

Lung Transplantation in Patients with Cystic Fibrosis

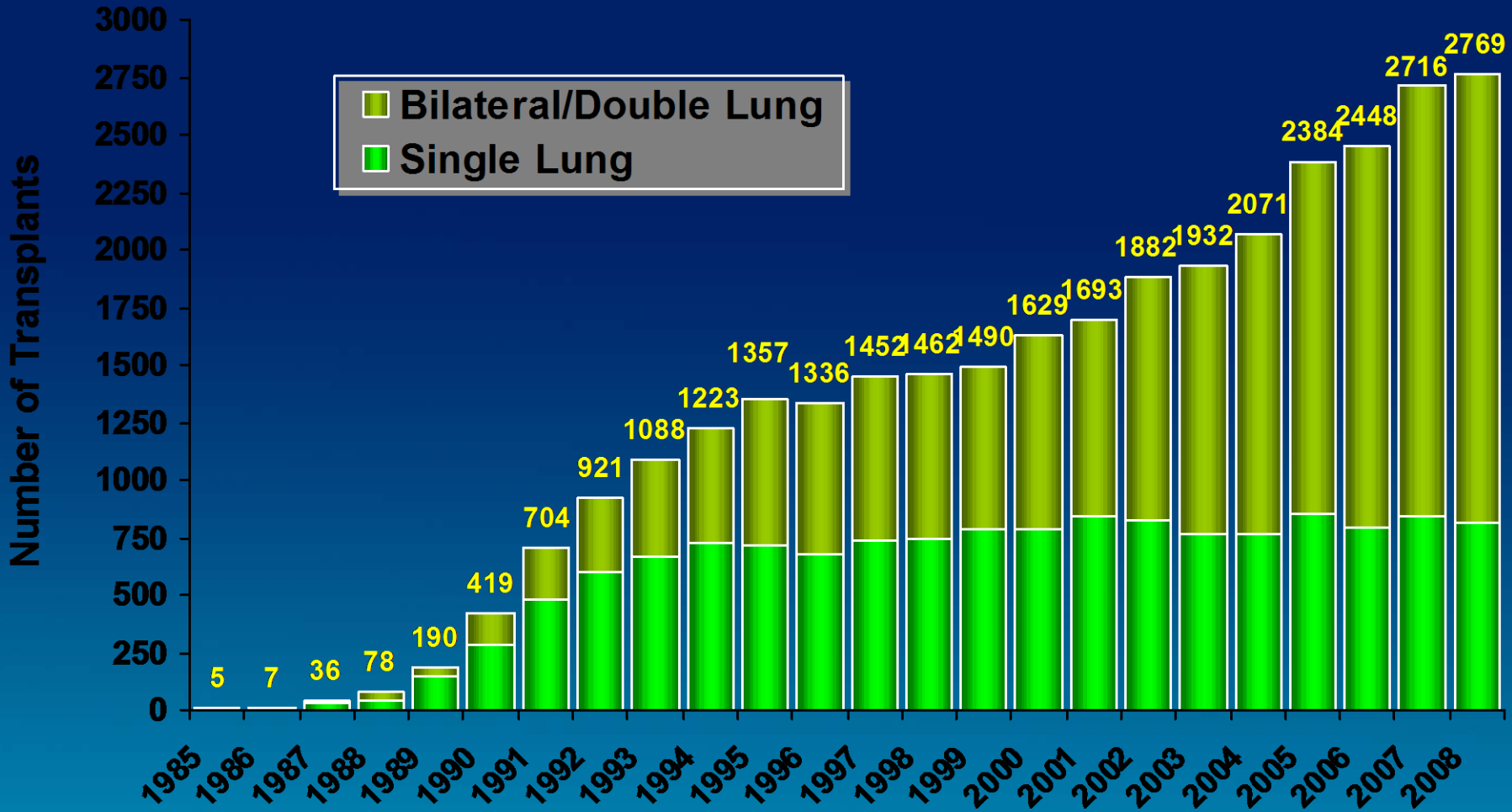
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NUMBER OF LUNG TRANSPLANTS REPORTED BY YEAR AND PROCEDURE TYPE



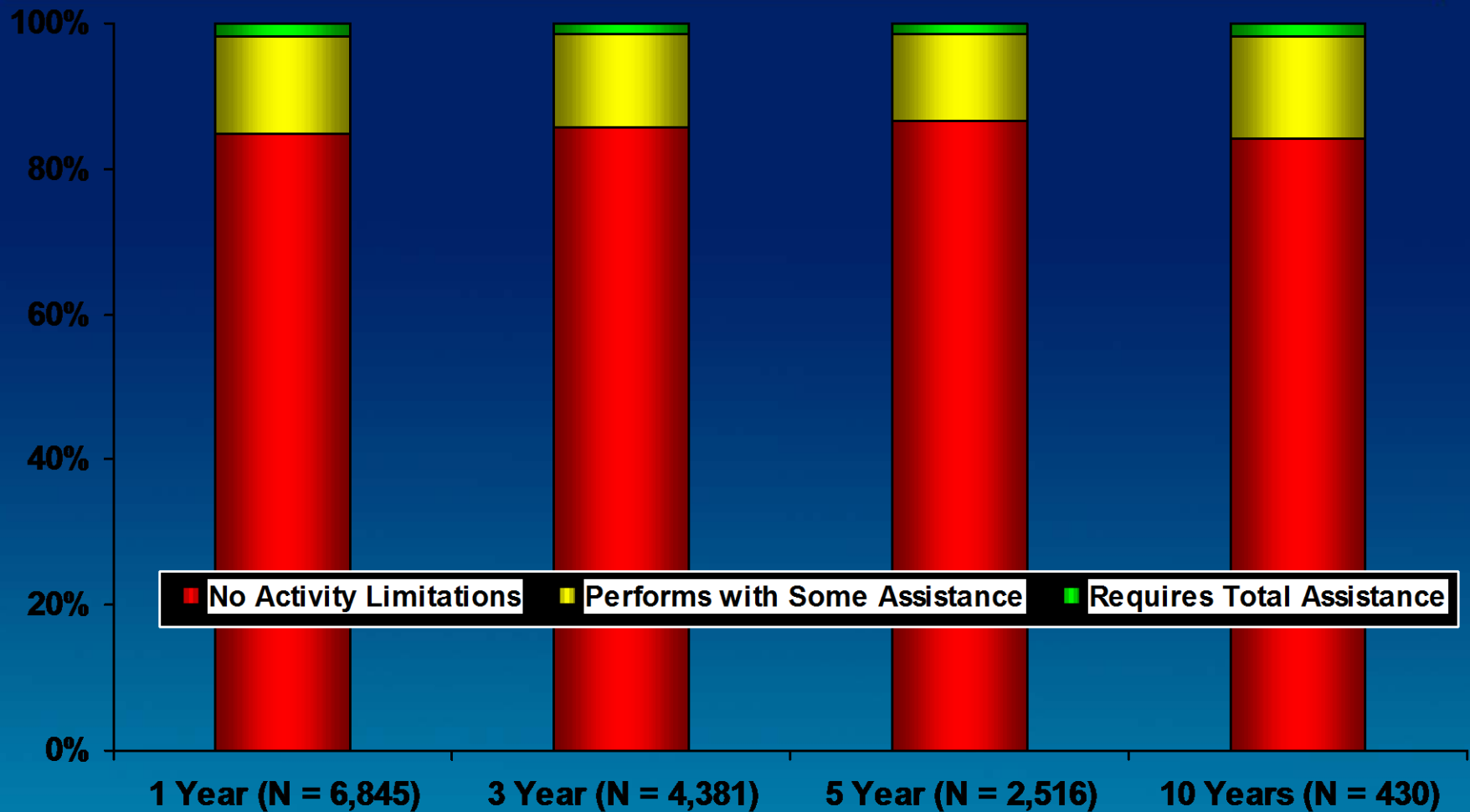
NOTE: This figure includes only the lung transplants that are reported to the ISHLT Transplant Registry. As such, this should not be construed as representing changes in the number of lung transplants performed worldwide.

