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Original Article

Methodology used in studies reporting chronic kidney disease prevalence: a systematic literature review

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ABSTRACT

Background. Many publications report the prevalence of chronic kidney disease (CKD) in the general population. Comparisons across studies are hampered as CKD prevalence estimations are influenced by study population characteristics and laboratory methods.

Methods. For this systematic review, two researchers independently searched PubMed, MEDLINE and EMBASE to identify all original research articles that were published between 1 January 2003 and 1 November 2014 reporting the prevalence of CKD in the European adult general population. Data on study methodology and reporting of CKD prevalence results were independently extracted by two researchers.

Results. We identified 82 eligible publications and included 48 publications of individual studies for the data extraction. There was considerable variation in population sample selection. The majority of studies did not report the sampling frame used, and the response ranged from 10 to 87%. With regard to the assessment of kidney function, 67% used a Jaffe assay, whereas 13% used the enzymatic assay for creatinine determination. Isotope dilution mass spectrometry calibration was used in 29%. The CKD-EPI (52%) and MDRD (75%) equations were most often used to estimate glomerular filtration rate (GFR). CKD was defined as estimated GFR (eGFR) <60 mL/min/1.73 m^2 in 92% of studies. Urinary markers of CKD were assessed in 60% of the studies. CKD prevalence was reported by sex and age strata in 54 and 50% of the studies, respectively. In publications with a primary objective of reporting CKD prevalence, 39% reported a 95% confidence interval.

Conclusions. The findings from this systematic review showed considerable variation in methods for sampling the general population and assessment of kidney function across studies reporting CKD prevalence. These results are utilized to provide recommendations to help optimize both the design and the reporting of future CKD prevalence studies, which will enhance comparability of study results.

Keywords: CKD, CKD-EPI equation, epidemiology, MDRD, systematic review

INTRODUCTION

Chronic kidney disease (CKD) is considered to be a major public health problem [1]. CKD has an important impact both at the patient level, by decreasing the quality of life and life expectancy, and at the population level, by increasing health-care costs and the demand for health-care services.

Since CKD prevalence estimation is central to CKD management and prevention planning at the population level [2], it is not surprising that many publications report CKD prevalence in the general population. It is common research practice to put study results into context by comparing them with previous publications to identify the regional CKD burden, assessing the impact on regional health-care systems and for tailoring preventive strategies to communities. In the case of CKD prevalence, such comparisons are likely hampered as CKD prevalence estimations are influenced by study population characteristics and by the methods used to assess kidney function [3, 4]. To realistically compare CKD prevalence across different population-based studies, methodological factors should be taken into account.

The purpose of this systematic literature review was to (i) identify all studies reporting on CKD prevalence in the European adult general population and (ii) to describe the methodology used in these studies. The findings from this review are utilized to provide recommendations that may help investigators to optimize both the design and the reporting of future CKD prevalence studies, which will enhance comparability of results across studies.

METHODS

Search strategy

A systematic literature search was performed in PubMed, MEDLINE and EMBASE to identify all original research articles reporting the prevalence of CKD in the adult general population. As Kidney Disease Outcomes Quality Initiative (KDOQI) published a guideline on CKD definition [5] in 2002, we included articles published between 1 January 2003, which is one year after the publication of the KDOQI guideline, and 1 November 2014, when our search was last updated. The database-specific search queries are presented in the Supplementary data, Appendix S1. Additionally, the representatives of national kidney foundations, renal registries and expert nephrologists in 39 European countries were asked to provide information on any relevant studies.

Study selection

Publications that presented original research, were designed to select a representative sample of a European adult general population and reported a CKD prevalence estimate were included. We excluded studies that ended subject recruitment prior to 1996 and studies lacking glomerular filtration rate (GFR) estimation based on serum creatinine. Cystatin C-based estimated GFR (eGFR) will lead to higher CKD prevalence estimates than creatinine-based eGFR [6]. For the sake of comparability, we chose not to include publications that solely reported cystatin C-based prevalence estimates. No language restrictions were applied. The literature search was done by two investigators (KB, ED). Any study that was judged relevant on the basis of its title was retrieved in abstract form, and if relevant, in full-text form. Any doubt about eligibility was resolved by discussion with another investigator (VS).

