Transition of young people Affected by Rare Renal Conditions

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The definition of rare diseases varies across the world

Europe: a disease or disorder is defined as rare when the prevalence is <1 in 2000 individuals

USA: the designation of rare disorder applies when <200,000 Americans are affected

Japan : one in 2500 people in and fewer than one in 500 000 people in China

The incidence of a rare disease can vary substantially between regions or ethnic groups

For example, congenital nephrotic syndrome of the Finnish type occurs more frequently in Finland (incidence of one in 8200 people) than in other parts of the world

Rare kidney diseases encompass $ 150 different conditions. The majority are inherited **(About 80% of rare diseases have an identified genetic origin)** while others, such as the primary glomerulonephritis's, have complex etiologies Conditions include :

congenital malformations

familial cystic renal diseases

Glomerulopathies

tubulopathies

microangiopathies

metabolic nephropathies

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Rare inherited kidney diseases: challenges, opportunities, and perspectives

Olivier Devuyst, **Nine V A M Knoers**, **Giuseppe Remuzzi**, and **Franz Schaefer for the Board of the Working Group for Inherited Kidney Diseases of the European Renal Association and European Dialysis and Transplant Association**

At least 10% of adults and nearly all children who receive renal-replacement therapy have an

inherited kidney disease. These patients rarely die when their disease progresses and can remain alive for many years because of advances in organ-replacement therapy

the fifth most common cause of end-stage renal disease after diabetes, hypertension, glomerulonephritis, and pyelonephritis

Genetics were first used in nephrology in the 1980s with the mapping of autosomal dominant polycystic kidney disease in 1985 and the first identification of a causal mutation for a monogenic kidney disorder (Alport's syndrome) in 1990

These breakthroughs were followed by identification of genes involved in classic disorders more than 160 rare kidney diseases :

- **nephrogenic diabetes insipidus**
- **autosomal dominant polycystic kidney disease type 1**
- **Liddle's syndrome**
- **Dent's disease**
- **Bartter's and Gitelman's syndromes**
- **nephropathic cystinosis**
- **Steroid-resistant nephrotic syndrome**

These disorders are caused by mutations in genes coding for a wide range of proteins including receptors, channels and transporters, enzymes, transcription factors, and structural components that might also have a role in extrarenal organs (bone, eye, brain, skin, etc)

Unknown genetic cause

Known monogenic causes :