ADULT LUNG RECIPIENTS

Cross-Sectional Analysis

Functional Status of Surviving Recipients

(Follow-ups: April 1994 – June 2009)



Lung Transplantation Procedure Options

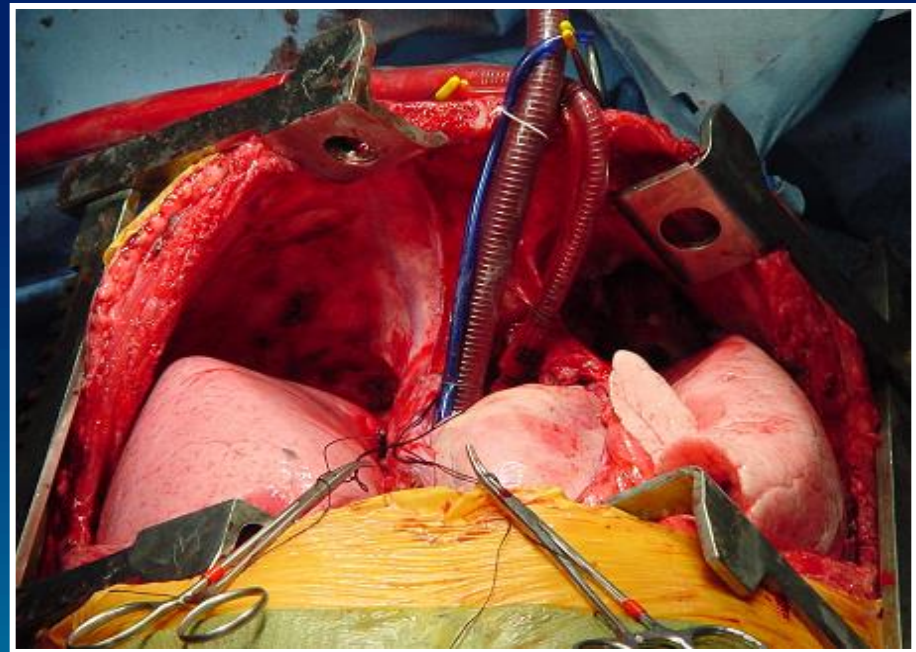
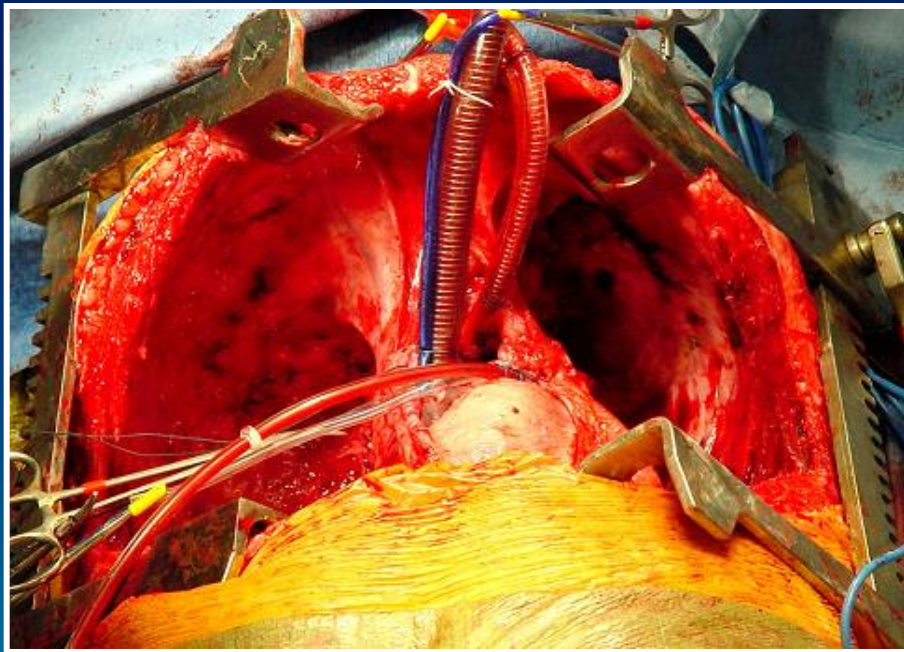
- **Double-lung transplantation**
 - Donor hearts could serve other patients
 - Avoids risk of accelerated atherosclerosis
- **Heart-lung transplantation**
 - Less commonly performed in the US
 - Fewer airway complications
- **Bilateral living lobar transplantation**
 - Reduced incidence and intensity of rejection
 - Circumvents the donor shortage problem
 - Considerable risk to donors
- **Split-lung transplantation**
 - Single donor can serve multiple recipients
 - Technically difficult procedure

Shennib H. *Arch Intern Med.* 1992.

Starnes VA, et al. *J Thorac Cardiovasc Surg.* 1994.

Boehler A. *Swiss Med Wkly.* 2003.

