Kennsla læknanema á 5. námsári

Chronic Kidney Disease in Children

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Introduction

- Chronic kidney disease (CKD) in children varies in severity, ranging from mild reduction in glomerular filtration rate (GFR) without long-term consequences to end-stage kidney disease (ESKD), necessitating dialysis or kidney transplantation for continued patient survival.

Introduction

- End-stage kidney disease reduces life expectancy as exemplified by the 30–150 times higher mortality in children and teenagers receiving dialysis compared with same age healthy individuals.
- Early institution of supportive therapies and drug treatment aimed at reducing CKD progression and extrarenal complications is essential.

Definition of CKD

- In the Kidney Disease Improving Global Outcome (KDIGO) CKD clinical practice guideline published in the year 2013, CKD is defined as:
  - Any abnormalities of kidney structure or function (kidney damage) with implications for health
  - Present for at least three consecutive months

CKD associated conditions

- Proteinuria
- Anaemia
- Metabolic acidosis and electrolyte disorders
- CKD-MBD
- Poor growth (short stature) – malnutrition
- Hypertension
- Dyslipidemia
- Increased CV-risk

Helstu fylgikvillar langvinns nýrnasjúkdóms (CKD) hjá börnum

Factors associated with CKD progression

- Optimal management of all modifiable risk is likely needed to attain maximum slowing of renal function decline in affected children and delay the need for kidney Tx.
  - Hypertension
    - Intensified treatment significantly slows progression
  - Metabolic acidosis
    - Treatment significantly slows progression
  - Proteinuria
    - Treatment slows progression in the short run only
  - Anaemia
    - Treatment may slow disease progression

Allra mögulegra leiða leitað til þess að draga úr hraða CKD progression

Staging of CKD

- Staging of CKD is primarily based on GFR, while the degree of proteinuria and a number of other factors, affecting prognosis, may predict individual patient outcome.

Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

Kidney Int Suppl (2013) 3 (1): 1–150.
doi:10.1038/kisup.2012.64

GFR categories (ml/min/ 1.73 m^2) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

Epidemiology of CKD in children

Prevalence in the US

- A total of 9921 children aged 0–21 years were receiving KRT at the end of December 2013,
- Giving a point prevalence of approximately 100 cases per million age-related population (pmarp).
  - 67.0 for kidney transplantation
  - 21 for hemodialysis (HD)
  - 2.5 for peritoneal dialysis (PD)

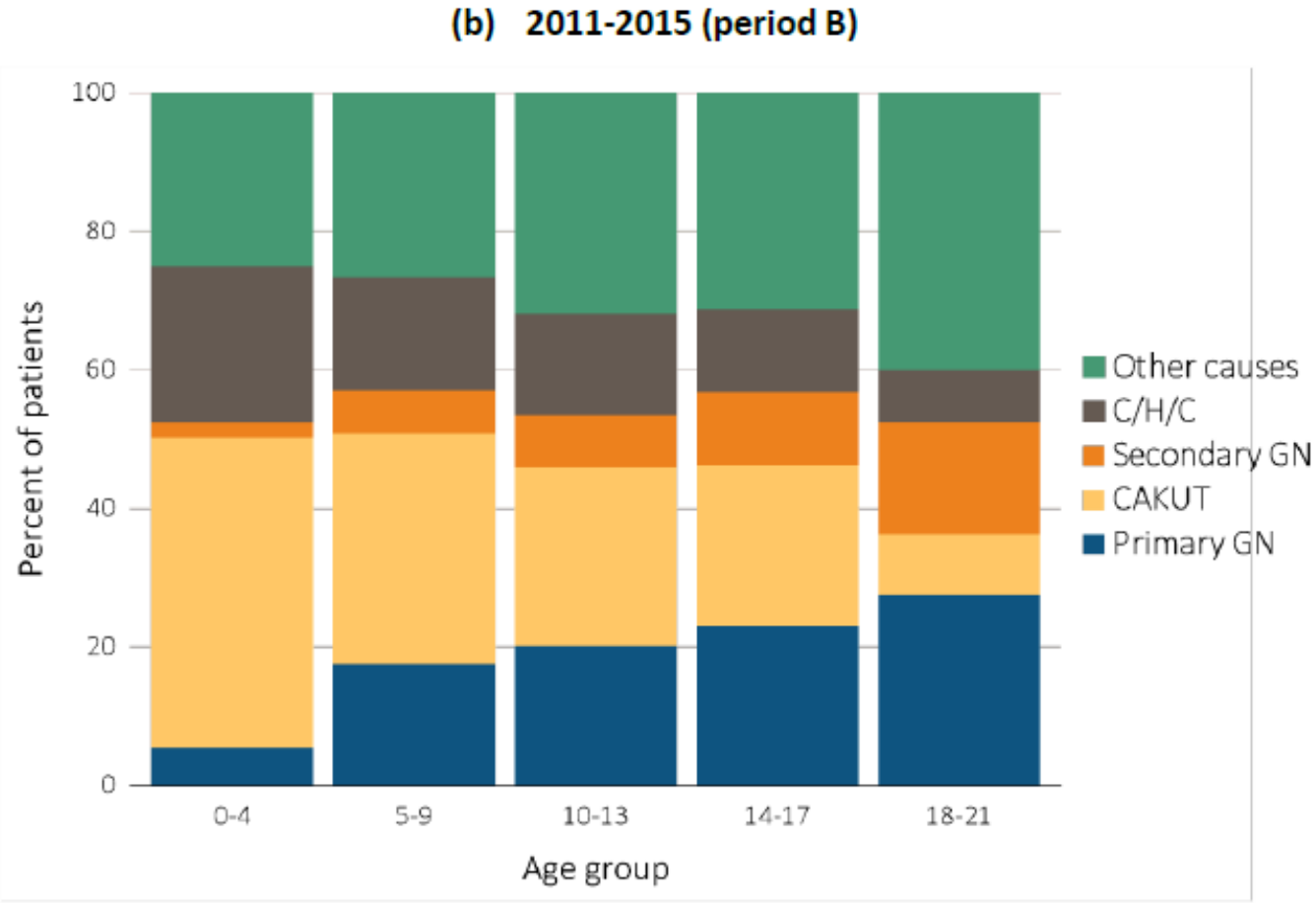
US - Incidence

- The number of US children 0–21 years of age who initiated KRT in the year 2013 was 1462
- Incidence rate of 14.8 per million per year
  - 8.6 for HD
  - 3.9 for PD
  - 2.3 received kidney transplantation as their first RRT modality.

Europe/EDTA - Epidemiology

- Children 0–19 years of age who initiated KRT in the year 2013
- Incidence rate of 8.3 per million per year
- Point prevalence end of year 2013 was 55.3 pmarp.
- These numbers are 50% of the US numbers
  - Black race/non-White

Etiology of CKD in Children



Data Source: Special analyses, USRDS ESRD Database. Abbreviations: CAKUT, congenital anomalies of the kidney and urinary tract; C/H/C, cystic/hereditary/congenital diseases; ESRD, end-stage renal disease; GN, glomerulonephritis

Table 7 Causes of CKD in the CKiD cohort [49]

Glomerular diagnosis $n = 129$ (22 %)	% (n)	Nonglomerular diagnosis $n = 457$ (78 %)	% (n)
Focal and segmental glomerulosclerosis	33 % (42)	Obstructive uropathy	26 % (118)
Hemolytic uremic syndrome	22 % (28)	Aplastic/hypoplastic/dysplastic kidneys	23 % (105)
Systemic immunologic disease	9 % (12)	Reflux nephropathy	19 % (87)
Familial nephritis	7 % (9)	Autosomal recessive polycystic kidney	4 % (19)
IgA nephropathy	5 % (7)	Renal infarct	4 % (18)
Chronic glomerulonephritis	5 % (7)	Syndrome of agenesis of abdominal musculature	2 % (11)
Membranoproliferative glomerulonephritis type I	3 % (4)	Pyelo/interstitial nephritis	2 % (9)
Idiopathic crescentic glomerulonephritis	2 % (3)	Cystinosis	2 % (9)
Membranous nephropathy	2 % (3)	Oxalosis	2 % (7)
Henoch-Schonlein purpura	2 % (3)	Medullary cystic disease	1 % (6)
Congenital nephrotic syndrome	2 % (2)	Wilms' tumor	1 % (4)
Membranoproliferative	2 % (2)	Autosomal-dominant polycystic kidney disease	<1 % (2)
Other	5 % (7)	Other	14 % (62)

CKD chronic kidney disease, *CKiD* chronic kidney disease in children study

Þekkja/kannast við helstu sjúkdóma sem valda CKD í börnum, mikið af meðfæddum vandamálum

Kidney Function

Purpose of kidney function assessment

- To identify individuals with reduced level of kidney function who are at risk of accelerated renal function decline.
  - Serum creatinine
  - Serum cystatin c
  - eGFR estimating equations
  - Direct GFR measurements

Helstu aðferðir til þess að áætla nýrnastarfsemi

Clinica Chimica Acta 490 (2019) 88–97

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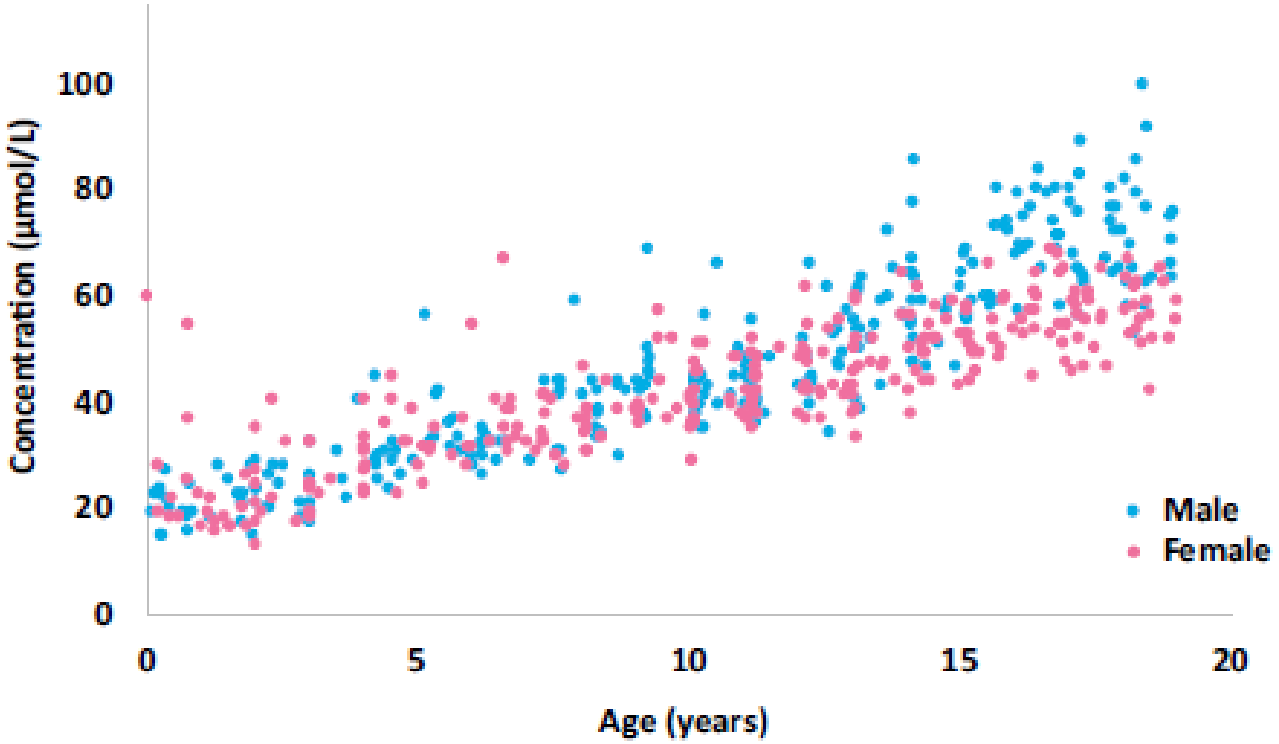
Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/cca