only 30–40% of cases of familial steroid-resistant nephrotic syndrome

40–50% of cases of congenital tubulopathy

50–60% of cases of atypical haemolytic uraemic syndrome

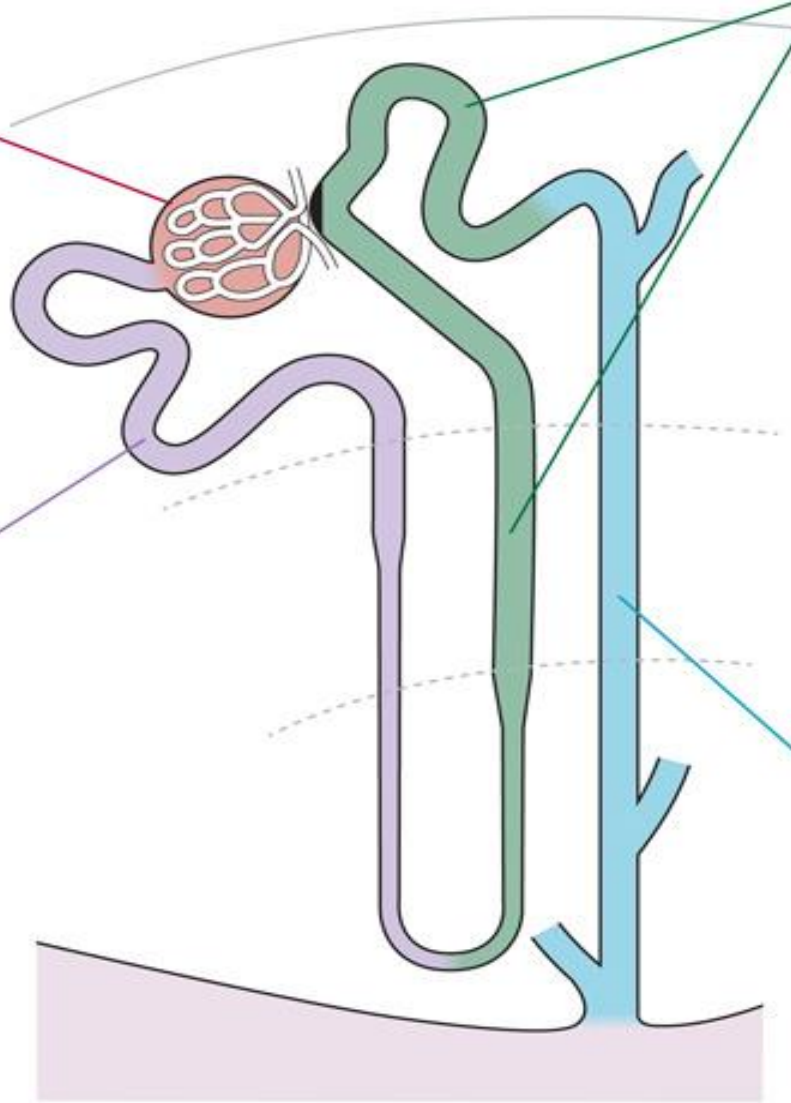
Poor appreciation of genetic studies , Even for well defined disorders such as Alport's, Bartter's, and Gitelman's syndromes

Clinical heterogeneity:

Many rare mendelian kidney diseases have a different prevalence in different populations and have substantial clinical heterogeneity in presence, age of onset, severity, and progression of symptoms

Glomerular diseases
- Congenital steroid-resistant nephrotic syndrome
- Denys-Drash syndrome, Frasier's syndrome
- Wilms' tumour, aniridia, genitourinary abnormalities, and mental retardation (WAGR) syndrome
- Pierson's syndrome
- Nail-patella syndrome
- Schimke immuno-osseous dystrophy
- Mitochondrial disorders with steroid-resistant nephrotic syndrome
- Fabry's disease
- Alport's syndrome
- Benign familial haematuria (thin basement membrane)
- Fechtner syndrome (Alport's syndrome with macrothrombocytopenia)
- Alport's syndrome with leiomyomatosis
- Familial amyloidosis

Proximal tubule
- Renal glucosuria
- Dicarboylic aminoaciduria
- Lysinuric protein intolerance
- Proximal renal tubular acidosis
- Hypophosphataemic rickets
- Nephropathic cystinosis
- Primary renal Fanconi's syndrome
- Fanconi-Bickel syndrome (hepatorenal glycogenosis)
- Lowe's syndrome
- Dent's disease, types 1 and 2
- Hereditary renal hypouricaemia
- Cystinuria, types 1–3



Thick ascending limb and distal convoluted tubule
- Bartter's syndrome, types 1–4
- Familial hypocalciuric hypercalcaemia
- Neonatal severe hyperparathyroidism
- Autosomal dominant hypocalcaemia
- Gitelman's syndrome
- Pseudohypoaldosteronism type 2 (Gordon's syndrome)
- SeSAME syndrome (EAST syndrome)
- Hypomagnesaemia, types 1–6
- Familial juvenile hyperuricaemic nephropathy

Collecting duct
- Liddle's syndrome
- Distal renal tubular acidosis
- Pseudohypoaldosteronism type 1
- Nephrogenic diabetes insipidus, types 1 and 2
- Nephrogenic syndrome of inappropriate antidiuresis

Rare Disease:

- Compromised health with a poor quality of life

For instance, children with severe congenital nephropathies, who can be dialyzed from neonatal age onwards, face many decades of life with end-stage renal disease and have a high likelihood of changes in physical, cognitive, and psychosocial development

- Multisystem complications that add to the typical challenges for rare disorder

variable phenotypes, fragmented clinical and biological data, an absence of standardization for diagnostic procedures, and poor knowledge for disease mechanisms and natural history

Rare inherited kidney diseases: why they are different?

