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# Changes in the epidemiology of kidney replacement therapy across Europe in 2020 – the first year of the COVID-19 pandemic: an ERA Registry study

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## ABSTRACT

**Background.** In 2020, the coronavirus disease 2019 (COVID-19) pandemic caused disruptions in kidney replacement therapy (KRT) services worldwide. The aim of this study was to assess the effect of the COVID-19 pandemic in 2020 on the incidence of KRT, kidney transplantation activity, mortality and prevalence of KRT across Europe.

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**Methods.** Patients receiving KRT were included from 17 countries providing data to the European Renal Association Registry. The epidemiology of KRT in 2020 was compared with average data from the period 2017–2019. Changes occurring during the first and second waves of the pandemic were also explored.

**Results.** The incidence of KRT was 6.2% lower in 2020 compared with 2017–2019, with the lowest point (-22.7%) during the first wave in April. The decrease varied across countries, was smaller in males (-5.2%) than in females (-8.2%) and was moderate for peritoneal dialysis (-3.7%) and haemodialysis (-5.4%) but substantial for pre-emptive kidney transplantation (-23.6%). The kidney transplantation rate decreased by 22.5%, reaching a nadir of -80.1% during the first wave, and was greatest for living donor kidney transplants (-30.5%). While in most countries the kidney transplantation rate decreased, in the Nordic/Baltic countries and Greece there was no clear decrease. In dialysis patients, mortality increased by 11.4% and was highest in those 65–74 years of age (16.1%), in those with diabetes as the primary renal disease (15.1%) and in those on haemodialysis (12.4%). In transplant recipients, the mortality was 25.8% higher, but there were no subgroups that stood out. In contrast to the rising prevalence of KRT observed over the past decrease across Europe, the prevalence at the end of 2020 (N = 317 787) resembled that of 2019 (N = 317 077).

**Conclusion.** The COVID-19 pandemic has had a substantial impact on the incidence of KRT, kidney transplant activity, mortality of KRT and prevalence of KRT in Europe with variations across countries.

Keywords: COVID-19, dialysis, Europe, kidney transplantation, mortality

## **KEY LEARNING POINTS**

### What was known:

- The coronavirus disease 2019 (COVID-19) pandemic has caused large reductions in healthcare services worldwide, including kidney replacement therapy (KRT).
- Among patients on KRT, a highly vulnerable population due to underlying chronic kidney disease and a high prevalence of multimorbidity, 28-day mortality due to COVID-19 was as high as 20%.

### This study adds:

- In 2020, the incidence of KRT was 6.2% lower compared with 2017–2019; whereas peritoneal dialysis as the first treatment decreased with 3.7%, that of haemodialysis declined by 5.4% and pre-emptive kidney transplantation by 23.6%.
- The kidney transplantation rate was 22.5% lower in 2020 compared with 2017–2019. The living donor kidney transplantation rate decreased more substantially (30.5%) than the deceased donor kidney transplantation rate (20.4%).
- When compared with 2017–2019, in 2020 mortality was 1.6% higher in patients receiving peritoneal dialysis, 12.4% higher in patients receiving haemodialysis and 25.8% higher in kidney transplant recipients.
- As a result, the 2020 prevalence of KRT was similar to that of 2019. This is in contrast to the usual 2% annual increase.

#### Potential impact:

- In 2020, fewer patients with end-stage kidney disease started KRT due to the COVID-19 pandemic and fewer patients received a kidney transplant.
- In addition to COVID-19-related mortality, patients may have died due to the impact of the pandemic on healthcare services and as a result of postponing the start of dialysis or kidney transplantation.
- COVID-19-related changes in the incidence, prevalence and mortality will affect future trend analyses by renal registries.

## **INTRODUCTION**

In 2020, the world was struck by the coronavirus disease 2019 (COVID-19) pandemic. Many people fell ill, including patients on kidney replacement therapy (KRT). During the early stages of the pandemic, analyses on the OpenSAFELY database revealed that the risk of dying from COVID-19 increased with decreasing kidney function [1]. Additionally, population-based renal registries and large cohort studies reported 90-day mortality rates due to COVID-19 as high as 30% in both dialysis and kidney transplant populations [2–6].

Less is known about how COVID-19 affected other aspects of the epidemiology of KRT. An early study from the USA [7] demonstrated a decrease in the incidence of KRT and pre-emptive transplant activity during the first pandemic wave, together with a modest shift from haemodialysis (HD) to peritoneal dialysis (PD) as a first treatment modality. In Europe, two regional KRT registries reported a decrease in both KRT incidence [8, 9] and prevalence [8] and an increase in mortality [8], while transplant organizations reported a marked reduction in kidney transplant activity across the globe [10, 11]. Currently an overview of the consequences of the COVID-19 pandemic on the epidemiology of KRT in Europe is lacking. The aim of this study was to investigate the effect of the COVID-19 pandemic across Europe during 2020 on the incidence of KRT, kidney transplant activity, mortality of KRT patients and the prevalence of KRT.

## METHODS Study population

The European Renal Association (ERA) Registry collects data on patients with end-stage kidney disease receiving KRT across Europe [12]. In this study, we included data from 17 countries: Austria, Belgium, Bosnia and Herzegovina, Denmark, Estonia, Finland, France, Greece, Iceland, Montenegro, The Netherlands, Norway, Serbia, Spain (Andalusia, Aragon, Asturias, Basque Country, Canary Islands, Cantabria, Castile and Léon, Castile-La Mancha, Catalonia, Community of Madrid, Extremadura, Galicia, Murcia, Navarre and Valencia), Sweden, Switzerland and the UK (England, Northern Ireland and Wales). Each registry collects data on



Figure 1: The incidence of confirmed COVID-19 cases and COVID-19 deaths in the general population.

the entire KRT population, representing a 100% population coverage, except for The Netherlands (94% for incidence analyses, 96% for prevalence analyses and 98% for transplant activity analyses) and Serbia (90%). Incomplete coverage was accounted for in the analyses. Data on children were unavailable for the registries of Dutch-speaking and French-speaking Belgium, Montenegro and the Spanish regions of Cantabria, Castile and Léon, Castile-La Mancha and Navarre. Informed consent was obtained by each registry in accordance with national and/or regional regulations. Compliance with ethical standards was confirmed by the Medical Ethical Committee of the Amsterdam Medical Centre (W21\_123 No. 21.136).

