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Exploration of the difference in incidence of renal replacement therapy between Flanders and the Netherlands—investigation of explanatory variables

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Abstract

Aim. This study investigates the difference in the incidence of renal replacement therapy (RRT) between Flanders and the Netherlands and possible explanations for this difference.

Methods. End-stage renal disease incidence data were obtained from the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA). Additional sources were the National Institute of Statistics (NIS), the Central Bureau of Statistics (CBS), the Organisation for Economic Cooperation and Development (OECD) health data and the WHO Health For All database (WHO-HFA).

Results. There is remarkable difference in incidence rate of RRT between Flanders and the Netherlands, with a higher rate in Flanders. This difference is already present in patients aged 45–64 years and increases with age, being >2-fold higher in subjects of ≥75 years. With respect to the renal diagnoses leading to need for RRT, a higher share of especially diabetes mellitus type 2 and renovascular disease was observed in Flanders. Remarkably, the difference in incidence rate of RRT is not associated with a difference in survival on RRT, not even in the elderly, arguing against a restricted access to RRT in the Netherlands. In the general

population, the expected number of healthy life years at birth is lower in Belgium than in the Netherlands, and in Belgium, the hospital discharge rates for diabetes, acute myocardial infarction and cerebrovascular accident and the number of coronary bypass procedures and percutaneous coronary interventions per capitum is higher, as is the prevalence of obesity.

Conclusions. Our data do not support the assumption that the differences in RRT incidence in the elderly between Flanders and the Netherlands are due to a more restricted access to RRT in the Netherlands but may be due to differences in underlying comorbidity and life style between the two populations.

Keywords: health care system; risk factors; RRT incidence; patient survival

Introduction

There is a considerable variability in the incidence of renal replacement therapy (RRT) between and within countries [1–3]. An example is the difference in RRT incidence that has been suggested between Flanders—the Dutch-speaking region of Belgium—and the Netherlands, with a higher incidence rate of RRT in Flanders [4]. This difference would be unexpected because of the apparent geographic, demographic and social similarities between these neighbouring regions.

Potential explanations for differences in incidence rate between neighbouring regions may be either patient, physician or health care system related. It has been suggested that physicians in the Netherlands are more restrictive in referring elderly patients and patients with more comorbidity to nephrologists for RRT [5, 6]. If true, a better survival of patients on RRT is to be expected in the Netherlands. Another explanation for a difference in incidence rates of RRT may be differences in the prevalence of risk factors for the development of chronic kidney disease (CKD) in the overall population. For instance, the recent epidemic of CKD in the USA has been attributed to the increase in prevalence of obesity and diabetes mellitus [7–9]. Thirdly, non-medical factors such as differences in health care system and health care resources may be of influence. It is even suggested that macroeconomic health care and renal service organisational factors have a greater influence on RRT incidence than general population age and health status factors do [10, 11].

Given these considerations, the aim of this study was to investigate the difference in incidence rate of RRT between Flanders and the Netherlands and to explore possible explanations for this difference. To this end, we studied RRT incidence, patient survival on RRT, prevalence of risk factors in the general population and health care system specification in both regions.

Methods

Population and procedure

Data on the socio-demographic characteristics of the general population for Flanders (and Belgium) were obtained from the National Institute of Statistics (NIS) and for the Netherlands from the Central Bureau of Statistics (CBS).

Data on the incidence of RRT and on patient survival on RRT were obtained from the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA). The ERA-EDTA Registry is a European Registry collecting data on RRT via the national and regional renal registries in Europe. The ERA-EDTA Registry received permission from the registries of Flanders and the Netherlands to use their data for this study. These registries cover all the dialysis centres and cover almost 100% of the population in Flanders and the Netherlands.