Data extraction

All publications were initially seen by one investigator (KB) and then independently reassessed by two additional investigators (ED for the first half and AK for the second half). For studies with multiple eligible publications, we selected the publication with a primary objective of reporting CKD prevalence or the most recent publication. Publications were assessed on method of population selection, which included the sampling frame (i.e. source used to identify subjects) and the sample

design (i.e. the method of sample selection). Additionally, we extracted information on the assessment of kidney function. The extracted data were categorized as follows:

(i) Creatinine assay was categorized as enzymatic, Jaffe, modified Jaffe, compensated Jaffe or unclear. The Jaffe method is known to suffer from interference by other substances [7], and multiple adaptations have been implemented to improve method specificity [7]. The compensated and modified Jaffe assays were developed to improve method specificity and minimize susceptibility of interfering substances [7]. The compensated Jaffe method is the use of a manufacturer-specific mathematical compensation [8]. The modified Jaffe assays are modifications of the method such as deproteinization of the sample prior to analysis or the addition of potassium ferricyanide [9].

(ii) Calibration was categorized as calibrated to the standardized isotope dilution mass spectrometry (IDMS) or calibrated by another method or calibrator.

(iii) Urinary albumin assay was categorized as dipstick, immunoassay (including both nephelometric and turbidometric immunoassays) or other.

(iv) The CKD definition was categorized as use of the KDOQI 2002 definitions [5] or use of other definitions. Use of chronicity criterion, i.e. persistence of albuminuria or decreased eGFR for at least 3 months, was assessed.

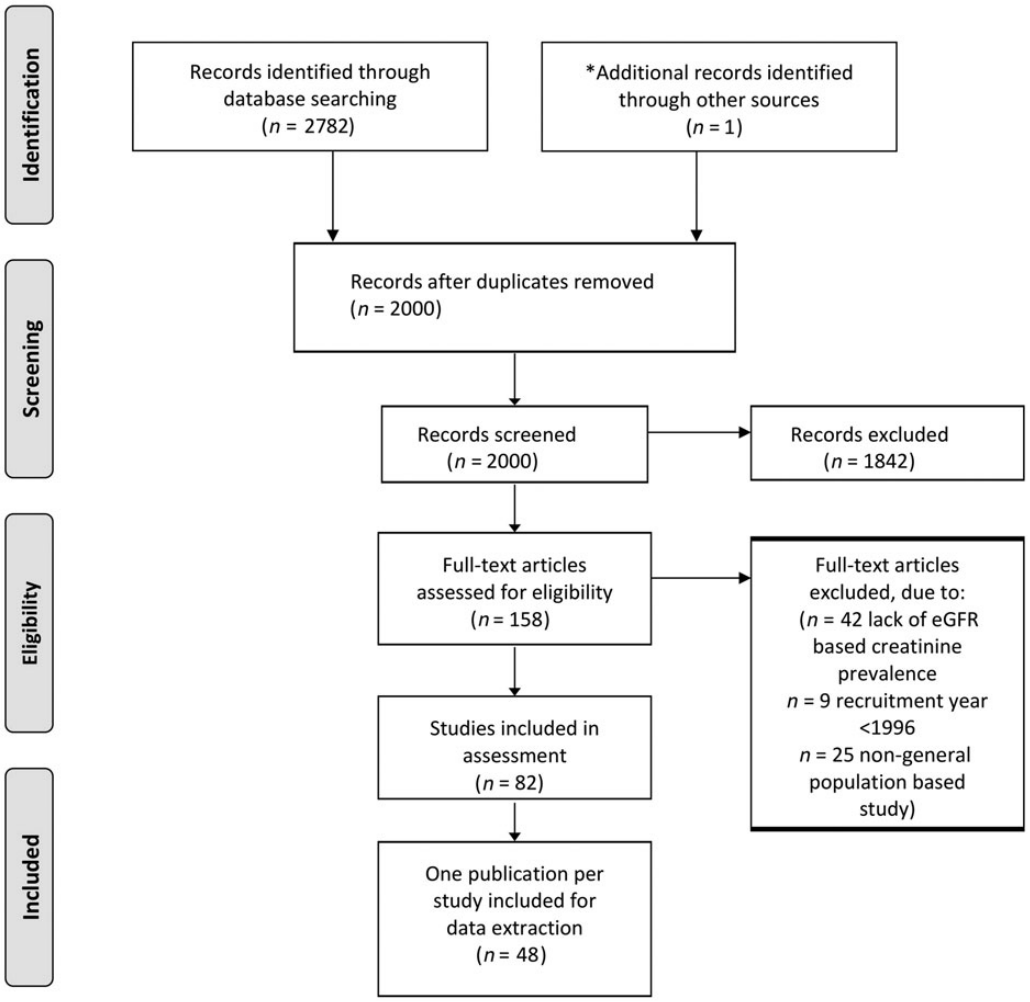
(v) Ethnicity reporting was categorized as 'yes' if publication reported collection of ethnicity data and as 'no' if 'ethnicity' data were not collected or if those were not reported.