## Data collection

The ERA Registry collects data on patient age at KRT initiation, sex, primary renal disease (PRD), KRT modality and date and cause of death. The cause of death was available for 42% of the patients who died between 2017 and 2020. Therefore, numbers relating to specific causes of death were extrapolated to match the total number of deaths in 2017–2019 and 2020. Data on the number of confirmed cases of COVID-19 and confirmed deaths due to COVID-19 in the general population of the participating countries were extracted from the website of the World Health Organization [13]. Population data were obtained from the statistical office of the European Union (Eurostat) [14] or via national statistics agencies.

## Analyses

Results are presented as absolute numbers, per million population (pmp) or per 1000 patient years (1000 py). Rates pmp or per million age-related population (pmarp) were calculated as the average number of patients per month (for pmarp per age group) divided by the mid-year general population, multiplied by one million. The mortality was calculated as the number of patients who died within a month divided by the total number of patient years on KRT in that same month. To enable comparisons between months, numbers were recalculated to a 30-day period.

We compared the epidemiology of KRT in 2020 with average data from the period 2017–2019 or, in case of KRT prevalence, with 31 December 2017, 2018 and 2019. In addition to changes in annual averages, we also explored changes occurring during the first and second waves of the pandemic. We defined each wave by identifying the month in which the first and second peak (or nadir) occurred during 2020, which were most commonly April and October. Differences between periods were modelled with Poisson regression. Analyses were stratified by age group, sex and diabetes versus other non-diabetic primary renal diseases. The incidence, prevalence and transplant activity analyses were also performed by country, however, regulations prevented comparisons of mortality at the country level. Differences between subgroups were tested using the  $\chi^2$  test of independence. P-values <.05 were considered statistically significant. All analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

## RESULTS

# COVID-19 cases and deaths in the general population in 2020

Figure 1 shows the incidence of confirmed COVID-19 cases and deaths in the general population of European countries participating in this study during 2020. The incidence of confirmed COVID-19 cases showed a minor peak during the first pandemic wave in April 2020 and a more substantial peak during the second wave in October–December 2020. The number of COVID-19-related deaths was higher during the first wave than during the second wave.

## Incidence of KRT

In 2020, 36 438 patients started KRT in the participating countries across Europe versus 38 863 per year on average during the period 2017–2019 (Table 1). This represents a 6.2% [95% confidence interval (CI) -7.7 to -4.8] decrease in the annual number of patients starting KRT, which was similar across age categories and among patients with and without diabetes as the PRD. However, the decrease in KRT incidence was smaller in males compared with females (P = .032), smallest for PD and largest for pre-emptive kidney transplantation. Between countries, substantial differences in the decrease in incidence was found for Estonia, Serbia, Austria, the UK, France and Spain, while there was no evidence for this in other participating countries.

Focusing on the first and second pandemic waves in 2020, the incidence rate of KRT decreased by a maximum of 22.7% during the first wave and 12.2% during the second wave (Fig. 2). The decrease in incidence during the first wave was similar across age groups, for females and males and in patients with diabetes as the PRD versus patients with other PRDs (Supplementary Fig. S1). However, the decrease during the first wave was larger for HD as the initial KRT modality than for PD, and was by far the largest for pre-emptive kidney transplantation (P < .001). In absolute numbers, the decrease in incidence was the largest for HD.

Table 1: The number of incident KRT patients and the absolute and relative differences between 2020 and 2017–2019 overall and by age group, sex, diabetes as the PRD, initial treatment modality and country.

