Pediatric Renal Transplantation

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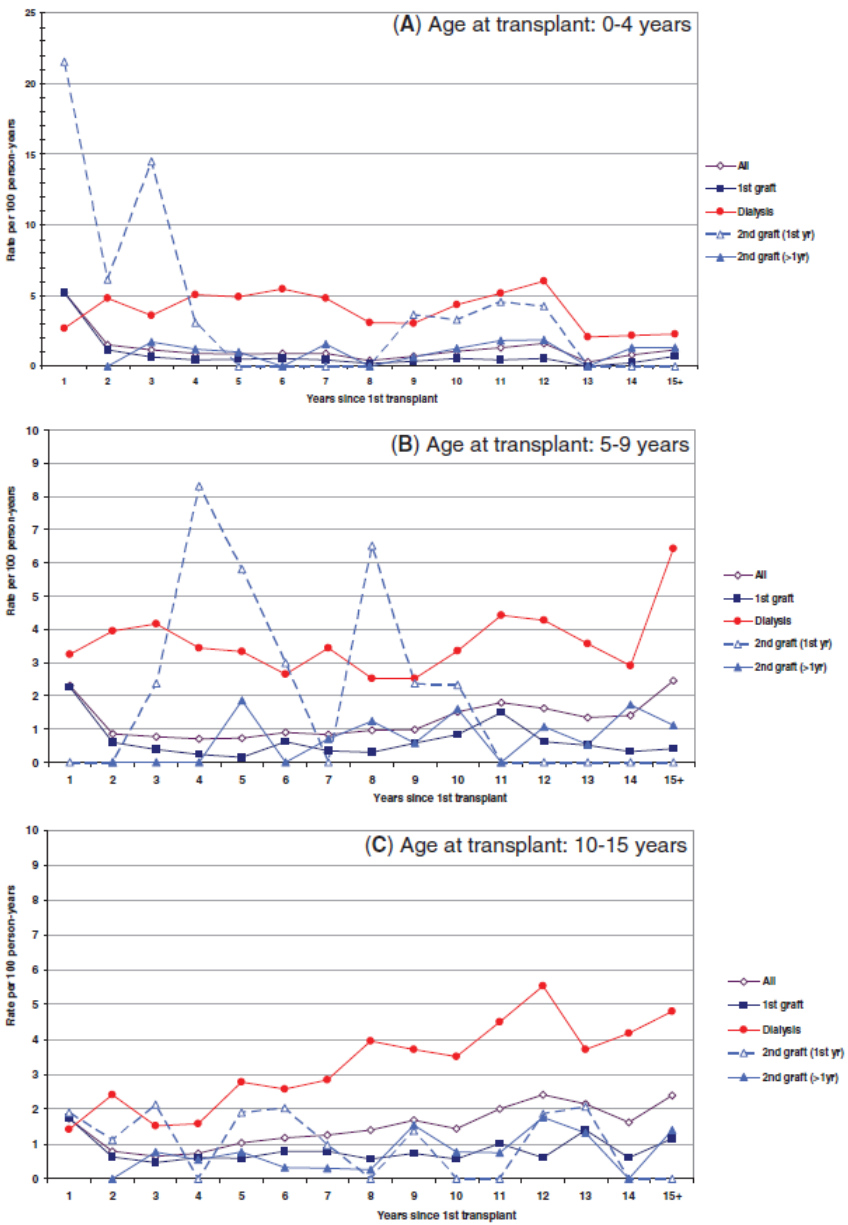
So many challenges!

- Limited number of patients
- Life threatening conditions
- Overall frailty
- Ethical and technical issues
- Brain development and cognitive outcomes
- Extrarenal involvement according to primary disease
- Body size
- Vessels size
- Body composition
- Pharmacokinetics of drugs, immature metabolism, protein binding
- Immune status
- Nutrition
- Etc.

Patient survival: Tx is the best option!

