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# Facilitating access to the renal transplant waiting list does not increase the number of transplantations: comparative study of two French regions

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## Abstract

**Background:** In France, there are important regional disparities of access to the renal transplant waiting list and transplantation. Our objectives were to compare the characteristics of patients with end-stage renal disease (ESRD) of two French regions (Ile-de-France and Bretagne) and to identify determinants of access to the waiting list and subsequent transplantation, with a focus on temporary inactive status (TIS) periods.

**Methods:** All 18–80-year-old incident patients who started dialysis in Ile-de-France or Bretagne between 2006 and 2009 were included ( $n = 6160$ ). Associations between patients' characteristics and placement on the waiting list or transplantation were assessed using a Fine and Gray model to take into account the competing risk of death and living donor transplantation.

**Results:** At the end of the follow-up (31 December 2013), more patients had undergone transplantation in Bretagne than in Ile-de-France (30 versus 27%), although the percentage of waitlisted patients was higher in Ile-de-France than in Bretagne (47 versus 33%). More patients were on TIS and with a longer median TIS duration in Ile-de-France. Independent of age and clinical characteristics, patients in Bretagne were less likely to be waitlisted than those in Ile-de-France [subdistribution hazard ratio 0.77 (95% confidence interval 0.7–0.9)]. After waitlisting, patients in Bretagne were four times more likely to be transplanted.

**Conclusions:** Our study highlights clinical practice differences in Bretagne and Ile-de-France and shows that facilitating access to the waiting list is not sufficient to improve access to renal transplantation, which also depends on organ availability.

**Key words:** chronic renal failure, dialysis, end-stage renal disease, epidemiology, kidney transplantation

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## Introduction

End-stage renal disease (ESRD) management is an important public health issue. Patients with ESRD need renal replacement therapy (haemodialysis, peritoneal dialysis or renal transplantation) to improve their survival. Renal transplantation is associated with better survival [1–3], better quality of life [4, 5] and lower cost [6] compared with dialysis. However, access to renal transplantation is often limited by organ shortage [7]. Previous studies found disparities in the access and evaluation of candidates for renal transplantation [8–13].

In France, the first step towards renal transplantation is placement on the French national renal transplant waiting list, which is managed by the Agence de la Biomédecine (ABM). Patients are placed on the list by a nephrologist after assessment of their medical status. Placement on the waiting list depends on the clinical team's practices, which may not be homogeneous between regions or even between transplant centres in the same region. Before the national guidelines, established by the Haute Autorité de Santé (French national health agency) in October 2015 [14], only European recommendations on the evaluation of patients to be placed on the list were used [15, 16].

After this first step, allocation of an organ from a deceased donor is based on the allocation score developed by ABM. This score includes the time on the waiting list, dialysis duration, age difference between the recipient and donor and donor-recipient immunological and biological compatibility (Supplementary data, Table S1). Its modulation was slightly different between regions and the grafts were allocated regionally until February 2015. Any waitlisted patient who is currently unavailable or unsuitable for transplantation is identified by a temporary inactive status (TIS) and cannot be transplanted. If the initial medical check-up is not finalized, this patient might be identified by an initial TIS period, although this does not correspond to a medical event limiting access to transplantation. Consequently, after placement on the waiting list, access to kidney transplantation depends on the allocation score, organ availability and also TIS.

A previous study in 11 French regions showed that after taking into account medical and non-medical factors, placement on the list was significantly associated with the region of residence, suggesting waitlisting practice differences [17]. For technical reasons, this study did not include the Ile-de-France region, where 18% of the French population live (INSEE). The cumulative incidence of placement on the waiting list in Ile-de-France is higher compared with other French regions, while the Bretagne region is in the average [18]. Therefore, the Ile-de-France and Bretagne regions are good candidates to study the variations of access to the waiting list. Nonetheless, the consequences of differences in waiting list access between regions in terms of eventual access to transplantation were not evaluated. Moreover, the link between TIS periods and access to renal transplantation have never been studied in France.

The objectives of this study were (i) to compare the characteristics of patients with ESRD in the Ile-de-France and Bretagne regions and (ii) to identify determinants of access to the renal transplant waiting list and renal transplantation, with a focus on TIS periods in these regions.

## Materials and methods

### Study population

All 18–80-year-old incident patients with ESRD who started dialysis between 1 January 2006 and 31 December 2009 in Bretagne

and Ile-de-France were extracted from the Renal Epidemiology and Information Network registry, a tool for public health decision support, evaluation and research [19]. Patients who received pre-emptive renal transplantation were not included.

ESRD incidence, after standardization for gender and age, was 174 per million population (pmp) in Ile-de-France and 126 pmp in Bretagne in 2013 [20].

### Collected data

Demographic and clinical data at first dialysis were extracted. Three demographic variables were taken into account: age group (18–39, 40–59, 60–69 and 70–80 years), gender and region of residence.

The following patients' clinical features at first dialysis (baseline) were studied: primary renal disease categorized in six groups [glomerulonephritis, pyelonephritis, diabetic nephropathy, hypertensive and vascular nephropathy, polycystic kidney disease and others (other causes and unknown)], modality and type of first dialysis (haemodialysis or peritoneal dialysis, emergency first dialysis and first dialysis session with a catheter), cardiovascular diseases (coronary artery disease, congestive heart failure, peripheral vascular disease, myocardial infarction, arrhythmia, aortic aneurism, cerebrovascular disease), diabetes, chronic respiratory disease, hepatic disease, active malignancy, physical disabilities (ambulation impairment, paraplegia or hemiplegia, member amputation, blindness) and HIV infection. Haemoglobin levels were categorized as <10, 10–12 and >12 g/dL. For waitlisted patients, the date of placement on the list, date of transplantation, blood group (A, B, O and AB), panel reactive antibody (PRA) level and TIS periods were recorded. If an inactive period was <75 days and started concomitantly with placement on the list ( $\pm 2$  days), it was considered as the period of completion of all medical examinations that are required for renal transplantation candidates and not as a TIS. Organ availability was quantified as the mean number of deceased donors per million population between the year of placement on the list and the year of transplantation or last follow-up. Date of death was also included.

