What's new in paediatric HD – a review of the recent literature

Rukshana Shroff

Great Ormond Street Hospital for Children
and Institute of Child Health
London, UK

Great Ormond Street Hospital

UCL

Outline

1. Vascular access

2. Intensified dialysis treatments

- Daily / nocturnal home HD
- HDF

Vascular Access – the Achille's heal of HD

AJN
American Journal
of Nephrology

**Patient-Oriented, Translational Research:
Research Article**

Am J Nephrol
DOI: 10.1159/000516212

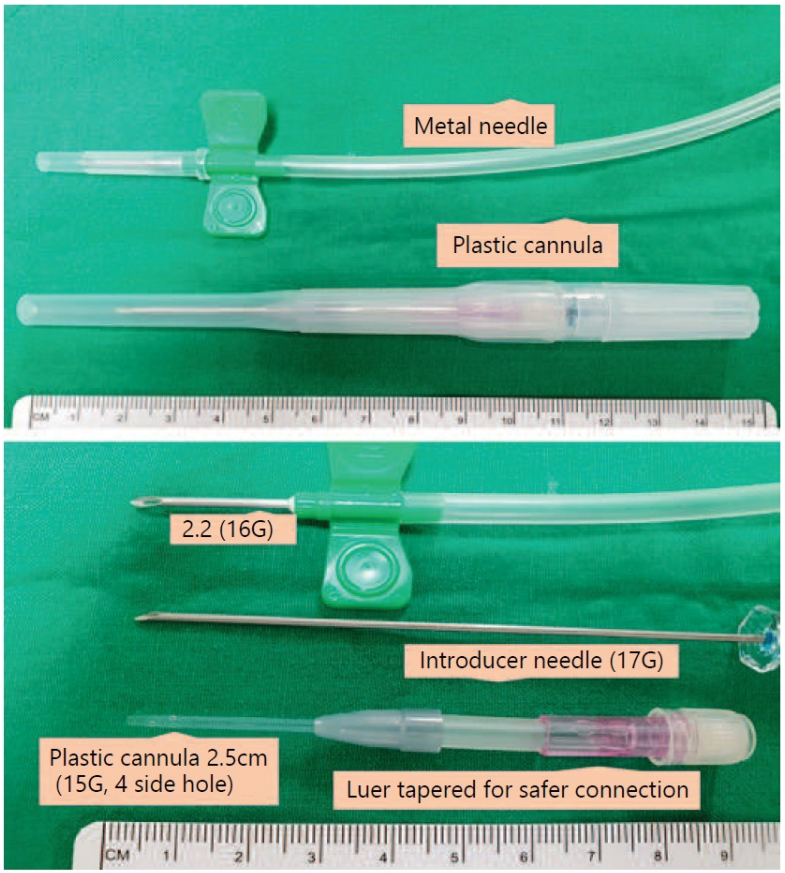
Received: January 20, 2021
Accepted: March 23, 2021
Published online: June 10, 2021

Efficacy and Safety of Plastic Cannulae Compared with Metal Needles in the Initial Use of an Arteriovenous Fistulae in Incident Hemodialysis Patients: A Randomized Controlled Study

Yong Seon Choi Hyung Seok Lee Narae Joo Pyoungju Park
Seung Nam Cho In Ju Youn Young Rim Song Sung Gyun Kim Jwa-Kyung Kim

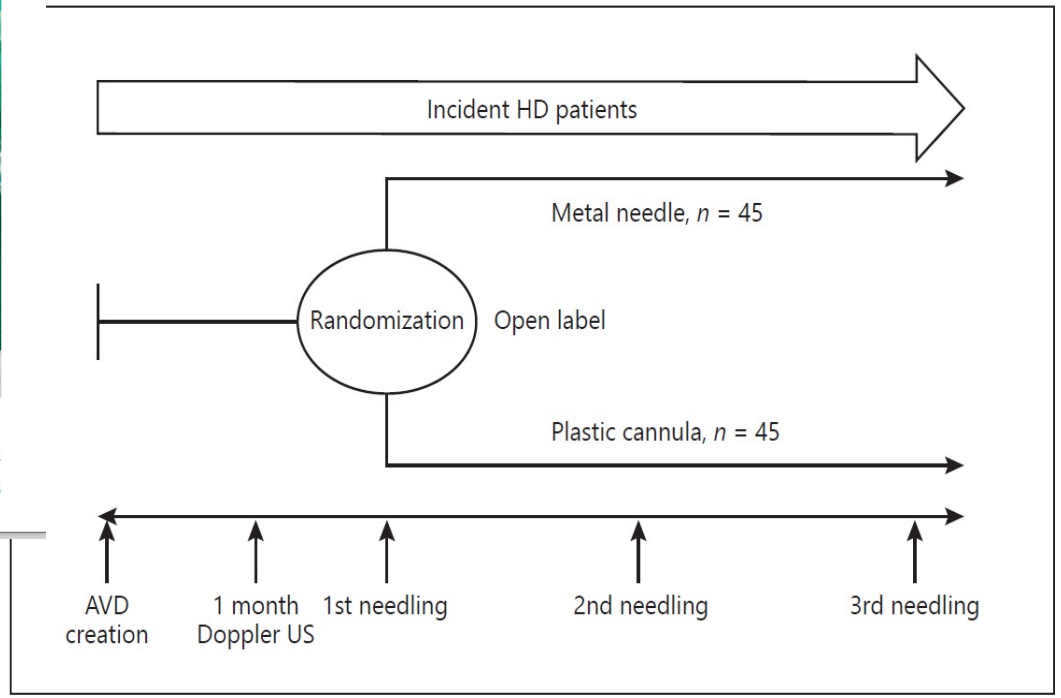
Kidney Research Institute & Department of Internal Medicine, Hallym University Sacred Heart Hospital, Anyang, South Korea

Randomised, open-label study of incident HD patients
N = 45 per arm
Metal needle vs plastic cannula
Primary end-point - initial cannulation failure rate, defined as the failure to successfully complete 3 consecutive dialysis sessions



Color version available online

Fig. 2. Comparison between a metal needle and a plastic cannula (top) and metal needle and plastic cannula (bottom) Comparisons of size and length.



Plastic cannulae improve cannulation success rate

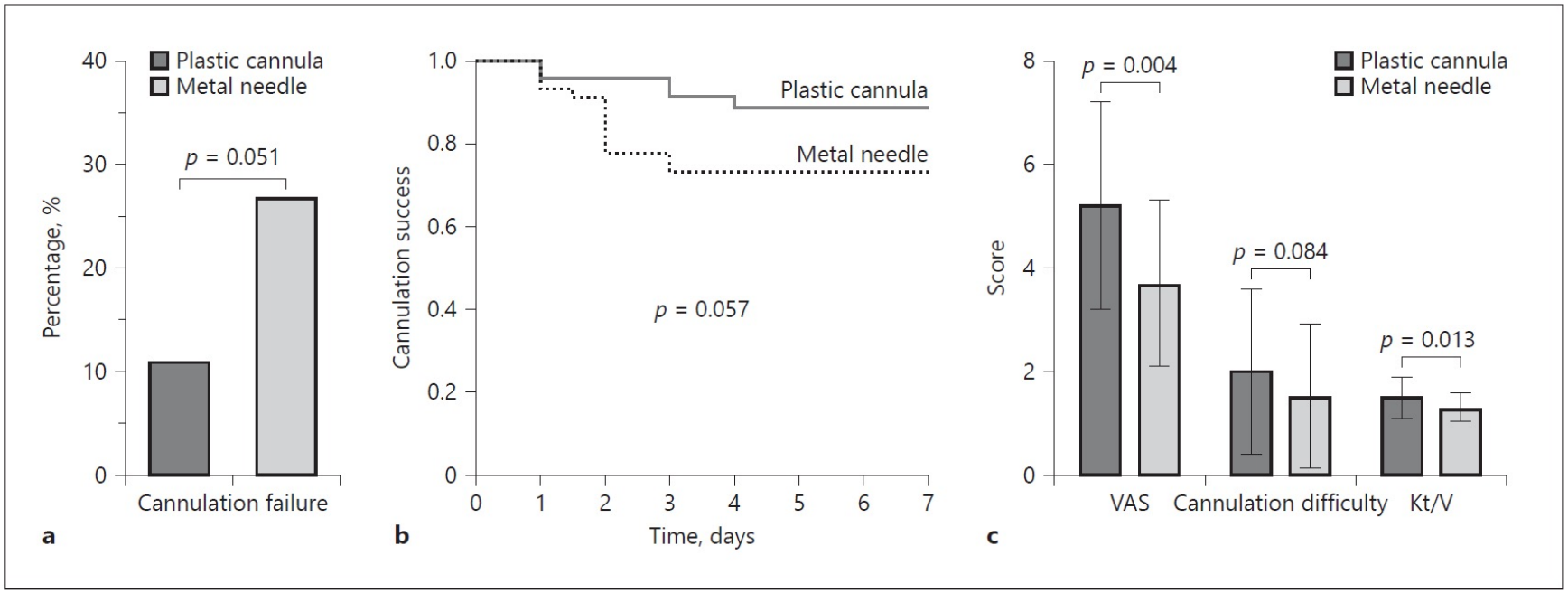
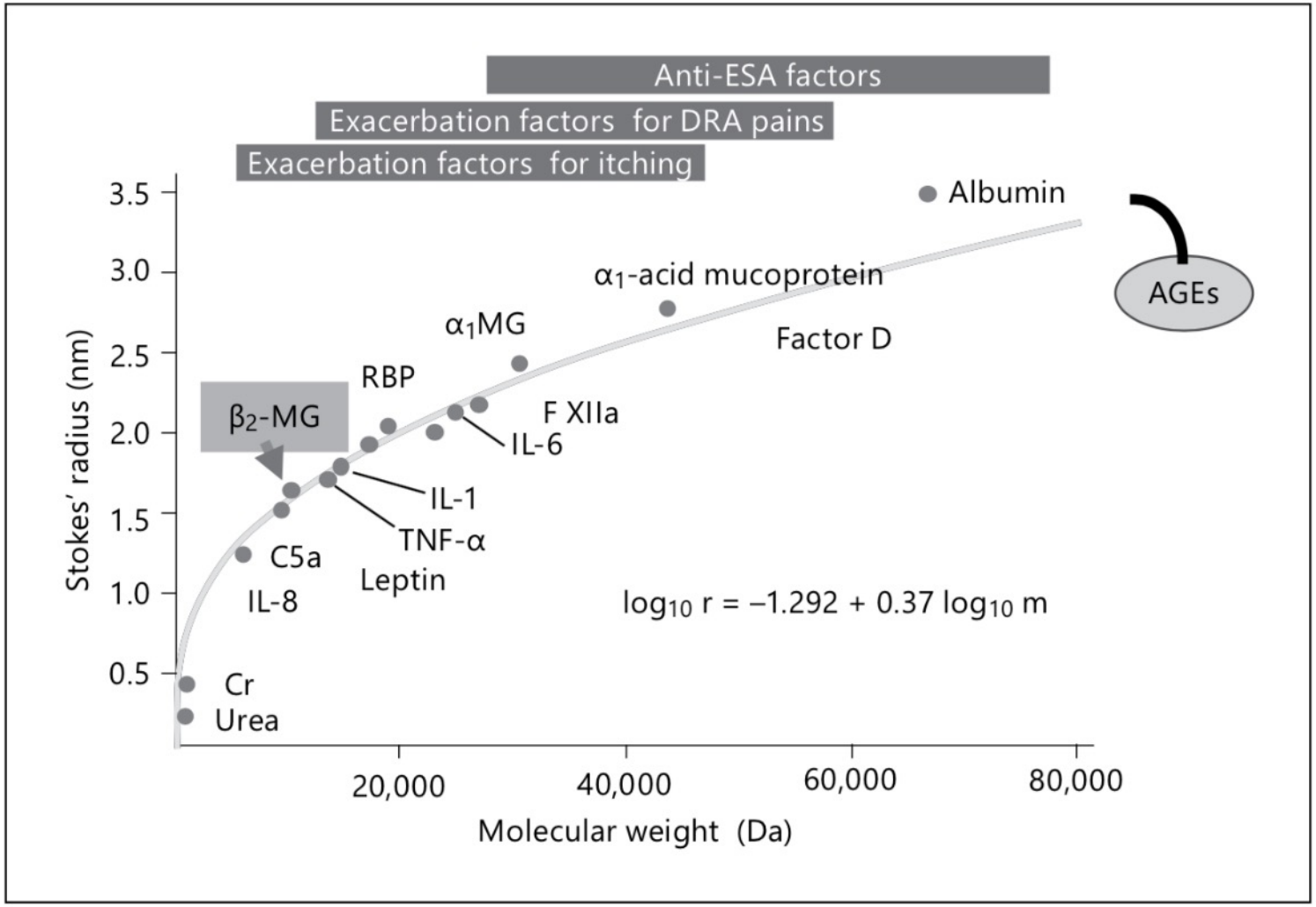


