European disparities in the incidence and outcomes of children with end-stage renal disease

Chesnaye, N.C.

Publication date
2017

Document Version
Other version

License
Other

Summary

Samenvatting

SUMMARY

In children, end-stage renal disease is a very rare condition affecting approximately 5 per million children every year in Europe. It requires life-long renal replacement therapy, consisting of either dialysis or renal transplantation to sustain life. Due to the rarity of paediatric end-stage renal disease, the statistical power to perform epidemiological research in this population has been lacking. The establishment of the European-wide registry for paediatric renal replacement therapy (ESPN/ERA-EDTA Registry) has helped alleviate this issue, and currently collects patient data annually from 36 European countries. The studies included in this thesis are based on data from this Registry .

In this thesis, we aimed to reveal health inequalities and improve outcomes in the European paediatric RRT population. Despite commitments and progress made by European Union Member States towards reducing health inequalities, we demonstrate that geographical disparities regarding the quality and provision of RRT to children have yet to be eliminated across Europe. Most of these disparities were attributable to an excess mortality risk and low incidence of paediatric RRT in several Eastern European countries. Country differences in their ability to accept and successfully treat the youngest patients, whom are the most complex and costly to treat, formed an important source of disparity within Europe. Geographical differences regarding the genetic susceptibility to certain renal diseases played only a marginal role in explaining the differences in RRT incidence and survival between countries, whereas macroeconomic indicators, in particular public health expenditure, strongly influenced both the quality of - and access to - paediatric RRT. Importantly, this implies that in countries with limited spending on health services, children in need of RRT are not only dying due to limited access to treatment, but also as a result of substandard care. Considering the austerity-driven cuts in healthcare budgets experienced by most European countries over the past few years, our results pose a challenge for health care policy makers in their aim to ensure universal and equal access to high-quality healthcare across Europe. Nonetheless, by revealing the magnitude of health-care inequalities in our population across Europe, we hope to increase the awareness amongst policy makers and in the paediatric nephrology community, and provide the evidence necessary to advocate policy change regarding resource allocation and clinical practice.

Patient survival is multifactorial, dependent on various patient and treatment characteristics, one of which is dialysis modality selection. We identified an initial survival advantage for those selected to initiate dialysis on PD, especially in children with a limited time under treatment of a nephrologist prior to dialysis, and in children over 5 year years of age, implying that when no contra-indications are present, these patients should ideally be started on PD. Specifically in infants, dialysis modality choice was not associated with mortality, nor with access to transplantation, suggesting that both modalities should be viewed as equally viable options in this population. These differential treatment effects in the paediatric dialysis population highlight the importance of focused clinical management in these subgroups.

Given the superior patient outcomes of renal transplantation compared to dialysis, it is fortunate that three-quarters of children with ESRD receive a transplant within 4 years after RRT initiation. However, approximately a quarter of these patients will lose their graft within 10 years after transplantation. A living donor should always be preferred over a deceased donor, as we demonstrate that even grafts from carefully selected older donors offer excellent graft survival probabilities. When a living donor is unavailable, the differential graft failure risk of deceased donor age and recipient age should be taken into account during the allocation process. Specifically, transplantation of the youngest deceased donors should be avoided in the youngest recipients, as graft failure rates in this group were especially high, particularly directly post-transplantation. In adolescents however, deceased donor age had little effect, likely owing to the overriding adverse effect of adolescence on graft survival probability. Currently, both recipient and deceased donor age definitions used by various donor allocation policies across Europe are heterogeneous, and require reappraisal and standardization taking these results into account.

SAMENVATTING

Wanneer de nieren niet of nauwelijks meer functioneren, spreken we van eindstadium nierfalen. Zonder levenslange behandeling met nierfunctie vervangende therapie (dialyse of transplantatie), is eindstadium nierfalen fataal. Gelukkig is deze aandoening in kinderen zeer zeldzaam, met een incidentie van ongeveer vijf op de miljoen per jaar in Europa. Door de kleine aantallen patiënten ontbreekt vaak de statistische power om epidemiologisch onderzoek uit te voeren in deze populatie. Om dit te verhelpen is een Europese registratie (ESPN/ERA-EDTA Registry) opgericht voor alle kinderen die behandeld worden met nierfunctie vervangende therapie. De registratie verzamelt momenteel data uit 36 Europese landen en vormt de basis van deze proefschrift.

Dit proefschrift heeft als doel de Europese verschillen in de incidentie en uitkomsten van nierfunctie vervangende therapie bij kinderen in kaart te brengen. Ondanks recente inspanningen van de Europese Unie om internationale verschillen in gezondheid te verminderen, tonen wij aan dat ongelijkheid in zowel toegang tot zorg, als de kwaliteit van zorg in deze populatie nog onaanvaardbaar groot blijkt. Het merendeel van deze verschillen was toe te wijzen aan een hoge patiënten sterfte en een lage incidentie van nierfunctie vervangende therapie in een aantal Oost-Europese landen. Hierin speelden de verschillen in de capaciteit van landen om de jongste patiënten (die medisch het meest complex zijn) succesvol in behandeling te nemen een belangrijke rol. Geografische verschillen in de relatieve distributie van het type primaire nierziekte konden deze verschillen niet verklaren. Macro-economische factoren daarentegen, met name overheidsuitgaven aan zorg, vormden de belangrijkste determinanten voor zowel toegang tot, als de kwaliteit van nierfunctie vervangende therapie. Dit impliceert dat in landen waar minder wordt uitgegeven aan zorg door de overheid, kinderen niet alleen sterven als gevolg van een beperkte toegang tot deze levensreddende behandeling, maar ook als gevolg van een lage kwaliteit van zorg. Vooral gezien de bezuinigingen op de zorg als gevolg van de financiële crisis zullen deze resultaten een uitdaging vormen voor beleidsmakers in hun streven naar een universele en eerlijke toegang tot kwalitatief hoogwaardige zorg in Europa. Desalniettemin, door de omvang van deze verschillen in kaart te brengen, hopen we bewustwording onder Europese/nationale beleidsmakers en kindernefrologen te stimuleren, en kennis te verschaffen zodat deze een kader bieden voor beleidswijzigingen zowel op klinisch gebied, als op het budgetteren van zorg.

Patiënt overleving in deze populatie is afhankelijk van meerdere patiënt- en behandelingsfactoren. Eén daarvan is het selecteren van de initiële dialysemodaliteit. Wij tonen aan dat patiënten die worden geselecteerd om met peritoneale dialyse te starten een betere overleving hebben gedurende het eerste dialysejaar vergeleken met patiënten die starten met hemodialyse. Dit behandeleffect was vooral evident bij kinderen die kort onder behandeling waren van een kindernefroloog vóór dialyse, en bij kinderen ouder dan vijf jaar. Dit impliceert dat, wanneer er geen contra-indicaties aanwezig zijn, kinderen bij voorkeur moeten starten op peritoneale dialyse. Specifiek bij kinderen onder de één jaar, vonden wij geen associatie tussen dialysemodaliteit en mortaliteit of transplantatiekans. De differentiële behandeleffecten bij kinderen die starten met dialyse benadrukken het belang van gerichte klinische behandeling in verschillende patiënt subgroepen.

Nier transplantatie bij kinderen biedt betere uitkomsten vergeleken met dialyse. In de praktijk wordt ongeveer driekwart van alle kinderen getransplanteerd binnen 4 jaar na het starten van nierfunctie vervangende therapie. Desondanks verliest ongeveer een kwart van deze kinderen binnen 10 jaar hun transplantaat. Wij hebben aangetoond dat een transplantaat van een levende donor betere overlevingskansen biedt vergeleken met een transplantaat van een overleden donor, zelfs als de levende donor op leeftijd is. Indien een levende donor niet voor handen is, adviseren wij tijdens het toewijzingsproces rekening te houden met het differentieel risico op transplantaat falen dat afhankelijk is van zowel de leeftijd van de overleden donor als de leeftijd van de patiënt. Transplantatie van de jongste overleden donors bij de jongste patiënten geeft namelijk een hoog risico op transplantaat falen, met name direct na transplantatie. Bij adolescente patiënten heeft de leeftijd van een overleden donor daarentegen weinig effect op transplantaat falen. Dit komt vermoedelijk door een overheersende negatief effect van adolescentie op de transplantaat overlevingskans. Ten tijde van het schijven van dit proefschrift is het toewijzingsbeleid van donor nieren in Europa zeer heterogeen, met name wat betreft de definities van donor en patiënt leeftijdscategorieën. Gezien het interactie effect tussen de leeftijd van patiënt en overleden donor op het risico van transplantaat falen, vereist dit evaluatie en harmonisatie van het donor toewijzingsbeleid in Europa.

