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Workshop on the State of the Science of Solid Organ Transplantation and Disability

Pediatric Liver and Intestine Transplantation

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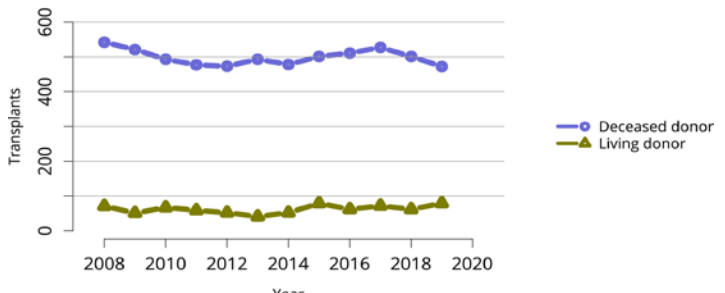
Strategy

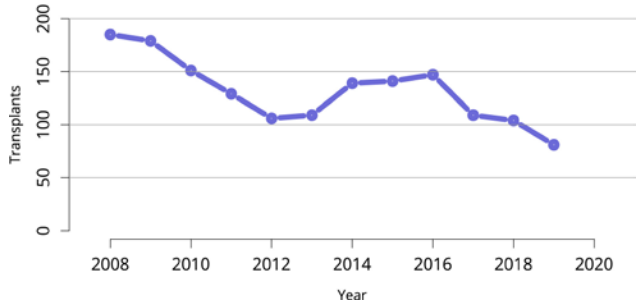
- Give you context for understanding the unique distinctions in pediatric liver and intestine transplantation
- Suggest a framework for looking at cycle of care in children
- Introduce the ideal outcome concept as a helpful measure to assess long term outcomes in children that may be helpful for disability determination

Pediatric Liver/Intestine Transplant At a Glance

Variable	Liver Transplantation	Intestine Transplantation
Annual volume in US	550-600 (551 in 2019)	90-100
Comparison to adult experience	>8000 transplants (2019)	Predominantly pediatric therapy
Key trends volume	Stable volume over past decade	Decreasing use
Key trends in medical space	Technical variant (split, living donor transplant offer option to reduce wait list mortality	Improvement in hormonal therapy have led to better non- transplant options
Support available for organ failure therapy available	No	Total parenteral nutrition
Retransplant	10% within 10-15 years	15% within 5 years