|                                    |                | Ir     | icidence—number | of patients starting KRT |                      |                      |
|------------------------------------|----------------|--------|-----------------|--------------------------|----------------------|----------------------|
| Characteristics                    | Mean 2017–2019 | 2020   | Difference, n   | Difference, % (95% CI)   | P-value <sup>a</sup> | P-value <sup>b</sup> |
| Overall                            | 38 863         | 36 438 | -2425           | -6.2 (-7.7 to -4.8)      | <.001                |                      |
| Age group (years)                  |                |        |                 |                          |                      |                      |
| 0-44                               | 4405           | 4090   | -315            | −7.1 (−11.4 to −2.9)     | <.001                | .460                 |
| 45–64                              | 11 449         | 10 690 | -759            | -6.6 (-9.3 to -4.0)      | <.001                |                      |
| 65–74                              | 10 710         | 10 230 | -480            | -4.5 (-7.2 to -1.8)      | <.001                |                      |
| ≥75                                | 12 300         | 11 428 | -872            | -7.1 (-9.6 to -4.5)      | <.001                |                      |
| Female                             | 13 631         | 12 510 | -1121           | -8.2 (-10.7 to -5.8)     | <.001                | .032                 |
| Male                               | 25 232         | 23 928 | -1304           | -5.2 (-6.9 to -3.4)      | <.001                |                      |
| DM as PRD                          | 9449           | 8802   | -647            | -6.8 (-9.8 to -3.9)      | <.001                | .192                 |
| No DM as PRD                       | 22 492         | 20 474 | -2018           | -9.0 (-10.9 to -7.1)     | <.001                |                      |
| HD at start of KRT                 | 31 070         | 29 389 | -1681           | -5.4 (-7.0 to -3.8)      | <.001                | <.001                |
| PD at start of KRT                 | 5640           | 5430   | -210            | -3.7 (-7.5 to -0.0)      | .046                 |                      |
| Pre-emptive kidney transplantation | 2118           | 1619   | -499            | -23.6 (-30.0 to -17.1)   | <.001                |                      |
| Austria                            | 1196           | 1085   | -111            | -9.3 (-17.5 to -1.0)     | .020                 | <.001                |
| Belgium                            | 2207           | 2100   | -107            | -4.8 (-10.8-1.1)         | .104                 |                      |
| Bosnia and Herzegovina             | 412            | 408    | -4              | -1.0 (-14.7-12.6)        | .881                 |                      |
| Denmark                            | 703            | 707    | +4              | +0.6 (-9.8-11.1)         | .909                 |                      |
| Estonia                            | 106            | 76     | -30             | -28.1 (-57.6-1.4)        | .028                 |                      |
| Finland                            | 540            | 522    | -18             | -3.4 (-15.4-8.6)         | .574                 |                      |
| France                             | 11 598         | 10 696 | -902            | -7.8 (-10.4 to -5.1)     | <.001                |                      |
| Greece                             | 2814           | 2749   | -65             | -2.3 (-7.6-2.9)          | .381                 |                      |
| Iceland                            | 40             | 38     | -2              | -5.0 (-49.4-39.4)        | .821                 |                      |
| Montenegro                         | 55             | 75     | +20             | +35.6 (+0.9–70.4)        | .086                 |                      |
| The Netherlands                    | 1922           | 1861   | -61             | -3.2 (-9.5-3.2)          | .324                 |                      |
| Norway                             | 581            | 543    | -38             | -6.6 (-18.3-5.1)         | .253                 |                      |
| Serbia                             | 620            | 474    | -146            | -23.5 (-35.5 to -11.6)   | <.001                |                      |
| Spain                              | 6803           | 6462   | -341            | -5.0 (-8.4 to -1.6)      | .003                 |                      |
| Sweden                             | 1145           | 1137   | -8              | -0.7 (-8.9-7.5)          | .867                 |                      |
| Switzerland                        | 849            | 846    | -3              | -0.4 (-9.9-9.2)          | .942                 |                      |
| UK                                 | 7273           | 6659   | -614            | -8.4 (-11.8 to-5.1)      | <.001                |                      |

DM: diabetes mellitus.

<sup>a</sup>P-value Poisson model comparing the 2020 count with the 2017–2019 average, within each (sub)group.

<sup>b</sup>P-value  $\chi^2$  test comparing the difference between the 2020 count and the 2017–2019 average between subgroups.

## Kidney transplant activity

In 2020, 10 593 kidney transplants were performed, which was 22.5% (95% CI -25.1 to -20.0) fewer than during 2017–2019 (Table 2). The decrease was similar across age groups, for males and females and for patients with and without diabetes as the PRD. At the level of the country, considerable differences were found. There was no statistically significant decrease in any of the countries in northern Europe, except for the UK, while there was a clear decrease in all other countries, with the exception of Greece. The number of living donor kidney transplants decreased more substantially than the number of deceased donor kidney transplants (P < .001).

Compared with 2017–2019, the kidney transplantation rate decreased by 80.1% during the first pandemic wave and by 29.2% during the second wave (Fig. 3). Comparing age groups, the decrease during the first wave was largest in patients  $\geq$ 75 years of age (0.062 pmp/day; 92.0%, P = .046), however, the absolute decrease was largest in patients 65–74 years of age (0.231 pmp/day; 87.1%) (Supplementary Fig. S2). The decrease during the first wave was similar in both sexes (P = .712), although the absolute decrease was larger for males (0.137 pmp/day) than females (0.084 pmp/day), while it was similar in patients with diabetes as the PRD versus patients with other PRDs (P = .547).



Figure 2: The incidence of KRT in 2017–2019 and 2020. The percentage change is provided for the months where the largest difference was found within the first and second pandemic waves.

The decrease in living donor kidney transplants during the first wave was larger than that for deceased donor kidney transplants (Fig. 3). However, when considering absolute numbers, the decrease in the living donor transplants (0.028 pmp/day) was far smaller than that of deceased donor transplants (0.085 pmp/day).

Table 2: The number of patients receiving a kidney transplant and the absolute and relative differences between 2020 and 2017–2019 overall and by age group, sex, diabetes as primary renal disease, donor type and country.

