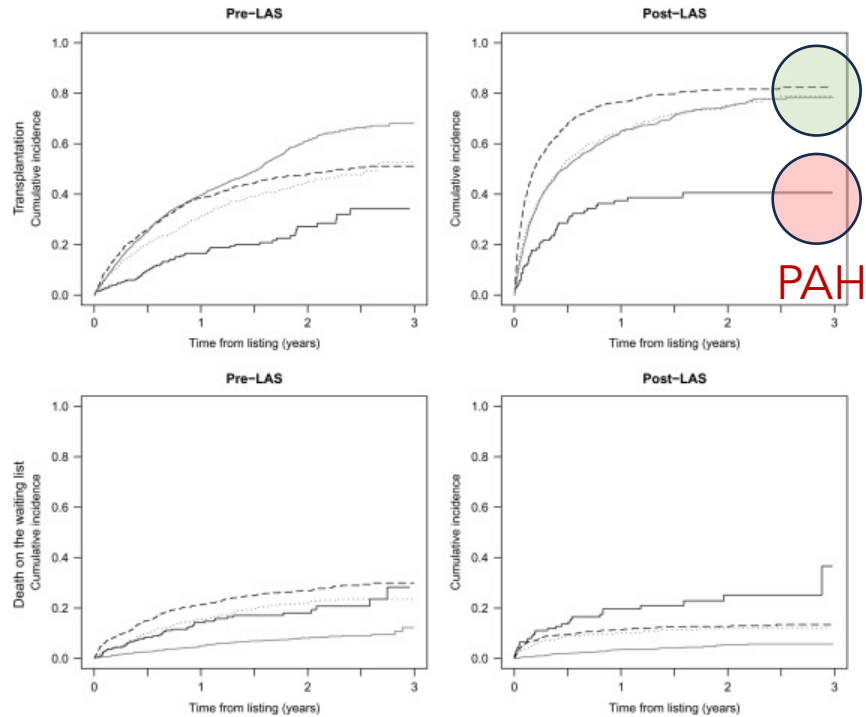
Some Eastern European countries



Changes in Lung allocation score in US

2015 Lung allocation score revision

Lung allocation score 2005



1 LAS results should not be considered definitive; they are merely a snapshot based upon the values entered and can vary daily.

Date of Birth * (mm/dd/yyyy)

Height * ft in cm Weight * lbs kg

Lung diagnosis code *
 Pulmonary arterial hypertension

Functional status

Diabetes

Assisted ventilation

Requires supplemental O₂

Predicted FVC Percentage (%) 6-minute walk distance (feet)

Pulmonary Artery Systolic Pressure (mmHg) Mean Pulmonary Artery Pressure (mmHg)

Cardiac index (CI) (L/min/m²) Central venous pressure (CVP) (mmHg)

1 If using a central venous test value for PCO₂ subtract 6 mmHg before entering the value.

PCO₂ (mmHg)
 Current
 Highest
 Lowest

Serum Creatinine (mg/dL)
 Current
 Highest
 Lowest

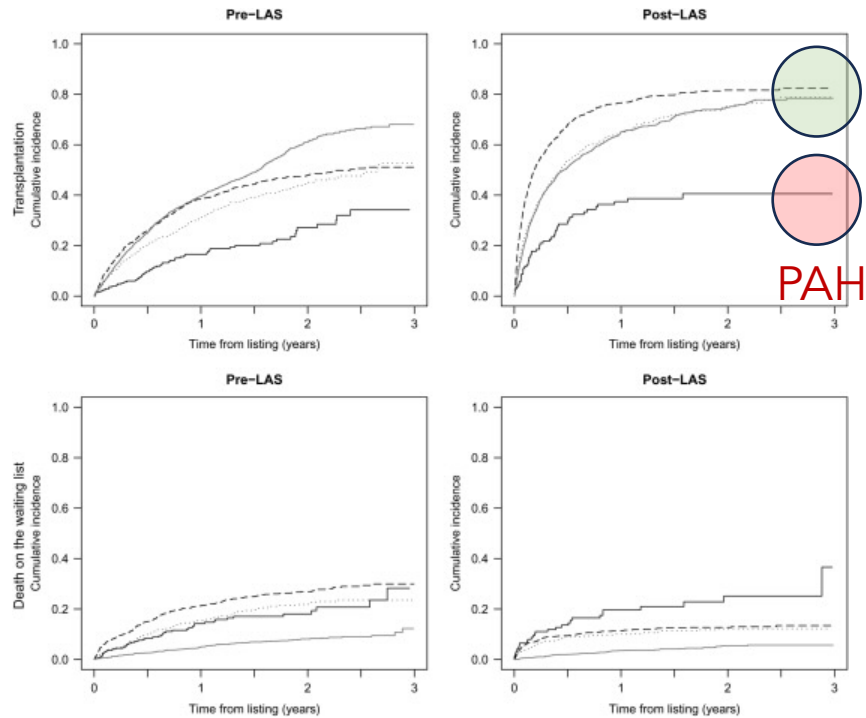
Total Bilirubin (mg/dL)
 Current
 Highest
 Lowest