### Statistical analysis

The patients' characteristics were described and compared using Pearson's  $\chi^2$  test. Continuous variables were expressed as mean  $\pm$  standard deviation. Means were compared using a Student test and medians using a non-parametric equality-of-medians test. Missing data were systematically imputed using multiple imputation by chained equation (MICE) with 10 imputations and one cycle, because missing data concerned only the haemoglobin level [21].

The outcomes of interest were

1. Placement on the renal transplant waiting list, regardless of the donor type (living or deceased). Death before waitlisting was considered as a competing event. Patients pre-emptively placed on the list before the beginning of dialysis were considered to be waitlisted at dialysis start. Times to outcomes (death, waiting-list placement) were calculated from the date of first dialysis. Non-waitlisted living patients were censored at the end of the follow-up (31 December 2013).
2. Deceased donor renal transplantation after placement on the list. Death before transplantation and living donor transplantation were considered as competing events. Times to outcomes (death, transplantation) were calculated from the date of placement on the list. Non-transplanted living patients were censored at the end of the follow-up.

- Deceased donor transplantation after first dialysis. Death before transplantation and living donor transplantation were considered as competing events. Times to outcomes (death, transplantation) were calculated from the date of first dialysis. Non-transplanted living patients were censored at the end of the follow-up.

The association between patients' characteristics (including the region of residence) and outcomes of interest was assessed using Fine and Gray univariate analyses [22]. Variables with a P-value <0.20 were included in the multivariate analysis. A P-value <0.05 was considered statistically significant. Results were reported as subdistribution hazard ratios (SHRs) with 95% confidence intervals (CIs) and P-values. The cumulative incidence function (CIF) curve, which represents the probability of transplantation after taking into account the competing risk of death before transplantation and living donor transplantation, was also used to compare the two regions. Statistical analyses were performed with STATA 13 software.

## Results

### Patients' characteristics

**Patients' characteristics.** Table 1 presents the baseline characteristics of the 6160 incident patients who started dialysis in Bretagne (18%) or Ile-de-France (82%) between 1 January 2006 and 31 December 2009. Their mean age was  $64.3 \pm 13.9$  years in Bretagne and  $60.1 \pm 15.1$  years in Ile-de-France ( $P < 10^{-4}$ ).

Significant differences were found in the percentage of patients with diabetes (28% in Bretagne and 39% Ile-de-France), an active malignancy (12% and 8%), a chronic respiratory disease (14% and 8%) and more than two cardiovascular diseases (29% and 19%) ( $P < 10^{-4}$  for all).

On 31 December 2013, 33% of patients in Bretagne and 47% in Ile-de-France were waitlisted (Figure 1). Among these patients, 18% were placed on the list at first dialysis or pre-emptively in Bretagne and 19% in Ile-de-France.

**Characteristics of waitlisted patients.** The gender of waitlisted patients (total number = 2748; 14% in Bretagne and 86% in Ile-de-France) was comparable between regions (Table 2). The mean age was  $51.8 \pm 13.0$  years in Bretagne and  $50.1 \pm 13.1$  in Ile-de-France ( $P = 0.016$ ).

Diabetes and hepatic disease were significantly more frequent in Ile-de-France than in Bretagne (27% versus 18% of patients with diabetes and 5% versus 2% with hepatic disease, respectively).

### Access to the renal transplant waiting list, TIS and access to deceased donor transplantation

**Access to the renal transplant waiting list.** In univariate analyses, age and most comorbidities, except HIV infection, limited access to the waiting list (Supplementary data, Table S2). Multivariate analyses (Table 3) confirmed that age was a limiting factor for placement. In addition, diabetic nephropathy was associated with a 47% lower chance of being waitlisted compared with polycystic kidney disease, whereas peritoneal dialysis was associated with a higher probability of placement on the list [SHR 1.26 (95% CI 1.1–1.4)]. The chance of being waitlisted was also lower for patients with diabetes (by 20%), with active malignancy (by 63%) and with more than three cardiovascular diseases (by 49%). Patients who had a first dialysis session with a catheter were less likely to be waitlisted [SHR 0.78 (95% CI 0.7–0.9)]. Finally, in the

multivariate model, patients in Bretagne were 23% less likely to be placed on the list than patients in Ile-de-France [SHR 0.77, (95% CI 0.7–0.9)].

**Temporary inactive status.** Overall, 1488 waitlisted patients had at least one TIS (42% in Bretagne and 56% in Ile-de-France;  $P < 10^{-4}$ ). The mean number of TIS periods was 2.4 per patient in Bretagne and 2.0 in Ile-de-France ( $P = 0.0002$ ). The TIS median duration was 6 months in Bretagne and 9 months in Ile-de-France ( $P = 0.014$ ). On average, TIS duration represented 52 and 41% of the time spent on the waiting list in Bretagne and Ile-de-France, respectively ( $P < 10^{-4}$ ).

In addition, 1041 patients were initially waitlisted with a TIS that had a median duration of 4 months in Bretagne and 5 months in Ile-de-France ( $P = 0.011$ ). Among these 1041 patients, 211 were waitlisted pre-emptively. For these patients, the median TIS duration was 6 months in both regions ( $P = 0.628$ ).

**Access to deceased donor transplantation after waitlisting.** At the end of the follow-up, 89% of waitlisted patients underwent renal transplantation, 4% were dead and 0.8% had a living donor transplant in Bretagne compared with 58%, 8% and 8%, respectively, in Ile-de-France.

