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Chronic kidney disease and end-stage renal disease—a review produced to contribute to the report 'the status of health in the European union: towards a healthier Europe'

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Abstract

The Report on the Status of Health in the European Union (EUGLOREH) is a project aimed at describing health problems in member states of the European Community. This project is an effort of more than 170 European experts and the collaboration of the health authorities or institutions from all EU Member States, major intergovernmental, International and European Organizations and Agencies. In this report, for the first time special emphasis is given to chronic diseases. Chronic kidney disease (CKD) is increasingly recognized as a major public health problem. However, with some notable exceptions, until now this disease has received scarce attention both at European level and at member states level. In 2007, the ERA-EDTA Registry was invited to contribute to EUGLOREH. The Registry made a major effort to gather published and unpublished information on the epidemiology of CKD and ESRD and to provide a comprehensive overview on CKD and ESRD in European countries. The review was completed in early 2008 and included into the final EUGLOREH published in the WEB as of 20 March 2009.

Keywords: CKD; ESRD; epidemiology; public health

Introduction

Chronic kidney disease (CKD) is increasingly recognized as a major public health problem. CKD can be detected via simple biochemical tests including a creatinine-based estimate of the glomerular filtration rate (GFR) [1]. CKD is now described based on internationally accepted definitions and diagnosed when structural or functional abnormalities of the kidneys persist for more than 3 months. The disease is categorized into five stages of increasing severity. Data derived from the National Health and Nutrition Examination Survey III (NHANES III) show that about 1 out of 10 adult Americans exhibit CKD [2]. Estimates in Asia and Australia [3,4] indicate that the problem is of the same magnitude in those countries. In Europe, several surveys have now been completed [5–11]; these studies indicate that CKD is of concern also in EU countries. CKD is a dangerous clinical condition for two reasons: first because renal impairment may prelude to the development of end-stage renal disease (ESRD), i.e. the disease stage where dialysis and transplantation are needed, second because it amplifies the risk for cardiovascular complications (Figure 1). Independent from other risk factors, patients with stage 4–5 CKD have a death risk for cardiovascular complications which is 2–4 times higher than that of the coeval general population, whilst patients with ESRD have a 100 times higher risk [12]. There is coherent, undisputable evidence that treatment can prevent or delay kidney disease progression and the resulting cardiovascular complications [13–20], but this knowledge has rarely been translated into public health policies. Moreover, early detection can prevent or delay progression to end-stage renal disease (ESRD).

CKD was not listed among chronic diseases in the 2005 WHO report [21,22]. However, it is exceedingly frequent in patients with cardiovascular diseases where it acts as a risk multiplier [19]. Furthermore, evidence is emerging that CKD is a risk factor for death and other clinical complications in other chronic diseases like in neoplasia and in chronic infections. Interpretative models are being developed to frame the link between CKD and other chronic diseases with the ultimate scope of devising policies aimed at improving clinical outcomes. Proteinuria and microalbuminuria [23,24] may be useful for the screening of CKD; indeed, studies are currently underway for further testing the value of these biomarkers at population level.

ESRD and the resulting cost of renal replacement treatments are still in an expanding phase [25]. Although the problem is well recognized, few countries have policies for CKD. The high prevalence of CKD, its contribution to cardiovascular risk and to other diseases and its economic implications are still largely overlooked by governments and health authorities and ignored by the population. In a

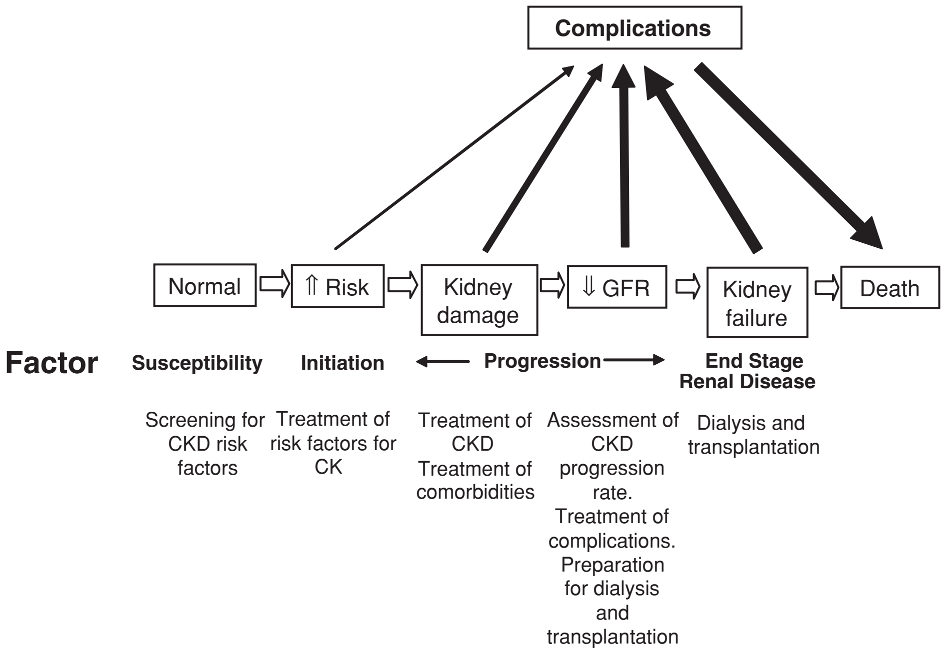

Fig. 1. Development and progression of CKD. Cardiovascular risk factors and the presence of cardiovascular disease convey an increased risk of progression to stages of in creasing severity. Arrow thickness denotes the propensity to complications (redrawn from Ref. [13]).

context where costs for other chronic diseases such as hypertension, diabetes and cardiovascular diseases are magnified by the epidemics of obesity [26] and consume a large fraction of health care resources, full recognition of CKD as a preventable disease is important. Indeed CKD prevention may also help to control the cardiovascular burden deriving from these diseases. Even though cardiovascular diseases largely remain the main contributor to the death toll of chronic diseases, communicable diseases are not yet under control in developed countries. CKD is very common in people with infectious diseases and neoplasia and amplifies the risk for adverse outcomes and the resulting costs in these conditions. For these reasons, health policies for CKD need to be harmonized with policies for other chronic diseases.