- Dialysis
- Transplantation



Age at Tx

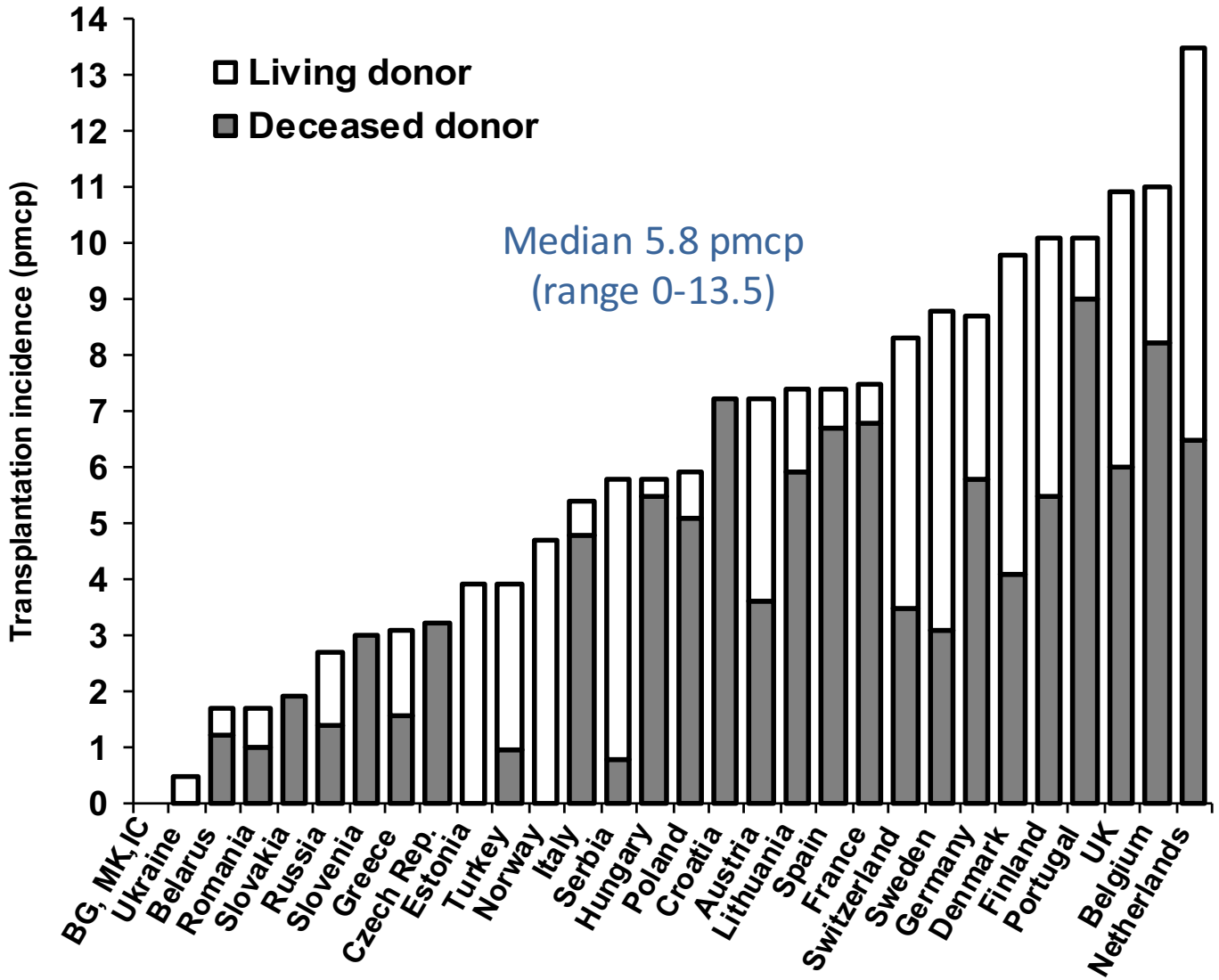
0-4 years

5-9 years

10-15 years

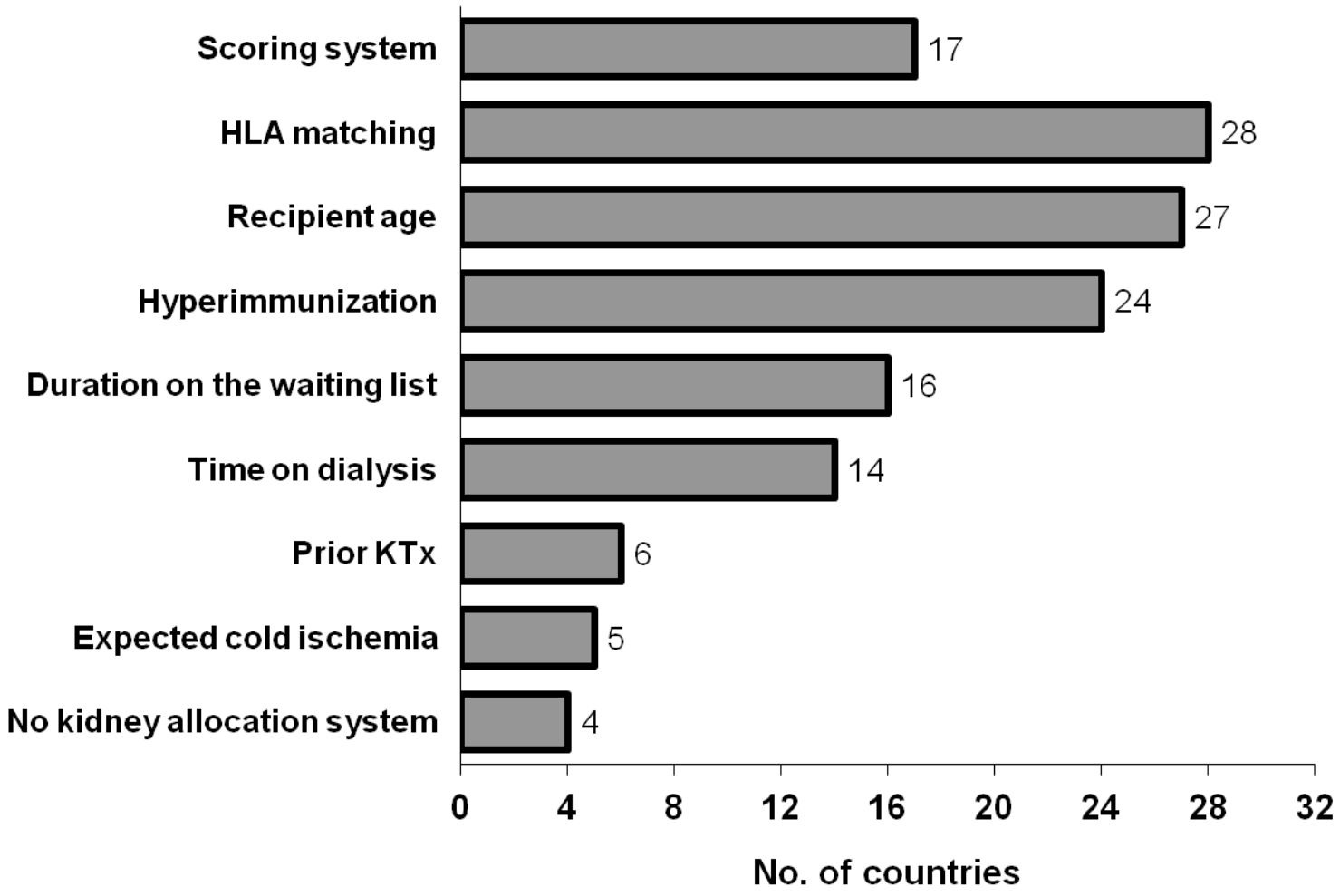
Foster *Am J Transplant* 2011

Incidence rate of pediatric KTx, Europe



Harambat *ESPN* 2012

Allocation systems for pediatric KTx, Europa



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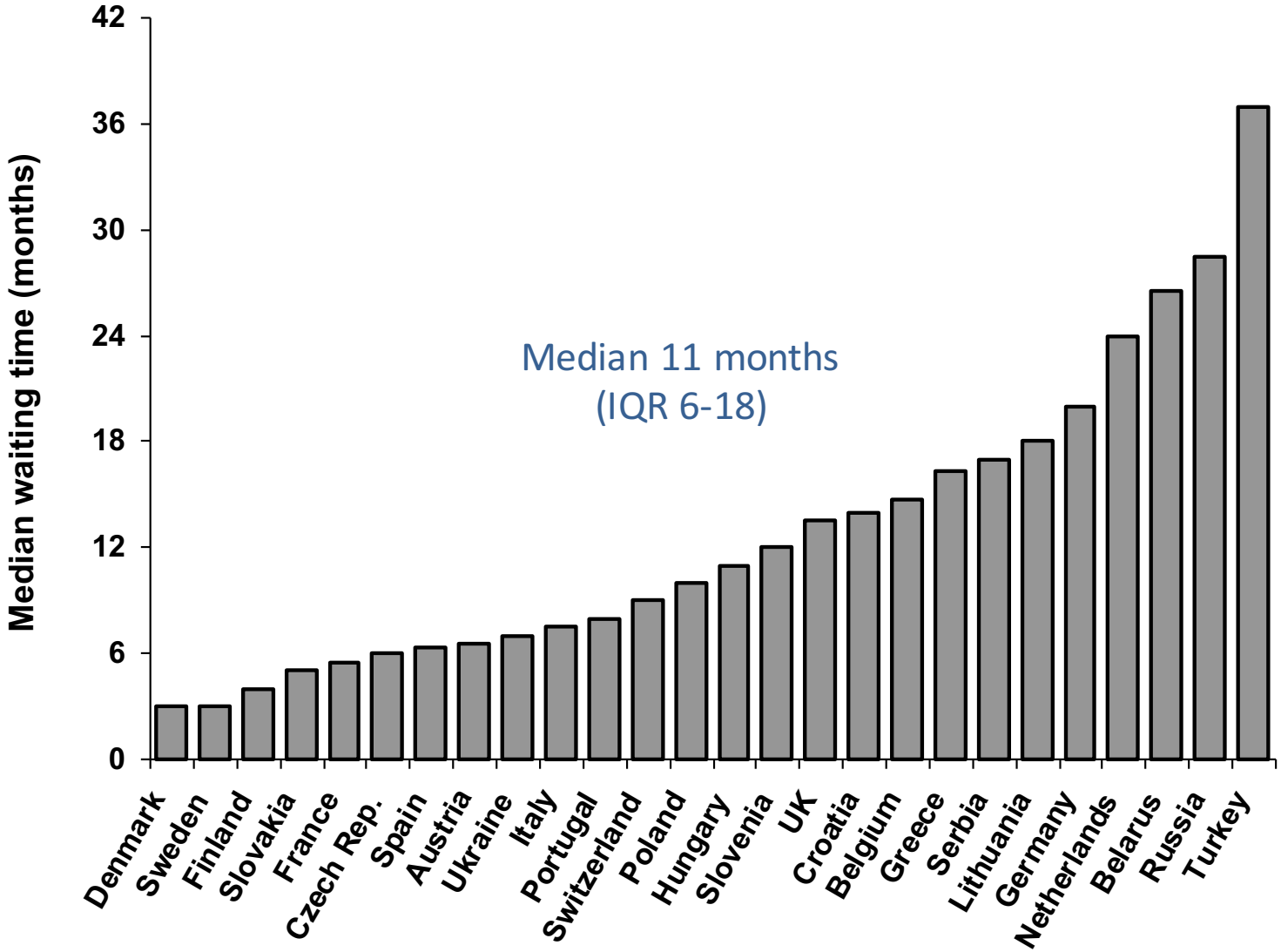
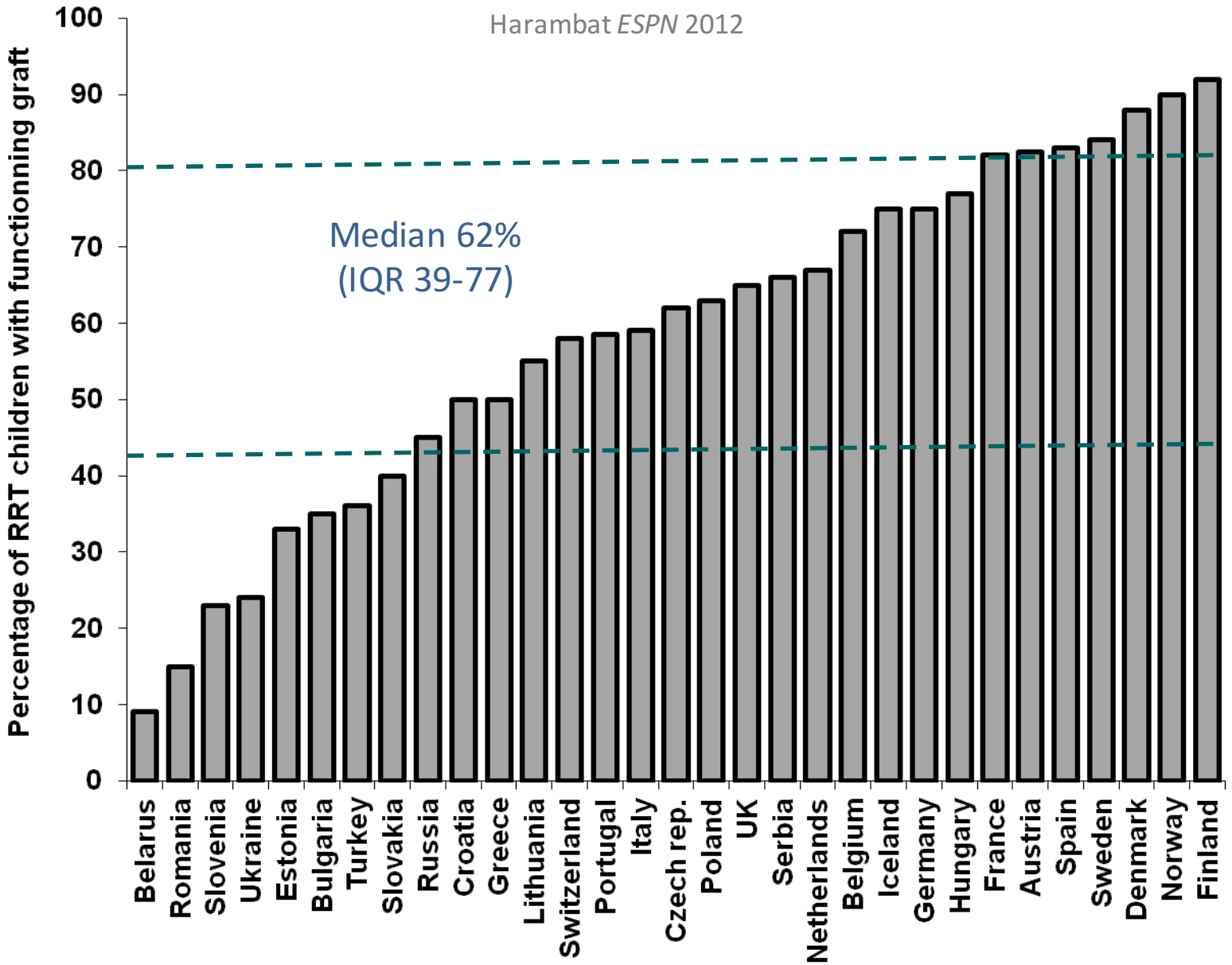
Waiting time for DD pediatric KTx, Europe



