



UK Kidney Association
Rare Renal



Effects of rare kidney disease on kidney failure: a longitudinal analysis of the UK National Registry of Rare Kidney Diseases (RaDaR) cohort



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Why are rare kidney diseases important?

Chronic Kidney Disease

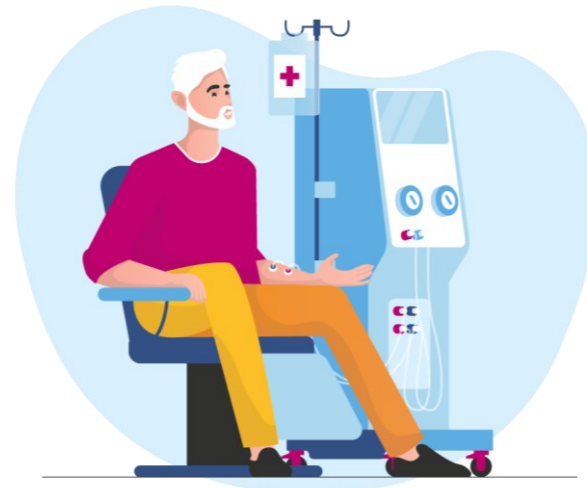
- >3 million of UK population
- £7.0 billion, 3.2% NHS spend
- Major health priority

End Stage Kidney Disease

- 69,000 patients

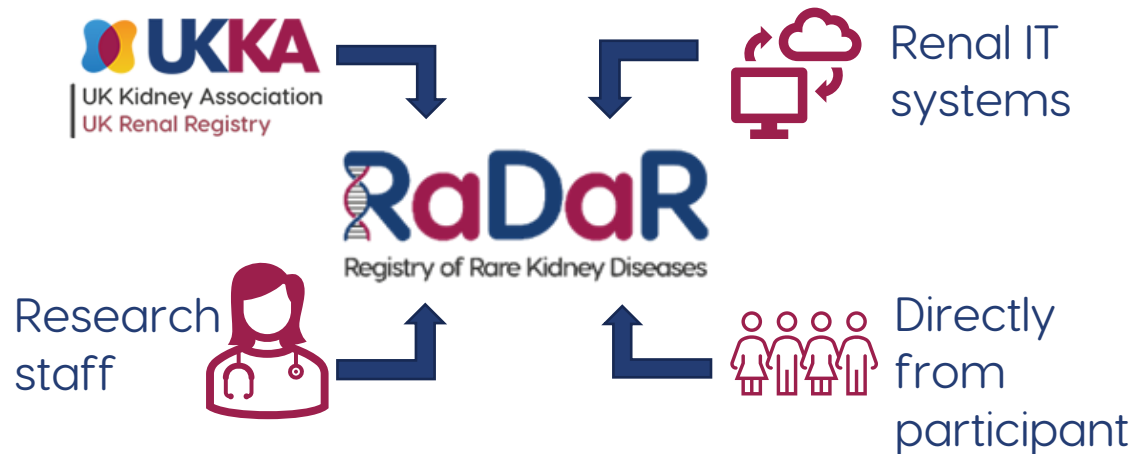
Rare Kidney Diseases

- 5-10% of patients with CKD
- **25%** of patients with ESKD
- Over-represented in kidney failure population