Finally, we extracted the following data on presentation of CKD prevalence results: the use of 95% confidence intervals (95%CI), the use of standardization of the prevalence estimate to a reference population and the presentation of results by age group and sex. If CKD prevalence was not the main focus of the publication, the use of 95%CI was rated as not applicable (n/a). The data extraction form is shown in the Supplementary data, Appendix S2.

RESULTS

Study selection

Figure 1 shows the selection process of inclusion and exclusion of publications in a flow chart. We retrieved 2000



*Only one study was solely identified through contacting national representatives and not by the database query.

FIGURE 1: Flow chart of publication selection.

individual publications of which only one study was solely identified through contacting national representatives. A total of 1842 publications were excluded based on title or abstract. Twenty-five publications were excluded as the study was not designed to select a representative sample of the general population, 9 studies were excluded as they ended recruitment prior to 1996 and 42 publications were excluded for not presenting a CKD prevalence estimate. Eighty-two publications fulfilled the inclusion criteria. Eighteen studies had multiple publications, highlighting various aspects of CKD (overall 34 publications). Finally, we included 48 publications of individual studies for the data extraction.

Data extraction

Table 1 describes the method of general population sample selection including the response per study. Details on the laboratory assessment of kidney function, the CKD definition used and on the reporting of CKD prevalence are presented in Table 2.

Population selection. All studies combined described a total of 247 342 subjects. The size of the study population ranged from 328 to 65 181 subjects. Twenty-three studies (48%) included virtually the entire age range of the adult population. The remaining (n = 25; 52%) studies restricted the recruitment of subjects to a higher age range.

Four studies (8%) used census data as the sampling frame to identify eligible study subjects. More than half of the studies (n = 26; 54%) did not report the sampling frame used. Fourteen studies (29%) were designed to select their population by age and sex stratification, and 12 studies (25%) selected a random sample. Ten studies (21%) did not provide details on the sample design, six of which referred to previous publications for more details.

The response was given in 31 studies (65%) and ranged from 10 to 87%. Of the 17 studies that did not report a response, 2 studies referred to a previous publication for details regarding responders and non-responders.

Assessment of kidney function. Serum creatinine was determined by Jaffe assay in the majority of studies (n = 32; 67%) and by enzymatic assay in six (13%) studies. Only few creatinine assays were calibrated to IDMS (n = 14; 29%). Urinary markers for kidney disease were assessed in 29 studies (60%), 15 of which (31%) used immunoassay to detect albuminuria. Seven studies (15%) used dipsticks to identify proteinuria, with confirmation of albuminuria by immunoassay in four studies (8%).

CKD definition. Almost all studies (n = 44; 92%) defined CKD as eGFR below 60 mL/min/1.73 m^2. Eighteen studies (38%) reported CKD prevalence defined as eGFR below 60 mL/min/1.73 m^2 and/or the presence of albuminuria >30 mg/g, and 15 studies (32%) reported CKD prevalence defined as albuminuria >30 mg/g. Although 10 studies (21%) additionally reported CKD according to another definition, only one study exclusively reported a CKD prevalence not defined by KDOQI.

The Modification of Diet in Renal Disease (MDRD) equation for unstandardized creatinine was used to estimate GFR in 22 studies (46%), and the MDRD equation for standardized creatinine was used in 14 studies (29%). Twenty-five studies (52%) used the CKD Epidemiology Collaboration (CKD-EPI) equation, and nine studies (19%) used the Cockcroft and Gault equation. Even though both the CKD-EPI and MDRD equations include an ethnicity variable, only 18 studies (38%) reported collecting ethnicity data. Eleven studies (23%) did not indicate whether ethnicity data were collected.

Reporting results. CKD prevalence reporting was the main objective in 36 publications, of which 39% reported a 95%CI. An age- and sex-standardized prevalence was reported in 12 studies (25%), of which 9 standardized to their national population. Although two studies standardized their population to the US population, only one study standardized to the European population. The presentation of CKD prevalence by strata was done by 31 studies, and these studies presented the CKD prevalence stratified per risk factor, mostly by age (n = 24; 50%) and by sex (n = 26; 54%).

DISCUSSION

We assessed 48 publications, published between 1 January 2003 and 1 November 2014, reporting CKD prevalence for the adult general population in 20 European countries. The results of this systematic literature review revealed considerable variation in general population sample selection methods and assessment of kidney function across studies. Moreover, often a clear description of the methods used was lacking, and the reporting of CKD prevalence was heterogeneous. These factors may have considerable influence on the prevalence estimates of CKD and need to be taken into account to allow comparison of CKD prevalence across studies.