Acknowledgements

Dankwoord

ACKNOWLEDGEMENTS

We would like to thank the patients, their parents and the staff of all the dialysis and transplant units who have contributed data via their national registries and contact persons. We also would like to thank E Levtchenko, D Haffner, Z Massy, A Bjerre, R Coppo, J Harambat, P Cochat, Z Massy, and C Stefanidis for being members of the ESPN/ERA-EDTA Registry Committee, D Shtiza, R Kramar, R Oberbauer, S Baiko, A Sukalo, K van Hoeck, F Collart, JM des Grottes, D Pokrajac, D Roussinov, D Batinić, M Lemac, J Slavicek, T Seeman, K Vondrak, JG Heaf, U Toots, P Finne, C Grönhagen-Riska, C Couchoud, M Lasalle, E Sahpazova, N Abazi, N Ristoka Bojkovska, K Rascher, E Nüsken, L Weber, G von Gersdorff, F Schaefer, B Tönshoff, K Krupka, B Höcker, L Pape, N Afentakis, A Kapogiannis, N Printza, G Reusz, Cs Berecki, A Szabó, T Szabó, Zs Györke, E Kis, R Palsson, V Edvardsson, R Chimenz, C Corrado, B Minale, F Paglialonga , R Roperto, G Leozappa, E Verrina, A Jankauskiene, B Pundziene, V Said-Conti, S Gatcan, O Berbeca, N Zaikova, S Pavićević, T Leivestad, A Zurowska, I Zagozdzon, C Mota, M Almeida, C Afonso, G Mircescu, L Garneata, EA Molchanova, NA Tomilina, BT Bikbov, M Kostic, A Peco-Antic, B Spasojevic-Dimitrijeva, G Milosevski-Lomic, D Paripovic, S Puric, D Kruscic, L Podracka, G Kolvek, J Buturovic-Ponikvar, G Novljan, N Battelino, A Alonso Melgar and the Spanish Pediatric Registry, S Schön, KG Prütz, L Backmän, M Stendahl, M Evans, B Rippe, CE Kuenhi, E Maurer, GF Laube, S Tschumi, P Parvex, A Hoitsma, A Hemke, and all centers participating in the RichQ study, R Topaloglu, A Duzova, D Ivanov, R Pruthi, F Braddon, S Mannings, A Cassula, MD Sinha for contributing data to the ESPN/ERA-EDTA Registry.

DANKWOORD

Na 4 jaar heb ik eindelijk mijn proefschrift afgerond, maar dit heb ik natuurlijk niet in mijn eentje gedaan! Hier wil ik graag iedereen bedanken die mee heeft geholpen, in welke vorm dan ook, bij het tot stand komen van dit proefschrift. Een aantal mensen wil ik graag in het bijzonder noemen.

Als eerste wil ik graag mijn promotores bedanken. Kitty, ik ben jou in het bijzonder dankbaar voor alle epidemiologische kennis die je mij de afgelopen jaren hebt bijgebracht. Ik kijk met veel plezier terug naar de samenwerking met jou de afgelopen 4 jaar, en ben daarom blij en trots dat je mij EQUAL toevertrouwt.

Karlijn, jouw enthousiasme voor de kindernefrologie was aanstekelijk. Na onze talloze onderzoeks besprekingen liep ik altijd terug naar mijn bureau vol met inspiratie en verse moed. Jouw kritische en creatieve blik hebben onze papers tot een hoger niveau getild. Samen met Kitty vormden we een efficiënt en gezellig team en dat zal ik helaas moeten missen nu je het AMC hebt verlaten.

Marjolein, regerende koningin van de ESPN registratie, onze samenwerking aan de jaarlijkse datastorm liep op een gegeven moment als een geoliede machine. De samenwerking ga ik missen, het dataploegen iets minder. Gelukkig zit je nog altijd twee deurtjes verderop. Ik denk met plezier terug aan alle congressen, van Italië tot Brazilië, die we samen vanaf mijn eerste dag op het AMC hebben meegemaakt.

Franz, Jerome, Jaap, your clinical knowledge was essential in bridging the gap between interesting research ideas and clinical relevance. It was my pleasure working with the very best paediatric nephrologists of Europe (or perhaps even the world?!). Even though I've now switched to adult nephrology, I am sure we will meet again soon.

(Ex-) kamergenoten, en triple-daters, jullie bedankt voor alle grapjes, gekkigheid, borrels, wandelingetjes naar de AH en de liters koffie die we samen hebben gedronken over de afgelopen jaren.

ERA team, en niet te vergeten onze guest-researcher Lidwien, bedankt voor alle gezelligheid tijdens onze diners, borrels, en team uitjes. Het is fijn om onderdeel uit te maken van een team dat elkaar op congressen steunt met de (presentatie) stress, en daarna de overwinning viert met borrels en (presidentiële) etentjes. Ik hoop dat er nog vele zullen volgen!

Verder wil ik iedereen van de afdeling KIK bedanken voor de altijd sympathieke, leerzame en constructieve sfeer.

I would also like to thank the members of the doctorate committee for taking the time to critically review my thesis and form the opposition during my defense ceremony.

Maria, wie had dat gedacht, dat ik dit nu in het Nederlands aan jou zou schrijven. Jouw kennis van de Nederlandse taal zal die van mij snel overstijgen. Ik heb een enorme respect voor jouw gedrevenheid; straks promoveren met duizend papers, het Nederlandse taal meester maken, en ook nog een master transplantatienefrologie erbij! Wat een fijne jaren hebben we achter de rug, met als hoogtepunten Brussel, Londen, Glasgow, en niet te vergeten alle Javastraat vrimibo's. Heel erg bedankt voor het paranimf zijn en alle bijbehorende verantwoordelijkheden. Ik hoop dat ik het net zo goed ga doen bij jouw promotie binnenkort!

Loes, BFF, Subba-queen, buuf, en nu ook paranimf! Bedankt voor het organiseren van het feest en alles wat daarbij komt kijken, maar vooral voor je vriendschap, inlevingsvermogen en begrip over de afgelopen jaren. Het heeft veel voor mij betekend!

Utrechtse en Amsterdamse vrienden, fijn dat jullie altijd bereid waren om een stress verlagende biertje met me te drinken en voor de ontelbare avonturen in het Amsterdamse/Utrechtse nachtleven!

Chiel, Oof, Tim, mijn 'stage' heb ik nu afgerond, hoor. Tegen de tijd dat jullie dit lezen ben ik ook al 'afgestudeerd'. Laten we snel weer een biertje drinken in jullie toekomstige woonplaats, Amsterdam.

Peim, autonoom kunstenaar, fotomodel, grafisch ontwerper, wat kun je niet? Ik ben heel blij met jouw ontwerp en vond het leuk om samen het creatief proces te doorlopen. Tot de volgende WYS photo shoot!

Dad and Sophie, thank you for always having confidence in me and for all the relaxing weekends in Assen. Mamma, je overvloed aan liefde en pedagogiek hebben me gemaakt tot wie ik ben en daarmee ben je dus ook deels verantwoordelijk voor het tot stand komen van deze proefschrift! Mike, straks mag jij ook promoveren. Ik heb er alle vertrouwen in dat het in South-Hampton helemaal goed komt en ben erg benieuwd naar je avonturen daarna!

Yara, bedankt voor het luisteren naar mijn spannende verhalen over de verschillende regressie-technieken. Je oprechtheid, empathie en liefde hebben hun sporen achtergelaten op mij. Op naar de volgende vakantie!

Curriculum Vitae

Portfolio

CURRICULUM VITAE

Nicholas Christopher Chesnaye werd op 13 februari 1985 geboren te Singapore. In 2003 behaalde hij zijn VWO diploma aan het Hondsrug College in Emmen. In 2007 behaalde hij zijn BSc Biomedische Wetenschappen aan de Universiteit van Utrecht, en in 2011 zijn MSc aan de Vrije Universiteit te Amsterdam. Ter afronding van zijn MSc liep hij stage bij de Centers for Disease Control and Prevention in de Vereinigde Staten, waar hij een maand veldwerk heeft verricht in Cambodja met als doel het nationale ontwormingsprogramma voor schoolkinderen te evalueren. Nicholas heeft vervolgens zijn onderzoeksstage gelopen bij het Intituut voor Tropische Geneeskunde Antwerpen, om in Vietnam onderzoek te doen naar de epidemiologie van malaria. Na zijn afstuderen is Nicholas begonnen als Clinical Research Associate Trainee bij de clinical research organisation Quintiles in Hoofddorp. In februari 2013 startte Nicholas met zijn promotieonderzoek binnen de ESPN/ERA-EDTA Registratie op de afdeling Klinische Informatiekunde van het Academisch Medisch Centrum te Amsterdam. Onder leiding van Prof. Dr. Kitty Jager en Dr. Karlijn van Stralen voerde hij het onderzoek in dit proefschrift uit. Na het afronden van zijn promotieonderzoek start Nicholas als internationale project coördinator van de EQUAL studie.