UK National Registry of Rare Kidney Diseases

- Formed in 2010
- Longitudinal data
- Retrospective data back to 1980s



109 renal units

England n=92

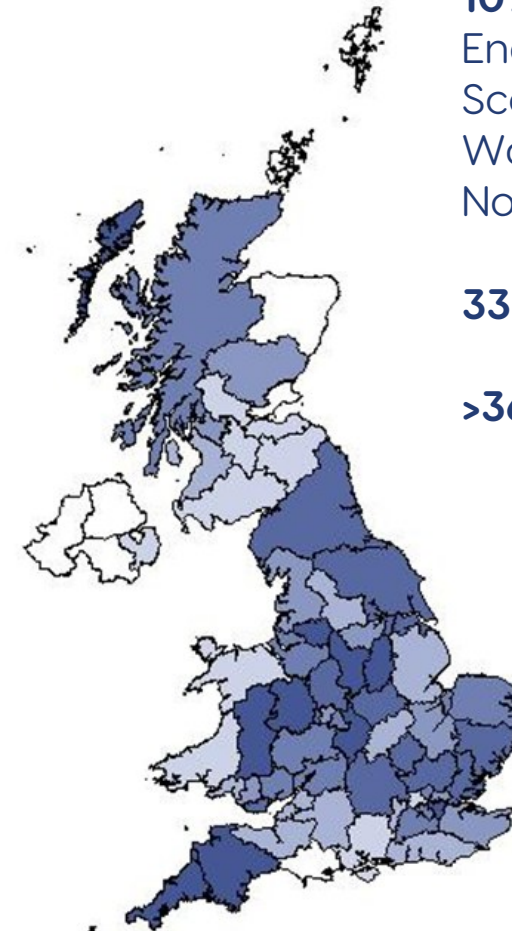
Scotland n=9

Wales n=3

Northern Ireland n=5

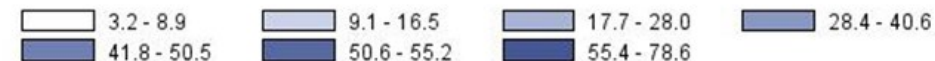
33 rare disease groups

>36,000 patients recruited



Largest rare kidney disease registry in the world

Patients per hundred thousand population



UK National Registry of Rare Kidney Diseases

Aims

To describe:

- **Clinical demographics**
- **Renal and patient survival**
- **Renal function trajectory and time in therapeutic window**

for individuals with rare kidney diseases in the UK

109 renal units

England n=92

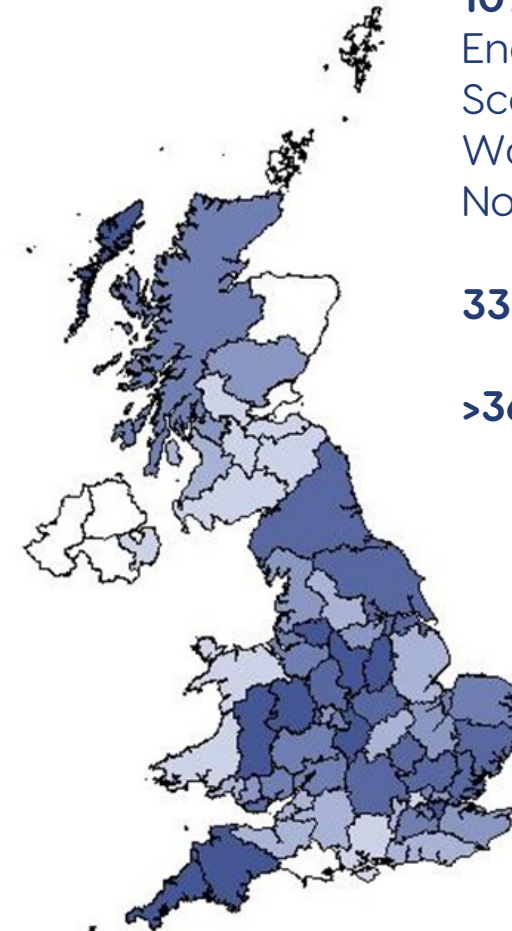
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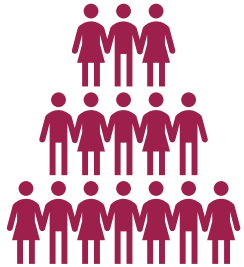
>36,000 patients recruited



Patients per hundred thousand population



Clinical Demographics



27285 patients

20 rare disease groups



**Median follow up
time 9.6 years
[IQR 5.9-16.7]**



Median age at diagnosis

All RaDaR – 41 years [23.7– 57.1]

Cystinosis – 2 years [0.7-9.9]

MGRS – 63 years [51.8-72.1]



Median eGFR at diagnosis

TBMN – 97.4 (69.1–111.2)

Gitelman Syndrome – 106.3 (93.1-120.5)