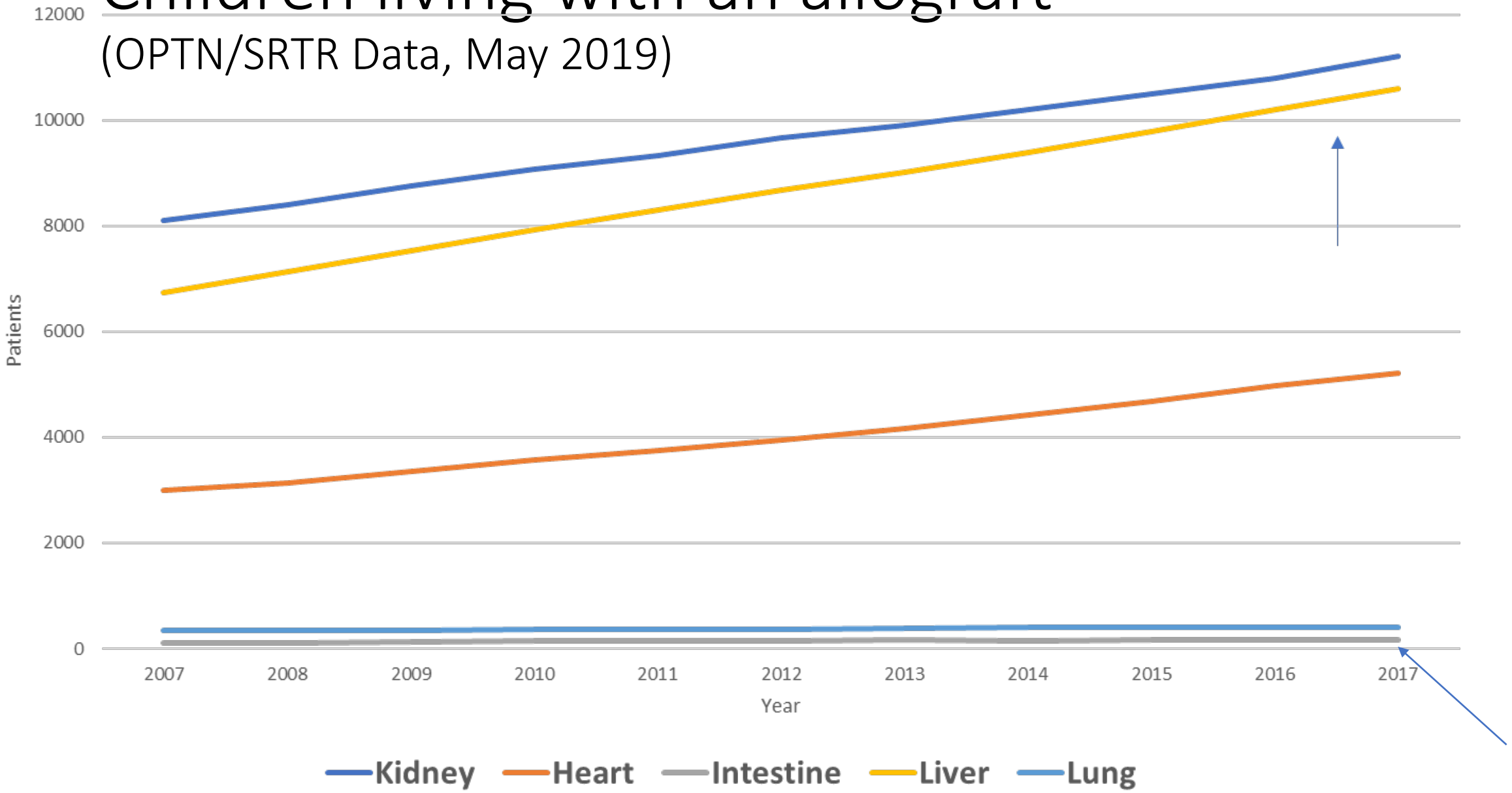
AJT, Volume: 21, Issue: S2, : 208-315
316,355, 17 February 2021, DOI:
