Alleviating the burden of ADPKD in Europe: estimating the impact of treatment on patient and health system outcomes in four EU countries

O'Reilly R[1], McEwan P[2,3], Bennett H[2], Robinson R[1]

[1] Otsuka Pharmaceutical Europe Ltd, Wexham, UK; [2] Health Economics & Outcomes Research Ltd, Monmouth, UK;
[3] School of Human & Health Sciences, Swansea University, Swansea, UK

INTRODUCTION AND AIMS

The aetiology of autosomal dominant polycystic kidney disease (ADPKD), related progression toward end-stage renal disease (ESRD) and eventual requirement for renal replacement therapy (RRT) has a significant impact on quality of life and healthcare resource use [1].

As the most common inherited kidney disease [2], ADPKD accounts for approximately 10% of patients receiving RRT in Europe [3].

Chronic kidney disease is associated with a greater than four-fold increase in healthcare costs, in part due to the incidence of associated comorbidities such as anaemia and cardiovascular disease. In 2012, the cost of dialysis treatment alone was estimated to make up 2% of healthcare budgets in Europe, and is predicted to double over the next five years [4].

This study aimed to:

- Quantify the current public health burden of ADPKD in four European countries in terms of ESRD incidence, dialysis and transplant requirements, life expectancy, quality of life and productivity.
- Assess the potential impact of slowing disease progression via treatment (based on data for tolvaptan) [5].

METHODS

The ADPKD Outcomes Model (ADPKD-OM) [6] was used to predict long-term patient and health system outcomes over a 50-year horizon in four European settings: UK, Sweden, Netherlands and Belgium.

Table 1 summarises the published sources utilised to inform model inputs; analysis was based on published country-specific data where available, applied to a patient cohort consistent with the CRISP study population at baseline (mean age 33.8) [7, 8].

Initiation of RRT was modelled once eGFR fell below thresholds of 7.8-8.5 ml/min/1.73m^2 and a minority of patients (10-12%) were assumed to receive conservative care at ESRD onset or transplant failure, dependent on country setting.

Point estimates of ESRD incidence, RRT requirements and undiscounted losses of working years, quality-adjusted life-years (QALYs) and life expectancy versus the general population were reported from probabilistic sensitivity analyses.

Table 1. Summary of sources informing key model inputs; country-specific sources shaded grey

Model parameter	UK	Sweden	Netherlands	Belgium
eGFR level at RRT initiation	[9]	[19]	[3]	[3]
Distribution of dialysis modalities	[10]	[20]	[23]	[24]
Probability of dialysis complications	[11]	[11]	None	None
Probability of transplant	[11, 12]	[20]	[24]	[28]
Transplant survival probabilities	[13]	[20]	[3]	[29]
Dialysis survival probabilities	[10]	[20]	[25]	[29]
Health-related utility: CKD 1-4	[14]	[21]	[14]	[14]
Health-related utility: CKD 5 and RRT	[15]	[21]	[15] [26]	[15,26]
Proportion of population employed	[16]	[22]	[27]	[30]
Proportion work time lost: CKD 1-5 (pre-RRT)	[17]	[21]	[21]	[21]
Proportion work time lost: RRT	[18]	[21]	[21]	[21]

CKD: chronic kidney disease, eGFR: estimated glomerular filtration rate, RRT: renal replacement therapy

Among treated patients, the annual rate of renal decline predicted under the natural history of ADPKD was subject to a constant reduction of 31.6% ± 7.8% and the incidence of serious pain events was reduced from 7 to 5 events per 100 patient years. No discontinuation of treatment was modelled prior to ESRD onset [5].

To estimate public health burden at a national level, results were scaled up based on an ADPKD prevalence rate of 4.28 per 10,000 population across countries [Otsuka data on file].

RESULTS

50-year predictions of ADPKD public health burden were significant across the four countries. Inter-country differences were primarily driven by the frequency of RRT modalities (e.g. higher probabilities of transplant in Sweden and Netherlands compared to UK and Belgium) and underlying mortality hazards.

