In Focus

Chronic kidney disease: who is affected, who is at risk and who cares?

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In this issue of the journal, Chudek et al. report the results from the PolSenior study, which was conducted cross-sectionally in the years from 2007–11 aiming to assess the health and socioeconomic status of the elderly (>65 years) in Poland. In total, 3793 subjects provided blood and urine samples as well as information on their medical history and completed a questionnaire. Creatinine was measured by Jaffe reaction and estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula; urinary albumin excretion was quantified by the albumin/creatinine ratio (ACR). Of the participants, 29.7% had a reduced eGFR (defined as a value <60 mL/min/1.73 m²), 12.5% had an ACR >30 mg/g creatinine and 36.5% were diagnosed with chronic kidney disease (CKD) according to the National Kidney Foundation (NKF) Kidney Disease Outcomes Quality Initiative (K/DOQI) definition (18.6% Stages I and II, 15.7% had reduced eGFR and elevated albuminuria, 65.7% of subjects with CKD had a decreased eGFR only). The prevalence of a decreased eGFR, albuminuria and CKD for the entire Polish elderly population was estimated to be 21.2, 12.3 and 29.4%, respectively [1].

The K/DOQI guidelines suggested using at least the values of eGFR and proteinuria/albuminuria to determine the stages of chronic renal disease. In Europe, several general population-based studies are available holding this information (see Table 1). Even though no study directly focused on the elderly, all provided at least some information about the effect of age on the prevalence of CKD (Table 2). In Groningen/Netherlands, all 85 421 inhabitants aged 28–75 years were invited to participate in the ‘Prevention of Renal and Vascular End stage Disease (PREVEND)’ prospective study. In total, 40 856 responded and a cohort was selected enriched for the presence of high albuminuria. The final study population consisted of 6000 out of the 7768 individuals with a urinary albumin excretion >10 mg/L and 2592 out of 3395 with albuminuria below this threshold. After excluding subjects with missing data, 8506 participants were analysed. In total, 6905 subjects had no renal disease (81.2%), 2.9% had CKD Stage I, 10% Stage II and 5.8% Stage III; 8 and 3 patients, respectively, were in Stages IV and V. The mean age of the population was 49 years and there was a strong association between increasing age and CKD class (the group without CKD had a mean age of 47.4 years, the one with Stage I 48.2 years, Stage II 56.5 years and Stage III patients were 63.2 years old on average) [2]. When extrapolating the prevalence data to the general population in the Netherlands the numbers changed slightly (1.3, 3.8 and 5.3% for Stages I, II and III, respectively, a total of 10.4%) [3].

In Norway, 70.4% of 92 939 individuals invited participated in a large-scale general health survey (second Health Survey of North Trondelag, HUNT II). The mean age of the population was 49 years. Whereas serum creatinine was determined in all participants, urinary albumin excretion was measured only in a 5% random sample. The prevalence of CKD Stages I–IV was 3.1, 3.4, 4.6 and 0.16%, respectively (total 11.3%) and thus comparable to the results obtained in Groningen. When looking at Modification of Diet in Renal Disease (MDRD) formula derived eGFR values only, there was a strong association between age and loss of renal function. As an example, 0.2% of the participants between 20 and 39 years had an eGFR between 30 and 59 mL/min/1.73 m² when compared with 18% in those older than 70 years [4].

Otero et al. published the results of a cross-sectional study performed in Spain. In total, 13 013 individuals stratified by age, sex and residence were targeted, 6464 were contacted and 2746 completed a questionnaire. The mean age was 50 years and the prevalence of CKD Stages I–IV was 0.99, 1.3, 6.5 and 0.27%, respectively. Again, a strong trend was observed with
especially higher stages of CKD being more prevalent in elderly subjects [5]. Viktorsdottir et al. used data from 19,381 subjects of the Reykjavik Heart Study, a population-based cohort study conducted in the years 1967–96, which included men born between 1907 and 1934 and women born between 1908 and 1935. In this study, urinary albumin excretion was estimated by dipstick, the mean age of the population was 54 years. Of the participants, 1.6% had Stages I and II, 7.4% Stage III and 0.2% Stage IV CKD. The prevalence of eGFR levels <60 mL/min/1.73 m² increased dramatically with age in males and even more pronounced in females with more than 53% of female participants aged over 80 years being affected [6].