(10.1111/ajt.16494)





Children living with an allograft

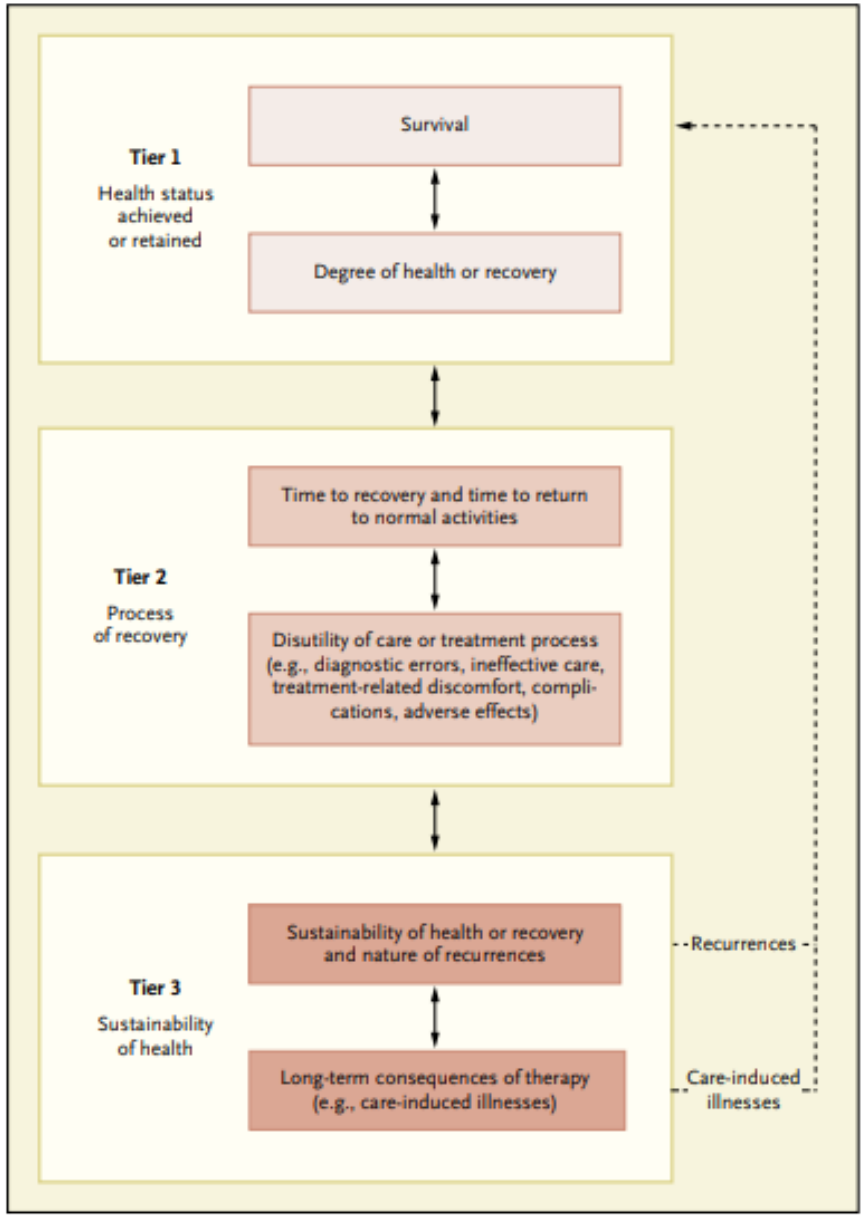
(OPTN/SRTR Data, May 2019)



