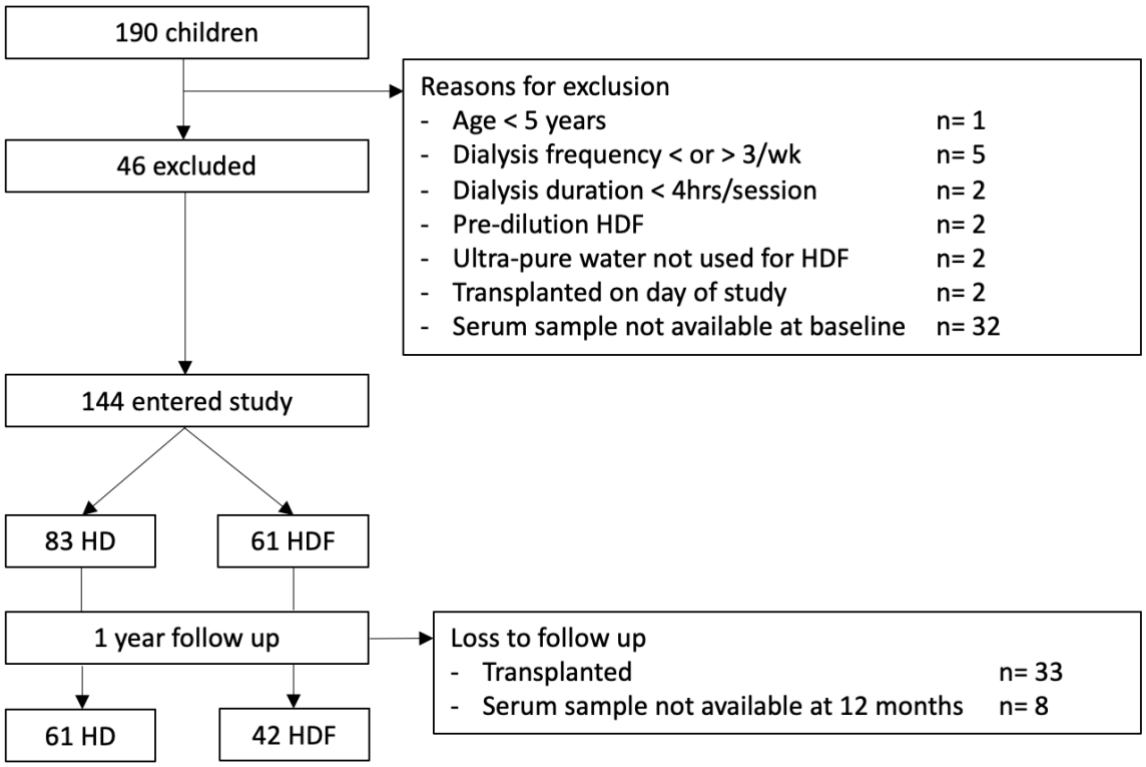
Supplemental Figure 1 Flow chart of study populations, including the number of children who were screened, underwent randomization, and completed 1-year follow-up in the HD and HDF arms