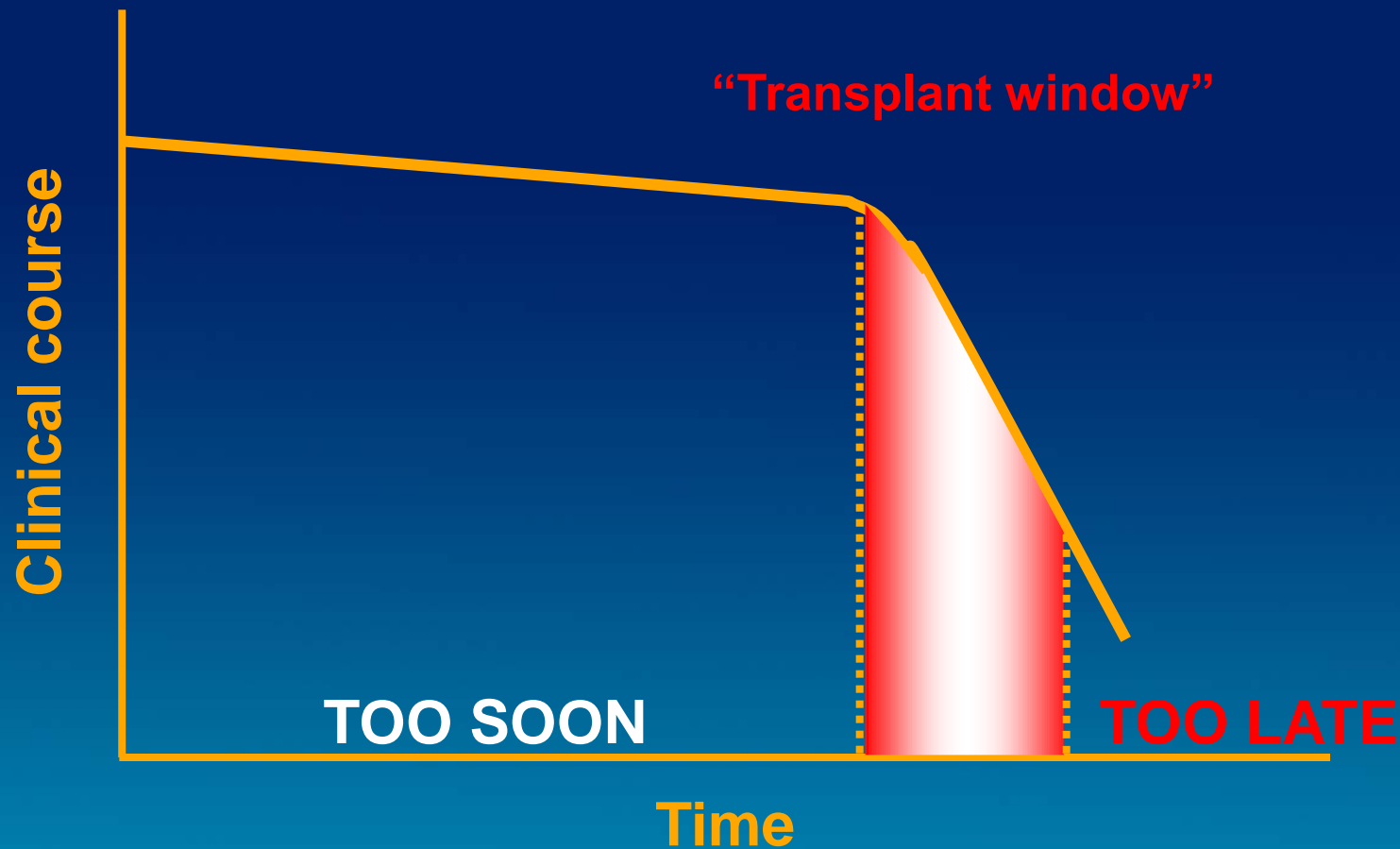
Double-Lung Transplantation



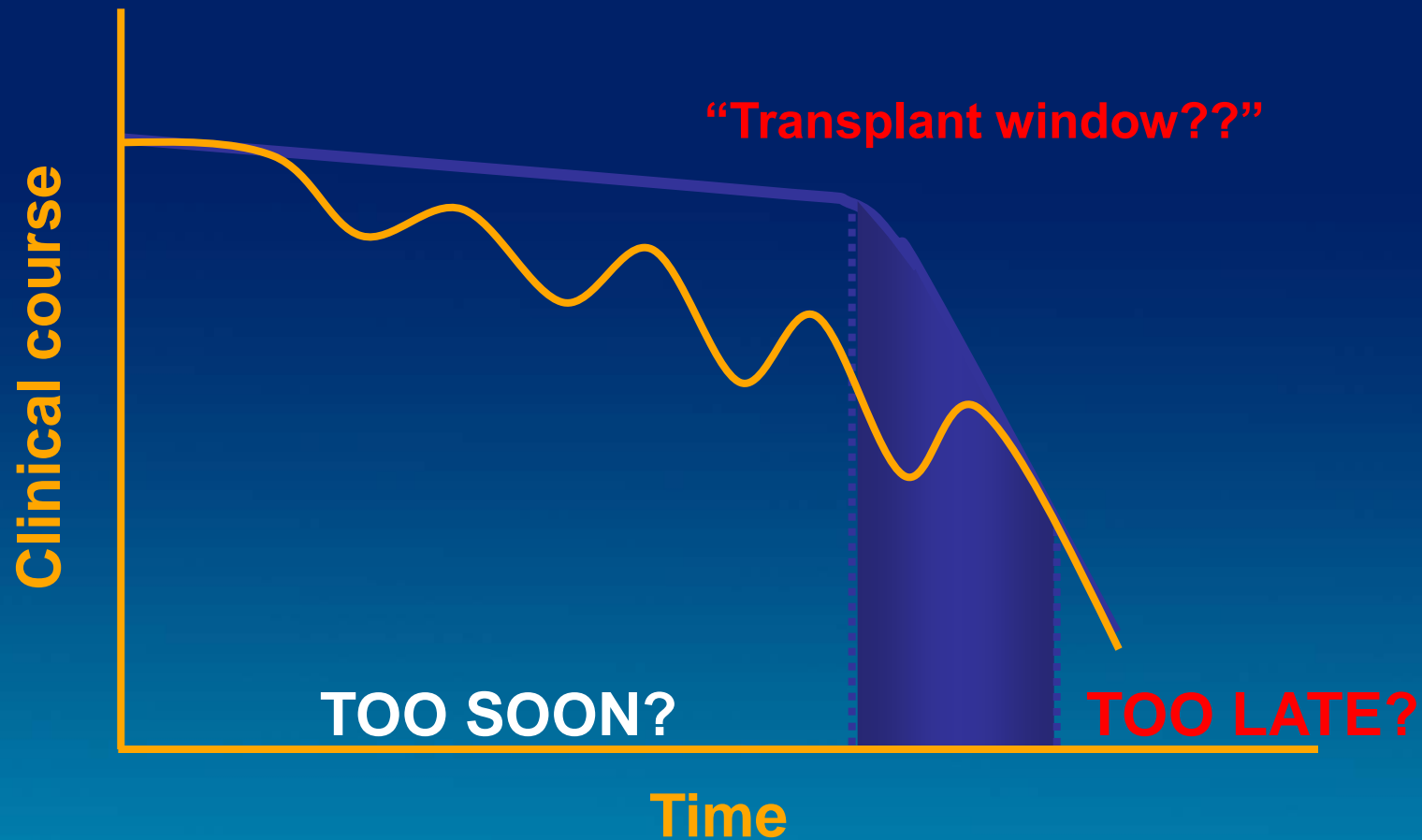
CF and Lung Transplant

- The course of CF is very unpredictable, and that makes the timing for transplant more difficult
- About 1600 CF recipients since 1991
- 120-150 recipients each year
- Second largest group to get transplanted
- CF recipients do better in general than non-CF recipients

Transplantation Window of Opportunity—in an Ideal World



Transplantation Window of Opportunity—in Reality



Difficult Questions to Ask Before Organ Transplantation

- When should a patient be referred for evaluation?
- When should a patient be placed on the waiting list?
- When should a patient have a transplant?