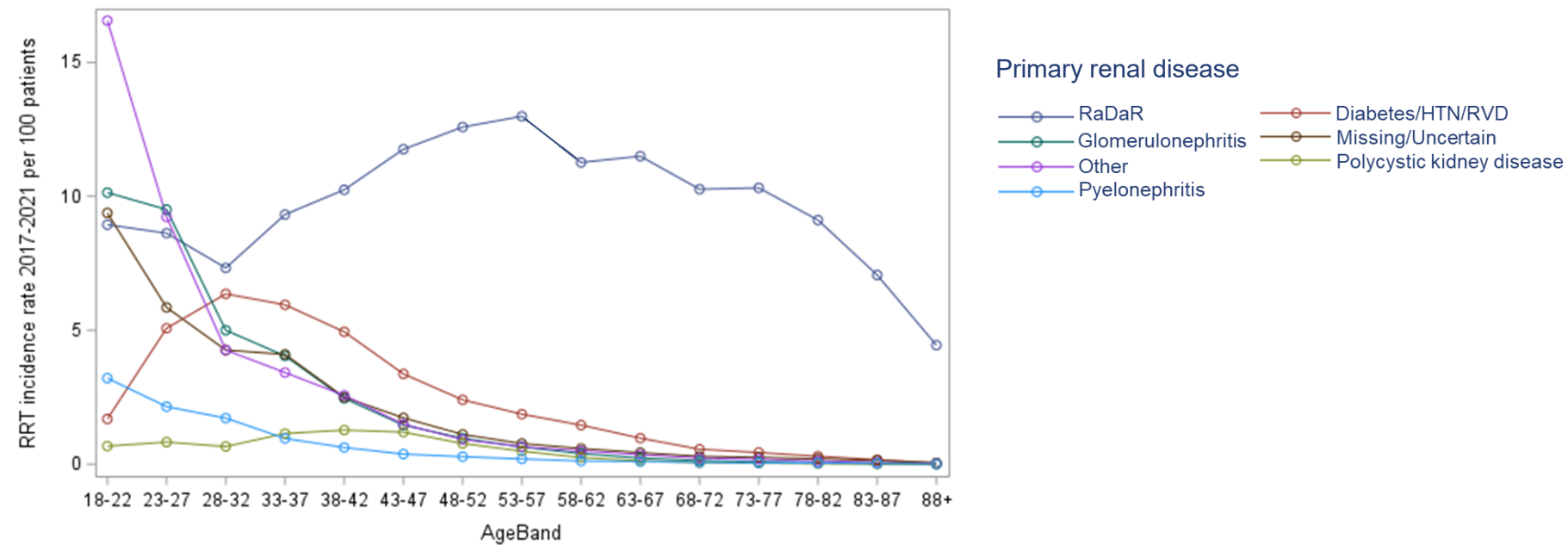
ANCA associated vasculitis- 30.5 (18.6–51.0)

Anti-GBM- 11.2 (6.7–17.5)

Incidence of ESKD



	RaDaR population (%) (95% CI)	General CKD population ^{1,2} (%)
1 year	8 (7,9)	0.2
3 year	19 (18,20)	0.6
5 year	28 (26, 29)	1



Higher rates of End Stage Kidney Disease for individuals with rare kidney diseases

1. QICKD study: de Lusignan S et al, Creatinine fluctuation has a greater effect than the formula to estimate glomerular filtration rate on the prevalence of chronic kidney disease. Nephron Clin Pract. 2011;117(3):c213-24. 2. UKRR annual report: Gilg J et al UK Renal Registry 14th Annual Report: Nephron Clin Pract 2012;120(suppl 1):c1-c27:1-28