Cepoi et al. measured serum creatinine and urinary protein excretion by dipstick in >60,000 individuals from the region of Iasi/Rumania. The mean age of the population studied was 55 years and CKD was defined as either eGFR <60 mL/min and/or an elevated urinary protein excretion. When using the MDRD equation, 6.69% of the subjects were affected; when the CKD-EPI equation was applied, this number changed to 7.32%. Patients with CKD were significantly older (71 years) than those without (54 years) [7].

Finally, Gambaro et al. studied 6200 Caucasians >40 years of age in northern Italy chosen randomly from patient lists of general practitioners. In total, 1.7% had CKD Stage I, 4.3 Stage

| Table 1. Prevalence of CKD in population-based studies in Europe, USA, Australia and Asia |
|---------------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Percentage of population CKD               | Stage I         | II              | III             | Total           | Mean age of study population | Comments |
| European studies                           |                 |                 |                 |                 |                              |          |
| De Zeeuw et al. [3]                        | 1.3             | 3.8             | 5.3             | 0.1             | 10.5               | 49        | PREVEND Study; details see text |
| Hallan et al. [4]                          | 3.1             | 3.4             | 4.5             | 0.2             | 11.2               | 49        | HUNT II Study; details see text |
| Otero et al. [5]                           | 1.0             | 1.3             | 6.5             | 0.3             | 9.1                | 50        | EPICRE Study; details see text |
| Viktorsdottir et al. [6]                   | 1.6, Stage I + II | 7.4            |                 | 0.2             | 9.2                | 53        | Reykjavik Heart Study; details see text |
| Gambaro et al. [8]                         | 1.7             | 4.3             | 6.4             | 0.1             | 12.5               | 60        | INCIPE Study; details see text |
| Chudek et al. [1]                          | 8.3, Stage I + II | 19.8           |                 | 1.1             | 29.2               | 71        | PolSen; details see text |
| US studies                                 |                 |                 |                 |                 |                              |          |
| Coren et al. [11]                          | 3.3             | 3.0             | 4.3             | 0.2             | 10.8               | 48        | NHANES III; a nationally representative sample of 15,625 non-institutionalized adults aged 20 years or older |
| Gambaro et al. [8]                         | 2.8             | 4.7             | 10.9            | 0.5             | 18.9               | 60        | Subpopulation >40 years drawn from NHANES III |
| Hui et al. [12]                            | 2.9             | 3.6             | 5.3             | 1.4             | 13.2               | 63        | ARIC; prospective cohort study in 15,792 individuals aged 45–64 years in four communities in the USA |
| Jassal et al. [13]                         | 8.0, Stage I and II | 32.0          |                 | 40.0            | 75                 | 50        | Rancho Bernardo Study; 1345 community dwelling well educated middle class Caucasians older than 50 years |
| Australian studies                         |                 |                 |                 |                 |                              |          |
| White et al. [14]                          | 1.4             | 4.3             | 7.5             | 0.3             | 13.5               | 52        |AusDiab Study; nation-wide, population-based survey of adults aged ≥25 years including 11,247 subjects; data calculated using MDRD formula |
| White et al. [14]                          | 2.3             | 3.4             | 5.5             | 0.3             | 11.5               | 52        |AusDiab Study; data calculated using CKD-EPI formula |
| Asian studies                              |                 |                 |                 |                 |                              |          |
| Xu et al. [15]                             | 8.9, Stage I + II | 1.4, Stage III and higher | 10.3           | 40               |                      |          | 13,626 Chinese subjects older than 20 years from the Beijing CKD health survey study, a clustered sample design study 4925 individuals from three communities near Beijing |
| Wang et al. [16]                           | 9.7             | 8.1             | 1.9, Stages III and higher | 19.7           | 52                 |          | 2353 out of 5593 residents older than 40 years served by a community hospital in the area of Beijing, testing included check for haematuria |
| Zhang et al. [17]                          | 1.9             | 4.3             | 5.2, Stages III and higher | 11.4           | 61                 |          |                      |