Gera sér grein fyrir að serum kreatínín hækkar með vaxandi vöðvamassa/aldri

Pediatric reference intervals for clinical chemistry assays on Siemens ADVIA XPT/1800 and Dimension EXL in the CALIPER cohort of healthy children and adolescents



Pathology (August 2015) 47(5), pp. 452–461

CHEMICAL PATHOLOGY

Trends and physiology of common serum biochemistries in children aged 0–18 years

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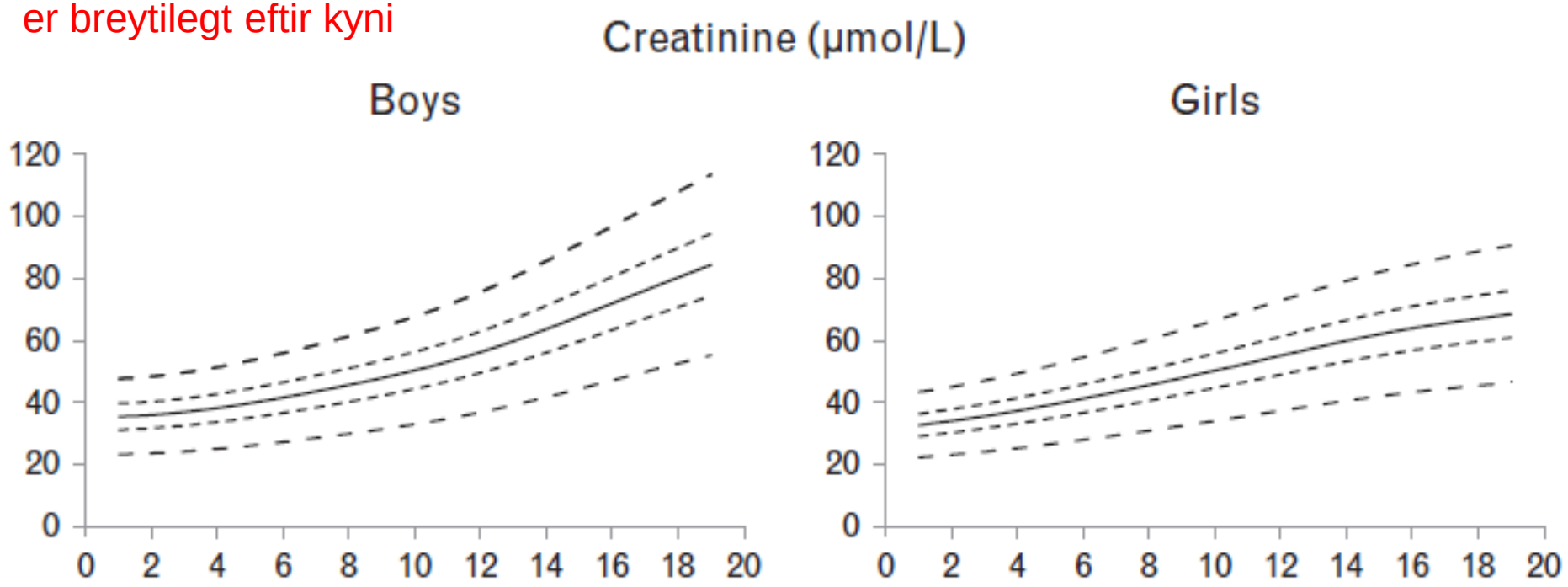
Gera sér grein fyrir að serum kreatínín hækkar með vaxandi vöðvamassa/aldri og er breytilegt eftir kyni



Pediatr Nephrol (2010) 25:2107–2113
DOI 10.1007/s00467-010-1533-y

ORIGINAL ARTICLE

Reference values for serum creatinine in children younger than 1 year of age

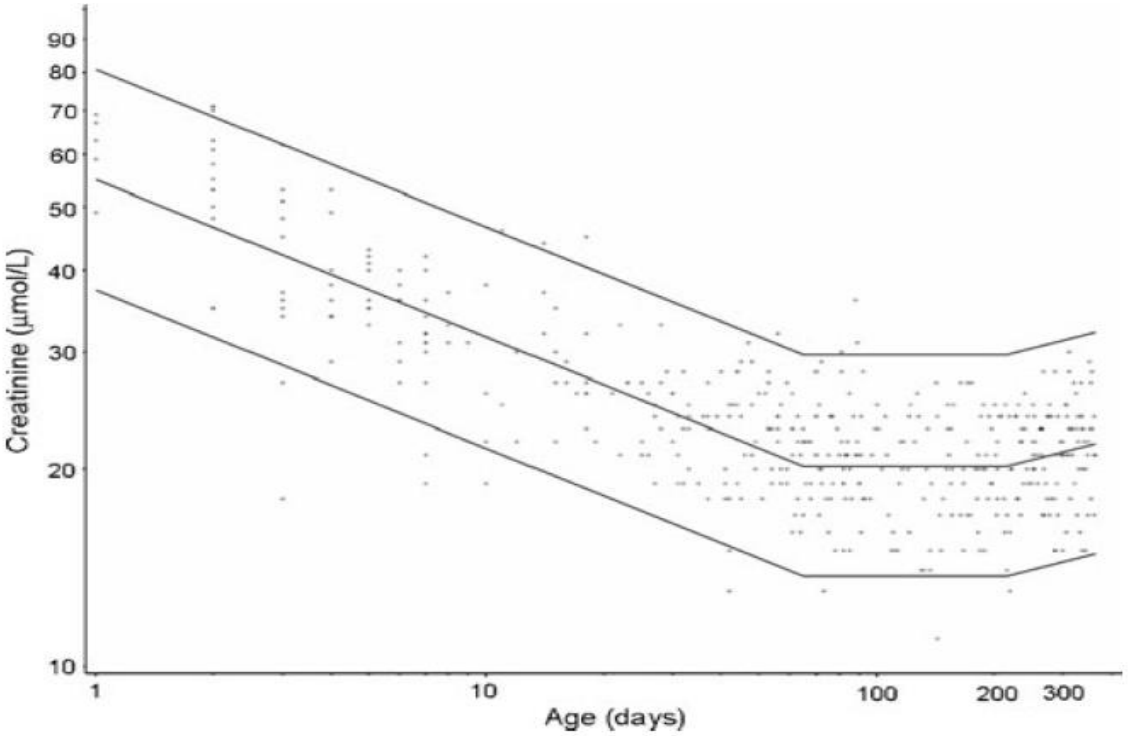


Fig. 1 Reference values of serum creatinine in children younger than 1 year of age. *Symbols* Individual serum creatinine value of each patient included in the study, *lines* geometric mean (*middle*) and the 2.5th (*lower*) and 97.5th (*upper*) percentiles

Serum kreatínín við fæðingu endurspeglar s-kreatínín móður. Nýrnastarfsemi er slök fyrstu vikurnar en batnar hægt og sígandi sem endurspeglast í lækkandi serum kreatíníngildum fyrstu 2-3 mánuðina.

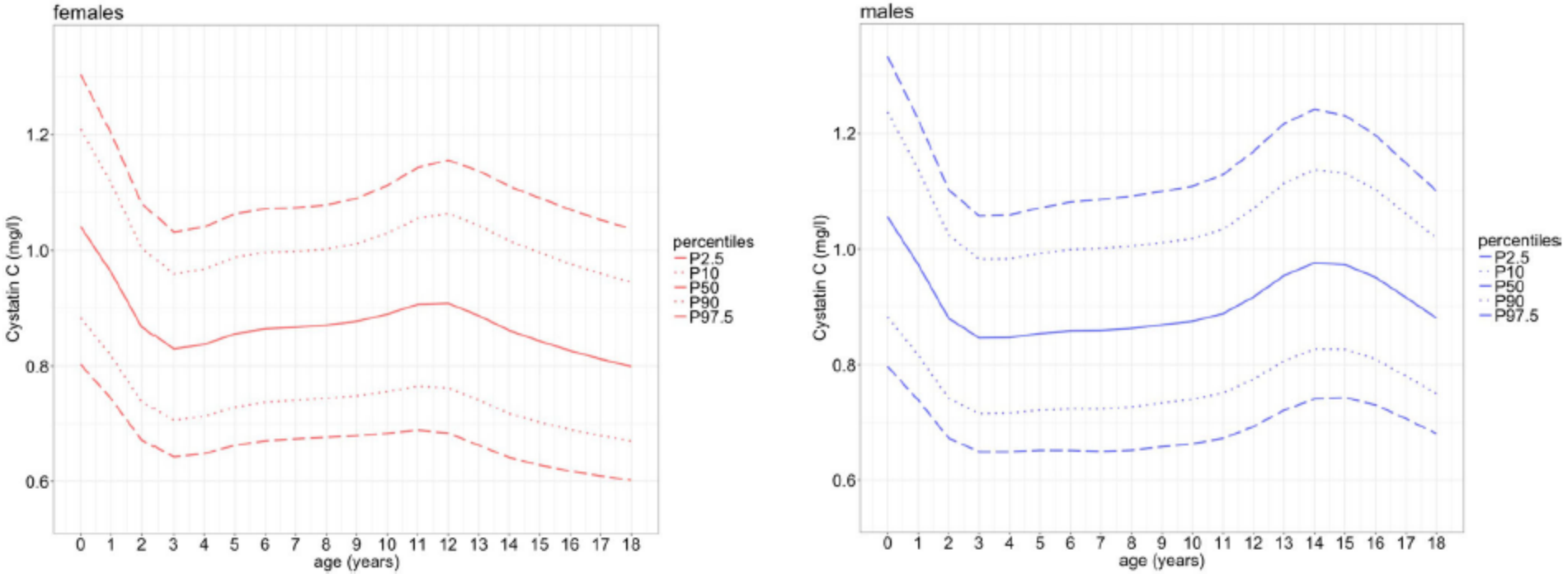


Fig. 3 Percentiles of cystatin C and its effector variable age for 0- to 18-year-old children of the LIFE Child cohort. Solid line = 50th percentile, dotted line = 10th and 90th percentile, dashed line = 2.5th and 97.5th percentile. P percentile. The percentiles were calculated using the ChildSDS package [37]. Note that just before the age of 12 years, the curves diverge and show different patterns for males and females thereafter. $n = 6217$ observations in 2803 participants

Viðmiðunargildi fyrir cystatin c. Vita að cystatin c er hentugt til þess að meta nýrnastarfsemi hjá einstaklingum með lítinn vöðvamassa (þegar serum kreatínín er ekki góður marker á nýrnastarfsemi).