PORTFOLIO
Name PhD student: Nicholas Christopher Chesnaye
PhD period: March 2013 – March 2017
Promotor: Prof. Dr. Kitty Jager

	Year	Workload (ECTS)
1. PhD training		
General courses		
Clinical Epidemiology	2013	0.6
Practical Biostatistics	2015	1.1
Observational Clinical Epidemiology	2015	0.6
Advanced Topics in Biostatistics	2016	2.1
Specific courses		
CME: Introductory Course on Epidemiology	2013	0.6
NIHES: International Comparison of Health Care Systems	2013	1.4
NDT - A Course For Reviewers To Be	2014	0.6
NIHES: Causal Mediation Analysis	2015	0.7
eBROK	2017	1.0
Seminars, workshops, and master classes		
Workshop 'Nephorology Registries and Genetic Renal Diseases', Genova, Italy	2013	0.6
Seminar '"Who wrote my paper" by Dr. Drummond Rennie', AMC	2013	0.3
Symposium 'Hot topics in pediatric end-stage renal disease', AMC	2013	0.3
Workshop 'Systematic review of measuring instruments', VUMC	2013	0.3
Masterclasses 'Advances in Epidemiologic Analysis', NIHES	2015	0.3
Symposium 'New Kids on the Block; wetenschappelijk onderzoek in de nefrologie', AMC	2015	0.3
Presentations (oral)		
Disparities in Treatment Rates of Paediatric End-Stage Renal Disease across Europe: Insights from the ESPN/ERA-EDTA Registry, ESPN/ERA-EDTA 47th congress, Porto, Portugal	2014	0.5
Mortality Risk in European Children with End-Stage Renal Disease on Dialysis, 52nd ERA-EDTA congress, London, United Kingdom	2015	0.5
Mortality Risk in European Children with End-Stage Renal Disease on Dialysis, ESPN/ERA-EDTA 48th congress, Brussel, Belgium	2015	0.5
Mortality Risk in European Children with End-Stage Renal Disease on Dialysis, 53rd ERA-EDTA congress, Vienna, Austria	2016	0.5
The Association of Donor and Recipient Age with Graft Survival in Pediatric Renal Transplant Recipients - an ESPN/ERA-EDTA Registry Study, IPNA 17th congress, Iguacu, Brazil	2016	0.5

Mortality Risk Disparities in Children with End-Stage Renal Disease across Europe - An ESPN-ERA/EDTA Registry Analysis, 54th ERA-EDTA congress, Madrid, Spain	2017	0.5
Presentations (poster)		
Disparities in Treatment Rates of Paediatric End-Stage Renal Disease across Europe: Insights from the ESPN/ERA-EDTA Registry, 51th ERA-EDTA congress, Amsterdam, The Netherlands	2014	0.5
Mortality Risk Disparities in Children with End-Stage Renal Disease across Europe - An ESPN-ERA/EDTA Registry Analysis, 53rd ERA-EDTA congress, Vienna, Austria	2016	0.5
Mortality Risk Disparities in Children with End-Stage Renal Disease across Europe - An ESPN-ERA/EDTA Registry Analysis, IPNA 17th congress, Iguacu, Brazil	2016	0.5
The Association of Donor and Recipient Age with Graft Survival in Pediatric Renal Transplant Recipients - an ESPN/ERA-EDTA Registry Study, 54th ERA-EDTA congress, Madrid, Spain	2017	0.5
(Inter)national conferences		
50th ERA-EDTA congress, Istanbul, Turkey	2013	1.0
51th ERA-EDTA congress, Amsterdam, The Netherlands	2014	1.0
ESPN/ERA-EDTA 47th congress, Porto, Portugal	2014	1.0
52nd ERA-EDTA congress, London, United Kingdom	2015	1.0
ESPN/ERA-EDTA 48th congress, Brussel, Belgium	2015	1.0
53rd ERA-EDTA congress, Vienna, Austria	2016	1.0
Seventeenth Congress of the International Pediatric Nephrology Association, Iguacu, Brazil	2016	1.0
EURenOmics Project and General Assembly Meeting, Paris, France	2016	1.0
54th ERA-EDTA congress, Madrid, Spain	2017	1.0
Other		
Journal club	2013-2017	2.0

2. Teaching

Lecturing		
CME: Introductory Course on Epidemiology, Kopenhagen, Denmark	2016	1.5
CME: Introductory Course on Epidemiology, Nicosia, Cyprus	2017	1.5
Supervising		
Gulfidan Yasar. Survival in children with end-stage renal disease.	2014-2015	1.0

LIST OF PUBLICATIONS

Chesnaye NC, van Stralen KJ, Bonthuis M, et al. *Survival in children requiring chronic renal replacement therapy*. Pediatr Nephrol 2017 May; Epub ahead of print

Chesnaye NC, van Stralen KJ, Bonthuis M, et al. *The association of donor and recipient age with graft survival in paediatric renal transplant recipients: an ESPN/ERA-EDTA Registry study*. Nephrol Dial Transplant 2017 Jul; Accepted

Chesnaye NC, Schaefer F, Bonthuis M, et al. *Mortality risk disparities in children receiving chronic renal replacement therapy for the treatment of end-stage renal disease across Europe - An ESPN-ERA/EDTA Registry analysis*. The Lancet 2017 May; 389(10084): 2128-2137

Vidal E, van Stralen KJ, **Chesnaye NC**, et al (2016) *Infants Requiring Maintenance Dialysis: Outcomes of Hemodialysis and Peritoneal Dialysis*. Am J Kidney Dis. 2017 May; 69(5): 617-625

Chesnaye NC, Schaefer F, Groothoff JW, et al. *Mortality risk in European children with end-stage renal disease on dialysis: Results from the ESPN/ERA-EDTA Registry*. Kidney Int 2016 Jun; 89(6): 1355–1362

Chesnaye NC, Schaefer F, Groothoff JW, et al. *Disparities in treatment rates of paediatric end-stage renal disease across Europe: insights from the ESPN/ERA-EDTA Registry*. Nephrol Dial Transplant 2015 Aug; 30(8): 1377–1385

Hafiz I, Berhan M, Keller A, Haq R, **Chesnaye NC**, et al. *School-based mass distributions of mebendazole to control soil-transmitted helminthiasis in the Munshiganj and Lakshmipur districts of Bangladesh: An evaluation of the treatment monitoring process and knowledge, attitudes, and practices of the population*. Acta Trop. 2015;141(Part B):385–90

Chesnaye NC, Bonthuis M, Schaefer F, et al. *Demographics of paediatric renal replacement therapy in Europe: a report of the ESPN/ERA-EDTA Registry*. Pediatr Nephrol 2014 Dec; 29(12): 2403–2410

Chesnaye NC, Sinuon M, Socheat D, Koporc K, Mathieu E. *Treatment coverage survey after a school-based mass distribution of mebendazole: Kampot Province, Cambodia*. Acta Trop. 2011 Apr;118(1):21-6

REFERENCES

1. Tjaden LA, Vogelzang J, Jager KJ, et al (2014) Long-term quality of life and social outcome of childhood end-stage renal disease. J Pediatr 165:336–342.
2. Tonelli M (2006) Chronic Kidney Disease and Mortality Risk: A Systematic Review. J Am Soc Nephrol 17:2034–2047.
3. Liyanage T, Ninomiya T, Jha V, et al (2015) Worldwide access to treatment for end-stage kidney disease: A systematic review. Lancet 385:1975–1982.
4. Warady BA, Chadha V (2007) Chronic kidney disease in children: the global perspective. Pediatr Nephrol 22:1999–2009.
5. Harambat J, van Stralen KJ, Kim JJ, Tizard EJ (2012) Epidemiology of chronic kidney disease in children. Pediatr Nephrol 27:363–373.
6. Gillen DL, Stehman-Breen CO, Smith JM, et al (2008) Survival advantage of pediatric recipients of a first kidney transplant among children awaiting kidney transplantation. Am J Transplant 8:2600–6.
7. Mendley SR, Zelko FA (1999) Improvement in specific aspects of neurocognitive performance in children after renal transplantation. Kidney Int 56:318–23.
8. McDonald SP, Craig JC (2004) Long-term survival of children with end-stage renal disease. N Engl J Med 350:2654–2662.
9. Goldstein SL, Graham N, Burwinkle T, et al (2006) Health-related quality of life in pediatric patients with ESRD. Pediatr Nephrol 21:846–850.
10. Van Arendonk KJ, Boyarsky BJ, Orandi BJ, et al (2014) National trends over 25 years in pediatric kidney transplant outcomes. Pediatrics 133:594–601.
11. NAPRTCS Collaborative Studies NAPRTCS 2014 Annual Transplant Report.
12. Neuhaus TJ, Goetschel P LE (1998) Small patients—high costs: economic aspects of medical treatment of children with early onset of chronic renal failure. Praxis (Bern 1994) 1593–1599.
13. Bunchman TE (1996) The ethics of infant dialysis. Perit Dial Int 16 Suppl 1:S505-8.
14. WHO Health 2020 policy framework and strategy.
15. Dhoul N, de Lusignan S, Dmitrieva O, et al (2012) Quality achievement and disease prevalence in primary care predicts regional variation in renal replacement therapy (RRT) incidence: an ecological study. Nephrol Dial Transplant 27:739–46.
16. Visser A, Noordzij M, Gansevoort RT, et al (2012) Exploration of the difference in incidence of renal replacement therapy between Flanders and the Netherlands--investigation of explanatory variables. Nephrol Dial Transplant 27:803–9.
17. Castledine CI, Gilg JA, Rogers C, et al (2012) How much of the regional variation in RRT incidence rates within the UK is explained by the health needs of the general population? Nephrol Dial Transplant 27:3943–50.
18. Judge A, Caskey FJ, Welton NJ, et al (2012) Inequalities in rates of renal replacement therapy in England: does it matter who you are or where you live? Nephrol Dial Transplant 27:1598–607.
19. Caskey FJ, Kramer A, Elliott RF, et al (2011) Global variation in renal replacement therapy for end-stage renal disease. Nephrol Dial Transplant 26:2604–10.
20. Kramer A, Stel VS, Caskey FJ, et al (2012) Exploring the association between macroeconomic indicators and