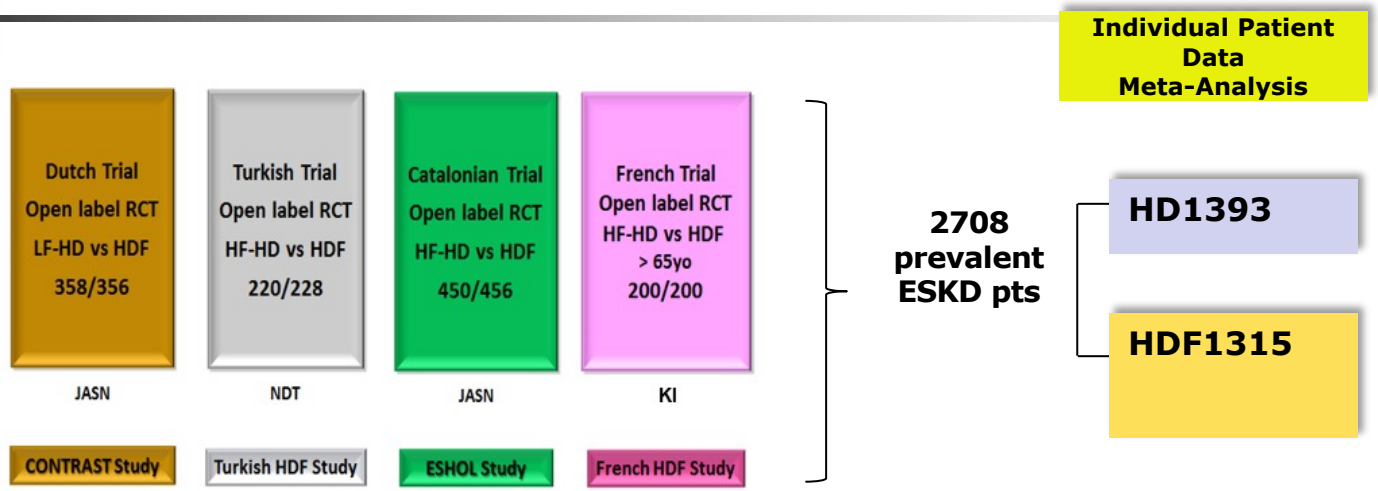
Fig. 3. Outcomes. **a–c** Metal needles had a higher initial cannulation failure rate regardless of AVF location than plastic cannulae (**a**, **b**). The patients' pain score, nursing staff cannulation difficulty score, and HD adequacy (Kt/V) were also compared (**c**). AVF, arteriovenous fistula; HD, hemodialysis.

Solute Clearences on HD vs HDF



Kawanishi H, Takemoto Y (eds): Scientific Aspects of Dialysis Therapy: JSDT/ISBP Anniversary Edition. Contrib Nephrol. Basel, Karger, 2017, vol 189, pp 17–23 (DOI: 10.1159/000450635)

HDF European Pooling Project
Four Randomized Clinical Trials



mode	HD	OI-HDF	OI-HDF	OI-HDF
OI-HDF dose		Lowest	Middle	Highest
Convection volume (l)	NA	18.0 (16.0–18.8)	21.0 (20.2–22.0)	25.7 (24.4–27.4)
Number	1393	433	447	435
Body surface area (m^2)	1.77 (0.22)	1.72 (0.23)	1.77 (0.20)	1.80 (0.20)
BMI post dialysis (kg/m^2)	25.2 (4.6)	24.7 (5.0)	24.9 (4.6)	25.8 (4.8)
Weight (kg)	68.7 (15.4)	66.2 (14.6)	68.9 (13.7)	71.5 (14.5)
Total body water (l)	35.1 (6.5)	34.6 (6.7)	35.3 (6.2)	35.0 (6.2)

Pooled individual patient analysis of four prospective trials compared thirds of delivered convection volume with hemodialysis. Convection volumes were either not standardized or standardized to weight, body mass index, body surface area, and total body water. Data were analyzed by multivariable Cox proportional hazards modeling from 2793 patients.

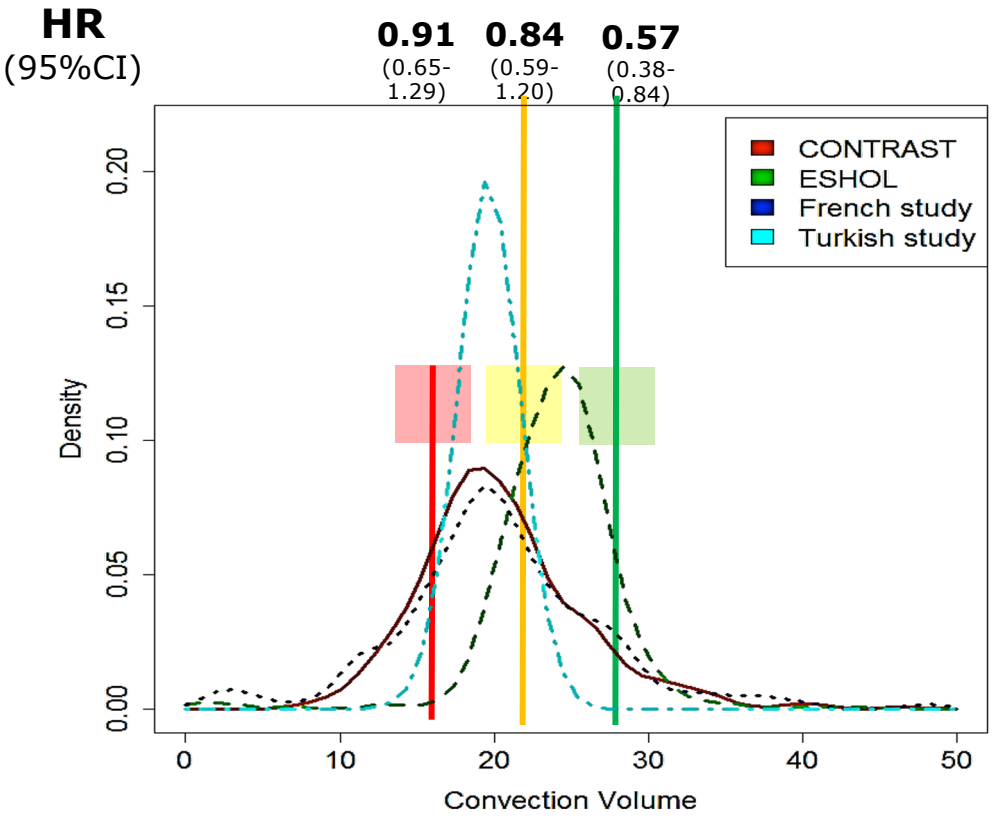
EUDIAL

Peters SAE et al, *Nephrol Dial Transplant* 2016;31(6):978-84.

