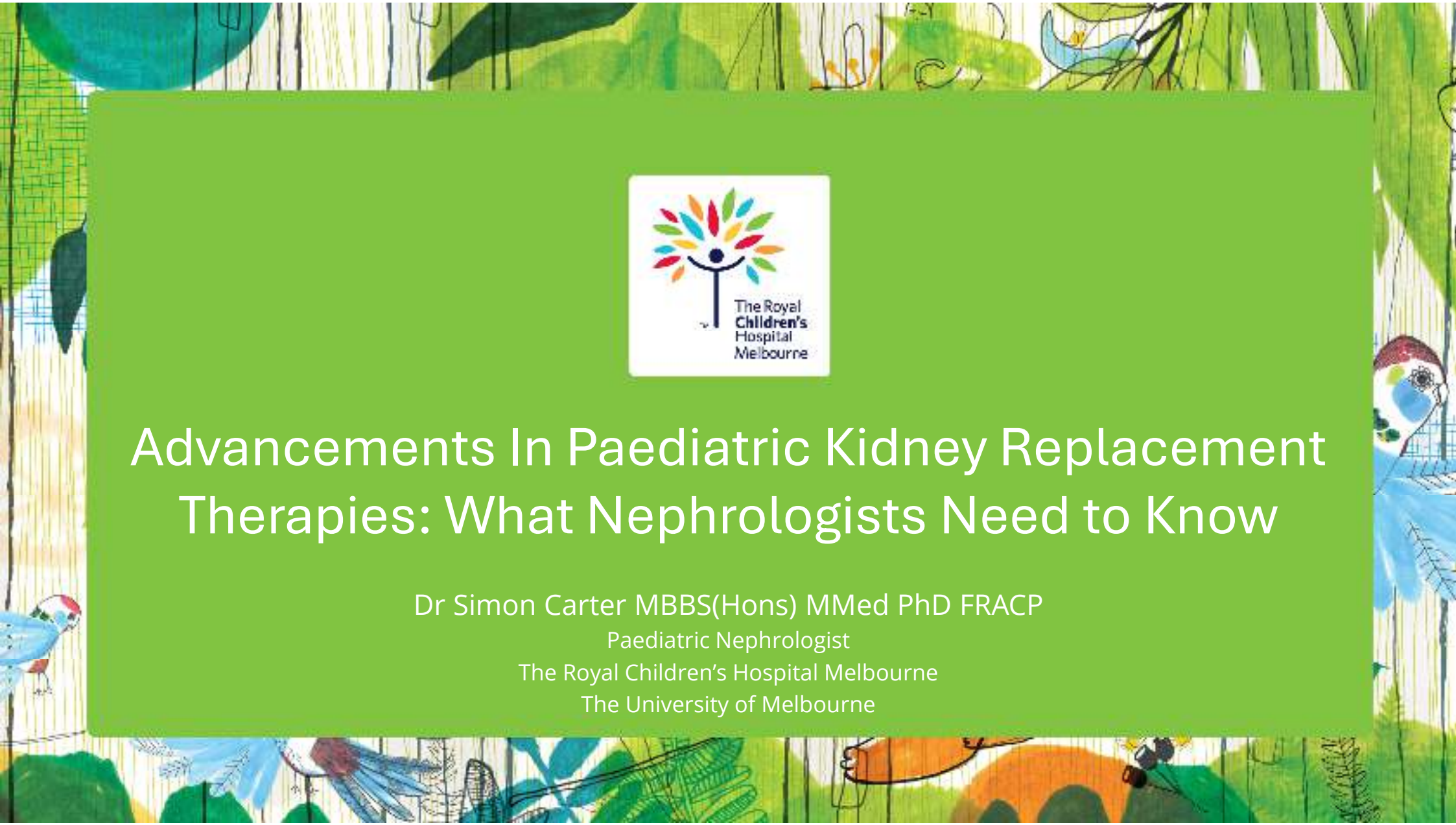
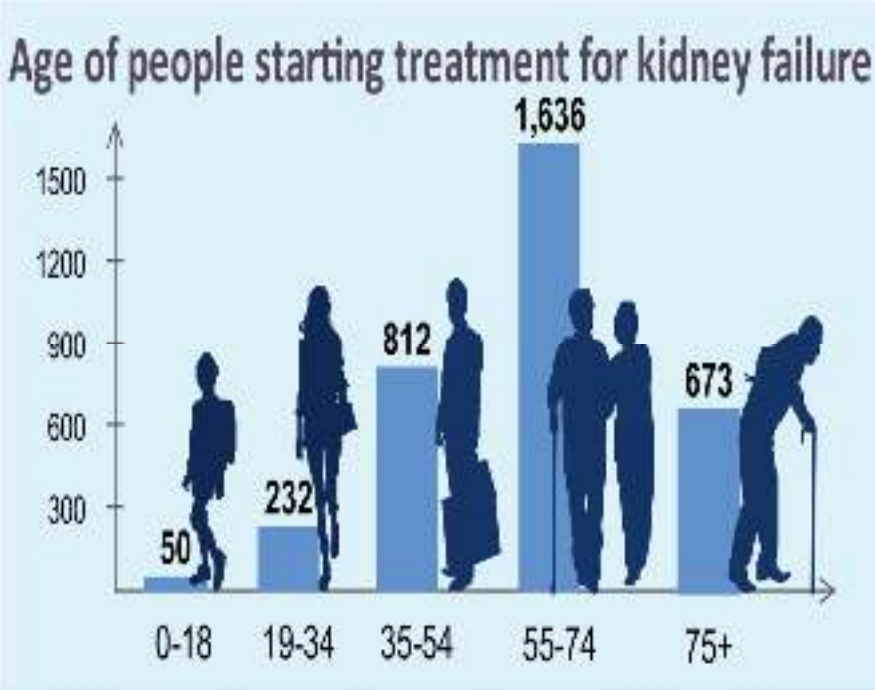
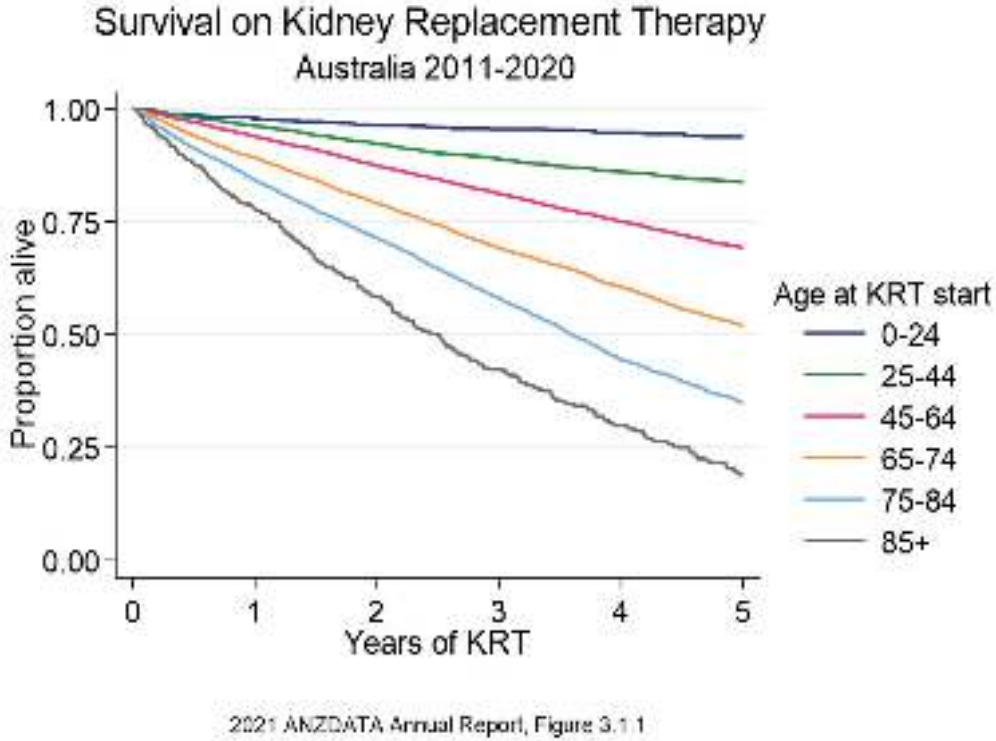