Data on the prevalence of risk factors for the development of CKD (diabetes, vascular diseases, overweight and tobacco use) in the general population are limited. Information on the prevalence of these risk factors was therefore obtained by studying hospital discharge rates for diabetes (ICD-10 E10-E14), myocardial infarction (ICD-10 I21-I22) and cerebrovascular accidents (ICD-10 I60-I69). These discharge rates include inhospital deaths but exclude day-care admissions and transfers to other care units within the same institution. Furthermore, information on prevalence of tobacco consumption, overweight and adiposity is presented as percentages of the total population. According to the World Health Organisation guidelines, a Body Mass Index >30 kg/m^2 is considered to reflect obesity. Data on discharge rates and on tobacco consumptions and obesity were obtained from the Organisation for Economic Cooperation and Development (OECD) health data [12] and from the WHO Health For All database (WHO-HFA) [13]. The OECD and WHO-HFA only provided information for Belgium as a whole and not for Flanders and Wallonia separately. Data on the health care system in both countries were also obtained from the WHO-HFA database. All data presented are related to the calendar year 2006, unless stated otherwise.

Statistical analyses

Descriptive statistics were used to compare the characteristics of the general population and the incidence rates of RRT between Flanders and the Netherlands. The incidence of RRT is defined as the number of new patients that started with RRT [dialysis or (pre-emptive) transplantation] per year and is expressed as number per million of the population (pmp). Incidence rates are presented for the overall population as well as for subgroups based on gender, age and primary renal disease. The incidence rates for the overall populations are adjusted for age and gender using the European standard population (EU25, 2000) as the reference population [14], whereas incidence rates for subgroups are presented in unadjusted form. To investigate trends over time, we report incidence rates for the period 1998–2006. Renal diseases leading to need for RRT were defined according to the ERA-EDTA coding system and classified into eight groups and the groups 'unknown' and 'missing'. Patient survival (cohort 1998–2006) was calculated from Day 1 on RRT and the event studied was all-cause mortality. Unadjusted survival probabilities were calculated using the Kaplan–Meier method according to Bie *et al.* [15]. Patients were censored in the case of recovery of renal function, loss to follow-up or end of follow-up time (31 December 2006). For the adjusted survival analyses, Cox regression models were used to compare the survival between patients in the Netherlands and Flanders adjusting for age, gender and primary renal disease. Descriptive statistics were also used to compare the prevalence of risk factors and health care resources in Flanders and the Netherlands.

Results

Characteristics of the general population in 2006

The total population in the Netherlands was in 2006 about two and a halve times larger than in Flanders. Characteristics as well as life expectancy of the total population in Flanders and in the Netherlands were nearly identical, with the Flemish population being slightly older (Table 1) and having a lower expectancy for number of healthy life years at birth than in the Netherlands (Table 2).

Incidence rate of RRT

Change in incidence rate of RRT between 1998 and 2006. Between 1998 and 2006, the annual incidence rate of RRT increased both in Flanders and in the Netherlands.

Table 1. Characteristics of the general population in Flanders and the Netherlands in 2006[a]

	Flanders	The Netherlands
Inhabitants	6 098 000	16 346 000
Age, %		
0–19 years	22.2	24.3
20–64 years	60.0	61.4
65+ years	17.8	14.3
Gender, % male	49.3	49.4
Foreign inhabitants, %	5.8	4.2

[a]Source: NIS and CBS.

Table 2. Life expectancy of the total population Belgium and the Netherlands in 2006[a]

	Belgium	The Netherlands
Life expectancy at birth[b]		
Male	76.61	77.6
Female	82.31	81.9
Life expectancy at age 65[b]		
Male	17.0	16.8
Female	20.6	20.2
Healthy life years at birth[c]		
Male	61.9	63.1
Female	61.7	65.0

[a]Life expectancy in Flanders is for male and female, respectively, 76.9 and 82.3 years.
[b]Source: OECD.
[c]Source: NIS and CBS.

In Flanders, the adjusted RRT incidence rate increased from 136.7 pmp in 1998 to 167.6 pmp in 2006 and in the Netherlands from 101.6 in 1998 to 113.3 pmp in 2006. Thus, over this 9-year period, incidence rates of RRT increased 22.6 and 11.5% in Flanders and the Netherlands, respectively.