dialysis mortality. Clin J Am Soc Nephrol 7:1655–63.
21. Robinson BM, Zhang J, Morgenstern H, et al (2014) Worldwide, mortality risk is high soon after initiation of hemodialysis. Kidney Int 85:158–65.
22. van Dijk P, Zwinderman A, Dekker F, et al (2007) Effect of general population mortality on the north-south mortality gradient in patients on replacement therapy in Europe. Kidney Int 71:53–9.
23. Schaefer F, Borzych-Duzalka D, Azocar M, et al (2012) Impact of global economic disparities on practices and outcomes of chronic peritoneal dialysis in children: insights from the International Pediatric Peritoneal Dialysis Network Registry. Perit Dial Int 32:399–409.
24. Wühl E, van Stralen KJ, Wanner C, et al (2014) Renal replacement therapy for rare diseases affecting the kidney: an analysis of the ERA-EDTA Registry. Nephrol Dial Transplant 29 Suppl 4:iv1-iv8.
25. White S (2008) How can we achieve global equity in provision of renal replacement therapy? Bull World Health Organ 86:229–237.
26. Shroff R, Ledermann S (2009) Long-term outcome of chronic dialysis in children. Pediatr Nephrol 24:463–74.
27. van de Luijtgaarden MWM, Noordzij M, Stel VS, et al (2011) Effects of comorbid and demographic factors on dialysis modality choice and related patient survival in Europe. Nephrol Dial Transplant 26:2940–2947.
28. Weinhandl ED, Foley RN, Gilbertson DT, et al (2010) Propensity-matched mortality comparison of incident hemodialysis and peritoneal dialysis patients. J Am Soc Nephrol 21:499–506.
29. Lukowsky LR, Mehrotra R, Kheifets L, et al (2013) Comparing mortality of peritoneal and hemodialysis patients in the first 2 years of dialysis therapy: a marginal structural model analysis. Clin J Am Soc Nephrol 8:619–628.
30. Mehrotra R, Chiu Y-W, Kalantar-Zadeh K, et al (2011) Similar outcomes with hemodialysis and peritoneal dialysis in patients with end-stage renal disease. Arch Intern Med 171:110–118.
31. Stokes JB (2012) Peritoneal dialysis is not a superior therapy to hemodialysis: A comparison. Blood Purif 33:160–164.
32. Noordzij M, Jager KJ (2014) Patient survival on dialysis in Korea: a different story? Kidney Int 86:877–880.
33. Wong CS, Hingorani S, Gillen DL, et al (2002) Hypoalbuminemia and risk of death in pediatric patients with end-stage renal disease. Kidney Int 61:630–637.
34. Mitsnefes MM, Laskin BL, Dahhou M, et al (2013) Mortality Risk Among Children Initially Treated With Dialysis for End-Stage Kidney Disease, 1990–2010. JAMA 309:1921–1929.
35. Lin HH, Tsai C-W, Lin PH, et al (2012) Survival analysis of pediatric dialysis patients in Taiwan. Nephrology (Carlton) 17:621–627.
36. Foster BJ, Dahhou M, Zhang X, et al (2011) Change in mortality risk over time in young kidney transplant recipients. Am J Transplant 11:2432–2442.
37. Cecka JM (2008) Kidney transplantation in the United States. Clin Transpl 1–18.
38. Pape L, Ehrich JHH, Offner G (2007) Young for young! Mandatory age-matched exchange of paediatric kidneys. Pediatr Nephrol 22:477–479.
39. Harmon WE, Alexander S, Tejani A, Stablein D (1992) The effect of Donor Age on Graft Survival in Pediatric Cadaver Renal Transplant Recipients - A Report Of The North American Pediatric Renal Transplant Cooperative Study. Transplantation 54(2):232--7.
40. Hayes JM, Novick AC, Streem SB, et al (1988) The use of single pediatric cadaver kidneys for

transplantation. Transplantation 45:106–10.
41. Pape L, Offner G, Ehrich JHH, et al (2004) Renal Allograft Function in Matched Pediatric and Adult Recipient Pairs of the Same Donor. Transplantation 77:1191–1194.
42. Harambat J, Van Stralen KJ, Schaefer F, et al (2013) Disparities in Policies , Practices and Rates of Pediatric Kidney Transplantation in Europe. Am J Transplant 13:2066–2074.
43. Dubourg L, Cochat P, Hadj-Aïssa A, et al (2002) Better long-term functional adaptation to the child's size with pediatric compared to adult kidney donors. Kidney Int 62:1454–1460.
44. Pape L, Hoppe J, Becker T, et al (2006) Superior long-term graft function and better growth of grafts in children receiving kidneys from paediatric compared with adult donors. Nephrol Dial Transplant 21:2596–2600.
45. Bresnahan BA, McBride MA, Cherikh WS, Hariharan S (2001) Risk factors for renal allograft survival from pediatric cadaver donors: an analysis of united network for organ sharing data. Transplantation 72:256–61.
46. Singh A, Stablein D, Tejani A (1997) Risk factors for vascular thrombosis in pediatric renal transplantation: a special report of the North American Pediatric Renal Transplant Cooperative Study. Transplantation 63:1263–7.
47. Schurman SJ, McEnery PT (1997) Factors influencing short-term and long-term pediatric renal transplant survival. J Pediatr 130:455–62.
48. Dharnidharka VR, Fiorina P, Harmon WE (2014) Kidney Transplantation in Children. N Engl J Med 371:549–558.
49. Pape L, Ehrich JHH, Zivicnjak M, Offner G (2005) Growth in children after kidney transplantation with living related donor graft or cadaveric graft. Lancet 366:151–153.
50. Tizard EJ, Verrina E, van Stralen KJ, Jager KJ (2009) Progress with the European Society for Paediatric Nephrology (ESPN)/ERA-EDTA Registry for children with established renal failure (ERF). Nephrol Dial Transplant 24:2615–7.
51. ESPN/ERA-EDTA (2013) http://www.espn-reg.org/.
52. Jager KJ, Zoccali C, Kramar R, Dekker FW (2007) Measuring disease occurrence. Kidney Int 72:412–5.
53. European Commission (2013) http://epp.eurostat.ec.europa.eu/.
54. ERA-EDTA Registry (2015) ERA-EDTA Registry Annual Report 2013.
55. Schwartz GJ, Muñoz A, Schneider MF, et al (2009) New equations to estimate GFR in children with CKD. J Am Soc Nephrol 20:629–37.
56. National Kidney Foundation (2006) KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for 2006 Updates: Hemodialysis Adequacy, Peritoneal Dialysis Adequacy and Vascular Access. Am J Kidney Dis 48:S1–S322.
57. Noordzij M, Leffondré K, van Stralen KJ, et al (2013) When do we need competing risks methods for survival analysis in nephrology? Nephrol Dial Transplant 1–8.
58. Pocock SJ, Clayton TC, Altman DG (2002) Survival plots of time-to-event outcomes in clinical trials: good practice and pitfalls. 359:1686–1689.
59. van Dijk PC, Jager KJ, de Charro F, et al (2001) Renal replacement therapy in Europe: the results of a collaborative effort by the ERA-EDTA registry and six national or regional registries. Nephrol Dial Transplant 16:1120–9.
60. European Mortality Database (2013) http://data.euro.who.int/.