Convective Dose predicts CV Mortality

Total Ultrafiltered Volume Distribution Per Study

EuDial Pooling Project



Peters SA et al, HDF Pooling Project Investigators. *Nephrol Dial Transplant.* 2015

The effects of HDF vs conventional HD on growth and cardiovascular markers in children - 3H (HDF, Hearts and Height) study*

Hypothesis

Children on HDF compared with HD have improved:

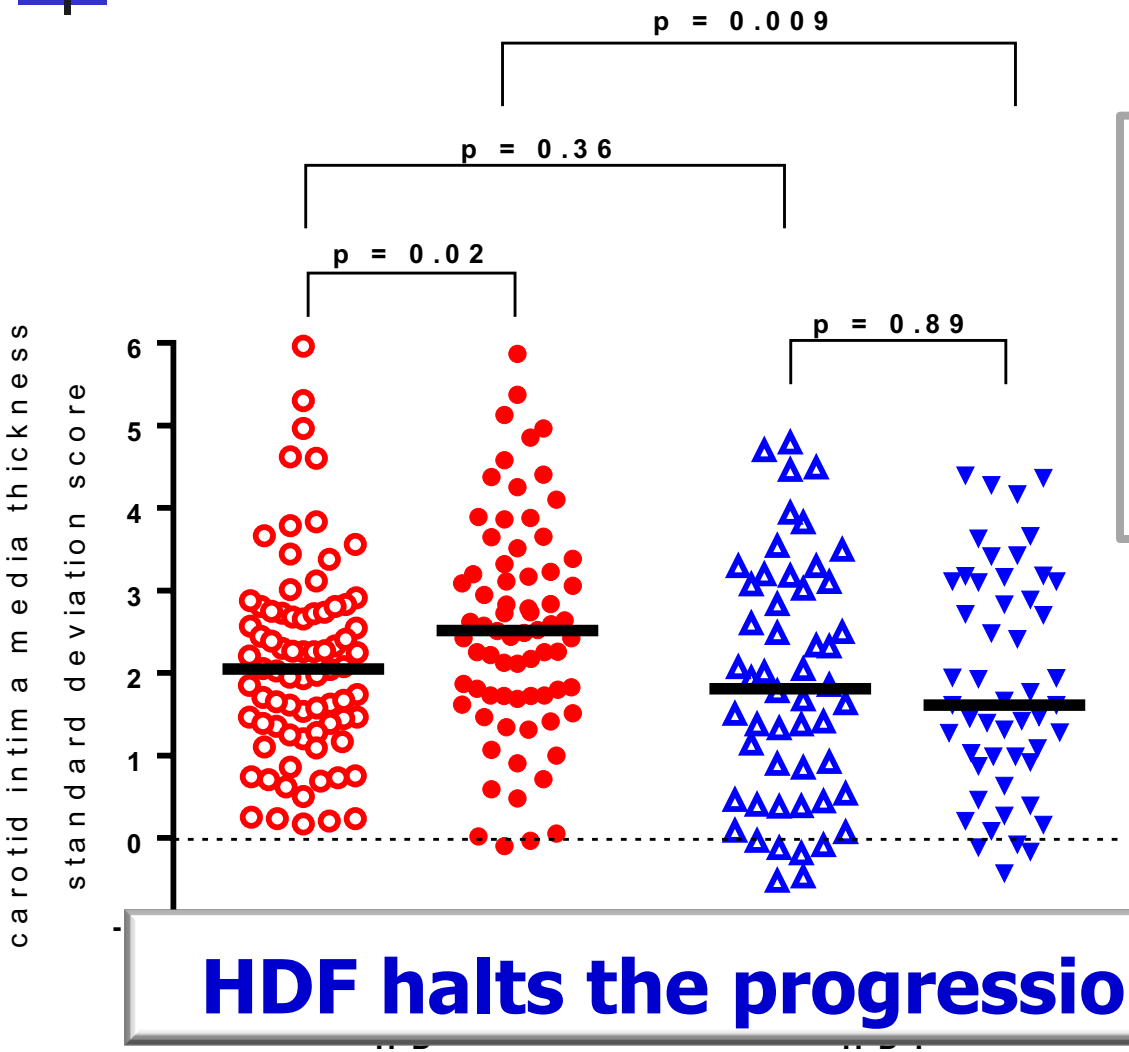
- Cardiovascular risk profile
- Growth and nutritional status
- Quality of life

Effects of HDF on:

- cardiovascular outcomes
- BP control
- bone disease
- growth and nutrition
- health related quality of life measures

Agbas et al; PLoS one 2018
Shroff et al; BMC Neph 2018
Shroff et al; JASN 2019
De Zan et al; Ped Nephrol 2021
Fischer et al; Kidney Int Reports 2021
Paglialonga et al; ESPN 2021

cIMT SDS at baseline and 1-year



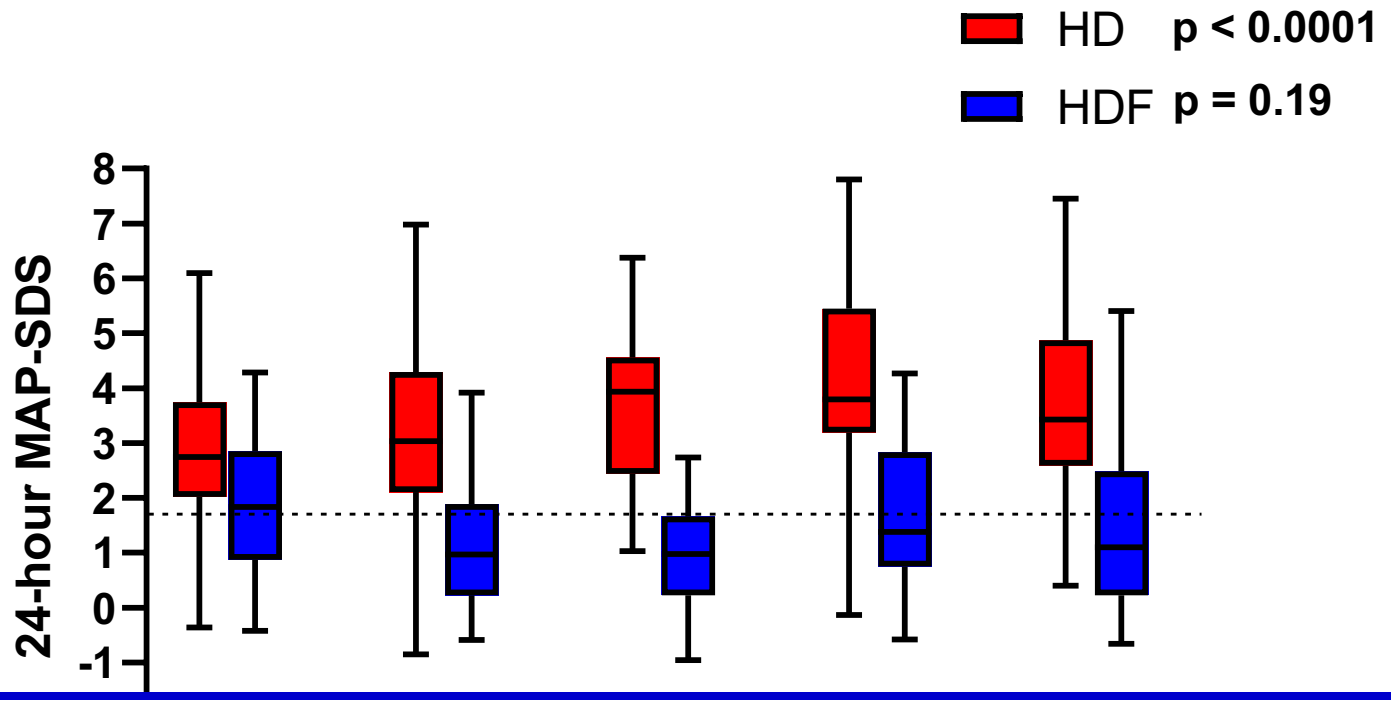
Predictors of higher cIMT-SDS at 12-months

- HD group
- Higher IDWG% and UF rate
- Higher systolic BP
- higher β2-microglobulin

HDF halts the progression of cIMT

Shroff et al; JASN 2019

Sustained improvement in BP on HDF compared to HD



Over a 1-year follow-up the MAP-SDS increased by 1 SDS in HD patients and 0.2 SDS in HDF patients.

HD modality and higher IDWG% are risk factors for a higher MAP-SDS over the one year follow up.

Dialysate sodium, BP and interdialytic weight gain

930 patients, 0-20 (12.9; 8.5-15.6) years, 2787 observations

- Dialysis modality: HD 64%, HDF 24%, intensified HD/F (>15 hours/week) 9/3%
- Dialysate Na: 138.5 (130-145) mmol/l
- Increased syst. / diast. BP: 46 / 27 % of patients
  62% on 2.2±1.1 (1-6) antihypertensives.

- Diast. BP-SDS independently predicted by: dNa (p=0.015)
  IDWG (<0.0001)
  age (p<0.0001)

- IDWG independently predicted by: dNa
  UF, syst. BP, low urine output/m²
  HD versus HDF,
  weekly dialysis time (all p<0.0001)

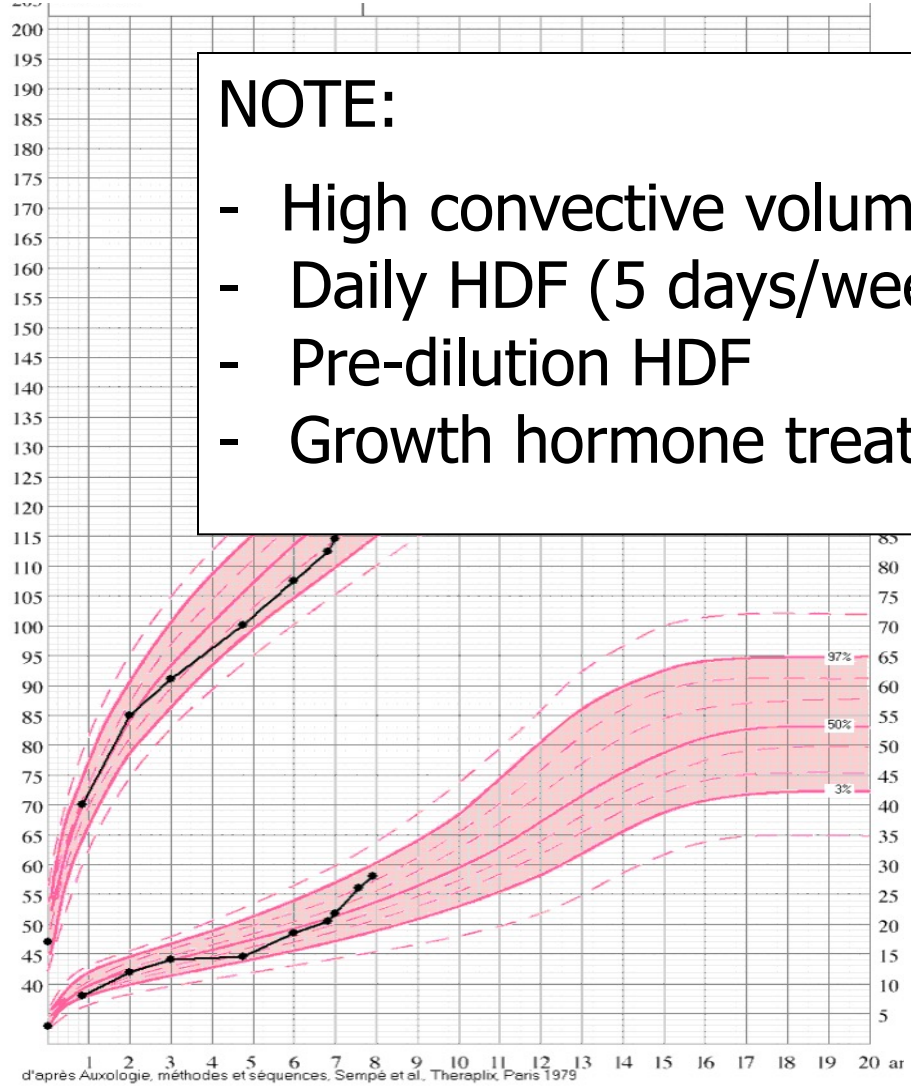
Dialysate sodium a therapeutic tool to improve blood pressure and IDWG ?