Harambat *ESPN* 2012

Proportion of RRT children with a functioning graft, Europe



Question 1: 1 right answer

The lower age limit for kidney Tx in children is

A. 0 to 6 months
B. 6 to 12 months
C. 12 to 18 months
D. 18 to 24 months
E. 24 to 36 months

Indication for kidney transplantation

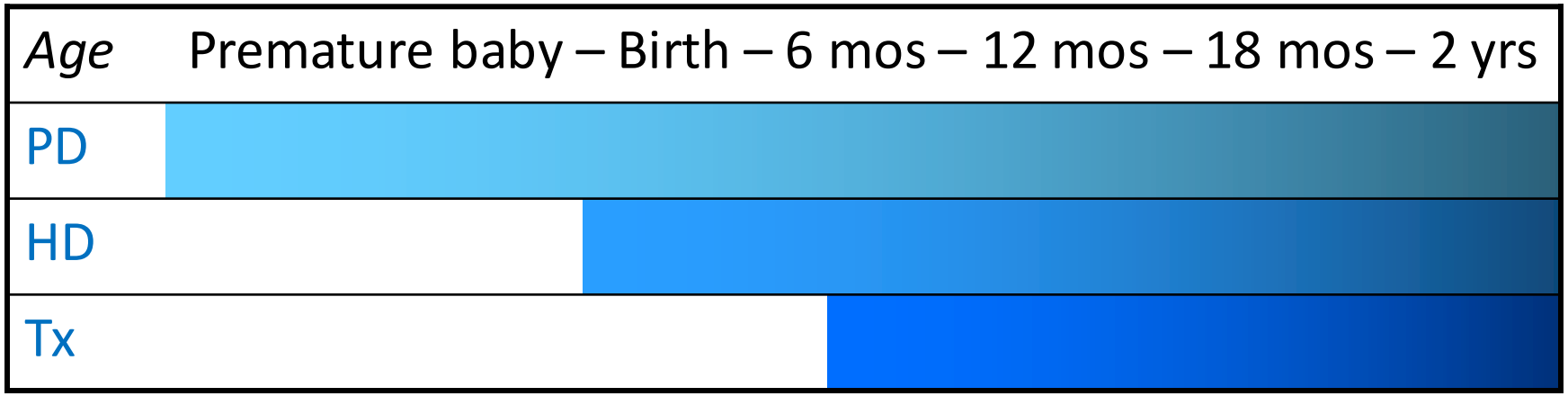
- Children with irreversible renal failure

- Min. age: 6 to 12 mos
- Min. BW: 5 to 10 kg

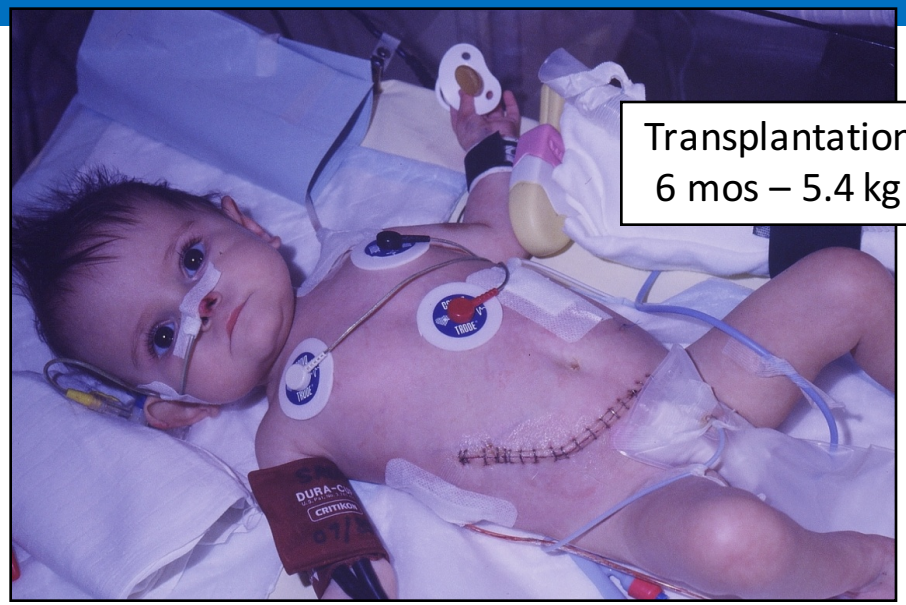
According to local experience & background

