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Special Feature

The increase in renal replacement therapy (RRT) incidence has come to an end in Sweden—analysis of variations by region over the period 1991–2010

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Abstract

Background. Renal replacement therapy (RRT) incidence has increased significantly in Sweden during the past decades. This study analyses variations in time and regional trends in RRT incidence in Sweden, adjusted for age and gender, focusing on the impact change in incidence during the last decade.

Methods. Using data from the Swedish Renal Registry (SRR) (21 counties in Sweden, total population 9 million), we identified all incident subjects starting RRT from 1991 through 2010. Only individuals alive following 90 days of RRT start were included. Gender- and age-specific standardized RRT incidences on an annual and regional basis were calculated, and differences between counties and variations over time were examined. We compared the overall age and gender-adjusted RRT incidence rates for Sweden by calendar year. Furthermore, we also calculated the age and gender-adjusted RRT incidence in each county during two time periods (1991–1999 versus 2000–2010).

Results. There were 20 172 new subjects treated with RRT between January 1991 and December 2010. The most common cause of end-stage renal disease (ESRD) was diabetes (24%) and hypertension/renal vascular disease (19%), followed by glomerulonephritis (16%). Sixty-four percent of new patients were male; the median age when commencing RRT was 66 years (10–90 percentiles; 39–80). The overall standardized RRT incidence reached its peak in 2000, and slowly decreased thereafter. A decrease in RRT incidence was observed over the study period in eight regions. The standardized RRT incidence varied between the different counties, from 0.82 to 1.19.

Conclusions. Adjusted for demographic changes in the population, an overall decrease in RRT incidence was observed from the year 2000 onwards—suggesting that the previously reported steady increase in RRT incidence is coming to an end in Sweden. Noteworthy differences were found between counties and in 8 out of 21 counties, a decreased incidence of RRT was found. Further studies need to identify the factors that contribute to this decrease.

Keywords: dialysis; geography; kidney disease; survival

Introduction

The prevalence of chronic kidney disease (CKD) defined as the estimated eGFR <60 mL/min/1.73 m^2 has reached epidemic proportions, with studies showing a prevalence of 10–13% [1]. Indeed, CKD is recognized as a growing global public health problem due to the rising rates of diabetes mellitus, obesity, hypertension and ageing populations [2–4]. Although only a small proportion of all CKD patients progress to end-stage renal disease (ESRD), needing the resource-intensive treatment with renal replacement therapy (RRT, dialysis or kidney transplantation), the cost of treatment for this patient group, roughly 0.1% of the population, comprise 1–2% of the total health care spending in high-income countries [2]. The RRT incidence is routinely collected by renal registries in many countries and shows a 45-fold variation across the world [5]. These variations in RRT incidence across countries are thought to be associated with economic, health care system and renal service factors, rather than population demographics and health status [2–4].

In Sweden, the overall RRT incidence has slowly increased from around 110 per million people (p.m.p.) during 1991–2000 to 122 p.m.p. during 2001–2010 [6]. This increase is generally attributed to a less restrictive RRT barrier together with a high patient acceptance of

RRT, especially among the elderly. However, there are substantial variations in the incidence of CKD between regions of Sweden and elsewhere [6–11], even when taking account that some patients are treated outside their home region [12].

The aim of the present epidemiological study was to examine in more detail the regional variations and time trends in standardized RRT incidence in Sweden between 1991 and 2010.

Material and methods

Chronic kidney disease and the Swedish National Health Service

Sweden comprises of 21 counties, with a total population of 9.4 million as of 31 December 2010 (www.scb.se). Stockholm County was the largest with 2.1 million inhabitants, accounting for 22% of the population. The population in Västra Götaland County and Skåne County is 1.6 and 1.2 million, respectively. They represent the catchment areas of the three largest nephrology centres in Sweden. The Swedish health care system was tax funded and offered universal access, and patients with RRT were treated by nephrologist inpatient and outpatient hospital care [13]. The decision to initiate RRT was made by nephrologists from clinical evaluations based on the Swedish guidelines originating from the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative guidelines [14] and the corresponding European guidelines [15].