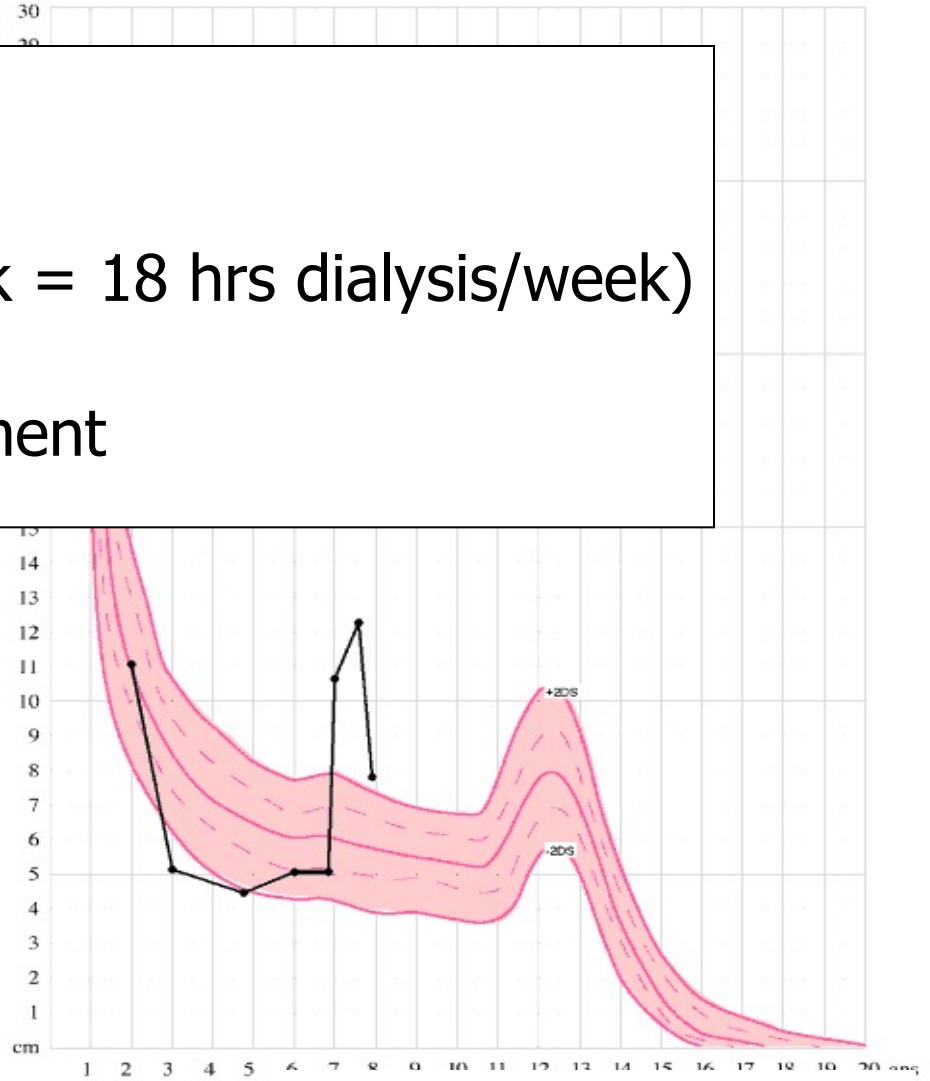
Slides courtesy of Dr Claus Schmitt

Improved growth on HDF

NOTE:

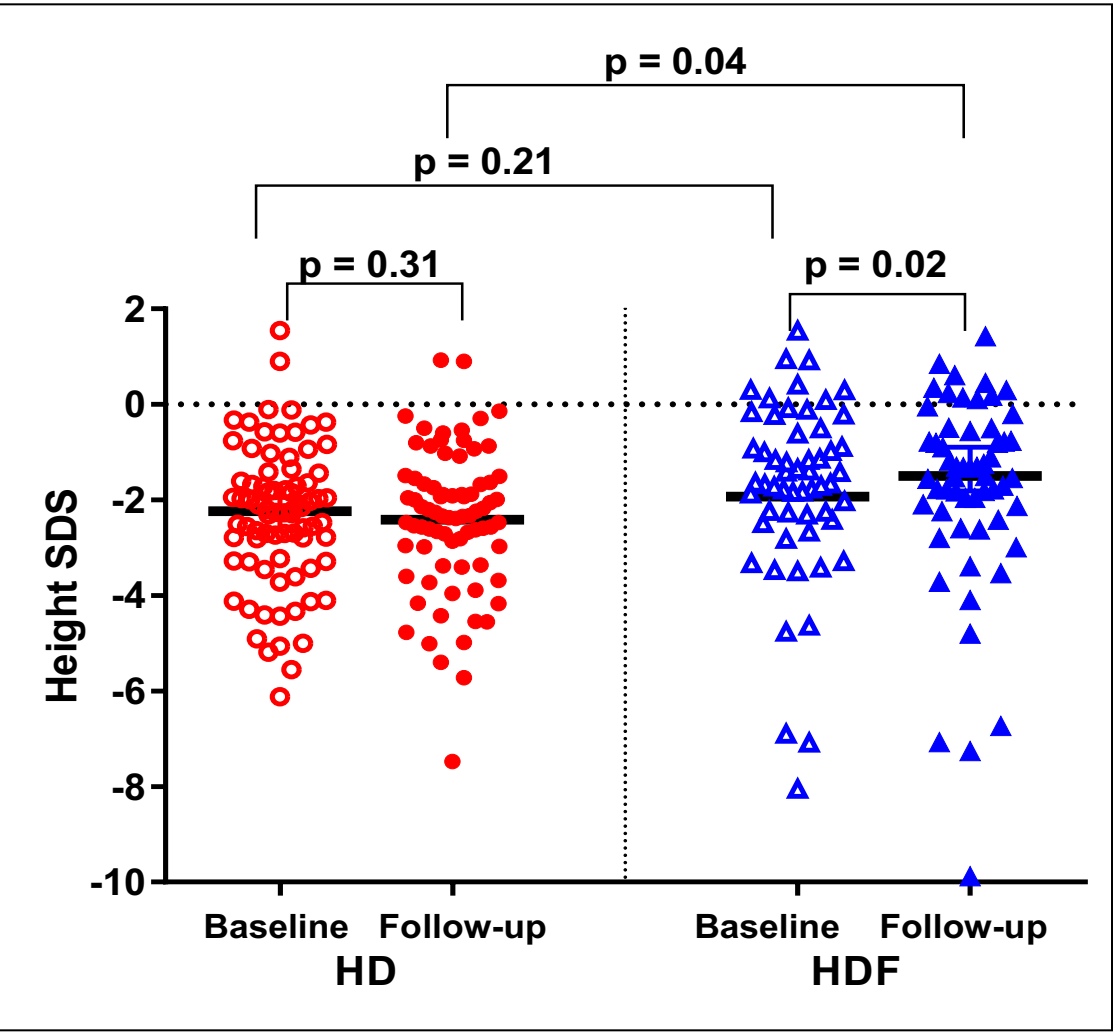
- High convective volume
- Daily HDF (5 days/week = 18 hrs dialysis/week)
- Pre-dilution HDF
- Growth hormone treatment





Fischbach et al; NDT, 2010

Change in Height SDS



15% on HD and 25% on HDF on growth hormone treatment

No difference in height-SDS in GH-Rx HDF vs HD patients (p = 0.08).

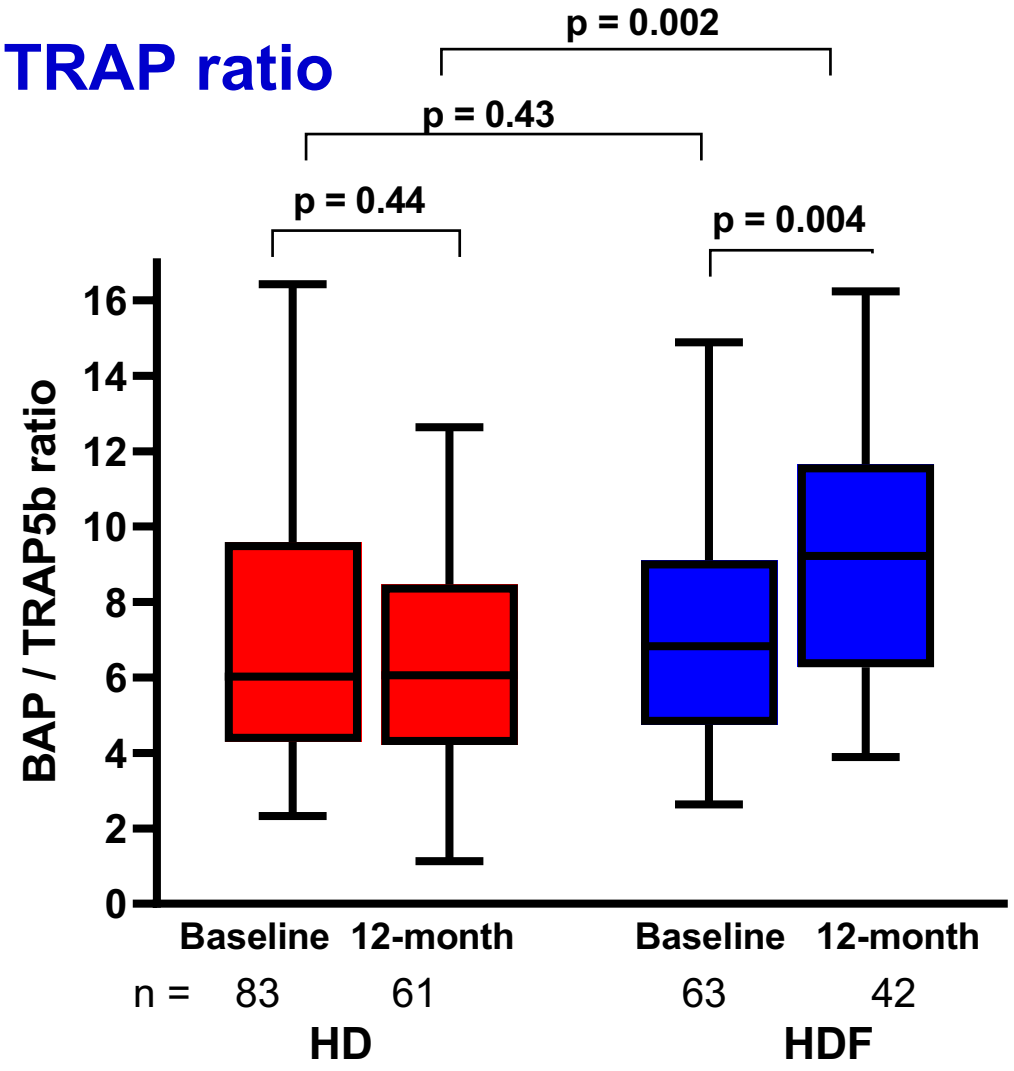
There was an inverse association between final height-SDS and β2-MG