Primary kidney disorders :

blood pressure

plasma composition

electrolyte and acid-base homoeostasis

cardiac excitability

growth dynamics and puberty

CNS and cognitive functions

Various aspects of renal function can also be affected in extrarenal rare disorders or polymalformative syndromes, including mitochondrial cytopathies

Patient organizations can foster these activities and provide support to the community.

Examples in rare kidney diseases include associations for cystic kidney disorders, primary hyperoxaluria, cystinosis, Lowe's syndrome, metabolic disorders, and so on Coalitions of patient organizations have been important stakeholders in health policies, helping to pass the US Orphan Drug Act in 1983 and to establish the Framework Programmed 7 research agenda in Europe

Transitioning from pediatric to adult care

Transition is defined as a well-planned process that occurs over time leading the adolescent or young adult patient to gain competency

Its aim is to enable the patients so that at transfer they can take full responsibility for their own healthcare

The patient is ready for transfer into adult based care if s/he knows and understands:

(a) his medical condition/illness

(b) his medication and other treatment, e.g. diet

(c) how/where to make appointments for medical care

(d) how to react in emergency period of puberty takes time

Consensus Statement on Transitions (2002, 2011)

Purposeful, **planned** process that addresses the **medical**, **psychosocial** and **educational/vocational needs** of young people with chronic medical conditions, as they move from child-centered to adult-oriented health care system

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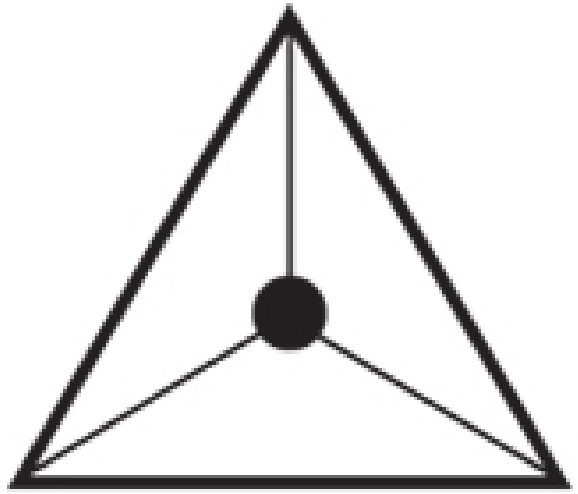
The Triple Aim