Advancements In Paediatric Kidney Replacement Therapies: What Nephrologists Need to Know

Dr Simon Carter MBBS(Hons) MMed PhD FRACP
Paediatric Nephrologist
The Royal Children's Hospital Melbourne
The University of Melbourne

Young people with kidney failure have good survival

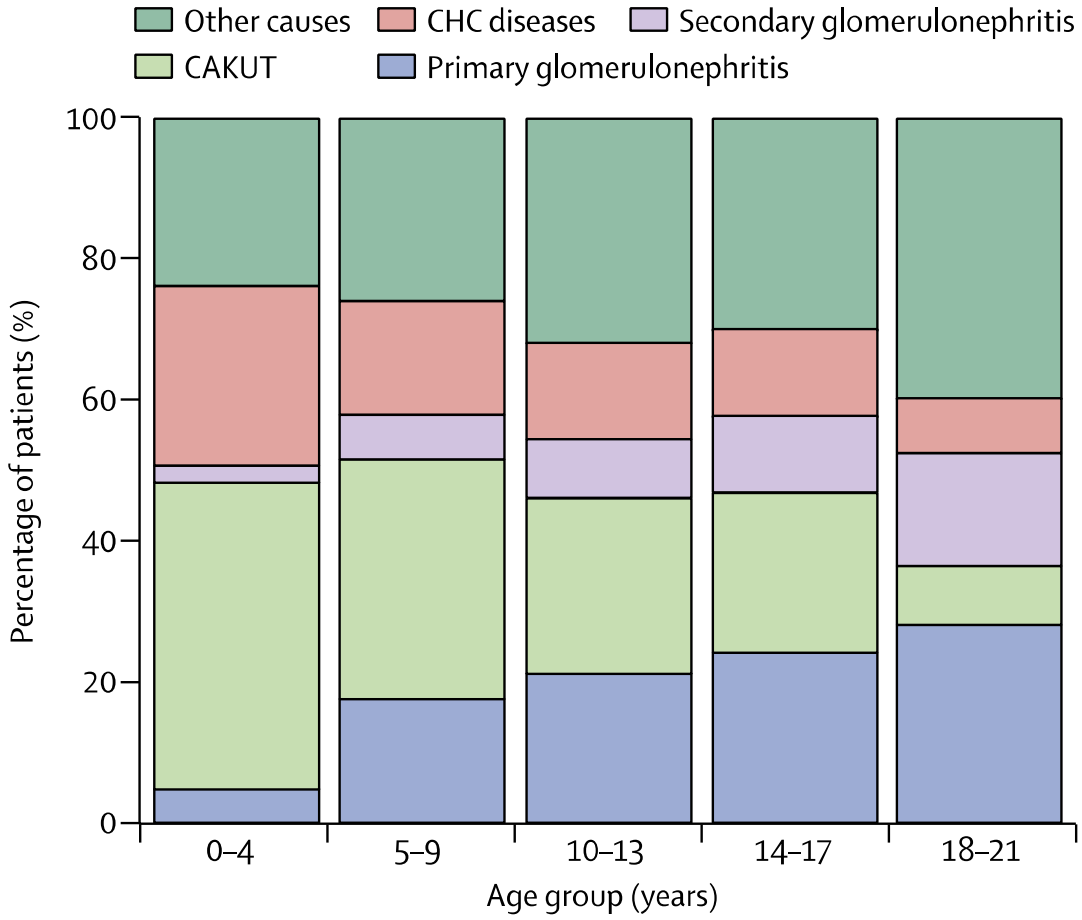




2021 ANZDATA Annual Report, Figure 3.1.1

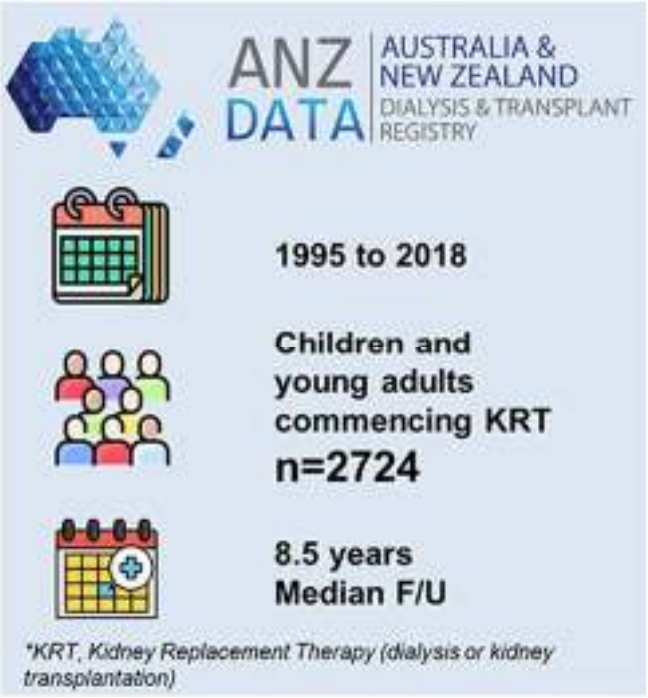
H McCarthy, C Davies, E Au, S Bateman, J Chen, K Hurst, G Irish, D Lee, S McDonald, W Mulley, M Roberts, T Sun, P Clayton. 46th Report, Chapter 12: Paediatric Patients with Kidney Failure Requiring Kidney Replacement Therapy. Australia and New Zealand Dialysis and Transplant Registry, Adelaide, Australia. 2023

Congenital (non-oliguric) causes are the largest group



Rees Lancet Child Adolesc Health 2017

Starting KRT?
Earlier is not necessarily better



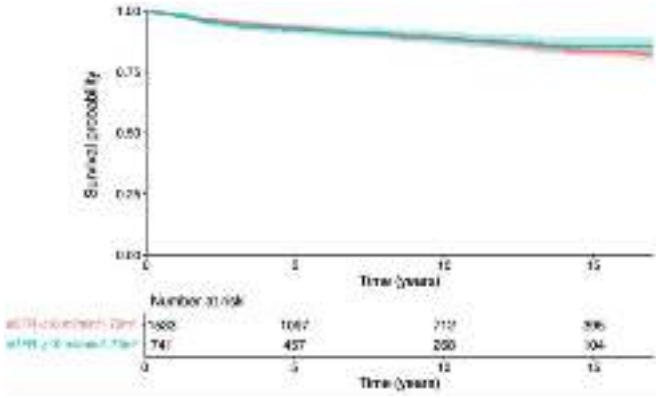
N=2354

Mean creatinine 707 µmol/l (513-999)

Mean eGFR 8 mL/min/1.73m^2 (6-11)

Median eGFR 9→11 between (10-12 months earlier start)