Mortality



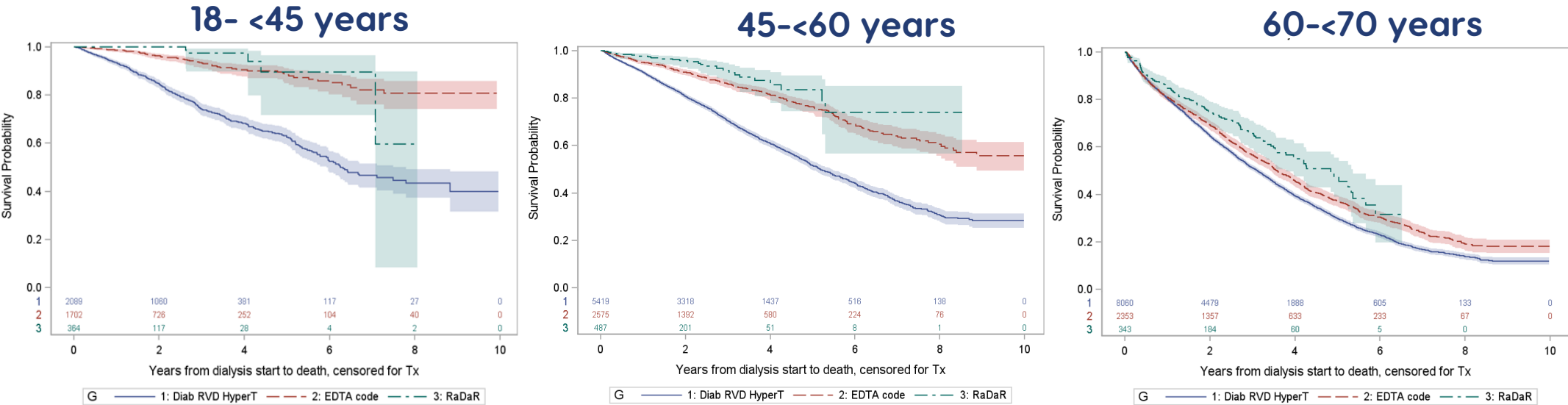
CKD
stage 3-5
not on
KRT



	Expected deaths	Observed	SMR (95% CI)
RaDaR (standardised ONS population)	221	507	2.29 (2.09 to 2.49)
RaDaR (standardised CKD population)*	166 [†]	70	0.42 (0.32 to 0.52)