|                                       |                | Num    | ber of patients rec | eiving a kidney transplant |                      |                      |
|---------------------------------------|----------------|--------|---------------------|----------------------------|----------------------|----------------------|
| Characteristics                       | Mean 2017–2019 | 2020   | Difference, n       | Difference, % (95% CI)     | P-value <sup>a</sup> | P-value <sup>b</sup> |
| Overall                               | 13 676         | 10 593 | -3083               | -22.5 (-25.1 to -20.0)     | <.001                |                      |
| Age group (years)                     |                |        |                     |                            |                      |                      |
| 0-44                                  | 3808           | 3035   | -773                | -20.3 (-25.1 to -15.5)     | <.001                | .703                 |
| 45–64                                 | 6310           | 4945   | -1365               | -21.6 (-25.4 to -17.9)     | <.001                |                      |
| 65–74                                 | 2659           | 2155   | -504                | -19.0 (-24.6 to -13.3)     | <.001                |                      |
| ≥75                                   | 554            | 458    | -96                 | −17.3 (−29.7 to −4.9)      | .003                 |                      |
| Female                                | 4838           | 3939   | -899                | -18.6 (-22.8 to -14.4)     | <.001                | .157                 |
| Male                                  | 8492           | 6654   | -1838               | -21.6 (-24.9 to -18.4)     | <.001                |                      |
| DM as PRD                             | 1953           | 1532   | -421                | -21.6 (-28.2 to -14.9)     | <.001                | .280                 |
| No DM as PRD                          | 9819           | 7397   | -2422               | -24.7 (-27.7 to -21.7)     | <.001                |                      |
| Deceased donor kidney transplantation | 10 737         | 8551   | -2186               | -20.4 (-23.2 to -17.5)     | <.001                | <.001                |
| Living donor kidney transplantation   | 2901           | 2016   | -885                | -30.5 (-36.2 to -24.8)     | <.001                |                      |
| Austria                               | 393            | 307    | -86                 | -21.8 (-36.8 to -6.9)      | .001                 | <.001                |
| Belgium                               | 445            | 308    | -137                | -30.8 (-45.3 to -16.3)     | <.001                |                      |
| Bosnia and Herzegovina                | 21             | 10     | -11                 | -52.4 (-127.7-22.9)        | .053                 |                      |
| Denmark                               | 256            | 278    | +22                 | +8.7 (-8.3-25.7)           | .335                 |                      |
| Estonia                               | 45             | 49     | +4                  | +8.2 (-32.2-48.6)          | .703                 |                      |
| Finland                               | 264            | 264    | 0                   | +0.1 (-17.0-17.2)          | .990                 |                      |
| France                                | 3665           | 2597   | -1068               | -29.1 (-34.2 to -24.1)     | <.001                |                      |
| Greece                                | 178            | 182    | +4                  | 2.1 (-18.6-22.7)           | .845                 |                      |
| Iceland                               | 9              | 10     | +1                  | +11.1 (-78.9-101.2)        | .819                 |                      |
| Montenegro                            | 5              | 0      | -5                  | -100 (-100 to -100)        | <.001                |                      |
| The Netherlands                       | 928            | 787    | -141                | -15.2 (-24.7 to -5.7)      | <.001                |                      |
| Norway                                | 259            | 240    | -19                 | -7.4 (-25-10.1)            | .388                 |                      |
| Serbia                                | 73             | 7      | -66                 | -90.5 (-168 to -12.9)      | <.001                |                      |
| Spain                                 | 3241           | 2619   | -622                | -19.2 (-24.3 to -14.0)     | <.001                |                      |
| Sweden                                | 455            | 419    | -36                 | -7.9 (-21.2-5.4)           | .223                 |                      |
| Switzerland                           | 343            | 293    | -50                 | -14.6 (-30.2-1.0)          | .048                 |                      |
| UK                                    | 3096           | 2223   | -873                | -28.2 (-33.6 to -22.7)     | <.001                |                      |

DM: diabetes mellitus.

<sup>a</sup>P-value Poisson model comparing the 2020 count with the 2017–2019 average, within each (sub)group.

 $^{b}$ P-value  $\chi^{2}$  test comparing the difference between the 2020 count and the 2017–2019 average between subgroups.



Figure 3: The overall, living and deceased kidney transplantation rate in 2017–2019 and 2020. The percentage change is provided for the months where the largest difference was found within the first and second pandemic waves. DD: deceased donor; LD: living donor; KTx: kidney transplantation.

## Mortality in dialysis and kidney transplant patients

During 2020, 28 935 patients died while on dialysis, an 11.4% (95% CI 9.8–13.1) increase compared with the average annual number of deaths for the period 2017–2019 (Table 3). Dialysis mortality increased in all age groups  $\geq$ 45 years, and the most prominent

increase was found for patients 65–74 years of age (P < .001). There was no difference in mortality change between males and females. However, in dialysis patients with diabetes as the PRD, the increase in mortality was greater than in patients with other PRDs (P = .020). Interestingly, mortality increased only in patients receiving HD, but not for patients receiving PD.

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Table 3: The number of deaths in dialysis and transplantation patients and the absolute and relative differences between 2020 and 2017–2019 overall and by age group, sex, diabetes

|                           |                |                  | Deaths         | on dialysis                         |                      |                      | De           | aths while   | e1 on a fu                        | nctioning kidney tı                  | ansplant.            |                      |
|---------------------------|----------------|------------------|----------------|-------------------------------------|----------------------|----------------------|--------------|--------------|-----------------------------------|--------------------------------------|----------------------|----------------------|
|                           | Moon           |                  | Д              | lifference                          |                      |                      | Moon         |              | Д                                 | ifference                            |                      |                      |
| Characteristics           | 2017-2019      | 2020             | и              | % (95% CI)                          | P-value <sup>a</sup> | P-value <sup>b</sup> | 2017–2019    | 2020         | и                                 | % (95% CI)                           | P-value <sup>a</sup> | P-value <sup>b</sup> |
| Overall                   | 25 963         | 28 935           | +2972          | 11.4 (9.8–13.1)                     | <.001                |                      | 4107         | 5166         | +1059                             | 25.8 (21.7–29.9)                     | <.001                |                      |
| Age group (years)         | 504            | С<br>Г<br>Г      | 977            | 0 1 (3 (31 0)                       | 157                  | 200                  | 146          | 174          | с <del>т</del><br>80 <del>т</del> | 18 0 (3 1-40 0)                      | 102                  | 646                  |
| 45-64                     | 4106           | 4608             | +502           | 2.2 (                               | (CT.) >              | /10.                 | 1199         | 1474         | +275                              | 23.0 (15.3–30.6)                     | <.001                | 010                  |
| 65-74                     | 6625           | 7690             | +1065          | 16.1 (12.8–19.4)                    | <.001                |                      | 1560         | 1947         | +387                              | 24.8 (18.1–31.4)                     | <.001                |                      |
| ≥75                       | 14 728         | 16 087           | +1359          | 9.2 (7.0–11.5)                      | <.001                |                      | 1202         | 1571         | +369                              | 30.7 (23.2–38.2)                     | <.001                |                      |
| Female<br>Male            | 9109<br>16 854 | 10 061<br>18 874 | +952<br>+2020  | 10.5 (7.6–13.3)<br>12.0 (9.9–14.1)  | <.001<br><.001       | .442                 | 1432<br>2675 | 1836<br>3330 | +404<br>+655                      | 28.2 (21.3–35.1)<br>24.5 (19.4–29.6) | <.001<br><.001       | .505                 |
| DM as PRD<br>No DM as PRD | 6944<br>19 019 | 7996<br>20 939   | +1052<br>+1920 | 15.1 (11.9–18.4)<br>10.1 (8.1–12.1) | <.001<br><.001       | .020                 | 718<br>3389  | 897<br>4269  | +179<br>+880                      | 25.0 (15.2–34.8)<br>26.0 (21.4–30.5) | <.001<br><.001       | .888                 |
| HD                        | 23 712<br>2251 | 26 648<br>2287   | +2936<br>+36   | 12.4 (10.6–14.1)<br>1.6 (–4.2–7.4)  | <.001<br>.590        | .001                 |              |              |                                   |                                      |                      |                      |