No change in mortality

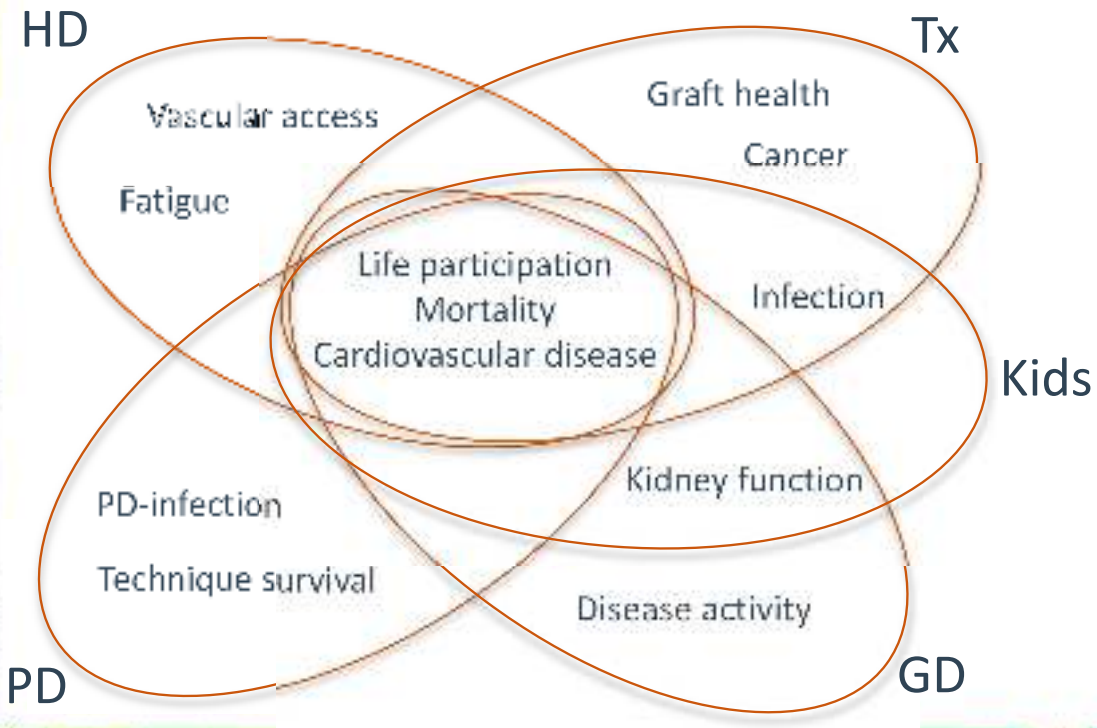


Cooper NEJM 2010 Larkins CJASN 2023 Winnicki J Am Soc Nephrol 2019

Balancing current and future outcomes

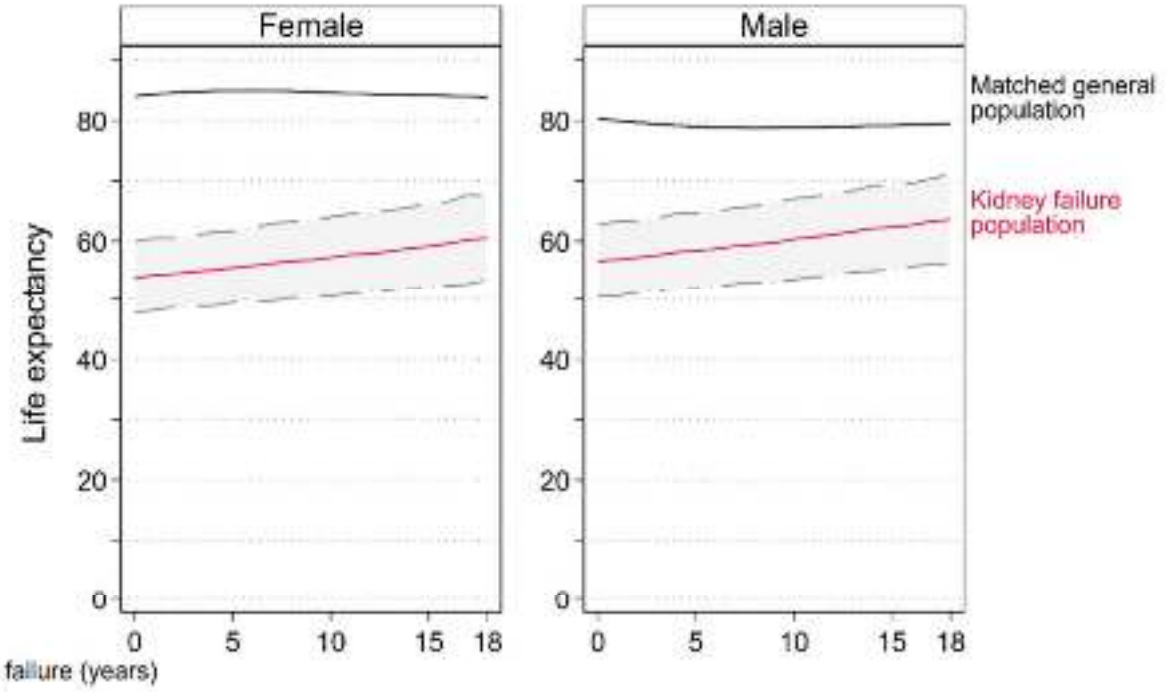
The SONG Initiative

To establish core outcomes for research across CKD



Hanson et al Kidney Int 2020

Life course in children with kidney failure



	Female					Male				
Dialysis (years)	20	20	21	21	22	22	23	23	24	24
Transplant (years)	35	31	27	24	22	36	32	28	25	23
Total years remaining	55	51	48	45	44	58	55	51	49	47