Outcome Measures Hierarchy -

Porter, What is value in Health Care?

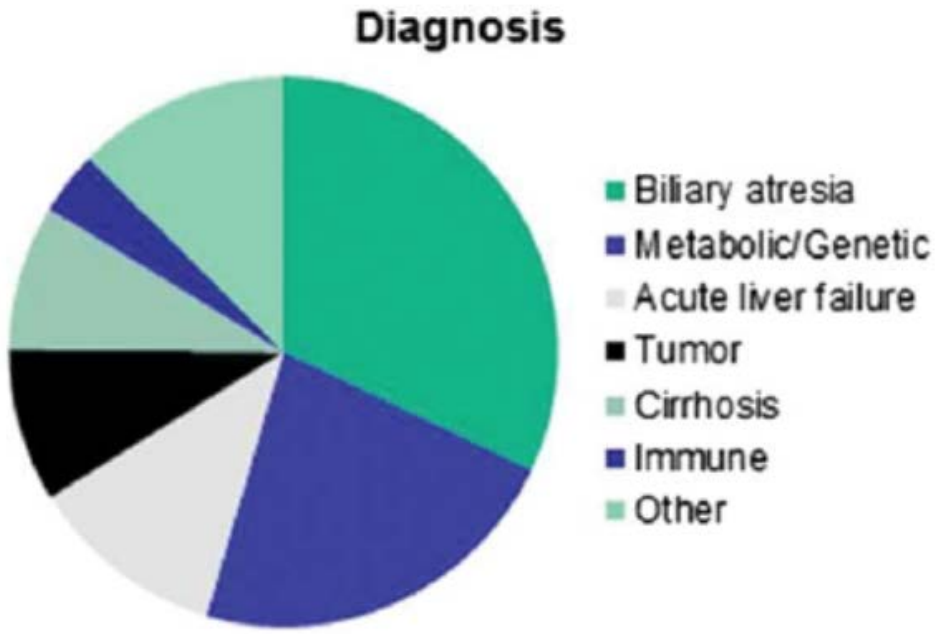
NEJM 12-23-2010, 2477-2481



Cycle of care in children is much longer than for adults with resultant period of potential impact of care being measured in decades.