Supplemental Table 1 Demographics of the study population at baseline

	HD	HDF	p
Number	83	61	
Age (years) n (%)			0.65
5 - 10	15 (18.1)	14 (23.0)	
10-15	28 (33.7)	22 (36.1)	
15-20	40 (48.2)	25 (41.0)	
Females; n (%)	36 (43.4)	35 (57.4)	0.10
Race (%)			0.48
Caucasian	60 (72.3)	43 (70.5)	
Asian	8 (9.6)	7 (11.5)	
African	5 (6.0)	7 (11.5)	
Mixed / Other	10 (12.1)	4 (6.6)	
Underlying renal diagnosis (%)			0.94
Cystic kidney disease	3 (3.6)	3 (4.9)	
Dysplasia	36 (43.4)	24 (39.3)	
Glomerulonephritis	17 (20.5)	14 (23.0)	
Others	21 (25.3)	17 (27.9)	
Unknown	6 (7.2)	3 (4.9)	
Comorbidity/genetic conditions			
Impaired cognitive development	17 (20.5)	13 (21.3)	0.90
Impaired motor development	7 (8.4)	6 (9.8)	0.77
Ocular or hearing abnormalities	3 (3.6)	3 (4.9)	0.70
Cardio-pulmonary	3 (3.6)	2 (3.3)	0.91
Genetic disorder/defined syndrome	15 (18.1)	15 (24.6)	0.34
Previous dialysis			
- Incident patients in study (%)	57 (68.7)	33 (54.1)	0.07
- Time on dialysis before 3H start	1.2 (0.22 – 1.4)	1.12 (0.18 – 1.6)	0.76
If previous dialysis			
- PD / HD or HDF / HD and PD (%)	57.7 / 23.1 / 19.2	46.4 / 39.3 / 14.3	0.44
- Time on dialysis before 3H (months)	25 (18 – 52)	30 (16 – 46)	0.80
Previous transplant			
- Yes (%)	13 (15.7)	19 (31.2)	0.03
- time with functioning graft (months)	35 (23 – 72)	72 (12 – 119)	0.84
- immunosuppression continued (yes; %)	11 (13.6)	11 (18.0)	0.43
Residual renal function (urine vol in ml/kg/day)	2.70 (0 – 12.82)	4.27 (0 – 17.75)	0.37
Anthropometry			
Height SDS	-2.21 (-3.30 to -1.61)	-1.41 (-2.67 to -0.51)	0.005
Body mass index SDS	-0.08 (-0.85 to 1.08)	-0.36 (-1.03 to 0.40)	0.22
Medications			
Native vitamin D (n; %)	32 (38.6)	38 (60.3)	0.005
Dosage (IU/day)	2700 (0 – 8400)	3120 (0 – 10,200)	0.08
Vitamin D analogs (n; %)	68 (81.9)	53 (84.1)	0.42
Dosage (mcg/day)	0.32 (0.2 to 1.35)	0.30 (0.2 to 1.25)	0.61
Phosphate binders:			0.71
- none	9 (10.8)	6 (9.8)	
- calcium based binders	47 (56.6)	30 (49.2)	
- Non-calcium based binders (sevelamer or lanthanum)	12 (14.5)	13 (21.3)	
- Both Ca based and non-Ca based binders	15 (18.1)	12 (19.7)	
Calcium supplements (n; %)	19 (22.9)	14 (23.0)	0.99
Cinacalcet (n; %)	5 (6.0)	5 (8.2)	0.61
Growth hormone (n; %)	11 (13.3)	12 (19.7)	0.30
Dialysis prescription			
Dialysate calcium			
1.25 vs 1.5 vs 1.75 mMol (%)	63.9 / 30.1 / 6.0	78.7 / 19.7 / 1/6	0.12

Dialysate bicarbonate <34 vs 34-36 vs >36mMol/L (%)	47.0 / 45.8 / 7.2	45.9 / 47.5 / 6.6	0.97

Data are presented as number (n) with percentage or as median and interquartile range. All dialysis related parameters are expressed as the mean of the previous four mid-week dialysis sessions.

Supplemental Table 2 Routine CKD mineral bone disease related measures at baseline and 12-months in the HD and HDF cohorts*

	HD (n = 61)			HDF (n = 42)		
	Baseline	**12 months**	**p**	**Baseline**	**12 months**	**p**
Albumin-corrected serum calcium (mMol/L)	2.4 (2.3, 2.5)	2.3 (2.2, 2.5)	0.63	2.5 (2.3, 2.6)	2.4 (2.3, 2.5)	0.71
Serum phosphate (mMol/L)	1.6 (1.3, 2.1)	1.7 (1.5, 2.1)	0.39	1.8 (1.3, 2.2)	1.8 (1.4, 2.0)	0.08
Serum magnesium (mMol/L)	1.0 (0.9, 1.2)	1.0 (0.9, 1.1)	0.82	1.0 (0.88, 1.2)	1.0 (0.94, 1.2)	0.77
Serum alkaline phosphatase (IU/L)	187 (113, 294)	222 (124, 313)	0.20	166 (111, 242)	196 (148, 320)	0.06
Serum parathyroid hormone (PTH; pMol/L)	32.6 (9.9 – 95.2)	44.1 (11.2 – 91.7)	0.27	29.8 (4.8 – 84.0)	21.8 (3.7 – 69.7)	0.08
Serum 25-hydroxy vitamin D (nMol/L)	29 (19, 40)	31 (15, 42)	0.59	38 (27, 48)	35 (19, 52)	0.37
Serum bicarbonate (mMol/L)	24 (18 – 26)	24 (17 – 25)	0.91	23 (19 – 24)	24 (18 – 26)	0.76

*Patients with paired data at baseline and 12 months are shown
Data are presented as median and interquartile range.