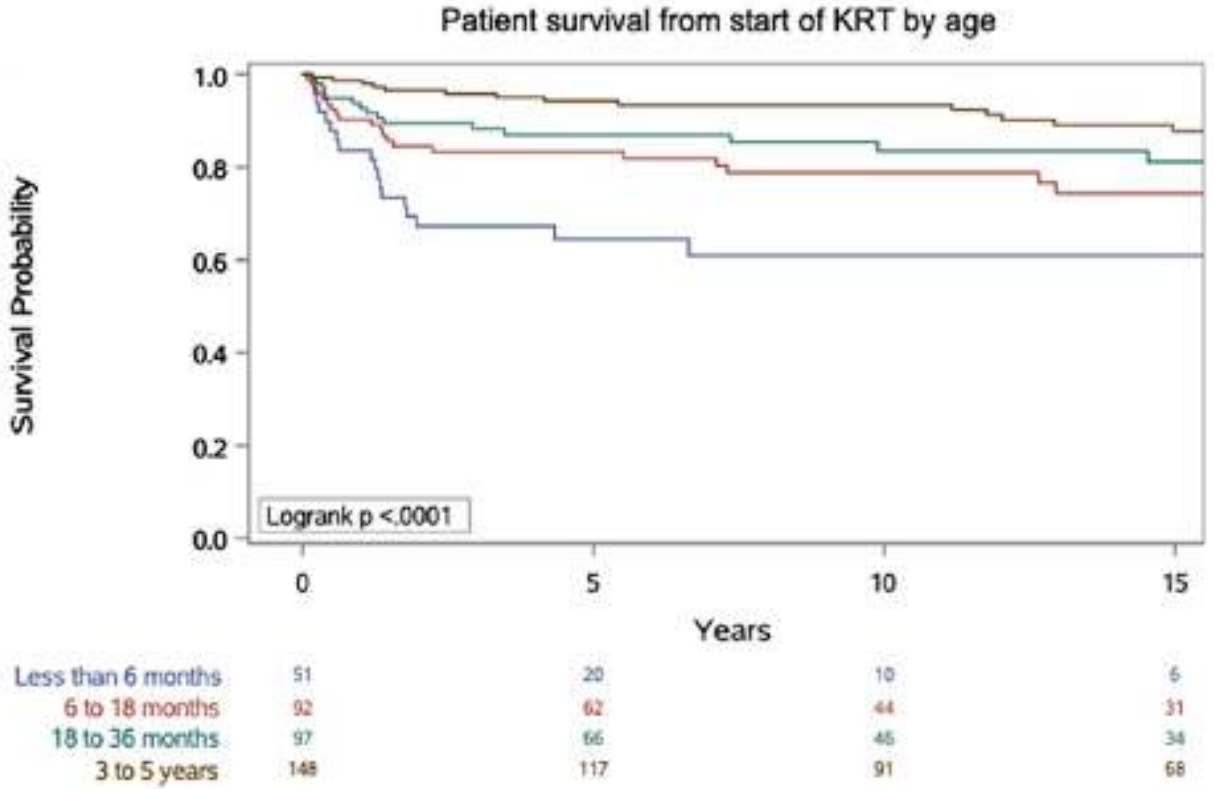
Wyld JASN 2023

Dialysis trends in pre-schoolers

	<6 mo	6-18 mo	18-36 mo	3-5 years
	N=51	N=91	N=97	N=149
Male sex	65%	74%	66%	57%
Weight (kg)	5.1	8.2	11.2	15.6
Diagnosis				
CAKUT	**57%**	50%	46%	45%
Cystic	10%	11%	10%	7%
Glomerular	8%	12%	13%	24%
Other	26%	26%	30%	24%
Initial therapy				
PD	**92%**	80%	70%	64%
HD	8%	17%	16%	17%
Transplant	-	2%	14%	19%

Larkins Ped Neph 2021

Survival decreases by age at KRT start



Larkins Paed Neph 2021

Neonatal dialysis is not extraordinary

- 63 – 86% neonates alive at 2-3 years
- Shifting landscape
- Who should we dialyse → who shouldn't

"chances of survival are now excellent, and RRT should be offered to all infants unless major extra-renal comorbidities are present"

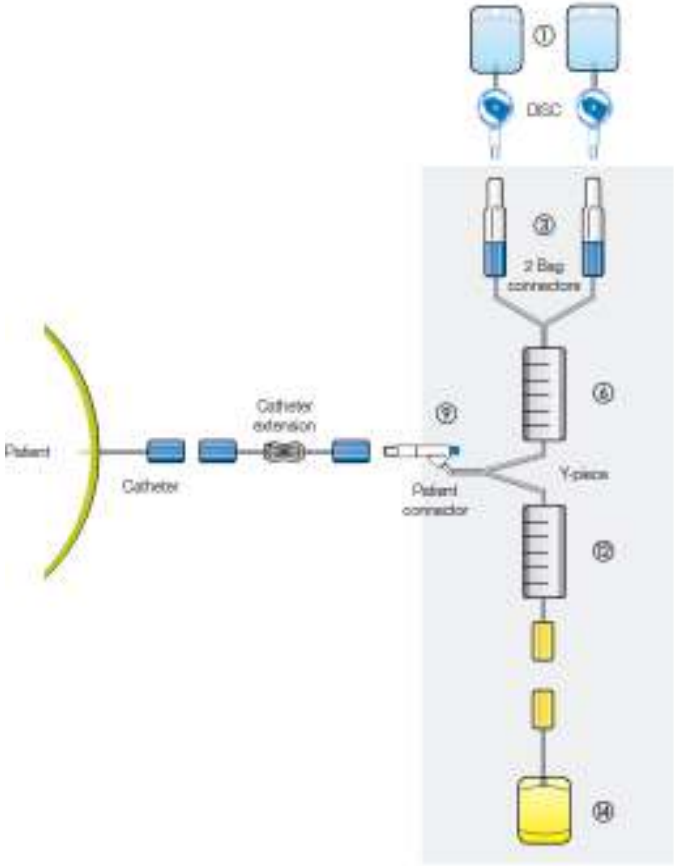
Sanderson J Peds 2021

Van Stralen NDT 2014

Wightman CJASN 2016

Neonatal PD prescription

- **Three manual systems (buretrol / scales)**
  - Fresenius PD-Paed system
  - Baxter system
  - Dialy-Nate system (Utah Medical products)
- **Automated (FV>100mL)**
- **Initial fill volumes 10-20ml/kg → 800-1400ml/m2**
- **Cycle duration 60-90 minutes**
  - for every hour longer dwell time 34ml less UF
- **May require salt supplementation**
  - unrecognized hypotension → anterior ischaemic optic neuropathy
  - NIPD can remove ~80mmol Na+/L dialysate - supplement with 2-5mmol/k/d NaCl



Nourse PDI 2021

Di Zazzo PD 2015; Akarkach AJKD 2020

Schaefer – IPPN 2019 (manuscript in process)

“Dialysis is easy… having two babies is challenging”

“Dialysis was never a problem”

Slide with thanks to A/Prof C Quinlan

Key aspects

Antenatal consult

Early contact
Early investigation

Early fluid management

Ethical challenges

Dëdicäted multi-disciplinary team

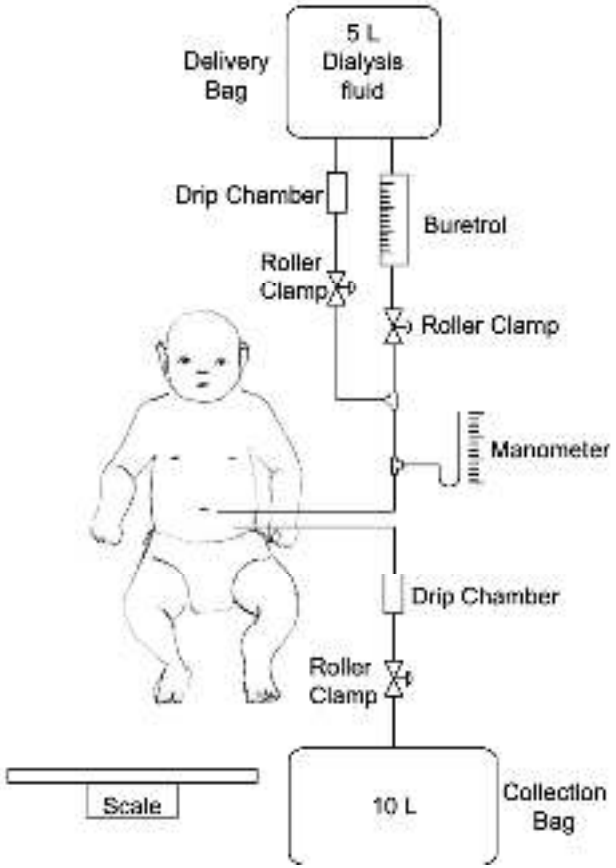
Which babies should we not dialyse?