Population sample selection

Although we restricted our search to studies that were designed to be representative of the general population, we observed great heterogeneity in population sample selection methods. Part of this variation was found in the sampling frame used to identify contact details of eligible subjects. The sampling frame should ideally include the entire target population [58], which in this case is the entire general population. National census or population registry data are ideal for sampling the general population; in principle, these should include all inhabitants of a country or region. However, general population surveys are typically limited to community-dwelling subjects who are physically and mentally capable to participate in such studies. At old age, a substantial proportion of those with age-related chronic diseases such as CKD may no longer fulfill these inclusion criteria, which may lead to substantial underestimation of the true prevalence of such diseases. In such circumstances, depending on the health system or country, general practitioner list- or registry-based approaches might be required to provide more valid estimates of true prevalence.

Additionally, there existed great variation in sample design. For example, some studies first performed stratification of population by age and sex, whereas others invited all inhabitants in the selected region. Both the sampling frame and

Table 1. Description of the method of general population sample selection per study

Author (Ref.)	Study name	Country	Time period	Number of subjects, *N*	Age range	Sampling frame	Sample design	Response, %
Aumann *et al.* [10]	SHIP	Germany	2001–6	2830	25–88	Not specified[a]	Multistage sampling	69
Bongard *et al.* [11]	MONA LISA	France	2006–7	4727	35–75	Electoral rolls	Age and sex stratified	Not given
Browne *et al.* [12]	SLAN	Ireland	2007	1098	45+	Other (Geo directory)	Multistage random sampling: by area and region	66
Capuano *et al.* [13]	VIP	Italy	1998–99 and 2008–9	2400	25–74	Electoral rolls	Age and sex stratified	Not given
Christensson *et al.* [14]	GAS	Sweden	2001–4	2815	60–93	Census	Stratified, age, sex and urban/rural location	60
Chudek *et al.* [15]	PolSenior	Poland	2007–11	3793	65+	Not specified[a]	Not specified[a]	32
Cirillo *et al.* [16]	Gubbio Population Study	Italy	Not specified	4574	18–95	Not specified[a]	Not specified[a]	Not given[a]
Codreanu *et al.* [17]	Early Detection and Intervention Program for Chronic Renal and Cardiovascular Disease in the Rep Moldova	Moldova	2006–7	973	18–77	Not specified	Not specified	Not given
De Nicola *et al.* [18]	CARHES	Italy	2008	4077	35–79	Electoral rolls	Age and sex stratified	45
Delanaye *et al.* [19]		Belgium	2008–9	1992	45–75	Not specified	Voluntary nature	Not given
Donfrancesco *et al.* [20]	MATISS	Italy	1993–96	2924	20–79	Electoral rolls	Age- and sex-stratified random sample	60
Formiga *et al.* [21]	Octabaix	Spain	2009	328	85	Not specified[a]	Not specified[a]	Not given
Fraser *et al.* [22]	HSE	England	2009–10	5799	16+	Other (address list)	Random two-stage sample	Not given[a]
Gambaro *et al.* [23]	INCIPE	Italy	2006	3629	40+	General practitioner list	Random sample	62
Gianelli *et al.* [24]	InChianti	Italy	1998–2000	676	65+	Not specified	Multistage stratified random sample	Not given
Goek *et al.* [25]	KORA	Germany	1999–1	1104	54–75	Not specified	Not specified	Not given
Gu *et al.* [26]	FLEMENGHO	Belgium	2005–10	797	18–89	Not specified	Not specified	78
Guessous *et al.* [27]	Swiss Study on Salt intake	Switzerland	2010–11	1145	15+	Other (phone directory)	Age- and sex-stratified random sample	10
Hallan *et al.* [28]	HUNT 2	Norway	1995–97	65 181	20+	Not specified	All inhabitants	70
Hernandez *et al.* [29]	IMAP	Spain	2007	2270	18–80	Not specified[a]	Random sample	Not given
Juutilainen *et al.* [30]	FINRISK	Finland	2002 and 2007	11 277	25–74	Census	Age- and sex-stratified random sample	71 in men 74 in women
Lieb *et al.* [31]	MONICA/KORA	Germany	Not specified	1187	25–74	Not specified	Age- and sex-stratified random sample	71
Meuwese *et al.* [32]	Leiden 85 + study	Netherlands	1997–99	558	85	Not specified	All in birth cohort	87
Nitsch *et al.* [33]	BWHHS	UK	1999–2001	3851	60–79	Not specified[a]	Random sample	60
Nitsch *et al.* [34]	SAPALDIA 2	Switzerland	1991 and 2002	6317	18+	Not specified[a]	Random sample	73
Otero *et al.* [35]	EPIRCE	Spain	2004–8	2746	20+	Census	Age-, sex- and region-stratified random sample	43
Pani *et al.* [36]	SardiNIA study	Italy	2001–	4471	14–102	Not specified[a]	Not specified[a]	56
Pattaro *et al.* [37]	MICROS	Italy	2002–3	1199	18+	Not specified[a]	Not specified[a]	Not given
Ponte *et al.* [38]	CoLaus	Switzerland	2003–6	5921	35–75	Population registry	Random sample	41
Redon *et al.* [39]	PREV-ICTUS	Spain	2005	6419	60+	General practitioner lists	Random sample	72
Robles *et al.* [40]	HERMEX	Spain	Not specified	2813	25–79	Other (health-care system database)	Age- and sex-stratified random sample	83
Roderick *et al.* [41]	MRC Older Age Study	UK	1994–99	13 179	75+	General practitioner list	Practices stratified by mortality score and deprivation score	73
Rothenbacher *et al.* [42]	ActiFE Ulm	Germany	2009–10	1471	65+	Census	Random sample	20
Rutkowski *et al.* [43]	PolNef	Poland	2004–5	2476	n/a	Other (address list)	Random sample	26
Sahin *et al.* [44]		Turkey	2005	1079	18–95	Not specified	Age, sex and region stratified	Not given
Schaeffner *et al.* [45]	BIS	Germany	2011	570	70+	Not specified[a]	Not specified[a]	Not given