Quality register sources

Renal replacement therapy patients. Data on dialysis initiation, type of dialysis, transplantation and transitions were collected from the Swedish Renal Registry (SRR), including all adult patients on RRT in Sweden [6, 16]. All RRT patients who had been reported to the SRR [16, 17] and who had undergone RRT at one of the participating 21 counties are included. For various reasons, such as complications related to initiation of dialysis, severe comorbidity or limited local dialysis capacity, some patients are treated outside their local dialysis centre. The calendar year ranged from 1 January 1991 to 31 December, 2010.

General population comparator cohort

We obtained data for the general population categorized by age (in 5-year groups) and gender from the Register of the Total Population held by Statistics Sweden for the calendar years 1991–2010.

Calculation of the standardized incidence rate. To calculate the incidence rates, we counted the number of new patients for each of the five age groups, namely <20, 20–44, 45–64, 65–75 and >75 years for the same county, by gender. These data were standardized using general population data from the same county divided based on the similar age and gender groups.

Statistical analysis

The population of Sweden and all incident cases were followed up until 1 January 2011. We calculated the age standardization incidence rate based upon the county's population [18]. Using Poisson's regression analysis, we made comparisons across counties; Sweden's national RRT incidence standard served as a reference. Multivariable Poisson's regression analyses were then fitted to obtain adjusted RRT incidence rate ratios. Due to the relatively small number of incident cases that would be observed in individual counties in a single year, county-level estimates were done in two time periods, i.e. 1991–1999 and 2000–2010.

We expressed continuous variables as median and 10–90 percentiles and categorical variables as percentage of the total. Differences between the three groups were analysed using the non-parametric Kruskal–Wallis analysis of variance. A chi-square test was used for categorical variables. Statistical significance was set at $P < 0.05$. All statistical analyses were performed using Stata statistical software (version 12.1) and SAS version 9.3 (SAS Campus Drive, Cary, NC, USA 27513).

Results

Patient baseline characteristics

According to SRR, a total of 20 172 patients initiated RRT between 1 January 1991 and 31 December 2010. Most patients resided in either Stockholm county (with the largest number of patients) [$n = 3391$, 65 (37–79) years, 37% female and 22% diabetes nephropathy (DN)], Västra Götaland county ($n = 3261$, 66 (39–80) years, 36% female and 24% DN) or Skåne county [$n = 2667$, 67 (38–80) years, 33% female and 26% DN]. The median age at the start of RRT increased from 66 (37–79) years in 1991–1999 to 67 (40–81, $P < 0.001$) in 2000–2010. Recorded clinical characteristics of the patients, divided by five age groups, are given in Table 1.

Incidence trend overall and by calendar year. When normalizing the RRT incidence to that of 1991, we observed that the total normalized incidence RRT reached its peak in the calendar year of 2000 (Figure 1), while there was a decreasing trend thereafter. As shown in Figure 2, we found remarkably higher standardized incidence rates of RRT (1991–2010) in men compared with female. We then divided the follow-up period into four 5-year periods to observe the standardized incidence rate in female (Figure 3A) and male (Figure 3B), respectively. We noticed that there was a decrease in the standardized incidence rate for both female and male 65–74 year olds in 2001–2005 and 2006–2010 compared with 1991–2000. For patients >75 years, there was an increasing trend for male patients in both 2001–2005 and 2006–2010 and likewise for female. The standardized incidence rate was relatively stable or decreased among female and male patients aged <65 years for 1991–2010 (Figure 3A and B).

Standardized incidence by county. The ratio between the age and gender-standardized incidence rates of 1991–1999 versus 2000–2010 showed a decrease in eight counties out of 21 and an increase in 15 (Figure 4)

County differences by Poisson's regression. The age and gender-standardized incidence rates of RRT for the whole

Table 1. Patient characteristics in the cohort of RRT ($n = 20\,172$). Data expressed as median and (10–90 percentiles) or percentages[a]

Age groups	<20 years	20–44 years	45–64 years	65–74 years	>75 years	Total
% of total	(2%)	(13%)	(31%)	(27%)	(27%)	100
Age, years	13(1–19)	37(26–44)	57 (48–64)	71(66–74)	79 (76–85)	66 (39–80)
Female, %	42	36	36	34	34	35
HD, first modality %	26	53	61	72	78	69
PD, first modality %	37	36	35	27	22	30
Rtx, first modality %	36	12	4	1	0	0.03
EDTA diagnosis						
DN, %	1	29	31	25	14	24
GN, %	20	30	18	13	10	16
HT/RVD,%	2	4	10	23	36	20
Other, %	77	36	41	38	40	40

[a]HD, haemodialysis; PD, peritoneal dialysis; Rtx, renal transplantation, DN, diabetes nephropathy; GN, glomerulonephritis; HT/RVD, hypertension/renal vascular disease.