Table 2. Percentage of population with the eGFR <60 mL/min/1.73 m² according to age group

<table>
<thead>
<tr>
<th>40–49 years</th>
<th>60–69 years</th>
<th>&gt;80 years</th>
<th>&gt;90 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>European studies</td>
<td>60–70</td>
<td>10.2a</td>
<td>38.0</td>
</tr>
<tr>
<td>Chudek et al. [1]</td>
<td>1.4b</td>
<td>6.3</td>
<td>18.6c</td>
</tr>
<tr>
<td>Hallan et al. [4]</td>
<td>3.3d</td>
<td>21.4e</td>
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<tr>
<td>Otero et al. [5]</td>
<td>2.0</td>
<td>14.0</td>
<td>44.0</td>
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<tr>
<td>Viktorsdottir et al. [6]</td>
<td>0.3</td>
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US studies


65–69 years.
40–59 years.
>70 years.
40–64 years.
>64 years.

especially higher stages of CKD being more prevalent in elderly subjects [5]. Viktorsdottir et al. used data from 19,381 subjects of the Reykjavik Heart Study, a population-based cohort study conducted in the years 1967–96, which included men born between 1907 and 1934 and women born between 1908 and 1935. In this study, urinary albumin excretion was estimated by dipstick, the mean age of the population was 54 years. Of the participants, 1.6% had Stages I and II, 7.4% Stage III and 0.2% Stage IV CKD. The prevalence of eGFR levels <60 mL/min/1.73 m² increased dramatically with age in males and even more pronounced in females with more than 53% of female participants aged over 80 years being affected [6].

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Finally, Gambaro et al. studied 6200 Caucasians >40 years of age in northern Italy chosen randomly from patient lists of general practitioners. In total, 1.7% had CKD Stage I, 4.3 Stage
II, 6.4 Stage III and 0.1% Stage IV. Even in this already selected population, the trend for higher prevalence with increasing age was preserved [8].

When European data are compared with US studies the overall prevalence of CKD in the general population is comparable (see Table 1, which also provides data from studies performed in Australia and Asia). This fact is interesting as the incidence of end-stage renal disease (ESRD) is much higher in the latter. De Jong et al. calculated that the incidence of ESRD as percentage of prevalence of CKD Stages III and IV in Norway (based on HUNT data) and the Netherlands (based on PREVEND) is 0.24 and 0.19, respectively, but 0.61 in the USA (this calculation being based on white participants in NHANES). The authors discussed that renal disease might progress at a faster rate in US patients [9]. Additionally, even within Europe the consequences of CKD (e.g. as measured by life years lost) vary significantly [10]. As far as the effect of age on the prevalence of CKD is concerned, there seems to also be a more pronounced effect in the USA (see Table 2).

In summary, all these studies support the conclusion that the prevalence of CKD dramatically increases with age and thus the number of renal patients is very likely to grow in the coming decades in parallel with the expected increase in life expectancy. There is, however, a continuing discussion as to whether currently used CKD classification systems applied in the general population are also appropriate for the elderly. It might be argued that there is a ‘physiological’ renal ageing process and thus low eGFR values in the elderly population might need a different interpretation than in younger subjects. The Chronic Kidney Disease Consortium analysed data from more than 2 million participants of general or vascular high-risk populations and CKD cohort studies on an individual level meta-analysis basis. Hazard ratios of mortality and ESRD according to eGFR and albuminuria were determined across age categories after multiple adjustments. Low eGFR and high albuminuria were associated with mortality and ESRD regardless of age. In general and high-risk populations the mortality risk associations with eGFR were weaker on the relative (probably due to the higher risk in the elderly reference population due to higher comorbidities) but stronger on the absolute scale at older ages. For albuminuria, the relative risk attenuation was smaller but the absolute increase in risk with age was even more pronounced. In cohorts specifically selected for CKD, age did not modify the risk of mortality. The authors concluded that a common definition and staging of CKD based on eGFR and albuminuria for all ages can be recommended [18].