Supplemental Table 3 Bone-specific biomarkers at baseline and 12-months in the HD and HDF cohorts*

	HD		HDF	
	Baseline	12 months	Baseline	12 months
Bone-specific alkaline phosphatase **BAP; (IU/L)** **z-score**	75 (32 – 96) 0.47 (-0.72, 2.10)	58 (49 - 73) -1.50 (-2.80, 0.44)	83 (34 – 102) 0.07 (-1.00, 0.91)	117 (69 – 138) 1.40 (0.34, 2.50)
Tartrate-resistant acid phosphatase 5b **TRAP-5b; (IU/L)** **z-score**	10.4 (0.9 – 14.2) 0.9 (-0.67, 1.9)	16.9 (7.8 – 21.1) 2.3 (0.84, 3.5)	11.3 (6.8 – 19.0) 0.64 (-0.46, 2)	9.1 (4.6 – 13.9) 0.17 (-0.84, 1.3)
Sclerostin (ng/ml)	0.92 (0.6, 1.5)	1.2 (0.68, 1.6)	0.72 (0.49, 0.97)	0.86 (0.57, 1.1)
Cross-linked C-telopeptide of type I collagen (CTX; ng/ml)	8.6 (5.6, 13)	9.4 (6, 14)	7.6 (4.7, 14)	8.9 (4.9, 12)
Intact FGF-23 (pg/ml)	487 (166, 1210)	1540 (522, 3489)	588 (235, 1345)	417 (146, 1300)
Klotho (pg/ml)	1225 (809, 1780)	1100 (697, 1760)	1420 (842, 2160)	1405 (868, 1903)
Inflammatory markers				
High-sensitivity CRP (g/L)	2.3 (0.7, 5.9)	4.0 (1.5, 8.5)	0.9 (0.4, 2.6)	1.1 (0.4, 2.8)
Interleukin-6 (IL-6; pg/ml)	315 (165, 600)	600 (295, 784)	28 (5, 146)	24 (5, 98)
Tumor Necrosis Factor (TNF)-α (pg/ml)	303 (165, 919)	647 (315, 1000)	15 (8.5, 74)	12 (8, 37)
Fetuin-A (g/L)	0.32 (0.26, 0.38)	0.32 (0.26, 0.42)	0.57 (0.44, 0.63)	0.53 (0.43, 0.63)

*The number of patients for each biomarker at each time point are shown on the respective Figures.
Data are presented as median and interquartile range.
All correlations are shown in the respective figures.

Supplemental Table 4 – Factors associated with height SDS at 12-month follow-up

	Unadjusted			**Adjusted 1**			**Adjusted 2* – including mediators**		
	Beta	**95% CI**	**P**	**Beta**	**95% CI**	**P**	**Beta**	**95% CI**	**P**
Dialysis modality (HD vs HDF)	-0.25	-0.46, -0.03	0.02	-0.24	-0.46, -0.01	0.04	-0.20	-0.42, 0.03	0.08
Dialysis vintage (per year longer)	0.01	-0.04, 0.06	0.58						
Weight adjusted urine output (per 10 higher)	0.06	-0.01, 0.13	0.10	0.05	-0.02, 0.12	0.16	0.05	-0.02, 0.12	0.16
Growth hormone medication (Yes vs no)	-0.08	-0.35, 0.19	0.57						
Physical activity (ref=3) 1 2	 -0.44 -0.18	 -0.75, -0.14 -0.45, 0.10	0.20						
Impaired motor development (Yes vs no)	0.02	-0.37, 0.41	0.93						
Potential mediators measured at one year:									
Beta-2 microglobulin (per 10 higher)	-0.04	-0.11, 0.04	0.33						
IL-6 (Per 100 higher)	-0.01	-0.03, 0.01	0.35						
TNF-α (Per 100 higher)	-0.01	-0.03, 0.02	0.70						
hs-CRP (per 10 higher)	0.03	-0.05, 0.12	0.40						
Calcium	0.36	-0.16, 0.88	0.18						
Phosphate	-0.19	-0.38, 0.01	0.06				-0.18	-0.39, 0.03	0.10
Vitamin D level (per 10 higher)	0.02	-0.03, 0.07	0.46						
Convective volume adjusted for BSA (Per 10 higher)	-0.08	-0.27, 0.11	0.43						

All independent variables measured at baseline. Results from linear regression models, additionally adjusted for baseline height and country. 95% CI = 95% confidence interval; BSA=body surface area.

Adjusted model 1: Adjusted for all potential confounders for the association between dialysis modality and bone disease with p<0.2 in univariable analyses n=118;

Adjusted model 2: Adjusted for all potential confounders, plus potential mediators measured at 12 months with p<0.2 in univariable analyses. n=117

STROBE Checklist - Hemodiafiltration is associated with reduced inflammation and increased bone turnover compared to conventional hemodialysis in children - the HDF, Heart and Height (3H) study

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4-5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6
Bias	9	Describe any efforts to address potential sources of bias	5-6
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	
		(*d*) If applicable, explain how loss to follow-up was addressed	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	7-8
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7-8
		(b) Indicate number of participants with missing data for each variable of interest	

		(c) Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	Report numbers of outcome events or summary measures over time	7-8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	8 -9-10
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9 - 10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10 - 11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	16

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.