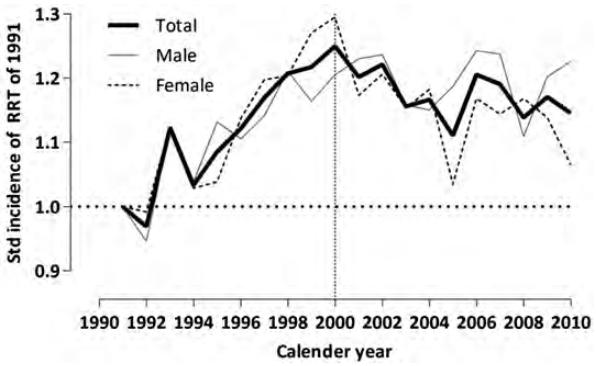

Fig. 1. Standardized incidence RRT by calendar year 1992–2010 normalized to incidence RRT of 1991. Total normalized incidence RRT shown by dark lines, male (grey lines) and female (dashed lines).

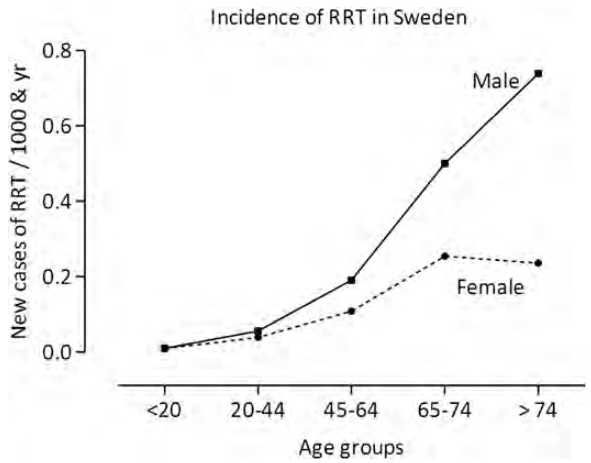

Fig. 2. The standardized incidence of ESRD requiring RRT in Sweden from 1991 to 2010 in male compared with female patients.

period (1991–2010) were calculated for the 21 counties (Table 2). Adjusted for age, gender and diagnosis, the RRT incidence was significantly lower in two counties: Halland IRR = 0.81 (95% CI, 0.75–0.89) and Stockholm [IRR = 0.90 (95% CI, 0.86–0.94)]. Whereas three counties showed a significantly higher RRT incidence—Östergötland [IRR = 1.14(95% CI, 1.08–1.22)], Gävleborg [IRR = 1.16 (95% CI, 1.08–1.25)] and Västernorrland [IRR = 1.14(95% CI, 1.05–1.23)].