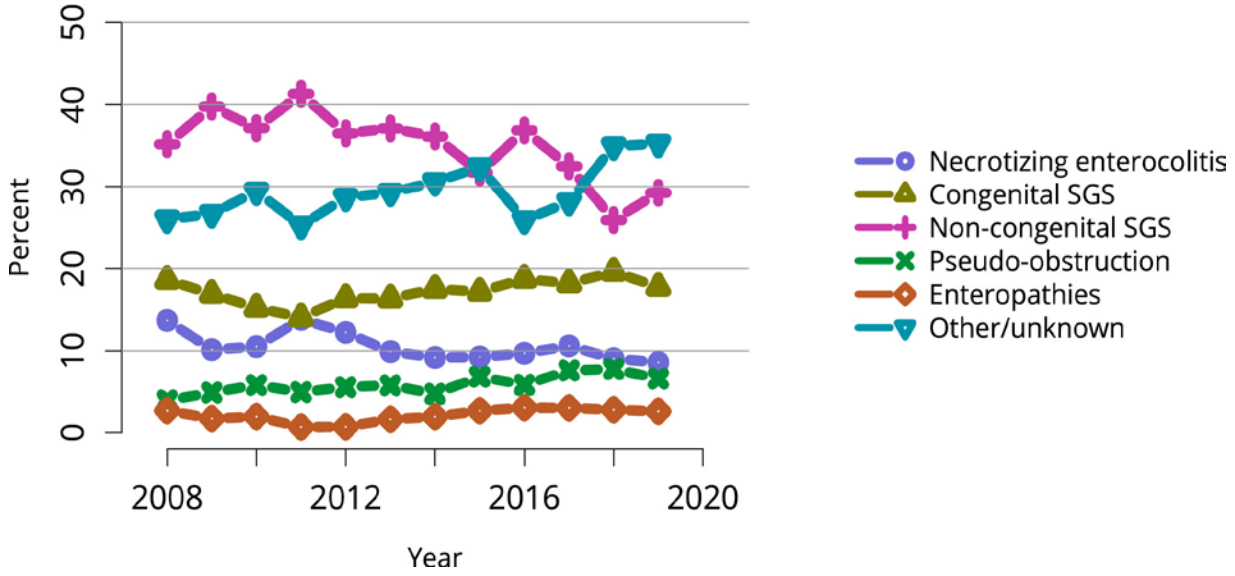
Disease states leading to transplant in children

Liver



HEPATOLOGY, Vol. 60, No. 1, 2014 Squires, et al

Intestine



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Understanding impact of metabolic disease

Disease	Chronic liver disease	Metabolic disease
Risk of Pre-existent Impairment	Rare	Moderate
Risk of post transplant impairment	Rare	Improved, but still possible

Mazariegos et al, Liver transplantation for pediatric metabolic disease, Molecular Genetics and Metabolism 111 (2014) 418–427

Metabolic diagnoses for which liver transplant has been reported.

Conditions with liver injury

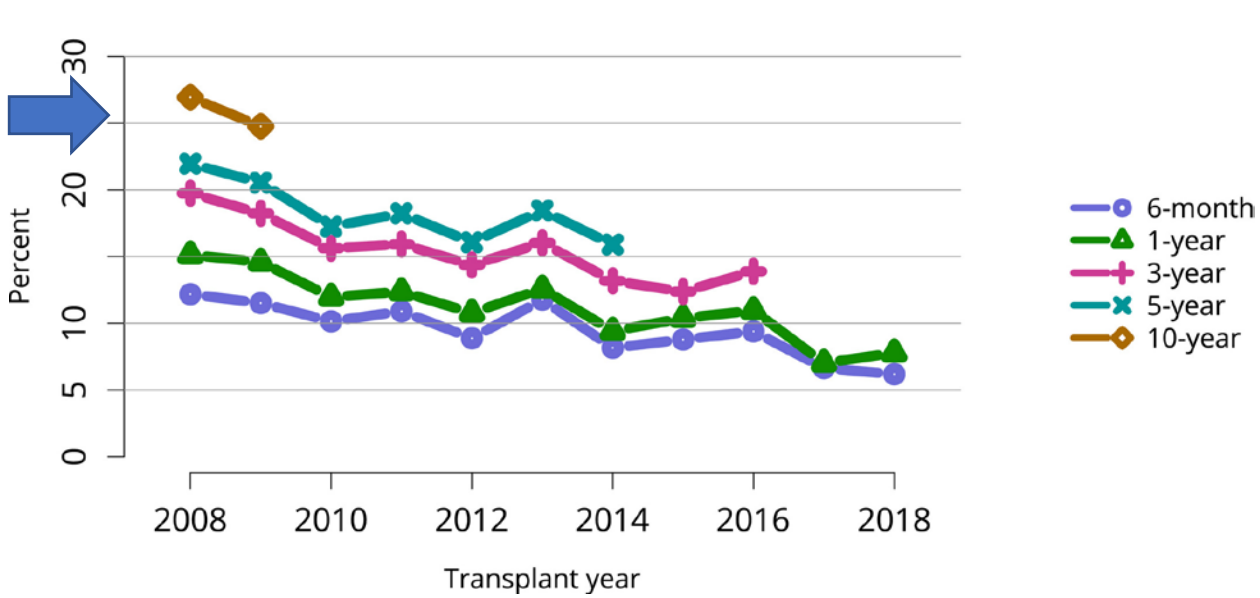
Intrahepatic	Extrahepatic
Alpha-1-antitrypsin deficiency (*SERPINA1*)	• Wilson disease • Cystic fibrosis • FIC-1 deficiency • Glycogen storage disease types Ib, III and IV • Non-alcoholic steatohepatitis • Gaucher disease • Niemann–Pick disease • Cholesterol ester storage disease • Mitochondrial cytopathies • Cerebrotendinous xanthomatosis • Citrin deficiency • Erythropoietic porphyria
• Tyrosinemia type I • GSD Type IV (*GBE1* gene) • BSEP deficiency • MDR-3 deficiency • Primary bile acid synthesis disorders • Hepatic porphyrias o Acute intermittent porphyria o Variegate porphyria • Glycogen storage disease type Ia • Hereditary fructose intolerance • Indian childhood cirrhosis	