(beta = -0.07 per 10 mg/L higher level; 95%CI = -0.14 to 0; p = 0.05).

Shroff et al; JASN 2019

Bone formation vs resorption ratios

BAP/ TRAP ratio



Fischer et al;
Kidney Int Reports 2021

Factors Predicting Catch Up Growth in IPHN

331 incident pts <16 yrs at entry
258 HD, 73 HDF, mean follow-up 1.5 years

	Parameter Estimate + SE	p
HDF dialysis mode	0.94 ±0.33	**0.002**
Age at baseline	0.03±0.03	0.29
Height SDS at baseline	0.039 ±0.08	**<0.0001**
Achieved Kt/V	0.38±0.27	0.15
Female gender	-0.03 ±0.03	0.69
Weekly dialysis time	-0.02 ±0.05	0.58
Blood flow	-0.004±0.002	**0.05**
Growth hormone use	0.26±0.32	0.41
Mean PTH	0.002±0.0003	0.47
Mean phosphate	-0.07±0.30	0.81

Factors Predicting Catch Up Growth in IPHN

Multivariable analysis, variables significant in univariate analysis included

	Parameter Estimate + SE	p
HDF dialysis mode	0.83 ±0.31	**0.008**
Height SDS at baseline	0.39 ±0.07	**<0.0001**
Blood flow	-0.003±0.001	**0.09**
Growth hormone use	0.30±0.31	0.32

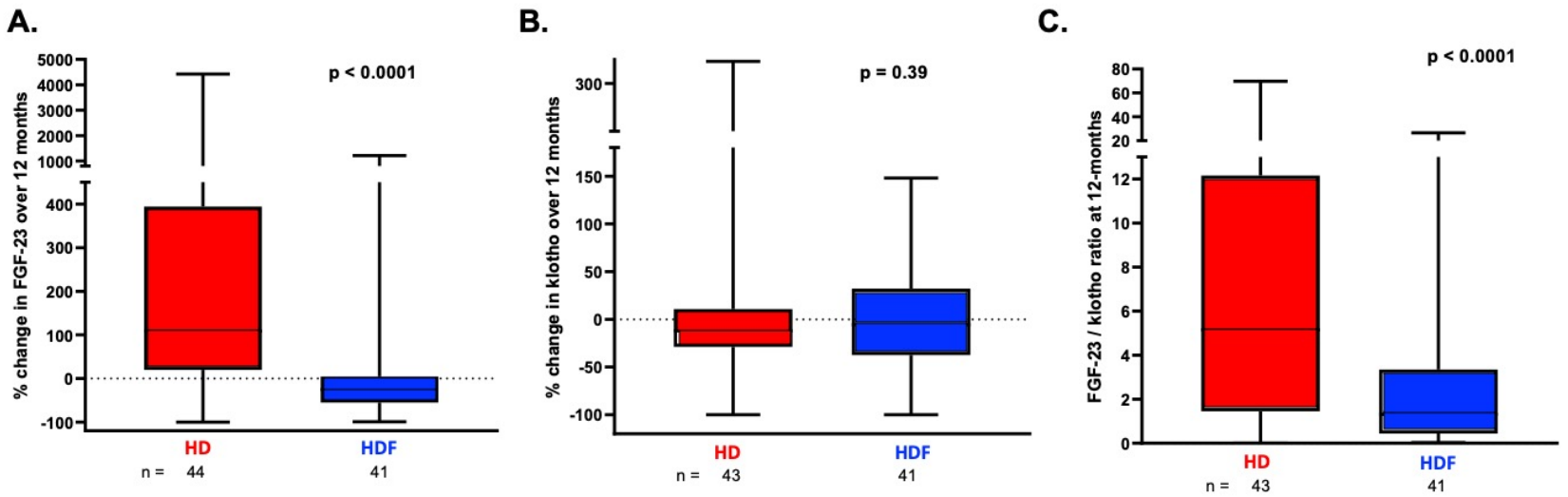
Slides courtesy of Dr Claus Schmitt

Anabolic effect of daily HDF

- Stimulates appetite - removal of circulating satiety factors (leptin, cholecystokinin, tryptophan)
- Correction of metabolic acidosis. Acidosis can:
  - activate the ubiquitin-proteosome pathway & increase protein degradation
  - suppresses endogenous GH secretion
- Minimises inflammatory cytokine release
- ? Removal of somatomedin and gonadotropin inhibitors by HDF
- ? reverses rhGH resistance

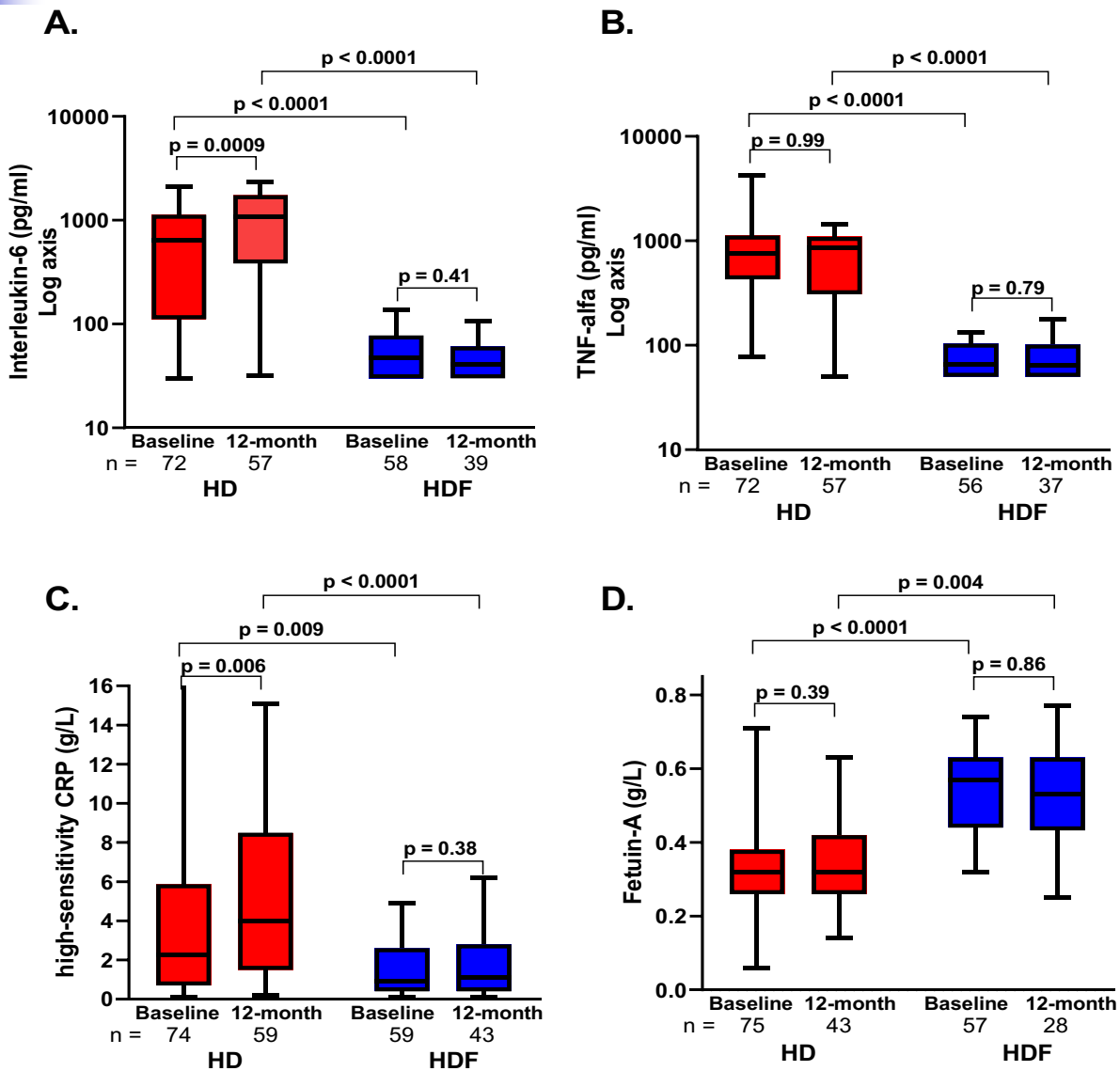
Schaefer et al, NDT 2010

FGF23 and klotho



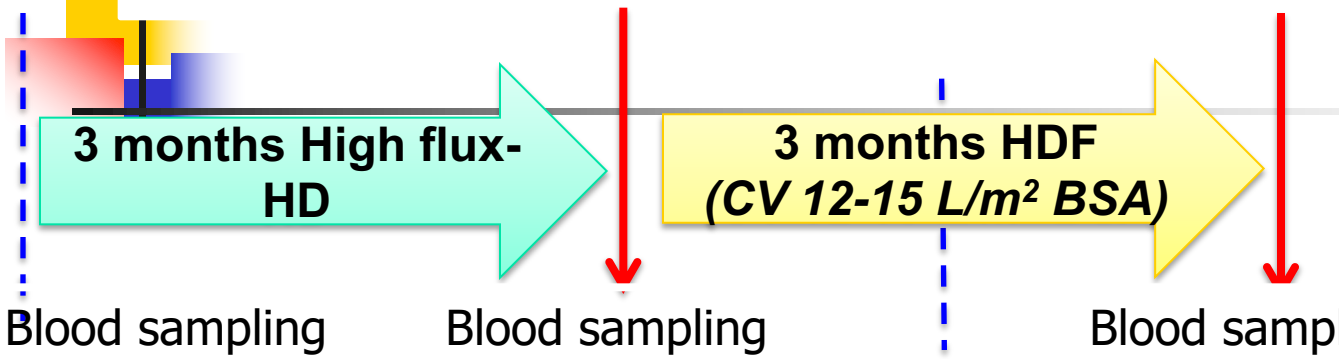
- **FGF23** levels ↓ by 25% in HDF but ↑ by 109% in HD.
- **Serum klotho** levels were comparable between HD and HDF cohorts and static over 12 months.
- The **FGF23/klotho ratio** was significantly higher in HD compared to HDF.
- On multivariable analysis those receiving HD had a 3.86 times higher FGF23/klotho ratio than those on HDF