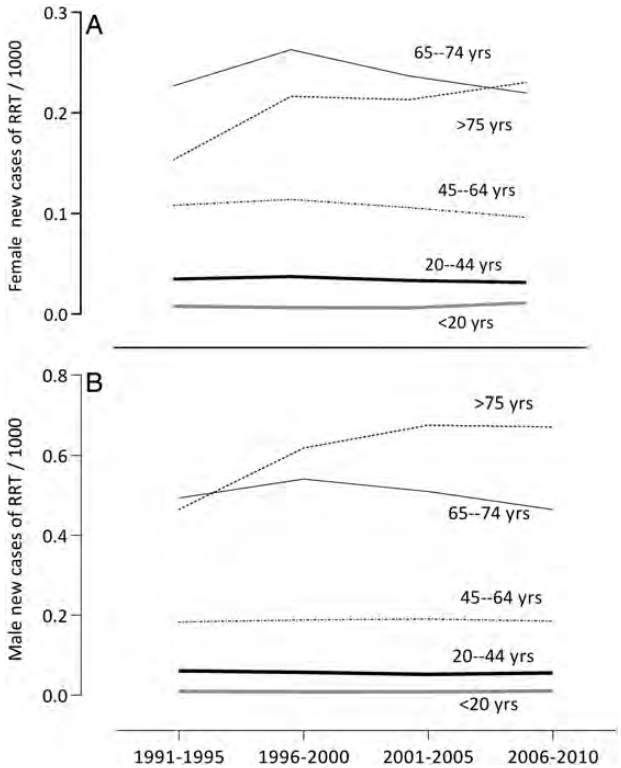

Fig. 3. (**A**) The incidence of ESRD in male patients in Sweden 1991–2010 in five age groups. (**B**) The incidence of ESRD in female patients in Sweden 1991–2010 in five age groups.

Discussion

In the present study, we investigate the standardized RRT incidence in the total population of Sweden between 1991 and 2010. Several similar studies have been reported, but our present study is unique, in that it is based upon two decades of follow-up. Adjusting for changes in population demographic factors, we report that the data suggest a significantly lower RRT incidence rate in Sweden for 2001–2010 when compared with 1991–2000. This decrease in incidence over time to great extent is attributable to declining incidence rates of patients in the population in 8 out of 21 counties of Sweden. We also found that for both male and female, the incidence rate increased in patients >75 years

between 1991 and 2010, while it decreased in those aged 65–74 years.

In a recent ERA-EDTA Registry report, an increase in the incidence rate was seen for Swedish patients in 2005–2009 [19]. In contrast, we observe only an increase in the incidence for male patients in 2001–2010, while there were decreased standardized incidence rates in female and male patients between 65 and 74 years in 2001–2010. The RRT incidence in patients under 65 years was stable during the whole 1991–2010 period which was similar to that observed in a recent report [20]. One reason for the overall decreased RRT incidence would be that the proportion of cases that are undetected, detected but not referred or referred but treated conservatively increases during the follow-up period. Consequently, it is not possible to be sure whether a low incidence is due to unmet need or to a genuinely lower incidence of ESRD. However, previous estimations of the proportion of untreated ESRD in Sweden show that of all new patients aged 18–74 with Stage 4–5 CKD <10% die before the start of RRT [21]. The effect of untreated ESRD on the RRT incidence would, however, be more pronounced among the elderly. This is opposed to our data which show that RRT incidence is still increasing among patients aged >75 years. The decreasing incidence among both males and females aged 65–74 years and the tendency of a decrease also in patients aged 45–64 years would then indicate a true decrease in the actual incidence, possibly as a consequence of better treatment in the earlier stages of CKD. In the USA, introduction of ameliorated glycaemic control in diabetic CKD and blood pressure treatment with ACE inhibitors and ARBs to attenuate progressive CKD have been observed to coincide with a plateau in the incidence of ESRD [22].

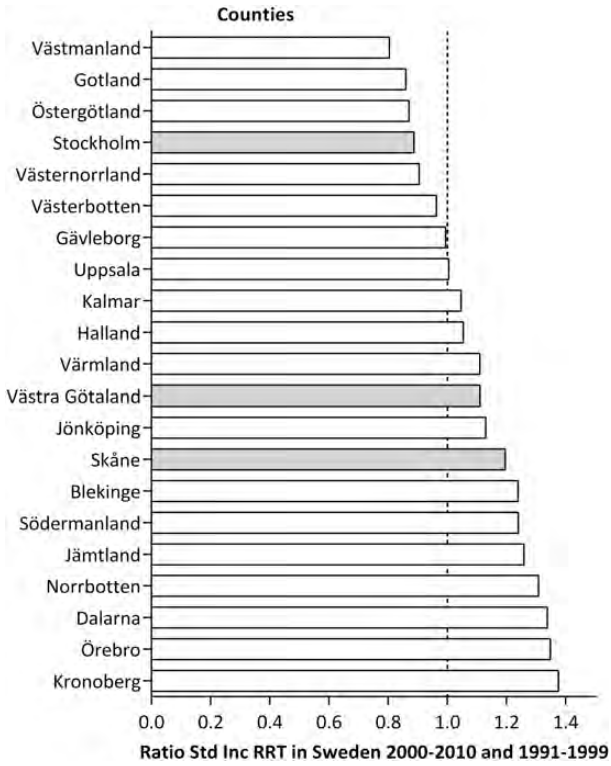

Fig. 4. The standardized incidence ratio between 2000 and 2010 versus 1991 and 1999 of patients requiring RRT in various regions of Sweden. The regions marked grey are Stockholm, Skåne and Västra Götaland which are main contributors of RRT population.