- Specifc caution to
  - ABO incompatibility
  - DSA (Donor-specific antibodies)
  - Malignancy within the previous 2 yrs
  - Active viral infection
  - Active (auto-) immune disease
  - Multiorgan failure
  - Major disability

Options according to age at start of RRT

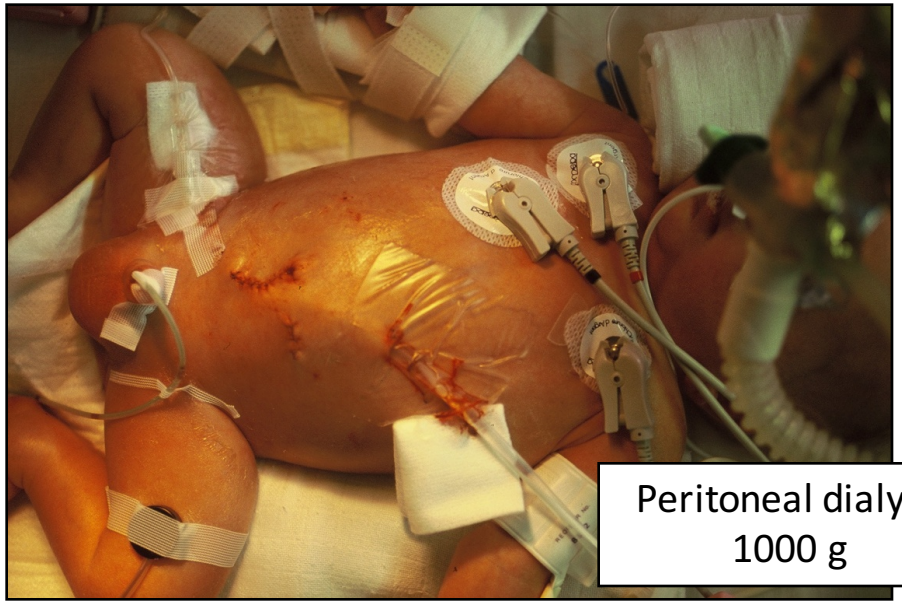


RRT options during the 1st year of life



Transplantation
6 mos – 5.4 kg

Hemodialysis
5 mos – 4.8 kg



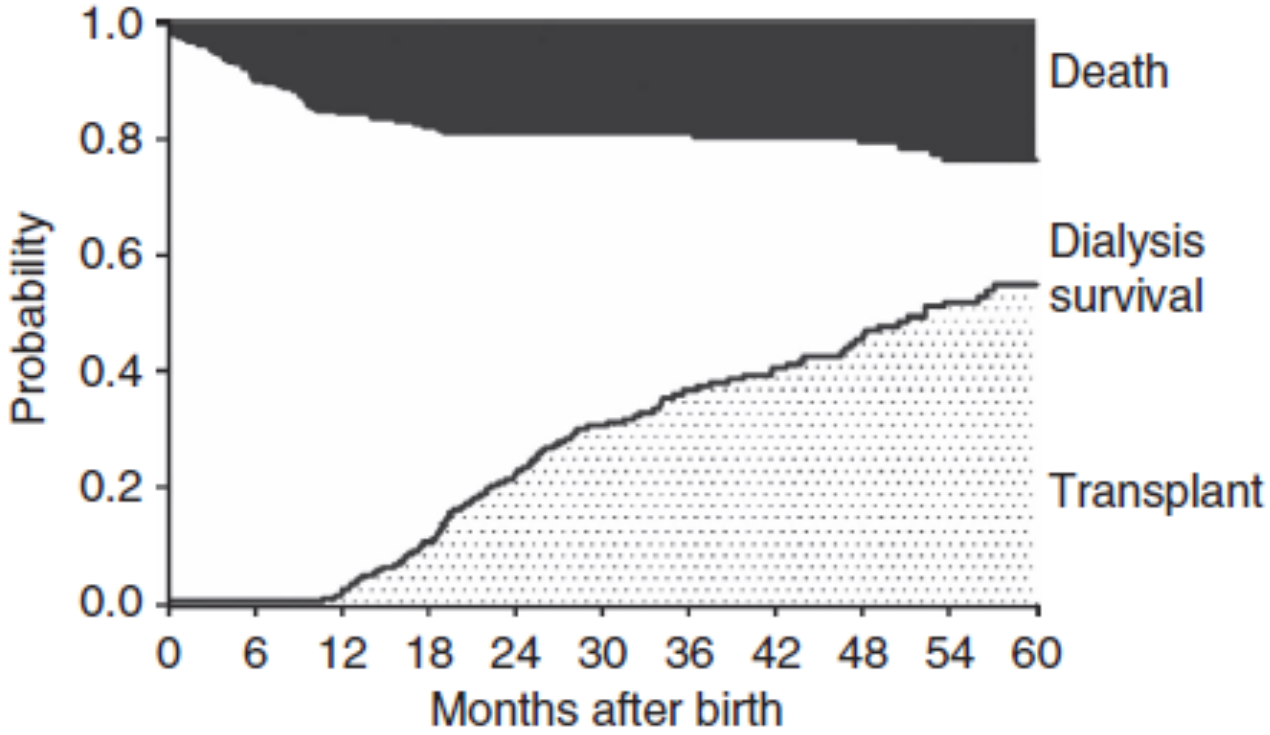
Peritoneal dialysis
1000 g

NAPRTCS Tx population 2010

Age Groupings (years)	N	%
0-1	614	5.3
2-5	1705	14.7
6-12	3804	32.8
13-17	4547	39.2
≥ 18	933	8.0

RRT in neonates: 264 patients from 32 countries

Mean follow-up: 29 mos
2-yr survival: 81%
5-yr survival: 76%



5-yr patient and graft survival: 96%

Van Stralen *Kidney Int* 2014

Question 2: 1 right answer

What is the average rate of Tx < 18 years among all kidney Tx?

A. 1 %
B. 2.5 %
C. 5 %
D. 7.5 %
E. 10 %

Pediatric kidney Tx activity, Europe

Country	Total Nb of Tx	Tx in children (%)
Croatia	109	4 (3.66%)
Czech Republic	427	15 (3.51%)
France	2423	81 (3.34%)
Germany	2478	117 (4.72%)
Israel	94	21 (22.3%)
Italy	1746	58 (3.32%)
Lithuania	63	2 (3.17%)
Netherlands	420	14 (3.33%)
Norway	256	9 (3.51%)
Poland	1067	38 (3.56%)
Spain	2057	68 (3.31%)
Sweden	372	13 (3.49%)
Turkey	665	59 (8.87%)
UK	1516	128 (8.44%)
Serbia	67	3 (4.47%)