Conditions without liver injury

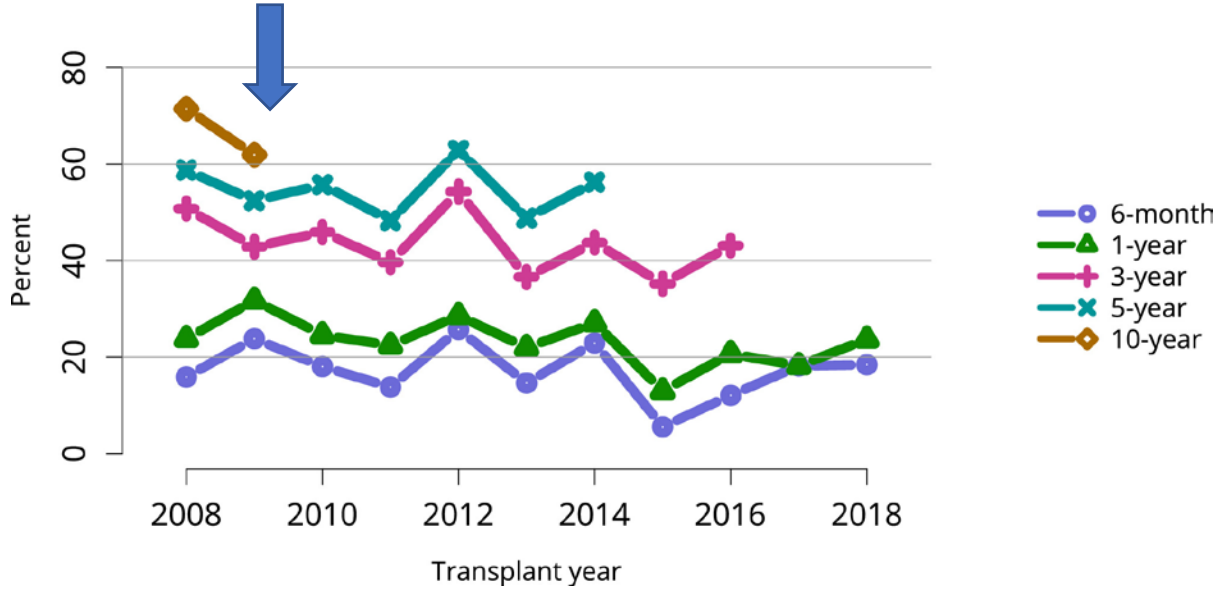
Intrahepatic	Extrahepatic
• Crigler–Najjar syndrome type 1 • Primary hyperoxaluria • Urea cycle disorders • Familial hypercholesterolemia • Fatty acid oxidation defects • Coagulation defects o Hemophilia A o Factors V and VII deficiency o Proteins C and S deficiencies • Factor H deficiency • Afibrinogenemia • Amyloidosis type 1	• Citrulinemia • Cystinosis • Branched amino acids disorders (organic acidemias) o Propionic acidemia o Methylmalonic acidemia o Mevalonic acidemia o Maple syrup urine disease