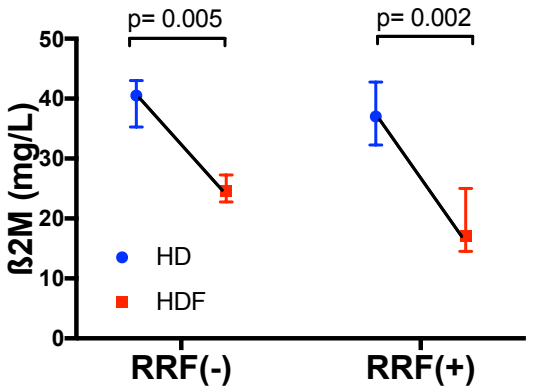
Reduced systemic inflammation in HDF



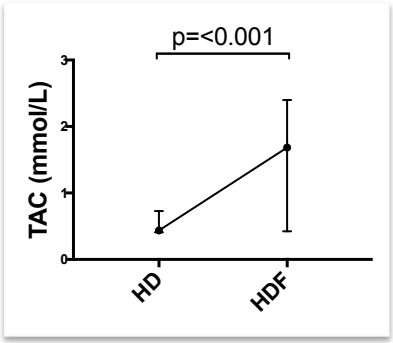
Fischer et al;
Kidney Int Reports 2021

HD → HDF - SWITCH STUDY

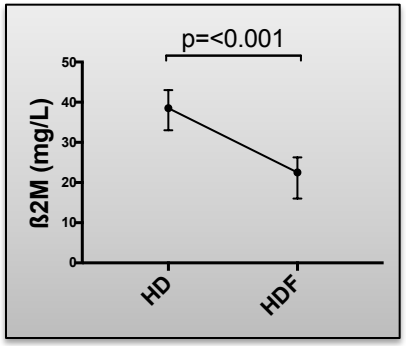


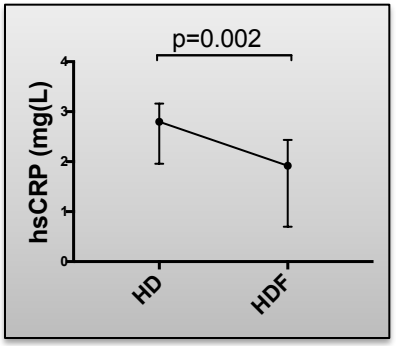


✓**Higher** antioxidant capacity

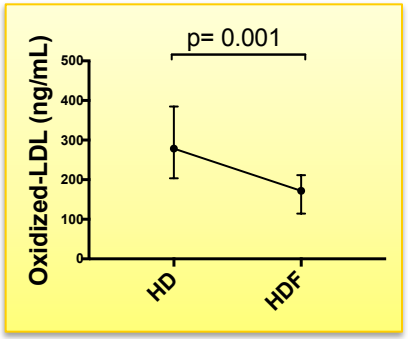


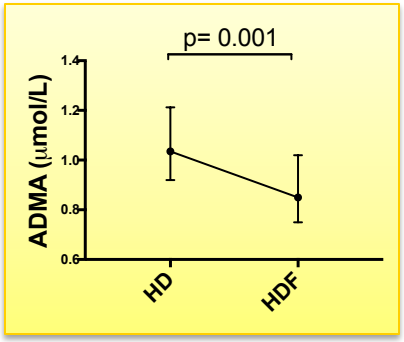
✓**Lower** inflammation (**ß2M, hsCRP**)

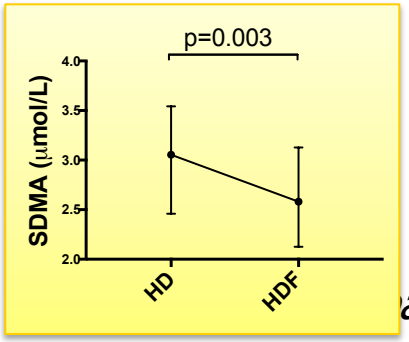


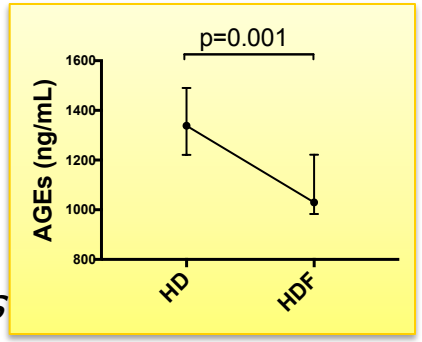


✓ **Lower** endothelial dysfunction markers (**ox-LDL,ADMA, SDMA, AGEs**)





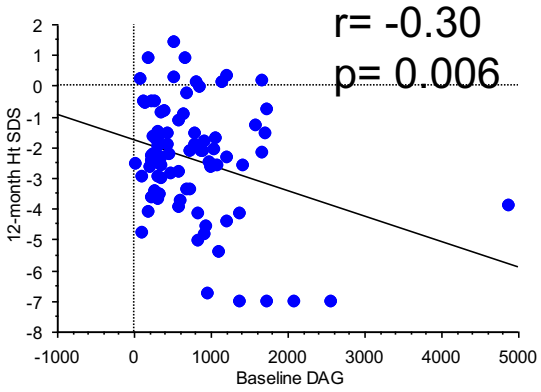


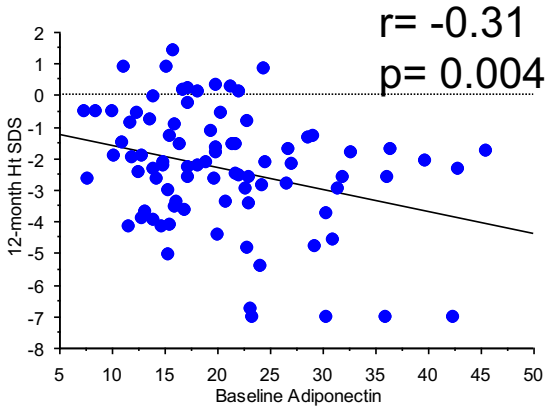


3H Nutrition and growth study: Ht SDS and nutrition-related hormones

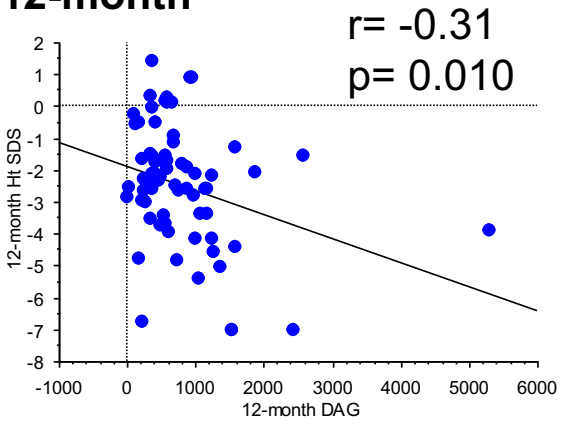
Presented at ESPN 2021
by Dr Fabio Paglialonga