Information on CKD in the pre-ESRD phases in children is scarce. Available data indicate that CKD at this age are rare [27,28]. Data on renal replacement therapy (RRT) for ESRD in children are collected by the renal registries in Europe. Although rare, CKD and ESRD in children pose unique challenges because of the many extra-renal manifestations of renal insufficiency that affect growth as well as development.

Economic impact of CKD

Apart from the morbidity, mortality and poor quality of life engendered by CKD and ESRD both in adults [29,30] and in children [31,32], these diseases impose high direct and indirect costs to society. CKD in the pre-ESRD phase entails a cost excess of $26.000 per case per year in the USA [33]. A considerable amount of healthcare funding in Europe is spent on treating dialysis patients. In 2001, it was estimated that in Italy 1.8% of the total health care budget was spent for ESRD patients, who represented 0.083% of the general population [34]. Renal transplantation is the most cost-effective renal replacement therapy [35]. The costs of treating patients living on a transplant are indeed by one-third to one-quarter lower than those spent on dialysis patients [36].

Data sources

The present review is based on a compilation of studies on the prevalence of CKD among children, adolescents and adults and on the data of the Registry of the European Renal Association-European Dialysis and Transplant Association (ERA-EDTA) that collects data in patients with ESRD on RRT. Available data on the prevalence of CKD (stages 1–5) in EU countries were summarized in presentations given at a recent convention on CKD in European countries made at the XLIV Congress of the ERA-EDTA (Barcelona, 21st–24th June 2007) [37] and unpublished information for some EU countries was derived from these presentations.

Data on CKD are very scarce. Whenever possible, the CKD data are presented according to the internationally accepted definition established by the Kidney Disease Improving Global Outcomes (KDIGO) initiative (Tables 1 and 2). Data about CKD in children are presented according to available GFR cut-offs. European data on CKD have been gathered both by using medical databases (Ireland, England, Italy) or population surveys. For the 27 EU Member countries, national surveys on the prevalence of CKD among adults are available for 12 countries. The data for the United Kingdom (UK) and Ireland and part of the Italian data were based on information derived from general

Table 1. KDIGO definition of chronic kidney disease

Structural or functional abnormalities of the kidneys for ≥3 months, as manifested by
1. *Kidney damage*, with or without decreased GFR, as defined by
• Pathologic abnormalities
• Markers of kidney damage
Urinary abnormalities (proteinuria)
Blood abnormalities (renal tubular syndromes)
Imaging abnormalities
• Kidney transplantation
2. *GFR <60 ml/min/1.73* m^2, with or without kidney damage

practitioners databases. Data from other countries are based on population samples representative of the general population of those countries. CKD data from medical databases overestimate the prevalence of diseases and this is apparent also in the data collected in this review.

In quite a number of EU Member States renal registries are able to provide complete and reliable individual patient data on the incidence and prevalence of RRT for ESRD to the ERA-EDTA Registry for international comparison. Other Member States, especially some larger ones, are not yet able to provide individual patient data covering their whole country (France, Germany, Italy, Spain and Portugal). Most new Member States as well as non-Member States have renal registries in development that will only include complete patient data in another few years. These different stages of development of renal registries hampered comparisons across Member States and non-Member States. On the other hand, the availability of individual patient data within one European ERA-EDTA Registry facilitated the comparisons as at least a large part of the data could be analysed using exactly the same methodology.

The ERA-EDTA Registry (http://www.era-edta-reg.org) collects individual and aggregated data from national and/or regional renal registries in Europe and countries bordering the Mediterranean Sea. The individual patient data are used for epidemiological analysis to calculate incidence, prevalence and patient survival. These are published in the Registry annual reports together with aggregated incidence and prevalence data that are received from other European countries. In addition, the Registry performs more focused studies using data from a segment of the catchment population with the aim of answering specific research questions. The resulting information may assist health authorities and health planners in the formulation of policies for the care of renal failure in the EU. For this report incidence and prevalence data on RRT were used from 42 registries in 29 countries. National and regional renal registries including individual patient data collect at least the date of birth and gender of each patient starting RRT in their coverage area together with information on primary renal disease and the start date and type of RRT. During the follow-up of the patients, the changes in treatment and the date and cause of death are registered. Registries collecting aggregated data usually perform yearly surveys among their renal centres. As availability of data depended on the existence of national and regional renal registries and the completeness of the coverage of their countries, data on RRT over the period 1992–2005 are incomplete. Seven EU-15 Member States (Austria, Belgium, Denmark, Finland, Greece, Sweden and The Netherlands) were able to provide complete individual patient data for the whole country over the entire period and six EU-15 Member States (France, Germany, Italy, Portugal, Spain and UK) provided individual or aggregated data either over a shorter period or with incomplete coverage of their country. Nine additional EU-27 Member States (Bulgaria, Czech Republic, Estonia, Hungary, Latvia, Poland, Romania, Slovakia and Slovenia) and a number of non-Member States were able to provide aggregated data over a shorter period. The data used for mortality analyses included patients who started RRT over the period 1996–2000 from 16 renal registries in 9 EU-15 Member States (Austria, Belgium, Denmark, Finland, Greece, Spain, Sweden, The Netherlands, UK) plus Iceland and Norway. The data on public health control tools and policies were collected from renal registries and from national experts in this area.