Graft failure among pediatric deceased donors

Liver



Intestine



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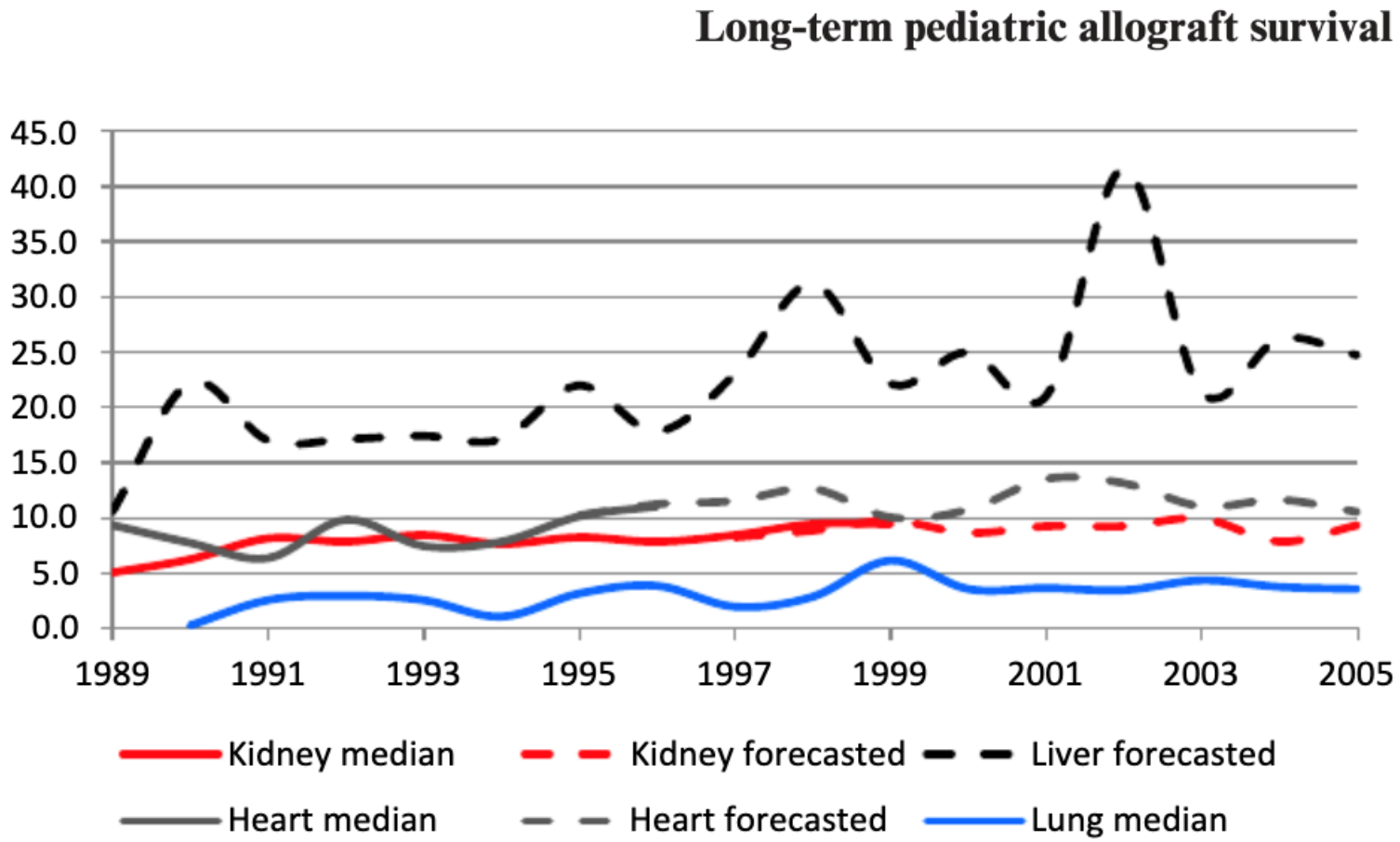
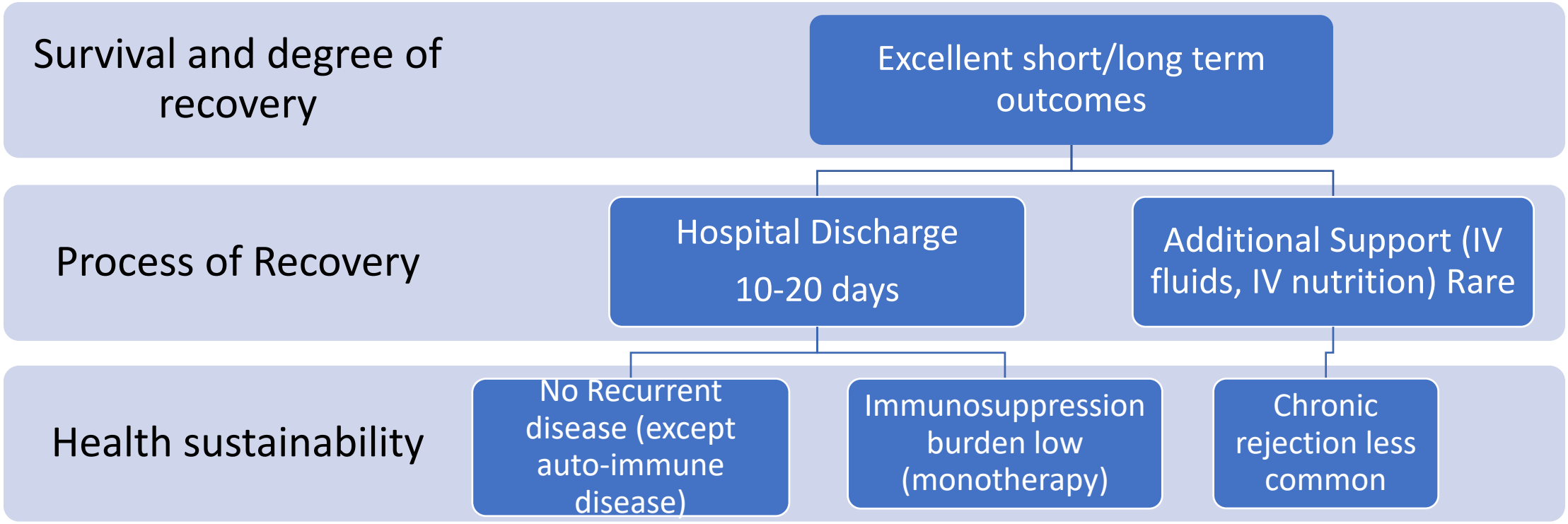
Pediatric graft half lives (median or forecasted, 1989-2008)