Reset Calculate

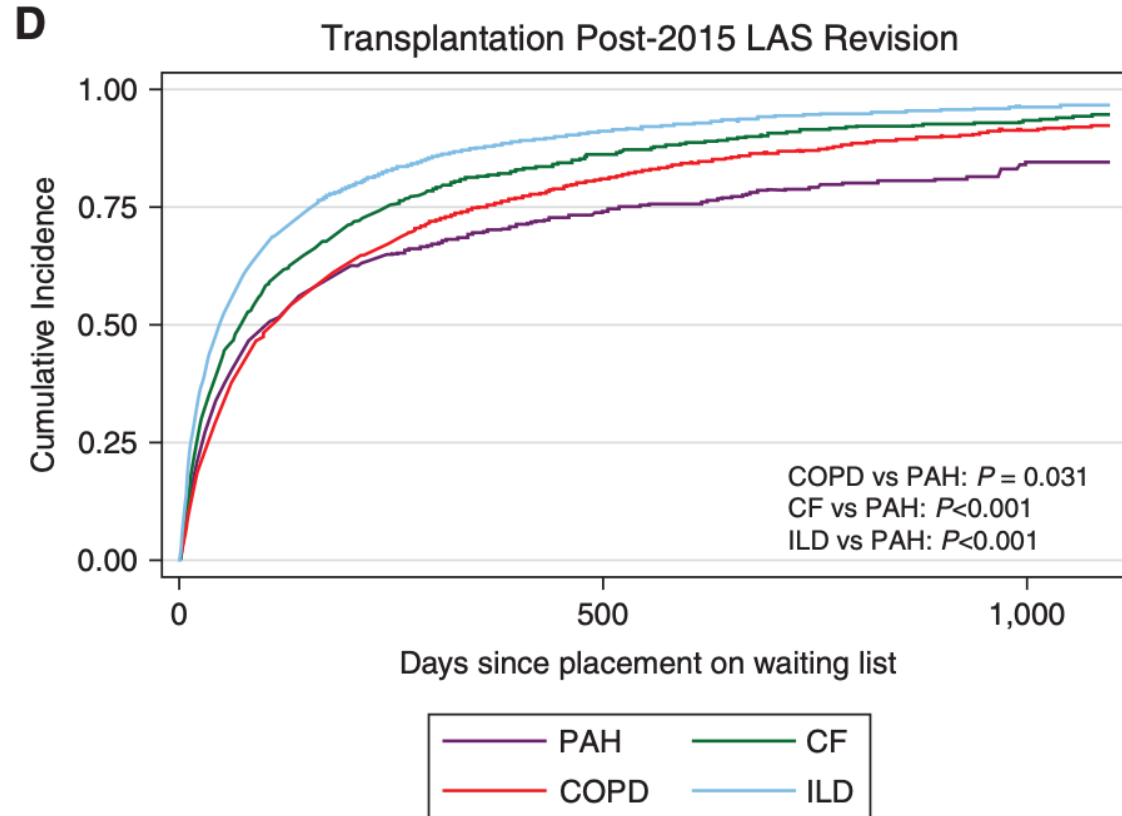
- Weighting Changed
- Parameter Added

Changes in Lung allocation score in US

