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Editorial Comment

EDITORIAL COMMENT

The last pre-pandemic European Renal Association Registry report: age at start of kidney replacement therapy in Europe

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ABSTRACT

The European Renal Association (ERA) Registry Annual Report 2019 will be its last pre-pandemic report. From 2020 on, registry data will incorporate any potential impact of coronavirus disease 2019 (COVID-19) on kidney replacement therapy (KRT) practices in Europe. The 2019 report focussed on age comparisons and found substantial differences in the distribution of primary renal disease, treatment modality, kidney donor type and the survival probabilities for different age categories. The report presents data that support a correlation ($R^2 = 0.43$, $P < 0.00001$) between the incidence of KRT per million population (pmp) and the median age at the start of KRT in the different regions and countries, suggesting that initiating KRT at an older median age may be a determinant of KRT incidence. The causes of the lower age at KRT in some countries should be explored. These may include, but are not limited to, KRT not being offered to the elderly or the elderly refusing KRT. In this regard, there was a correlation between the median age at the start of KRT and per capita gross domestic product (GDP) ($R^2 = 0.26$, $P < 0.0046$), suggesting that the availability of resources may be a factor that limits the offer of KRT to the elderly. The UK may represent a case to study these issues. Both age at initiation of KRT and KRT incidence are below the European median and lower than that expected for GDP. Furthermore, there are differences between the various countries within the UK, as well as documented racial differences, the latter being a piece of information missing for most European countries.

Keywords: age, chronic kidney disease, incidence, kidney replacement therapy, racial differences

This issue of *CKJ* contains the latest edition of the European Renal Association (ERA) Registry Annual Report, corresponding to 2019 [1]. This is an important document, as it represents the last pre-pandemic annual report and will serve as the baseline that will allow the interpretation of data in the 2020 and subsequent reports. Chronic kidney disease (CKD) is the most common risk factor for severe coronavirus disease 2019 (COVID-19) and the risk factor that most increases the risk for COVID-19 death [2–4]. The risk of death is especially high for persons on kidney replacement therapy (KRT), be it dialysis or transplantation [2]. Transport to and from haemodialysis (HD) was a key risk factor for COVID-19 in HD patients early in the pandemic [5]. Additionally, patients with CKD, and especially kidney transplant recipients, display an accelerated loss of anti-severe acute respiratory syndrome coronavirus 2 antibodies following infection as well as suboptimal response to vaccines [6, 7]. Thus the COVID-19 pandemic is expected to have a major impact on KRT incidence and prevalence as well as on incident and prevalent KRT age in the ERA Registry Annual Report from 2020 onwards. In this regard, it is worth reflecting on age comparisons in the 2019 report as a baseline to interpret later COVID-19 era data.

Boenink *et al.* [1] found substantial differences in the distribution of primary renal disease, treatment modality, kidney

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donor type and survival probabilities for different age categories among patients in the ERA Registry. These differences may guide the approach of practicing physicians to patient care, since for certain age ranges, often repeated statistics derived from the whole KRT population may not apply but may still guide, e.g. what differential diagnosis physicians will consider based on their overall frequency among persons with CKD. In this regard, the median ERA Registry age at the start of KRT was 67.9 years and the median age for prevalent patients was 60.5 years. However, the two most common causes of CKD for patients <65 years of age were glomerulonephritis and miscellaneous, but not diabetes as it is the case for those >65 years of age and for the full KRT population. Indeed, 'miscellaneous' was the most common cause of CKD for those <45 years of age, representing 60% of CKD cases <19 years of age. There is clearly a need to better define what 'miscellaneous' means and what the major categories are for each age range. There is evidence that genetic kidney diseases [i.e. genetic kidney diseases other than autosomal domain polycystic kidney disease (ADPKD)] may represent an important proportion of miscellaneous causes [8]. However, by clumping them together under 'miscellaneous' and separating them from ADPKD, we may be driving them away from the minds of physicians, thus limiting their recognition in clinical practice. Further differences were found in treatment modality, kidney donor type and survival probabilities for different age categories [1]. Among the latter, it is worth emphasizing the dramatic impact of being on KRT on expected remaining lifetime in younger persons. The life expectancy of patients on dialysis was ~70% shorter than in the general population and for kidney transplant recipients it was ~40% shorter. In absolute terms, this represents >40 years shorter life expectancy for someone 20 years of age on dialysis and ~20 years shorter for the 20-year-old kidney transplant recipient. Absolute numbers better transmit the sense of urgency regarding investing in research on CKD and its therapy aimed at improving these dismal outcomes [9, 10]. We should strive to dispel the idea that many health policy planners have that CKD is not a major health issue since, at worst, kidney function can be easily replaced [11].