DM: diabetes mellitus. <sup>a</sup> P-value Poisson model comparing the 2020 count with the 2017–2019 average, within each (sub)group. <sup>b</sup> P-value  $\chi^2$  test comparing the difference between the 2020 count and the 2017–2019 average between subgroups. Excess mortality in kidney transplant recipients in 2020 [25.8% (95% CI 21.7–29.9)] was larger than that in patients receiving dialysis. There was no difference in transplant mortality between regions, age groups, males and females or patients with diabetes as the PRD versus patients with other PRDs (Table 3).

The increase in mortality in HD patients was 47.9% during the first pandemic wave and 26.5% during the second wave. In PD patients, no increase in mortality during the first pandemic wave was found, while it temporarily decreased to 20% between May and July and increased to 22.5% during the second wave. In kidney transplant recipients, this increase in mortality was 86.6% and 48.3%, respectively (Fig. 4).

In 2020, there were 2972 excess deaths among patients on dialysis, of which 2468 (83%) were due to an infectious cause of death (COD) (Supplementary Fig. S3). We found that there were 2215 excess deaths due to viral pulmonary infection and 653 due to generalized viral infection, while these were partially compensated for by fewer deaths due to septicaemia (n = 214) and bacterial pulmonary infection (n = 170). Among kidney transplant patients there were 1059 excess deaths, of which 742 (70%) were due to an infectious COD (Supplementary Fig. S3). Of these, 546 excess deaths were due to viral pulmonary infection and 249 due to generalized viral infection, whereas, similar to the CODs in dialysis patients, other infectious causes of death such as septicaemia (n = -41) were lower than in 2017–2019 in transplant recipients.

## Prevalence of KRT

On 31 December 2020, 317 787 patients in the participating countries were receiving KRT (Table 4). This was similar to the prevalence on 31 December 2019 (N = 317 077). This finding differs from the usual 2% annual increase in the prevalence of KRT in European countries, as was the case when comparing the 2018 and 2019 prevalence (Table 4). The relative difference between the 2019 and 2020 prevalence was similar across age groups, sexes and for patients with and without diabetes as the PRD, but not across countries. While for kidney transplant recipients the prevalence increased by 0.7% (P = .005), it remained stable for patients receiving dialysis. When comparing the change in prevalence between 2017–2019 and 2019–2020, we found that the change was most substantial in the oldest age groups for patients receiving dialysis and for kidney transplant recipients (Supplementary Fig. S4).

## DISCUSSION

In contrast to most previous studies investigating KRT patients affected by COVID-19, this study focused on the effects of the pandemic on the European KRT population as a whole. In our comparative analysis between 2020 and the years 2017–2019, we found a 6.2% decrease in the annual number of patients starting KRT, reaching the lowest point (-22.7%) during the first pandemic wave in April. This decrease was smaller in males than in females and was least pronounced for PD, followed by a larger decrease for HD and a substantial decrease for pre-emptive kidney transplantation. The kidney transplantation rate decreased by 22.5%, reaching a nadir of -80.1% during the first wave, particularly affecting living donor kidney transplants. The largest decrease was observed in patients ≥65 years of age. In dialysis patients, mortality increased by 11.4% and this increase was highest in dialysis patients 65–74 years of age, in those with diabetes as the PRD and in those on HD. In kidney transplant recipients, the mortality in 2020 was 25.8% higher than in 2017–2019, peaking at 86.6%



Figure 4: The mortality rate in HD, PD and kidney transplant patients in 2017–2019 and 2020. The percentage change is provided for the months where the largest difference was found within the first and second pandemic waves. KTx: kidney transplantation.

during the first wave. In contrast to the increasing prevalence of KRT observed over the past decades across Europe, the year 2020 marked an anomaly caused by the increase in mortality coupled with a decline in the number of new cases, with the prevalence at the end of 2020 resembling that of 2019.

## Incidence of KRT

In 2020, the incidence of KRT in Europe decreased to 136 pmp [12], a level that was last seen in 2013 [16]. The decrease in the incidence of KRT in European males compared with females was lower when expressed as a percentage (5.2% versus 8.2%, respectively) but higher when expressed in numbers (n = 1304 versus 1121, respectively), which is due to the usually higher incidence of KRT among males [17]. This more modest decrease in males may indicate a smaller proportion of males postponing dialysis or opting for conservative care when compared with females. The decrease in KRT incidence varied widely across Europe, with the largest decreases observed in larger countries such as France, Spain and the UK. While the exact causes underlying these differences remain unclear, potential contributing factors may include varying degrees of overwhelmed healthcare systems, high CKD patient mortality or differences in policies aimed at delaying KRT initiation to minimize COVID-19 exposure in the clinic [8].

The decrease of 6.2% in the incidence of KRT in Europe was more substantial than in the USA (1%) [18]. Although the first pandemic wave appears to have had a similar impact on access to KRT [19], in Europe the second wave seems to have had a greater effect than in the USA [20]. It is uncertain if the decreases in KRT incidence in Europe and the USA reflected the choices of patients and/or their treating physicians, barriers to care, a permanent choice for conservative care or a higher mortality in patients with advanced CKD [8, 18, 19]. It may have been a combination of these factors, especially because neither European nor US data showed a catch-up effect later in the year.