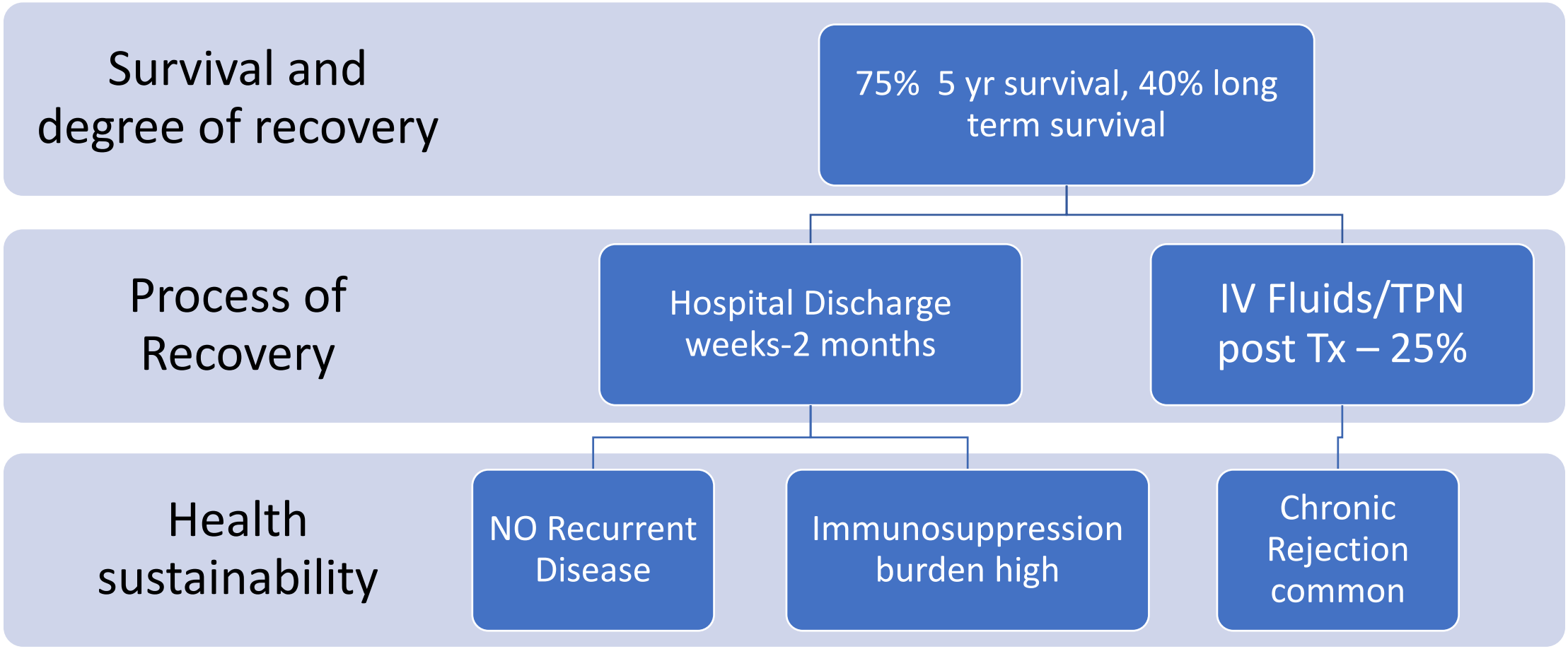


Dharnidharka et al, Lack of significant improvements in long- term allograft survival in pediatric organ transplantation Pediatric Transplantation 2015:19, 477-483

Pediatric Liver Transplantation



Pediatric Intestine Transplantation



Toward a more wholistic view: the “Ideal outcome” metric

Table IV. The ideal SPLIT 10-year survivor of pediatric LT

Medical variable: result reported at 10-year visit	Patient data available, n	Patients who answered “yes” to variable as phrased, n (%)	Patients missing data, n (%)
Sustainability of allograft			
1 No retransplantation	167	147 (88%)	0
2 No chronic rejection; confirmed diagnosis previously/presently	167	152 (91%)	0
3 Serum ALT normal	166	148 (89%)	1 (1%)
4 Serum TB normal	165	161 (98%)	2 (2%)
5 Serum albumin normal	162	160 (99%)	5 (3%)
6 Serum GGT normal	149	126 (85%)	18 (11%)
Absence of immunosuppression-induced comorbid conditions			
7 No PTLD; previous diagnosis of tissue-confirmed PTLD	167	158 (94%)	0
8 No renal dysfunction; cGFR <90 mL/min/1.73 m^2	118	107 (91%)	49 (29%)
9 Acceptable linear growth; >−2 SD for healthy population	121	112 (93%)	46 (27%)
10 No diabetes	167	165 (99%)	0
Absence of need for additional medications			
11 No ongoing use of prednisone	167	135 (81%)	0
12 No use of antihypertensive agent	167	146 (87%)	0
13 No use of antiseizure medication	167	167 (100%)	0

Vicky Ng et al : Health Status of Children Alive 10 years after Pediatric Liver Transplant J Pediatrics 2012: 160-820-6

Summary

- Evaluating pediatric liver and intestine transplant through the outcomes hierarchy paradigm is helpful to identify the distinct challenges children face thru the transplant journey
- As compared to adults, pediatric span of care is measured in decades
- Although long term outcomes favor liver transplant, the incidence of metabolic disease in liver candidates yields more children who may be at risk of pre-transplant neurologic injury/disability
- Ideal outcome metrics including quality of life measures have begun to be studied in liver transplantation, but are at an early stage in intestine recipients.