Split by age group, the incidence rate in Flanders and the Netherlands among patients aged 20–64 years was nearly the same in 2006 as it was in 1998. The increase in incidence of RRT was therefore due to the rise in incidence among patients aged 65–74 years (8.4% in Flanders and 6.5% in the Netherlands) and especially in those aged ≥75 years (89.9% in Flanders and 69.7% in the Netherlands).

Incidence of RRT by age group and gender in 2006. In 2006, the adjusted incidence rate of RRT in the overall population was 1.5-fold (167.6/113.3) higher in Flanders when compared to the Netherlands. Figure 1a illustrates the unadjusted incidence rate at Day 1 of RRT by age group. The incidence rate among the age group of 20–44 years was similar for Flanders and the Netherlands, but in the age groups of 45–64, 65–74 and ≥75 years, the incidence rates were, respectively, 1.3-, 1.4- and 2.3-times higher in Flanders than in the Netherlands.

Figure 1b shows the age-specific incidence rates by gender. The incidence of RRT among women and men ≥75 years was, respectively, 2.5- and 2.1-times higher in Flanders than in the Netherlands.

Incidence of RRT by primary renal disease in 2006. Table 3 shows the adjusted incidence rate of RRT pmp by primary renal diseases for all ages. Nearly, all primary renal diseases were more frequent in Flanders than in the Netherlands, but especially diabetes mellitus type 2 and renal vascular disease as cause of end-stage renal failure were more common in Flanders when compared with the Netherlands (2.5- and 2.3-times, respectively).

The adjusted incidence by primary renal diagnosis per age group showed the same pattern, with one exception. The incidence rate for RRT due to diabetes mellitus type II and renal vascular disease among patients of ≥75 years was especially high in Flanders (169.6 and 272.3 pmp, respectively) when compared to the Netherlands (36.8 and 89.1 pmp, respectively), indicating a 4.6- and 3.1-times higher incidence rate in Flanders.

Survival probabilities (cohort 1998–2006)

Figure 2a shows the crude survival probabilities of incident RRT patients per age group from Day 1 of RRT in Flanders and the Netherlands over the period 1998–2006. The 90-day survival rate was almost similar between Flanders and the Netherlands for all age groups, with in the Netherlands slightly worse survival. The 1-, 2- and 5-year survival probabilities for patients in the Netherlands were 1.5–6.0% lower in comparison with Flanders.

The adjusted survival analyses among incident patients per age group also demonstrate that the 1-, 2- and 5-year survival probability was slightly lower in the Netherlands when compared to Flanders, and that this differences increased with longer observation time (Figure 2b).

Factors that may influence the incidence of RRT

Prevalence of risk factors for CKD in the general population in 2006. Table 4 shows that hospital discharge rates for diabetes, acute myocardial infarction and cerebrovascular accident were higher in Belgium than in the Netherlands. Also, the number of coronary bypass procedures and percutaneous coronary interventions per capitum and the percentage of the population with obesity were higher in Belgium than in the Netherlands. Lifestyle factors such as fat consumption and the average number of calories available per person per day are also higher in Belgium. Only the percentage of the population that used tobacco was higher in the Netherlands.

Health care resources in 2006. In 2006, Flanders had 27 and the Netherlands 64 dialysis centres. The number of nephrologists per 1000 of the population was 1.75 higher in Belgium than in the Netherlands. The number of physicians per 1000 of the population was similar between Belgium and the Netherlands, but the number of nurses was 1.66-times higher in Belgium (Table 5). The number of hospital and the acute care beds per 1000 inhabitants were, respectively, 1.47- and 1.43-times higher in Belgium than in the Netherlands. The total expenditure on health per capita was $3179 in Belgium and $3320 in the Netherlands.