Data description and analysis

Incidence

Children and adolescents. CKD in the pre-ESRD phases in childhood and adolescence in the above-mentioned population-based registry in Italy (Italkid) have shown an incidence rate of CKD (defined as a GFR <75 ml/min per 1.74 m^2) of 12.1 cases per million of the age-related population (pmarp) [27]. In the Swedish study (considering children and adolescents in the 6 months–16 years range) the corresponding figure was 7.7 cases/year pmarp (<30 ml/min per 1.74 m^2) [28]. In 2005, the incidence rate of RRT

Table 2. Current CKD classification based on severity and therapy

Stage	Description	GFR (mL/min per 1.73 m^2)	ICD 9 CM Code	Treatment
1	Kidney damage with normal or ↑ GFR	≥90	585.1	
2	Kidney damage with mild ↓ GFR	60–89	585.2	1–5 T if kidney transplant recipient
3	Moderate ↓ GFR	30–59	585.3	
4	Severe ↓ GFR	15–29	585.4	
5	Kidney failure	<15 (or dialysis)	585.5	
			585.6 (if ESRD)	
			V codes for dialysis or transplantation	5 D if dialysis (HD or PD)

Table 3. Incidence of RRT (pmarp) in countries providing individual patient data to the ERA-EDTA Registry over the entire period 1992–2005, by age group, gender and cause of renal failure (crude)

	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
0–14	8.5	8.0	7.6	8.7	7.1	8.2	9.2	8.0	9.5	9.0	10.1	8.5	8.7	7.1
15–64	73.9	80.4	77.7	79.9	79.7	83.6	82.7	83.8	86.1	84.2	83.2	82.4	84.7	82.0
65+	212.8	244.9	260.5	292.5	315.4	332.3	347.5	363.0	381.1	398.3	409.1	421.1	437.0	429.3
Males	100.8	110.5	110.3	122.5	126.2	133.1	137.9	141.2	145.4	150.9	150.7	153.7	159.5	156.9
Females	63.9	72.8	74.5	76.3	79.6	84.5	83.9	87.2	92.4	90.7	93.2	93.1	96.4	93.2
DM	13.6	16.2	17.0	19.4	20.1	21.5	22.0	22.8	25.5	25.6	26.9	27.2	28.5	27.6
Hypertension/CVD	10.9	12.8	13.5	14.8	15.7	17.6	17.3	18.2	18.8	20.1	20.4	20.4	21.6	20.4
Glomerulonephritis/ sclerosis	15.5	16.6	16.6	16.1	16.2	16.4	15.3	16.0	16.3	15.7	15.0	15.0	14.2	14.3
Other cause	42.0	45.6	45.0	48.6	50.5	52.9	55.7	56.7	57.8	58.9	59.2	60.2	63.1	62.2
Total	82.0	91.3	92.1	99.0	102.5	108.4	110.4	113.7	118.4	120.3	121.4	122.9	127.4	124.5

Table 4. Incidence of RRT over the period 1992–2005 (per million population) in countries providing individual patient data to the ERA-EDTA Registry, by country (adjusted for the age and gender distribution of the EU25 population)

	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Austria	108.4	111.0	109.5	117.2	115.5	127.8	128.8	134.7	131.7	137.3	133.6	137.9	154.9	145.5
Belgium, Dutch-speaking			113.4	123.9	123.6	130.7	137.1	143.6	140.7	149.7	160.4	159.2	159.9	159.3
Belgium, French-speaking	86.5	112.1	112.6	99.5	116.3	115.3	132.8	156.8	152.9	172.2	169.1	155.0	178.5	170.2
Denmark	70.1	98.1	86.1	97.6	98.8	106.5	112.2	126.9	133.7	141.7	133.1	133.6	131.2	117.5
Finland	62.5	73.9	65.4	76.2	80.5	76.8	92.5	93.0	96.6	90.6	92.2	93.0	93.4	89.3
Greece	84.4	77.2	91.5	97.7	103.1	107.6	112.5	117.5	144.9	155.8	154.6	168.3	176.6	169.9
Iceland	46.8	77.9	64.9	58.5	23.6	64.3	84.1	44.6	71.6	94.3	89.4	82.8	83.7	79.5
Italy												127.5	127.2	
Norway	70.1	72.4	74.5	82.3	73.4	87.0	94.9	92.5	94.4	96.6	92.8	96.9	101.8	100.6
Spain, Andalucia	76.8	85.1	89.2	94.8	101.7	107.8	125.4	113.6	130.7	125.1	136.5	133.9	137.4	138.8
Spain, Aragon													107.9	
Spain, Asturias												113.9		84.9
Spain, Basque country	61.3	76.7	76.9	74.5	88.4	95.8	100.9	91.3	112.4	109.0	88.4	117.0	111.6	106.5
Spain, Cantabria												144.7	149.3	158.3
Spain, Castile and Leon												92.9	95.3	
Spain, Castile-La Mancha												103.2	111.2	122.1
Spain, Catalonia	97.4	109.4	112.6	123.4	133.1	129.7	128.8	142.9	136.9	133.7	138.4	140.8	129.7	125.7
Spain, Extremadura														110.2
Spain, Valencia	115.6	127.2	118.0	132.0	134.9	135.0	157.2	153.0	163.3	139.0	150.0	147.0	155.0	137.4
Sweden	99.0	114.9	105.7	110.9	113.7	115.7	120.6	118.2	121.8	118.9	119.3	112.3	112.6	108.6
The Netherlands	84.8	92.6	93.7	95.4	98.8	103.6	100.5	102.7	102.2	104.9	107.7	107.5	108.9	106.7
UK, England/Wales							90.3	90.9	92.8	96.4	96.9	97.6	101.7	102.2
UK, Scotland	73.8	86.3	80.9	92.3	86.6	104.2	110.5	114.9	112.4	102.9	109.3	119.3	111.2	117.8

for ESRD in children aged 0–14 was 7.1 patients pmarp (Table 3).

Adults. CKD incidence in adults has been studied very little [38] and is marred with difficulties [39]. No data have been published in Europe. In the Atherosclerosis Risk in Communities (ARIC) Study in the USA, a study which enrolled individuals 45–64 years old, the incidence rate of 3–5 CKD was 7.8 per 1000 patient years [40]. Similarly scarce are the data concerning changes in CKD over time, whilst the correlation with changes in the incidence of ESRD are mainly based on NHANES surveys and on a survey made in Norway. In the USA, the incidence of ESRD appears to be increasing faster than that observed for CKD [41]. Indeed, nine new cases of ESRD developed in 1983 for every 1000 prevalent patients with CKD in 1978. By comparison, 16 cases of ESRD had developed in 1996 for every 1000 patients with CKD in 1991. A similar finding in terms of the relative stability of CKD versus a marked increase in ESRD was noticed in a second study that examined NHANES data [2]. In Europe, similar data are available only in Norway. The prevalence of 1–5 CKD in Norway was 10.2% which is similar to the current prevalence in the USA (11%). This contrasts with ESRD incidence rates which are three times higher in the United States compared to Norway. In a recent comparative study [8], the relative risk for progression from CKD stage 3 or 4 to ESRD in US white patients compared to Norwegian patients was 2.5. This was only modestly modified by adjustment for age, gender, and diabetes. Age and GFR at the beginning of dialysis were similar, hypertension and cardiovascular mortality in the populations were comparable, but US white patients were referred later to a nephrologist and had a higher prevalence of obesity and diabetes.