Univariate analyses (Supplementary data, Table S2) showed that, after placement on the waiting list, patients in the 70–80-year age group had higher chances of undergoing transplantation. Diabetes, more than three cardiovascular diseases (compared with no cardiovascular disease) and hepatic disease were associated with a lower probability of transplantation. In the multivariate model (Table 3), patients in the 60–69 and 70–80-year age groups were more likely to undergo transplantation than 18–39-year-old patients. Diabetes [SHR 0.78 (95% CI 0.6–1)] and more than three cardiovascular diseases [SHR 0.63 (95% CI 0.4–0.9); compared with no cardiovascular disease] were significantly associated with a reduced likelihood of transplantation. The probability of transplantation was also reduced for patients with at least one TIS period (by 56%). In the multivariate model, patients in Bretagne were 4.52 times more likely to be transplanted than patients in Ile-de-France. Time spent on the waiting list before transplantation was shorter for patients in Bretagne than in Ile-de-France (CIF attained 50%, 12.7 months after placement on the list in Bretagne versus 45.4 months in Ile-de-France) (Supplementary data, Figure S1). This difference remained when only patients without TIS were considered (5.3 months in Bretagne and 33.9 months in Ile-de-France).

In the multivariate model taking into account organ availability (Supplementary data, Table S3), the greater the organ availability, the higher was the probability of transplantation. Nevertheless, after taking region into account, organ availability was not significantly associated with access to renal transplantation. This fact may be related to the greater level of organ availability in Bretagne during the study period.

**Access to deceased donor transplantation after first dialysis.** Overall, 30% of all incident patients (waitlisted and non-waitlisted) in Bretagne underwent renal transplantation compared with 27% in Ile-de-France. In univariate analyses (Supplementary data, Table S2) as in multivariate analyses (Table 3), old age and comorbidities, except HIV infection, were associated with a lower probability of transplantation after dialysis start. In the multivariate model, patients in Bretagne were 2.07 times more likely to undergo transplantation than patients in Ile-de-France.

Table 1. Characteristics of incident patients

|                                        | Patients' baseline characteristics |                        |                            | Patients placed on the list at the end of the follow-up, % |                       |
|----------------------------------------|------------------------------------|------------------------|----------------------------|------------------------------------------------------------|-----------------------|
|                                        | Bretagne<br>n (%)                  | Ile de France<br>n (%) | P-value                    | Bretagne<br>33.5                                           | Ile de France<br>47.1 |
| Gender                                 |                                    |                        |                            |                                                            |                       |
| Female                                 | 435 (38.9)                         | 1785 (35.4)            | <b>0.027</b>               | 34.0                                                       | 46.8                  |
| Male                                   | 683 (61.1)                         | 3257 (64.6)            |                            | 33.2                                                       | 47.2                  |
| Age (years)                            |                                    |                        |                            |                                                            |                       |
| 18-39                                  | 78 (7)                             | 602 (11.9)             | <b>&lt;10<sup>-4</sup></b> | 88.5                                                       | 89.2                  |
| 40-59                                  | 288 (25.8)                         | 1617 (32.1)            |                            | 68.8                                                       | 76.3                  |
| 60-69                                  | 246 (22)                           | 1166 (23.1)            |                            | 35.0                                                       | 43.7                  |
| 70-80                                  | 506 (45.3)                         | 1657 (32.9)            |                            | 4.3                                                        | 5.7                   |
| Primary renal disease                  |                                    |                        |                            |                                                            |                       |
| Polycystic kidney disease              | 120 (10.7)                         | 327 (6.5)              | <b>&lt;10<sup>-4</sup></b> | 72.5                                                       | 83.5                  |
| Hypertensive and vascular nephropathy  | 263 (23.5)                         | 1204 (23.9)            |                            | 17.1                                                       | 37.5                  |
| Diabetic nephropathy                   | 130 (11.6)                         | 1305 (25.9)            |                            | 26.9                                                       | 33.5                  |
| Glomerulonephritis                     | 164 (14.7)                         | 607 (12)               |                            | 51.2                                                       | 72.5                  |
| Pyelonephritis                         | 57 (5.1)                           | 148 (2.9)              |                            | 49.1                                                       | 54.1                  |
| Others                                 | 384 (34.3)                         | 1451 (28.8)            |                            | 25.0                                                       | 47.7                  |
| First modality of dialysis             |                                    |                        |                            |                                                            |                       |
| Haemodialysis                          | 990 (88.6)                         | 4634 (91.9)            | <b>&lt;10<sup>-4</sup></b> | 33.0                                                       | 46.2                  |
| Peritoneal dialysis                    | 128 (11.4)                         | 408 (8.1)              |                            | 37.5                                                       | 57.4                  |
| Diabetes                               |                                    |                        |                            |                                                            |                       |
| No                                     | 800 (71.6)                         | 3084 (61.2)            | <b>&lt;10<sup>-4</sup></b> | 38.6                                                       | 56.5                  |
| Yes                                    | 318 (28.4)                         | 1958 (38.8)            |                            | 20.8                                                       | 32.2                  |
| Active malignancy                      |                                    |                        |                            |                                                            |                       |
| No                                     | 988 (88.4)                         | 4660 (92.4)            | <b>&lt;10<sup>-4</sup></b> | 36.6                                                       | 49.5                  |
| Yes                                    | 130 (11.6)                         | 382 (7.6)              |                            | 10.0                                                       | 17.3                  |
| Chronic respiratory disease            |                                    |                        |                            |                                                            |                       |
| No                                     | 965 (86.3)                         | 4636 (91.9)            | <b>&lt;10<sup>-4</sup></b> | 36.7                                                       | 49.4                  |
| Yes                                    | 153 (13.7)                         | 406 (8.1)              |                            | 13.7                                                       | 20.0                  |
| HIV infection                          |                                    |                        |                            |                                                            |                       |
| No                                     | 1113 (99.6)                        | 4901 (97.2)            | <b>&lt;10<sup>-4</sup></b> | 33.5                                                       | 46.5                  |
| Yes                                    | 5 (0.4)                            | 141 (2.8)              |                            | 40.0                                                       | 65.2                  |
| Hepatic disease                        |                                    |                        |                            |                                                            |                       |
| No                                     | 1058 (94.6)                        | 4754 (94.3)            | 0.651                      | 34.7                                                       | 47.2                  |
| Yes                                    | 60 (5.4)                           | 288 (5.7)              |                            | 13.3                                                       | 45.5                  |
| Physical disabilities                  |                                    |                        |                            |                                                            |                       |
| 0                                      | 949 (84.9)                         | 4358 (86.4)            | 0.175                      | 38.0                                                       | 52.7                  |
| ≥1                                     | 169 (15.1)                         | 684 (13.6)             |                            | 8.3                                                        | 11.0                  |
| Cardiovascular disease                 |                                    |                        |                            |                                                            |                       |
| 0                                      | 552 (49.4)                         | 3010 (59.7)            | <b>&lt;10<sup>-4</sup></b> | 52.4                                                       | 59.7                  |
| 1                                      | 243 (21.7)                         | 1055 (20.9)            |                            | 21.0                                                       | 36.2                  |
| 2                                      | 154 (13.8)                         | 552 (10.9)             |                            | 11.7                                                       | 20.8                  |
| ≥3                                     | 169 (15.1)                         | 425 (8.4)              |                            | 10.1                                                       | 18.4                  |
| Haemoglobin (g/dL)                     |                                    |                        |                            |                                                            |                       |
| 10-12                                  | 429 (38.4)                         | 1463 (29)              | <b>&lt;10<sup>-4</sup></b> | 35.9                                                       | 48.1                  |
| 10                                     | 462 (41.3)                         | 2176 (43.2)            |                            | 30.1                                                       | 46.6                  |
| >12                                    | 178 (15.9)                         | 774 (15.4)             |                            | 39.9                                                       | 50.8                  |
| Missing                                | 49 (4.4)                           | 629 (12.5)             |                            | 22.4                                                       | 41.8                  |
| Emergency first dialysis session       |                                    |                        |                            |                                                            |                       |
| No                                     | 796 (71.2)                         | 3961 (78.6)            | <b>&lt;10<sup>-4</sup></b> | 37.4                                                       | 48.7                  |
| Yes                                    | 322 (28.8)                         | 1081 (21.4)            |                            | 23.9                                                       | 41.2                  |
| First dialysis session with a catheter |                                    |                        |                            |                                                            |                       |
| No                                     | 691 (61.8)                         | 2582 (51.2)            | <b>&lt;10<sup>-4</sup></b> | 40.5                                                       | 52.7                  |
| Yes                                    | 427 (38.2)                         | 2460 (48.8)            |                            | 22.2                                                       | 41.2                  |