61. The Malaysian Dialysis & Transplant Registry (2013) 20th Report of the Malaysian Dialysis & Transplant Registry.
62. National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases. (2012) United States Renal Data System, USRDS 2012 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States.
63. Australia and New Zealand Dialysis and Transplant Registry ANZDATA Registry Report 2012.
64. National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases (2011) U.S. Renal Data System, USRDS 2014 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States.
65. van Stralen KJ, Tizard EJ, Jager KJ, et al (2010) Determinants of eGFR at start of renal replacement therapy in paediatric patients. Nephrol Dial Transplant 25:3325–32.
66. Samuel SM, Tonelli MA, Foster BJ, et al (2011) Survival in pediatric dialysis and transplant patients. Clin J Am Soc Nephrol 6:1094–1099.
67. Roberts MA, Polkinghorne KR, McDonald SP, Ierino FL (2011) Secular trends in cardiovascular mortality rates of patients receiving dialysis compared with the general population. Am J Kidney Dis 58:64–72.
68. van der Heijden BJ, van Dijk PCW, Verrier-Jones K, et al (2004) Renal replacement therapy in children: data from 12 registries in Europe. Pediatr Nephrol 19:213–221.
69. Vogelzang JL, van Stralen KJ, Jager KJ, Groothoff JW (2013) Trend from cardiovascular to non-cardiovascular late mortality in patients with renal replacement therapy since childhood. NDT 28:2082–2089.
70. Groothoff JW, Gruppen MP, Offringa M, et al (2002) Mortality and causes of death of end-stage renal disease in children: a Dutch cohort study. Kidney Int 61:621–629.
71. Wolfe I, Thompson M, Gill P, et al (2013) Health services for children in western Europe. Lancet 381:1224–34.
72. ESRI ArcGIS Desktop 10.2. 11.
73. Ralph P, Coop G (2013) The geography of recent genetic ancestry across Europe. PLoS Biol 11:e1001555.
74. Benjamini, Y Hochberg Y (2000) On the Adaptive Control of the False Discovery Rate in Multiple Testing With Independent Statistics. J Educ Behav Stat 25:60–83.
75. World Bank Database (2013) http://data.worldbank.org/.
76. Wiesel A, Queisser-Luft A, Clementi M, et al (2005) Prenatal detection of congenital renal malformations by fetal ultrasonographic examination: an analysis of 709,030 births in 12 European countries. Eur J Med Genet 48:131–44.
77. Tattersall J, Dekker F, Heimbürger O, et al (2011) When to start dialysis: updated guidance following publication of the Initiating Dialysis Early and Late (IDEAL) study. Nephrol Dial Transplant 26:2082–6.
78. Statistical Methodology and Applications Branch Surveillance Research Program National Cancer Institute. Joinpoint Regression Program, Version 4.0.4.
79. Chesnaye N, Bonthuis M, Schaefer F, et al (2014) Demographics of paediatric renal replacement therapy in Europe: a report of the ESPN/ERA-EDTA registry. Pediatr Nephrol 29(12):2403–2410.
80. WHO (2013) Health, health systems and economic crisis in Europe Impact and policy implications.
81. Ehrich JHH, El Gendi AA, Drukker A, et al (2005) Demography of paediatric renal care in Europe: organization and delivery. Nephrol Dial Transplant 20:297–305.
82. Wisk LE, Witt WP (2012) Predictors of delayed or forgone needed health care for families with children.

Pediatrics 130:1027–37.
83. Schell CO, Reilly M, Rosling H, et al (2007) Socioeconomic determinants of infant mortality: a worldwide study of 152 low-, middle-, and high-income countries. Scand J Public Health 35:288–97.
84. Europeristat (2010) European Perinatal Health Report: Health and Care of Pregnant Women and Babies in Europe in 2010.
85. Richardus JH, Graafmans WC, Verloove-Vanhorick SP, Mackenbach JP (2003) Differences in perinatal mortality and suboptimal care between 10 European regions: results of an international audit. BJOG 110:97–105.
86. van Stralen KJ, Borzych-Dużalka D, Hataya H, et al (2014) Survival and clinical outcomes of children starting renal replacement therapy in the neonatal period. Kidney Int 86:168–174.
87. Damen-Elias HAM, De Jong TPVM, Stigter RH, et al (2005) Congenital renal tract anomalies: outcome and follow-up of 402 cases detected antenatally between 1986 and 2001. Ultrasound Obstet Gynecol 25:134–43.
88. Scott JES (2002) Fetal, perinatal, and infant death with congenital renal anomaly. Arch Dis Child 87:114–7.
89. Joseph KS, Kinniburgh B, Hutcheon JA, et al (2013) Determinants of increases in stillbirth rates from 2000 to 2010. Cmaj 185:345–351.
90. Khoshnood B, Greenlees R, Loane M, Dolk H (2011) Paper 2: EUROCAT public health indicators for congenital anomalies in Europe. Birth Defects Res A Clin Mol Teratol 91 Suppl 1:S16-22.
91. Hanlon M, Burstein R, Masters SH, Zhang R (2012) Exploring the relationship between population density and maternal health coverage. BMC Health Serv Res 12:416.
92. S. R. Alexander MH (1993) Continuous peritoneal dialysis for children: a decade of worldwide growth and development. Kidney Int Suppl 40:S65–S74.
93. Chesnaye NC, Schaefer F, Groothoff JW, et al (2015) Disparities in treatment rates of paediatric end-stage renal disease across Europe: Insights from the ESPN/ERA-EDTA registry. Nephrol Dial Transplant 30:1377–1385.
94. Spiegelhalter DJ (2005) Funnel plots for comparing institutional performance. Stat Med 24:1185–1202.
95. Merlo J, Chaix B, Yang M, et al (2005) A brief conceptual tutorial of multilevel analysis in social epidemiology: linking the statistical concept of clustering to the idea of contextual phenomenon. J Epidemiol Community Health 59:443–449.
96. Aelvoet W, Terryn N, Blommaert A, et al (2016) Community-acquired pneumonia (CAP) hospitalizations and deaths: is there a role for quality improvement through inter-hospital comparisons? Int J Qual Health Care 28:22–32.
97. Legrand C, Duchateau L, Sylvester R, et al (2006) Heterogeneity in disease free survival between centers: Lessons learned from an EORTC breast cancer trial. Clin Trials 3:10–18.
98. Merlo J, Yang M, Chaix B, et al (2005) A brief conceptual tutorial on multilevel analysis in social epidemiology: investigating contextual phenomena in different groups of people. J Epidemiol Community Health 59:729–736.
99. Jager K, Zoccali C, MacLeod A, Dekker F (2008) Confounding: What it is and how to deal with it. Kidney Int 73:256–260.
100. OECD (2012) Health at a Glance: Europe 2012. OECD
101. Covic A, Schiller A (2010) Burden of disease - prevalence and incidence of ESRD in selected European regions and populations. Clin Nephrol 74 Suppl 1:S23-7.

102. Rutkowski B (2006) Highlights of the epidemiology of renal replacement therapy in Central and Eastern Europe. Nephrol Dial Transplant 21:4–10.
103. Dussault G, Fronteira I, Cabral J (2009) Migration of health personnel in the WHO European Region.
104. Buchan J (2006) Migration of health workers in Europe: policy problem or policy solution?
105. Buchan J, Perfilieva G (2006) Health Worker Migration in the European Region: Country Case Studies and Policy Implications.
106. European Society for Paediatric Nephrology. http://espn-online.org/training.
107. Chavers BM, Molony JT, Solid CA, et al (2015) One-Year Mortality Rates in US Children with End-Stage Renal Disease. Am J Nephrol 41:121–128.
108. Groothoff JW (2005) Long-term outcomes of children with end-stage renal disease. Pediatr Nephrol 20:849–853.
109. Chesney RW (2002) The development of pediatric nephrology. Pediatr Res 52:770–778.
110. Carey WA, Martz KL, Warady BA (2015) Outcome of Patients Initiating Chronic Peritoneal Dialysis During the First Year of Life. Pediatrics 136:e615–e622.
111. Laskin BL, Mitsnefes MM, Dahhou M, et al (2014) The mortality risk with graft function has decreased among children receiving a first kidney transplant in the United States. Kidney Int 87:1–9.
112. Hattori M, Sako M, Kaneko T, et al (2015) End-stage renal disease in Japanese children: a nationwide survey during 2006-2011. Clin Exp Nephrol 19:933–938.
113. National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases. (2015) United States Renal Data System. 2015 USRDS annual data report: Epidemiology of kidney disease in the United States.
114. NAPRTCS (2011) NAPRTCS 2011 Annual Report.
115. Alexander RT, Foster BJ, Tonelli MA, et al (2012) Survival and transplantation outcomes of children less than 2 years of age with end-stage renal disease. Pediatr Nephrol 27:1975–1983.
116. Bunchman TE (1995) Chronic dialysis in the infant less than 1 year of age. Pediatr Nephrol S18-22.
117. Mekahli D, Shaw V, Ledermann SE, Rees L (2010) Long-term outcome of infants with severe chronic kidney disease. Clin J Am Soc Nephrol 5:10–17.
118. Kari JA, Gonzalez C, Ledermann SE, et al (2000) Outcome and growth of infants with severe chronic renal failure. Kidney Int 57:1681–1687.
119. Shooter M, Watson A (2000) The ethics of withholding and withdrawing dialysis therapy in infants. Pediatr Nephrol 14:347–351.
120. Zurowska AM, Fischbach M, Watson AR, et al (2013) Clinical practice recommendations for the care of infants with stage 5 chronic kidney disease (CKD5). Pediatr Nephrol 28:1739–1748.
121. Pollack S, Eisenstein I, Tarabeih M, et al (2015) Long-term hemodialysis therapy in neonates and infants with end-stage renal disease: a 16-year experience and outcome. Pediatr Nephrol 31:305–313.
122. Hogan J, Couchoud C, Bonthuis M, et al (2016) Gender Disparities in Access to Pediatric Renal Transplantation in Europe: Data from the ESPN/ERA-EDTA Registry. Am J Transplant 16:2097–2105.
123. Laskin BL, Mitsnefes MM, Dahhou M, et al (2014) The mortality risk with graft function has decreased among children receiving a first kidney transplant in the United States. Kidney Int 87:1–9.
124. Laster M, Soohoo M, Hall C, et al (2016) Racial–ethnic disparities in mortality and kidney transplant outcomes among pediatric dialysis patients. Pediatr. Nephrol.