Lung allocation score 2005



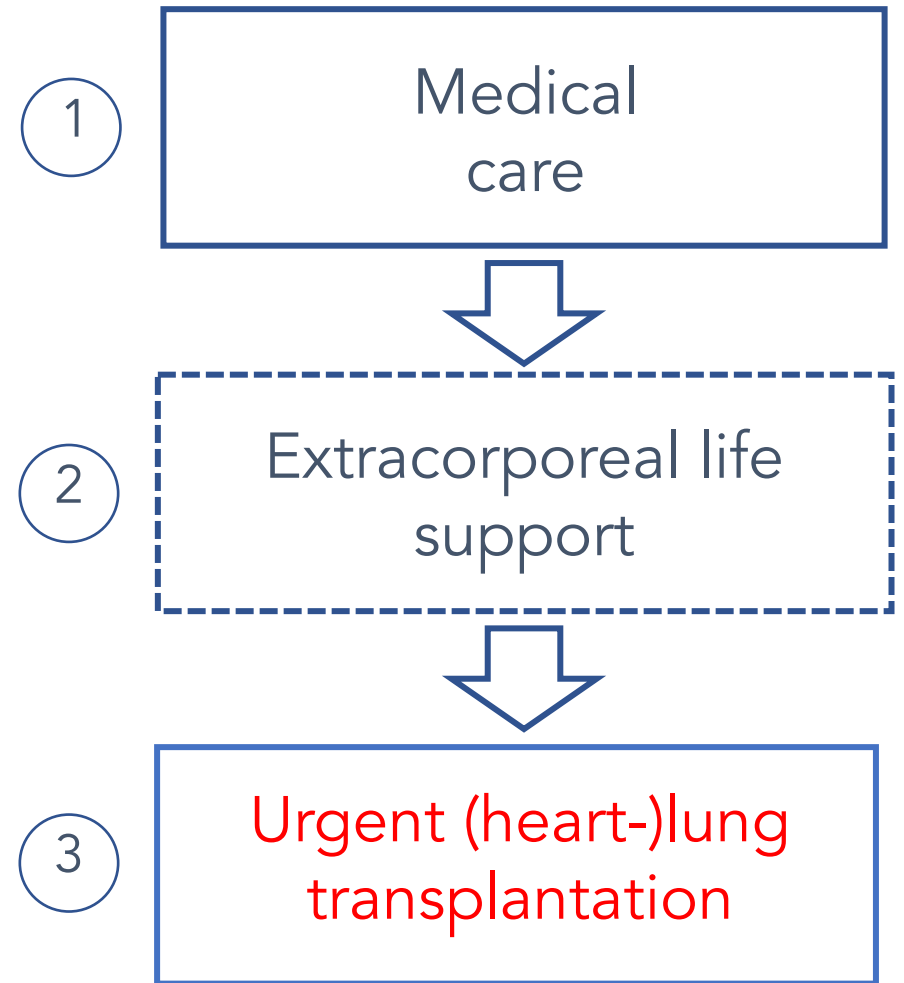
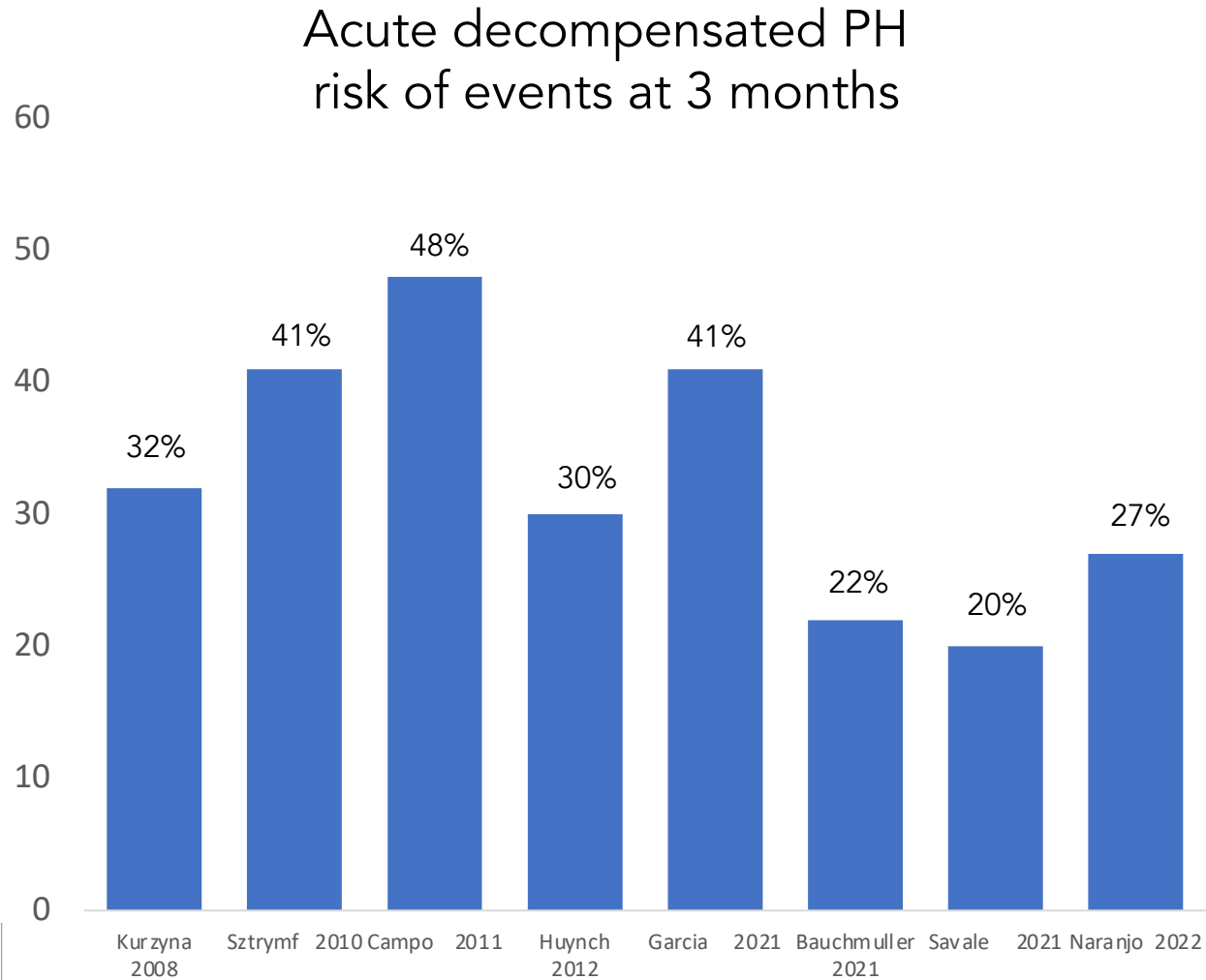
2015 Lung allocation score revision