In Europe, a decrease in the incidence was seen for all KRT modalities, but in the USA the overall decrease of 1% was caused by a 3.4% decrease in HD, while the incidence of PD and preemptive transplantation increased by 16.3% and 8.1%, respectively [18]. As in the USA, the rate of COVID-19 hospitalization was three to four times higher in HD patients compared with patients receiving PD, with US investigators relating this finding to the protective effect of the home setting of PD [18]. Although this may explain part of the shift in the first dialysis modality from HD to PD in the USA, it seems that such a shift did not occur in Europe.

## Kidney transplant activity

In Europe, kidney transplant activity was  $\approx$ 20% lower in 2020 compared with 2017–2019, which was very different in the USA, where transplant activity was 5.8% higher in 2020, although both regions showed a substantial decrease during the first pandemic wave [18, 20]. This reduction in the number of transplants during the pandemic waves may be ascribed to a lack of access to care due to limited availability of staff for non-COVID care and reduced access to elective surgery together with potential hesitancy on the part of patients and their nephrologists with respect to hospital admission considering the need for high doses of immunosuppressants and increased infection risk immediately following the transplant. In many European countries, kidney transplantation (except for paediatric transplantation and urgent cases) was completely suspended during the first wave of COVID-19. On the other hand, we found that some countries, such as the Nordic countries and Greece, managed to sustain their kidney transplant activity during the pandemic.

The decrease in the number of living donor kidney transplants (30.5%) was more substantial than that of deceased donor transplants (20.4%). It is likely that living donor transplant programs were hesitant to expose donors to COVID-19 in hospital settings [10]. In addition, the capacity to perform the donor evaluation may have been reduced. Moreover, in contrast to deceased donor kidney transplantation, living donor kidney transplantation can usually be postponed. Also, in the USA, the number of living donor kidney transplants was lower in 2020 than in 2017–2019, although the decrease was only around half of that in Europe (17.8% versus 30.5%).

With respect to deceased donor kidney transplants, limited access to the intensive care unit (ICU) for the purpose of organ preservation as well as a lower availability of donors due to the reduction in road traffic accidents and rejection of COVID-19positive donors may have contributed to the decline in the transplantation rate. From this perspective, the difference in the effect of the pandemic on the number of deceased donor transplants in Europe (-20.4%) and the USA (+15.3%) is striking. In Europe, the attitude of nephrologists towards kidney transplantation during the first two pandemic waves was guided by hospitals, especially their ICUs, being overwhelmed by the number of COVID-19 patients and, second, by the fear of higher mortality due to high doses of immunosuppressants immediately after the transplant. It is important to note that, on average, the participating European countries have less than half the ICU capacity per 100 000 inhabitants compared with the USA (11 versus 26 beds, respectively) [21, 22]. In addition, the number of road traffic victims in 2020