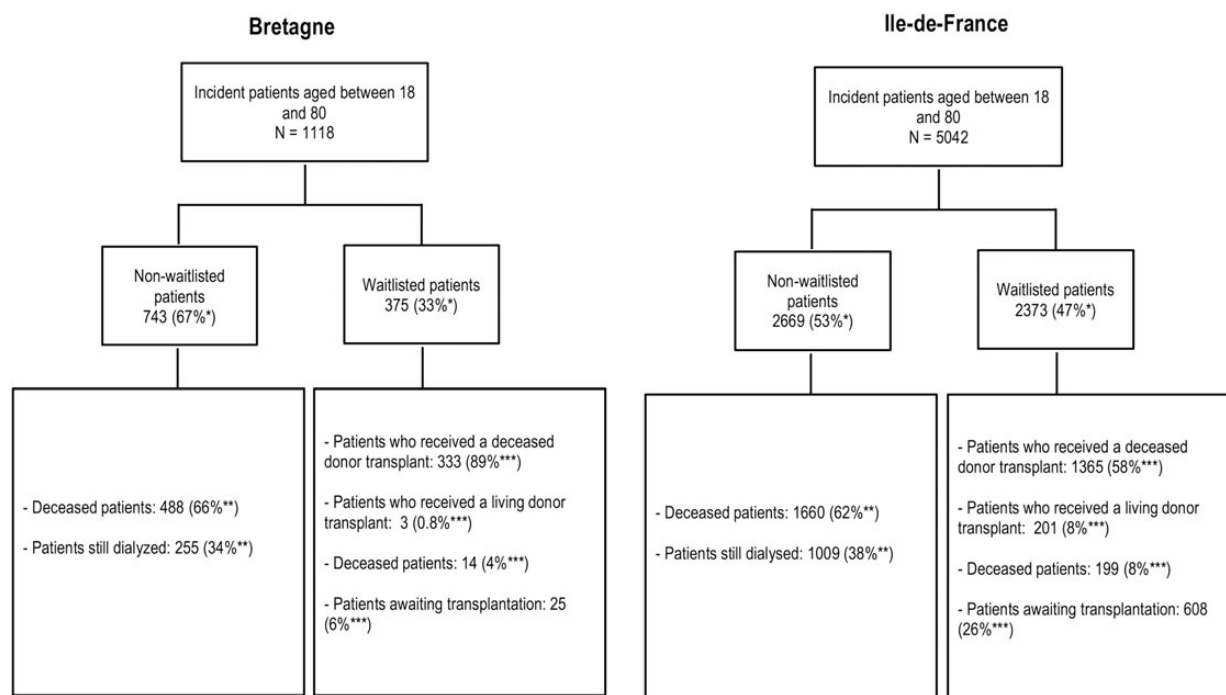
HIV, human immunodeficiency virus.

P values highlighted in bold correspond to P<0.05 (P values statistically significant)

## Discussion

This study compared access to the renal transplant waiting list and transplantation in two French regions (Bretagne and Ile-de-France) and shows that waitlisting strategies are stricter in

Bretagne than in Ile-de-France. Despite easier access to the waiting list, the likelihood of renal transplantation after dialysis start is reduced by half for patients in Ile-de-France. Indeed, once waitlisted, access to renal transplantation outweighed the reduced



\*Ratio based on incident patients, \*\*Ratio based on non-waitlisted patients, \*\*\* Ratio based on waitlisted patients

Fig. 1. Summary of the patients' status in Ile-de-France and Bretagne at the end of the follow-up (31 December 2013).