Scheven *et al.* [46]	PREVEND	The Netherlands	1997–98	8121	28–75	Not specified	All inhabitants	48
Stasevic *et al.* [47]		Kosovo + Metohia	2006	423	18+	Not specified	All inhabitants	43
Stengel *et al.* [48]	3C	France	1991–2001	8705	65+	Electoral rolls	Random sample	37
Suleymanlar *et al.* [49]	CREDIT	Turkey	Not specified	10 056	18+	Not specified	Age, sex and region stratified	Not given
Tavira *et al.* [50]	RENASTUR	Spain	2010–12	592	55–85	Not specified	Random sample	Not given
Van Pottelbergh *et al.* [51]	Crystal	Russia	2009	611	65–91	General practitioner list	All registered on list	66
Viktorsdottir *et al.* [52]	RHS	Iceland	1967–96	19 256	33–85	Not specified	All in birth cohort	Not given
Vinhas *et al.* [53]	PREVADIAB	Portugal	2008–9	5167	20–79	Other (universal health card)	Age, sex and region stratified	84
Wasen *et al.* [54]		Finland	1998–99	1246	64–100	Not specified	All residents born ≤1933	83
Wetmore *et al.* [55]		Iceland	2001–3	1630	18+	Not specified	Random sample	71
Zambon *et al.* [56]	ProV.A.	Italy	1995–97	3063	65+	Other (health district registries)	Age- and sex-stratified random sample	77 in men 64 in women
Zhang *et al.* [57]	ESTHER	Germany	2000–2	9806	50–74	General practitioners	All participants who underwent a general health check-up	Not given

N, Number of subjects with creatinine measurement; n/a, not applicable.
[a]Authors refer to previous publication.

sample design influence the response and non-response bias [58], which in turn may influence the representativeness of the resulting sample for the general population and consequently of the CKD prevalence estimate. Collecting information on non-responders may help to assess the possibility and likely direction of non-response bias [58].

Assessment of kidney function

Serum creatinine and albuminuria measurements. There was great variation in the laboratory methods used in studies that reported details of those methods, especially in the calibration of serum creatinine. Differences in creatinine assays are important to take into account in CKD prevalence comparisons, as Jaffe methods overestimate serum creatinine and therefore overestimate CKD prevalence [59]. In 2006, IDMS standardization has been implemented to reduce the systematic bias in creatinine determination and to increase inter laboratory comparability [7]. The publications that clearly reported the use of IDMS standardization were only published in 2010 or later.

Ethnicity. In equations used to estimate GFR, like MDRD and CKD-EPI, the variable 'ethnicity' is included to adjust for ethnicity-specific differences. Ethnicity may, therefore, influence CKD prevalence estimates; even so, less than half of the publications reported collection of ethnicity data. Since in most European countries the vast majority of the European population is Caucasian, the lack of ethnicity data is unlikely to influence the CKD prevalence of most countries. In the future, however, the proportion of Caucasian subjects in the European population may change, making the collection of ethnicity data more important.

CKD definition. Despite the KDOQI guideline on CKD that was published in 2002 [5] and updated by Kidney Disease Improving Global Outcomes (KDIGO) in 2012 [60], we observed great variation in the definition of CKD, both in eGFR equations used and in cut-off values for both eGFR and albuminuria. For future studies, it is advisable to report CKD as recommended in the updated KDIGO guideline, including six eGFR categories and three albuminuria categories, as this classification allows presentation by mortality and progression risk [61]. The chronicity criterion was never used, mainly because follow-up data on serum creatinine were not collected. In more recent studies, CKD was most commonly defined using the CKD-EPI equation, as recommended by KDOQI [5].