Another interesting aspect of the study by Chudek is the fact that only 3.2% of the elderly subjects with CKD were aware of their disease [1]. A similar lower percentage has been reported in some US studies. For example in the KEOP study, a free screening programme, which was targeting patients at risk for CKD, 60% tested positive for microalbuminuria, but <4% had ever been told that they had kidney disease [19]. Platinga et al. analysed data from the NHANES survey covering the years 1999–2004. Awareness improved over time in those with CKD Stage 3 only from 4.7% in 1999 to 9.2% in 2003–04. The numbers were significantly better for men and those with proteinuria, diabetes and hypertension [20]. The presence of albuminuria markedly increased CKD awareness in a study by Tuot et al. [21], who also used NHANES data, whereas other complications of CKD like hyperkalemia, hyperphosphatemia, elevated blood urea nitrogen or anaemia did only to a smaller extent. Nonetheless, 90% of individuals with two to four markers and 84% with >5 markers of CKD were unaware of their disease. Clearly, more advanced renal disease also increases awareness [22]. Better awareness was demonstrated by Gorini et al., who assessed eGFR in 573 volunteers (aged 21–62 years) in central Italy. Of the subjects, 55% had an eGFR <90 mL/min/1.73 m² and ~45% showed an awareness of CKD [23]. Low level of awareness may reflect poor health-care provider recognition and confusion regarding appropriate diagnosis and intervention, particularly at earlier stages of kidney disease leading to a lack of education of patients. It has been shown in other areas of medicine that increasing awareness improves treatment pattern [24, 25], and thus one might speculate that achieving a higher level of awareness might also improve outcome in CKD. The Kidney Early Evaluation Program assessed awareness of subjects at high risk for CKD at the time of the initial screening and followed the subjects longitudinally [26]. Among those with eGFR <60 mL/min/1.73 m², 9% were aware of their disease. Compared with those unaware, these individuals had a lower eGFR (49 versus 62), a higher prevalence of albuminuria, diabetes, cardiovascular disease and cancer. Hence, it was not surprising that subjects aware were more likely to progress to ESRD and die when compared with those unaware (4 versus 17% and 22 versus 19%). Surprisingly, however, even after statistical adjustment for demographics, socioeconomic factors, comorbidity and severity of CKD at screening, aware participants continued to demonstrate this increased risk (HR 1.37; 95% CI 1.07–1.75; P < 0.0123 for ESRD and HR 1.27; 95% CI 1.07–1.52 P < 0.0077 for mortality). Even though the authors clearly state that they do not conclude that unawareness conveys a survival advantage, they nonetheless suggest that awareness on its own is not necessarily sufficient to reduce the poor outcomes associated with CKD.

Finally, Chudek et al. [1] additionally used their data to look for socioeconomic factors that are associated with CKD. The disease was more prevalent in urban dwellers, non-smokers and alcohol abstainers and in those with low physical activity.