*excluding patients without eGFR values

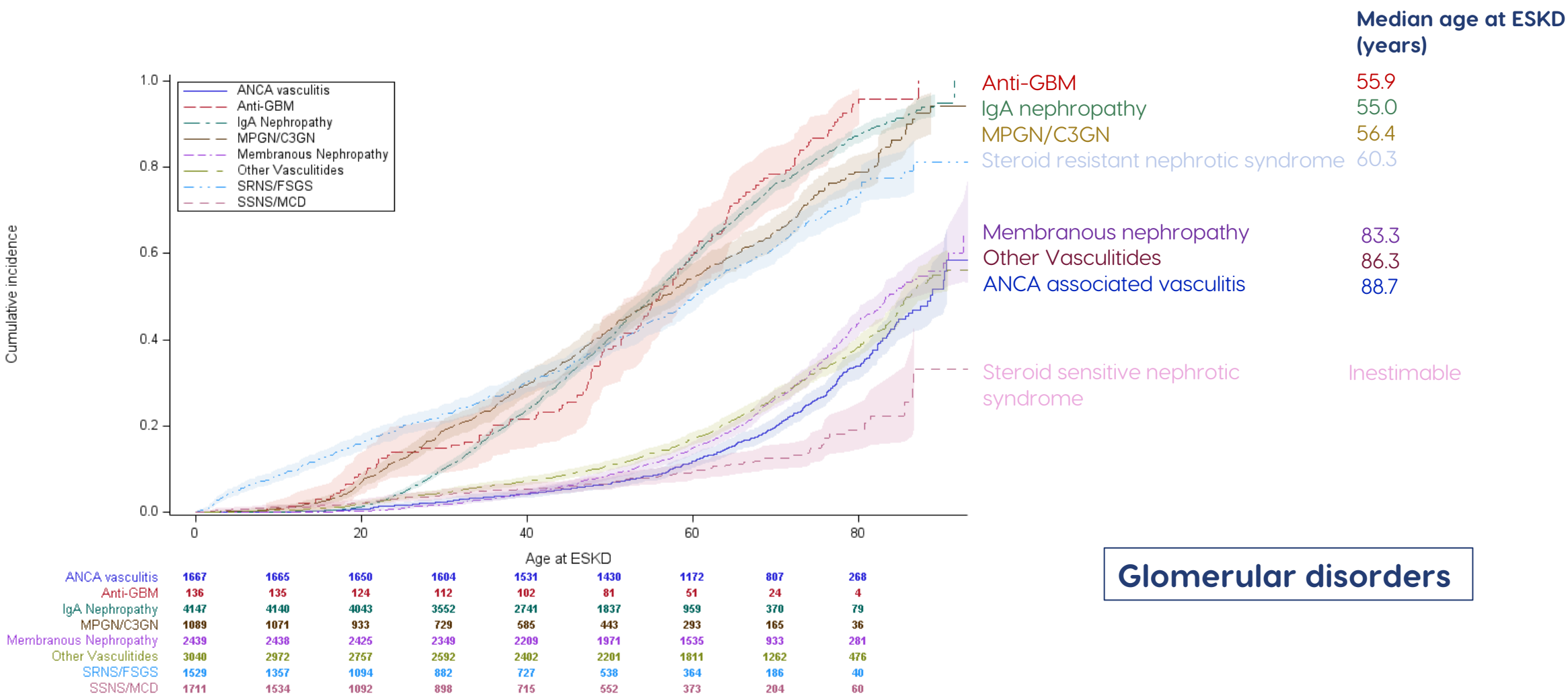
Kidney
Replacement
Therapy



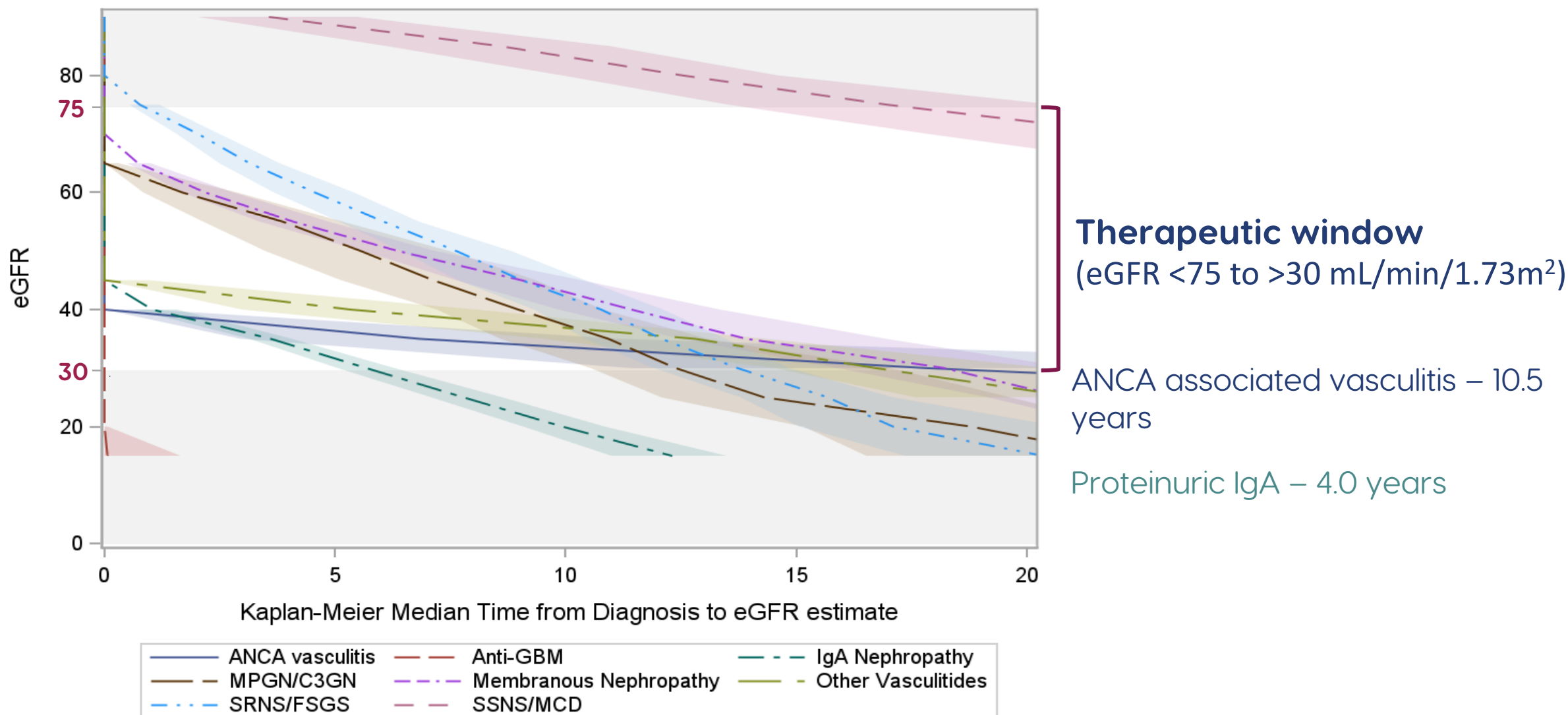
Lower mortality for individuals with rare kidney diseases (CKD and KRT)