- Semi-urgent medical assessment inc genetics
- Zone of parental discretion
- ‘Transplantability’ not necessarily a reason not to dialyze
- ‘Relational potential'
- Evolve our language around these discussions
- Challenge assumptions: resources, rurality, intellectual disability

Van Amstel AJKD 2021

Continuous flow PD

- **Randomized cross-over trial**
- **n=15 children**
  - Age 0.2-35 months, weight 2.3-14kg
  - 8 post cardiac surgery, rest shocked due to sepsis, HUS, gastro
- **1:1 PD/CFPD**
- **2x 8.5Fr Cook PD catheters**
- **IAP <15cmH20**
- **Inflow 50-100mL/min/1.73m2**
  - outflow 52.5ml/min/1.73m2
- **Outcomes:**
  - feasibility, UF, clearance



Nourse P *Perit Dial Int* 2021

Continuous flow PD

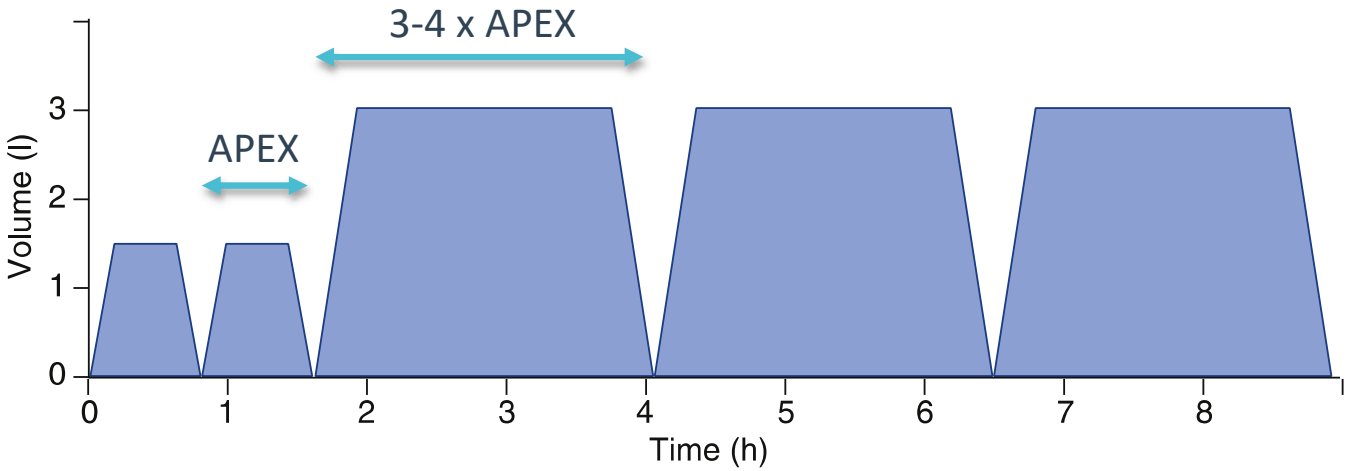
- **UF: 1.05 vs 4.1 mL/k/hr mean difference: 3.05 (2.6-9.2 fold increase)**
- **Clearance:**
  - urea mean difference 5.58ml/min/1.73m2; creatinine 4.33
  - Middle molecules ~2x conventional PD clearance
- **Complications**
  - usual PD complications, *raised IAP*
- **Use 6x as much fluid; two-fold higher protein loss**

- **Indications: poor tolerance of high fill volumes**

Raina *et al* Adv Chronic Kidney Dis 2021

Nourse Ped Neph 2023

Adapted peritoneal dialysis



The concept of adapted APD small/short exchange followed by large/long exchange to optimize dialytic sodium removal

Exchange favoring UF

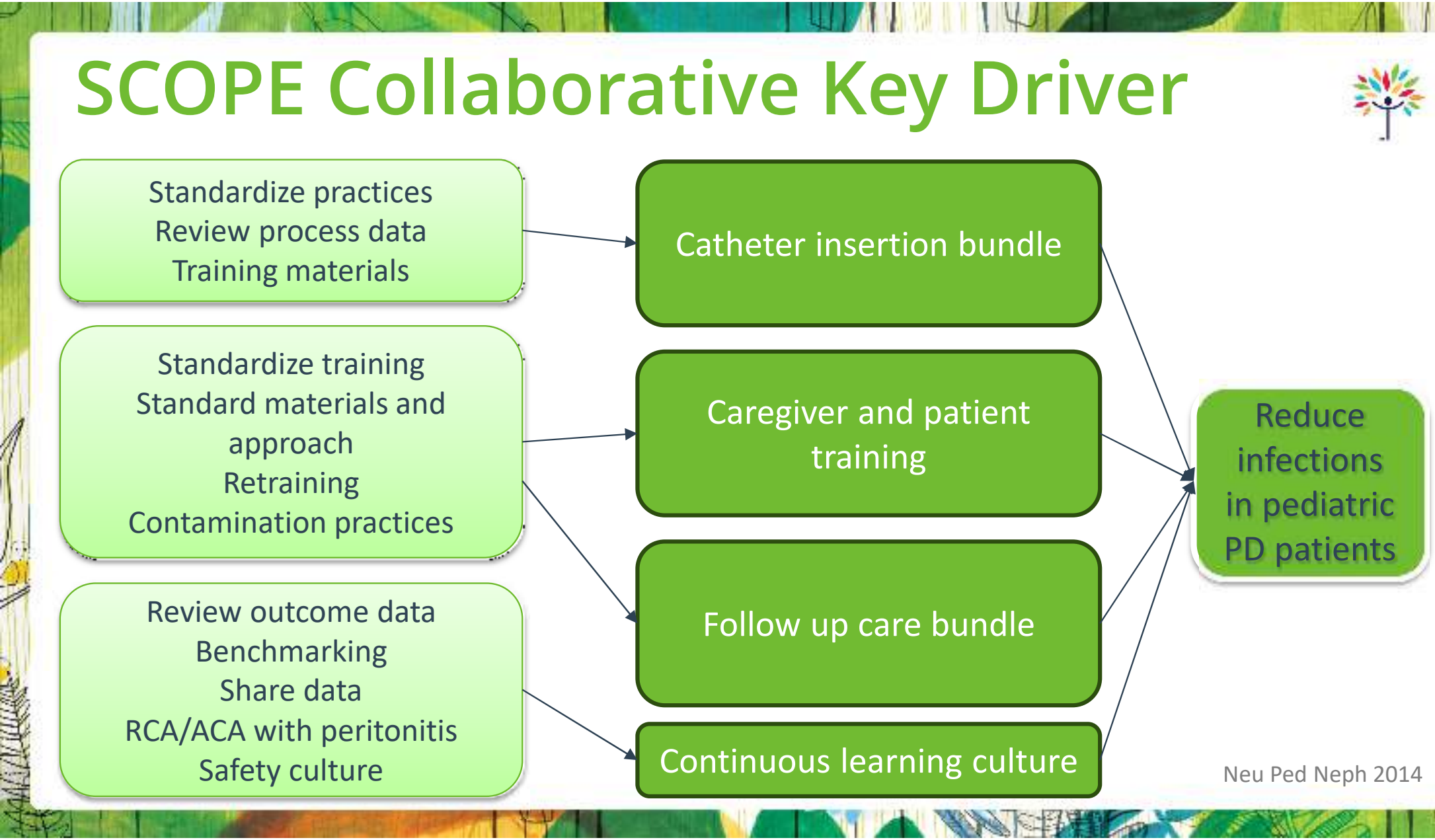
Short/small cycle
(Free water transfer via AQP-1)
- Hemoconcentration
- Incomplete drainage (low IPP)
- Low NaD

Exchange favoring dialytic Na removal

Long/large cycle
(Small pore recruitment)
- Na-coupled water transport
- Long diffusion time
- High diffusion gradient (NaPl/NaD)

Fischbach KI 2016

SCOPE Collaborative Key Driver



Neu Ped Neph 2014

Standardising training in paediatric PD

SCOPE

- 2168 pts
- Median 8 sessions; total 21.5hrs
- ISPD compliance (23%, all):
  - 1:1 training 95%
  - Trained >10 days after 67%
  - Session time under 3hrs 52%
  - Home visit performed 74%