Pediatr Nephrol. 2019; 34(3): 449–457

CLINICAL EPIDEMIOLOGY www.jasn.org

New Equations to Estimate GFR in Children with CKD

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eGFR = Ht (cm) x 36.5 mcmol/L)/SCr mcmol/L

J Am Soc Nephrol 20: 629–637, 2009. doi: 10.1681/ASN.2008030287

Direct measurement of kidney function (GFR)

- Isotope-labeled markers such as
  - ^{51}Cr-EDTA, ^{99}mTc-DTPA, and ^{125}Iiothalamate
  - and iohexol, a nonradioactive low-osmolar contrast agent widely used in clinical laboratories.
  - Unit: mL/min./1.73m^2

Helstu aðferðir til þess að mæla nýrnastarfsemi

Normal kidney function by age

Age (years)	^{51}Cr-EDTA clearance, mL/min/1.73m^2 (mean and SD
≤ 0.1	52.0 ± 9.0
0.1 - 0.3	61.7 ± 14.3
0.3 - 0.7	71.7 ± 13.9
0.7 – 1	82.6 ± 17.3
1.0 - 1.5	91.5 ± 17.8
1.5 - 2.0	94.5 ± 18.1
> 2.0	104.4 ± 19.9

Piepsz, A., Tondeur, M., & Ham, H. (2006). Revisiting normal (51)Cr-ethylenediaminetetraacetic acid clearance values in children. Eur J Nucl Med Mol Imaging, 33(12), 1477

Clinical characteristics

Causes of CKD in children by presenting clinical and laboratory features

Hypoplastic and dysplastic nephropathies often present with fluid and electrolyte losses and growth failure.

Glomerulopathies typically present with hypertension, hematuria (microscopic, macroscopic), edema and oligo-anuria.

Tubular and Interstitial Nephropathies may present with loss of electrolytes (hypokalemia, hypophosphatemia), polyuria, polydipsia, urinary concentrating difficulties, enuresis and metabolic acidosis.

Proteinuria

Evaluation

- Proteinuria is a hallmark of kidney disease.
- Measurement of urine protein content plays a central role in any diagnostic work-up for kidney disease.

Normal urinary protein excretion

- Normal urinary protein excretion is <240 mg/m^2/day in children <6 months of age and <150 mg/m^2/day in older children
  - Uromodulin secreted by the renal tubules makes up close to 50% of renal protein excretion
  - Approximately 30–40% is albumin
  - Filtered low molecular weight (LMW) plasma proteins, such as beta-2-microglobulin and retinol-binding protein, account for the remaining 10–20%.

Proteinuria assessment

- Standard urine dipstick analysis primarily detects albumin but not tubular and/or overflow proteinuria.
- trace = <300 mg/L
- 1+ = 300 to <1000 mg/L
- 2+ = 1–3 g/L
- 3+ = 3–20 g/L
- 4+ = >20 g/L

Proteinuria assessment

- Urinary albumin excretion of:
  - <30 mg/24 h (albumin-to-creatinine ratio (ACR)) of <3 mg/mmol is normal
  - 30–300 mg/24 h (ACR,3–30 mg/mmol) represents a moderate increase
  - >300 mg/24 h (ACR, >30 mg/mmol) is severely increased

Til upplýsingar, þarf ekki að kunna

Physiological proteinuria

- Orthostatic proteinuria
- Febrile proteinuria
- Exercise proteinuria
  - In all these situations, proteinuria is transient and absent when tested in a first morning urine sample collected directly after getting up, after recovery from the febrile condition, or after recovery from strenuous exercise, respectively.

Þekkja helstu orsakir “physiologic proteinuria”

Pathologic/abnormal proteinuria

- Increased glomerular membrane permeability (glomerular proteinuria)
  - albuminuria
- Reduced tubular reabsorption of LMW weight proteins (tubular proteinuria)
- Increased filtered LMW protein load exceeding the tubular reabsorptive capacity (overflow proteinuria)

Þekkja helstu orsakir “pathologic proteinuria”

Management of proteinuria/albuminuria

- Treatment of underlying disease
- ACE/ARB
  - May reduce rate of CKD progression

Anemia

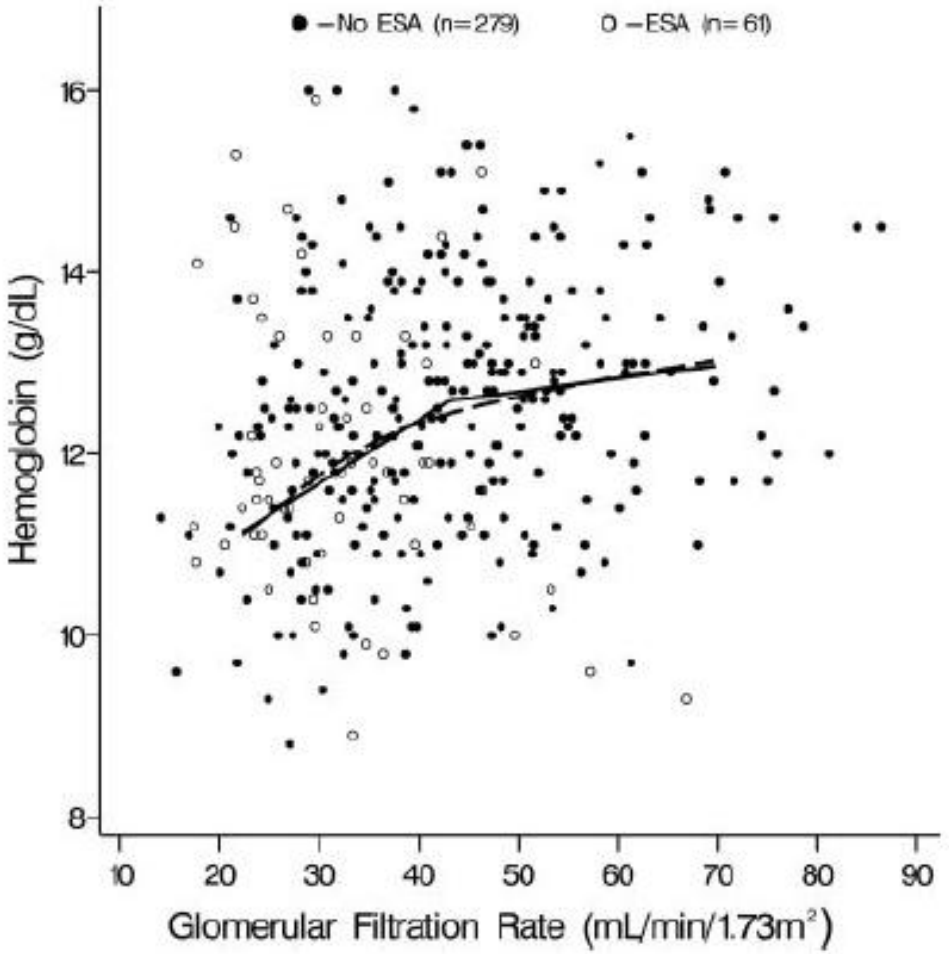

Figure 1. Hemoglobin *versus* GFR in children with chronic kidney disease (CKD): Linear threshold model (solid line) and nonparametric smoothing model (dashed line) describing relationship of hemoglobin concentration and GFR in 340 pediatric patients with CKD.

Fadrowski JJ, et al (2008) Clin J Am Soc Nephrol 3 (2):457–462

Definition of anemia in children with CKD

- According to the 2012 KDOQI recommendations, the diagnosis of anemia should be made in children with CKD when Hgb concentration is
- <110 g/L) in children 0.5–5 years,
- <115 g/L) in children 5–12 years,
- <120 g/L) in children 12–15 years, and
- <130 g/L in males and <120 g/L in females >15 years of age

- The anemia is normocytic with an inappropriately decreased reticulocyte count.

Evaluation of anemia in CKD

- A complete blood count (CBC), which should include Hgb concentration, red cell indices, white blood cell count and differential, and platelet count
- Absolute reticulocyte count
- Serum ferritin concentration (aim for >100 ng/mL)
- Serum iron and total iron-binding capacity,
- Transferrin saturation (should aim for >20%)
- Serum vitamin B12 and folate levels.

Pediatric Nephrology
DOI 10.1007/978-3-642-27843-3_59-1

Management of Chronic Kidney Disease in Children

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Table 10 Common causes of anemia in chronic kidney disease

Erythropoietin deficiency
Iron deficiency
Dietary iron deficiency
Gastrointestinal loss, phlebotomy, menses
Poor absorption of enteral iron
Iron depletion from ESA use
Chronic inflammation
Complement activation from dialysis
Systemic inflammatory diseases (systemic lupus erythematosus, Wegener's granulomatosis, etc.)
Surgical procedures
Bone marrow suppression
Inhibitory factors
Hyperparathyroidism
Medications (immunosuppressive drugs)
Increased red cell turnover
Carnitine deficiency
Primary renal disease (hemolytic uremic syndrome)
Malnutrition
B12 or folate deficiency
Carnitine deficiency
Aluminum toxicity

Mechanism of anemia in CKD

- Anemia affects all patients with advanced CKD and is primarily caused by reduced erythropoietin production by the failing kidneys
- The erythrocyte life span is shortened in children with CKD
- Iron deficiency (frequent blood drawing)
- Hepcidin levels increased in CKD due to decreased kidney clearance
  - Hepcidin may be the key mediator in the inflammation-related iron-restricted erythropoiesis in patients with CKD, in effect causing a “functional iron deficiency.”
  - Preventing iron release from the reticuloendothelial system and limiting iron bioavailability

Treatment of anemia

- Correct identified causes of anemia
- Elemental iron 6 mg/kg/day if
  - Transferrin saturation <20% or Ferritin <100 ng/mL
  - And always prior to ESA treatment
- Erythropoietin-Stimulating Agents/ESA
  - NeoRecormon (rHuEPO; x 2-3 per week)
  - Aranesp (Darbepoetin-alfa/longer half-life)
- Avoid blood transfusions

Treatment of anemia

- Correct identified causes of anemia
- Elemental iron 6 mg/kg/day if (Ekki muna skammta)
  - Transferrin saturation <20% or Ferritin <100 ng/mL
  - And always prior to ESA treatment
- Erythropoietin-Stimulating Agents/ESA
  - NeoRecormon (rHuEPO; x 2-3 per week)
  - Aranesp (Darbepoetin-alfa/longer half-life)
- Avoid blood transfusions

Treatment of anemia

- The treatment of CKD was revolutionized in 1986 with the introduction of recombinant human erythropoietin (rHuEPO) therapy
- Studies in pediatric CKD patients have documented improvements in appetite, exercise tolerance, oxygen consumption, intelligence testing scores, and quality of life with the correction of anemia.
- Severe left ventricular hypertrophy has also been associated with low hemoglobin values
  - treatment of anemia has been associated with a significant reduction in left ventricular mass index

Metabolic acidosis

Metabolic acidosis

- The daily net acid production in individuals with normal kidney function is approximately
  - 1–3 mEq/kg body weight in infants,
  - 1 mEq/kg body weight in older children
  - Approximately 20–60 mEq in postpubertal children and adults

Metabolic acidosis

- When GFR falls below 25–50 mL/min/1.73 m^2 and the residual functional renal parenchyma can no longer generate enough bicarbonate to buffer endogenous acid load
- Increased anion gap acidosis is the predominant type in children with CKD although a significant proportion of affected individuals have the normal anion gap pattern.
- Consequences
  - Metabolic bone disease
  - Growth retardation in children
  - Acceleration of CKD progression

Kannast við þessar 3 afleiðingar metabolic acidosis í CKD hjá börnum

Þarf ekki að kunna, heldur vita af. sbr fyrri skyggnu.