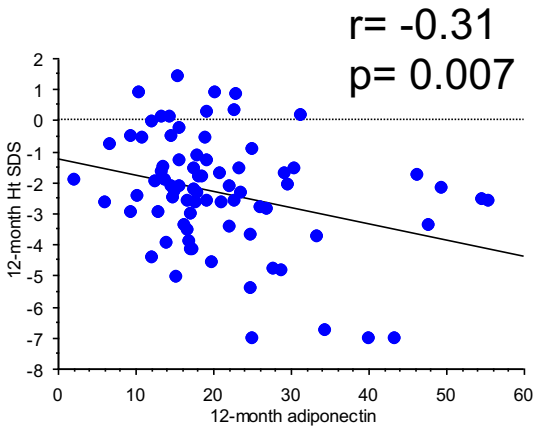
Baseline

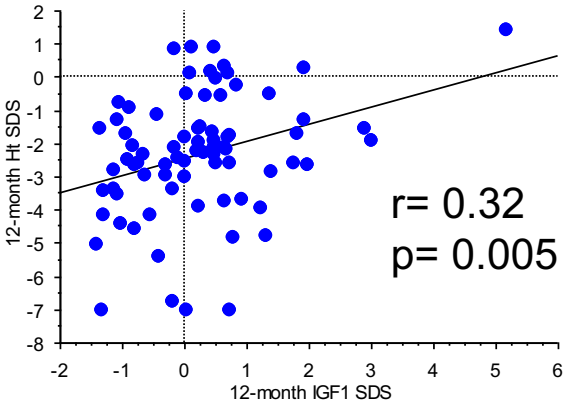




12-month







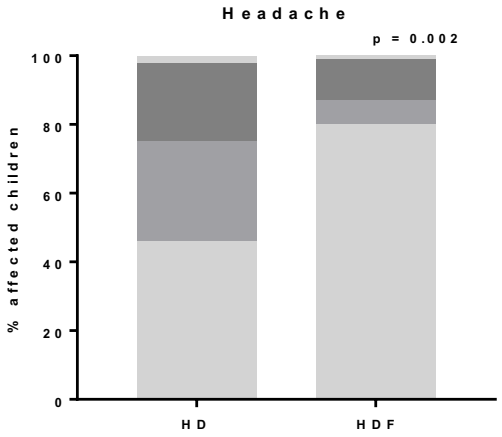
DAG
-> anorexia

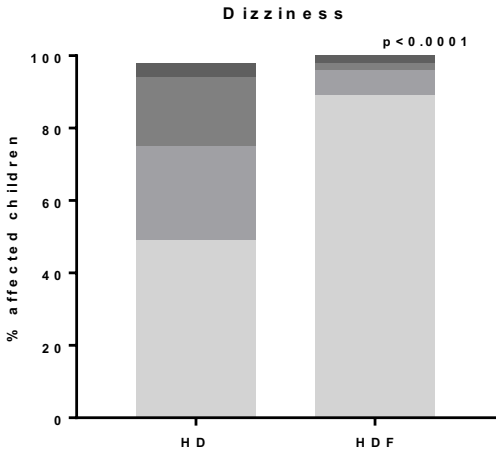
Adiponectin
-> PEW

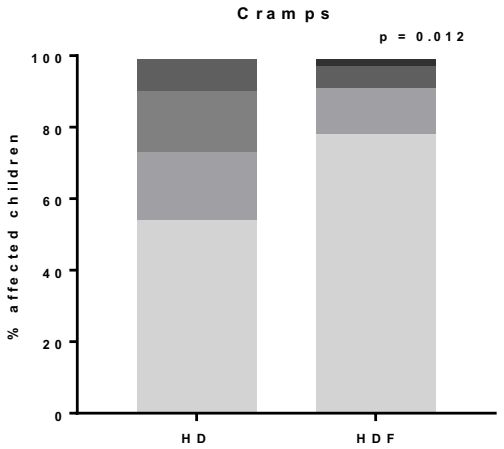
IGF-1 SDS
-> anabolism

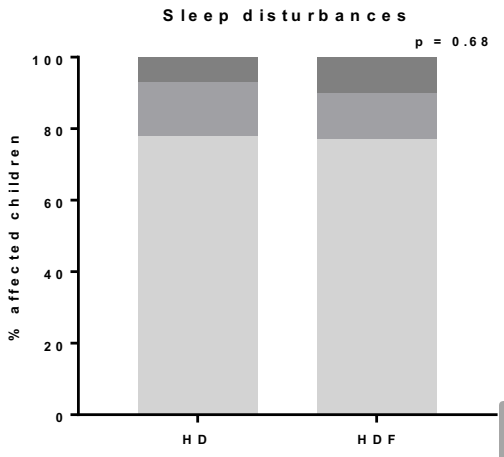
Patient related outcomes

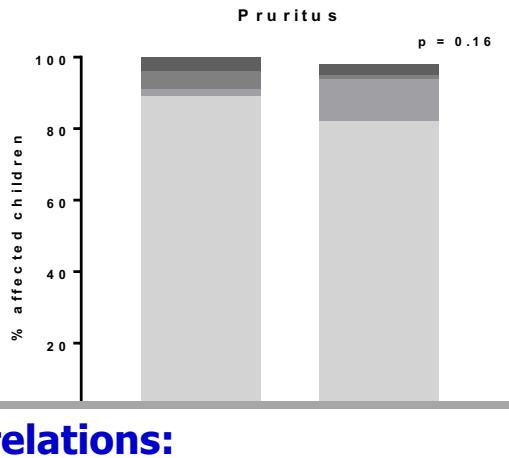
Self-reporting on 6-monthly questionnaires

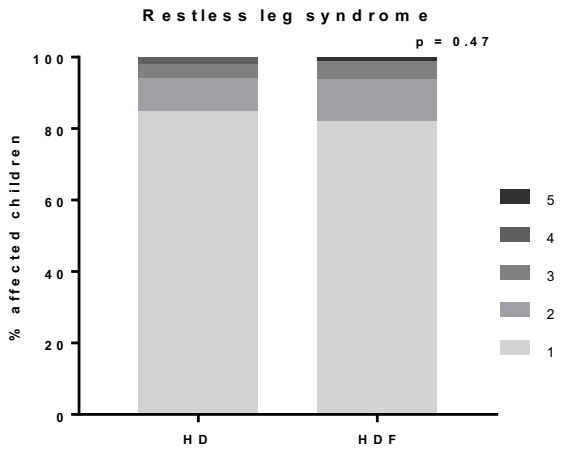








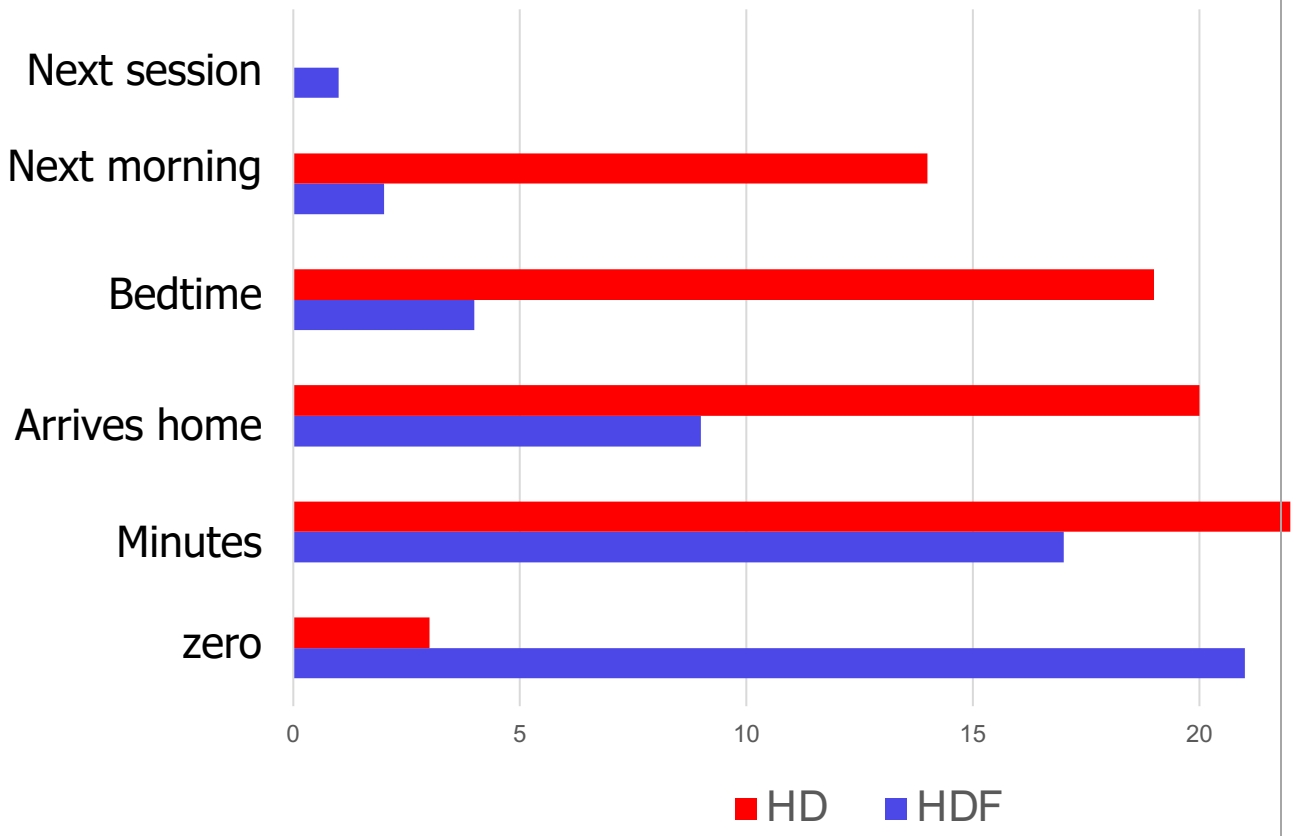


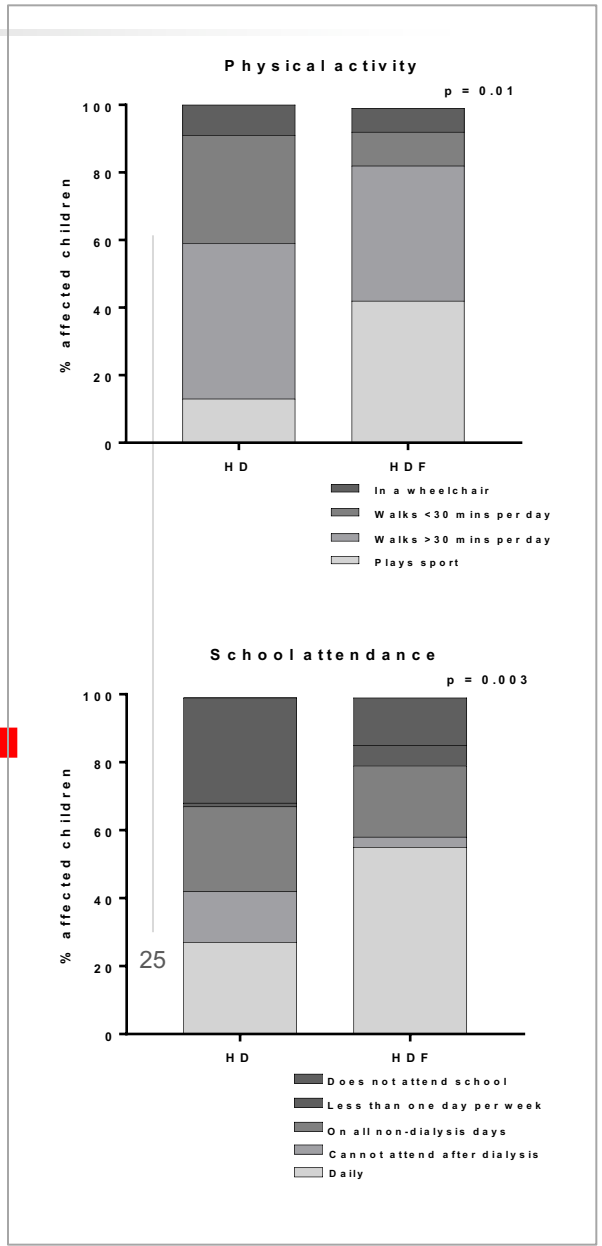


Correlations:

- ultrafiltration volume per session
- hemoglobin

PROMs – post-dialysis recovery time



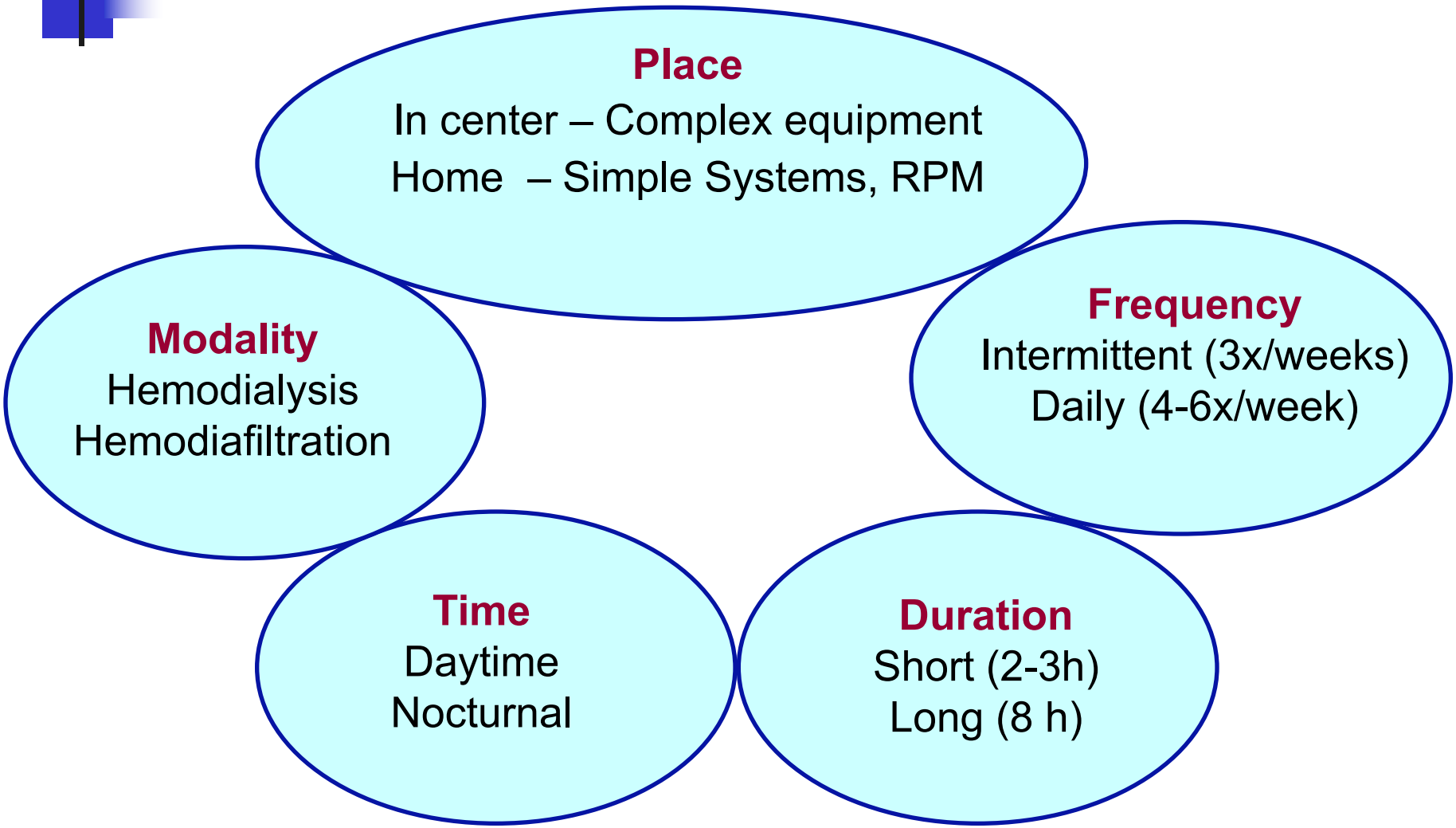


Benefits of HDF over conventional HD

- In children, HDF halts the progression of vascular changes compared to conventional HD
- HDF is associated with an early and sustained improvement in:
  - fluid status
  - Reduced inflammation and oxidative stress
  - Improved endothelial function
- Children on HDF have a small but significant increase in height SDS and increased bone formation
- Improved patient outcomes on HDF

Need a randomised study to make definitive conclusions!

Intensified Hemodialysis: Modalities



Home Haemodialysis

Advantages

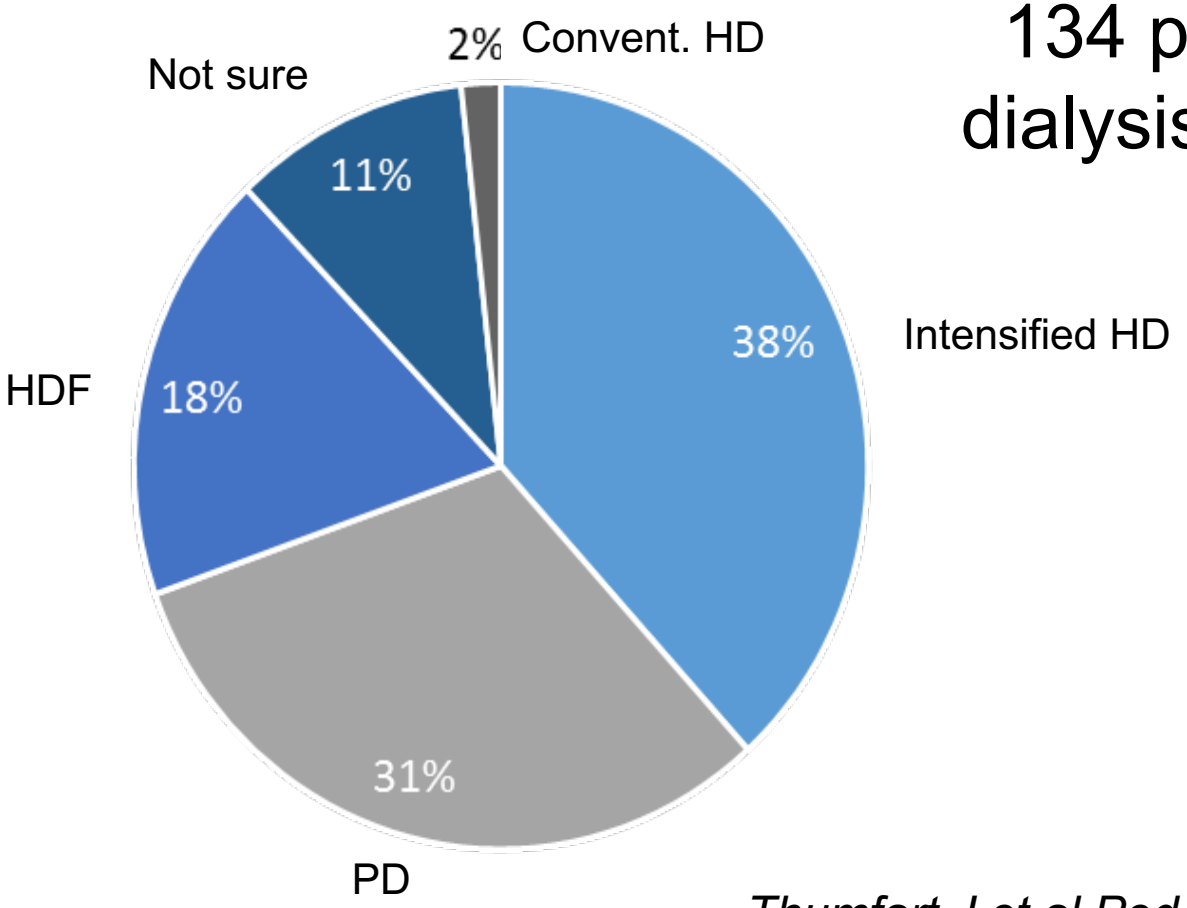
- Quality of life
- Schooling
- Reduced/no fluid and diet restrictions
- Reduced medication burden
- BP control
- Improved recovery time
- Nutrition and growth
- Energy levels
- Can be performed anywhere (inc. at home and abroad)
- Independence - teenagers
- Long term HD patient
- Nocturnal or daytime
- It is not everyday!

Disadvantages

- Carer burden
- Patient burden
- Daunting
- Utility bills
- CVC/Fistula infections
- Exit site infections
- CVC/fistula problems
- Machine breakdown
- Body image
- Needs a committed family/teenager and appropriate housing

IPDN - real life data

Which dialysis modality do you believe offers the best overall patient outcomes?



134 pediatric dialysis centers

Thumfart J et al Ped Nephol 2018

IPDN - real life data

- 2017: Only 38% of centers offer int. HD(F) in patient subgroups
  Barriers to expansion of intensified HD programs:
  - lack of adequate funding (66%)
  - shortage of staff (63%)
  - lack of expertise / motivation 21 / 14%

- 5/2019
  - HDF 18%
  - iHD(F) 8%

- 9/2021:
  - HDF 26%
  - iHD(F) 12%

Slide courtesy of Dr Claus Schmitt

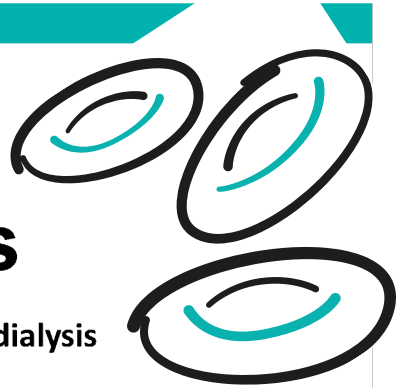
Conclusions

- Paediatric dialysis research:
- Registries
- Retrospective data
- prospective observational studies

Need RCTs to develop evidence based practice!

For more details…..

NHS
Great Ormond Street Hospital for Children
Learning Academy



Advances in Paediatric Dialysis

This 2-day virtual conference is aimed at doctors and nurses working with children on dialysis

It forms part of the core curriculum for training in Paediatric Dialysis. From the basic principles of dialysis and practical workshops on PD and HD to state-of-the-art lectures, this is your opportunity to hear experts discuss different dialysis modalities (PD, HD, HDF and home HD) as well as the CKD and dietetic management of children on dialysis.

Date: 10th and 11th February 2022

Time: 13:00-17:00 GMT

Who can attend?

- Junior Doctors (Fellows)
- Consultants
- Dialysis nurses and technicians
- Allied health professionals
- Industry Members

Course Director: Rukshana Shroff

Faculty: The GOSH team & international speakers

For queries please contact: PGME.Education@gosh.nhs.uk