

NEWSLETTER - N° 33 - May, 2025



## Late Breaking Clinical Trials contribution: Exploring the Margins of Transplant Survival Benefit





By Rachel Hellemans, Nephrologist at Antwerp University Hospital and Nick Chesnaye, Epidemiologist at the ERA Registry

The seminal work of Wolfe et al., published by the NEJM in 1999, has long served as the landmark paper describing the universal transplant survival benefit over dialysis in patients with kidney failure. However, nowadays, kidney transplantation is more often offered to older comorbid patients, using less-than-ideal donor kidneys, while dialysis survival has improved. Current literature lacks answers on the transplant survival benefit in several patient subgroups in the current era.

Therefore, in this study we evaluated the survival benefit of deceased donor kidney transplantation compared to continued dialysis in the most recent time period while considering patient age, patient co-morbidities, donor quality and donor retrieval type.

As a randomized clinical trial to study transplant survival benefit over dialysis is not feasible due to ethical reasons, we rely on observational data to explore this topic. However, by applying the innovative target trial emulation method to mimic the strict design criteria of a randomized clinical trial, we avoid biases commonly found in observational research, and achieve a level of evidence that closely approximates a true randomized clinical trial.

Our study is based on 64,013 patients  $\geq 20$  years, from Catalonia, Denmark, France, Norway, and the United Kingdom from the ERA Registry database, who were on dialysis while waitlisted for a first deceased donor kidney-only transplant between 2000 and 2019. This large database allowed us to study the margins of transplant benefit in specific recipient/donor combinations, particularly in the oldest recipients.

The results of this study will be presented at the Late Breaking Clinical Trials session at the ERA congress. We believe that our findings will greatly stimulate the discussion on future standard-of-care in kidney transplantation.

For more details, please attend the session on Late Breaking Clinical Trials I: Cutting-Edge Clinical Trials in Nephrology on Thursday, June 5, 2025, 11:15 – 12:30 CEST





# What are the potential risk factors for KRT in your country?

## By Eva Pella, Nephrologist, Former research fellow at the ERA Registry



Data from the ERA Registry show that kidney replacement therapy (KRT) incidence varies considerably across European countries. In 2022, KRT incidence rates ranged from 61 per million population (pmp) in Ukraine to 306 pmp in Cyprus.<sup>1</sup>

A higher KRT incidence could be explained by a higher prevalence of and risk factors for chronic kidney disease (CKD) in the general population, a faster progression from CKD to kidney failure and/or a higher access to KRT. Macroeconomic factors could affect all these aforementioned factors by influencing sociocultural, infrastructural and educational development in a country, but several other factors might also be at play.

Recently, we conducted the most extensive and up-to-date overview of 67 national factors potentially related to the incidence of KRT across European countries. Country specific information on factors potentially related to KRT incidence included geographic, socioeconomic, sociocultural, and health-related factors and factors related to CKD and national capacity for CKD prevention and was derived from online sources (such as the World Health Organization). In this study, 38 European countries were included, and divided into 12 low (0-100 pmp), 21 middle (100-200 pmp), and 5 high (>200 pmp) KRT incidence countries. Among the factors evaluated, median age at KRT initiation, physical inactivity prevalence, and population density were significantly positively correlated with KRT incidence (Figure).

Although we cannot prove causality, our findings could serve as a source for individual countries to explore the factors potentially underlying their KRT incidence and compare this with that of other countries. Moreover, our results could be used by policy makers, stakeholders and nephrologists to optimize healthcare (planning) regarding KRT initiation and in turn reduce disparities in KRT incidence.

## For more details, please attend the Moderated e-Poster Session on Chronic kidney disease (Epidemiology & outcome) on Thursday, June 5, 2025, 12:30-14:15 CEST



#### Median age at KRT initiation and KRT incidence

<sup>1</sup>Boenink R, Bonthuis M, Boerstra BA et al., The ERA Registry Annual Report 2022: Epidemiology of Kidney Replacement Therapy in Europe, with a focus on sex comparisons. Clin Kidney J. 2024 Dec 12;18(2):sfae405



kererences:



## The prevalence of reduced kidney function across Europe: a comparison of KDIGO and ageadapted definitions of CKD



#### By Megan Astley, PhD student at the ERA Registry

Chronic kidney disease (CKD) is typically diagnosed when an individual's estimated glomerular filtration rate (eGFR) is below 60 mL/min per 1.73 m<sup>2</sup> for at least three consecutive months, as described in the KDIGO guidelines.<sup>1</sup> However, this singular threshold does not consider the physiological age-related decline in kidney function that occurs in healthy individuals.<sup>2</sup> To account for these age-related changes in kidney function, age-adapted definitions of CKD are proposed, which would use age-specific eGFR thresholds to identify reduced kidney function. One of the proposed thresholds is the categorical age-adapted eGFR threshold which uses three age groups with a progressively lower eGFR thresholds.

But, there are biological and logical concerns about reclassifying individuals from having CKD to not having CKD when they transition into the next age group without any change in their eGFR. An alternative approach that avoids this pitfall involves using a continuous age-adapted eGFR threshold based on a lower percentile of eGFR reference values derived from a healthy population. Recently, the European CKD Burden Consortium determined continuous age-and sex-adapted eGFR thresholds based on the 5<sup>th</sup> and 2.5<sup>th</sup> percentiles of the eGFR distribution derived from over 1.5 million healthy (non-diseased) European adults. We then compared the prevalence of reduced eGFR in more than 2.5 million adults from a multinational European general population according to these two new continuous age- and sex-adapted eGFR thresholds, the categorical age-adapted eGFR threshold, and the KDIGO eGFR threshold.