Is low serum bicarbonate associated with CKD progression in children?

CJASN
Clinical Journal of American Society of Nephrology

Data from

CKiD Chronic Kidney Disease in Children Study

Children with Non glomerular disease
n - 603
Children with Glomerular disease
n - 255

Median Follow up Time:
Children with Non glomerular disease
4 years
Children with Glomerular disease
3 years

Non glomerular Disease

39% had HCO3 ≤ 22mEq/L

36% were treated with alkali Rx

Glomerular Disease

31% had HCO3 ≤ 22mEq/L

18% were treated with alkali Rx

Primary outcome

Composite of

50% ↓ in eGFR or Kidney Replacement Therapy (KRT)

Non glomerular Disease	Adjusted Hazard Ratios
HCO3 ≤ 18	1.28 (95%CI: 0.84, 1.94)
HCO3 19-22	0.91 (95%CI: 0.65, 1.26)
HCO3 > 22	Ref

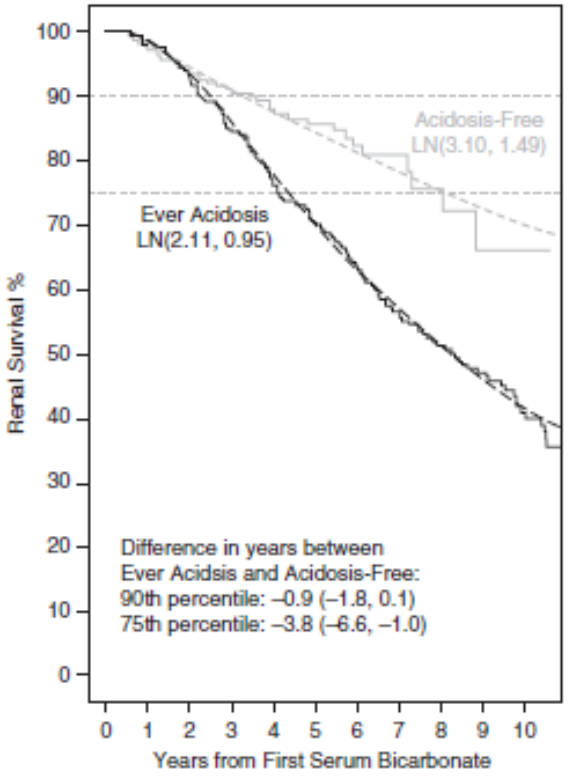
Glomerular Disease	
HCO3 ≤ 18	2.16 (95%CI: 1.05, 4.44)
HCO3 19-22	1.74 (95%CI: 1.07, 2.85)
HCO3 > 22	Ref

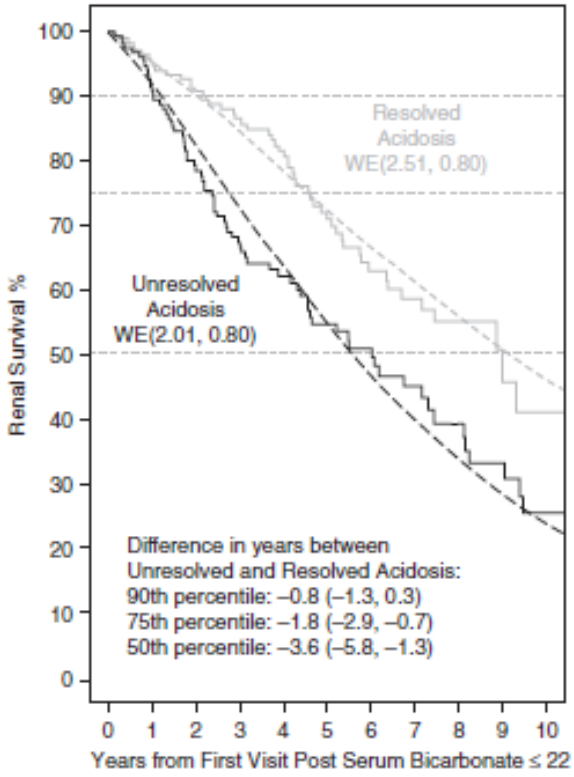
Conclusion: In children with glomerular disease, low bicarbonate was linked to a higher risk of CKD progression. Less than half of all children with low bicarbonate reported treatment with alkali therapy. Long-term studies of alkali therapy's effect in pediatric CKD are needed.

Denver D. Brown, Jennifer Roem, Derek K. Ng, Kimberly J. Reidy, et al. ***Low Serum Bicarbonate and CKD Progression in Children.*** CJASN doi: 10.2215/CJN.07060619. **Visual Abstract by Aakash Shingada, MD**

CJASN May 2020, CJN.07060619; DOI: https://doi.org/10.2215/CJN.07060619

50% decline in eGFR or KRT





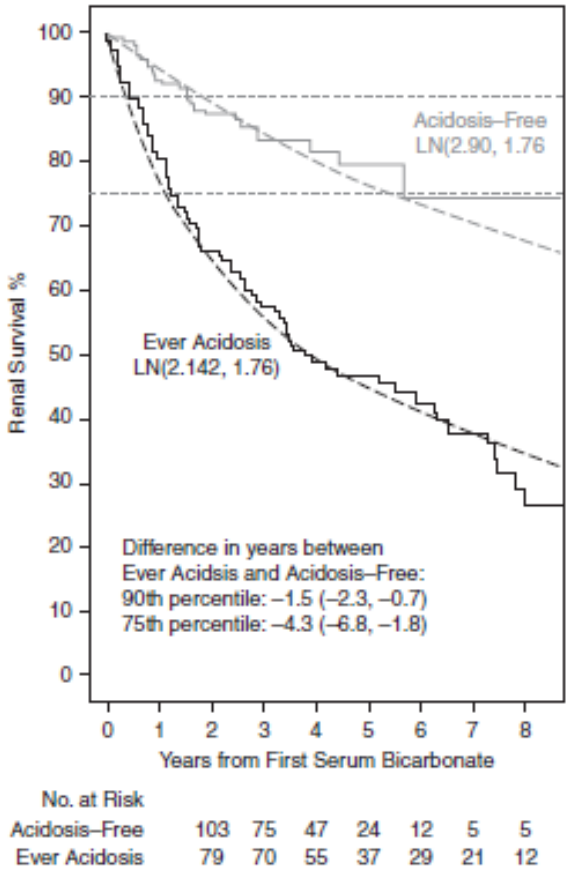
Þarf ekki að kunna, heldur vita af, acidosis veldur CKD progression.

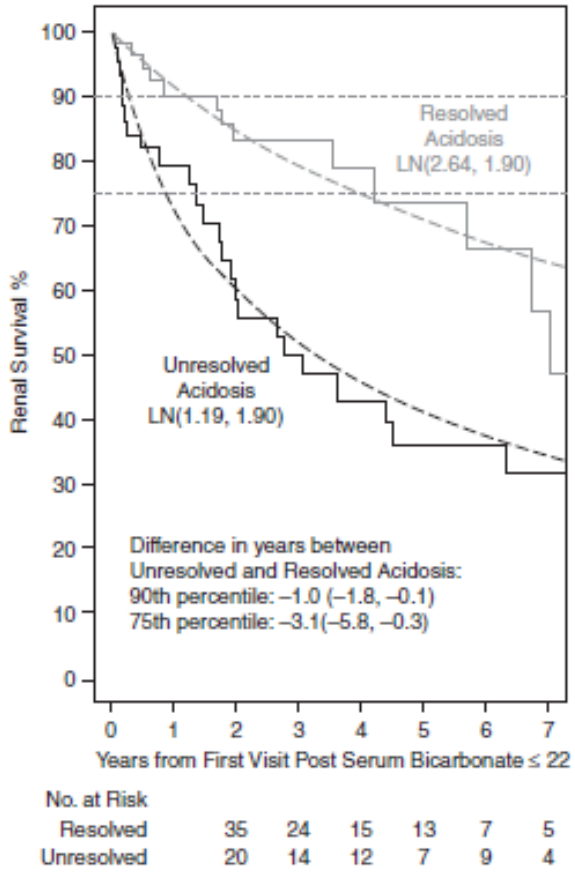
	Non-glomerular (n=603)		Non-glomerular, ever acidosis (n=338)	
	Never Acidosis (n=187)	Ever Acidosis (n=416)	Resolved (n=188)	Unresolved (n=150)
Composite outcome, n (%)	39 (21)	151 (36)	53 (28)	74 (49)
50% reduction in eGFR	10 (26)	48 (32)	13 (25)	26 (35)
Kidney replacement therapy	29 (74)	103 (68)	40 (75)	48 (65)

Figure 1. | Survival time to 50% decline in eGFR or KRT (transplant or dialysis) by "ever acidosis" following the first bicarbonate measurement among 603 participants with non-glomerular disease (left). Event-free time by acidosis persistence following the first visit after participants become acidotic among 338 participants with non-glomerular disease who were ever acidotic (right). Parametric Weibull or Lognormal distributions for each group with location (β) and scale (σ) and denoted as WE(β, σ) or LN(β, σ), respectively, are shown by dashed lines. Percentiles provided due to differences in the proportion of participants who reached the composite event. The relative percentile measure of association summarizes the difference in time (years) for the p^{th} percentile of the exposed group (*e.g.*, those with acidosis) compared to the unexposed group (*e.g.*, those without acidosis).