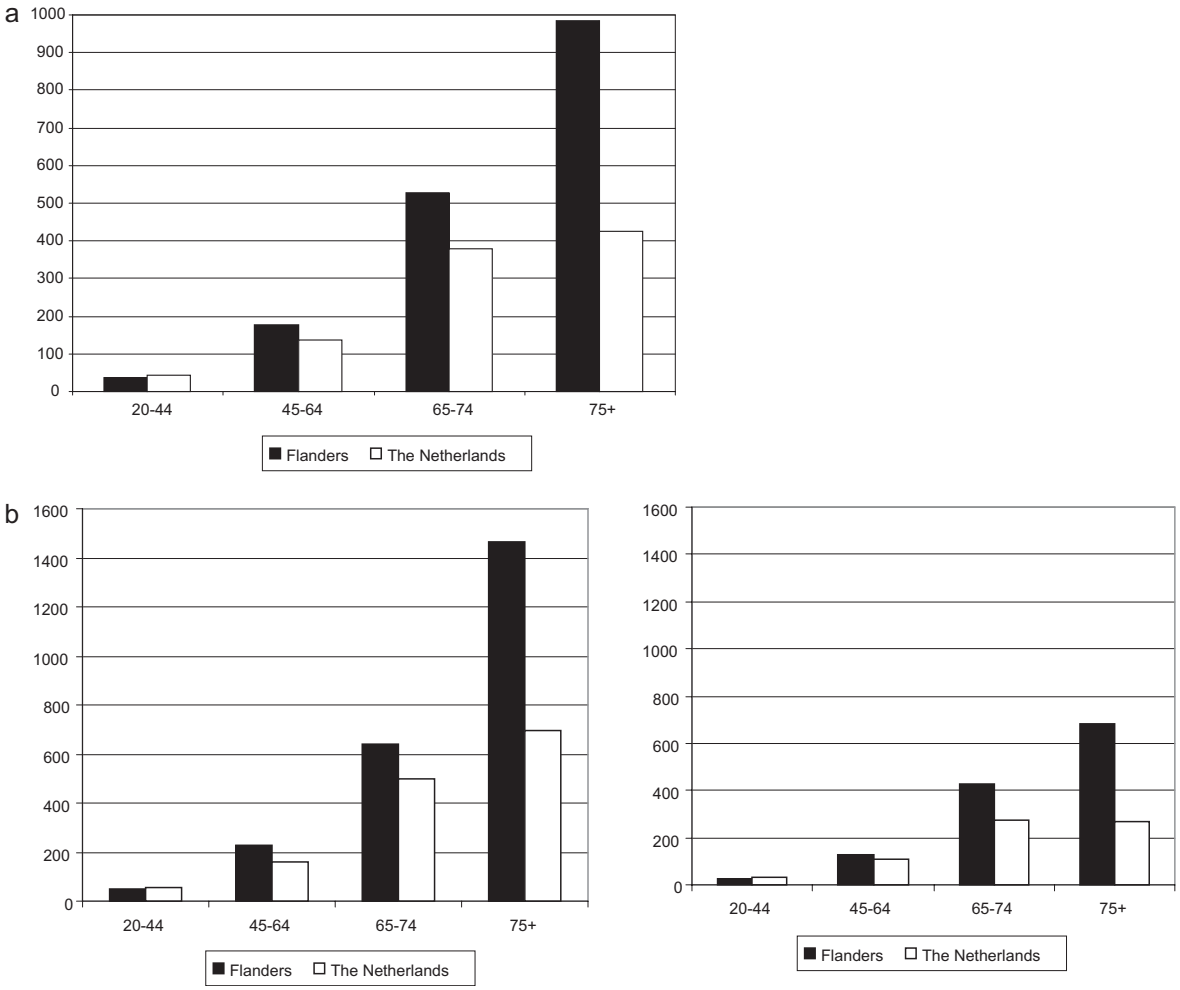

Fig. 1. (**a**) Incidence of RRT in Flanders and the Netherlands pmp in 2006 by age group, (unadjusted). (**b**) Incidence of RRT for male (left) and female (right) pmp in 2006 by age group (unadjusted). pmp, per million population.

Table 3. Incidence at start of RRT per million population and percentages by primary renal diagnosis in 2006, adjusted for age and gender[a]

	Flanders		The Netherlands	
	Incidence (pmp)	%	Incidence (pmp)	%
Glomerulonephritis	14.4	8.6	10.4	9.2
Diabetes mellitus				
Type 1	5.5	3.3	5.4	4.8
Type 2	31.8	19.0	12.5	11.0
Renal vascular disease	31.5	18.8	13.9	12.3
Hypertension	14.7	8.8	13.3	11.7
Pyelonephritis	10.8	6.4	4.2	3.7
Polycystic kidney disease	8.5	5.1	5.8	5.1
Miscellaneous	34.0	20.3	17.7	15.6
Unknown	16.4	9.8	14.8	13.1
Missing	NA[b]	NA[b]	15.2	13.4

[a]Source: ERA-EDTA.
[b]Not applicable.