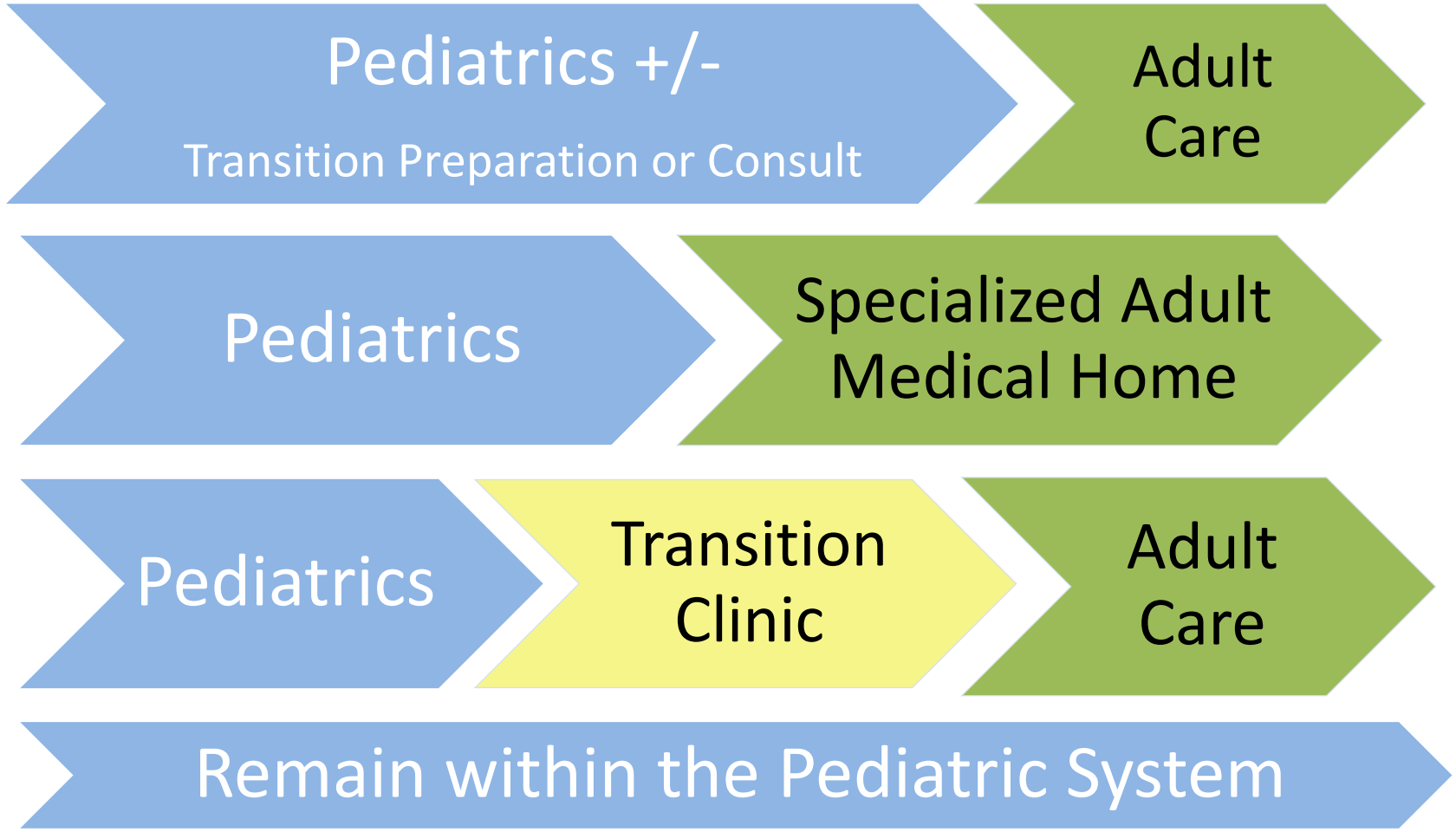
Improving
patient experience



Improving
population outcomes

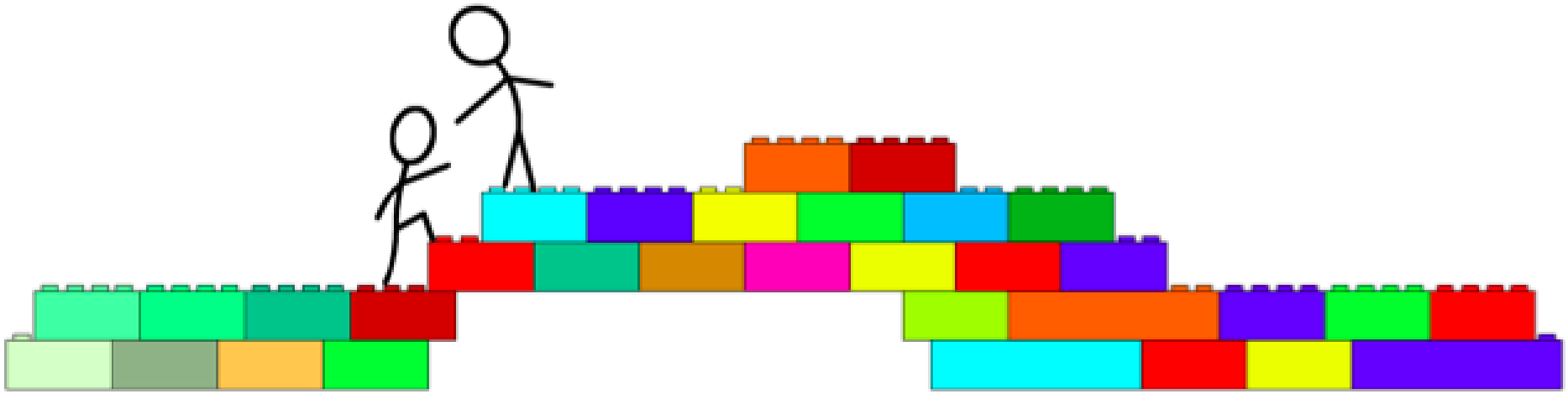
Lowering
per capita costs

Transition Processes Now




همیشه یک برنامه سالم درمانی باید داشته باشیم
مریضا معمولا به یک برنامه سالم برای زندگی سالم
نیاز دارن، نه یک برنامه برای درمان صرفا
کی نوبت من میشه که برم صحبت کنم؟
من مثل یه آدم غریبه میمونم بین این همه آدم
تبدیل، یک معذل بسیار مهم و بسیار خطرناک به شمار میره

Bridging The Gap



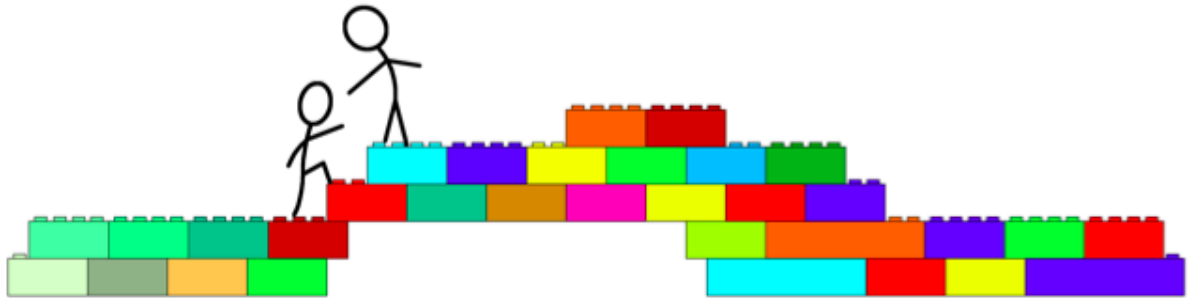
Bridging The Gap:

Transition of young people Affected by Rare Renal Conditions

Build and support self-management skills

Tele-mediated specialty support

Guide patients & families through service changes



~15% net reduction in annual per capita medical spending for target population

what happens during transition from child to adult services from age 14 to 25 years?

Young people with CKD have very specific medical needs and experience their condition in distinctive ways:

steroids may dramatically alter their appearance and mood

CKD may stunt their growth

Lifestyle modifications may be extreme (such as fluid and diet restrictions)

Medications may have unpleasant side effects

Treatments (such as dialysis) can be very time consuming and restrictive, and depending on the modality may involve employed or unpaid carers, and regular travel to hospital

Impact on reproductive choices and lifestyle ambitions as well as education options, such as choice of school, university or apprenticeships, career choices, travel, relationships and ability or choice to live independently in Adulthood

http://www.kidney-international.org

Transition from pediatric to adult renal services: a consensus statement by the International Society of Nephrology (ISN) and the International Pediatric Nephrology Association (IPNA)

Alan R. Watson[1], Paul N. Harden[2], Maria E. Ferris[3], Peter G. Kerr[4], John D. Mahan[3] and Maher Fouad Ramzy[5], Consensus Panel Members

The number of young patients graduating from pediatric to adult renal care has progressively increased due to improved management resulting in patient survival rates of 85–90%.