CJASN May 2020, CJN.07060619; DOI: https://doi.org/10.2215/CJN.07060619

50% decline in eGFR or KRT





Þarf ekki að kunna, heldur vita af, acidosis veldur CKD progression.

	Glomerular (n=255)		Glomerular, ever acidosis (n=105)	
	Never Acidosis (n=108)	Ever Acidosis (n=147)	Resolved (n=55)	Unresolved (n=50)
Composite outcome, n (%)	26 (24)	64 (44)	13 (24)	24 (48)
50% reduction in eGFR	16 (62)	20 (31)	6 (46)	9 (38)
Kidney replacement therapy	10 (38)	44 (69)	7 (54)	15 (62)

Figure 2. | Survival time to 50% decline in eGFR or KRT (transplant or dialysis) by "ever acidosis" following the first bicarbonate measurement among 255 participants with glomerular disease (left). Event-free time by acidosis persistence following the first visit after participants become acidotic among 105 participants with glomerular disease who were ever acidotic (right). Parametric Lognormal distributions for each group with location (β) and scale (σ) and denoted as LN(β, σ) are represented by dashed lines. Percentiles provided due to differences in the proportion of participants who reached the composite event. The relative percentile measure of association summarizes the difference in time (years) for the p^{th} percentile of the exposed group (*e.g.*, those with acidosis) compared to the unexposed group (*e.g.*, those without acidosis).

CJASN May 2020, CJN.07060619; DOI: https://doi.org/10.2215/CJN.07060619

Metabolic acidosis - Treatment

- The goal of alkali therapy in children with CKD is to maintain serum bicarbonate ≥22 mEq/L
  - Calculate and replace deficit
    - Bicarb distribution volume = 0,5 L/kg body weight
    - 10 kg child = 5 L
  - Provide maintenance
    - 1-3 mmol/kg/day
  - Replace ongoing losses
- Sodium bicarbonate
- Sodium/Potassium citrate (2 mmol alkali/mL)

CKD-MBD

Chronic kidney disease mineral and bone disorder

- Defined as a systemic disorder of mineral and bone metabolism associated with CKD manifested by either one or more of the following factors:
  - abnormalities in phosphorus, calcium, vitamin D, and parathyroid hormone (PTH) metabolism;
  - abnormal bone histology, reduced skeletal strength, and retardation of linear growth;
  - and (3) vascular and other soft tissue calcifications

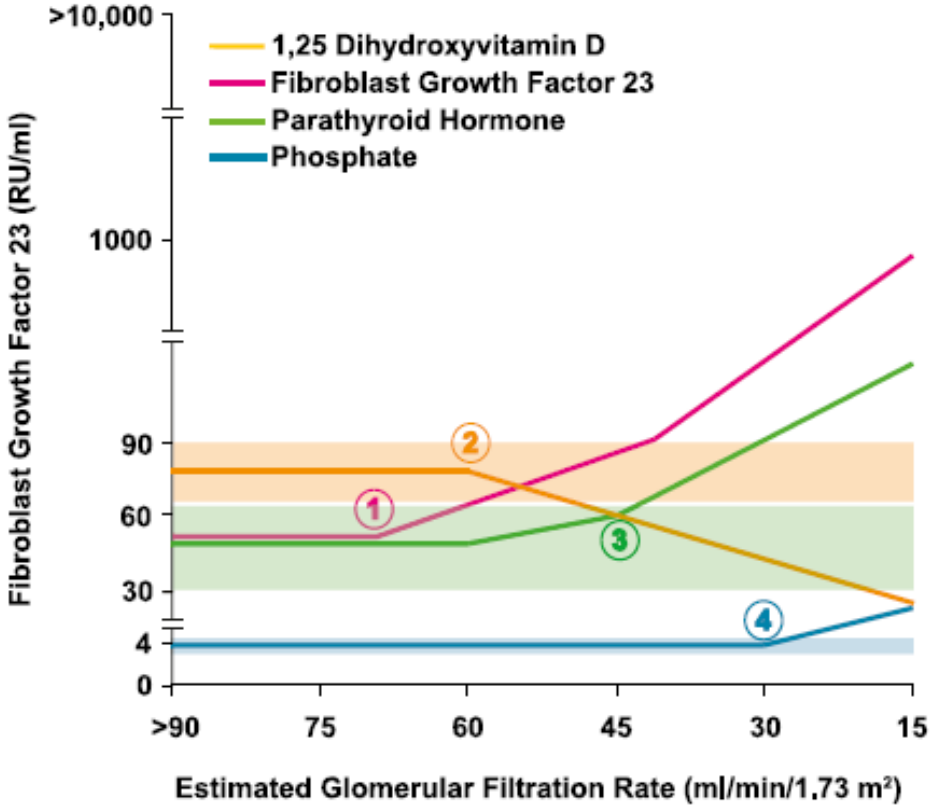


Figure 2. Biochemical phenotype of disordered mineral metabolism in CKD. The graph summarizes evolution of abnormal mineral metabolism along the spectrum of CKD. Depicted values are based on published literature. The *x*-axis represents glomerular filtration. The *y*-axis represents circulating levels of individual analytes with temporal changes in and normal ranges of FGF23 shown in red, 1,25 dihydroxyvitamin D (1,25D) shown in purple, parathyroid hormone (PTH) shown in green, and phosphate shown in blue. Elevated FGF23 is the earliest alteration in mineral metabolism in CKD (1). Elevations in FGF23 levels cause the early decline in 1,25D levels (2) that leads to secondary hyperparathyroidism (3). All of these changes occur prior to elevations in serum phosphate levels (4). This figure is reproduced from Wolf,[102] with permission from the American Society of Nephrology.

Treatment of CKD-MBD in patients with CKD G3a–G5D

- Patients with levels of intact PTH progressively rising or persistently above the upper normal limit for the assay must be evaluated for modifiable factors, including hyperphosphatemia, hypocalcemia, high phosphate intake, and vitamin D deficiency.
  - Should be guided by serial assessments of phosphate, calcium, and PTH levels, considered together.
  - Elevated phosphate levels should be lowered toward the normal range by a) reduced dietary intake; b) administration of phosphate binders
  - In children, maintain serum calcium in the age appropriate normal range.

Growth - nutrition

Growth failure in CKD

- Short stature is a major complication in children with reduced kidney function
  - In the first 2 years of life, malnutrition (protein and calories) is a major factor contributing to the growth failure
  - Perturbations of the GH/insulin-like growth factor axis predominate in older children
  - Other factors
    - Acid-base and electrolyte disorders.

Pediatric Nephrology (2020) 35:519–531
https://doi.org/10.1007/s00467-019-04426-0

GUIDELINES

Energy and protein requirements for children with CKD stages 2-5 and on dialysis–clinical practice recommendations from the Pediatric Renal Nutrition Taskforce

Til upplýsinga, þurfið ekki að kunna

Vanessa Shaw[1,2] · Nonnie Polderman[3] · José Renken-Terhaerdt[4] · Fabio Paglialonga[5] · Michiel Oosterveld[6] · Jetta Tuokkola[7] · Caroline Anderson[8] · An Desloovere[9] · Laurence Greenbaum[10] · Dieter Haffner[11] · Christina Nelms[12] · Leila Qizalbash[13] · Johan Vande Walle[9] · Bradley Warady[14] · Rukshana Shroff[15,16] · Lesley Rees[15,16]

Table 1 Energy and protein requirements for infants, children and adolescents with CKD2–5D aged 0–18 years

SDI for energy and protein: birth[a] to 18 years				
Month	SDI[b] energy (kcal/kg/day)	SDI protein (g/kg/day)	SDI protein (g/day)	
0	93–107	1.52–2.5	8–12	
1	93–120	1.52–1.8	8–12	
2	93–120	1.4–1.52	8–12	
3	82–98	1.4–1.52	8–12	
4	82–98	1.3–1.52	9–13	
5	72–82	1.3–1.52	9–13	
6–9	72–82	1.1–1.3	9–14	
10–11	72–82	1.1–1.3	9–15	
12	72–120	0.9–1.14	11–14	
Year	SDI energy (kcal/kg/day)		SDI protein (g/kg/day)	SDI protein (g/day)
–	Male	Female		
2	81–95[c]	79–92[c]	0.9–1.05	11–15
3	80–82	76–77	0.9–1.05	13–15
4–6	67–93	64–90	0.85–0.95	16–22
7–8	60–77	56–75	0.9–0.95	19–28
9–10	55–69	49–63	0.9–0.95	26–40
11–12	48–63	43–57	0.9–0.95	34–42
13–14	44–63	39–50	0.8–0.9	34–50
15–17	40–55	36–46	0.8–0.9	Male: 52–65 Female: 45–49

Pediatric Nephrology (2020) 35:519–531
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GUIDELINES

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Til upplýsinga, þurfið ekki að kunna

Table 2 Suggested addition of energy modules to formulas

Energy module	Age	Amount of CHO/fat module added to formula	Final concentration of CHO/fat in formula (% or g/100 mL)
Glucose polymer	< 6 months	3–5 g (+ 7 g CHO from infant formula[a])	10–12
	6 months–1 year	5–8 g (+ 7 g CHO from infant formula[a])	12–15
	> 1 year	8–18 g (+ 12 g CHO from pediatric formula[a])	20–30
Fat emulsion (50% fat content)	< 1 year	3–5 ml (+ 3.5 g fat from infant formula[a])	5–6
	> 1 year	9 ml (+ 4.5 g fat from pediatric formula[a])	9

Adapted from Shaw V (ed) *Clinical Paediatric Dietetics*, 4th edition (2015). Chichester: Wiley Blackwell, page 18

CHO carbohydrate

[a] CHO and fat contents of formulas vary

hGH resistance in children with CKD

- In healthy children the binding of hGH to the GH receptor results in the synthesis of insulin-like growth factor 1 (IGF-1) which mediates its peripheral activity
- In CKD there is resistance to GH as there is poor growth in association with normal or high GH levels and decreased IGF-1 bioactivity.
  - Resistance to hGH caused by increased serum concentrations of IGF-binding proteins, which concentration is inversely correlated to GFR
  - Metabolic acidosis reduces hGH secretion and action

Growth in children with chronic kidney disease: a report from the Chronic Kidney Disease in Children Study

Nancy M. Rodig · Kelly C. McDermott · Michael F. Schneider · Hilary M. Hotchkiss · Ora Yadin · Mouin G. Seikaly · Susan L. Furth · Bradley A. Warady

Table 2 Median and interquartile range of baseline age–sex-specific height SDS by sex and eight different age strata among 799 CKiD study participants