There is also a possibility that earlier start of dialysis may affect the RRT incidence rates [23]. In Sweden, dialysis is generally started when the eGFR according to the MDRD equation is 7.6 mL/min/1.73 m^2 [21]. However, recent observations in the SRR demonstrate significant differences in the eGFR at the start of dialysis between regions [6]. Notably, the county of Halland has both the highest eGFR at the start of dialysis, but nevertheless significantly lower RRT incidence rates compared with the rest of Sweden.

The observed regional differences in the rate of incident RRT may be due to several factors: differences in renal morbidity, underlying population health characteristics, behaviour (propensity to seek healthcare), referral patterns of general practitioners or strategies of nephrological and

Table 2. The standardized incidence of ESRD patients requiring RRT in Sweden from 1991 to 2010 in various counties

Counties	Crude IRR (95% CI)	P	IRR (95% CI)[a]	P	IRR (95% CI)[b]	P
Stockholm	0.83 (0.79–0.85)	**0.001**	**0.91 (0.88–0.94)**	**0.001**	**0.90 (0.86–0.94)**	**0.001**
Uppsala	0.87 (0.81–0.95)	0.002	0.96 (0.88–1.03)	0.28	0.94 (0.87–1.03)	0.17
Södermanland	1.07 (0.99–1.16)	0.06	1.04 (0.96–1.12)	0.37	1.03 (0.95–1.11)	0.44
Östergötland	1.16 (1.10–1.22)	0.001	1.15 (1.08–1.22)	0.001	1.14 (1.08–1.22)	0.001
Jönköping	1.00 (0.93–1.07)	0.97	0.98 (0.91–1.06)	0.60	0.97 (0.90–1.04)	0.48
Kronoberg	0.94 (0.85–1.04)	0.27	0.91 (0.83–1.02)	0.06	0.91 (0.82–1.01)	0.06
Kalmar	1.14 (1.06–1.24)	0.001	1.05 (0.97–1.15)	0.08	1.05 (0.96–1.04)	0.24
Gotland	1.06 (0.89–1.25)	0.52	1.02 (0.86–1.21)	0.80	1.02 (0.86–1.20)	0.84
Blekinge	1.09 (0.99–1.21)	0.07	1.02 (0.92–1.14)	0.71	1.01 (0.91–1.12)	0.88
Skåne	1.04 (0.99–1.07)	**0.09**	**1.03 (0.99–1.07)**	**0.17**	**1.02 (0.98–1.06)**	**0.42**
Halland	0.83 (0.76–0.91)	0.001	0.82 (0.76–0.90)	0.001	0.81 (0.75–0.89)	0.001
Västra Götaland	0.96 (0.93–0.99)	**0.04**	**0.97 (0.93–1.01)**	**0.08**	**1.01 (0.97–1.05)**	**0.72**
Värmland	1.14 (1.06–1.23)	0.001	1.06 (0.98–1.14)	0.14	1.03 (0.96–1.11)	0.39
Örebro	1.11 (1.03–1.19)	0.006	1.07 (0.99–1.15)	0.08	1.07 (0.99–1.16)	0.06
Västmanland	1.13 (1.05–1.22)	0.002	1.10 (1.02–1.19)	0.01	1.10 (1.02–1.19)	0.01
Dalarna	1.08 (1.00–1.16)	0.05	1.01 (0.93–1.08)	0.98	0.99 (0.92–1.07)	0.86
Gävleborg	1.29 (1.20–1.38)	0.001	1.19 (1.12–1.28)	0.001	1.16 (1.08–1.25)	0.001
Västernorrland	1.25 (1.16–1.34)	0.001	1.15 (1.06–1.23)	0.001	1.14 (1.05–1.23)	0.001
Jämtland	1.19 (1.06–1.32)	0.001	1.09 (0.98–1.21)	0.10	1.08 (0.98–1.21)	0.12
Västerbotten	0.92 (0.85–1.01)	0.06	0.93 (0.86–1.02)	0.08	0.93 (0.86–1.02)	0.12
Norrbotten	1.05 (0.97–1.13)	0.25	1.03 (0.93–1.09)	0.81	0.99 (0.92–1.08)	0.95