Across settings, approximately 93% of patients were predicted to reach ESRD within 50 years under the natural history of ADPKD, at a mean age of 53 years. One transplant was predicted for every 2.1 patients in the Netherlands, 2.4 in Sweden and 2.7 in the UK, compared to 4.5 in Belgium. The estimated mean time on dialysis per patient ranged from 3.1 years in Sweden to 5.4 years in Belgium (Figure 1).

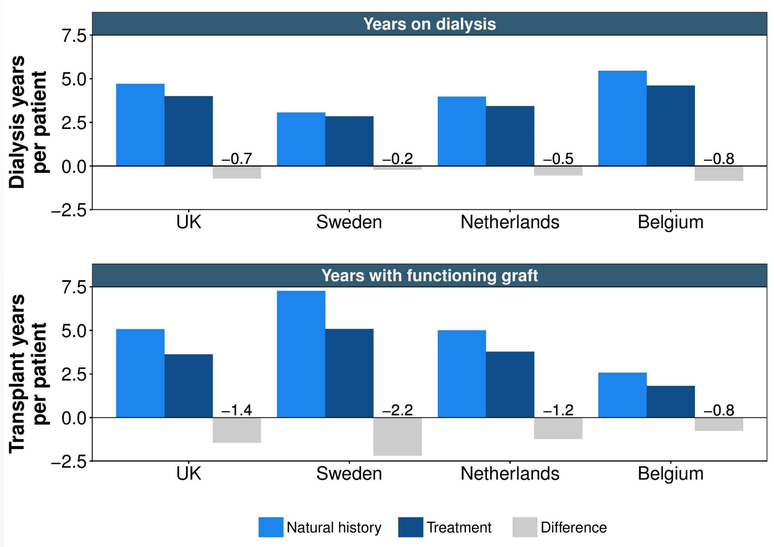

Figure 1. Mean RRT requirements estimated per ADPKD patient, with and without treatment

ADPKD was estimated to reduce life expectancy by up to 15.9 years (Belgium) and result in the loss of up to 19.9 QALYs (Sweden) and 9.1 (Sweden) working years compared to the general population.

Treatment was estimated to reduce the 50-year incidence of ESRD by approximately 6% and increase the mean age at onset by almost 5 years. Mean estimated time spent on dialysis per patient consequently fell by between 3 and 10 months (Figure 1), depending on modelled setting. Between 53 and 96 fewer transplants were predicted for every 1,000 ADPKD patients treated (Figure 2).

As a result of treatment, gains of between 2.6 and 3.9 QALYs, 2.8 and 3.6 life years, and 2.5 and 3.4 working years were estimated per patient compared to natural history. Estimated benefits were largest for Belgium (QALYs and life years) and the UK (working years); the settings associated with the largest predicted reductions in dialysis burden (Figure 2).

Corresponding with the trend in population size and absolute ADPKD prevalence across countries, estimated national level burden was lowest in Sweden (<5,000 ADPKD cases) and highest in the UK (>25,000 ADPKD cases). The potential impact of treatment on national-level burden also followed this trend (Figure 3).

Based on projections of ADPKD progression and tolvaptan treatment effect associated with a population enriched for rapid progression (TEMPO 3:4), the 50-year benefits of treatment would translate to ranges of approximately:

- 230-1,660 incident ESRD cases avoided *(Sweden-UK)*
- 250-2,240 transplants avoided *(Belgium-UK)*
- 860-19,370 dialysis years avoided *(Sweden-UK)*
- 10,500-76,300 QALYs gained *(Sweden-UK)*
- 11,800-84,200 life years gained *(Sweden-UK)*
- 10,100-91,900 working years gained *(Sweden-UK)*