→no association with PDI

IPPN

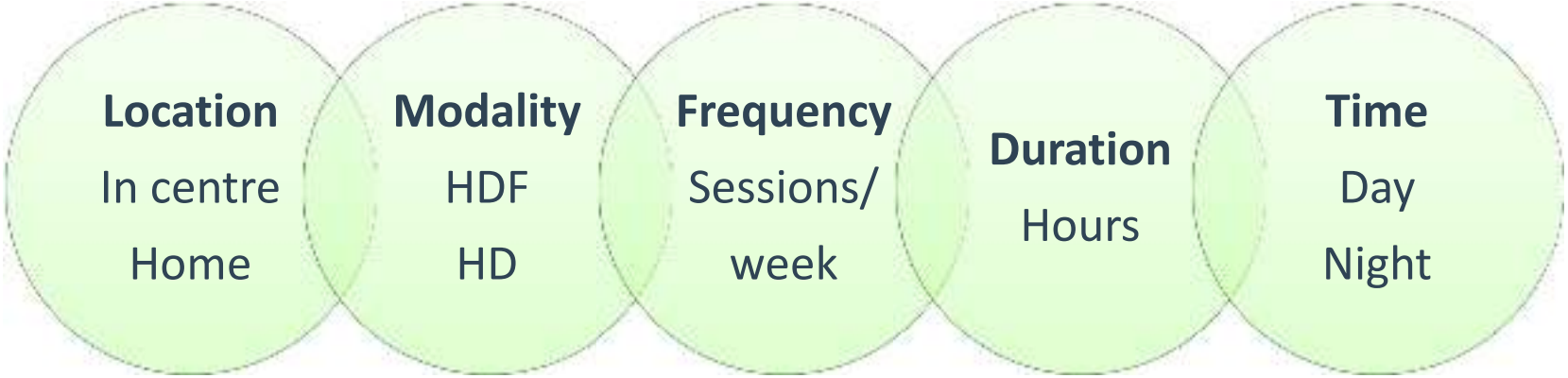
- 50 centres, 1033 pts
- Overall peritonitis rate 0.41
  - Higher rates with more infants on PD
  - Training time <20hrs
  - Lower GDP
  - Fewer training tools

Kamath Ped Neph 2023

Holloway PDI 2001

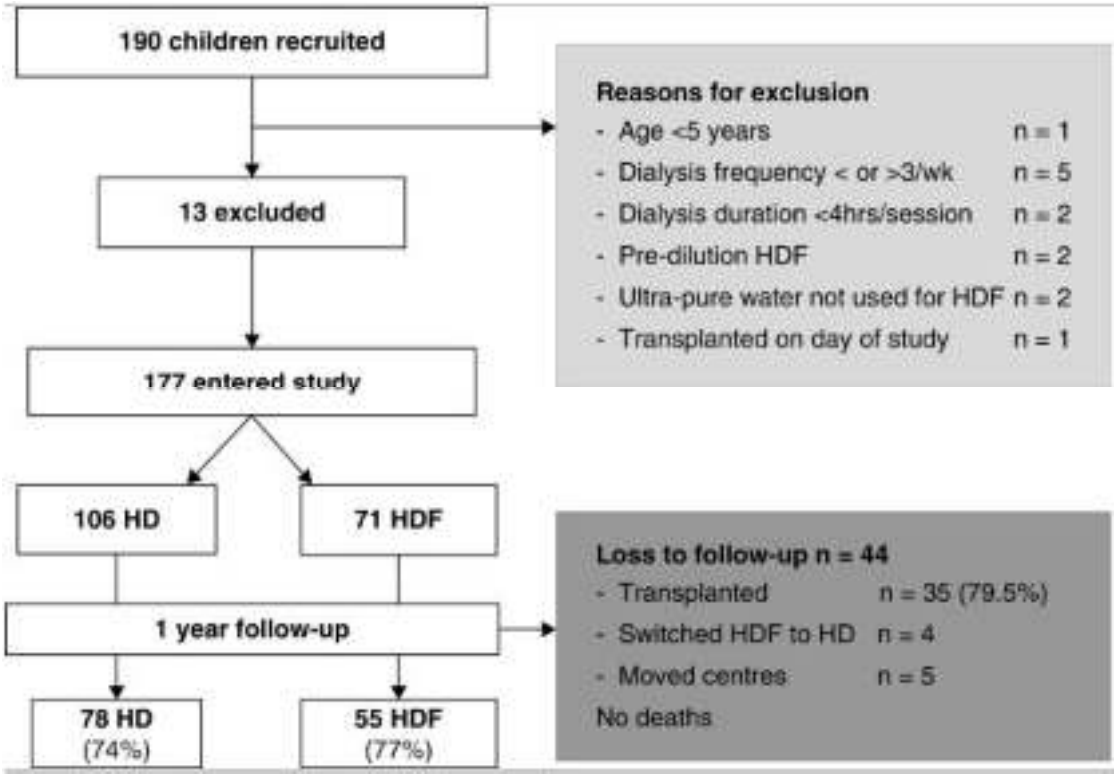
Begin Ped Neph 2023

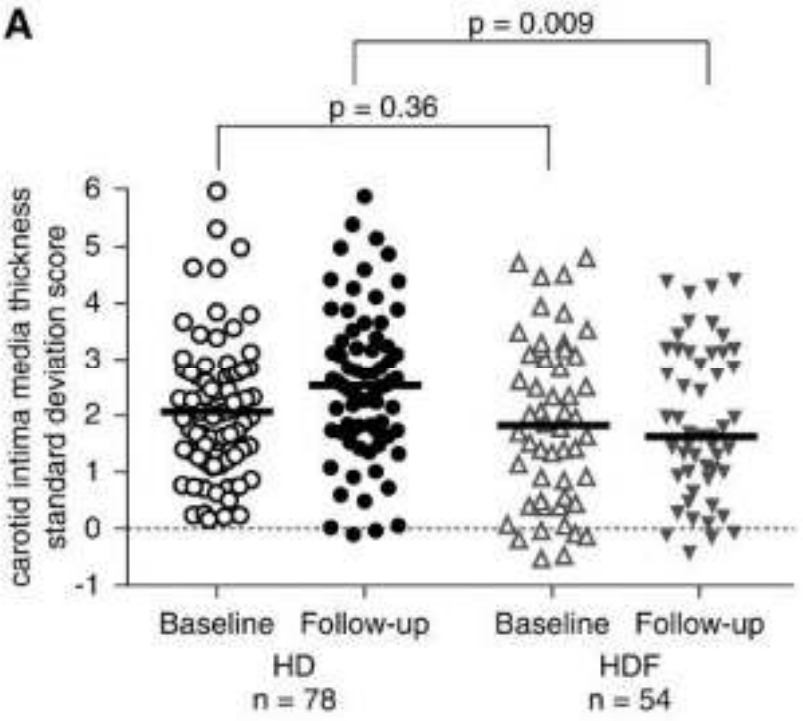
Intensification of dialysis (HD)