Discussion

This study was designed to investigate the difference in incidence of RRT that has been suggested to exist between Flanders and the Netherlands and to explore possible explanations for this difference in RRT incidence. Our data show that there indeed is a considerable difference in RRT incidence between Flanders and the Netherlands, even after adjusting for age and gender. The higher incidence rate in Flanders was already present in the age group 45–65 years and increased progressively with age. Among patients aged ≥75 years, the crude RRT incidence was even more than twice as high in Flanders as it was in the Netherlands. Incident RRT patients in Flanders had more often diabetes mellitus type II and renal vascular disease as cause of end-stage renal disease (ESRD) leading to RRT. In the general population, the expected number of healthy life years at birth was lower in Belgium than in the Netherlands, and the hospital discharge rates for diabetes, acute myocardial infarction and cerebrovascular accident and the number of coronary bypass procedures and percutaneous coronary interventions per capitum were higher in Belgium, as was the prevalence of obesity.

What may be the explanation for the higher incidence of especially elderly patients with diabetic nephropathy or renal vascular disease entering RRT programmes in Flanders when compared to the Netherlands. It has been

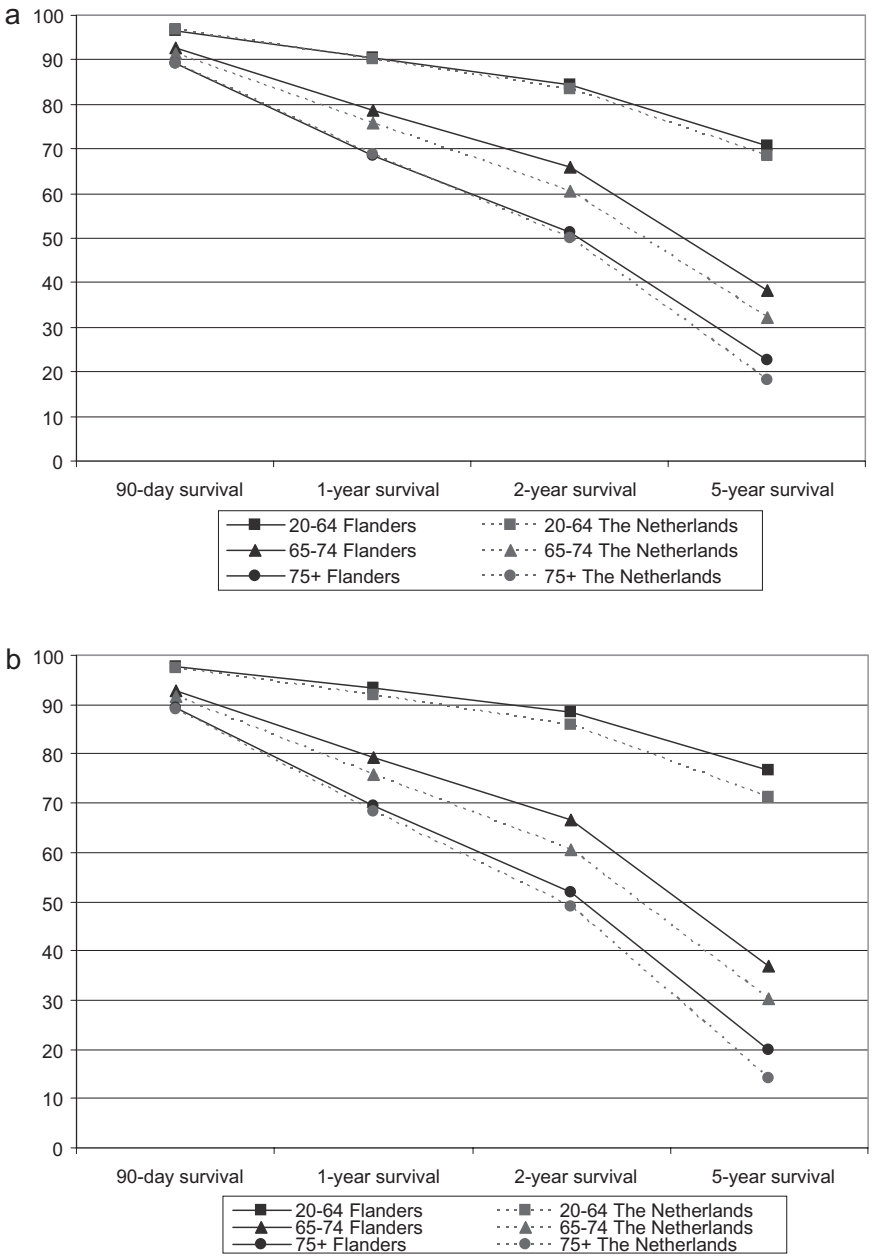

Fig. 2. (**a**) 90-day, 1, 2 and 5-year survival probabilities (cohort 1998–2006): incident RRT patients by age group, unadjusted, from Day 1 of RRT. (**b**) 90-day, 1, 2 and 5-year survival probabilities (cohort 1998–2006): incident RRT patients by age group, adjusted, from Day 1 of RRT. Adjusted for age, gender and primary renal disease. Source: ERA-EDTA.

suggested that physicians in the Netherlands are more restrictive in referring elderly patients and patients with more co-morbidity to nephrologists for RRT [5, 6]. If true, it would be expected that patient survival on RRT would be better in the Netherlands. Importantly, despite the more favourable characteristics of the RRT population in the Netherlands, the survival probability of incident RRT patients was similar or even worse for patients in the Netherlands