125. Parekh RS, Carroll CE, Wolfe RA, Port FK (2002) Cardiovascular mortality in children and young adults with end-stage kidney disease. J Pediatr 141:191–197.
126. Chavers BM, Li S, Collins AJ, Herzog CA (2002) Cardiovascular disease in pediatric chronic dialysis patients. Kidney Int 62:648–653.
127. Mitsnefes M, Stablein D (2005) Hypertension in pediatric patients on long-term dialysis: a report of the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS). Am J Kidney Dis 45:309–315.
128. Flynn JT, Mitsnefes M, Pierce C, et al (2008) Blood pressure in children with chronic kidney disease: a report from the Chronic Kidney Disease in Children study. Hypertension 52:631–637.
129. Tjaden LA, Noordzij M, van Stralen KJ, et al (2015) Racial Disparities in Access to and Outcomes of Kidney Transplantation in Children, Adolescents, and Young Adults: Results From the ESPN/ERA-EDTA. Am J Kidney Dis 67:293–301.
130. National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases (2008) U.S. Renal Data System, USRDS 2008 Annual Data Report: Atlas of End-Stage Renal Disease in the United States.
131. Sule S, Fivush B, Neu A, Furth S (2011) Increased risk of death in pediatric and adult patients with ESRD secondary to lupus. Pediatr Nephrol 26:93–98.
132. Harambat J, van Stralen KJ, Espinosa L, et al (2012) Characteristics and outcomes of children with primary oxalosis requiring renal replacement therapy. Clin J Am Soc Nephrol 7:458–465.
133. Wong CS, Gipson DS, Gillen DL, et al (2000) Anthropometric measures and risk of death in children with end-stage renal disease. Am J Kidney Dis 36:811–819.
134. Ku E, Glidden D, Hsu CY, et al (2016) Association of Body Mass Index with Patient-Centered Outcomes in Children with ESRD. J Am Soc Nephrol 27:551–558.
135. Furth SL, Hwang W, Yang C, et al (2002) Growth failure, risk of hospitalization and death for children with end-stage renal disease. Pediatr Nephrol 17:450–455.
136. Furth SL, Stablein D, Fine RN, et al (2002) Adverse Clinical Outcomes Associated With Short Stature at Dialysis Initiation: A Report of the North American Pediatric Renal Transplant Cooperative Study. Pediatrics 109:909–913.
137. Ku E, Fine RN, Hsu C, et al (2016) Height at First RRT and Mortality in Children. Clin J Am Soc Nephrol 11:832–839.
138. Pruthi R, O'Brien C, Casula A, et al (2013) UK Renal Registry 15th annual report: Chapter 4 demography of the UK paediatric renal replacement therapy population in 2011. Nephron Clin Pract 123 Suppl:81–92.
139. Tsai H, Yang L, Chin T, et al (2010) Outcome and risk factors for mortality in pediatric peritoneal dialysis. Perit Dial Int 30:233–239.
140. Neu AM, Sander A, Borzych-Duzalka D, et al (2012) Comorbidities in chronic pediatric peritoneal dialysis patients: a report of the International Pediatric Peritoneal Dialysis Network. Perit Dial Int 32:410–418.
141. Shroff R, Rees L, Trompeter R, et al (2006) Long-term outcome of chronic dialysis in children. Pediatr Nephrol 21:257–264.
142. Wood EG, Hand M, Briscoe DM, et al (2001) Risk factors for mortality in infants and young children on dialysis. Am J Kidney Dis 37:573–579.
143. Ledermann SE, Scanes ME, Fernando ON, et al (2000) Long-term outcome of peritoneal dialysis in infants. J Pediatr 136:24–29.
144. Ellis EN, Pearson D, Champion B, Wood EG (1995) Outcome of infants on chronic peritoneal dialysis. Adv

Perit Dial 11:266–269.
145. Hijazi R, Abitbol CL, Chandar J, et al (2009) Twenty-five Years of Infant Dialysis: A Single Center Experience. J Pediatr 155:111–117.
146. Amaral S, Sayed BA, Kutner N, Patzer RE (2016) Preemptive kidney transplantation is associated with survival benefits among pediatric patients with end-stage renal disease. Kidney Int 90:1100–1108.
147. Korevaar JC, Feith GW, Dekker FW, et al (2003) Effect of starting with hemodialysis compared with peritoneal dialysis in patients new on dialysis treatment□: A randomized controlled trial. Kidney Int 64:2222–2228.
148. Chesnaye NC, Schaefer F, Groothoff JW, et al (2016) Mortality risk in European children with end-stage renal disease on dialysis. Kidney Int 89:1355–1362.
149. Vidal E, van Stralen KJ, Chesnaye NC, et al (2016) Infants Requiring Maintenance Dialysis: Outcomes of Hemodialysis and Peritoneal Dialysis. Am. J. Kidney Dis. epub:
150. Chang HJ, Han KH, Cho MH, et al (2014) Outcomes of chronic dialysis in Korean children with respect to survival rates and causes of death. Korean J Pediatr 57:135–139.
151. Van De Luijtgaarden MWM, Jager KJ, Segelmark M, et al (2016) Trends in dialysis modality choice and related patient survival in the ERA-EDTA Registry over a 20-year period. Nephrol Dial Transplant 31:120–128.
152. National Institutes of Health National Institute of Diabetes and Digestive and Kidney Diseases (2011) U.S. Renal Data System, USRDS 2011 Annual Data Report: Atlas of Chronic Kidney Disease and End-Stage Renal Disease in the United States.
153. Bargman JM, Thorpe KE, Churchill DN (2001) Relative contribution of residual renal function and peritoneal clearance to adequacy of dialysis: a reanalysis of the CANUSA study. J Am Soc Nephrol 12:2158–2162.
154. Liao C-T, Chen Y-M, Shiao C-C, et al (2009) Rate of decline of residual renal function is associated with all-cause mortality and technique failure in patients on long-term peritoneal dialysis. Nephrol Dial Transplant 24:2909–2914.
155. Guzzo I, Mancini E, Kengne Wafo S, et al (2009) Residual renal function and nutrition in young patients on chronic hemodialysis. Pediatr Nephrol 24:1391–1397.
156. Chadha V, Blowey DL, Warady BA (2001) Is growth a valid outcome measure of dialysis clearance in children undergoing peritoneal dialysis? Perit Dial Int 21 Suppl 3:S179-184.
157. Borzych D, Rees L, Ha IS, et al (2010) The bone and mineral disorder of children undergoing chronic peritoneal dialysis. Kidney Int 78:1295–1304.
158. Wright S, Klausner D, Baird B, et al (2010) Timing of Dialysis Initiation and Survival in ESRD. Clin J Am Soc Nephrol 5:1828–1835.
159. Korevaar JC, Jansen MA, Dekker FW, et al (2001) When to initiate dialysis: effect of proposed US guidelines on survival. Lancet 358:1046–1050.
160. Lee J, An JN, Hwang JH, et al (2014) Effect of Dialysis Initiation Timing on Clinical Outcomes: A Propensity-Matched Analysis of a Prospective Cohort Study in Korea. PLoS One 9:e105532.
161. Atkinson MA, Oberai PC, Neu AM, et al (2010) Predictors and consequences of higher estimated glomerular filtration rate at dialysis initiation. Pediatr Nephrol 25:1153–61.
162. Cooper BA, Branley P, Bulfone L, et al (2010) A Randomized, Controlled Trial of Early versus Late Initiation of Dialysis. N Engl J Med 363:609–619.