A further finding relates to differences in the median age at the start of KRT and the median age of prevalent patients on KRT [1]. The median age at the start of KRT ranged from 54.0 years (Ukraine) to 74.4 years (Greece). Similarly, the median prevalent age ranged from 55.0 years (Ukraine) to 69.0 years (Israel). Since the prevalence of CKD is known to increase with increasing age, the focus of research should be on countries with a lower median age at the start of KRT. There are several potential reasons why a low age at the start of KRT may be concerning: it may represent inadequate care of younger persons at risk for CKD or lack of access to KRT for the elderly or excess mortality of elderly CKD patients before they need KRT. There are alternative explanations that are of lesser concern, such as the refusal of KRT by the elderly based on their system of values and beliefs. However, patient opinion is frequently greatly influenced by information provided by healthcare professionals. In any case, there is a need for careful examination of the reasons driving the younger age at initiation of KRT in several countries and regions. A simple approach may provide some clues about what factors should be further studied. Thus there was a correlation between age at initiation of KRT and incidence of KRT per million population (pmp) ($R^2 = 0.43$, $P < 0.00\,001$). This finding is not unexpected as, as indicated above, the prevalence of CKD increases with increasing age. It suggests that access to and acceptance of KRT by the elderly is one of the factors contributing to differences in the incidence of KRT between countries and regions. Another correlate