Our findings demonstrate a fundamental shift in who would be classified as having reduced eGFR, particularly among younger and older adults, depending on the eGFR threshold. These results offer valuable new insights regarding the discussion about accounting for age-related changes in kidney function when defining CKD. However, the association with clinical outcomes and age-adapted eGFR thresholds needs to be established before its incorporation into the definition of CKD can be considered.

#### For more details, please attend the ERA Registry Symposium (S 0.4) on Thursday, June 5, 2025, 16:30 - 18:00 CEST

#### References:

<sup>1</sup> Stevens PE, Ahmed SB, Carrero JJ, et al. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney International. 2024;105(4, Supplement):S117-S314.

<sup>2</sup> Delanaye P, Jager KJ, Bökenkamp A, et al. CKD: A Call for an Age-Adapted Definition. J Am Soc Nephrol. 2019;30(10):1785-805.





## Annual CME Introductory course on Epidemiology



On March 13-14, 2025, the CME Introductory Course on Epidemiology was held in Thessaloniki, Greece for the 36<sup>th</sup> time. Several enthusiastic nephrologists and nephrology researchers from across Europe and beyond attended the course to learn about basic epidemiological principles and to practice these in interactive hands-on sessions.

This epidemiology course is organized by the ERA Registry once a year throughout Europe. If you are also interested to attend the course, we hope to welcome you in 2026! Please follow the ERA through the socials and website for any updates.





### ERA Registry Activities during the 62<sup>nd</sup> ERA congress June 4-7, 2025, Vienna

#### **REGISTRY COMMITTEE**

Roser Torra, Spain - ERA President Alberto Ortiz, Spain - Chair Miha Arnol, Slovenia Anders Åsberg, Norway Sevcan Bakkaloglu, Türkiye – ESPN representative Pietro Manuel Ferraro, Italy Jaakko Helve, Finland Julien Hogan, France – ESPN representative Viktorija Kuzema, Latvia Belén Ponte, Switzerland J Emilio Sánchez-Álvarez, Spain Mårten Segelmark, Sweden

#### **REGISTRY STAFF**

Vianda Stel, PhD Director | PI | Epidemiologist Kitty Jager, MD, PhD PI | Epidemiologist Anneke Kramer, PhD Data lead | Medical Informatician Nick Chesnaye, PhD EQUAL coordinator | Epidemiologist Marjolein Bonthuis, PhD Epidemiologist Rianne Boenink, PhD Epidemiologist Megan Astley, MSc PhD student Britt Boerstra, MSc PhD student Marin Hoekstra, MSc PhD student Arno Weerstra, MSc Software Engineer Özlem Gök Pasayigit Management assistant Ronald Cornet, PhD IT advisor | Medical Informatician



in collaboration with Ö G N N Ö Seellschaft für Nephrologie

#### Late breaking clinical trials I: Cutting-Edge Clinical trials in Nephrology Thursday, June 5, 11:15 - 12:30 CEST (Hall A Plenary Room)

 Exploring the Margins of Survival Benefit in Deceased Donor Kidney Transplantation: An International Target Trial Emulation – Rachel Hellemans

#### **ERA Registry Symposium**

#### Thursday, June 5, 16:30 - 18:00 CEST (Hall F1)

- The prevalence of reduced kidney function across Europe: a comparison of KDIGO and ageadapted definitions of CKD – **Megan Astley**
- Treatment trajectories of patients on kidney replacement therapy Brittany Boerstra
- Premature kidney ageing as cause of kidney failure Alberto Ortiz

#### FC 6: Kidney transplantation: Epidemiological insights Thursday, June 5, 11:15 - 12:30 CEST (Hall F1)

• Trends in all-cause and cause-specific mortality in adult first kidney transplant recipients with and without diabetes as cause of kidney failure: an ERA Registry study – Laia Oliveras

#### Chronic kidney disease

Thursday, June 5, 12:30 - 14:15 CEST (Moderated e-poster: XWall 2 Schubert Die Forelle)
An overview of 67national-level factors potentially related to the incidence of kidney replacement therapy across European countries – Eva Pella

#### Chronic kidney disease

#### Thursday, June 5, 15:00 - 16:15 CEST (Focussed Oral Room 4)

• Causal assessment of CKD-MBD phenotypes and CKD progression through a g-formula analysis- Insights from the EQUAL Study – **Lorenza Magagnoli** 

#### **Kidney transplantation**

#### Thursday, 5 June, 16:30 - 18:00 CEST (Focussed Oral Room 8)

 Time trends in European paediatric kidney transplantation: an ESPN/ERA Registry study – Iris Montez de Sousa

#### Chronic kidney disease

#### Thursday, June 5, 16:3 - 18:00 CEST (Focussed Oral Room 9)

 Burden of pruritus in older CKD stage 4-5 patients: 7-year follow-up of the EQUAL study – Enise Çelebi

#### Physiology, cell biology & genetic diseases

#### Friday, June 6, 08:15 - 09:45 CEST (Focussed Oral Room 1)

• Incidence and outcomes of kidney replacement therapy for kidney failure due to inherited tubulopathies in Europe: findings from the ERA Registry – **Marta Giaccari** 

#### **Kidney transplantation**

#### Friday, June 6, 08:15 - 09:45 CEST (Focussed Oral Room 8)

• Sex differences in transplant outcomes and survival for children on kidney replacement therapy: data from the ESPN/ERA Registry – Lucy Plumb

#### Dialysis

#### Friday, June 6, 16:30 - 18:00 CEST (Focussed Oral Room 5)

• Association between healthcare expenditure per capita and adoption of early home dialysis and kidney transplantation – **Jan Dominik Kampmann** 

