Young people with, or at risk of Autosomal Dominant Polycystic Kidney Disease

Paul Winyard, UCL Great Ormond Street Institute of Child Health.

Jan Dudley, Bristol Royal Hospital for Children
In children and young people:

- Should they be told that they might have ADPKD?
- Is there any reason to diagnose asymptomatic ADPKD?
Classical view on children with ADPKD:

a) 1-2% early presentation
b) 98-99% slowly progressive
c) No point in worrying children by talking about it or doing any tests until they can decide for themselves

Hypertension (>95 percentile) - 22%
Hyperlipidemia - 54%
Proteinuria (>150 mg/d) - 7%

Note 98 % normal renal function
Presymptomatic screening of ADPKD is not currently recommended for at-risk children. For at-risk adults the potential benefits of presymptomatic diagnosis usually outweigh the risks, ........
ADPKD in children: “the screening of asymptomatic children with a positive family history is not recommended. ….. the early detection and treatment of hypertension is important. Screening for hypertension in all at-risk children from the age of 5 years might be a pragmatic approach”.
“Diagnostic screening of asymptomatic children is not recommended. However, expert opinion advises screening for hypertension from 5 years of age in at-risk children, to identify and treat hypertension and prevent later cardiovascular complications”.
Blood pressure in ADPKD

Blood pressure:
• 25% hypertensive as adolescents
• 67% hypertensive by age 30

Cysts progressively developing with age; corresponding loss of normal functioning tissues

GFR normal until age 40+
Dear friends,

we are glad to present the ADPKiDs study that has been established with the support from the ERA-EDTA Working Group on Inherited Kidney Diseases (WGIKD) and has been endorsed by the European Society of Pediatric Nephrology (ESPN).

This study has two very simple goals, namely to establish a European cohort of children with autosomal dominant polycystic kidney disease (ADPKD) and to assess the prevalence of (pre)-hypertension by Ambulatory Blood Pressure Monitoring (ABPM).

Francesco Emma, Franz Schaefer

1. age < 18 years
2. at least 1 renal cyst
3. positive family history for ADPKD or proven PKD1/PKD2 mutation
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Francesco Emma, Franz Schaefer

**310 patients enrolled in 22 European centres,**

1. mean age $11.5 \pm 4.2$ years
2. 34% on BP medicines or ABPM > 95th centile
3. Night time: 35% non-dippers and 19% isolated ↑BP

IPNA, Brazil, September 2016
Hypertension in autosomal dominant polycystic kidney disease: a meta-analysis

Matko Marlais\textsuperscript{1}, Oliver Cuthell\textsuperscript{2}, Dean Langan\textsuperscript{1}, Jan Dudley\textsuperscript{2}, Manish D Sinha\textsuperscript{3}, Paul J D Winyard\textsuperscript{1}
Hypertension in autosomal dominant polycystic kidney disease: a meta-analysis

Mean Age vs. % with Hypertension

% with Hypertension

Mean Age (years)
How do we know that mildly elevated blood pressure is bad for children?
4,860 men aged 20-39 at inception; mean 24.5 years of follow-up after age 40
Renal volume, renin-angiotensin-aldosterone system, hypertension, and left ventricular hypertrophy in patients with autosomal dominant polycystic kidney disease.

- 5-yr follow-up
- progressive increase LVMI in hypertensive group
- half with borderline developed frank hypertension
- BP well controlled ACEI

Children with hypertension or borderline hypertension had a significantly greater left ventricular mass index (LVMI).
Grant to investigate blood pressure in children and young people with ADPKD

Matko Marlais, Manish Sinha, Paul Winyard
Evelina and GOS/ICH

• Clinic BP, 24hr BP, Central BP, Cardiac echo
• Pilot study - 50 children/young people
There are no UK guidelines on management of ADPKD in Children and Young People

A survey of UK management of childhood ADPKD

• **Aim**
  – To ascertain current practice amongst UK paediatric nephrologists

• **Method**
  – Case-based approach to establish patterns in practice
  – Questionnaire x 2 – 1 child, 1 young adult
Management of Children with Possible ADPKD

We are a group of Paediatric Nephrologists interested in polycystic kidney disease to assess how children and young people affected by ADPKD are currently managed around the UK.

This survey contains similar questions for two different scenarios when the diagnosis is proved or just suspected.

Please feel free to give frank answers - there is probably no correct response for most of these questions at the moment but we hope to develop better guidelines for future management, particularly as new treatments are developed. Free text comments also appreciated.

Yours sincerely
Amanda Richardson, Maanasa Polubothu, Manish Sinha, Larissa Kerecuk and Paul Winyard
(NB: this is a confidential survey, not open to the public and the results will be kept secure)

SCENARIO 1
A four year old boy has been diagnosed with ADPKD following a routine ultrasound via the GP because his mother has a family history of the condition. He is referred to your specialist centre to review and develop a management plan.

Examination is unremarkable with height on the 50th centile, weight 7th centile and BP on 60th centile.

- Would you perform DNA analysis to confirm the diagnosis?
  - Yes
  - No

- Would you
  - Refer back to GP
  - Refer back to local hospital

If you said Yes to any of the above, what instructions do you give to his GP/local hospital?

- Once 6 mths
- Every 2 yrs
- Never
- Other - please specify

If you follow this type of patient in your clinic, how often would you?

- Review him
- Check BP
- Perform
## Estimated Number of children with ADPKD at each centre

<table>
<thead>
<tr>
<th>Centre</th>
<th>Lowest Estimate</th>
<th>Highest Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOSH</td>
<td>15</td>
<td>100</td>
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<tr>
<td>ECH</td>
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<td>20</td>
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<td>Cardiff</td>
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<td>Nottingham</td>
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</tr>
<tr>
<td>SPIN</td>
<td>20</td>
<td>(258)</td>
</tr>
</tbody>
</table>
Results

How often would you review?