Table 5. Incidence of RRT (at day 1) over the period 2000–2005 (per million population) in countries providing aggregated patient data to the ERA-EDTA Registry, by country (crude)

	2000	2001	2002	2003	2004	2005
Bosnia-Herzegovina		61.0	109.7	108.0	107.8	103.9
Croatia	106.1	112.2	118.1	131.4	155.1	143.6
Czech Republic		162.9	171.6		166.0	174.5
Estonia						57.2
France					138.7	139.1
Germany	175.0	184.0	174.0	186.1	194.3	203.4
Hungary				198.6		
Italy				150.3	173.0	161.9
Latvia			58.7		100.0	69.1
Macedonia, the Former Yugoslav Republic of			72.7	83.0	84.5	97.9
Poland	68.0		99.1	104.6	96.1	120.0
Portugal			200.2	203.6	215.4	204.6
Romania						85.7
Serbia-Montenegro	97.2	91.9	137.2	117.4	94.6	
Slovakia*			139.0		155.7	184.7
Slovenia					126.7	124.5
Spain				131.9	123.8	126.0
Turkey*						186.9

*Dialysis patients only.

In 2005, the incidence rates of RRT for ESRD ranged from 57 patients pmp in Estonia to 205 patients pmp in Portugal (Tables 4 and 5). The incidence rate of RRT for ESRD in 2005 steeply increased with age and was higher in males than in females (Table 3). Whereas incidence rates in Canada (160 pmp in 2005) are similar to those in Europe, incidence rates in US whites (286 pmp in 2005) [42] are 1.5–3 times as high as in Europe. This is partly due to a higher US incidence rate of diabetic ESRD.

Trends in incidence over time

There is no information on the trends of the CKD incidence rate in children/adolescents or adults. In the 1992–2005 period, the incidence rate of RRT increased by more than 50% (Table 3). This was primarily due to the fact that the incidence rate in patients over 65 years of age had more than doubled. Whereas the incidence of RRT for diabetic and hypertensive ESRD became twice as high, the incidence of RRT for ESRD due to glomerulonephritis/glomerulosclerosis remained stable. Although there are considerable differences in absolute incidence rates of RRT for ESRD across countries, there was a consistent increase in incidence rates in virtually all Member States at least until 2002. This was mainly driven by an increase in the incidence rates of RRT for diabetic and hypertensive ESRD [43,44]. After 2002, the incidence rates have tended to stabilize. The stabilization, or even decrease in some causes of ESRD, has prompted some investigators to suggest that treatment strategies for the prevention of ESRD have finally started to bear fruit [45,46]. The increasing incidence rates together with improvements in survival of RRT patients [47] resulted in a concomitant increase in the prevalence of RRT over the past decades that is posing a still increasing economic burden on Member States.

Socioeconomic variation in incidence

The incidence rate of RRT was higher in socially deprived areas of the UK than it was in other areas [48].

Prevalence

Children and adolescents. Information on CKD in the pre-ESRD phases for children and adolescents is very limited [27,49]. Data in a population-based registry in Italy including all people <20 years reported a prevalence of CKD (defined as a GFR <75 ml/min per 1.74 m^2) of 74.7 cases pmarp [27]. In a survey in Sweden in a more restricted age-range (6 months-16 years) and applying a lower GFR cut-off for defining CKD (<30 ml/min per 1.74 m^2), the corresponding figure was 21 cases pmarp [28].

The prevalence of ESRD undergoing RRT in children (<20 years) in Europe is about 60 cases pmarp [50]. In 2005, the prevalence of RRT in the 0- to 14-year age group was 43 pmarp (Table 6).

Adults. The prevalence of CKD by stage (as defined in Tables 1 and 2) in The Netherlands [7] and in Spain [51] is shown in Figure 2. The prevalence of stage 3–5 CKD—i.e. the stages showing a higher risk for CV complications and for evolution to ESRD [52]—in population-based studies ranges from 3.57% (Norway) [8] to 7.2% (Germany) [53] in males and from 6.2% (Italy) [10] to 10.2% (Iceland) [5] in females (Figure 3), while higher figures are reported

Table 6. Prevalence of RRT over the period 1992–2005 (per million age related population) in countries providing individual patient data to the ERA-EDTA Registry, by age group, gender and cause of renal failure (crude)

	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
0–14	40.5	41.2	41.6	43.8	42.8	42.9	45.9	44.9	44.7	44.3	45.3	43.7	43.6	43.3
15–64	533.1	559.7	578.7	598.7	617.5	639.3	646.7	666.0	684.5	693.1	705.8	740.1	747.3	748.5
65+	796.6	882.7	1000.6	1091.6	1183.8	1279.9	1290.3	1376.0	1456.8	1518.1	1609.0	1725.3	1808.0	1880.4
Males	573.6	612.2	643.5	682.9	719.5	758.5	775.7	809.7	841.9	866.1	894.3	949.0	975.2	994.7
Females	390.3	415.7	447.5	466.1	486.3	509.9	505.1	525.2	545.2	554.4	573.0	603.0	615.9	624.9
DM	46.4	52.0	58.1	63.2	68.6	74.1	75.4	80.8	87.6	91.8	98.2	105.4	110.6	113.1
Hypertension/CVD	39.1	43.8	48.9	53.7	58.3	63.2	63.1	67.4	71.9	75.4	79.7	84.3	88.8	91.8
Glomerulonephritis/ sclerosis	135.4	141.2	147.1	152.1	157.1	162.7	156.1	160.4	164.2	164.3	165.9	170.5	170.3	170.4
Other cause	259.3	275.1	289.7	303.5	316.7	331.9	343.1	356.1	367.0	375.9	387.1	412.8	422.8	431.4
Total	480.2	512.1	543.7	572.5	600.8	631.9	637.7	664.7	690.7	707.4	730.8	773.0	792.5	806.7