Table 2. Characteristics of patients placed on the waiting list

|                                       | Baseline characteristics of patients placed on the waiting list |                        |                   | Deceased donor-transplanted patients at the end of the follow-up, % |               |
|---------------------------------------|-----------------------------------------------------------------|------------------------|-------------------|---------------------------------------------------------------------|---------------|
|                                       | Bretagne<br>n (%)                                               | Ile de France<br>n (%) | P-value           | Bretagne                                                            | Ile de France |
|                                       | 375 (13.6)                                                      | 2373 (86.4)            |                   | 88.8                                                                | 57.5          |
| Gender                                |                                                                 |                        |                   |                                                                     |               |
| Female                                | 148 (39.5)                                                      | 836 (35.2)             | 0.112             | 39.9                                                                | 35.9          |
| Male                                  | 227 (60.5)                                                      | 1537 (64.8)            |                   | 60.1                                                                | 64.1          |
| Age (years)                           |                                                                 |                        |                   |                                                                     |               |
| 18–39                                 | 69 (18.4)                                                       | 537 (22.6)             | 0.123             | 19.2                                                                | 23.0          |
| 40–59                                 | 198 (52.8)                                                      | 1233 (52)              |                   | 52.0                                                                | 50.2          |
| 60–69                                 | 86 (22.9)                                                       | 509 (21.4)             |                   | 22.5                                                                | 21.8          |
| 70–80                                 | 22 (5.9)                                                        | 94 (4)                 |                   | 6.3                                                                 | 5.0           |
| Primary renal disease                 |                                                                 |                        |                   |                                                                     |               |
| Polycystic kidney disease             | 87 (23.2)                                                       | 273 (11.5)             | <10 <sup>-4</sup> | 24.9                                                                | 14.5          |
| Hypertensive and vascular nephropathy | 96 (25.6)                                                       | 692 (29.2)             |                   | 25.5                                                                | 27.3          |
| Diabetic nephropathy                  | 35 (9.3)                                                        | 437 (18.4)             |                   | 8.4                                                                 | 17.0          |
| Glomerulonephritis                    | 45 (12)                                                         | 451 (19)               |                   | 10.5                                                                | 19.3          |
| Pyelonephritis                        | 84 (22.4)                                                       | 440 (18.5)             |                   | 22.5                                                                | 18.9          |
| Others                                | 28 (7.5)                                                        | 80 (3.4)               |                   | 8.1                                                                 | 3.0           |
| First modality of dialysis            |                                                                 |                        |                   |                                                                     |               |
| Haemodialysis                         | 327 (87.2)                                                      | 2139 (90.1)            | 0.081             | 86.5                                                                | 90.1          |
| Peritoneal dialysis                   | 48 (12.8)                                                       | 234 (9.9)              |                   | 13.5                                                                | 9.9           |
| Diabetes                              |                                                                 |                        |                   |                                                                     |               |
| No                                    | 309 (82.4)                                                      | 1742 (73.4)            | <10 <sup>-4</sup> | 84.7                                                                | 76.1          |
| Yes                                   | 66 (17.6)                                                       | 631 (26.6)             |                   | 15.3                                                                | 23.9          |
| Active malignancy                     |                                                                 |                        |                   |                                                                     |               |
| No                                    | 362 (96.5)                                                      | 2307 (97.2)            | 0.46              | 97.3                                                                | 97.7          |
| Yes                                   | 13 (3.5)                                                        | 66 (2.8)               |                   | 2.7                                                                 | 2.3           |