Reporting methods

A clear description of the population sample selection methods and assessment of kidney function may facilitate a more fair comparison of CKD prevalence across studies. Studies should, therefore, preferably report this in detail in the method section of their publication. Unfortunately, many studies did not report the sampling frame used. In addition, information about biological sample collection (e.g. nature of collecting procedure, participants conditions, time between sampling and further processing) and sample storage conditions (duration of storage, thawing cycles, etc.) should also be reported [62].

Table 2. Laboratory assessment of kidney function, CKD definition used and details on the reporting of CKD prevalence per study

Author (Ref.)	Creatinine assay	IDMS	Albuminuria	CKD definition	eGFR equation	Ethnicity	CI	Age and sex standardized	Stratified prevalence
Aumann *et al.* [10]	Jaffe	Other	n/a	2	CKD-EPI + other	Yes	n/a	No	Yes: other
Bongard *et al.* [11]	Jaffe	No	n/a	2	MDRD (old)	No	Yes	Yes to national pop.	No
Browne *et al.* [12]	Modified Jaffe	Yes	Other	1 + 2	CKD-EPI + new MDRD	No	Yes	Yes to national pop.	Yes: age, sex and other
Capuano *et al.* [13]	Modified Jaffe	No	n/a	2	CG	No	No	Yes to national pop.	Yes: age, sex and other
Christensson *et al.* [14]	Unclear	Other	n/a	Other	CKD-EPI, MDRD (old) + CG	Yes	No	No	Yes: age and sex
Chudek *et al.* [15]	Jaffe	Unclear	If dipstick − → immunoassay	1 + 2 + 3	CKD-EPI	No	No	No	Yes: age, sex and other
Cirillo *et al.* [16]	Modified Jaffe	No	Immunoassay	2	MDRD (old)	Yes	Yes for *N* Not for %	Yes to national pop.	Yes: age and sex
Codreanu *et al.* [17]	Unclear	No	Other	2 + 3	MDRD (old)	No	No	No	Yes: age, sex and other
De Nicola *et al.* [18]	Enzymatic	Yes	Immunoassay	1 + 2 + 3	CKD-EPI	No	Yes	No	No
Delanaye *et al.* [19]	Compensated Jaffe	Yes	n/a	2	CKD-EPI + new MDRD	No	No	No	Yes: sex
Donfrancesco *et al.* [20]	Enzymatic	Yes	n/a	2	CKD-EPI	No	No	No	Yes: sex
Formiga *et al.* [21]	Compensated Jaffe	No	n/a	2	MDRD (old)	No	No	No	No
Fraser *et al.* [22]	Enzymatic	Yes	Not specified	1 + 2 + 3 + other	CKD-EPI + new MDRD	Yes	No	Unclear	Yes: other
Gambaro *et al.* [23]	Modified Jaffe	Other	If dipstick + → immunoassay	1 + 2 + 3	CKD-EPI	Yes	Yes	Yes to US pop.	Yes: age, sex and other
Gianelli *et al.* [24]	Modified Jaffe	No	n/a	2	MDRD (old) and CG	No	No	No	No
Goek *et al.* [25]	Compensated Jaffe	Unclear	n/a	2	CKD-EPI	No	n/a	No	No
Gu *et al.* [26]	Modified Jaffe	Unclear	Not specified	2	CKD-EPI + MDRD (old)	No	No	No	No
Guessous *et al.* [27]	Compensated Jaffe	Unclear	Unclear	1	CKD-EPI	Yes	n/a	No	No
Hallan *et al.* [28]	Jaffe	Other	Immunoassay	1 + 2 + 3	New MDRD	Yes	Yes	Yes to national + US pop.	Yes: age, sex and other
Hernandez *et al.* [29]	Not specified	Unclear	Not specified	1 + other	CKD-EPI	Yes	n/a	No	Yes: other
Juutilainen *et al.* [30]	Enzymatic	Yes	n/a	2 + other	CKD-EPI + new MDRD	No	no	No	Yes: age and sex
Lieb *et al.* [31]	Enzymatic	No	Immunoassay	3 + other	MDRD (old)	No	n/a	No	No
Meuwese *et al.* [32]	Jaffe	No	n/a	2	CKD-EPI + MDRD (old)	No	n/a	No	No
Nitsch *et al.* [33]	Modified Jaffe	Other	n/a	2	MDRD (old)	Yes	n/a	No	Yes: other
Nitsch *et al.* [34]	Jaffe	Other	n/a	2	MDRD (old) and CG	Yes	Yes	No	Yes: age and sex
Otero *et al.* [35]	Unclear	Unclear	Unclear	1 + 2	MDRD (old)	Yes	Yes	Yes to national pop.	Yes: age, sex and other
Pani *et al.* [36]	Not specified	Other	Not specified	1 + 2 + 3	CKD-EPI + new MDRD	No	Yes	No	Yes: age and sex
Pattaro *et al.* [37]	Enzymatic	Yes	n/a	2	CKD-EPI, new MDRD + other	No	Yes	No	Yes: age
Ponte *et al.* [38]	Compensated Jaffe	Yes	Immunoassay	1 + 2 + 3	CKD-EPI + new MDRD	Yes	Yes	No	Yes: age and sex
Redon *et al.* [39]	Jaffe	Yes	Immunoassay	2	CG	No	n/a	No	No
Robles *et al.* [40]	Modified Jaffe + enzymatic	No	Dipstick	2 + other	CKD-EPI + new MDRD	Yes	Yes	Yes to EU pop.	Yes: age and sex
Roderick *et al.* [41]	Modified Jaffe	Yes	Immunoassay	2 + other	MDRD (old)	No	Yes	No	Yes: age and sex
Rothenbacher *et al.* [42]	Modified Jaffe	No	If dipstick + → immunoassay	1 + 2 + 3	CKD-EPI + new MDRD	No	No	No	Yes: age and sex
Rutkowski *et al.* [43]	Modified Jaffe	Unclear	n/a	1 + 2 + 3	MDRD (old)	No	No	No	No