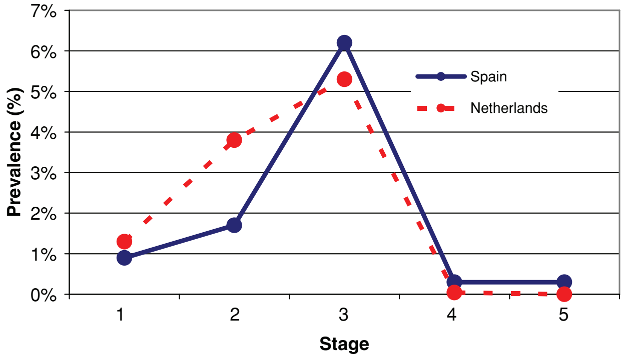

Fig. 2. Prevalence of chronic kidney disease per stage in two EU countries.

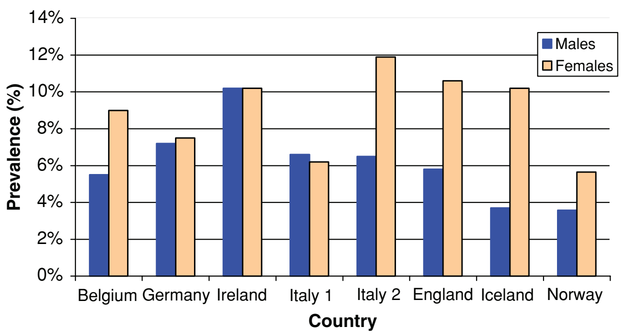

Fig. 3. Prevalence of stages 3–5 of chronic kidney disease by gender in selected countries.

in medical databases [54]. The stage 3–5 CKD prevalence was either similar in males and females (Germany, Italy) or higher in females (Belgium [11], England [54], Iceland [5], Norway [8,9]). The prevalence of stage 3–5 CKD was indeed 1.3–1.5 times higher in medical databases in Ireland, England and Italy than in population based studies in Belgium, Netherlands, Spain, Italy, Iceland, Norway. The prevalence of stage 3–5 CKD appears reasonably similar across EU countries and more frequent in females than in males. The higher prevalence on CKD in females, which flies in the face of ESRD statistics where men are disproportionally affected (Table 6), may depend on the fact that the GFR, as estimated by the MDRD equation [1], is lower in females than in males. Furthermore, the performance of this equation in people with normal or mildly impaired GFR may be sub-optimal [55]. In all countries where this information was available, the prevalence of stage 3–5 CKD increased with age (Figure 4).

In 2005, the crude prevalence of RRT for ESRD at the country level varied from 321 patients pmp in Romania to 1057 patients pmp in Germany (Tables 7 and 8). It increased with age and was more than 50% higher in males compared to females (Table 6). The prevalence of RRT in Europeans is lower than that in US whites (1209 pmp) and in Canadians (1003 pmp) [42].

Trends in the prevalence over time

There is still very scarce information on time-trends of CKD. The most solid source of information remains the periodic surveys made in the USA (NHANES III and NHANES IV performed between 1988 and 1994 and between 1999 and 2004, respectively). In those surveys, the prevalence of stage 1–5 CKD rose from 14.5% (NHANES III) to 16.8% (NHANES IV) [37,56], while the prevalence of stages 3–5 remained almost unmodified at about 6%. None of these data are available in European countries.

In Europe, over the period 1992–2005 (Table 6), the overall crude prevalence of RRT for ESRD increased from 480 to 807 patients per million population (pmp). This was due to a 40% increase in the 15–64 age group and a more than 130% increase in the 65+ age group. In the 0–14 age group, however, the prevalence remained stable throughout the period.

Mortality

A recent meta-analysis has shown that the risk of mortality in CKD rises exponentially with decreasing GFR [42]. Mortality in ESRD patients is very high. Five-year mortality rates in incident RRT patients are 52% in all patients, and 21%, 32% and 73% for patients aged 0–14, 15–64 and over 65 years of age, respectively (Table 9). Five-year mortality

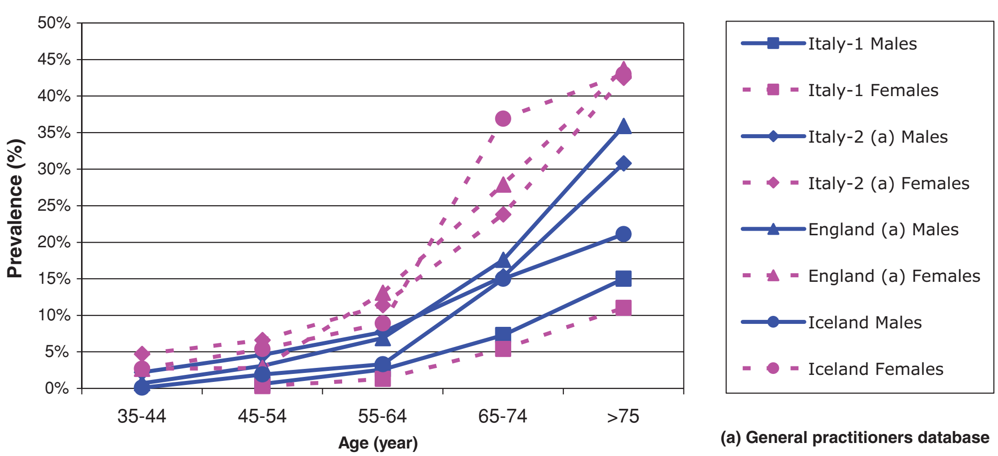

Fig. 4. Prevalence of stages 3–5 of chronic kidney disease by age and sex in selected countries.