Referral for Lung Transplant

- Patient readiness
- Transplant team readiness and comfort level
- Local transplant center culture
- Wait times (less important now because of LAS)

Lung Allocation Score

- New scoring system since May 2005
- “How bad you need it + How well you’ll do with it”
- Applies to transplant candidates > 12 yrs
- Scores range from 0-100
- Scores can be updated

Lung Allocation Score: Clinical Information

- Diagnosis
- Age
- Height and Weight (BMI)
- Diabetes
- Use of supplemental oxygen
- Six minute walk distance
- PASP
- PCWP
- FVC
- Serum Creatinine
- Functional Status
- Assisted Ventilation

Lung Allocation Score: *CF Variables That Are Not Included*

- FEV_1
- pCO_2
- Infections
- Antibiotic Sensitivity of Infections
- Hemoptysis
- Frequency of Exacerbations

The Kerem Survival Model

Significant predictors of 2-year survival

Single covariate analysis

FEV₁ and FVC

Female gender

Low arterial pO₂

High arterial pCO₂

Low weight-for-height

Multiple covariate analysis

FEV₁

Female gender

Age

Consensus Guidelines for Referral of Lung Transplant Candidates with CF

- $FEV_1 \leq 30\%$ of predicted with rapid, progressive respiratory deterioration
 - Increasing number of hospitalizations
 - Massive hemoptysis
 - Recurrent pneumothorax
 - Increasing cachexia
 - Rapid fall in FEV_1
- Hypoxemia: $PaO_2 < 55$ mm Hg
- Hypercapnia: $PaCO_2 > 50$ mm Hg
- $< 50\%$ survival in 2 years
- Early referral is recommended for young female patients, who have particularly poor prognosis

The Validated Predictive 5-Year Survival Model of CF

FEV₁ % equivalency*

Increased survival:

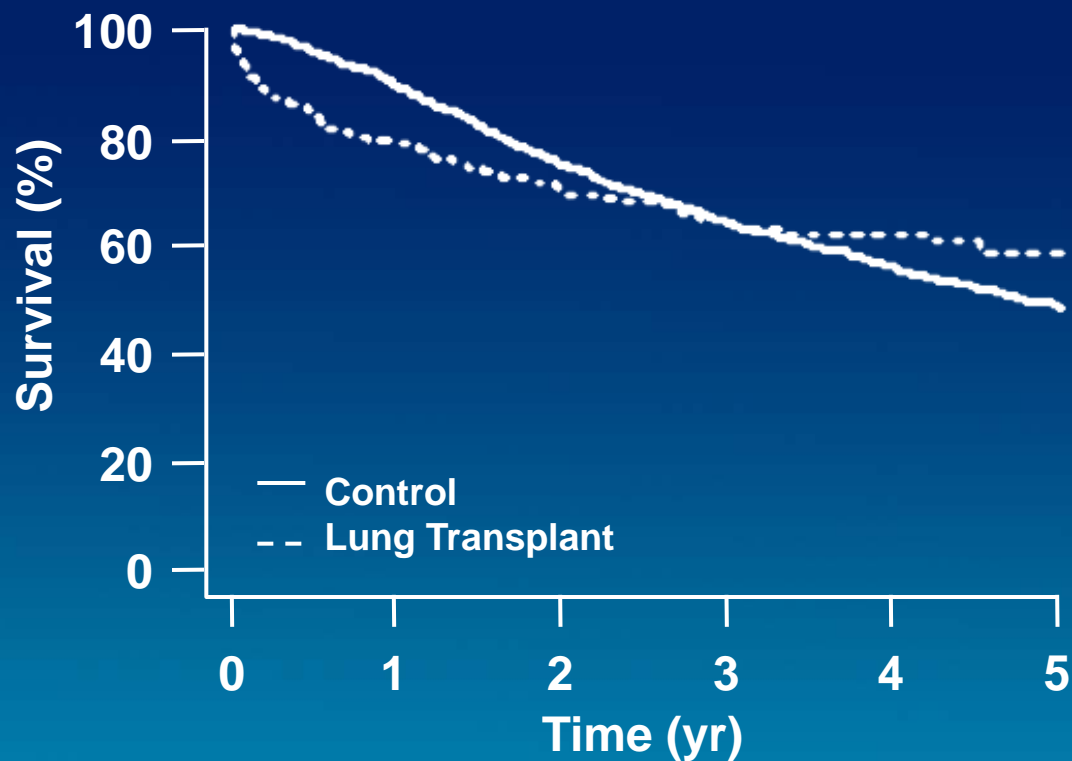
- Pancreatic sufficiency +12
- Higher weight-for-age z-score +10
- *Staphylococcus aureus* infection +6
- Higher FEV₁% +1

Decreased survival:

- *Burkholderia cepacia* infection -48
- Diabetes mellitus -13
- Acute pulmonary exacerbation -12
- Female gender -6
- Increasing age -0.7

*Difference in FEV₁ (% predicted) required for equivalent effect on survival

Equivocal Survival Benefit of Lung Transplantation in Patients with $FEV_1 \leq 30\%$



Predicting the “Right Time” for Transplant

- Study to look at who was listed too late
- Evaluated who was listed for transplant but died before receiving new lungs
- Rationale is that there are things that the transplant centers integrate with the variables collected by the CFF Registry and UNOS
- Four transplant centers

Predicting the “Right Time” for Transplant

Variables that increased risk of death

- $FEV_1 < 30\%$ predicted
- Shorter height
- $P_aCO_2 > 50\text{mmHg}$
- Need for nutritional intervention

Variables that decreased risk of death

- Referral from a CF Center
- Listing after 1996

International Guidelines for the Selection of Lung Transplant Candidates: 2006 Update