Adult renal services are being exposed to an increasing number of adolescent and young adult patients who have either transitioned from pediatric care or presented directly to adult services

It is recognized that there are substantial risks of non-adherence at the time of transfer from pediatric to adult care and among the cohort of patients aged <25 years who are managed in adult care

European Journal of Human Genetics (2019) 27:1783–1790
https://doi.org/10.1038/s41431-019-0460-z

ESHG

ARTICLE

Current management of transition of young people affected by rare renal conditions in the ERKNet

Martin Kreuzer[1] · Jens Drube[1] · Jenny Prüfe[1] · Franz Schaefer[2] · Lars Pape[1] · Members of the ERKNet Taskforce 'QoL & Transition'

ERKNet is the "European Reference Network for Rare Kidney Diseases", a consortium of 38

expert paediatric and adult nephrology centres in 12 European countries which provide healthcare to more than 40,000 patients with rare kidney conditions:

Age of first introduction of the concept of transition of 36 ERKNet experts; the ISN/IPNA consensus recommendation is displayed as shaded area:

3% <12 28%=12-14 25%=14-16 19%= 16-18 25%>18

Clin Exp Nephrol (2016) 20:918–925
DOI 10.1007/s10157-016-1231-6

ORIGINAL ARTICLE

Transition of adolescent and young adult patients with childhood-onset chronic kidney disease from pediatric to adult renal services: a nationwide survey in Japan

Motoshi Hattori[1] · Masayuki Iwano[2] · Mayumi Sako[3] · Masataka Honda[4] ·

148 institutions:C-CKD total of 3138 patients divided into a transfer (n = 1260) and a non transfer (n = 1878)

The most frequent primary kidney disease in both the transfer (23.5 %) and non-transfer (22.6 %) groups:

IgA nephropathy (IgAN), followed by minimal change NS (16.7 and 15.0 %, respectively), CAKUT (12.9 and 10.7 %, respectively), focal segmental glomerulosclerosis (5.3 and 5.4 %, respectively), lupus nephritis (4.7 and 3.8 %, respectively), IgA vasculitis nephritis (3.8 and 3.5 %, respectively) and Alport syndrome (3.9 and 3.2 %, respectively)

The peak age at transfer was 20–24 years, with 65.5 % of these patients transferred from pediatric to adult renal services before age 25 years. The remaining 34.5 % were transferred after age 25 years

Reasons for transfer : Proposed transfer (the most common reason)Life events, including employment, furtherance of education at a higher level, moving to new addresses, marriage and pregnancy

Educational levels:

Of the patients in these two groups, 42.9 and 44.3 %, respectively, were in college or graduate school

Employment status:

20.7 and 24.0 %, respectively, were unemployed at the time of this survey.

Common Elements in Rare Kidney Diseases: Conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference

OPEN

Ségolène Aymé[1], Detlef Bockenhauer[2], Simon Day[3], Olivier Devuyst[4,16], Lisa M. Guay-Woodford[5,16], Julie R. Ingelfinger[6], Jon B. Klein[7], Nine V.A.M. Knoers[8], Ronald D. Perrone[9], Julia Roberts[10], Franz Schaefer[11], Vicente E. Torres[12], Michael Cheung[13], David C. Wheeler[14] and Wolfgang C. Winkelmayer[15]; for Conference Participants[17]

The age at which a patient makes the transition from pediatric to adult care varies between and within countries. For example, in Singapore, the age of transition is 12 years ,whereas in the USA, patients in their 20s can still be in the transition process

Kidney Disease: Improving Global Outcomes (KDIGO) convened a global, multidisciplinary Controversies Conference to address 5 central issues in rare kidney diseases:

1-Diagnostic challenges

2-Management of kidney functional decline and progression of chronic kidney disease (CKD)

3-Challenges in clinical study design

4- Translation of advances in research to clinical care

5-Provision of practical Integrated patient support

Pediatr Nephrol (2014) 29:2379–2385
DOI 10.1007/s00467-014-2864-x

ORIGINAL ARTICLE

Differences between paediatric and adult presentation of ESKD in attainment of adult social goals

Helen Lewis · Stephen D. Marks

Young adults (n = 296, 52 % male, 79 % Caucasian and 73 % with functioning renal allograft) with a mean age at first presentation of ESKD and current age of 17 and 25 years of whom 5 % still attended paediatric services.