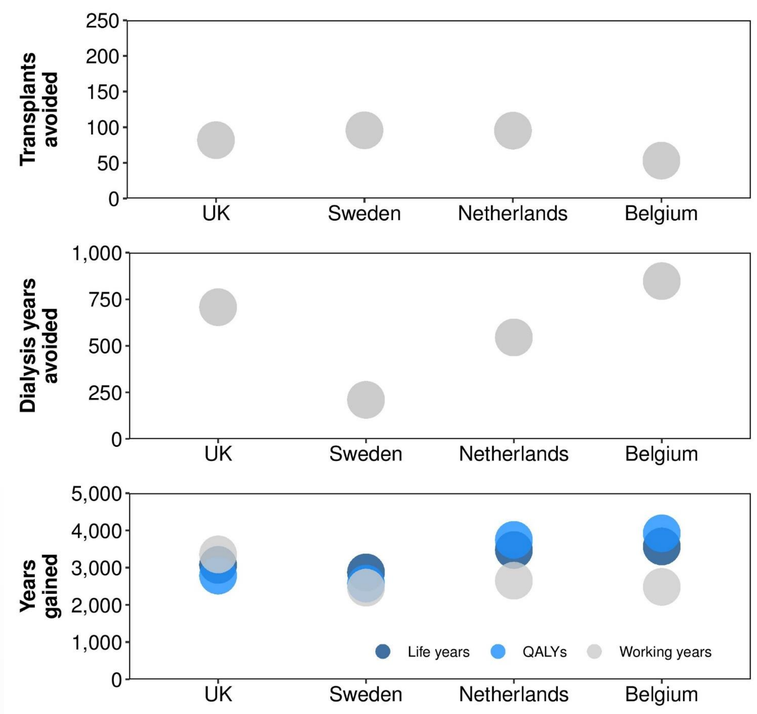

Figure 2. Predicted impact of treatment on health burden of ADPKD, estimated per 1,000 patients

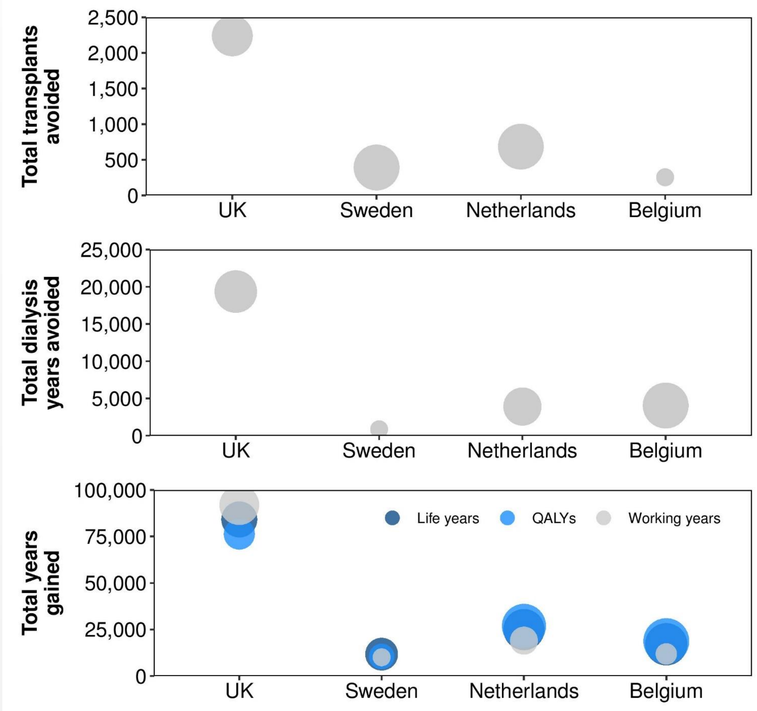

Figure 3. Predicted impact of treatment on health burden of ADPKD, estimated at national level

Size of bubble represents magnitude of treatment benefit per patient

CONCLUSIONS

Despite being classified as a rare disease, ADPKD represents a significant burden to patients, healthcare systems and society across Europe.

With the availability of a therapeutic option capable of slowing disease progression, meaningful life expectancy and quality of life gains may be achieved for patients.

Further, significant societal productivity gains may be made, and financial and logistical pressures of delivering care to those with ESRD eased for healthcare providers.