Average % Tx in children

4.5 %

Cochat *Comprehensive Pediatric Nephrology* 2008

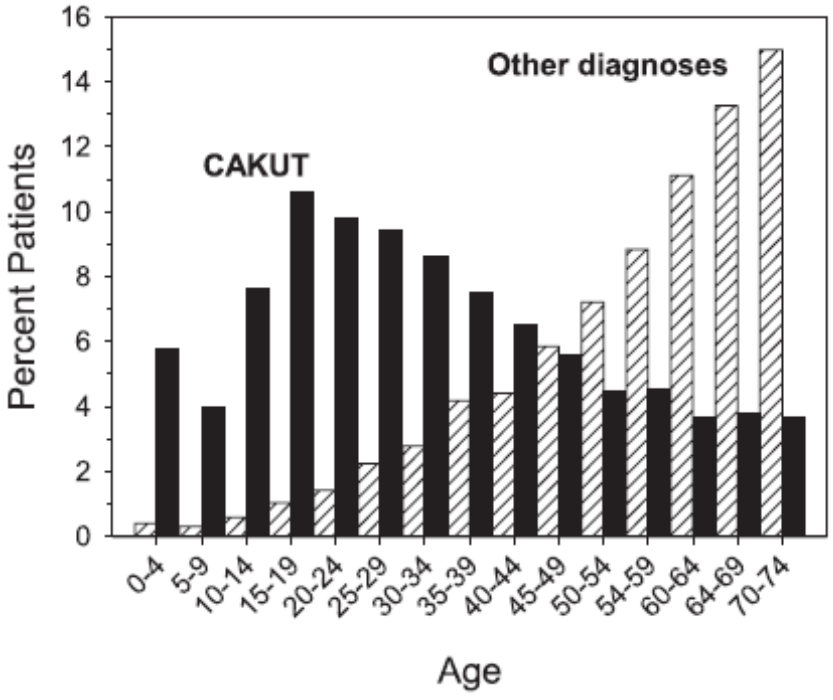
Question 3: 1 right answer

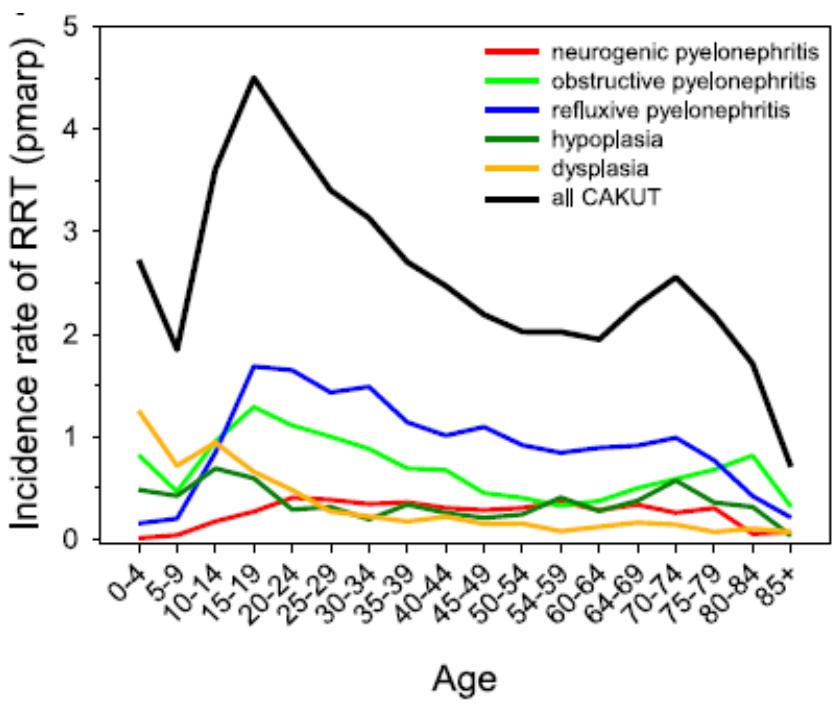
What is the main cause of ESRD in children < 5 years of age?

A. Congenital abnormalities of the kidney and urinary tract
B. Steroid-resistant nephrotic syndrome
C. Inherited renal diseases
D. Hemolytic uremic syndrome
E. Chronic pyelonephritis

CAKUT among RRT: Epidemiology

ERA-EDTA Registry – 4765 patients from 1990 to 2009





Wühl *Clin J Am Soc Nephrol* 2013

Primary disease

Primary Diagnosis		
Aplasia/hypoplasia/dysplasia kidney	1681	15.8
Obstructive uropathy	1630	15.3
Focal segmental glomerulosclerosis	1246	11.7
Reflux nephropathy	549	5.2
Chronic glomerulonephritis	340	3.2
Polycystic disease	323	3.0
Medullary cystic disease	287	2.7
Congenital nephrotic syndrome	277	2.6
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Cystinosis	221	2.1
Membranoproliferative glomerulonephritis - Type I	186	1.7
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Idiopathic crescentic glomerulonephritis	181	1.7
SLE nephritis	159	1.5
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Berger's (IgA) nephritis	135	1.3
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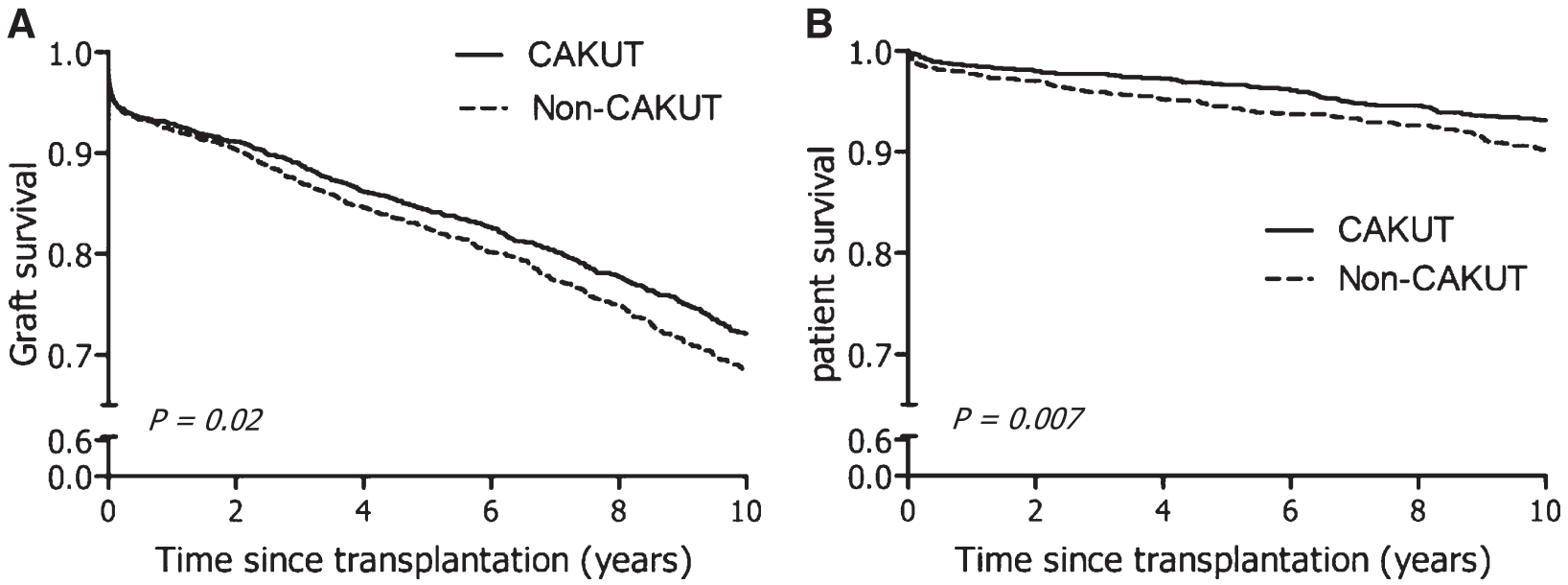
Membranoproliferative glomerulonephritis - Type II	85	0.8
Wegener's granulomatosis	66	0.6
Wilms tumor	56	0.5
Drash syndrome	55	0.5
Oxalosis	55	0.5
Membranous nephropathy	47	0.4
Other systemic immunologic disease	34	0.3
Sickle cell nephropathy	16	0.2
Diabetic glomerulonephritis	11	0.1
Other	1110	10.4
Unknown	663	6.2