Lower socioeconomic status has been reported to be associated with CKD, and some have recommended screening this high-risk group [27]. However, the strength of the association of various parameters used as a measure of socioeconomic status with CKD varies with region. In a recent paper, individuals who participated in the 1999–2002 NHANES and in the Dutch PREVEND study, which was performed in 1997–98 in the area of Groningen, were examined. CKD was defined as a GFR <60 mL/min/1.73 m² or albuminuria >30 mg/day and the association with income and education was determined. In the US population, CKD was strongly associated with income (as was hypertension, smoking, high BMI and diabetes) but education was not, whereas in PREVEND the prevalence of renal disease was more dependent on education than on income. The authors argue that in the USA access to health
care is traditionally more income dependent than in countries with free access to health care and that the gap between high- and low income level was much higher in the USA than for example in the Netherlands (ratio 7.1 in NHANES versus 3.3 in PREVEND). However, education also exhibits a significant role in living a healthy lifestyle (e.g., by affecting an individuals’ ability to resolve adverse health issues, perform self-control, enhance uptake of information and use of health care resources as well as allow effective physician–patient communication and food and lifestyle choices). Therefore, if one accepts that socioeconomic factors are not only associated with the incidence of CKD but are causally related, the recommendations for approaching this problem have to differ in various countries [28]. Interestingly, in participants >65 years, in both NHANES and PREVEND, neither income nor education were significantly associated with CKD, which may be due to the fact that this subpopulation in developed economies usually receive state financial benefits and aid in accessing health care. The association between socioeconomic parameters and renal disease might also vary according to comorbidity. In the Pittsburgh Epidemiology of Diabetes Complication study, ESRD and coronary artery disease incidence over 20 years was significantly higher in patients with type 1 diabetes without a college degree, whereas the incidence of autonomic neuropathy was greater in individuals with low-income/non-professionals. HbA1c was inversely correlated with income. The authors concluded that lower socioeconomic status might lead to poorer self-management and thus greater complications from diabetes [29].

CONFLICT OF INTEREST STATEMENT

I declare that the results presented in this paper have not been published previously in whole or part, except in abstract format.

(See related article by Chudek et al. The prevalence of chronic kidney disease and its relation to socioeconomic conditions in an elderly Polish population: results from the national population-based study PolSenior. Nephrol Dial Transplant 2014; 29: 1073–1082.)

REFERENCES


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Putting the patient first: should we nudge them or shove them?

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There has been unprecedented pressure on people and health-care systems since the global financial crash. The resulting changes to health-care systems, as described by Ronco et al. in this edition of NDT, have been in the context of a number of other major current trends in health-care delivery: a marked demographic change with an ageing population; a rise in the burden of chronic disease including the increasing ascertainment of chronic kidney disease; and patient empowerment with higher expectations of services. So, what do we mean by ‘putting the patient first’?

The global financial crash of 2008 dramatically changed the governmental and fiscal landscape and put unprecedented pressure on people and health-care systems [1]. As described by Ronco et al. in this edition of NDT, the health-care expenditure clamp-down that followed had to occur in the context of a number of other major current trends in health-care delivery: a marked demographic change with an ageing population; a rise in the burden of chronic disease including the increasing ascertainment of chronic kidney disease (CKD); and patient empowerment with higher expectations of services. Although in places their commentary appears to unquestioningly flatter some of the health-policy initiatives discussed—one of the authors was the Minister for Health responsible for introducing several of them [2]—its high-level health-policy perspective makes interesting and thought provoking reading.

Part of the solution to the fiscal crisis in health-care may lie in altering individual patient, health professional and ultimately population and institutional behaviour. Politicians can choose to do this with either a carrot or a stick; a nudge or a shove. A nudge, according to Thaler and Sunstein, who have influenced policy makers worldwide [3], is any feature of a person’s context that encourages them to behave in a particular way [4]. Rather than restricting choice, as happens with legislation (i.e. a shove), nudges are designed to increase the likelihood that the more responsible choice is made. One of the best-known examples of nudge theory is the introduction of physical targets (the image of a fly) in the urinals of Amsterdam’s public toilets which had an impressive effect on men’s behaviour in relation to urinating into the bowl. Putting to one side for a moment the criticisms of nudging—many of the cited examples of nudges involve the simple provision of information or the exertion of pressure which seems to contradict their definition [5]—can we find similar solutions for health care?

Ronco et al. contend that patients have moved from being passive recipients of health care to active consumers with greater expectations. They highlight that 8 out of 10 patients use the internet after visiting their primary care physician in the USA, yet other reports show that fewer than 2 in 10 are accessing official data comparing the quality of health care to aid decision-making regarding the best facility or provider of health care [6]. A Cochrane review concluded that there is no consistent evidence that the public release of performance data changes consumer behaviour or improves care [7]. Part of the explanation for the gap between the use of official and unofficial data sources on the internet may be that we, the medical