Sahin *et al.* [44]	Enzymatic	Yes	Not specified	2	New MDRD	No	No	No	Yes: age, sex and other
Schaeffner *et al.* [45]	Unclear	Unclear	Immunoassay	2	CKD-EPI + other	Yes	n/a	No	No
Scheven *et al.* [46]	Modified Jaffe	Unclear	If dipstick + → immunoassay	1 + 2 + 3	CKD-EPI	No	n/a	No*	No
Stasevic *et al.* [47]	Jaffe	Yes	Unclear	2 + 3 + other	MDRD (old)	No	No	No	No
Stengel *et al.* [48]	Jaffe	Yes[a]	Immunoassay	1 + 2	CKD-EPI + new MDRD	No	No	No	Yes: age and sex
Suleymanlar *et al.* [49]	Not specified	No	Not specified	1 + 2 + 3	MDRD (old)	Yes	No	Yes to national pop.	Yes: age and sex
Tavira *et al.* [50]	Modified Jaffe	No	n/a	2	MDRD (old)	Yes	n/a	No	No
Van Pottelbergh *et al.* [51]	Modified Jaffe	No	Dipstick	2	MDRD (old) and CG	No	No	No	Yes: age and sex
Viktorsdottir *et al.* [52]	Modified Jaffe	No	n/a	1 + 2 + 3	MDRD (old) and CG	Yes	No	Yes to global pop.	Yes: age and sex
Vinhas *et al.* [53]	Jaffe	Unclear	Immunoassay	2	MDRD (old)	No	Yes	Yes to national pop.	Yes: age, sex and other
Wasen *et al.* [54]	Unclear	Yes	n/a	2 + other	New MDRD and CG	No	No	No	Yes per sex
Wetmore *et al.* [55]	Jaffe	Other	Dipstick	2	New MDRD and CG	Yes	No	No	No
Zambon *et al.* [56]	Modified Jaffe	No	Immunoassay	2 + other	CKD-EPI and MDRD (old)	Yes	n/a	Yes to national pop.	No
Zhang *et al.* [57]	Modified Jaffe	Other	n/a	2 + other	MDRD (old)	No	No	No	Yes: age, sex and other

Albuminuria = method of albuminuria measurement; CKD definition 1 = eGFR below 60 mL/min/1.73 m^2 and or the presence of albuminuria >30 mg/g (i.e. CKD Stages 1–5); 2 = eGFR below 60 mL/min/1.73 m^2 (i.e. CKD Stages 3–5); 3 = albuminuria >30 mg/g. Ethnicity = 'yes' if collection is reported; 'no' if not reported or not collected. CI, confidence interval given for prevalence estimate; CG, Cockcroft and Gault equation; n/a, not applicable.

[a]In order to standardize creatinine values, 1720 frozen serum samples were remeasured in a single laboratory with an IDMS-traceable enzymatic assay. Hereafter, equations relating the Jaffe and IDMS-traceable creatinine were developed to standardize all baseline values as follows: ScrIDMS = 0.86 × ScrJaffe + 4.40. *Population corrected for sampling design (i.e. oversampling of albuminuria).