CAKUT 40%

NAPRTCS 2010

CAKUT and kidney Tx: Better outcomes

ERA-EDTA registry – 4765 patients from 1990 to 2009



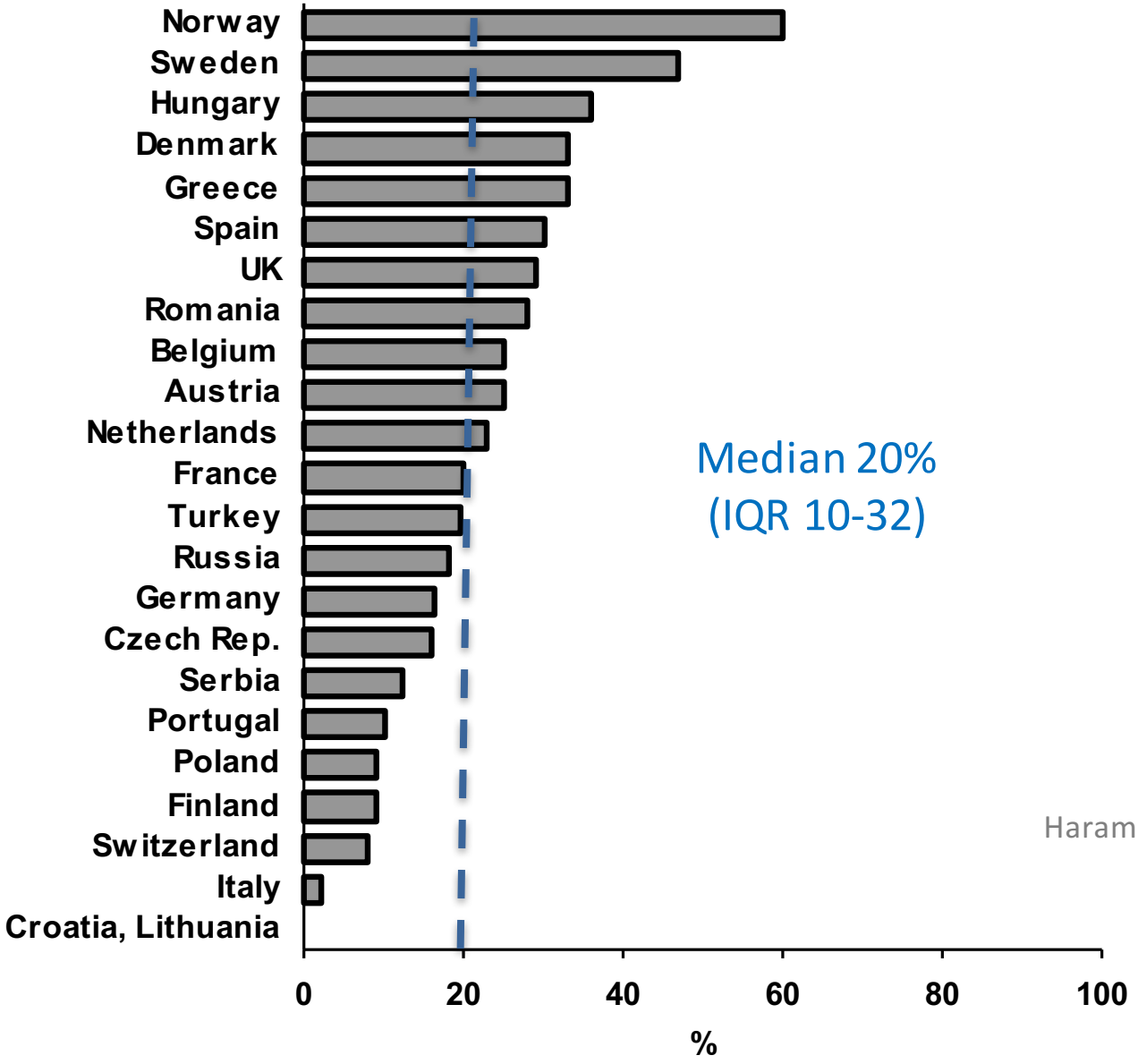
Wühl *Clin J Am Soc Nephrol* 2013

Question 4: 1 or more right answer(s)

Preemptive kidney transplantation

A. Should be the preferred option in most ESRD children
B. Cannot be recommended du to the risk of non-adherence
C. Can be proposed irrespective of the primary disease
D. Provides the same graft survival than in dialysis children
E. Relies on local facilities

Preemptive kidney Tx in children, Europe



Harambat *ESPN* 2012

Transplant characteristics

Primary Transplants	N	%
Total Primary Transplants	9198	100.0
Preemptive	2241	24.4
Splenectomy	57	0.6
Native tissue removed	2007	21.8
Maintenance hemodialysis	2645	28.8
Maintenance peritoneal dialysis	3578	38.9
Both maintenance hemo & peritoneal dialysis	533	5.8

NAPRTCS 2010

The best option for RRT children in preemtive Tx

Dialysis should be limited to those children who cannot benefit from preemptive Tx

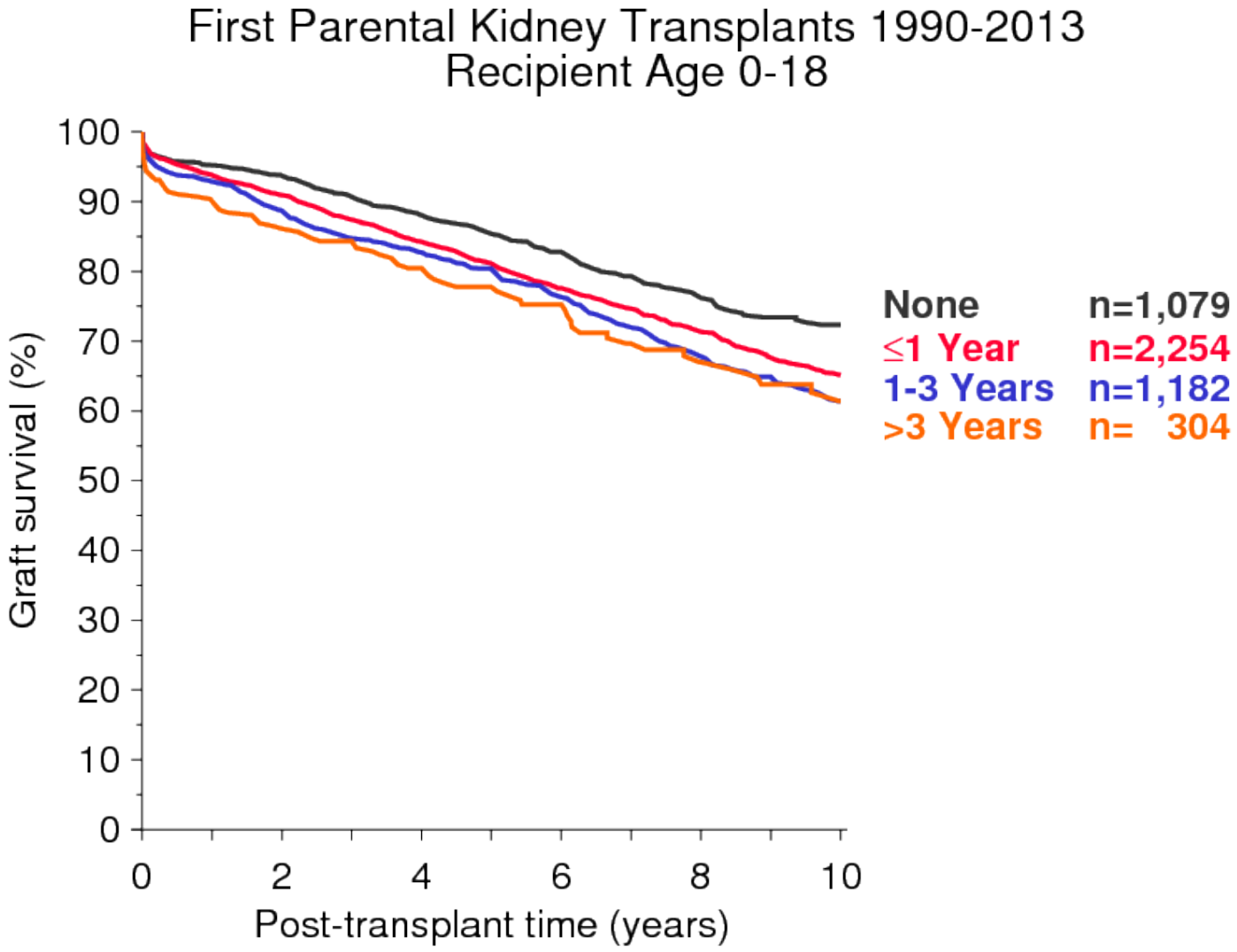
Advantages

- Avoids dialysis (school attendance, social and family life)
- Avoids vascular/peritoneal access
- Better results than non-preemptive Tx
- Cost effectiveness

Drawbacks

- Timing for registration on the waiting list?
- Increased risk of non-adherence?