Table 7. Prevalence of RRT over the period 1992–2005 (per million population) in countries providing individual patient data to the ERA-EDTA Registry, by country (adjusted for the age and gender distribution of the EU25 population)

	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Austria	552.5	584.9	618.1	651.8	673.0	704.9	723.8	745.8	764.9	798.1	815.0	840.8	879.2	907.0
Belgium, Dutch-speaking			589.4	624.9	648.3	677.1	706.2	735.1	760.7	795.9	826.1	847.9	877.7	910.0
Belgium, French-speaking	505.6	550.4	591.6	609.4	645.0	666.5	704.1	749.9	782.8	827.4	875.4	914.8	964.6	995.2
Denmark	410.1	447.7	465.2	491.5	518.9	543.7	570.7	611.4	644.6	684.9	710.9	738.0	758.1	764.9
Finland	379.5	410.3	434.0	453.5	472.5	487.5	517.8	544.1	577.2	599.7	617.6	638.1	656.6	675.1
Greece	470.1	493.2	531.5	567.9	604.4	642.4	680.1	720.5	760.0	787.1	807.3	846.5	850.5	872.8
Iceland	314.3	353.5	398.0	400.3	338.5	365.0	417.5	384.1	407.3	457.0	490.8	535.8	532.7	528.6
Italy												900.2	981.2	
Norway	414.0	434.7	454.8	476.5	496.1	517.0	549.5	580.5	608.4	632.6	659.5	687.2	724.8	742.8
Spain, Andalucia	556.9	593.9	626.1	658.6	694.0	734.0	783.5	809.2	849.3	866.5	909.9	940.2	969.9	1000.8
Spain, Aragon													715.1	
Spain, Asturias												760.1		804.0
Spain, Basque country	467.8	503.4	542.6	572.8	610.6	654.1	696.0	722.9	764.9	796.1	800.3	831.5	864.5	901.6
Spain, Cantabria												1118.6	1141.9	1133.6
Spain, Castile and Leon												753.9	782.1	
Spain, Castile-La Mancha												831.3	840.3	869.3
Spain, Catalonia	722.9	755.7	792.1	819.3	845.8	876.3	907.6	928.7	950.7	965.9	980.4	997.9	1029.2	1021.9
Spain, Extremadura														817.1
Spain, Valencia	704.4	747.5	789.5	821.1	865.8	885.1	934.7	962.0	1006.3	986.5	1006.2	1002.7	1040.8	1028.0
Sweden	515.9	557.7	575.8	596.9	619.0	637.2	661.7	679.5	698.6	716.7	736.4	745.7	763.8	774.1
The Netherlands	481.6	503.0	523.2	543.5	561.4	586.4	604.3	622.8	638.6	646.6	671.4	690.4	711.4	738.9
UK, England/Wales							528.2	544.1	559.8	572.0	597.3	681.6	675.1	670.7
UK, Scotland	435.1	462.3	483.4	510.9	535.1	567.8	595.6	622.5	649.6	661.8	679.6	700.6	712.0	735.2

Table 8. Prevalence of RRT over the period 2000–2005 (per million population) in countries providing aggregated patient data to the ERA-EDTA Registry, by country (crude)

	2000	2001	2002	2003	2004	2005
Bosnia-Herzegovina		365.0	399.9	432.4	486.2	525.1
Bulgaria				333.4	339.8	
Croatia	620.2	656.5	698.7	789.7	807.3	835.7
Czech Republic		662.6	695.3	707.8	757.6	
Estonia		245.0	273.1	313.8	342.2	394.2
France					944.7	933.2
Germany	870.0	919.0	918.1	948.5	997.6	1057.2
Hungary				438.5		
Italy				995.4	1099.3	1007.4
Latvia			265.5		390.4	334.8
Macedonia, the Former Yugoslav Republic of			522.1	540.3	547.7	601.4
Poland	318.0		404.6	456.9	321.5	536.7
Portugal			1097.2	1128.2		
Romania					277.8	321.0
Serbia-Montenegro	372.6	396.6	492.8	491.2	402.4	
Slovakia			487.9		498.0	581.1
Slovenia					869.3	901.0
Spain				920.8	888.7	899.5
Turkey		361.0		433.5	475.0	527.1

in patients on dialysis is almost five times as high as that after kidney transplantation: 60% and 13%, respectively.

Mortality on RRT is lower in Europe compared to the USA [48,49,57]. Also within Europe there are considerable differences in patient survival [58]. Studies to investigate the reasons for international differences in outcomes in haemodialysis patients are in progress [59].

Trends in mortality over time

Previous analyses have shown that compared to patients starting dialysis in the cohort 1980–1984, dialysis patients in the more recent cohorts had a 6% (cohort 1990–1994) and 12% (cohort 1995–1999) lower risk of death. The mortality risk reduction in transplant recipients was much higher: 32% and 56%, respectively [60].

In conclusion, there is still a paucity of data on CKD. The available data suggest that the prevalence of stage 3–5 CKD is reasonably similar across EU countries and higher in females than in males. Although there are considerable differences in absolute incidence rates of RRT for ESRD across countries, there was a consistent increase in incidence rates in virtually all Member States, at least until 2002. This was mainly driven by an increase in the incidence rates of RRT for diabetic and hypertensive ESRD. After 2002, the incidence rates have tended to stabilize. The stabilization, or even decrease in some causes of ESRD, have prompted some investigators to suggest that treatment strategies for the prevention of ESRD have finally started to bear fruit [45,46]. While patient survival is improving the mortality among ESRD patients is still very high. Although the better survival of transplant recipients is, at least in part, due to selection bias, the survival of RRT patients could be considerably improved at reduced costs by increasing organ donation rates. The increasing incidence rates together with improvements in survival of RRT patients [47] resulted in a

Table 9. 90-day, 1-, 2- and 5-year mortality rates in incident RRT patients (cohort 1996–2000), in countries providing individual patient data to the ERA-EDTA Registry, by age group, gender and cause of renal failure (crude)