Reporting results

Another observed difference was the presentation of the results on CKD prevalence estimates. Part of this variation is likely explained by the fact that CKD prevalence was not the main focus of 12 publications. However, even in publications with the main focus on CKD prevalence, there was great variation in reporting. All studies did report unadjusted prevalence estimates, yet they were mostly reported without a 95%CI. The reporting of the 95%CI is necessary as it provides an indication of how much uncertainty there is in the prevalence estimate.

Future studies should preferably report CKD prevalence standardized to the European population to enable international comparison, at least across Europe. In the case of regional prevalence estimates, additional standardization to the national population is required for within-country comparison. This standardization is essential when comparing CKD prevalence estimates from different countries or regions to avoid the influence of differences in national or regional age and sex distributions.

European CKD Burden Consortium

In 2012, the European CKD Burden Consortium was established, including both nephrologists and epidemiologists, to enhance comparability of CKD prevalence across European regions and countries.

Box 1 provides an overview of the methodology used by the European CKD Burden Consortium to compare CKD prevalence results across different general population-based studies in Europe. This methodology facilitates comparability by providing a detailed description of the population selection method and the response of each study to help assess representativeness of the study population sample. Additionally, the figures and tables clearly show the serum creatinine method used (i.e. Jaffe versus enzymatic) and whether IDMS calibration standardization was used.

Furthermore, a uniform definition of CKD based on the KDIGO guideline was established [60]. CKD was defined as the presence of albuminuria >30 mg/g and/or an eGFR of <60 mL/min/1.73 m^2 as calculated by the CKD-EPI equation. The chronicity criterion was not applied, for none of the assessed general population-based studies had this available.

The Consortium will additionally harmonize reporting of results in their publications. All CKD prevalence estimates will be presented as unadjusted rates and standardized to the EU27 population of 2005 [63] and include a 95%CI. As the occurrence of CKD is associated with age and not all study populations cover the entire range of the adult population, the CKD prevalence will also be presented for different age ranges, i.e. 20–44, 45–64, 65–74 and 75–84 years. Additionally, the prevalence estimates will be presented with stratification for the presence of the following risk factors: diabetes, hypertension and obesity. This stratification is useful to determine if differences in CKD prevalence are caused by differences in risk factor presence or differences in overall health status of the general population. Whether disparities in CKD prevalence are explained by important risk factors for CKD will guide policy makers to focus on secondary or primary prevention.

Box 1: Recommended methodology for comparison of CKD prevalence results across general population-based studies as used by European CKD Burden Consortium

Recommended tools	Details
1. General population sampling	
Sampling methods	Describe: – sampling frame, i.e. source used to identify subjects – sample design, i.e. method of subject selection (e.g. age stratified, random)
Response	Report the response in percentages
2. Assessment of kidney function	
Serum creatinine assay	Describe assay used, i.e. Jaffe or enzymatic
Albuminuria assay	Describe assay used, e.g. immunoassay and dipstick
IDMS calibration standardization	Describe if IDMS calibration standardization was used (yes/no)
CKD definition	Use of the same definition of CKD: CKD Stages 1–5: eGFR < 60mL/min/1.73 m^2 calculated by the CKD-EPI equation, and/or ACR > 30 mg/g. CKD Stages 3–5: eGFR < 60mL/min/1.73 m^2 calculated by CKD-EPI equation.
3. Presentation of results	
CKD prevalence estimate	Report: – unadjusted and adjusted CKD prevalence (e.g. standardized to the EU27 population) – 95%CI
CKD prevalence estimate by strata	Report: – stratified by age groups: 20–44, 45–64, 65–74 and 75–84 years – stratified by diabetic, hypertension and obesity status
Serum creatinine determination	Indicate in tables and figures which studies use: – Jaffe or enzymatic assay – IDMS calibration standardization

Implications

This systematic literature review revealed considerable variation in general population sample selection methods and assessment of kidney function across studies. In addition, a clear description of the methods used was often lacking, and the reporting of CKD prevalence was heterogeneous. The approach of The European CKD Burden Consortium will not eliminate the differences in population selection methods and laboratory assessment of kidney function. However, the recommendations regarding the reporting of both methods and results of CKD prevalence studies may enhance comparability of CKD prevalence results across Europe and even worldwide [64]. Our recommendations may be used by investigators to optimize both the design and the reporting of future CKD prevalence studies.

SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

CONFLICT OF INTEREST STATEMENT

The authors hereby declare that the results presented in this article have not been published previously in whole or part, except in abstract format.

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