Age (years)	Males (*N*=505)		Females (*N*=294)	
	N (%)	Height SDS (IQR)	*N* (%)	Height SDS (IQR)
1 to <3	28 (6)	−0.71 (−1.46 to −0.21)	15 (5)	−0.63 (−1.42 to 0.13)
3 to <5	54 (11)	−0.75 (−1.48 to −0.03)	17 (6)	−0.28 (−1.25 to 0.16)
5 to <7	44 (9)	−0.56 (−1.42 to 0.04)	26 (9)	−1.16 (−1.82 to −0.68)
7 to <9	64 (13)	−0.57 (−1.50 to 0.29)	37 (13)	−0.83 (−1.31 to −0.26)
9 –to<11	67 (13)	−0.36 (−1.18 to 0.32)	47 (16)	−0.78 (−1.63 to −0.05)
11 to <13	65 (13)	−0.59 (−1.31 to 0.06)	39 (13)	−0.76 (−1.67 to 0.76)
13 to <15	78 (15)	−0.26 (−1.18 to 0.69)	50 (17)	−0.63 (−1.65 to 0.17)
15 to <18	105 (21)	−0.36 (−1.00 to 0.25)	63 (21)	−0.31 (−1.06 to 0.47)
Overall	505 (100)	−0.49 (−1.30 to 0.24)	294 (100)	−0.68 (−1.46 to 0.13)

CKiD study, Chronic Kidney Disease in Children study

Lengdarvöxtur mjög skertur hjá börnum með langt genginn CKD

Vaxtarhormón virkar mjög vel hjá börnum með CKD

EFFECT OF GROWTH HORMONE TREATMENT ON THE ADULT HEIGHT OF CHILDREN WITH CHRONIC RENAL FAILURE

DIETER HAFFNER, M.D., FRANZ SCHAEFER, M.D., RICHARD NISSEL, M.D., ELKE WÜHL, M.D., BURKHARD TÖNSHOFF, M.D., AND OTTO MEHLS, M.D., FOR THE GERMAN STUDY GROUP FOR GROWTH HORMONE TREATMENT IN CHRONIC RENAL FAILURE*

EFFECT OF GROWTH HORMONE TREATMENT ON THE ADULT HEIGHT OF CHILDREN WITH CHRONIC RENAL FAILURE

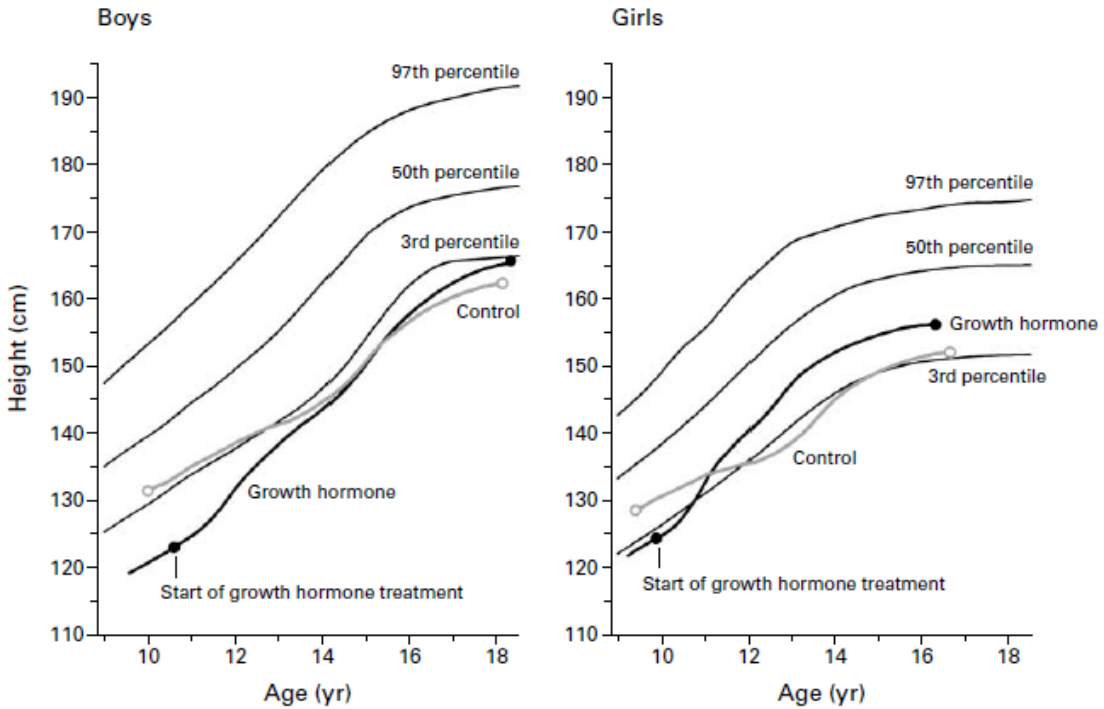

Figure 2. Synchronized Mean Growth Curves during Growth Hormone Treatment for 38 Children (32 Boys and 6 Girls) with Chronic Renal Failure, as Compared with 50 Control Children with Chronic Renal Failure Not Treated with Growth Hormone, According to Sex.

Normal values are indicated by the 3rd, 50th, and 97th percentiles. The circles indicate the time of the first observation (the start of growth hormone treatment in the treated children) and the end of the pubertal growth spurt.

N Engl J Med 2000; 343:923-930

EFFECT OF GROWTH HORMONE TREATMENT ON THE ADULT HEIGHT OF CHILDREN WITH CHRONIC RENAL FAILURE

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The New England Journal of Medicine

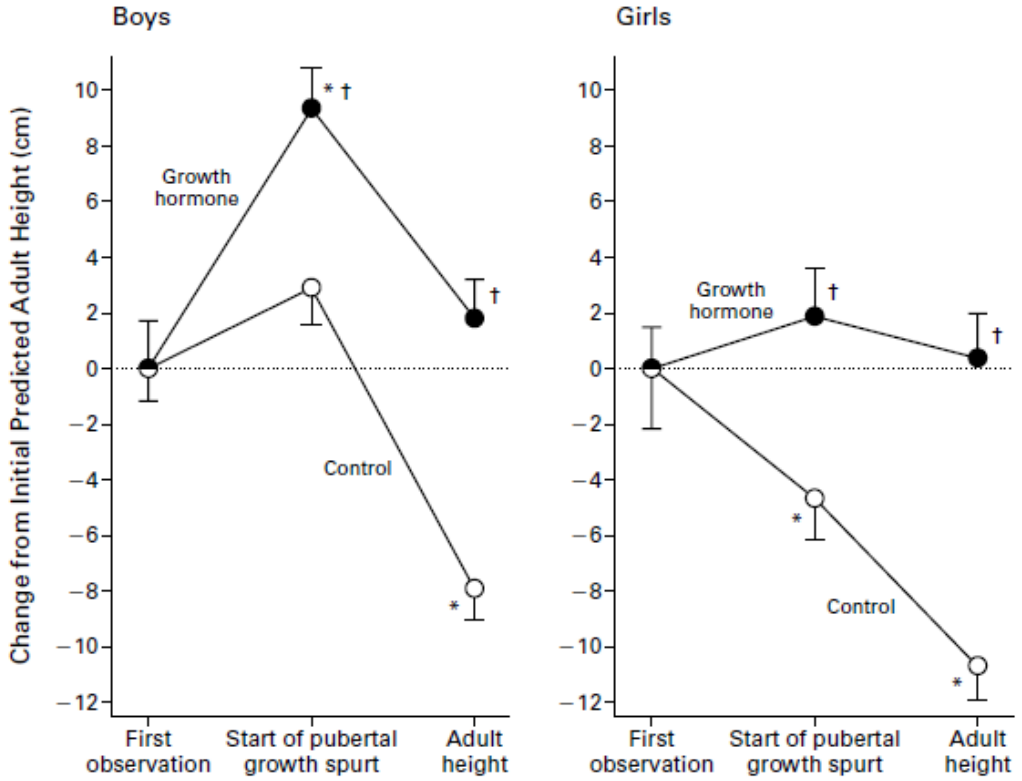

Figure 3. Change from Initially Predicted Adult Height at Base Line in 38 Children (32 Boys and 6 Girls) with Chronic Renal Failure Who Received Growth Hormone Treatment, as Compared with 50 Control Children with Chronic Renal Failure Who Did Not Receive Growth Hormone, According to Sex.

Values are means ±SD. Asterisks indicate significant differences from the previous period ($P<0.001$), and daggers significant differences from the children who were not treated with growth hormone ($P<0.001$).

Vaxtarhormón virkar mjög vel hjá börnum með CKD

N Engl J Med 2000; 343:923-930

Hypertension

Definition of Hypertension (1-18 years of age)

	Age < 13 years (for age, sex and height)	Age ≥ 13 years*
Normal BP	< 90th %	< 120 / < 80
Elevated BP	≥ 90th and < 95th %	120 to 129 / < 80
Hypertension	≥ 95th %	≥ 130 / 80
Stage 1	≥ 95th and < 95th % + 12 mm Hg	130 – 139 / 80 – 89
Stage 2	≥ 95th + 12 mm Hg	≥ 140 / 90

*An examination of the new pediatric BP tables (excluded those with BMI ≥ 85th %tile) indicates that the 90th percentile for adolescents ≥13 years of age was close to a systolic BP of 120 mm Hg and diastolic BP of 80 mm Hg. Also, the 95th percentile in adolescents ≥13 years of age approximates 130 mm Hg. These definitions interface with the 2017 AHA guidelines.

To cite: Flynn JT, Kaelber DC, Baker-Smith CM, et al. Clinica Practice Guideline for Screening and Management of Hig Blood Pressure in Children and Adolescents. *Pediatrics* 2017;140(3):e20171904

How do we defince childhood hypertension?

- Age, gender and height specific blood pressure reference values, now widely used for the diagnosis of childhood hypertension, both in the clinic and scientific research.
- The reference values (blood pressure percentiles) are based on the normative distribution of 60,000 single BP measurements in healthy children.
  - Overweight children now excluded from the normative data set

Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents

Joseph T. Flynn, MD, MS, FAAP,[a] David C. Kaelber, MD, PhD, MPH, FAAP, FACP, FACMI,[b] Carissa M. Baker-Smith, MD, MS, MPH, FAAP, FAHA,[c] Douglas Blowey, MD,[d] Aaron E. Carroll, MD, MS, FAAP,[e] Stephen R. Daniels, MD, PhD, FAAP,[f] Sarah D. de Ferranti, MD, MPH, FAAP,[g] Janis M. Dionne, MD, FRCPC,[h] Bonita Falkner, MD,[i] Susan K. Flinn, MA,[j] Samuel S. Gidding, MD,[k] Celeste Goodwin,[l] Michael G. Leu, MD, MS, MHS, FAAP,[m] Makia E. Powers, MD, MPH, FAAP,[n] Corinna Rea, MD, MPH, FAAP,[o] Joshua Samuels, MD, MPH, FAAP,[p] Madeline Simasek, MD, MSCP, FAAP,[q] Vidhu V. Thaker, MD, FAAP,[r] Elaine M. Urbina, MD, MS, FAAP,[s] SUBCOMMITTEE ON SCREENING AND MANAGEMENT OF HIGH BLOOD PRESSURE IN CHILDREN

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Til upplýsingar, alls ekki að kunna utanað, skilgreining á háþrýstingi breytileg eftir aldri, kyni og hæð, sjá nánar í fyrirlestri um háþrýsting.