163. Rama I, Grinyó JM (2010) Malignancy after renal transplantation: the role of immunosuppression. Nat Rev Nephrol 6:511–519.
164. Bartosh SM, Leverson G, Robillard D, Sollinger HW (2003) Long-term outcomes in pediatric renal transplant recipients who survive into adulthood. Transplantation 76:1195–1200.
165. Smith J, Martz K, Blydt-Hansen TD (2013) Pediatric kidney transplant practice patterns and outcome benchmarks , 1987 – 2010□: A report of the North American Pediatric Renal Trials and Collaborative Studies. Pediatr Transplant 17:149–157.
166. Webster AC, Craig JC, Simpson JM, et al (2007) Identifying high risk groups and quantifying absolute risk of cancer after kidney transplantation: A cohort study of 15 183 recipients. Am J Transplant 7:2140–2151.
167. Ploos van Amstel S, Vogelzang JL, Starink M V, et al (2015) Long-Term Risk of Cancer in Survivors of Pediatric ESRD. Clin J Am Soc Nephrol 10:2198–2204.
168. Luyckx VA, Naicker S, McKee M (2013) Equity and economics of kidney disease in sub-Saharan Africa. Lancet 382:103–104.
169. Sinha A, Bagga A (2014) Maintenance dialysis in developing countries. Pediatr Nephrol 211–219.
170. Harambat J, Ekulu PM (2016) Inequalities in access to pediatric ESRD care: a global health challenge. Pediatr Nephrol 31(3):353–358.
171. Miller MEY, Williams JA (2009) Chronic Renal Failure in Jamaican Children – an Update (2001 – 2006). West Indian Med J 58:231–234.
172. Asinobi AO, Ademola AD, Ogunkunle OO, Mott SA (2014) Paediatric end-stage renal disease in a tertiary hospital in South West Nigeria. BMC Nephrol 15:25.
173. Mong Hiep TT, Janssen F, Ismaili K, et al (2008) Etiology and outcome of chronic renal failure in hospitalized children in Ho Chi Minh City, Vietnam. Pediatr Nephrol 23:965–970.
174. Gulati S, Mittal S, Sharma RK, Gupta A (1999) Etiology and outcome of chronic renal failure in Indian children. Pediatr Nephrol 13:594–596.
175. Nahas AM El, Bello AK (2010) Chronic kidney disease: the global challenge. Lancet 365:331–340.
176. Kramer A, Stel VS, Tizard J, et al (2009) Characteristics and survival of young adults who started renal replacement therapy during childhood. Nephrol Dial Transplant 24:926–933.
177. Vogelzang JL, Heestermans LWAA, van Stralen KJ, et al (2013) Simultaneous reversal of risk factors for cardiac death and intensi fi ed therapy in long-term survivors of paediatric end-stage renal disease over the last 10 years.
178. Dobrowolski LC, van Huis M, van der Lee JH, et al (2016) Epidemiology and management of hypertension in paediatric and young adult kidney transplant recipients in The Netherlands. Nephrol Dial Transplant 31:1947–1956.
179. Groothoff JW, Gruppen MP, Offringa M, et al (2002) Increased arterial stiffness in young adults with end-stage renal disease since childhood. J Am Soc Nephrol 13:2953–2961.
180. Gruppen MP, Groothoff JW, Prins M, et al (2003) Cardiac disease in young adult patients with end-stage renal disease since childhood: A Dutch cohort study. Kidney Int 63:1058–1065.
181. Rianthavorn P, Ettenger RB, Malekzadeh M, et al (2004) Noncompliance with immunosuppressive medications in pediatric and adolescent patients receiving solid-organ transplants. Transplantation 77:778–782.
182. Van Arendonk KJ, James NT, Boyarsky BJ, et al (2013) Age at graft loss after pediatric kidney

transplantation: exploring the high-risk age window. Clin J Am Soc Nephrol 8:1019–1026.
183. Watson AR (2000) Non-compliance and transfer from paediatric to adult transplant unit. Pediatr Nephrol 14:469–472.
184. IPNA (2017) IPNA website. https://www.ipna-online.org/. Accessed 6 Feb 2017
185. Liu FX, Rutherford P, Smoyer-Tomic K, et al (2015) A global overview of renal registries: a systematic review. BMC Nephrol 16:1–10.
186. Verrina E, Edefonti A, Gianoglio B, et al (2004) A multicenter experience on patient and technique survival in children on chronic dialysis. Pediatr Nephrol 19:82–90.
187. Mandrekar JN Cutpoint Determination Methods in Survival Analysis using SAS.
188. Vonesh EF (2004) The differential impact of risk factors on mortality in hemodialysis and peritoneal dialysis. 66:2389–2401.
189. Heaf JG, Løkkegaard H, Madsen M (2002) Initial survival advantage of peritoneal dialysis relative to haemodialysis. Nephrol Dial Transpl 17:112–117.
190. Perl J, Wald R, McFarlane P, et al (2011) Hemodialysis vascular access modifies the association between dialysis modality and survival. J Am Soc Nephrol 22:1113–21.
191. Termorshuizen F (2003) Hemodialysis and Peritoneal Dialysis: Comparison of Adjusted Mortality Rates According to the Duration of Dialysis: Analysis of the Netherlands Cooperative Study on the Adequacy of Dialysis 2. J Am Soc Nephrol 14:2851–2860.
192. Vonesh EF, Snyder JJ, Foley RN, Collins AJ (2006) Mortality studies comparing peritoneal dialysis and hemodialysis: what do they tell us? Kidney Int Suppl 70:S3-11.
193. Jansen MAM, Hart AAM, Korevaar JC, et al (2002) Predictors of the rate of decline of residual renal function in incident dialysis patients. Kidney Int 62:1046–53.
194. Boehm M, Winkelmayer WC, Arbeiter K, et al (2010) Late referral to paediatric renal failure service impairs access to pre-emptive kidney transplantation in children. Arch Dis Child 95:634–638.
195. Jander A, Nowick M, Tkaczyk M, et al (2006) Does a late referral to a nephrologist constitute a problem in children starting renal replacement therapy in Poland? - A nationwide study. Nephrol Dial Transplant 21:957–961.
196. Kennedy SE, Bailey R, Kainer G (2012) Causes and outcome of late referral of children who develop end-stage kidney disease. J Paediatr Child Health 48:253–8.
197. Warady B a., Abraham AG, Schwartz GJ, et al (2015) Predictors of Rapid Progression of Glomerular and Nonglomerular Kidney Disease in Children and Adolescents: The Chronic Kidney Disease in Children (CKiD) Cohort. Am. J. Kidney Dis.
198. Ivarsen P, Povlsen J V (2014) Can peritoneal dialysis be applied for unplanned initiation of chronic dialysis? Nephrol Dial Transplant 29:2201–6.
199. Foley RN, Chen S-C, Solid CA, et al (2014) Early mortality in patients starting dialysis appears to go unregistered. Kidney Int 86:1–7.
200. Watson AR, Hayes WN, Vondrak K, et al (2013) Factors influencing choice of renal replacement therapy in European paediatric nephrology units. Pediatr Nephrol 28:2361–8.
201. Geary DF (1998) Attitudes of pediatric nephrologists to management of end-stage renal disease in infants. J Pediatr 154–156.
202. Laakkonen H, Holtta T, Lonnqvist T, et al (2008) Peritoneal dialysis in children under two years of age.

Nephrol Dial Transplant 23:1747–1753.
203. Vidal E, Edefonti A, Murer L, et al (2012) Peritoneal dialysis in infants: the experience of the Italian Registry of Paediatric Chronic Dialysis. Nephrol Dial Transplant 27:388–395.
204. Wedekin M, Ehrich JHH, Offner G, Pape L (2010) Renal replacement therapy in infants with chronic renal failure in the first year of life. Clin J Am Soc Nephrol 5:18–23.
205. Teh JC, Frieling ML, Sienna JL, Geary DF (2011) Attitudes of caregivers to management of end-stage renal disease in infants. Perit Dial Int 31:459–465.
206. Feber J, Schärer K, Schaefer F, et al (1994) Residual renal function in children on haemodialysis and peritoneal dialysis therapy. Pediatr Nephrol 8:579–583.
207. Kiliś-Pstrusińska K, Wasilewska A, Medyńska A, et al (2013) Psychosocial aspects of children and families of children treated with automated peritoneal dialysis. Pediatr Nephrol 28:2157–2167.
208. Donckerwolcke RA, Bunchman TE (1994) Hemodialysis in infants and small children. Pediatr Nephrol 8:103–6.
209. Shroff R, Wright E, Ledermann S, et al (2003) Chronic hemodialysis in infants and children under 2 years of age. Pediatr Nephrol 18:378–83.
210. Feinstein S, Rinat C, Becker-Cohen R, et al (2008) The outcome of chronic dialysis in infants and toddlers--advantages and drawbacks of haemodialysis. Nephrol Dial Transplant 23:1336–45.
211. Quinlan C, Bates M, Sheils A, et al (2013) Chronic hemodialysis in children weighing less than 10 kg. Pediatr Nephrol 28:803–809.
212. Bonthuis M, van Stralen KJ, Verrina E, et al (2012) Use of national and international growth charts for studying height in European children: development of up-to-date European height-for-age charts. PLoS One 7:e42506.
213. Ehrich JH, Rizzoni G, Brunner FP, et al (1992) Renal replacement therapy for end-stage renal failure before 2 years of age. Nephrol Dial Transplant 7:1171–7.
214. Goldstein SL, Macierowski CT, Jabs K (1997) Hemodialysis catheter survival and complications in children and adolescents. Pediatr Nephrol 11:74–7.
215. Chalem Y, Ryckelynck J-P, Tuppin P, et al (2005) Access to, and outcome of, renal transplantation according to treatment modality of end-stage renal disease in France. Kidney Int 67:2448–53.
216. Fuggle S V, Allen JE, Johnson RJ, et al (2010) Factors affecting graft and patient survival after live donor kidney transplantation in the UK. Transplantation 89:694–701.
217. Gill JS, Gill J, Rose C, et al (2006) The older living kidney donor: Part of the solution to the organ shortage. Transplantation 82:1662–6.
218. Øien CM, Reisaeter AV, Leivestad T, et al (2007) Living donor kidney transplantation: the effects of donor age and gender on short- and long-term outcomes. Transplantation 83:600–6.
219. Van Arendonk KJ, King E a., Orandi BJ, et al (2015) Loss of Pediatric Kidney Grafts During the "High-Risk Age Window": Insights From Pediatric Liver and Simultaneous Liver-Kidney Recipients. Am J Transplant 15:445–452.
220. Smith JM, Ho PLM, McDonald RA (2002) Renal transplant outcomes in adolescents: a report of the North American Pediatric Renal Transplant Cooperative Study. Pediatr Transplant 6:493–499.
221. Foster BJ, Pai ALH (2014) Adherence in Adolescent and Young Adult Kidney Transplant Recipients. Open Urol Nephrol J 7:133–143.