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|                              | Prevalenc | e, number of | patients rece | iving KRT |       | Mean average d   | lifference 201       | 7–2019               |        | Difference           | 2019-2020            |                      |
|------------------------------|-----------|--------------|---------------|-----------|-------|------------------|----------------------|----------------------|--------|----------------------|----------------------|----------------------|
| Characteristics              | 2017      | 2018         | 2019          | 2020      | и     | % (95% CI)       | P-value <sup>a</sup> | P-value <sup>b</sup> | u      | % (95% CI)           | P-value <sup>a</sup> | P-value <sup>b</sup> |
| Overall<br>Age groun (years) | 302 830   | 309 919      | 317 077       | 317 787   | +7158 | 2.3 (1.8–2.8)    | <.001                |                      | +710   | 0.2 (-0.3-0.7)       | .207                 |                      |
| 156 Graup Ucura)<br>0-44     | 47 476    | 47 425       | 47 399        | 47 043    | -26   | -0.1(-1.4-1.2)   | .905                 | <.001                | -356   | -0.8 (-2.0-0.5)      | .102                 | .288                 |
| 45-64                        | 116 600   | 118 716      | 120 557       | 120 804   | +1841 | 1.7 (0.9–2.5)    | <.001                |                      | +247   | 0.2 (-0.6-1.0)       | .477                 |                      |
| 65-74                        | 73 285    | 76 069       | 78 630        | 79 294    | +2561 | 3.6 (2.6–4.6)    | <.001                |                      | +664   | 0.8 (-0.1-1.8)       | .018                 |                      |
| ≥75                          | 65 467    | 67 708       | 70 490        | 70 645    | +2782 | 3.8 (2.7–4.8)    | <.001                |                      | +155   | 0.2 (-0.8-1.3)       | .559                 |                      |
| Female                       | 114 363   | 116 854      | 119 398       | 119 412   | +2544 | 2.2 (1.4–3.0)    | <.001                | .690                 | +14    | 0.0 (-0.8-0.8)       | .968                 | .512                 |
| Male                         | 188 467   | 193 065      | 197 679       | 198 375   | +4614 | 2.4 (1.8–3.0)    | <.001                |                      | +696   | 0.4 (-0.3-1.0)       | .117                 |                      |
| DM as PRD                    | 51109     | 52 670       | 54 117        | 53 771    | +1447 | 2.9 (1.7-4.1)    | <.001                | .251                 | -346   | -0.6(-1.8-0.6)       | .137                 | .278                 |
| No DM as PRD                 | 206 448   | 210 799      | 214 895       | 215 105   | +4096 | 2.0 (1.4–2.6)    | <.001                |                      | +210   | 0.1 (-0.5-0.7)       | .651                 |                      |
| HD                           | 138 303   | 140 734      | 143 623       | 143 185   | +2889 | 1.9 (1.2–2.6)    | <.001                | .071                 | -438   | -0.3 (-1.0-0.4)      | .248                 | .095                 |
| PD                           | 15 095    | 15 117       | 15 189        | 15 395    | +72   | 0.3 (-1.9-2.6)   | .558                 |                      | +206   | 1.4 (-0.9-3.6)       | .095                 |                      |
| Kidney transplantation       | 148 275   | 153 036      | 157 457       | 158 561   | +4421 | 3.0 (2.3–3.8)    | <.001                |                      | +1104  | 0.7 (0.1–1.4)        | .005                 |                      |
| All dialysis                 | 153 398   | 155 851      | 158 812       | 158 580   | +2961 | 1.7 (1.0–2.5)    | <.001                |                      | -232   | -0.1 (-0.8-0.5)      | .560                 |                      |
| Austria                      | 9123      | 9155         | 9184          | 9181      | +31   | 0.3 (-2.6-3.2)   | .741                 | <.001                | с<br>Г | 0.0 (-2.9-2.9)       | .982                 | <.001                |
| Belgium                      | 14 675    | 14 993       | 15 266        | 15 234    | +296  | 2.0 (-0.3-4.3)   | .388                 |                      | -32    | -0.2 (-2.5-2.0)      | .855                 |                      |
| Bosnia and Herzegovina       | 2683      | 2731         | 2704          | 2547      | +11   | 0.4 (-4.9-5.7)   | .745                 |                      | -157   | -5.8 (-11.2 to -0.4) | .030                 |                      |
| Denmark                      | 5545      | 5580         | 5605          | 5685      | +30   | 0.5 (-3.2-4.3)   | .692                 |                      | 80     | 1.4 (-2.3-5.1)       | .452                 |                      |
| Estonia                      | 950       | 1000         | 1034          | 1049      | +42   | 4.3 (-4.5-13.1)  | .255                 |                      | 15     | 1.5 (-7.1-10.0)      | .742                 |                      |
| Finland                      | 5027      | 5108         | 5204          | 5303      | +89   | 1.7 (-2.1-5.6)   | .212                 |                      | 66     | 1.9 (-1.9-5.7)       | .334                 |                      |
| France                       | 88 403    | 90 530       | 92 559        | 92 864    | +2078 | 2.3 (1.4–3.2)    | <.001                |                      | 305    | 0.3 (-0.6-1.2)       | .479                 |                      |
| Greece                       | 14 225    | 14 703       | 15 166        | 15 169    | +471  | 3.3 (1.0–5.5)    | <.001                |                      | ŝ      | 0.0 (-2.2-2.3)       | .986                 |                      |
| Iceland                      | 259       | 265          | 291           | 302       | +16   | 6.1 (-10.7-22.8) | .222                 |                      | 11     | 3.8 (-12.3-19.9)     | .651                 |                      |
| Montenegro                   | 192       | 195          | 228           | 241       | +18   | 9.2 (-10.0-28.4) | .094                 |                      | 13     | 5.7 (-12.4-23.8)     | .548                 |                      |
| The Netherlands              | 17 135    | 17 456       | 17 846        | 17 931    | +356  | 2.1 (0.0–4.2)    | .019                 |                      | 85     | 0.5 (-1.6-2.5)       | .653                 |                      |
| Norway                       | 5178      | 5276         | 5382          | 5464      | +102  | 2.0 (-1.9-5.8)   | .176                 |                      | 82     | 1.5 (-2.2-5.3)       | .431                 |                      |
| Serbia                       | 5098      | 5359         | 5621          | 5516      | +262  | 5.0 (1.2–8.8)    | <.001                |                      | -105   | -1.9 (-5.6-1.8)      | .320                 |                      |
| Spain                        | 58 522    | 690 09       | 61 809        | 62 138    | +1644 | 2.8 (1.6–3.9)    | <.001                |                      | 329    | 0.5 (-0.6-1.6)       | .350                 |                      |
| Sweden                       | 9930      | 10 037       | 10 246        | 10 332    | +158  | 1.6 (-1.2-4.3)   | .084                 |                      | 86     | 0.8 (-1.9-3.6)       | .549                 |                      |
| Switzerland                  | 7927      | 8077         | 8298          | 8528      | +186  | 2.3 (-0.8-5.4)   | .054                 |                      | 230    | 2.8 (-0.3-5.8)       | .076                 |                      |
| UK                           | 57 958    | 59 385       | 60 634        | 60 303    | +1338 | 2.3 (1.1–3.4)    | <.001                |                      | -331   | -0.5 (-1.7-0.6)      | .341                 |                      |
| DM: diabetes mellitus.       |           |              |               |           |       |                  |                      |                      |        |                      |                      |                      |

<sup>a</sup> P-value Poisson model comparing the count with the count of the previous year, within each (sub)group. <sup>b</sup>P-value  $\chi^2$  test comparing the difference between the count and the count of the previous year between subgroups... Downloaded from https://academic.oup.com/ndt/advance-article/doi/10.1093/ndt/gfae043/7695927 by Universitat Politecnica de Valencia user on 30 September 2024

decreased by 17% in Europe compared with 2019 [23], but only by 6.8% in the USA [24]. Also, border restrictions in Europe may have contributed to the lower number of deceased donor transplants as a result of less cross-border exchange.

# Mortality in dialysis and kidney transplant patients

Interestingly, mortality on dialysis increased for patients receiving HD but not for those on PD, where it even temporarily decreased. Again, this may be attributed to the protective effect of the home setting of PD, but also to the fact that, in general, patients receiving PD are healthier than HD patients. In line with this, European data during the first wave suggest that the number of patients receiving PD who were diagnosed with COVID-19 was less than half of those treated with HD [3].

In European dialysis patients, the increase in mortality in 2020 was lower than in their US counterparts (11.4% versus 15.8%) [18]. US Renal Data System investigators noted that during the first pandemic wave, hospitalization rates for cardiovascular events were substantially lower, and they suggested that part of the excess mortality may be attributed to disruptions in ordinary healthcare utilization, as patients may have been unable or unwilling to seek necessary acute care [19]. However, our data do not show excess cardiovascular deaths in dialysis patients in Europe. The same is true for the general population in Europe [25].