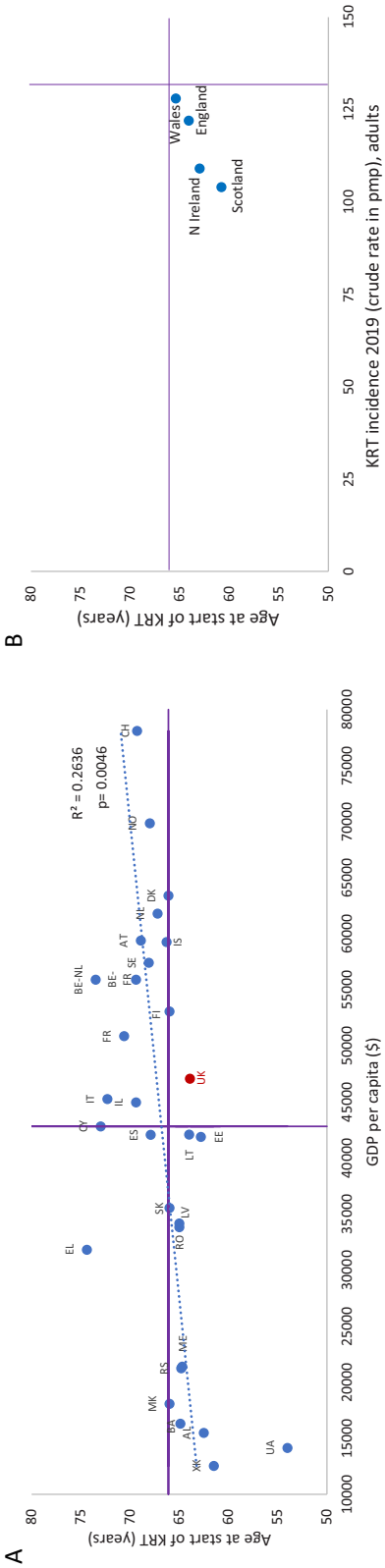

FIGURE 1: Correlation between age at the start of KRT and per capita GDP and data for countries in the UK. (**A**) Correlation between age at the start of KRT and per capita GDP. The UK is represented as we could not find data on GDP per capita on the UK countries from the same source as for the other countries in the graph. Note that the UK is the only country in the lower right quadrant (higher GDP, younger age at start of KRT). (**B**) Age at the start of KRT in UK countries is plotted against the incidence of KRT pmp. Note that there was a relationship between age at the start of KRT and the incidence of KRT, suggesting that findings may be explained by a lower use of KRT among the elderly rather than by a higher incidence of kidney failure in younger persons. UA, Ukraine; XK, Kosovo; AL, Albania; EE, Estonia; LT, Lithuania; ME, Montenegro; RS, Serbia; BA, Bosnia and Herzegovina; LV, Latvia; RO, Romania; FI, Finland; MK, North Macedonia; SK, Slovakia; DK, Denmark; IS, Iceland; NL, Netherlands; ES, Spain; NO, Norway; SE, Sweden; AT, Austria; CH, Switzerland; BE-FR, Belgium, French-speaking; IL, Israel; FR, France; IT, Italy; CY, Cyprus; BE-NL, Belgium, Dutch-speaking; EL, Greece; UK, United Kingdom; SCT, Scotland; NIR, Northern Ireland; ENG, England; WLS, Wales. Source of GDP data: https://www.imf.org/en/Publications/WEO/weo-database/2021/October/ (25 November 2021, date last accessed) and https://www.ons.gov.uk/economy/grossdomesticproductgdp/datasets/regionalgrossdomesticproductallnutslevelregions (25 November 2021, date last accessed). Purple lines represent median values for the countries in the ERA Registry shown in (**A**).

of older age at initiation of KRT was the per capita gross domestic product (GDP) ($R^2 = 0.26$, $P < 0.0046$) (Figure 1A). This may also be considered an expected finding, as countries with more abundant resources can provide adequate pre-dialysis care (thus delaying the need for KRT to an older age) and KRT for a greater number of citizens (thus being able to offer KRT to the elderly). However, there was no correlation between age at initiation of KRT and the median age of the population (Supplementary data, Figure S1), suggesting that, at least within the age range of European countries, the age pyramid of the population had little impact on the age at the start of KRT.

A case study regarding age at KRT initiation is represented by the UK. It was the only Western European country with an age at the start of KRT below the median despite having a per capita GDP above the median (Figure 1A). Assessment of individual UK countries suggests that a younger age at the initiation of KRT was related to a lower overall incidence of KRT (Figure 1B). This argues against a higher prevalence of kidney failure in young persons as the driver for the younger age at the start of KRT and suggests that KRT is not being started in older persons in the same manner as in other European countries with a similar GDP. It would be worth making an in-depth analysis of KRT practices in the UK versus other European countries with a similar population size and GDP but higher age at the start of KRT, such as Italy, France or even Spain, despite the smaller population and lower GDP per capita of the latter. As pointed out in the past, large discrepancies in the incidence of KRT or, as in the present case, in the age at KRT initiation call for benchmarking studies to try to clarify whether this is due to overindication of KRT in some countries or underindication of KRT in others [12]. Further information may be found in the 23rd Annual Report of the UK Renal Registry, which contains data through 31 December 2019 [13]. Among the UK renal centres that contributed data on non-dialysis CKD, the median age of persons with an estimated glomerular filtration rate <30 mL/min/1.73 m^2 was 78.0 years compared with a median age of 59.6 years for those on KRT. This further supports that in the UK, KRT is less commonly prescribed in the elderly than in other European countries with a similar GDP. For adults, it reports a median age of incident KRT patients of 64.2 years, but this was dependent on ethnicity (White 66.3 years, Asian 62.3 years and Black 56.3 years). This ethnicity distribution raises questions about access to KRT for elderly Blacks and Asians, although alternative explanations are possible, including suboptimal access to kidney care for these persons that fails to prevent CKD progression in younger persons. Could the remarkably lower age at starting KRT in Blacks explain the overall lower-than-expected age at KRT initiation in the UK? Likely not. Although the race distribution in France is not officially known, estimates suggest that ~3–5% of the population is Black, which may be greater than the 3% reported for England, while Blacks in Scotland, the UK country with the youngest age at KRT initiation, represent <1% of the population [14, 15].