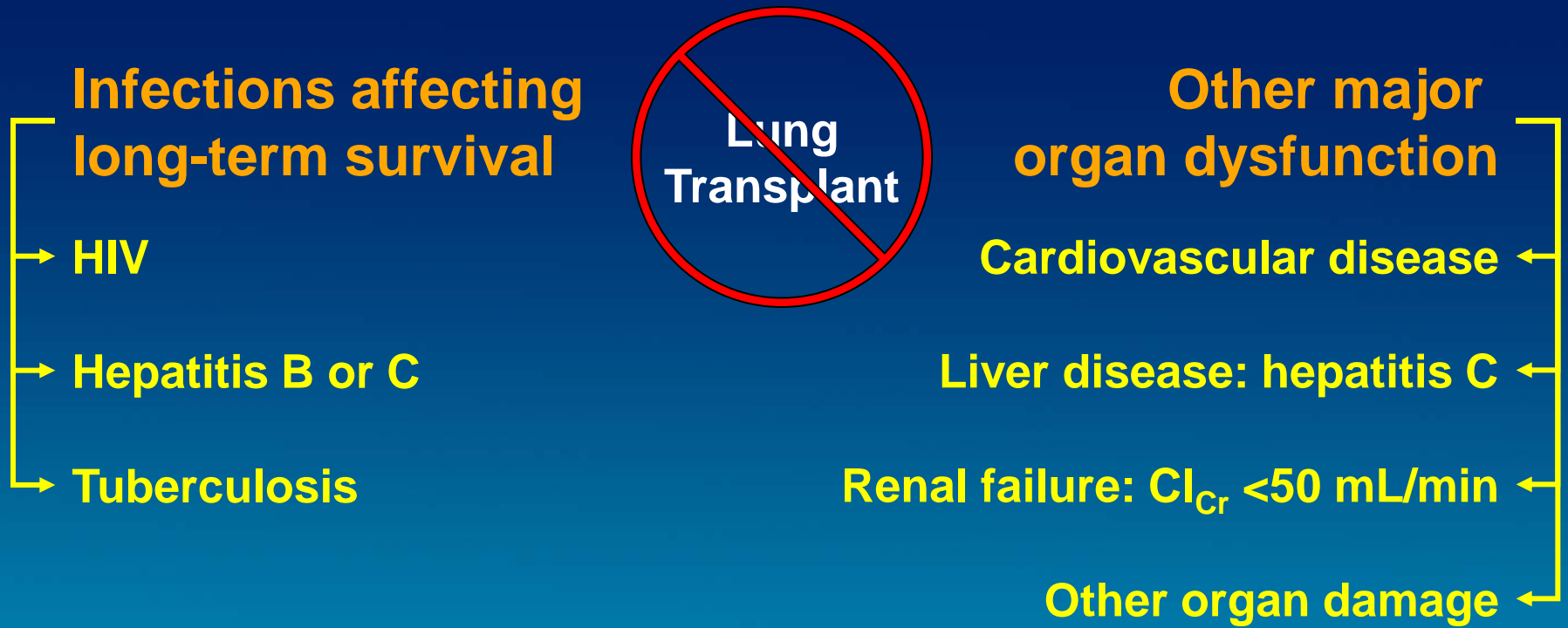
- Guidelines for referral:
 - FEV₁ below 30% predicted or a rapid decline in FEV₁
 - in particular young female patients
 - Exacerbation of pulmonary disease requiring ICU stay
 - Increasing frequency of exacerbations requiring abx
 - Refractory/recurrent pneumothorax
 - Recurrent hemoptysis not controlled by embolization

International Guidelines for the Selection of Lung Transplant Candidates: 2006 Update

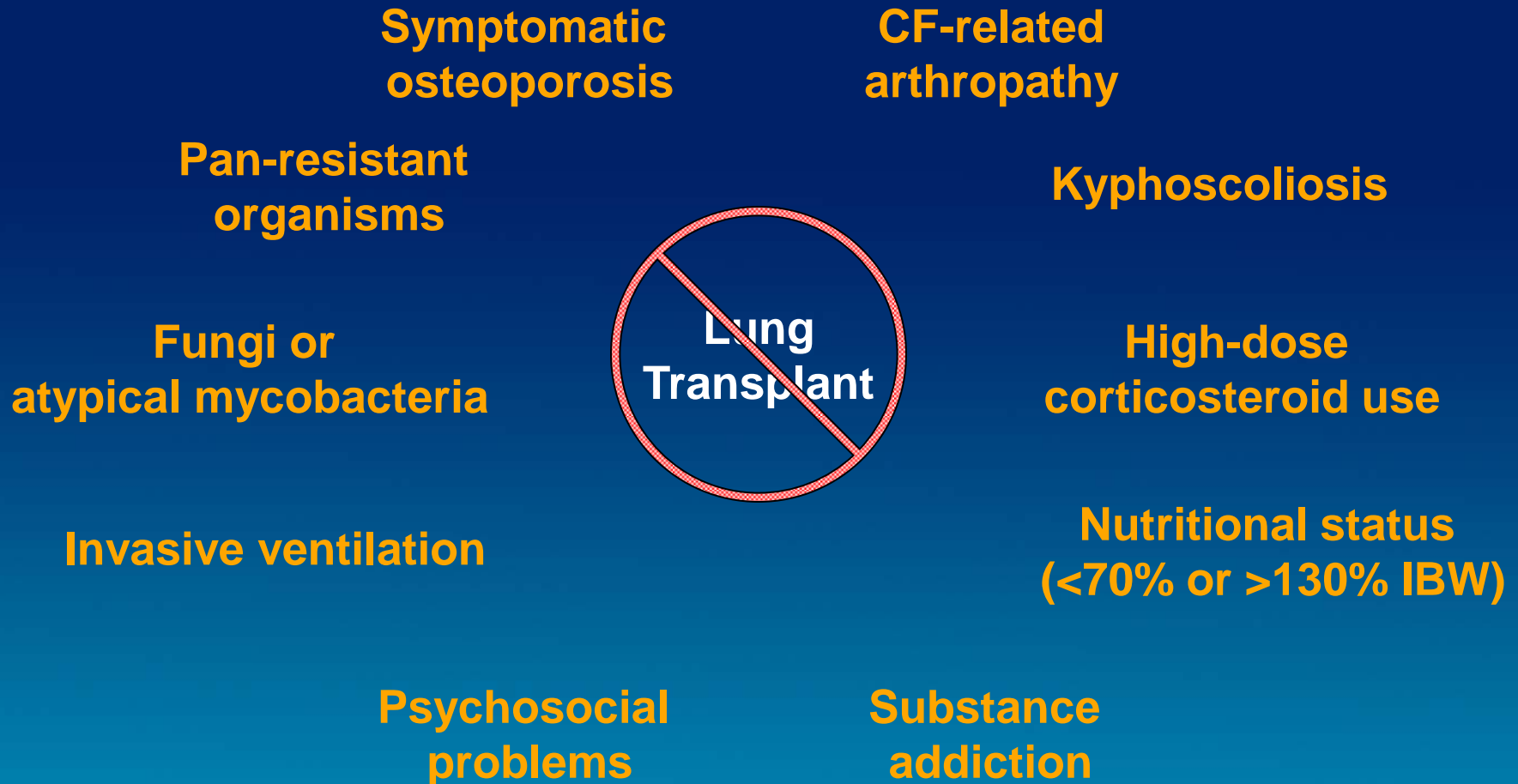
- Guidelines for transplant:
 - Oxygen-dependent respiratory failure
 - Hypercapnia
 - Pulmonary hypertension