The 25.8% increase in mortality of European kidney transplant recipients was lower than that in US patients (32.4%). It remains unclear to what extent this is linked to a more substantial decrease in transplant activity in Europe, which in turn reduced the need for high doses of immunosuppressive medications shortly after transplantation. Nevertheless, the impact of fewer transplantations on the prognosis of individual KRT patients, weighting the risk of remaining on dialysis versus a higher short-term risk of death for a limited period after transplantation, has been shown to be limited, as long as the pause in the kidney transplant activity was not prolonged [26, 27].

## Prevalence of KRT

In Europe in 2020, the prevalence of KRT was 0.2% higher than in 2019, although the Madrid region showed a 1.8% decrease in prevalence [8], suggesting some variation across the continent. In the USA, prevalence declined by 0.5% from 2019 to 2020 [18]. The difference in the change in prevalence is difficult to interpret, as the incidence and mortality rates of KRT patients were also very different between Europe and the USA in pre-COVID times.

## Strengths and limitations

A strength of this study is the large number of countries participating in the ERA Registry, which covers a geographically diverse area in Europe. At the same time, this study was unable to include data from countries in Eastern Europe, nor Germany, Italy and Turkey. In addition, we cannot rule out the possibility that difficulties in collecting data may have occurred in some countries during the pandemic, potentially influencing the quality of the data registered. Lastly, as regulations prevented comparisons of mortality at the country level, we were unable to identify any COVID-19-related mortality patterns across Europe.

## CONCLUSION

The COVID-19 pandemic has had a substantial impact on the incidence and prevalence of KRT, kidney transplant activity and mortality of KRT across Europe, with variations across countries. Any geographical differences, both within Europe and between Europe and the USA, are difficult to interpret due to international differences and changes in COVID-19 policies over time. For example, when compared with the USA, Europe showed a greater decrease in incidence and a decrease in transplant activity, whereas the latter increased in USA. In addition, mortality in European dialysis patients was similar to that in US patients, whereas mortality in kidney transplant recipients was lower. In retrospect, however, it is impossible to speculate on whether the more 'conservative' attitude in Europe-more often postponing dialysis and reducing kidney transplant activity—was rational with respect to patient safety. In particular, the consequences of a decision to abandon deceased donor kidney transplantation based on medical concerns of a higher short-term mortality post-transplant are difficult to assess in light of an improved long-term prognosis when compared with remaining on dialysis. This should be the subject of further research.

## SUPPLEMENTARY DATA

Supplementary data are available at Nephrology Dialysis Transplantation online.

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## **AUTHORS' CONTRIBUTIONS**

A.K., K.J.J., N.C.C., A.O. and V.S.S. were responsible for the conceptualization and methodology. A.K. was responsible for the formal analysis. H.W.K., G.Y.H., H.J.K., S.-W.K., J.T.P. and E.L. were responsible for the investigation. A.K. and K.J.J. wrote the original draft. A.K., K.J.J., N.C.C., J.K., K.H., J.C.F., S.T.A., R.S., P.F., M.H.H., A.Å., D.N., P.A., S.S.S., J.E.S., M.S., H.R., M.O., D.R., R.P., C.S.P., O.L.R.A., C.L., M.L., S.A.B., A.O. and V.S.S. reviewed and edited the manuscript. All authors read and approved the final manuscript.

## DATA AVAILABILITY STATEMENT

The data underlying this article cannot be shared with any third party because the national and regional registries that provided data to the ERA Registry remain the owners of the data.

## **CONFLICT OF INTEREST STATEMENT**

K.J.J. reports research funding from the ERA, grants from the European Society for Paediatric Nephrology and ERA and board membership from the Share RR working group and International Society of Nephrology (ISN), all outside the submitted work. J.C.F. reports honoraria for presentations from the Donation and Transplantation Institute, outside the submitted work. R.S. reports lectures fees from Menarini, AstraZeneca, Boehringer Ingelheim and Novo Nordisk and travel support from Menarini and AstraZeneca, outside the submitted work. P.F. reports grants from Finska läkaresällskapet and Liv och Hälsa and consulting fees from Baxter, AstraZeneca and GSK, outside the submitted work. D.N. reports board membership for the UK Kidney Association, outside the submitted work. P.A. reports honoraria for presentations from CSL Behring (Vifor) and board membership for the Swiss Society of Nephrology, outside the submitted work. M.S. reports grants from the Swedish Kidney Foundation, Skåne University Hospital Foundations, IngaBritt and Arne Lundbergs stiftelse and consulting fees from Hansa Biopharma, AstraZeneca, Vifor and Otsuka, outside the submitted work. H.R. reports board membership for the Balkan Cities Association of Nephrology, Dialysis, Transplantation and Artificial Organs (BANTAO), Mediterranean Kidney Society (MKS) and European Association of Professors Emeriti (EAPE), outside the submitted work. M.O. reports board membership for the Estonian Society of Nephrology and the ISN Eastern and Central Europe Regional Board, outside the submitted work. R.P. reports grants from the Icelandic Research Fund and board membership for the Icelandic Society of Transplantation and the Icelandic Society of Internal Medicine, outside the submitted work. M.L. reports board membership for the Serbian Society of Nephrology, outside the submitted work. A.O. reports grants from Sanofi; consultancy or speaker fees or travel support from Advicciene, Astellas, AstraZeneca, Amicus, Amgen, Boehringer Ingelheim, Fresenius Medical Care, GSK, Bayer, Sanofi-Genzyme, Menarini, Mundipharma, Kyowa Kirin, Eli Lilly, Alexion, Freeline, Idorsia, Chiesi, Otsuka, Novo Nordisk, Sysmex and Vifor Fresenius Medical Care Renal Pharma; Directorship of the Catedra Mundipharma-UAM of diabetic kidney disease and the Catedra AstraZeneca-UAM of chronic kidney disease and electrolytes; board membership for the European Renal Association and stock

options from Telara Farma, all outside the submitted work. V.S.S. reports research funding from the ERA, outside the submitted work. The remaining authors declare no conflicts of interest.

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