[†]Go AS et al, Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med. 2004 Sep 23;351(13):1296–305. doi: 10.1056/NEJMoa041031

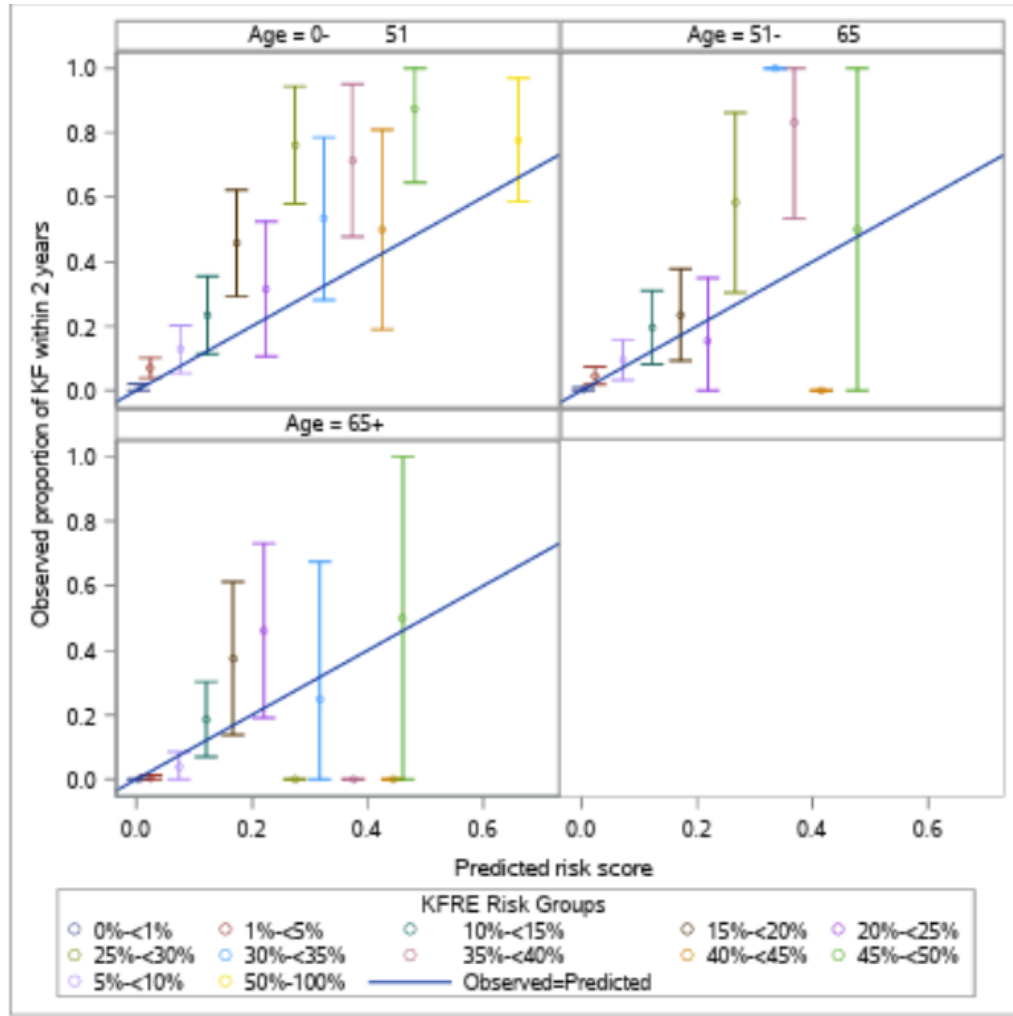
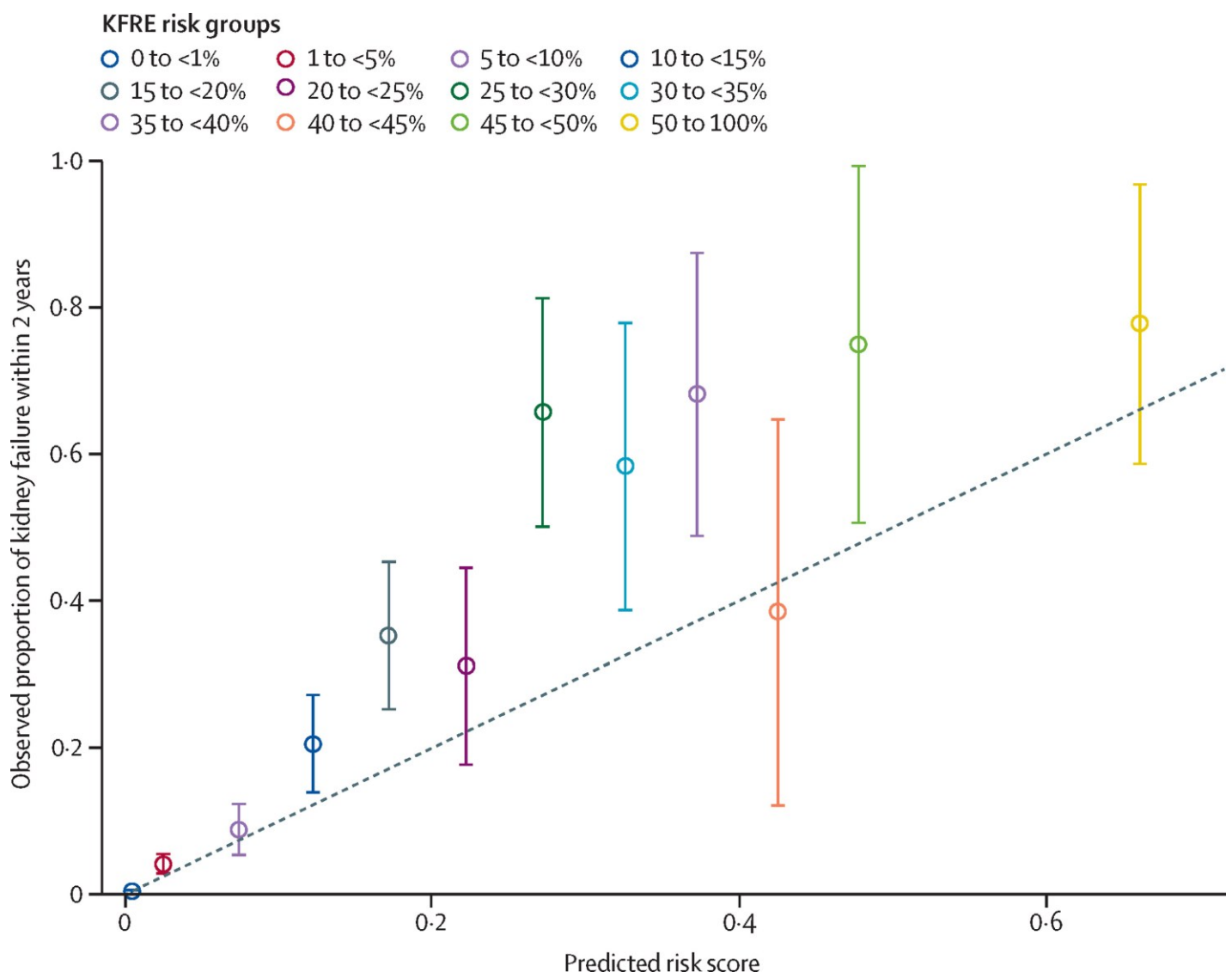
Kidney and patient outcomes in individual rare kidney diseases- age at ESKD