Lung Composite Allocation Score (CAS) (since March 2023)

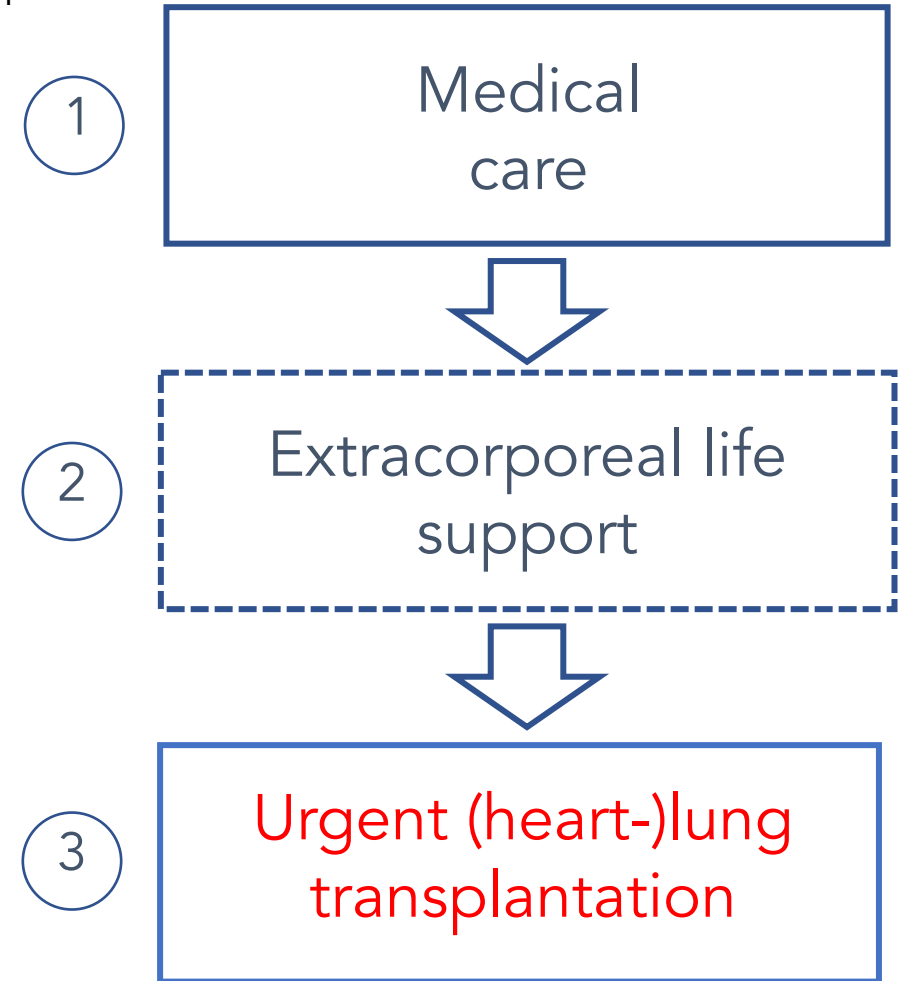
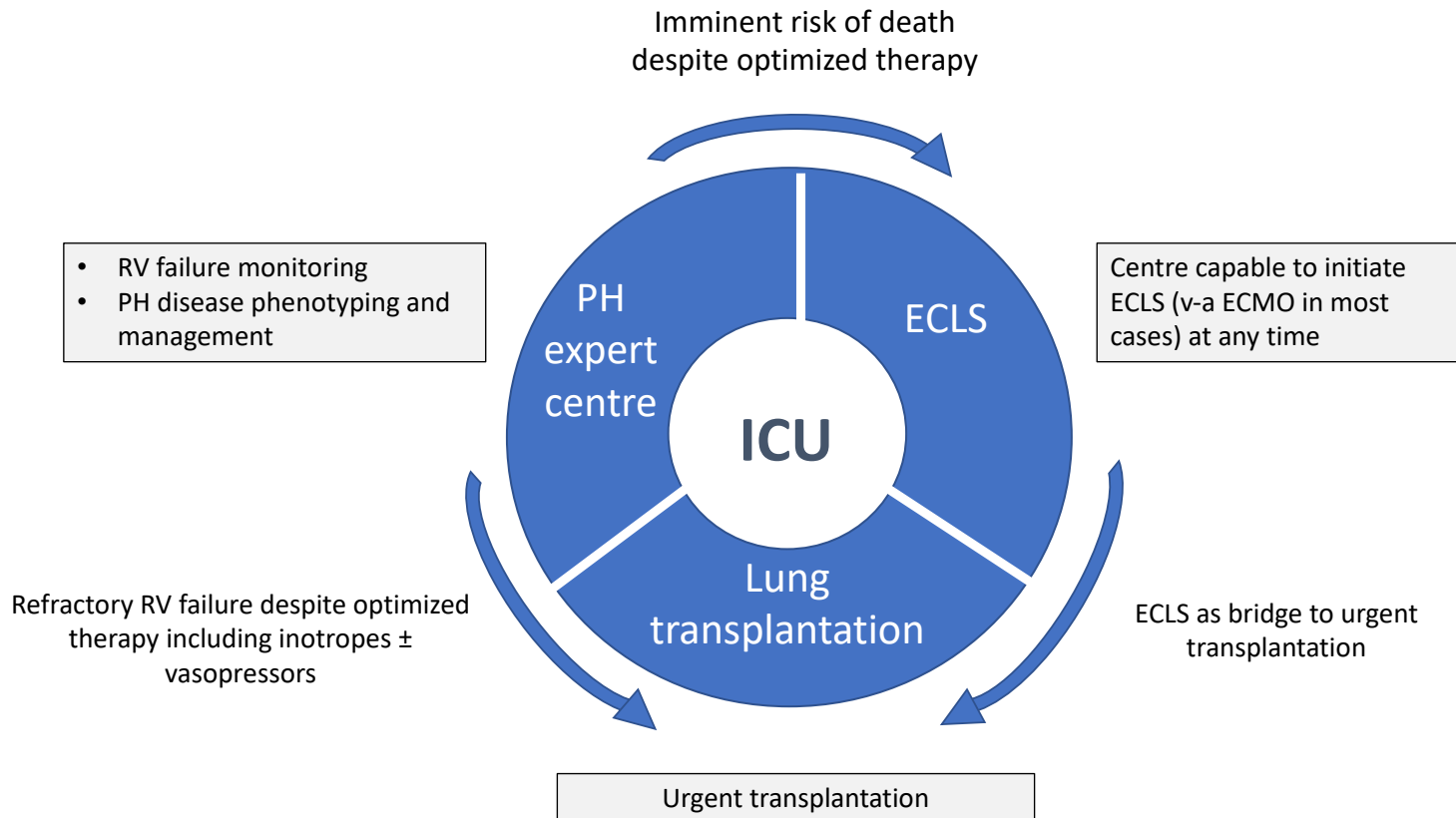
- 1:1 weighting of the waitlist urgency measure and the post-transplant survival measure (and not 2:1)
- Post-transplant survival measure from estimating the likelihood of 5-years post-transplant survival (and not 1-year survival)
- LAS component : 50% of the overall score => 50% dependent on the recipient candidate's biology