Table continues

Table 2. Continued

|                                        | Baseline characteristics of patients placed on the waiting list |                        |                            | Deceased donor–transplanted patients at the end of the follow-up, % |               |
|----------------------------------------|-----------------------------------------------------------------|------------------------|----------------------------|---------------------------------------------------------------------|---------------|
|                                        | Bretagne<br>n (%)                                               | Ile de France<br>n (%) | P-value                    | Bretagne                                                            | Ile de France |
|                                        | 375 (13.6)                                                      | 2373 (86.4)            |                            | 88.8                                                                | 57.5          |
| Chronic respiratory disease            |                                                                 |                        |                            |                                                                     |               |
| No                                     | 354 (94.4)                                                      | 2292 (96.6)            | <b>0.037</b>               | 95.8                                                                | 97.2          |
| Yes                                    | 21 (5.6)                                                        | 81 (3.4)               |                            | 4.2                                                                 | 2.8           |
| HIV infection                          |                                                                 |                        |                            |                                                                     |               |
| No                                     | 373 (99.5)                                                      | 2281 (96.1)            | <b>0.001</b>               | 99.4                                                                | 97.5          |
| Yes                                    | 2 (0.5)                                                         | 92 (3.9)               |                            | 0.6                                                                 | 2.5           |
| Hepatic disease                        |                                                                 |                        |                            |                                                                     |               |
| No                                     | 367 (97.9)                                                      | 2242 (94.5)            | <b>0.005</b>               | 97.9                                                                | 95.2          |
| Yes                                    | 8 (2.1)                                                         | 131 (5.5)              |                            | 2.1                                                                 | 4.8           |
| Physical disabilities                  |                                                                 |                        |                            |                                                                     |               |
| 0                                      | 361 (96.3)                                                      | 2298 (96.8)            | 0.56                       | 97.3                                                                | 97.6          |
| ≥1                                     | 14 (3.7)                                                        | 75 (3.2)               |                            | 2.7                                                                 | 2.4           |
| Cardiovascular disease                 |                                                                 |                        |                            |                                                                     |               |
| 0                                      | 289 (77.1)                                                      | 1798 (75.8)            | 0.422                      | 79.3                                                                | 78.4          |
| 1                                      | 51 (13.6)                                                       | 382 (16.1)             |                            | 13.2                                                                | 14.9          |
| 2                                      | 18 (4.8)                                                        | 115 (4.8)              |                            | 3.9                                                                 | 4.3           |
| ≥3                                     | 17 (4.5)                                                        | 78 (3.3)               |                            | 3.6                                                                 | 2.4           |
| Haemoglobin (g/dL)                     |                                                                 |                        |                            |                                                                     |               |
| 10–12                                  | 154 (41.1)                                                      | 704 (29.7)             | <b>0.001</b>               | 40.8                                                                | 30.5          |
| <10                                    | 139 (37.1)                                                      | 1013 (42.7)            |                            | 36.3                                                                | 40.6          |
| >12                                    | 71 (18.9)                                                       | 393 (16.6)             |                            | 19.5                                                                | 18.3          |
| Missing                                | 11 (2.9)                                                        | 263 (11.1)             |                            | 3.3                                                                 | 10.5          |
| Emergency first dialysis session       |                                                                 |                        |                            |                                                                     |               |
| No                                     | 298 (79.5)                                                      | 1928 (81.2)            | 0.414                      | 80.8                                                                | 81.6          |
| Yes                                    | 77 (20.5)                                                       | 445 (18.8)             |                            | 19.2                                                                | 18.4          |
| First dialysis session with a catheter |                                                                 |                        |                            |                                                                     |               |
| No                                     | 280 (74.7)                                                      | 1360 (57.3)            | <b>&lt;10<sup>-4</sup></b> | 76.9                                                                | 61.2          |
| Yes                                    | 95 (25.3)                                                       | 1013 (42.7)            |                            | 23.1                                                                | 38.8          |
| TIS                                    |                                                                 |                        |                            |                                                                     |               |
| No                                     | 218 (58.1)                                                      | 1042 (43.9)            | <b>&lt;10<sup>-4</sup></b> | 63.7                                                                | 52.6          |
| Yes                                    | 157 (41.9)                                                      | 1331 (56.1)            |                            | 36.3                                                                | 47.4          |
| Blood groups                           |                                                                 |                        |                            |                                                                     |               |
| O                                      | 174 (46.4)                                                      | 1048 (44.2)            | 0.269                      | 46.2                                                                | 38.5          |
| A                                      | 142 (37.9)                                                      | 854 (36)               |                            | 39.0                                                                | 44.7          |
| B                                      | 44 (11.7)                                                       | 370 (15.6)             |                            | 11.1                                                                | 11.0          |
| AB                                     | 15 (4)                                                          | 101 (4.3)              |                            | 3.6                                                                 | 5.8           |
| PRA level                              |                                                                 |                        |                            |                                                                     |               |
| <85%                                   | 360 (96)                                                        | 2133 (89.9)            | <b>&lt;10<sup>-4</sup></b> | 96.4                                                                | 91.9          |
| ≥85%                                   | 15 (4)                                                          | 240 (10.1)             |                            | 3.6                                                                 | 8.1           |

HIV, human immunodeficiency virus; TIS, temporary inactive status; PRA: panel reactive antibody.

access to the waiting list in Bretagne, where patients were 4.5 times more likely to undergo transplantation and also more rapidly (3.6 times shorter waiting time). This is also the first study in France on TIS and its association with transplantation. In Ile-de-France, more patients had at least one TIS period and TIS cumulative duration was longer. However, relative to the overall time on the waiting list, waitlisted patients in Bretagne spent more time on TIS. These findings highlight differences of practice patterns and variations of access to renal transplantation in these two French regions.

Unlike previous studies in Scotland [12] or in the UK [11, 23], our analysis took into account all major comorbidities. Furthermore, our study is based on a robust methodology that considered the competing risk of death and of living

donor transplantation to study access to the waiting list and transplantation.

After adjustment for age, all comorbidities reduced the chance of waitlisting. These findings are consistent with the few previous French studies [17, 24]. After taking into account age and the clinical characteristics, the chance of being waitlisted was 23% lower for patients in Bretagne than in Ile-de-France. Waitlisted patients had more comorbidities in Ile-de-France than in Bretagne. Moreover, mortality while on the waiting list was higher in Ile-de-France (8%) than in Bretagne (4%). These results suggest that nephrologists in Bretagne use stricter criteria than those in Ile-de-France for selecting eligible candidates for renal transplantation. During the study period, local policies of placement on transplant waiting lists (defined within each

Table 3. Association between patients' characteristics and outcomes of interest (multivariate Fine and Gray model)