TABLE 5 BP Levels for Girls by Age and Height Percentile

Age (y)	BP Percentile	SBP (mm Hg)							DBP (mm Hg)						
		Height Percentile or Measured Height							Height Percentile or Measured Height						
		5%	10%	25%	50%	75%	90%	95%	5%	10%	25%	50%	75%	90%	95%
1	Height (in)	29.7	30.2	30.9	31.8	32.7	33.4	33.9	29.7	30.2	30.9	31.8	32.7	33.4	33.9
	Height (cm)	75.4	76.6	78.6	80.8	83	84.9	86.1	75.4	76.6	78.6	80.8	83	84.9	86.1
	50th	84	85	86	86	87	88	88	41	42	42	43	44	45	46
	90th	98	99	99	100	101	102	102	54	55	56	56	57	58	58
	95th	101	102	102	103	104	105	105	59	59	60	60	61	62	62
	95th + 12 mm Hg	113	114	114	115	116	117	117	71	71	72	72	73	74	74
2	Height (in)	33.4	34	34.9	35.9	36.9	37.8	38.4	33.4	34	34.9	35.9	36.9	37.8	38.4
	Height (cm)	84.9	86.3	88.6	91.1	93.7	96	97.4	84.9	86.3	88.6	91.1	93.7	96	97.4
	50th	87	87	88	89	90	91	91	45	46	47	48	49	50	51
	90th	101	101	102	103	104	105	106	58	58	59	60	61	62	62
	95th	104	105	106	106	107	108	109	62	63	63	64	65	66	66
	95th + 12 mm Hg	116	117	118	118	119	120	121	74	75	75	76	77	78	78
3	Height (in)	35.8	36.4	37.3	38.4	39.6	40.6	41.2	35.8	36.4	37.3	38.4	39.6	40.6	41.2
	Height (cm)	91	92.4	94.9	97.6	100.5	103.1	104.6	91	92.4	94.9	97.6	100.5	103.1	104.6
	50th	88	89	89	90	91	92	93	48	48	49	50	51	53	53
	90th	102	103	104	104	105	106	107	60	61	61	62	63	64	65
	95th	106	106	107	108	109	110	110	64	65	65	66	67	68	69
	95th + 12 mm Hg	118	118	119	120	121	122	122	76	77	77	78	79	80	81
4	Height (in)	38.3	38.9	39.9	41.1	42.4	43.5	44.2	38.3	38.9	39.9	41.1	42.4	43.5	44.2
	Height (cm)	97.2	98.8	101.4	104.5	107.6	110.5	112.2	97.2	98.8	101.4	104.5	107.6	110.5	112.2
	50th	89	90	91	92	93	94	94	50	51	51	53	54	55	55
	90th	103	104	105	106	107	108	108	62	63	64	65	66	67	67
	95th	107	108	109	109	110	111	112	66	67	68	69	70	70	71
	95th + 12 mm Hg	119	120	121	121	122	123	124	78	79	80	81	82	82	83

TABLE 5 BP Levels for Girls by Age and Height Percentile

Age (y)	BP Percentile	SBP (mm Hg)						
		Height Percentile or Measured Height						
		5%	10%	25%	50%	75%	90%	95%
1	Height (in)	29.7	30.2	30.9	31.8	32.7	33.4	33.9
	Height (cm)	75.4	76.6	78.6	80.8	83	84.9	86.1
	50th	84	85	86	86	87	88	88
	90th	98	99	99	100	101	102	102
	95th	101	102	102	103	104	105	105
	95th + 12 mm Hg	113	114	114	115	116	117	117
2	Height (in)	33.4	34	34.9	35.9	36.9	37.8	38.4
	Height (cm)	84.9	86.3	88.6	91.1	93.7	96	97.4
	50th	87	87	88	89	90	91	91
	90th	101	101	102	103	104	105	106
	95th	104	105	106	106	107	108	109
	95th + 12 mm Hg	116	117	118	118	119	120	121
3	Height (in)	35.8	36.4	37.3	38.4	39.6	40.6	41.2
	Height (cm)	91	92.4	94.9	97.6	100.5	103.1	104.6
	50th	88	89	89	90	91	92	93
	90th	102	103	104	104	105	106	107
	95th	106	106	107	108	109	110	110
	95th + 12 mm Hg	118	118	119	120	121	122	122
4	Height (in)	38.3	38.9	39.9	41.1	42.4	43.5	44.2
	Height (cm)	97.2	98.8	101.4	104.5	107.6	110.5	112.2
	50th	89	90	91	92	93	94	94
	90th	103	104	105	106	107	108	108
	95th	107	108	109	109	110	111	112
	95th + 12 mm Hg	119	120	121	121	122	123	124
5	Height (in)	40.8	41.5	42.6	43.9	45.2	46.5	47.3
	Height (cm)	103.6	105.3	108.2	111.5	114.9	118.1	120
	50th	90	91	92	93	94	95	96
	90th	104	105	106	107	108	109	110
	95th	108	109	109	110	111	112	113
	95th + 12 mm Hg	120	121	121	122	123	124	125

Til upplýsingar, alls ekki að kunna utanað, skilgreining á háþrýstingi breytileg eftir aldri, kyni og hæð, sjá nánar í fyrirlestri um háþrýsting.

Blood pressure control and progression of renal disease

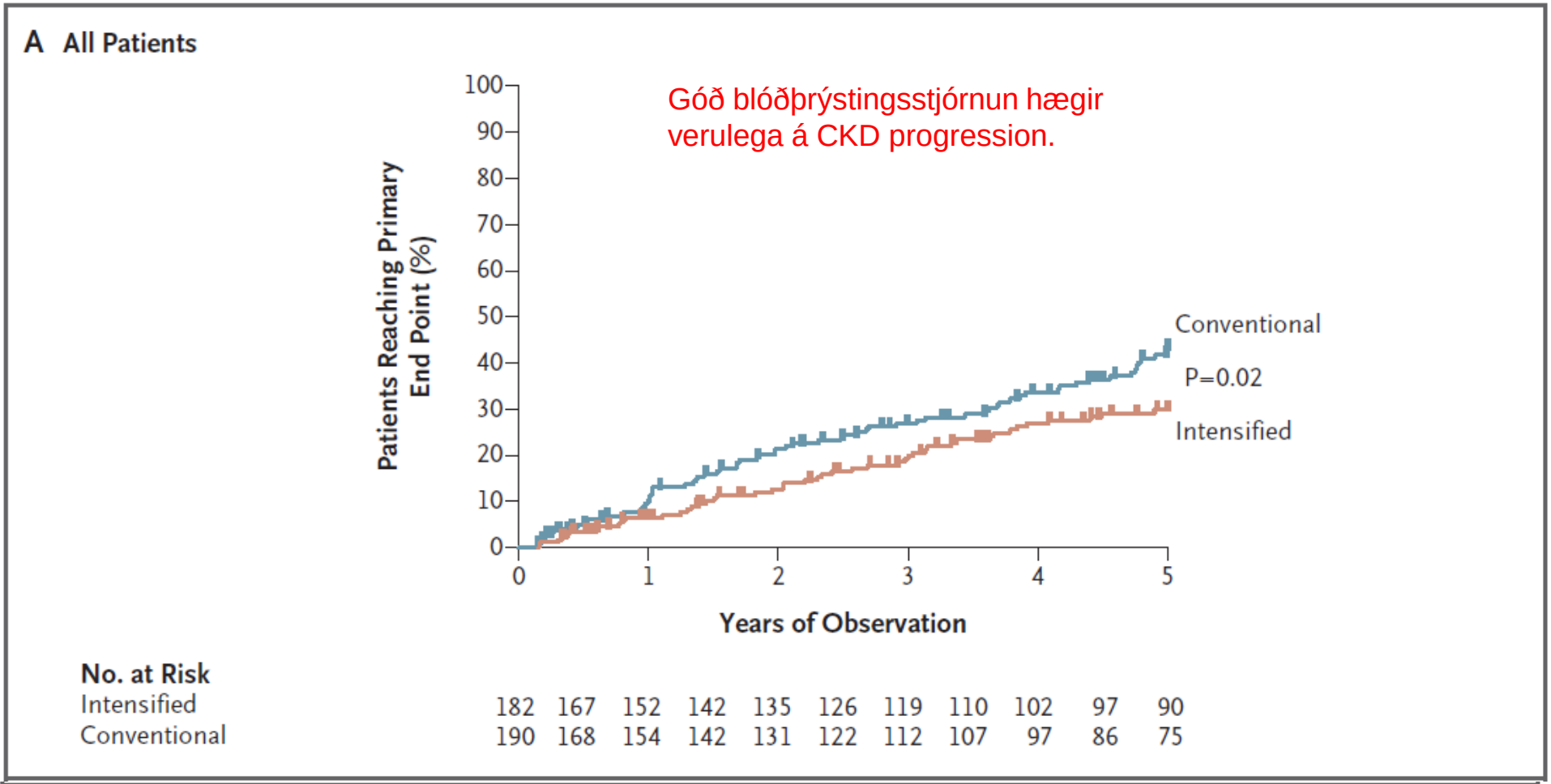


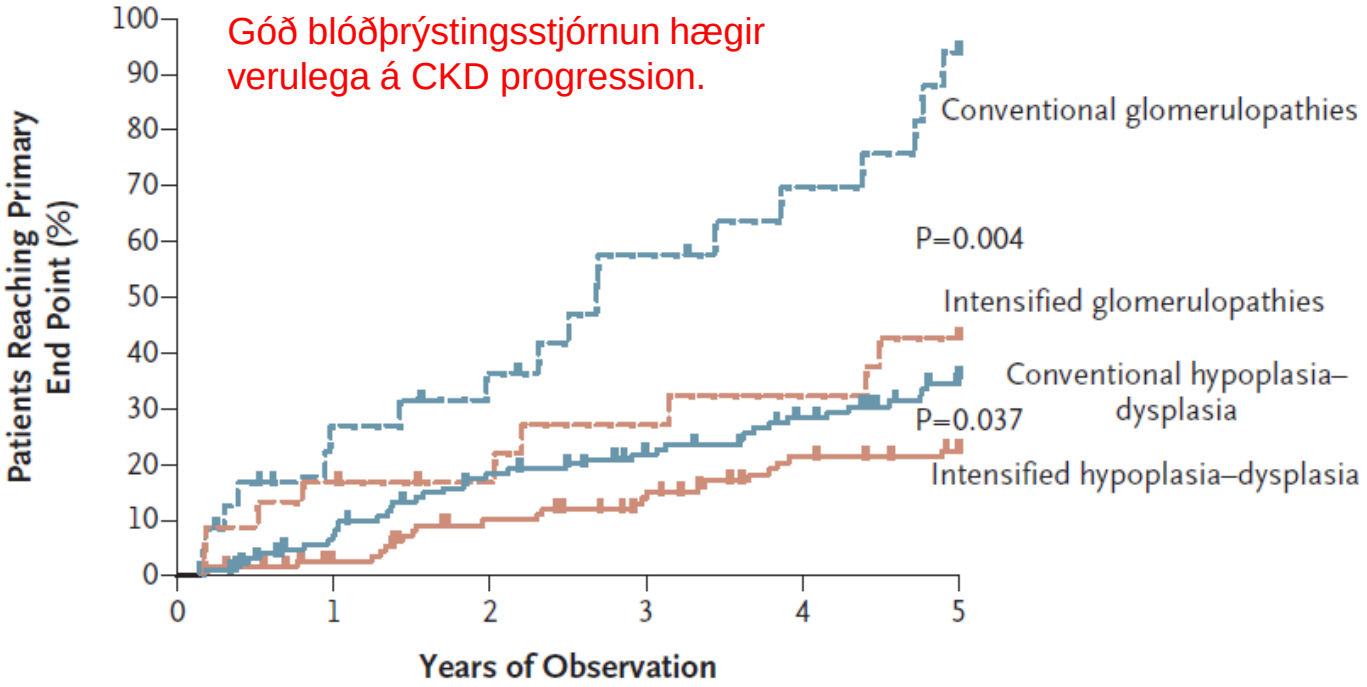
Figure 2. Progression of Renal Disease, According to Blood-Pressure–Control Group.