	90-day mortality			1-year mortality			2-year mortality			5-year mortality		
	%	*95% CI*		%	*95% CI*		%	*95% CI*		%	*95% CI*	
0–14	3.6	2.4	5.2	10.0	8.1	12.3	15.0	12.8	17.5	20.8	18.5	23.4
15–64	2.8	2.7	3.0	9.1	8.8	9.3	16.0	15.7	16.3	32.1	31.8	32.5
65+	9.2	8.9	9.4	25.0	24.7	25.3	40.7	40.4	41.0	72.5	72.3	72.6
Males	6.2	6.0	6.5	17.5	17.1	17.8	28.9	28.5	29.2	52.3	52.1	52.6
Females	5.9	5.7	6.1	16.9	16.6	17.2	28.2	27.9	28.5	52.4	52.2	52.6
DM	5.8	5.5	6.2	19.6	19.1	20.1	36.1	35.6	36.6	67.2	67.0	67.5
Hypertension/CVD	7.1	6.7	7.6	20.3	19.7	20.8	33.8	33.3	34.4	62.9	62.6	63.2
Glomerulonephritis/ sclerosis	3.2	2.9	3.5	8.5	8.0	9.0	14.8	14.3	15.4	31.8	31.2	32.4
Other cause	6.6	6.4	6.8	17.7	17.4	18.0	27.7	27.4	28.0	49.1	48.8	49.3
Total	6.0	5.9	6.2	17.1	16.9	17.4	28.5	28.2	28.7	52.4	52.2	52.6

concomitant increase in the prevalence of RRT over recent decades that is posing a still increasing economic burden on Member States.

Risk factors for CKD

Hypertension and diabetes [61], obesity [62] and perhaps non-traditional risk factors such as anaemia, hyperphosphatemia, high plasma C reactive protein and fibrinogen, high sympathetic activity and accumulation of endogenous inhibitors of nitric oxide synthase [63] appear to be the main drivers of CKD at population level. Patients with neoplasia and with chronic infectious diseases such as HIV and viral hepatitis (HBC) and patients exposed to nephrotoxic drugs are at higher risk for CKD. There are no data on the relationship between socio-economic status and CKD. It is likely that these links actually exist. Social inequalities affect the health of disadvantaged people for various reasons including access to education and health promotion initiatives and the psychosocial consequences of socio-economic inequalities. This is true for diseases such as hypertension [64] and diabetes [65,66] in adults and obesity in children [67]. Since these risk factors are also the main drivers of CKD, it appears likely that socioeconomic factors are also linked to CKD. According to data from the UK Renal Registry [48], the prevalence of RRT was higher in socially deprived areas of the UK.

Currently, diabetes mellitus is the most common cause of RRT for ESRD, affecting more than 22% of the incident patients.

Apart from international differences in the incidence rates of RRT for diabetic ESRD and differences in stages of economic development across EU Member States, the causes for the considerable differences in the overall incidence rates of RRT between Member States are largely unknown. The incidence of RRT is the outcome of a complex interplay of many factors that have effects in different directions. The number of patients developing ESRD will, among other factors, be affected by the age and gender distribution in the general population, by the prevalence of underlying causes of ESRD, by the access to and quality of health care and by survival from so-called competing risks (e.g. cardiovascular mortality in the general population) [47]. Another factor that must be considered is that once patients have developed ESRD, they may or may not be taken into RRT. There are no data available that support or refute the hypothesis of restriction of RRT, at least not in Western European countries.

Control tools and policies

Secondary prevention

It is still uncertain whether screening the general population for CKD is cost-effective [23,68]. Targeting individuals with cardiovascular risk factors or with cardiovascular disease (i.e. those individuals in whom CKD acts as a risk amplifier) and diabetics appears to be a reasonable approach to the problem [14]. Mass screening through the measurement of albumin excretion has been advocated by investigators in Groningen (The Netherlands) and a cost-effectiveness analysis in support of this contention has been provided [24]. Patients with neoplasia and with chronic infectious diseases such as HIV and viral hepatitis (HBC and HBB) are at higher risk for CKD. When the risk of complications due to modifiable factors is high, for example when nephrotoxic drugs should be used for the treatment of neoplasia, screening for CKD appears advisable. Both in patients with neoplasia and in those with chronic infections, screening for CKD could be implemented using the existing infrastructures used for the detection of these diseases.

Policies

- The Danish Health Ministry has had a quality improvement program for RRT, administered by the Danish Society of Nephrology since 2000. Up until now, the eight parameters collected have been mainly biochemical, but as of 2009, quality measures will be based on patient outcomes, referral patterns and hospital administration.
- In Greece, the Ministry of Health has not issued any objectives, nor has undertaken any initiative relating to the incidence and the course of CKD. The only activities to inform the general population on the epidemiological

problem of CKD have been related to the campaign of the Hellenic Society of Nephrology, particularly during the World Kidney Day, in the last 2 years.