than in Flanders. Our results showed furthermore that the difference in RRT incidence started already among patients <65 years of age with a similar pattern of distribution of the primary renal disease categories in all age groups. These data therefore do not suggest that patient selection has an important role in explaining the difference in incidence rates for RRT between Flanders and the Netherlands. Another study, in which we investigated the likelihood of referral of primary care physicians and internists, did also not provide indications for a more restrictive referral policy in the Netherlands [16].

Differences in health care system and resources might also explain differences in the incidence of RRT. For instance, it has been suggested that a higher reimbursement for technical activities (like dialysis) and lower reimbursement for intellectual activities (like prevention and counselling) could limit nephrologists' interest in preventing the progression of CKD [17]. A lower gross domestic product (GDP) per capita and a lower proportion of GDP spent on healthcare predicted RRT incidence negatively [18]. The

Table 4. Risk factors for the development of ESRD and life style factors in 2006[a]

	Belgium	The Netherlands
Discharge rate for[b]		
Diabetes	194	69
Acute myocardial infarction	154	141
CABG	135.4	58.2
PCI	435.1	144.6
Cerebrovascular accidents	292	195
% of population who are current smokers	22.0	30.8
% of population with obesity	12.7	10.9
Pure alcohol consumption, litres per capita	9.7	10.6
Average number of calories available per person per day	3675	3218
% of total energy available from fat	39.7	37.5

[a]Source: OECD and WHO-HFA.
[b]CABG, coronary artery bypass graft; PCI, percutaneous coronary intervention, per 100 000 population.

Table 5. Health Care Resources in 2006 per 1000 population for the whole of Belgium and the Netherlands[a]

	Belgium	The Netherlands	Ratio
Practising physicians[b]	4.0	3.9	1.03
Practising nurses	14.8	8.9	1.66
Nephrologists[c]	0.021	0.012	1.75
Hospital beds	6.6	4.5	1.47
Acute care beds	4.3	3.0	1.43
Total expenditure on health per capita, $	3179	3320	0.96

[a]Source: WHO-HFA.
[b]Physicians includes generalists and specialists.
[c]Data were obtained from the EVEREST study and based on 2003–05.