Thumfart Ped Neph 2018

The HDF, Heart and Heights

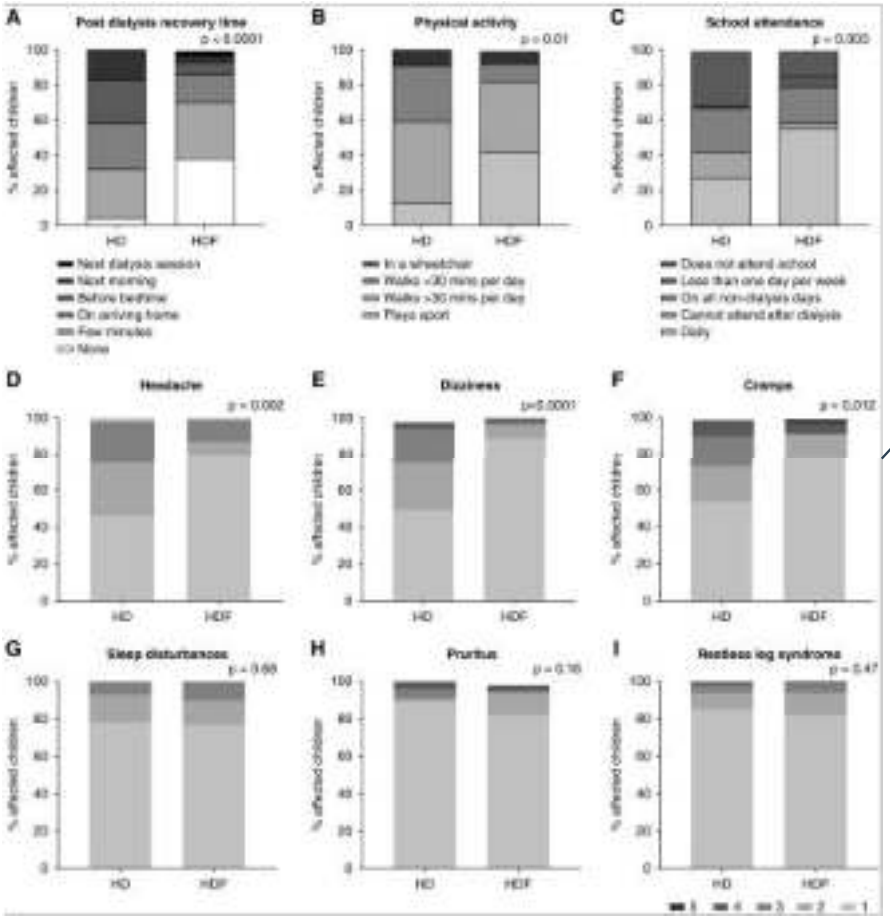




HD: +0.47 increase in cIMT (95%CI 0.07 – 0.87, p=0.02)

Shroff JASN 2019

Improved patient symptoms



24hr BP increased +0.65 SD vs static in HDF group

Residual RF at baseline	HD, n= 78	HDF, n=55
0	32 (41)	21 (38)
0-200	18 (23)	7 (13)
201-500	11 (14)	9 (16)
500+	17 (22)	18 (33)

Paglialonga J Ren Nutr 2023

Shroff JASN 2019

Infant HD poses unique challenges

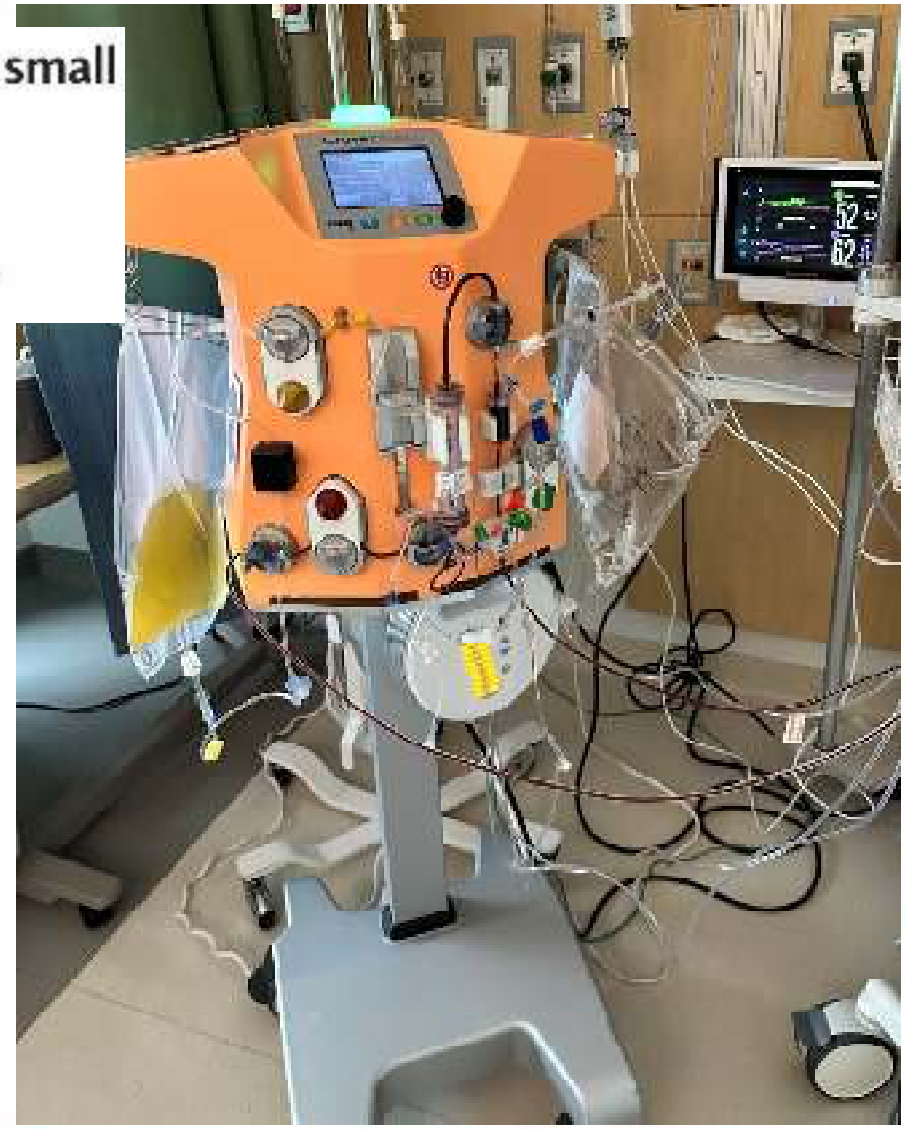
- Access
- Volume control – extracorporeal volume + UF (will tolerate up to 16ml/kg if no UF required
  - Theoretical minimal wt: Fres 5008 (15.6kg) 6008 (12kg), Baxter AK98 (6.6kg)
- Haemodynamic stability
- Anticoagulation: bleeding, citrate lock
- Temperature
- Resources, expertise and staffing

Ped Neph 2005; 20:1054-66

Continuous renal replacement therapy in neonates and small infants: development and first-in-human use of a miniaturised machine (CARPEDIEM)

Claudio Ronco, Francesco Garzotto, Alessandra Brendolan, Monica Zanella, Massimo Bellettato, Stefania Vedovato, Fabio Chiarenza, Zaccaria Ricci, Stuart L Goldstein

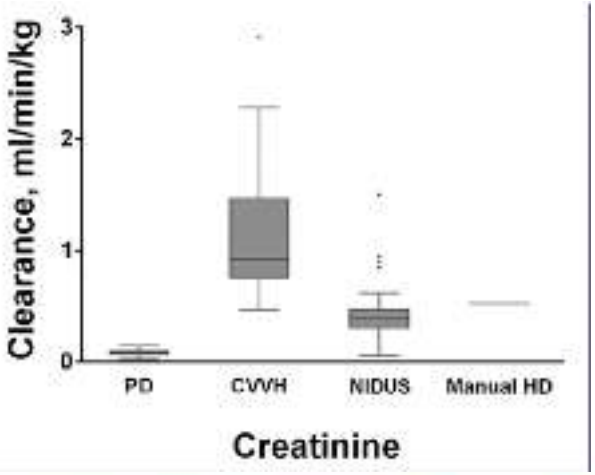
- Various modalities
  - pre- and post-dilution CVVH, PLEX, exchange transfusion, CVVHDF, SPAD
- Patient weight 2.5-10kg (>1.8 kg); 5Fr dual lumen
- Filter SA – 0.075, 0.15 and 0.25 sqm
- Extracorporeal volume 27, 33 or 42mL
- Blood flow rates 5-50 mL/min
- Small solute clearance 25-35mL/kg/hr
- Heparin or Citrate protocols
- Exceptionally sensitive UF/replacement scales +/- 1g
- Replace lines every 24 hours