Graft survival according to waiting time

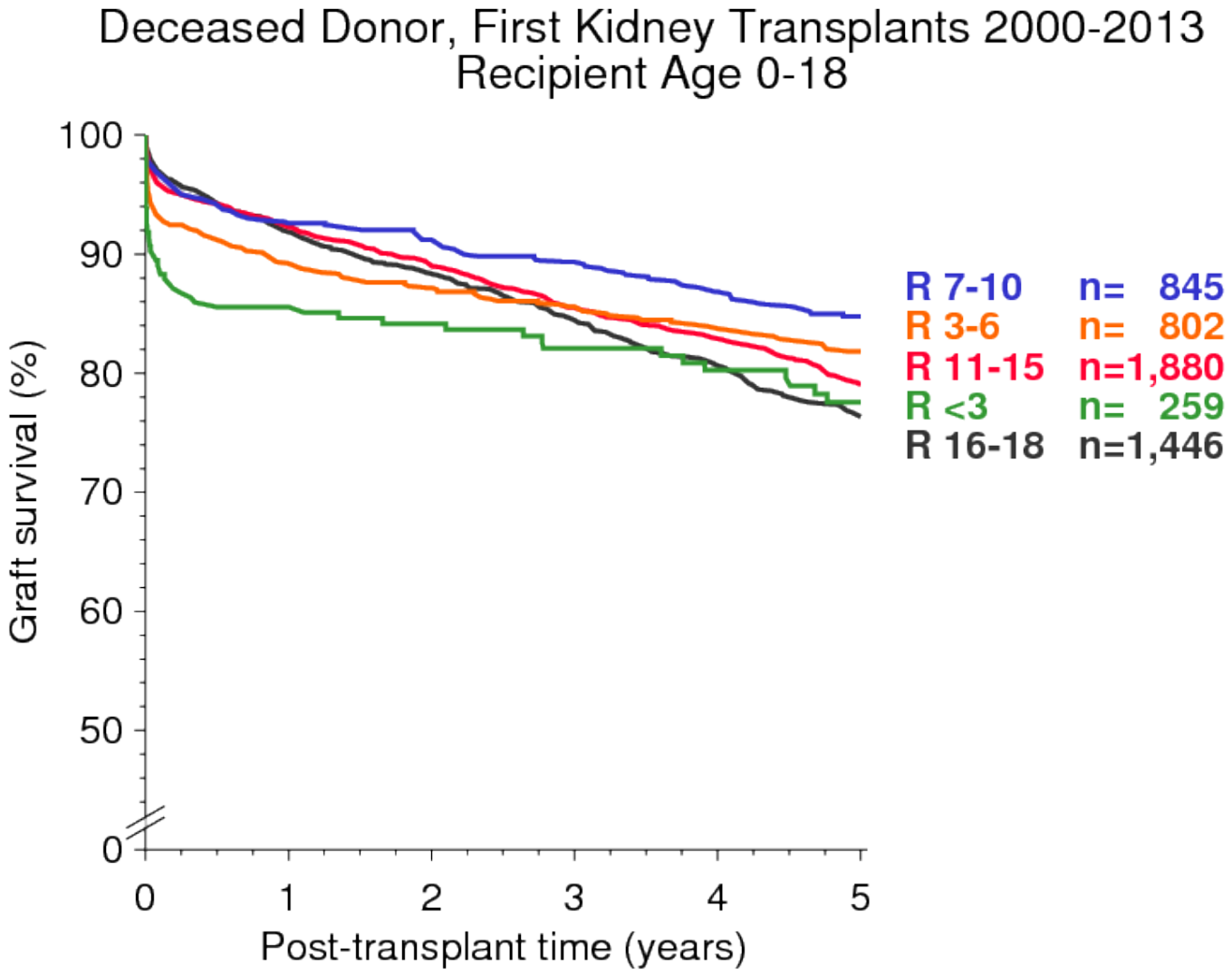


Question 5: 1 or more right answer(s)

In kidney Tx children, 5 year-graft survival

A. Is independent of age
B. Depends on age at Tx
C. Is better in infants
D. Is better in school age children
E. Is better in adolescents

Graft survival according to recipient age



Question 5: 1 right answer

In kidney Tx children, the main cause for graft failure is

A. Vascular thrombosis
B. Recurrence of the primary disease
C. Acute rejection
D. Chronic allograft nephropathy
E. Post-transplant lymphoproliferative disorder

Causes of graft failure

Cause	Index Graft Failures		Subsequent Graft Failures		All Graft Failures	
	N	%	N	%	N	%
Total	2367	100.0	317	100.0	2684	100.0
Death with functioning graft	220	9.3	23	7.3	243	9.1
Primary non-function	60	2.5	2	0.6	62	2.3
Vascular thrombosis	239	10.1	38	12.0	277	10.3
Other technical	28	1.2	4	1.3	32	1.2
Hyper-acute rejection	13	0.6	4	1.3	17	0.6
Accelerated acute rejection	33	1.4	8	2.5	41	1.5
Acute rejection	308	13.0	41	12.9	349	13.0
Recurrence of original kidney disease	152	6.4	31	9.8	183	6.8
Renal artery stenosis	15	0.6	0	0.0	15	0.6
Bacterial/viral infection	45	1.9	5	1.6	50	1.9
Cyclosporine toxicity	11	0.5	0	0.0	11	0.4
De novo kidney disease	7	0.3	2	0.6	9	0.3
Patient discontinued medication	108	4.6	8	2.5	116	4.3
Malignancy	31	1.3	2	0.6	33	1.2
Other/Unknown	272	11.5	32	10.1	304	11.3

chronic allograft nephropathy – i.e., nonadherence in most patients!

Question 6: 1 or more right answer(s)

In children after kidney Tx, these diseases have a 80 to 100 % risk of graft loss to recurrence

A. Focal segmental glomerulosclerosis
B. Atypical HUS due to factor H mutation
C. Primary hyperoxaluria type 1
D. Lupus nephritis
E. IgA nephropathy

Primary disease

Primary Diagnosis		
Aplasia/hypoplasia/dysplasia kidney	1681	15.8
Obstructive uropathy	1630	15.3
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Reflux nephropathy	549	5.2
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Potential risk of recurrence 24%

NAPRTCS 2010

Recurrent renal diseases: an overview

Recurrence of the full primary renal disease		
High risk of graft loss	*Low risk of graft loss*	*Late risk of graft loss*
Primary hyperoxaluria type 1	IgA nephropathy	Type 1 diabetes
Steroid resistant NS / FSGS	Lupus nephritis	Sickle cell disease
Atypical HUS	ANCA-associated GN	
Membranoproliferative GN		
Membranous nephropathy		

Recurrence of specific features	
Alloimmunization	*Urinary tract malformations*
Nephrin, podocin Alport syndrome	Posterior urethral valves