The cumulative probability of reaching the primary composite end point of a 50% decline in the glomerular filtration rate or progression to end-stage renal disease is shown for all patients (Panel A) and for patients with renal hypoplasia–dysplasia or glomerulopathies (Panel B).

Wuhl E et al. N Engl J Med, 2009

Blood pressure control and progression of renal disease

B Glomerulopathies or Hypoplasia–Dysplasia



No. at Risk

Intensified glomerulopathies	28	21	19	18	17	15	15	14	14	12	12
Conventional glomerulopathies	24	20	16	15	13	11	8	6	5	4	1
Intensified hypoplasia–dysplasia	125	118	112	102	97	93	88	81	76	74	71
Conventional hypoplasia–dysplasia	139	127	116	108	101	98	91	88	78	70	63

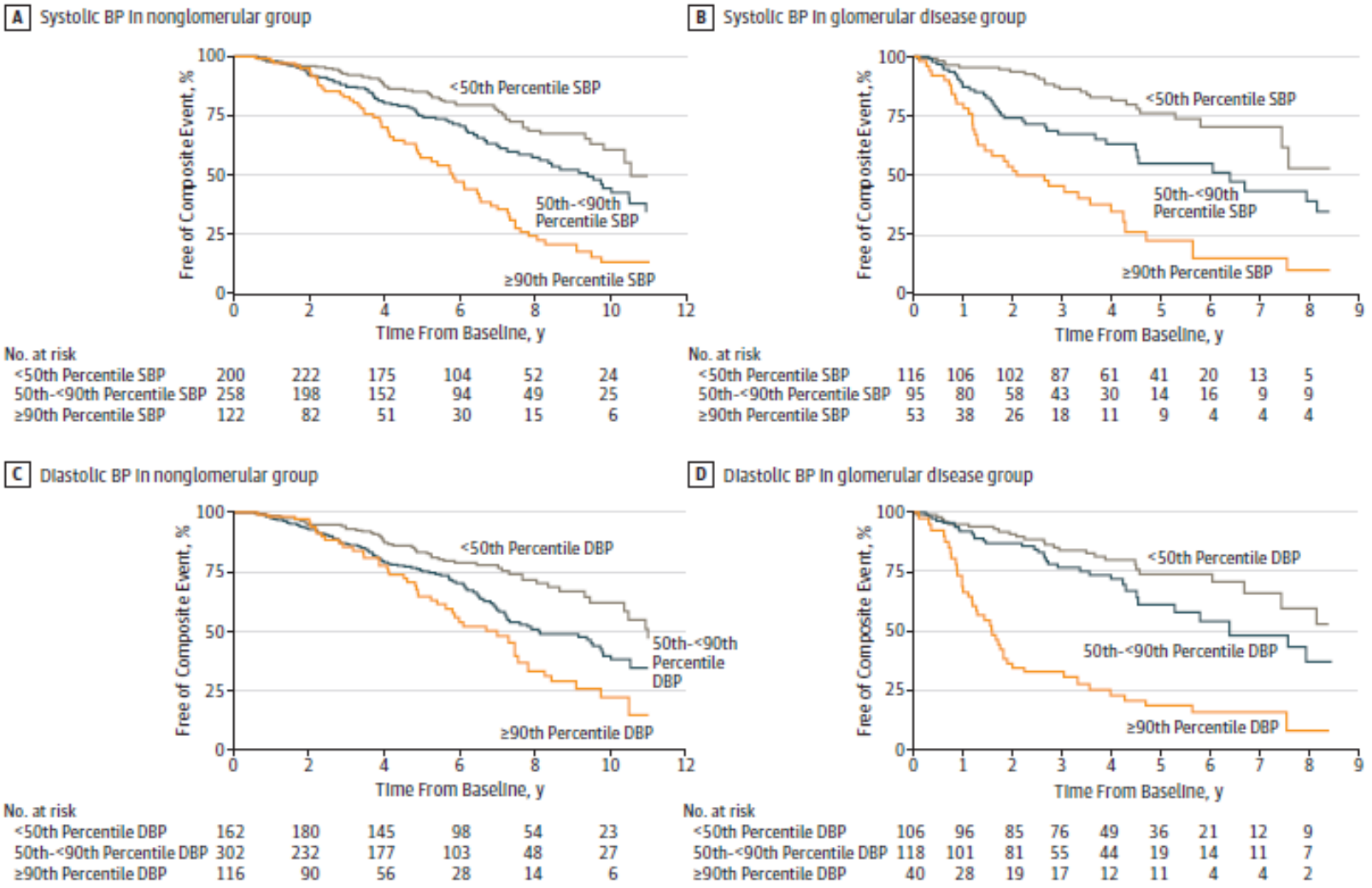
Figure 2. Progression of Renal Disease, According to Blood-Pressure–Control Group.

The cumulative probability of reaching the primary composite end point of a 50% decline in the glomerular filtration rate or progression to end-stage renal disease is shown for all patients (Panel A) and for patients with renal hypoplasia–dysplasia or glomerulopathies (Panel B).

Wuhl E et al. N Engl J Med, 2009

A composite renal outcome (50% GFR reduction from baseline, estimated GFR less than 15 mL/min/1.73m2, or dialysis or transplant)

Figure 1. Unadjusted Survival Curves of Progression to the Composite Renal Outcome by Time-Varying Blood Pressure (BP) Percentile Categories



The reference group includes those with BP of less than the 50th percentile compared with groups with BP from the 50th to less than 90th percentiles and at least 90th percentile for systolic BP (SBP) and diastolic BP (DBP).

CKiD study JAMA Netw Open. 2020;3(2):e1921213. doi:10.1001/jamanetworkopen.2019.21213

The latest pediatric KDIGO CKD clinical BP management guideline

- To initiate antihypertensive treatment when manually measured blood pressure is consistently above the 90th percentile for age, sex, and height;
- To consistently achieve systolic and diastolic readings less than or equal to the 50th percentile (particularly those with proteinuria), when not limited by symptomatic hypotension.
- To prescribe ARB or ACEi to this population of children in whom treatment with BP-lowering drugs is indicated, independent of the degree of proteinuria.

Dyslipidemia

Assessment of lipid status in children with CKD

- In children with newly identified CKD (including those treated with chronic dialysis or kidney transplantation), we recommend evaluation with a lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides).
- In children with CKD (including those treated with chronic dialysis or kidney transplantation), we suggest annual follow-up measurement of fasting lipid levels.

KDIGO Clinical Practice Guideline
for Lipid Management
in Chronic Kidney Disease

Til upplýsingar, ekki kunna

Table 5 | Plasma lipid concentrations for children and adolescents[7]

Category	Acceptable	Borderline High (75%)	High (95%)
Total Cholesterol	<4.4 (<170)	4.4–5.2 (170–199)	>5.2 (≥200)
LDL-C	<2.8 (<110)	2.8–3.3 (110–129)	≥3.4 (≥130)
Non-HDL-C	<3.1 (<120)	3.1–3.7 (120–144)	≥3.8 (≥145)

Abbreviations: LDL-C, low-density lipoprotein cholesterol; Non-HDL-C, non-high-density-lipoprotein cholesterol.
Values given are in mmol/l (mg/dl). Values for plasma lipid and lipoprotein levels are from the National Cholesterol Education Program (NCEP) Expert Panel on Cholesterol Levels in Children. Non-HDL-C values from the Bogalusa Heart Study are equivalent to the NCEP Pediatric Panel cut points for LDL-C.

Pharmacological lipid-lowering treatment in children

- In children less than 18 years of age with CKD (including those treated with chronic dialysis or kidney transplantation), we suggest that statins or statin/ezetimibe combination not be initiated.
- In children with CKD (including those treated with chronic dialysis or kidney transplantation) and hypertriglyceridemia, we suggest that therapeutic lifestyle changes be advised.
- It must be emphasized that these recommendations are weak and reflect the lack of evidence for benefit and safety associated with long-term statin use

Cardiovascular disease

Left ventricular hypertrophy

- Left ventricular hypertrophy
  - Hypertension
  - Anemia
  - Elevated levels of FGF23
- Coronary calcifications
  - Related to CKD-MBD
  - High calcium and phosphate

Formal Preparation of the Family for Kidney Transplantation

Modifiable factors affecting the rate of childhood CKD progression

- Formal preparation of the child and the family for the development of ESRD and available treatment options should according to the K/DOQI guidelines be initiated when the child reaches CKD stage 4, when eGFR has declined to <30 mL/min./1.73 m^2
- Earlier and less formal education regarding the future need for RRT is likely to be beneficial and should be considered much earlier in the course of progressive CKD.
- Optimal timing of transplant surgery is when the outcome of conservative CKD management is less than that expected following successful kidney transplantation.

Summary - I

- Regardless of age, chronic kidney disease is defined as any abnormality of kidney structure or function adversely affecting health present for a minimum of three consecutive months.
- The clinical disease spectrum is wide, ranging from mild renal affection such as urine sediment abnormalities, disordered tubular function, and/or structural renal anomalies with normal kidney function (GFR) to end-stage kidney failure requiring RRT for continued patient survival.

Summary - II

- The risk for CKD progression is present in all affected individuals and increases as the disease advances.
- Therefore, early diagnosis and timely institution of supportive therapies including proper nutrition and drug treatment aimed at reducing CKD progression and supporting normal homeostatic mechanisms are important.
- Meticulous medical management of hypertension, proteinuria, metabolic acidosis and electrolyte disorders, CKD-MBD, anemia, and all other modifiable risk is likely needed to attain maximum slowing of renal function decline in affected children.