Outcomes of patients aged >23 years and in stable health (n=146) were compared between paediatric and adult presentation, with 30 and 20 % of patients, respectively, registered as disabled (p=0.02).

Educational attainment, based on percentage of those not achieving the General Certificate of Secondary Education (GCSE) level for England, was lower in the paediatric presentation group than in the adult one (7 vs. 18 %, respectively; p=0.04).

Transition From Pediatric to Adult Renal Care: Education, Preparation, and Collaboration for Successful Patient Outcomes

Angela Degnan, LCSW, LSCSW, NSW-C, Sarah Henderson, LMSW,
Amy Nau, RN, MSN, MBA, Children's Mercy Hospital, Kansas City, MO

Kennedy and Sawyer (2008) define "transition" as the period of preparation prior to and after the event of transfer

The literature has recently indicated a significant improvement in success rates and as many as 90% of dialysis and transplant patients are living past 21 years old

transition education program was developed and implemented by the dialysis and kidney transplant program at Children's Mercy Hospital. The program, entitled"Kidney Education for Your Success (K.E. Y.S.)," is designed to be initiated when the patient reaches age 12 and to continue until the patient is transferred to adult care

Phase1=12-14 Phase2=15-17 Phase3=18-20 Phas4=21 through transfer to adult care

Clin Exp Nephrol. 2014 Dec;18(6):939-43. doi: 10.1007/s10157-014-0941-x. Epub 2014 Feb 2.

The problem of transition from pediatric to adult healthcare in patients with steroid-sensitive nephrotic syndrome (SSNS): a survey of the experts

Masataka Honda [1], Kazumoto Iijima, Kenji Ishikura, Kazunari Kaneko

About one-third of pediatric nephrologists (PNs) did not transfer patients to adult units, and half of PNs followed patients after they reached adulthood (i.e., age >20 years)

The dose of steroids after puberty varied between doctors, but 74 % of PNs provided short-term daily therapy. 72 % of PNs informed the patients of the shift in steroid dose, but 26 % of PNs did not

About two-thirds of PNs did not consult with adult nephrologists before the transition from pediatric to adult care

No institute had a transition program for SSNS and 2 institutes had transition coordinators

Child health

Qualitative synthesis

Transition from paediatric to adult care for chronic diseases may cause insecurity and unpreparedness for new relationships and surroundings FREE

Thelma Begley

A total of 18 studies : 368 participants between 1999 and November 2010

Fegran and colleagues identified the following overarching theme that emerged from the data analysis, 'being in limbo moving from familiar to unknown ward cultures and achieving responsibility'

The four associated subthemes were:

facing changes in significant relationships

moving from familiar to an unknown

being prepared for transfer

achieving responsibility

Age of transfer from paediatric to adult care in the studies reviewed ranged from 14 to 22 years.

Stage	Number	%
3a	41	8.4
3b	10	2
4	116	22.7
5	322	62.5
Total	489	100
Age groups(years)		
<1	38	7.8%
1-5	76	15.5
5-10	175	32.1
>10	218	44.6
Gender		
Male	254	51.6
Female	235	48.1

Causes	Number	%
Congenital structural anomalies	204	41.4
Glomerular diseases	118	24.1
Renal Tubular disease	40	8.2
Hereditary renal diseases	75	15.3
Stone	26	5.3
Other	26	5.3
Total	489	100

Treatment	conservative	217	44.4
	PD	57	11.6
	HD	175	35.7
	TX	40	8.2
Prognosis	Alive	396	81.0
	Death	93	19.0
	Total	489	100.0

277 بیمار با سندروم فانکونی در طی 10 سال بین 6ماه تا 20 سال با میانگین وزنی 13.9 و قد96.43 بررسی شدند

	Minimum	Maximum	Mean	Std. Deviation
GFR	8.80	144.77	58.16	22.77447

stage	Number	%
1	24	7.3
2	103	31.3
3a	70	21.1
3b	58	17.5
4	18	5.4
5	4	1.2