Different from recurrence	
De novo *renal diseases*	*Specific deposits*
Membranous GN, thrombotic microangiopathy	Cystinosis, Fabry

Recurrent renal diseases: an overview

Table 1 | Recurrence of primary disease after first renal transplantation[2,3,6]

Primary disease	Recurrence rate (%)	Graft loss due to recurrence (%)	Usual time to recurrence
SRNS	14–50*	40–60	Early, within the first days or weeks
MPGN type I	30–77	17–50	Late
MPGN type II	66–100	25–61	Late
Primary hyperoxaluria type I	90–100	80–100	Early, within the first few days
Atypical haemolytic uraemic syndrome	0 (*DGKE*) 17 (*MCP*) 90 (*CFH, CFI*)	0 (*DGKE*) 10 (*MCP*) 86 (*CFH, CFI*)	Early, within the first days or weeks
IgA nephropathy	32–60	3–7	Late
Henoch–Schönlein purpura nephritis	31–100	8–10	Late
Lupus nephritis	0–30	0–5	Late
ANCA-associated vasculitis	<20	No data available	Late

Bacchetta *Nat Rev Nephrol* 2015

Question 7: 1 or more right answer(s)

In children with a functioning renal graft, statural growth

A. Returns to normal velocity
B. Is retarded in 10 to 20% of patients
C. Depends on steroid exposure
D. Depends on GFR
E. Requires the use of rhGH in one third of cases

Post-transplant growth

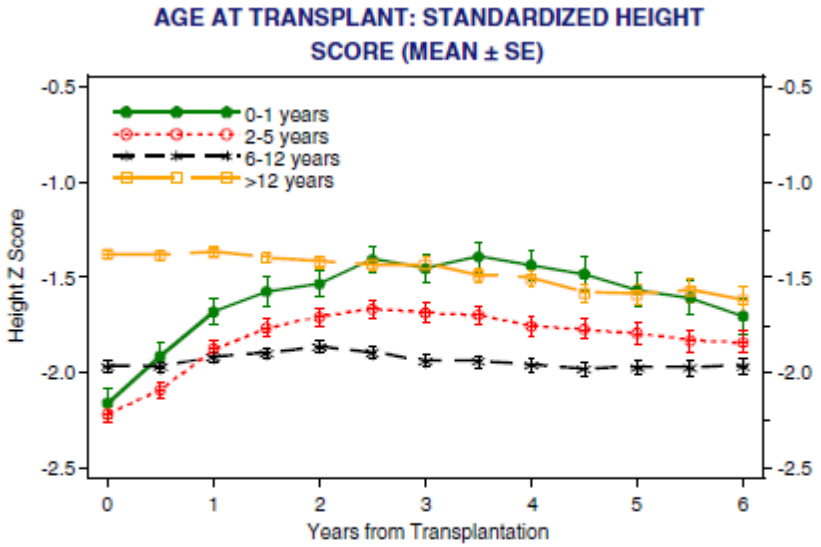


Fig. 1 Age at transplantation. Standardized height score [mean ± standard error (SE)]

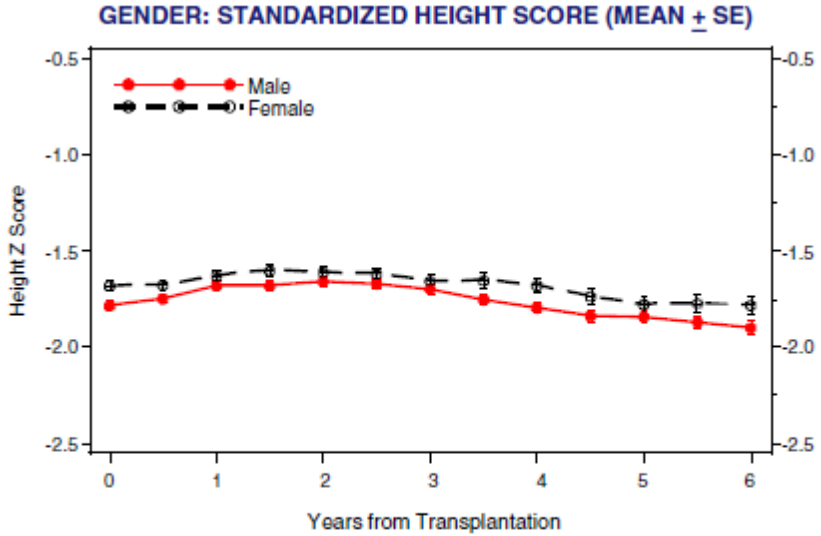
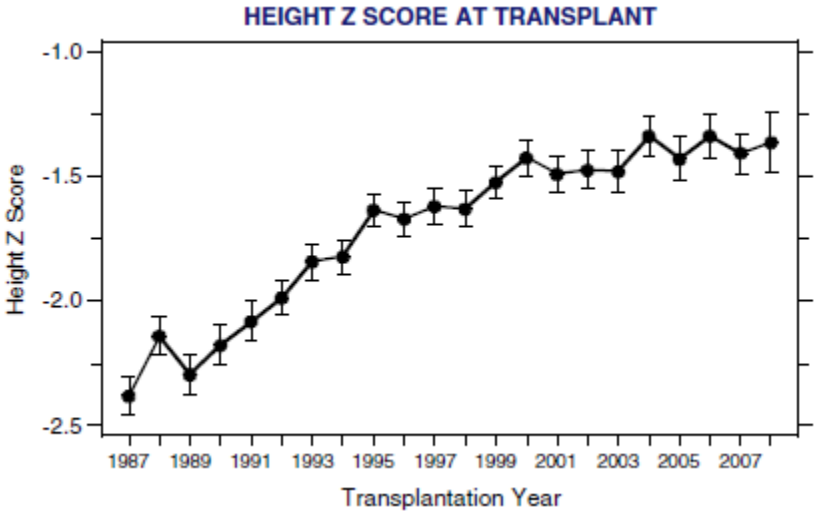
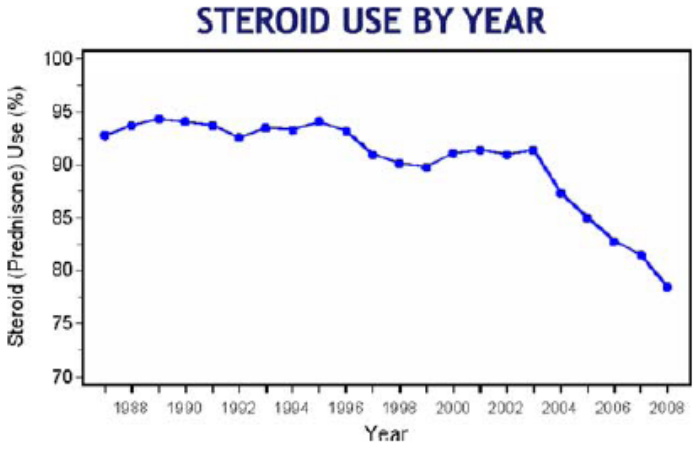


Fig. 3 Gender. Standardized height score [mean ± standard error (SE)]





Fine *Pediatr Nephrol* 2009

Conservative methods to optimize growth velocity post-Tx

Causes of growth impairment	Methods
Reduced GFR	Prevention and management of chronic allograft nephropathy
	Treatment of acute rejection episodes
	Drug compliance
Steroid therapy	Daily low or alternate day steroid therapy
	Steroid avoidance/withdrawal under evaluation
Bone disease	Target PTH within normal range in CKD stage 2–3 and < 2× upper limit in CKD stage 4
	Target plasma phosphate within age-appropriate normal range
Metabolic acidosis	Target plasma bicarbonate > 22 mmol/L
Malnutrition	Adequate nutritional intake
Comorbidities	Assessment and control of comorbidities which may impair growth (chronic inflammation, liver, lung or heart diseases)

Harambat *Pediatr Nephrol* 2009

Thank you for your attention!