222. Arbus GS, Rochon J, Thompson D (1991) Survival of cadaveric renal transplant grafts from young donors and in young recipients. Pediatr Nephrol 5:152–157.
223. Briscoe DM, Kim MS, Lillehei C, et al (1992) Outcome of renal transplantation in children less than two years of age. Kidney Int 42:657–662.
224. Postlethwaite RJ, Johnson RJ, Armstrong S, et al (2002) The outcome of pediatric cadaveric renal transplantation in the UK and Eire. Pediatr Transplant 6:367–77.
225. Jahnukainen T, Bjerre A, Larsson M, et al (2016) The second report of the Nordic Pediatric Renal Transplantation Registry 1997-2012: More infant recipients and improved graft survivals. Pediatr Transplant 20:364–371.
226. Opelz G, Collaborative Transplant Study (1988) Influence of recipient and donor age in pediatric renal transplantation. Transpl Int 1:95–98.
227. Dale-Shall AW, Smith JM, McBride MA, et al (2009) The relationship of donor source and age on short- and long-term allograft survival in pediatric renal transplantation. Pediatr Transplant 13:711–718.
228. Opelz G, Döhler B (2010) Pediatric kidney transplantation: analysis of donor age, HLA match, and posttransplant non-Hodgkin lymphoma: a collaborative transplant study report. Transplantation 90:292–297.
229. Dharnidharka VR, Stevens G, Howard RJ (2005) En-bloc kidney transplantation in the United States: An analysis of United Network of Organ Sharing (UNOS) data from 1987 to 2003. Am J Transplant 5:1513–1517.
230. Sharma A, Fisher RA, Cotterell AH, et al (2011) En Bloc Kidney Transplantation From Pediatric Donors: Comparable Outcomes With Living Donor Kidney Transplantation. Transplantation 92:564–569.
231. Dion M, Rowe N, Shum J, et al (2014) Donation after Cardiac Death Pediatric En Bloc Renal Transplantation. J Urol 193:1–5.
232. Winnicki E, Dharmar M, Tancredi D, Butani L (2016) Comparable Survival of En Bloc versus Standard Donor Kidney Transplants in Children. J Pediatr 173:1–6.
233. Cransberg K, Van Gool JD, Davin JC, et al (2000) Pediatric renal transplantations in the Netherlands. Pediatr Transplant 4:72–81.
234. Eurotransplant Foundation (2013) Eurotransplant Manual – version 3.0. Eurotransplant Foundation, Leiden
235. Foster BJ, Dahhou M, Zhang X, et al (2013) Relative importance of HLA mismatch and donor age to graft survival in young kidney transplant recipients. Transplantation 96:469–75.
236. Simpson CM, McTaggart SJ, Sterne JAC, et al (2005) Grandparent donors in paediatric renal transplantation. Pediatr Nephrol 20:1636–1641.
237. Papachristou F, Stabouli S, Printza N, et al (2016) Long-term outcome of pediatric kidney transplantation: A single-center experience from Greece. Pediatr Transplant 500–506.
238. WHO (2011) Rio Political Declaration on Social Determinants of Health.
239. Caskey FJ, Schober-Halstenberg H-J, Roderick PJ, et al (2006) Exploring the differences in epidemiology of treated ESRD between Germany and England and Wales. Am J Kidney Dis 47:445–54.
240. Couchoud C, Guihenneuc C, Bayer F, et al (2012) Medical practice patterns and socio-economic factors may explain geographical variation of end-stage renal disease incidence. Nephrol Dial Transplant 27:2312–22.
241. Hommel K, Rasmussen S, Kamper A-L, Madsen M (2010) Regional and social inequalities in chronic renal replacement therapy in Denmark. Nephrol Dial Transplant 25:2624–32.
242. Böger CA, Gorski M, Li M, et al (2011) Association of eGFR-related loci identified by GWAS with incident

CKD and ESRD. PLoS Genet 7:3–10.
243. Köttgen A, Glazer NL, Dehghan A, et al (2011) Multiple Novel Loci are Associated with Indices of Renal Function and Chronic Kidney Disease. 41:712–717.
244. Stiller CA, Parkin DM (1990) International variations in the incidence of childhood lymphomas. Paediatr Perinat Epidemiol 4:303–324.
245. Stiller CA (2004) Epidemiology and genetics of childhood cancer. Oncogene 23:6429–44.
246. Hölttä T, Bonthuis M, Van Stralen KJ, et al (2016) Timing of renal replacement therapy does not influence survival and growth in children with congenital nephrotic syndrome caused by mutations in NPHS1: data from the ESPN/ERA-EDTA Registry. Pediatr Nephrol 2317–2325.
247. Bodenheimer T (2013) High and Rising Health Care Costs. Part 2: Technologic Innovation.
248. Sorenson C, Drummond M, Bhuiyan Khan B (2013) Medical technology as a key driver of rising health expenditure: disentangling the relationship. Clinicoecon Outcomes Res 5:223–34.
249. Bech M (2010) The influence of economic incentives and regulatory factors on the adoption of treatment technologies: a case study of technologies used to treat heart attacks. 18:1114–1132.
250. Vecchi AF De, Dratwa M, Wiedemann ME (1999) Nephrology Dialysis Transplantation Healthcare systems and end-stage renal disease (ESRD) therapies — an international review : costs and reimbursement / funding of ESRD therapies. 14:31–41.
251. Dor A, Pauly M V, Eichleay M a, Held PJ (2007) End-stage renal disease and economic incentives: the International Study of Health Care Organization and Financing (ISHCOF).
252. Kollée LAA, Cuttini M, Delmas D, et al (2009) Obstetric interventions for babies born before 28 weeks of gestation in Europe: results of the MOSAIC study. BJOG 116:1481–91.
253. Fan ZJ, Lackland DT, Lipsitz SR, et al (2007) Geographical patterns of end-stage renal disease incidence and risk factors in rural and urban areas of South Carolina. Health Place 13:179–87.
254. Couchoud C, Guihenneuc C, Bayer F, Stengel B (2010) The timing of dialysis initiation affects the incidence of renal replacement therapy. Nephrol Dial Transplant 25:1576–8.
255. Grassmann A, Gioberge S, Moeller S, Brown G (2005) ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. Nephrol Dial Transplant 20:2587–93.
256. Boyle PJ, Kudlac H, Williams AJ (1996) Geographical variation in the referral of patients with chronic end stage renal failure for renal replacement therapy. QJM 89:151–7.
257. Mircescu G, Capsa D, Covic M, et al (2004) Nephrology and renal replacement therapy in Romania--transition still continues (Cinderella story revisited). Nephrol Dial Transplant 19:2971–80.
258. Rodwell C, Aymé S (2015) Rare disease policies to improve care for patients in Europe. Biochim Biophys Acta - Mol Basis Dis 1852:2329–2335.
259. Union E (2011) European Union Committee of Experts on Rare Diseases: recommendations on qual- ity criteria for centres of expertise for rare diseases in Member States.
260. Yeates K, Ghosh S, Kilonzo K (2013) Developing nephrology programs in very low-resource settings: challenges in sustainability. Kidney Int Suppl 3:202–205.
261. Jiang Y, Shen Y, Lau KKH (2014) Survey of chronic haemodialysis in children between 2007 and 2012 in China. Nephrology 19:375–378.
262. Wühl E, Trivelli A, Picca S, et al (2009) Strict blood-pressure control and progression of renal failure in children. N Engl J Med 361:1639–50.

263. Chaudhary K, Sangha H, Khanna R (2011) Peritoneal dialysis first: rationale. Clin J Am Soc Nephrol 6:447–56.
264. Juergensen E, Wuerth D, Finkelstein SH, et al (2006) Hemodialysis and peritoneal dialysis: patients' assessment of their satisfaction with therapy and the impact of the therapy on their lives. Clin J Am Soc Nephrol 1:1191–1196.
265. Rubin HR, Fink NE, Plantinga LC, et al (2004) Patient ratings of dialysis care with peritoneal dialysis vs hemodialysis. JAMA 291:697–703.
266. Karahalios A, Baglietto L, Carlin JB, et al (2012) A review of the reporting and handling of missing data in cohort studies with repeated assessment of exposure measures. BMC Med. Res. Methodol. 12:
267. Ehrich JHH, Kerbl R, Pettoello-Mantovani M, Lenton S (2015) Opening the Debate on Pediatric Subspecialties and Specialist Centers: Opportunities for Better Care or Risks of Care Fragmentation? J Pediatr 167:1177–1178.
268. Ethier J, Mendelssohn DC, Elder SJ, et al (2008) Vascular access use and outcomes: An international perspective from the dialysis outcomes and practice patterns study. Nephrol Dial Transplant 23:3219–3226.