- In Poland in 2007, a programme to detect CKD in an early phase was presented to a Parliamentary Health Commission. Unfortunately, the plan has not yet been accepted at national level.
- The public health policy in Finland is that all patients should receive RRT when deemed necessary. The patient association—which is supported by the Finnish Government—has issued a declaration on the quality of care for renal patients.
- In Spain, there is no single agenda for CKD and ESRD at national level, as the national health authorities have decided to incorporate these subjects into public health policies on cardiovascular disease and diabetes mellitus.
- Since April 2007, German dialysis centres, by law, have regularly electronically reported four quality indicators. Since the beginning of 2008, a central organization has provided information to the centres about their quality based on these parameters in relation to the national average. It is planned that after 2008, dialysis centres will face disadvantages (most likely monetary), if more than 15% of their patients fail defined limits.
- In The Netherlands, quality assurance is a vital element of the dialysis care system. The government has stepped back from a system of planning and licensing; now market parties are assumed to take responsibility for the provision and quality of health care. At present, there is a system of quality control, auditing and certification of dialysis providers. Nearly 90% of the dialysis centres have a quality certificate. The development of an efficient system for benchmarking clinical performance data is currently in progress.
- In 2001 in France, the so-called 'Graft plan' was set to improve organ donation and transplant activity. In 2002 new regulations on RRT established that planning of the supply of care should be related to population needs, assessed at regional level. In 2004, the French Ministry of Health established a list of 100 public health objectives; two of which concerned chronic renal failure: (1) to stabilize (or decrease) the incidence of ESRD and (2) to reduce the impact of chronic renal failure on quality of life, especially in dialysis patients. Since 2005, it has been mandatory for laboratories to provide both serum creatinine and equation-based GFR estimates for any creatinine prescription in order to improve CKD diagnosis. Policies regarding evaluation of care including CKD are currently in progress.
- In Italy, in March 2007, a report by the Istituto Nazionale di Statistica did not list CKD among chronic diseases. On September 26th 2007, after a special convention held in Rome, the Ministry of Health agreed that a public health policy should be developed to counter this disease. A proposal for a survey on the prevalence of CKD at community level has been submitted by the Italian Society of Nephrology to the Ministry of Health and it is possible that this survey will be included in the framework of an ongoing cardiovascular prevention project of the Istituto Superiore di Sanità. As for ESRD, reporting on quality of treatment is still not compulsory.
- The UK Renal Registry monitors the quantity and quality of RRT care using electronic methods of data transfer from hospital based clinical renal IT systems. The NHS Healthcare Commission monitors quality improvement in England & Wales through the UK registry, while NHS Quality Improvement Scotland (QIS) does this in Scotland. The UK Renal Association has developed detailed guidelines and standards for audit measures in Renal Services. The NHS in England and also in Wales has published a national service framework for renal services. Although CKD has hitherto been an underdiagnosed condition, recent changes in the measurements of the kidney function and the introduction of CKD into the Quality and Outcomes Framework (QOF), which rewards GPs, have now made the UK a world leader in this field. Under QOF, GPs are now paid partly on the basis of how well they manage patients with CKD. This helps ensuring that once people are diagnosed with CKD, they get high quality advice and support in modifying the lifestyle factors which exacerbate the effects of their diseases. Early figures indicate that in the year up to March 2007, the first in which this system was in operation, roughly 1.5 million people were diagnosed with CKD, creating an opportunity to provide potentially life-saving advice and treatment. CKD receives 27 points in QOF, with a further 9 for diabetes directly related to kidney disease. This significantly supports the implementation of the Renal National Service Framework (NSF) quality requirements which aim to minimise the impact of kidney disease in its early stages.
- The Ministry of Health in Norway has started a process to create a national action plan for CKD, including secondary prevention, dialysis and kidney transplant.
- The Austrian Ministry of Health commissioned an institute (OEBIG) to issue an Austrian Health Plan (OESG). Regulations concerning the provision of ESRD treatment throughout Austria have been indicated in this Health Plan. The Plan also stated that the Austrian Dialysis and Transplantation Registry (OEDTR) shall take care of quality assurance in ESRD treatment. The Health Plan found its way to regional health legislation and planning in all nine Austrian counties via an agreement between the federal government and the counties, the so called '§15a-Vereinbarung'.
- In the Czech Republic, RRT is freely available for all citizens. The average waiting time for transplantation is about 2 years. Accessibility of dialysis therapy is possible in 92 dialysis centres; in 2006, there were 464 patients pmp under dialysis treatment. The registry of patients that issues The Statistical Yearbook of Dialysis Treatments is organized by the Czech Society of Nephrology in cooperation with the Dialysis Centres.
- There are no public health policies on CKD or RRT in Estonia and Sweden. We lack information on all other countries.
- NephroQUEST [69] is an initiative promoted by the ERA-EDTA registry and co-funded by the European

Commission whose aim is to give assistance in the collection of clinical performance indicators in RRT that are comparable at international level.

Future developments

There is a need for an integrated strategy of community management of CKD, including self-care and long-term conditions. New models and new technologies (e.g. telemedicine) may be very helpful in this respect. The RenalPatientView, which is being rolled out in a number or renal units in the UK offers a web-based system to provide support to kidney patients.

Monitoring and evaluation are essential in the prevention of ESRD and in the improvement of survival and quality of life of those patients for whom ESRD cannot be prevented. Under the umbrella of the ERA-EDTA Registry, most of the national and regional renal registries in EU Member States have started to collaborate within the QUEST initiative [69]. This initiative includes not only European collaborative studies on different aspects on the quality of ESRD care, but also projects to stimulate the future EU wide availability of comparable data on clinical performance indicators in RRT. The availability of these data would facilitate (inter)national benchmarking and the collection of new epidemiological knowledge. In addition, such data will assist policy makers and other stakeholders in guiding their decisions. The NephroQUEST project that has recently been funded under the Public Health Programme of the European Commission will help making these data available through the standardization of clinical performance indicators, the development of techniques to automatically extract clinical data from electronic medical records and by bringing renal registries in development up to high quality standards.

As already summarized in the paragraph on policies a growing number of Member States have developed national health policies regarding RRT for ESRD. In contrast, only very few countries have developed this kind of policy for CKD. The development of these policies, however, including full recognition of CKD as a preventable disease and the development of meaningful screening strategies and prevention programs is vital. As stated in the introduction, these policies for CKD will need to be harmonized with policies for other chronic diseases. However, in Europe there is still no document on pan-European or national health plans of the calibre of Healthy People 2010 (http://www.healthypeople.gov/), i.e. a document that challenges individuals, communities and professionals to take specific steps to ensure that good health, as well as long life, are enjoyed by all. In Healthy People 2010, specific goals have been fixed for curbing ESRD in the American population. Indicators on these goals are currently being monitored (http://www.ep.niddk.nih.gov/Divisions/kuh/kidneyHP2010.htm).

In most Member States, multinational dialysis companies have taken over or set up haemodialysis centres. Over the next few years, the number of these private centres is expected to grow. On the other hand, in Europe the availability of cadaver kidneys for renal transplantation is far below the demand. As patient survival and quality of life are higher in transplant recipients compared to dialysis patients, whereas costs of treatment are lower, it is important to increase organ donation rates. Some countries (Spain, Scandinavian countries, Austria) have successfully implemented policies that ensure superior donation rates. Legislation and the development and promulgation of specific policies at European level may be of help for improving organ donation rates in other countries.

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