The counties which are marked bold are Stockholm, Skåne and Västra Götalands, major contributors to the RRT population. We adjusted for [a]gender and age and [b]primary renal disease (categorized into four groups) and diabetes (type I or II).

preventative care. Regardlessly, the rates of incident RRT vary substantially both within Sweden—from 70 to 213 p.m.p. (non-standardized rates) in 2006 [6]—and between countries—from 125 p.m.p. in Europe [Iceland and Finland (80 p.m.p.) and Germany (213 p.m.p.)] to 360 p.m.p. in the USA in 2006 [24, 25]. Thus, ethnic and public health care system differences aside, it appears to be clear that standards of referral and preventative care are of central importance and may be improved in many instances. Supporting this claim, the Swedish population is relatively homogenous, with equal access and public health financed care and standardizing for regional differences changed the RRT incidence rates relatively little (Table 2).

However, a recently published study analysing factors associated with RRT incidence showed that the RRT incident rates are affected by macroeconomic and renal service factors [26]. The decreasing incidence rates in eight counties, and among them the two largest catchment areas, may be due to improved general population health status and demographic characteristics of the counties. Also, the differences in diabetic ESRD have been reported to affect regional incidence rates in Australia and Denmark, who like Sweden have homogenous populations [12, 27]. While regional differences due to higher rates of diabetic ESRD have been reported also in Sweden [6], we found a lower rate of RRT incidence in patients with diabetes resident in Stockholm when compared with other regions. This may suggest that preventative strategies are more important for the RRT incidence. Comparing our results on regional differences with studies from Australia [7], UK [28] and the USA [29], we were unable to confirm the previously observed higher rates of RRT incidence in rural areas and in areas with lower physician density as a proxy for health care availability. This difference may be explained by the large differences in social security and access to health care present between Sweden and the USA. Also, the Australian data concern indigenous groups, perhaps less likely to seek regular preventative care.

The SRR has 100% coverage of the general population. This work thus provides a robust and novel calculation of catchment area influence—while all previous estimates have been based on regional reporting and subjective interpretation of the data [22, 30–37]. To enable regional variation to be studied at the county level, complex statistical methods have been used to adjust for clustering in the estimates.

One potential limitation of the study is that the RRT incidence is based on 90-day survival in chronic RRT. Patients who experienced early mortality or had reversible renal failure are not included, as well as patients who started short-term RRT during intensive care. To include only patients who have been given treatment for at least 3 months is a common procedure and increases the comparability of our findings with others [24, 25].

In conclusion, our aggregated analysis of the total population suggests that the previously reported steady increase in RRT incidence has now come to an end in Sweden. Instead, the RRT incidence in Sweden has reached a plateau and is declining steadily, especially in patients aged 65–74 years. We also report updated and detailed incidence rates for RRT in all counties of Sweden, as well as remarkable differences in the adjusted incidence rate of RRT between counties. In 8 out of 21 counties, a decreasing RRT incidence over time was found. However, further studies are needed to understand the specific causes underlying the decline of the RRT incidence in selected counties of Sweden, while explaining the increasing rates in others.

Authors' contribution

A.R.Q and C-G.E. initiated the study. A.R.Q. and C.-G.E together made the statistical analysis and wrote the first draft of the report, which all co-authors subsequently critically reviewed and contributed to. K-G.P. is a general secretary of the Swedish RRT registry and provided all data used in the analysis. C.-G.E., K-G.P., M.S., M.E. and A. R.Q have all contributed substantially to the design, evaluation and reporting of this work.

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Conflict of interest statement. None declared.

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