Absolute Contraindications to Lung Transplantation

Active malignancy <5 years

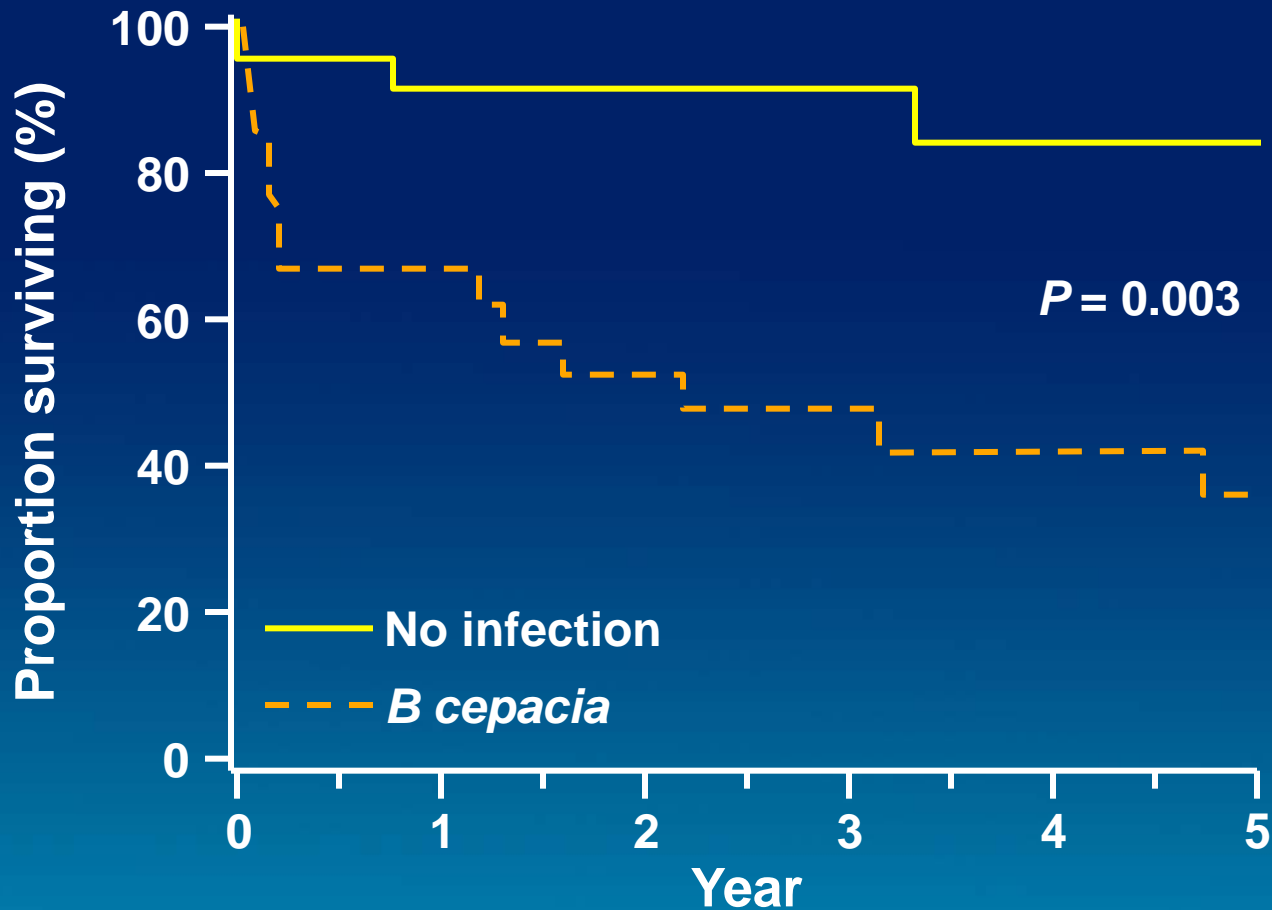


Relative Contraindications to Lung Transplantation



Postoperative Issues specific to CF Lung Transplant Recipients

Excess Mortality Associated with Preoperative *B cepacia* Infection



Post-transplant Survival Influenced by *B cepacia* Genomovar Type

Deaths (N) in patients infected with

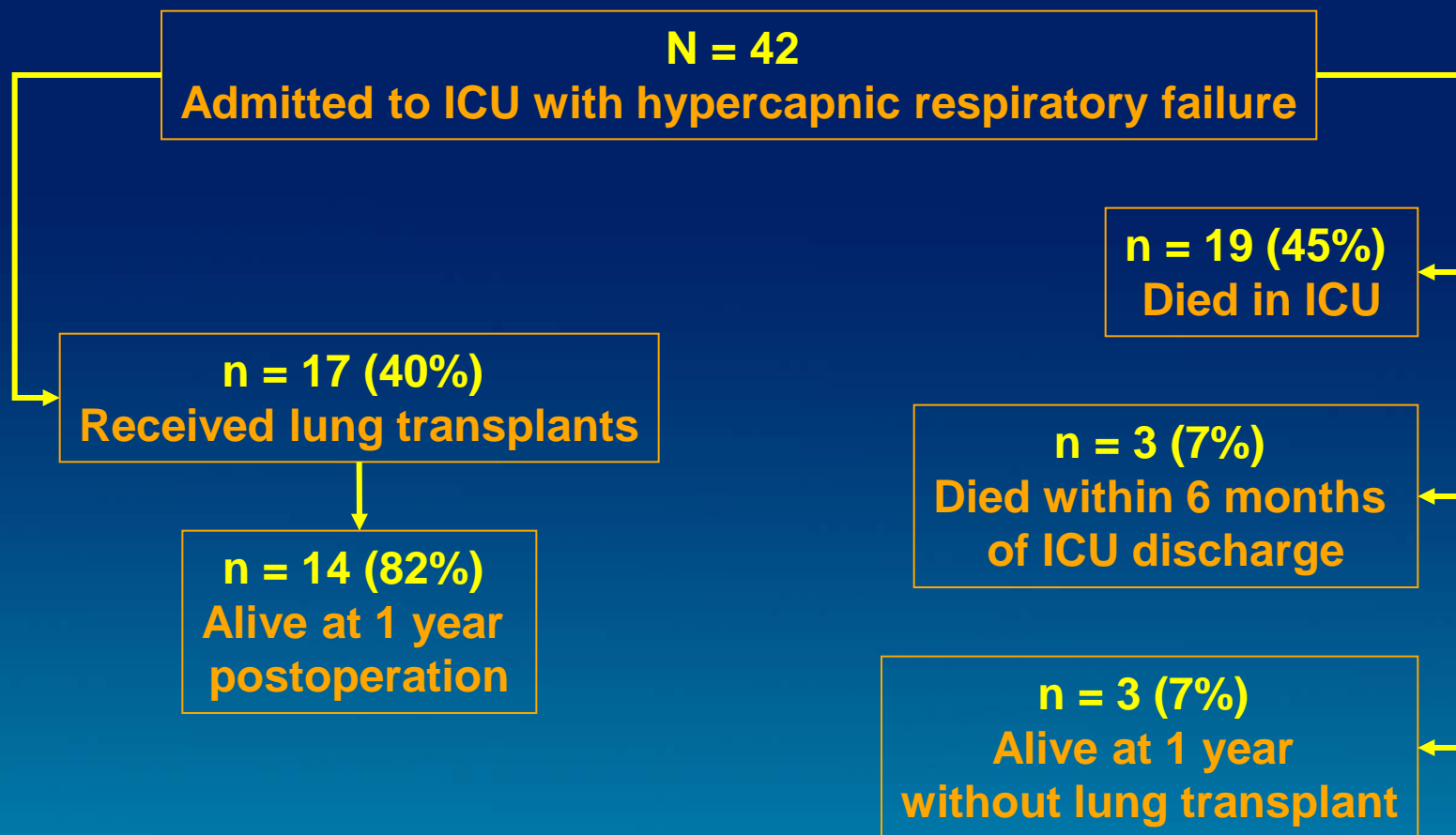
Study	Genomovar III	Non-genomovar III	<i>P</i> value*
Aris	5	0	0.035
De Soyza	4	0	0.007

*Genomovar III vs non-genomovar III

Aris RM, et al. *Am J Respir Crit Care Med.* 2001.

De Soyza A, et al. *Lancet.* 2001.

Lung Transplantation in Adult CF Patients with History of Acute Respiratory Failure



Potential Surgical Complications of Lung Transplantation

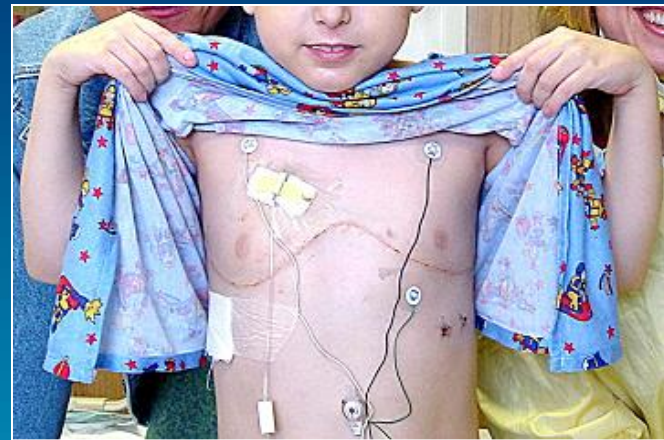
Complication	Prevalence (%)
Most serious	
• Primary graft failure due to ischemia-reperfusion injury/diffuse alveolar damage	15-35
• Anastomotic complications: vascular or airway	7