Ronco Lancet 2014

Newcastle Infant Dialysis and Ultrafiltration System (NIDUS)

- Uncouples blood flow from dialysis 5-12.5ml aliquots
- Child weight 0.8-8kg
- Single lumen access 2.7Fr of CVL
- Neoflux1 0.045m2 circuit volume 9.5mL; ECV 9-17mL
- Heparin only
- Blood flow rates 20-45ml/min
- UF 0-60ml/hr
- 24 hr sessions
- More accurate than CRRT
  - 2.95 vs 18.75mL/hr



Lambert et al. PCCM 2023
Lambert et al. BMJ Open 2021

https://allmedgroup.com/innovation/

Equity in childhood KRT

- 80% paediatric KRT occurs in Europe, North America and Japan (18-100 pmarp)
- YLL 16-32 years: females lose >7 years, younger age
- Health spending: %GDP explains 67% of mortality variation
- Age-at-start correlates with GDP per capita
  - IPDN: children <3 yrs 8% low per capita GNI vs 27-33%

Wyld JASN 2023

Ploos van Amstel Am J kidney Dis 2021

Rees Lancet Child Adolesc Health 2017

The Royal
Children's
Hospital
Melbourne

NEOKID

Neonatal KIDNEY Collaborative Australia & New Zealand Chapter

Volume assessment

- **Bioimpedance spectroscopy**
  - Limited evidence <5 years
- **Circulating natriuretic peptide**
- **Lung ultrasound**
- **Inferior vena cava diameters**
- **Heavy water dilution studies**

Eng *et al.* Nephrol Dial Transplant 2018

Surgical considerations

- Omentectomy
- Nephrectomy in ARPKD?
- Gastrostomy?
- Colostomy

Burgmaier Sci Rep 2020; Liebau Ped Neph 2021; van Lieburg Ped Neph 2001; Hassinger Ped Neph, 2013

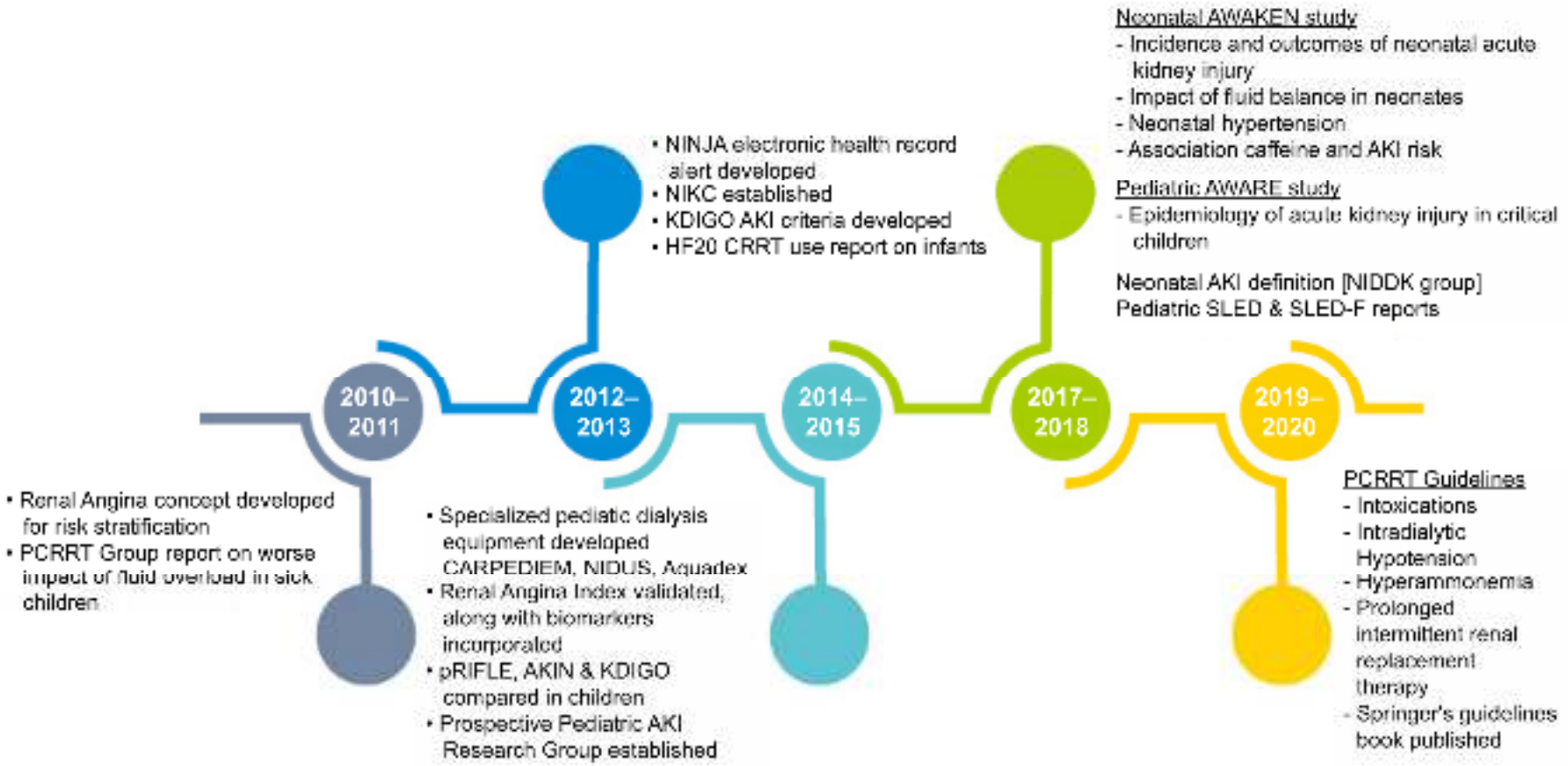
Rasmussen Ped Surg 2022

PD in premature neonates

- 101 babies reported (1982-2022)
- Mean 26+8 weeks
- 640 – 1005g
- Variety of tubing used
- Mean of 3 days on PD
- Mortality 58%
- Recovery renal function 45%

Burgmaier PDI 2020 Stojanovic PDI 2017 Bellos PDI 2021

Landmark studies in paediatric AKI



Sethi Kidney Res Clin Pract 2021

PD in acute kidney injury?

PD post cardiac surgery

- Early time to negative FB
- Shorter time on mechanical ventilation
- Lower inotrope requirements
- Fewer electrolyte imbalances
- Improved mortality: decrease of 47% (30 days) 44% (90 days)
- Low complication rate

PD post STEC-HUS

- 389 Argentinian children
- 37 centres 2015-2019
- Mean age 2.7 years
- 8 days PD
- Catheter malfunction 93 (24%)
- Peritonitis 75 (19%)**
- Leak 45 (11%)
- Bleeding 23 (6%)
- Discontinuation 3.8%

Coccia Ped Neph 2021

For larger infants, greater UF:

Aquadex Flex Flow Machine

- CVVHF weight >20kg (<20kg off label)
- ECV 33mL
- SA 0.12m2
- BFR 10-40ml/min
- UFR 500ml/hr
- Circuit life 72 hours

Prismaflex HF20 filter set (Gambro)

- >8kg (FDA) – 2.3-5.4kg off label
- Dual lumen 6.5Fr catheter
- ECV 60mL
- SA 0.2m2
- BFR 20-100ml/min
- UFR 540-1440 ml/hr
- Circuit life 56+/- 32hr

Raina *et al* Adv Chronic Kidney Dis 2021