REFERENCES

1. Miskulin DC, et al. Am J Kidney Dis 2014; 63: 214–226
2. Ong AC, et al. Lancet. 2015 May 16;385(9981):1993-2002
3. Spithoven EM, et al. Nephrol Dial Transplant. 2014 Sep;29 Suppl 4:iv15-25.
4. European Kidney Health Alliance. Is kidney disease really such an important issue for Europe? 2012. Available from: www.era-edta.org/images/2012_EKHA-policy_paper.pdf
5. Torres VE, et N Engl J Med 2012; 367: 2407-2418.
6. Robinson R, et al. Development of a model to predict disease progression in autosomal dominant polycystic kidney disease (ADPKD). ERA-EDTA 2015
7. Chapman AB, et al. Kidney Int. 2003 Sep;64(3):1035-45.
8. Grantham JJ, et al. N Engl J Med. 2006 May 18;354(20):2122-30.
9. Shaw C, et al. Nephrol Dial Transplant. 2014 Oct;29(10):1910-8.
10. UK Renal Registry 2013. Nephron Clin Pract 2013;125:29-169
11. National Institute for Health and Care Excellence. NICE clinical guideline 125. 2011. Available from: www.nice.org.uk/guidance/cg125/resources/guidance-peritoneal-dialysis-pdf
12. NHS Blood and Transplant. Transplant activity in the UK. 2009. Available from: www.organdonation.nhs.uk/statistics/transplant_activity_report/archive_activity_reports/pdf/ukt/transplant_activity_uk_2008-2009.pdf
13. NHS Blood and Transplant. Organ donation and transplantation: activity report 2012/13. Available from: www.organdonation.nhs.uk/statistics/transplant_activity_report/archive_activity_reports/pdf/ukt/activity_report_2012_13.pdf
14. Gorodetskaya et al. Kidney Int. 2005;68(6):2801-8.
15. Lee AJ, et al. Curr Med Res Opin. 2005;21(11):1777-83.
16. Office of National Statistics. Labour Force Survey Jan-Mar 2015. Available from: www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-363535
17. European ADPKD Forum. Translating science into policy to improve ADPKD care in Europe. 2015. Available from: www.pkdinternational.org/EAF_ADPKD_Policy_Report_2015
18. Sennfält et al. Perit Dial Int. 2002;22(1):39-47.
19. Tattersall J, et al. Nephrol Dial Transplant. 2011 Jul;26(7):2082-6.
20. Svenskt njurregister. Årsrapport. 2013. Available from: www.medscinet.net/snr/rapporterdocs/%C3%85rsrapport%202013%20SNR.pdf
21. Eriksson DL, et al. Costs and quality of life in patients with autosomal dominant polycystic kidney disease - A cross-sectional study in Denmark, Finland, Norway and Sweden. Data on File, 2015.
22. Statistika Centralbyrån (SCB), 2014. Available from: www.scb.se
23. Adarkwah CC, et al. Kidney Blood Press Res. 2013;37(2-3):168-80.
24. ERA-EDTA Registry. Annual report 2012. Available from: www.era-edta-reg.org/files/annualreports/pdf/AnnRep2012.pdf
25. RENINET database [accessed 07/2014]
26. De Wit GA, et al. Nephrol Dial Transplant. 2002 Jan;17(1):86-92.
27. Centraal Bureau voor de Statistiek. Available from: Statline.cbs.nl
28. Pippias M, et al. Clin Kidney J. 2015 Jun;8(3):248-61
29. ERA-EDTA Registry. Survival report 2010: Belgium, French-speaking.
30. Statistics Belgium. Available from: statbel.fgov.be/en/statistics/figures/labour_market_living_conditions/employment/figures

Presented at 53rd ERA-EDTA Congress, Vienna, 21st-23rd May 2016

Otsuka

53 ERA
23--SP
Renal development and cystic diseases.
Karl OReilly
DOI: 10.3252/pso.eu.53era.2016
ePosters supported by F. Hoffmann- La Roche Ltd.
53rd CONGRESS ERA-EDTA VIENNA MAY 21-24 2016
Held jointly with Österreichische Gesellschaft für Nephrologie
PosterSessionOnline.com