Emergency allocation programs



Emergency allocation programs

An urgent donor lung allocation system is required to facilitate achievement of early transplantation and reduce the risk of prolonged circulatory assistance



Emergency allocation programs in France and the UK (No LAS)

French/UK graft allocation rules

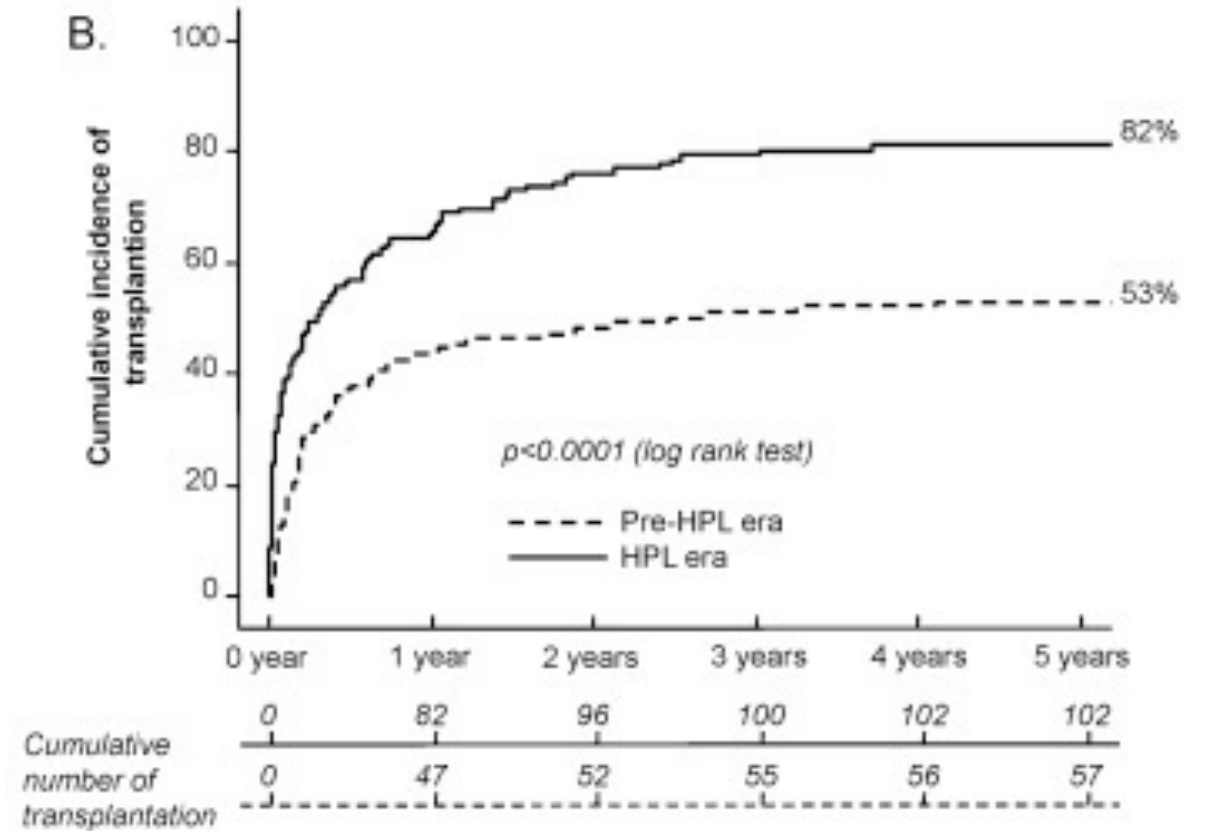
No score at time of listing



Acute PAH decompensation in ICU



Emergency allocation program
(national priority)



Conclusion

- **Access to transplantation for PAH remains challenging**, with a wide variability depending on the healthcare system and the graft allocation rules.
- Evaluation of a LTx programme should be considered at an early stage in **the treatment algorithm**
- **Patients be engaged** in discussions about transplantation as a treatment option early in their treatment course
- Final decision should be **jointly** made between the patient and medical team
- **Decisions to refer and then list** patients should be comprehensive and include risk assessment, comorbidities, anticipated wait list times and donor pool.
- Development of **urgent transplant program**