|                                        | Access to waiting list for incident patients (N = 6160) |         |                   | Access to transplantation <sup>a</sup> after placement on the list (N = 2748) |         |                   | Access to transplantation <sup>a</sup> after dialysis start (N = 6160) |         |                   |
|----------------------------------------|---------------------------------------------------------|---------|-------------------|-------------------------------------------------------------------------------|---------|-------------------|------------------------------------------------------------------------|---------|-------------------|
|                                        | SHR                                                     | 95% CI  | P-value           | SHR                                                                           | 95% CI  | P-value           | SHR                                                                    | 95% CI  | P-value           |
| Gender                                 |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| Female                                 | 1.00                                                    |         |                   | 1.00                                                                          |         |                   | 1.00                                                                   |         |                   |
| Male                                   | 1.06                                                    | 1–1.2   | 0.144             | 0.96                                                                          | 0.9–1.1 | 0.495             | 1.07                                                                   | 1–1.2   | 0.217             |
| Age (years)                            |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| 18–39                                  | 1.00                                                    |         |                   | 1.00                                                                          |         |                   | 1.00                                                                   |         |                   |
| 40–59                                  | 0.78                                                    | 0.7–0.9 | <10 <sup>−4</sup> | 0.97                                                                          | 0.8–1.1 | 0.648             | 0.82                                                                   | 0.7–0.9 | <b>0.002</b>      |
| 60–69                                  | 0.37                                                    | 0.3–0.4 | <10 <sup>−4</sup> | 1.38                                                                          | 1.2–1.6 | <10 <sup>−4</sup> | 0.57                                                                   | 0.5–0.7 | <10 <sup>−4</sup> |
| 70–80                                  | 0.04                                                    | 0–0.1   | <10 <sup>−4</sup> | 2.59                                                                          | 2–3.4   | <10 <sup>−4</sup> | 0.08                                                                   | 0.1–0.1 | <10 <sup>−4</sup> |
| Primary renal disease                  |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| Polycystic kidney disease              | 1.00                                                    |         |                   | 1.00                                                                          |         |                   | 1.00                                                                   |         |                   |
| Glomerulonephritis                     | 0.78                                                    | 0.7–0.9 | <b>0.001</b>      | 0.82                                                                          | 0.7–1   | <b>0.019</b>      | 0.72                                                                   | 0.6–0.9 | <10 <sup>−4</sup> |
| Hypertensive and vascular nephropathy  | 0.58                                                    | 0.5–0.7 | <10 <sup>−4</sup> | 0.87                                                                          | 0.7–1   | 0.104             | 0.63                                                                   | 0.5–0.8 | <10 <sup>−4</sup> |
| Diabetic nephropathy                   | 0.53                                                    | 0.4–0.7 | <10 <sup>−4</sup> | 0.97                                                                          | 0.7–1.3 | 0.817             | 0.70                                                                   | 0.5–0.9 | <b>0.007</b>      |
| Pyelonephritis                         | 0.72                                                    | 0.6–0.9 | <b>0.005</b>      | 0.78                                                                          | 0.6–1   | 0.077             | 0.62                                                                   | 0.5–0.8 | <b>0.001</b>      |
| Others                                 | 0.53                                                    | 0.5–0.6 | <10 <sup>−4</sup> | 0.76                                                                          | 0.6–0.9 | <b>0.001</b>      | 0.53                                                                   | 0.4–0.6 | <10 <sup>−4</sup> |
| First modality of dialysis             |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| Haemodialysis                          | 1.00                                                    |         |                   | Not significant                                                               |         |                   | Not significant                                                        |         |                   |
| Peritoneal dialysis                    | 1.26                                                    | 1.1–1.4 | <10 <sup>−4</sup> |                                                                               |         |                   |                                                                        |         |                   |
| Diabetes                               |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| No                                     | 1.00                                                    |         |                   | 1.00                                                                          |         |                   | 1.00                                                                   |         |                   |
| Yes                                    | 0.8                                                     | 0.7–0.9 | <b>0.002</b>      | 0.78                                                                          | 0.6–1   | <b>0.016</b>      | 0.68                                                                   | 0.6–0.8 | <10 <sup>−4</sup> |
| Active malignancy                      |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| No                                     | 1.00                                                    |         |                   | Not significant                                                               |         |                   | 1.00                                                                   |         |                   |
| Yes                                    | 0.37                                                    | 0.3–0.5 | <10 <sup>−4</sup> |                                                                               |         |                   | 0.34                                                                   | 0.2–0.5 | <10 <sup>−4</sup> |
| Chronic respiratory disease            |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| No                                     | 1.00                                                    |         |                   | Not significant                                                               |         |                   | 1.00                                                                   |         |                   |
| Yes                                    | 0.64                                                    | 0.5–0.8 | <10 <sup>−4</sup> |                                                                               |         |                   | 0.52                                                                   | 0.4–0.7 | <10 <sup>−4</sup> |
| Cardiovascular disease                 |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| 0                                      | 1.00                                                    |         |                   | 1.00                                                                          |         |                   | 1.00                                                                   |         |                   |
| 1                                      | 0.76                                                    | 0.7–0.9 | <10 <sup>−4</sup> | 0.88                                                                          | 0.8–1   | 0.115             | 0.76                                                                   | 0.7–0.9 | <10 <sup>−4</sup> |
| 2                                      | 0.58                                                    | 0.5–0.7 | <10 <sup>−4</sup> | 0.76                                                                          | 0.5–1.1 | 0.103             | 0.52                                                                   | 0.4–0.7 | <10 <sup>−4</sup> |
| ≥3                                     | 0.51                                                    | 0.4–0.6 | <10 <sup>−4</sup> | 0.63                                                                          | 0.4–0.9 | <b>0.027</b>      | 0.39                                                                   | 0.3–0.5 | <10 <sup>−4</sup> |
| Physical disabilities                  |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| 0                                      | 1.00                                                    |         |                   | Not significant                                                               |         |                   | 1.00                                                                   |         |                   |
| ≥1                                     | 0.37                                                    | 0.3–0.5 | <10 <sup>−4</sup> |                                                                               |         |                   | 0.35                                                                   | 0.3–0.5 | <10 <sup>−4</sup> |
| HIV infection                          |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| No                                     | 1.00                                                    |         |                   | Not significant                                                               |         |                   | Not significant                                                        |         |                   |
| Yes                                    | 0.6                                                     | 0.5–0.7 | <10 <sup>−4</sup> |                                                                               |         |                   |                                                                        |         |                   |
| Hepatic disease                        |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| No                                     | 1.00                                                    |         |                   | Not significant                                                               |         |                   | 1.00                                                                   |         |                   |
| Yes                                    | 0.71                                                    | 0.6–0.8 | <10 <sup>−4</sup> |                                                                               |         |                   | 0.63                                                                   | 0.5–0.8 | <10 <sup>−4</sup> |
| Haemoglobin (g/dL)                     |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| 10–12                                  | 1.00                                                    |         |                   | Not significant                                                               |         |                   | Not significant                                                        |         |                   |
| <10                                    | 0.87                                                    | 0.8–1   | <b>0.004</b>      |                                                                               |         |                   |                                                                        |         |                   |
| >12                                    | 1.02                                                    | 0.9–1.2 | 0.76              |                                                                               |         |                   |                                                                        |         |                   |
| Emergency first dialysis session       |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| No                                     | Not significant                                         |         |                   | Not significant                                                               |         |                   | Not significant                                                        |         |                   |
| Yes                                    |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| First dialysis session with a catheter |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| No                                     | 1.00                                                    |         |                   | Not significant                                                               |         |                   | 1.00                                                                   |         |                   |
| Yes                                    | 0.78                                                    | 0.7–0.9 | <10 <sup>−4</sup> |                                                                               |         |                   | 0.71                                                                   | 0.6–0.8 | <10 <sup>−4</sup> |
| TIS                                    |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| No                                     | Available only for waitlisted patients                  |         |                   | 1.00                                                                          |         |                   | Available only for waitlisted patients                                 |         |                   |
| Yes                                    |                                                         |         |                   | 0.44                                                                          | 0.4–0.5 | <10 <sup>−4</sup> |                                                                        |         |                   |
| Blood groups                           |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| O                                      | Available only for waitlisted patients                  |         |                   | 1.00                                                                          |         |                   | Available only for waitlisted patients                                 |         |                   |
| A                                      |                                                         |         |                   | 2.23                                                                          | 2–2.5   | <10 <sup>−4</sup> |                                                                        |         |                   |
| B                                      |                                                         |         |                   | 0.73                                                                          | 0.6–0.9 | <10 <sup>−4</sup> |                                                                        |         |                   |
| AB                                     |                                                         |         |                   | 2.76                                                                          | 2.1–3.7 | <10 <sup>−4</sup> |                                                                        |         |                   |