In conclusion, further research is needed into KRT epidemiology in different age groups across countries, given the widely variable clinical characteristics, treatments and outcomes, as well as on men and women of different age ranges. A key urgent need is to understand the differences in incident and prevalent CKD age in different countries, as this may hold clues to optimal care regarding the initiation of KRT and the outcome results of such decisions. Given the highly variable clinical practice regarding KRT in the elderly, we are missing a great opportunity to advance our knowledge regarding the optimal management of kidney failure in these persons. Eventually, some countries will learn that their approach was misguided, either by excessive or defective offers of KRT initiation, but only the evaluation of outcomes associated with the different approaches will provide answers.

SUPPLEMENTARY DATA

Supplementary data are available at *ckj* online.

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CONFLICT OF INTEREST STATEMENT

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REFERENCES

1. Boenink R, Astley ME, Huijben JA *et al*. The ERA Registry Annual Report 2019: summary and age comparisons. *Clin Kidney J* 2022 (this issue)
2. ERA-EDTA Council; ERACODA Working Group. Chronic kidney disease is a key risk factor for severe COVID-19: a call to action by the ERA-EDTA. *Nephrol Dial Transplant* 2021; 36: 87–94
3. Williamson EJ, Walker AJ, Bhaskaran K *et al*. Factors associated with COVID-19-related death using OpenSAFELY. *Nature* 2020; 584: 430–436
4. Clark A, Jit M, Warren-Gash C *et al*. Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study. *Lancet Glob Health* 2020; 8: e1003–e1017
5. Rincón A, Moreso F, López-Herradón A *et al*. The keys to control a COVID-19 outbreak in a haemodialysis unit. *Clin Kidney J* 2020; 13: 542–549
6. Quiroga B, Soler MJ, Ortiz A *et al*. Safety and immediate humoral response of COVID-19 vaccines in chronic kidney disease patients: the SENCOVAC study. *Nephrol Dial Transplant* 2021; doi: 10.1093/ndt/gfab313
7. Carriazo S, Mas-Fontao S, Seghers C *et al*. Increased one-year mortality in hemodialysis patients with COVID-19: a prospective, observational study. *Clin Kidney J* 2021; https://doi.org/10.1093/ckj/sfab248
8. Torra R, Furlano M, Ortiz A *et al*. Genetic kidney diseases as an underrecognized cause of chronic kidney disease: the key role of international registry reports. *Clin Kidney J* 2021; 14: 1879–1885
9. Vanholder R, Annemans L, Bello AK *et al*. Fighting the unbearable lightness of neglecting kidney health: the decade of the kidney. *Clin Kidney J* 2021; 14: 1719–1730

10. Ortiz A, AIRG-E, EKPF *et al*. RICORS2040: the need for collaborative research in chronic kidney disease. *Clin Kidney J* 2021; https://doi.org/10.1093/ckj/sfab170
11. Ortiz A, Covic A, Fliser D *et al*. Epidemiology, contributors to, and clinical trials of mortality risk in chronic kidney failure. *Lancet* 2014; 383: 1831–1843
12. Gonzalez-Espinoza L, Ortiz A. 2012 ERA-EDTA Registry Annual Report: cautious optimism on outcomes, concern about persistent inequalities and data black-outs. *Clin Kidney J* 2015; 8: 243–247
13. UK Kidney Association. UK Renal Registry 23rd Annual Report—data to 31 December 2019, Bristol, UK. https://renal.org/audit-research/annual-report (27 November 2021, date last accessed)
14. Wikipedia. *Black British People*. https://en.wikipedia.org/wiki/Black_British_people (27 November 2021, date last accessed)
15. Wikipedia. *Black People in France*. https://en.wikipedia.org/wiki/Black_people_in_France (27 November 2021, date last accessed)