Most common	
• Phrenic/vocal cord paresis	3-30
• Gastroparesis	25-30

Potential Medical Complications Following Lung Transplantation

- Obliterative bronchiolitis (BOS/chronic rejection)
- Acute rejection
- Infection: viral, bacterial, fungal, protozoal
- Toxicity of immunosuppressives
 - Nephrotoxicity
 - Hypertension
 - Hirsutism, gingival hyperplasia
- Diabetes
- Hyperlipidemia
- Post-transplant lymphoproliferative disease (EBV)

Recommended Follow-up of Transplant Recipients

- Regular monitoring of PFTs, chest x-rays, and blood tests
 - Creatinine, complete blood count, liver function tests, CMV infection
- Post-transplant bronchoscopy; surveillance with BAL and transbronchial biopsy following:
 - Decline in PFTs
 - Change in chest x-ray
 - Onset of new symptoms
 - Acute rejection



Special Issues for the CF Patient

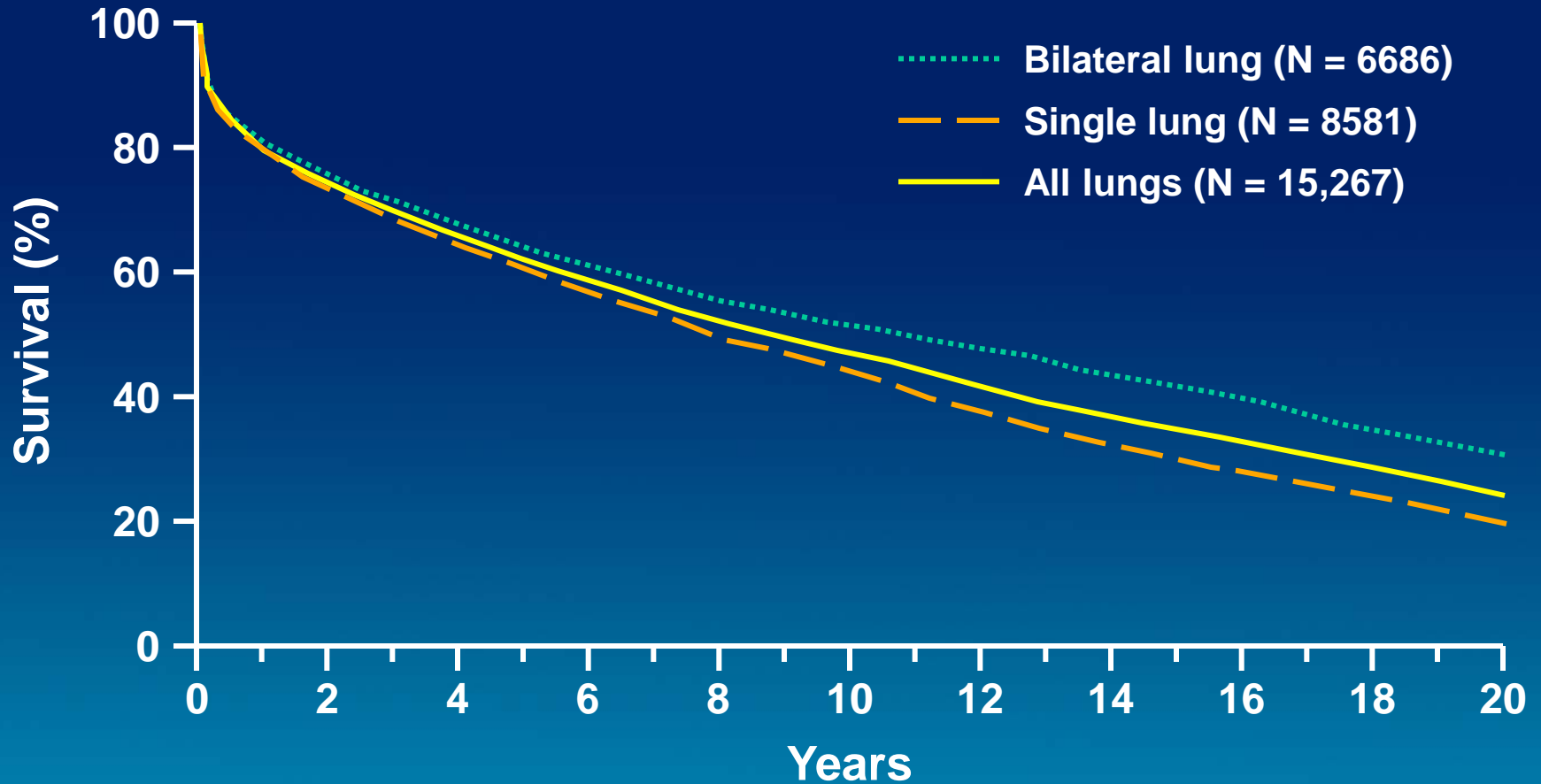
- Colonization vs. infection
- Sinus disease
- GI Issues:
 - GERD
 - Pancreatic Insufficiency
 - Nutrition
 - DIOS
- CFRD
- Osteoporosis
- Psychosocial