- Once - then refer back
- 3 mths
- 6 mths
- Yearly
- Every 2 yrs
- Every 5 yrs
- Never
How often would you perform routine cardiac echo?

- Once - then refer back
- 3 mths
- 6 mths
- Yearly
- Every 2 yrs
- Every 5 yrs
- Never
ADPKD in Children Guideline
Working Group

Renal Association / BAPN / RCPCH

Jan Dudley, Matko Marlais, Tess Harris, Paul Winyard, Oliver Cuthell, Dick Sandford, Sarah Borrows, Lukas Foggensteiner, Kay Turner and Lucy Moore

Expected date of publication: 2018
Telling children / young people they may have ADPKD

1. Who should do it?
2. At what age?
3. Concerns about consent and long term implications?
Parents' and children's communication about genetic risk: a qualitative study, learning from families' experiences

Alison Metcalfe,1,* Gill Plumridge,2 Jane Coad,3 Andrew Shanks,2 and Paramjit Gill2

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Abstract

Little is known about how parents explain to their children their risk of inheriting a gene that may cause disease in the child or in the child's future progeny. This study explored how genetic risk information is shared between family members and the factors affecting it, to ascertain the implications for children, young people and their parents to inform future service development and provision. A volunteer group of parents, children (8–11 years) and young people (12+ years) in families affected by or at risk of one of six inherited genetic conditions was interviewed. The
Parents' and children's communication about genetic risk: a qualitative study, learning from families' experiences

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 7 years</td>
<td>Children began to notice and question visible difference and some asked if they were likely to be affected in the same way as what they observed. Some understood that the condition was a result of the biological relationship between parents and child in the same way as eye colour.</td>
</tr>
<tr>
<td>8 - 11 years</td>
<td>Children understood the condition in terms of what they could see and how it currently affects their daily lives. Most understood the notion of hereditary in terms of the condition being passed down through the family but had no idea of hereditary patterns.</td>
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<tr>
<td>12 - 14 years</td>
<td>Children began to understand more about the condition in terms of expected future symptoms and about mortality. Most understood hereditary in terms of their relationship to their parent(s) but not to their future children. Most use genetic language but without an underlying understanding, and they could not describe hereditary patterns accurately or quantify risk.</td>
</tr>
<tr>
<td>15 - 17 years</td>
<td>Young people understood that they may carry a gene that could or would affect their health. They had a clearer understanding of mortality although still not always the stages of progression. They were more able to describe hereditary patterns and began to realise the implications for their own future children.</td>
</tr>
<tr>
<td>18 years plus</td>
<td>Young adults began to understand the wider implications of the condition and relate it more to themselves. They realised how it might influence their career choices and personal relationships and how their decisions relating to genetic testing had impact on other family members.</td>
</tr>
</tbody>
</table>

Children seemed to accept information at a relatively superficial level. There were some behavioural problems or signs of stress when they were not given information in difficult family situations.

Children continued to accept information at a relatively superficial level and looked for positives and did not let the condition become the central focus of their lives.

A period of rebellion for some children who became angry and questioned 'why me?' Some children challenged treatments and routines.

Young people reported upset and shock as they better understood the mortality, responded to test results or faced surgery. However they looked for positives and did not let the condition monopolise their life.

The most difficult time emotionally. Young adults were coming to terms with the implications of the condition at a time when so many other important life decisions and choices are being made.
What do ADPKD parents think?

MUM 1
I have 3 children with ADPKD, the oldest being diagnosed at 9 after suffering a burst cyst, the youngest (with many cysts and hypertension) at 2. Originally we were not going to screen them and just have annual BP checks but after worries about their blood pressure we requested scans. I have been very happy with the care we have received from probably 4 different paediatric nephrologists. The care is great, depending on their problems I would say once a year is the norm for them to be seen, but I do have a local contact point if we were to have any problems or worries. Some doctors have said they will do annual blood tests, some have said every 3 or 4 years but I would hope if I was concerned they would do it before then.

MUM 2
I have 2 children aged 3 and 5. I was diagnosed with ADPKD last July. I have told my GP about my sons’ chances of having ADPKD, they just said he can be scanned when they're 20. No referral or anything.

MUM 3
I have one son aged 11 with ADPKD. He was diagnosed 2 years ago. I am very happy with the care we have received from the paediatric nephrologist. He checks urine, BP and bloods. He is very forthcoming with info regarding new drugs etc. My son was scanned at 2 weeks old and there was some small cysts visible at that point on his kidneys. He has complained of back ache and pain at the bottom of his stomach so I suspect he is getting symptoms.

MUM 4
I have three children (3 & 11 month old twins) and due to my eldest being in hospital with a nasty virus this week they found cysts on an ultrasound :-(. She will now be reviewed by a consultant. I do not have anyone else to ask for a second opinion.
Interventions for preventing the progression of autosomal dominant polycystic kidney disease (Review)

Bolignano D, Palmer SC, Ruospo M, Zoccali C, Craig JC, Strippoli GFM

There is currently insufficient evidence to show that drugs used for people with ADPKD can protect kidney function to delay needing dialysis or a kidney transplant. Further evidence from large, well-designed clinical studies is needed to inform healthcare decision making before these drugs can be chosen routinely to achieve better health outcomes for people with ADPKD.
ADPKD in children and young people

- Primarily a cardio-vascular disease
- We don’t have proper guidelines
- Major ethical and financial implications of changing practice
In children and young people:

- Should they be told that they might have ADPKD?
- Is there any reason to diagnose asymptomatic ADPKD?