GDP per capita is higher in the Netherlands, but a lower proportion of GDP is spent on health care. The number of nephrologists is higher in Belgium, as is the number of practising nurses and hospital beds. Other non-medical factors that have been mentioned to affect incidence of RRT are health care system related such as financing of renal care [2, 10] and societal factors such as physician's referral behaviour and patients attitude to RRT [6, 19, 20]. As yet, there is limited understanding whether such factors are of importance. The international collaboration of nephrologists, epidemiologists and health economists that recently started the EVEREST study may help to explain to what extent the variation in RRT between populations is caused by such economic and organisational factors [10].

Our data show that the percentage of the general population with obesity was higher in Belgium than in the Netherlands. Obesity is an important risk factor for ESRD but also for diabetes and cardiovascular diseases. In line with these data, we found that the hospital discharge rate for diabetes and cardiovascular disease-related admissions was higher in Belgium than in the Netherlands. This confirms the findings of an earlier study in which the general population in Flanders was found to have a higher prevalence of diabetes than in the Netherlands [21]. These data together with the fact that especially diabetes mellitus type 2 and renal vascular disease were found as causes for the higher RRT incidence in Flanders lead to the hypothesis that differences in the prevalence of risk factors for ESRD explain the difference in RRT incidence rates between Flanders and the Netherlands. Other epidemiological studies have provided evidence supporting this hypothesis as explanation for regional differences in RRT incidence [1, 2, 22]. Another risk factor for ESRD is the proportion of foreign inhabitants in a country, since in general, these subjects have a higher chance of CKD due to genetic reasons and/or due to the fact that they predominantly belong to a lower socio-economic class [23]. However, both the Flemish and the Netherlands population are relatively homogeneous with only 5.8 and 4.2% foreign inhabitants, respectively. Racial differences are therefore not likely to play a role.

An important strength of this study is that the data on the incidence of RRT are based on robust and complete data of national registries covering all centres that offer RRT. This study has also limitations. Firstly, because a valid registry of the prevalence of risk factors for ESRD is not available in Flanders and the Netherlands we had to rely on other data sources, which included hospital discharge rates and self-reports. These data are only available for the whole of Belgium instead of for Flanders specifically. Though the incidence of RRT in Flanders is similar to that in the other (French speaking) part of Belgium [24]. It may be, however, that there are differences in health between these regions. Secondly, previous studies showed that the ratio of RRT incidence to CKD prevalence is much higher in the USA than in Europe [9, 25]. This may be explained by initiation of RRT at a higher residual Glomerular Filtration Rate [11] or a higher rate of progression of CKD to ESRD in the USA [9]. A higher progression rate may be due to, for instance, less attention for nutritional status, anaemia management and use of renin–angiotensin system inhibitors [9]. Unfortunately, information on these variables is not available for Belgium and the Netherlands on a nationwide level. Data from the Netherlands Cooperative Study on the Adequacy of Dialysis (NECOSAD, $N = 264$) and data from the Dialysis Outcomes and Practice Patterns Study (DOPPS, $N = 116$) for Flanders collected between 2002 and 2004 suggest, however, that RRT is started in these regions at a similar level [blood creatinine of 6.6 (SD of 2.7) mg/dL in Flanders and 7.9 (SD of 3.2) mg/dL in the Netherlands (personal communication DOPPS, Els Boeschoten, Jennifer Bragg-Gresham, and NECOSAD)].

In conclusion, there is remarkable difference in incidence rate of RRT between Flanders and the Netherlands, with a higher incidence rate in Flanders, which increases with age. This difference in incidence rate does not result in a difference in survival, as would be expected in case patient selection would be present. Our data thus do not support the assumption that this difference is due to a more restricted access to RRT in the Netherlands. As especially diabetes mellitus type 2 and renal vascular disease leading to need for RRT are high in Belgium when compared to the Netherlands, and that there is a higher prevalence of obesity and higher number of cardiovascular intervention and diabetes-related hospital admissions in Belgium, we hypothesize that a difference in underlying comorbidity and lifestyle between the two

populations may explain the observed difference in RRT incidence.

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Conflict of interest statement. None declared.

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