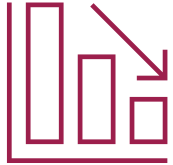
Kidney and patient outcomes in individual rare kidney diseases- time in therapeutic window



Kidney Failure Risk Equation



Rare Kidney Diseases ≠ Chronic Kidney Disease



Lower mortality rates compared to CKD population



Higher rates of End Stage Kidney Disease compared to CKD population

- **Without treatments and interventions that specifically target and delay progress of rare kidney diseases, there may not be a meaningful decrease in burden of End Stage Kidney Disease, even with better treatments for CKD**
- **A need for rare kidney disease specific clinical trials**



Significant heterogeneity in age at kidney failure, death and time in therapeutic window between Rare Disease Groups

- **Aid patient prognostication**
- **Inform health resource planning**
- **Identify when in disease course novel treatments or interventions might be best targeted**

Effects of rare kidney diseases on kidney failure: a longitudinal analysis of the UK National Registry of Rare Kidney Diseases (RaDaR) cohort



Katie Wong, David Pitcher, Fiona Braddon, Lewis Downward, Retha Steenkamp, Nicholas Annear, Jonathan Barratt, Coralie Bingham, Constantina Chrysoschou, Richard J Coward, David Game, Sian Griffin, Matt Hall, Sally Johnson, Durga Kanigicherla, Fiona Karet Frankl, David Kavanagh, Larissa Kerecuk, Eamonn R Maher, Shabbir Moomhala, Jenny Pinney, John A Sayer, Roslyn Simms, Smeeta Sinha, Shalabh Srivastava, Frederick W K Tam, Andrew Neil Turner, Stephen B Walsh, Aoife Waters, Patricia Wilson, Edwin Wong, Christopher Mark Taylor, Dorothea Nitsch, Moin Saleem, Dettlef Bockenhauer, Kate Bramham, Daniel P Gale, for the RaDaR consortium*

Summary

Background Individuals with rare kidney diseases account for 5–10% of people with chronic kidney disease, but constitute more than 25% of patients receiving kidney replacement therapy. The National Registry of Rare Kidney Diseases (RaDaR) gathers longitudinal data from patients with these conditions, which we used to study disease progression and outcomes of death and kidney failure.

Methods People aged 0–96 years living with 28 types of rare kidney diseases were recruited from 108 UK renal care facilities. The primary outcomes were cumulative incidence of mortality and kidney failure in individuals with rare kidney diseases, which were calculated and compared with that of unselected patients with chronic kidney disease. Cumulative incidence and Kaplan–Meier survival estimates were calculated for the following outcomes: median age at kidney failure; median age at death; time from start of dialysis to death; and time from diagnosis to estimated glomerular filtration rate (eGFR) thresholds, allowing calculation of time from last eGFR of 75 mL/min per 1.73 m² or more to first eGFR of less than 30 mL/min per 1.73 m² (the therapeutic trial window).

Findings Between Jan 18, 2010, and July 25, 2022, 27 285 participants were recruited to RaDaR. Median follow-up time from diagnosis was 9.6 years (IQR 5.9–16.7). RaDaR participants had significantly higher 5-year cumulative incidence of kidney failure than 2.81 million UK patients with all-cause chronic kidney disease (28% vs 1%; p<0.0001), but better survival rates (standardised mortality ratio 0.42 [95% CI 0.32–0.52]; p<0.0001). Median age at kidney failure, median age at death, time from start of dialysis to death, time from diagnosis to eGFR thresholds, and therapeutic trial window all varied substantially between rare diseases.

Interpretation Patients with rare kidney diseases differ from the general population of individuals with chronic kidney disease: they have higher 5-year rates of kidney failure but higher survival than other patients with chronic kidney disease stages 3–5, and so are over-represented in the cohort of patients requiring kidney replacement therapy. Addressing unmet therapeutic need for patients with rare kidney diseases could have a large beneficial effect on long-term kidney replacement therapy demand.

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Introduction

Chronic kidney disease is an umbrella term for conditions resulting in impaired kidney function, and can be divided into five stages defined by estimated glomerular filtration rate (eGFR). Chronic kidney disease stages 3, 4, and 5 represent moderate to severe disease and affect an estimated 6–1% of the UK population over the age of 16 years and 32.7% of those older than 75 years.¹ The most common causes of chronic kidney disease stage 3 in high-income and middle-income countries are diabetes and hypertension.²

Rare diseases are generally defined as affecting fewer than 200 000 individuals in the USA,³ or fewer than five

per 10 000 individuals in Europe.⁴ Approximately 80% of rare diseases are inherited.⁵ Rare kidney diseases, as defined by the Kidney Disease: Improving Global Outcomes global organisation, include more than 150 conditions⁶ and have an estimated prevalence of 60–80 cases per 100 000 people in Europe and the USA.⁵

More than 50% of children and those younger than 20 years receiving kidney replacement therapy have a rare kidney disease.⁷ In contrast to earlier chronic kidney disease stages, glomerulonephritis (which comprises multiple individually rare disorders) accounts for more UK adults receiving kidney replacement therapy than do common causes of chronic kidney disease, such as

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- Wider medical field
- Regulators/health service

Thank you



All patients and families who have kindly agreed to participate in RaDaR



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