Table continues



Table 3. Continued

|               | Access to waiting list for incident patients (N = 6160) |         |                   | Access to transplantation <sup>a</sup> after placement on the list (N = 2748) |         |                   | Access to transplantation <sup>a</sup> after dialysis start (N = 6160) |         |                   |
|---------------|---------------------------------------------------------|---------|-------------------|-------------------------------------------------------------------------------|---------|-------------------|------------------------------------------------------------------------|---------|-------------------|
|               | SHR                                                     | 95% CI  | P-value           | SHR                                                                           | 95% CI  | P-value           | SHR                                                                    | 95% CI  | P-value           |
| PRA level     |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| <85%          | Available only for waitlisted patients                  |         |                   | 1.00                                                                          |         |                   | Available only for waitlisted patients                                 |         |                   |
| ≥85%          |                                                         |         |                   | 0.75                                                                          | 0.6–0.9 | 0.002             |                                                                        |         |                   |
| Region        |                                                         |         |                   |                                                                               |         |                   |                                                                        |         |                   |
| Ile-de-France | 1.00                                                    |         |                   | 1.00                                                                          |         |                   | 1.00                                                                   |         |                   |
| Bretagne      | 0.77                                                    | 0.7–0.9 | <10 <sup>-4</sup> | 4.52                                                                          | 3.8–5.4 | <10 <sup>-4</sup> | 2.07                                                                   | 1.8–2.4 | <10 <sup>-4</sup> |

HIV, human immunodeficiency virus; TIS, temporary inactive status; PRA, panel reactive antibody.

<sup>a</sup>Deceased donor transplantation.

transplant centre) were implemented in France. Furthermore, with nine transplant centres in Ile-de-France and only two in Bretagne, differences in placement strategies could be accentuated. The recent recommendations of October 2015 [14] may allow better practice harmonization and limit such differences.

Our study shows that the probability of transplantation, once waitlisted, was higher for patients >60 years of age than for patients between 18 and 39 years of age. In France, the percentage of donors >65 years of age increased by a factor of 19 between 1998 and 2013 (to 37.5%) compared with the percentage of donors between 50 and 64 years of age (30%), which remained stable [18]. The higher chances of transplantation for the oldest waitlisted patients may be explained by the fact that the French allocation score favours age-matching between recipient and donor.

After adjustment for age and clinical characteristics, waitlisted patients in Bretagne were 4.5 times more likely to be transplanted than patients in Ile-de-France.

The CIF of transplantation after placement attained 50% 3.6 times earlier in Bretagne. After excluding patients with a TIS period, this delay was still longer in Ile-de-France than in Bretagne. Conversely, the rate of pre-emptive transplantation was 4% in both regions. These differences might be explained by the local organ allocation policy and the number of locally available organs, which is proportional to the number of deceased donors, which was still higher in Bretagne during the study period. In addition, organ availability was associated with transplantation after waitlisting only when the region was not included in the multivariate model. We interpreted these findings as resulting from the association between 'organ availability' and 'region' variables, of which 'region' should be considered as the main factor contributing to transplantation access (organ availability was higher in Bretagne during the study period). This limited access to renal transplantation was not attenuated by a more active policy of inclusion on the waiting list. Therefore, local strategies for promoting/limiting access to the waiting list may not influence the likelihood of receiving a successful transplantation, which remains mainly dependent on organ availability.

The percentage of patients with a TIS period, which is considered as a poor indicator of access to transplantation, has increased in France during the last 6 years [20]. Our study shows that there were more patients on TIS in Ile-de-France than in Bretagne. The median TIS duration was ~3 months longer in Ile-de-France than in Bretagne. Among pre-emptively waitlisted patients, the median TIS duration was the same in both regions, suggesting that nephrologists in these two regions have similar pre-emptive waitlisting practices.

This study has some limitations. Patients in Ile-de-France represented 82% of the entire sample. This size difference did not allow comparison of determinants of access to the waiting list and transplantation in the two regions. In addition, our analyses took into account the TIS periods, but not the reason for such TIS.

In conclusion, this study shows variations of clinical practices concerning waitlisting and TIS between nephrologists in Bretagne and Ile-de-France. More patients, and specifically more patients with comorbidities, were placed on the list in Ile-de-France than in Bretagne. Moreover, more patients had at least one TIS period in Ile-de-France than in Bretagne. However, access to renal transplantation (from the time of waitlisting or of dialysis initiation) was higher in Bretagne, where organ availability was higher during the study period. We conclude that waitlisting more patients is not sufficient to improve access to renal transplantation in the absence of a proportional increase in the number of available organs. Future work should evaluate access to transplantation after the new national recommendations for placement on the waiting list and the new national organ allocation score to harmonize practices and reduce differences between regions.

## Supplementary data

Supplementary data is available online at <http://ndt.oxfordjournals.org>.

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## Conflict of interest statement

None declared.

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