French Lung Transplant Experience for CF

- Compared two five year periods (2000-2005 and 2005-2010)
 - Improved one year survival (75% to 88%) due to: extensive use of thoracic epidurals leading to increased early extubations

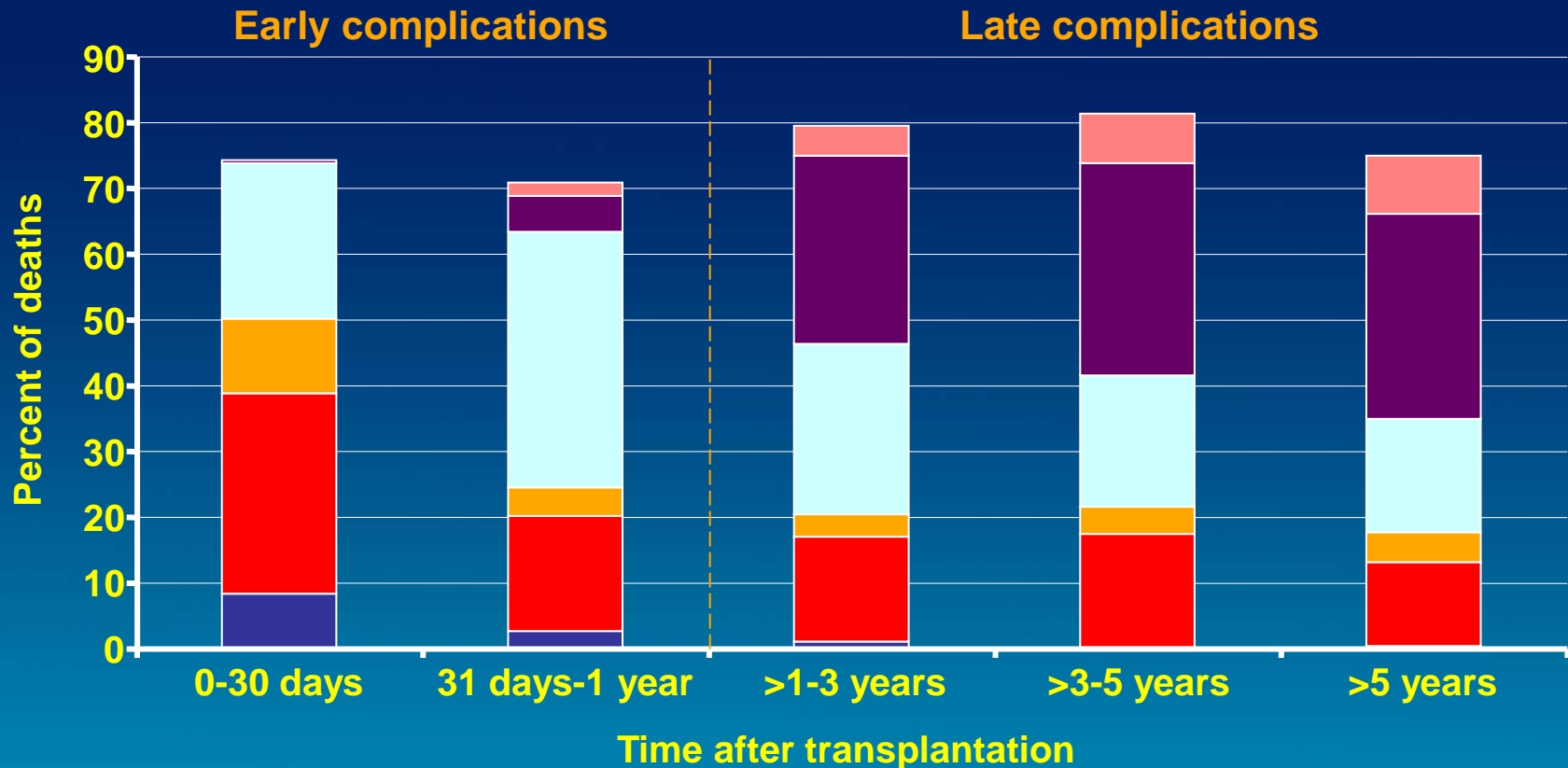
Mordant et al. European Journal of Cardiothoracic Surgery.
2010

Survival of Transplant Recipients by Procedure Type



Causes of Death in Lung Transplant Recipients

- Technical complication
- Graft failure
- Cardiovascular disease
- Infection – Non-CMV
- Chronic rejection
- Malignancy – Non-lymphoma



Summary

- CF is the third most common indication for lung transplant
- Decision of transplantation is derived from a **comprehensive evaluation** that **MUST** take into account several indicators of disease severity: FEV₁, increase in O₂ need, hypercapnia, need for non-invasive ventilation, functional status & pulmonary hypertension.

Summary

- Post-transplant survival of CF patients is similar or even greater than survival of patients w/ other conditions