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CHAPTER 2:

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

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on behalf of the European CKD Burden Consortium

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ABSTRACT

Background

Many publications report chronic kidney disease (CKD) prevalence 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 reporting the prevalence of CKD in the European adult general population, which were published between January first 2003 and November first 2014. 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 dilute mass spectrometry calibration was used in 29%. The CKD-EPI (52%) and MDRD (75%) equation were most often used to estimate Glomerular Filtration Rate (eGFR). CKD was defined as eGFR <60 ml/min/1.73m² in 92% of studies. Urinary markers of CKD were assessed in 60% of studies. CKD prevalence was reported by sex and age strata in 54% and 50% of 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.

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 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 1) identify all studies reporting on CKD prevalence in the European adult general population and 2) 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 KDOQI published a guideline on CKD definition (5) in 2002, we included articles published since January 1st 2003 which is one year after the publication of the KDOQI guideline. Our search was last updated on November 1st 2014. The database-specific search queries are presented in appendix 1. 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 were included that presented original research, were designed to select a representative sample of a European adult general population and reported a CKD prevalence estimate. We excluded studies which ended subject recruitment prior to 1996 and studies lacking GFR estimation based on serum creatinine. Cystatin C-based eGFR will

lead to higher CKD prevalence estimates than creatinine-based eGFR (6). For the sake of comparability we chose not to include publications which 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:

1. 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).
2. Calibration was categorized as calibrated to the standardized isotope dilution mass spectrometry (IDMS) or calibrated by another method or calibrator.
3. Urinary albumin assay was categorized as dipstick, immunoassay (including both nephelometric and turbidometric immunoassays) or other.
4. 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.
5. Ethnicity reporting was categorized as “yes” if publication reported collection of ethnicity data and as “no” if ‘ethnicity’ data was not collected or if this was 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 appendix 2.

RESULTS

Study selection

Figure 1 shows the selection process of in- and ex-clusion of publications in a flow chart. We retrieved 2000 individual publications of which only one study was solely identified through contacting national representatives. 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, nine studies were excluded as they ended recruitment prior to 1996 and forty-two 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 forty-eight 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 twelve 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 which did not report a response, two 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

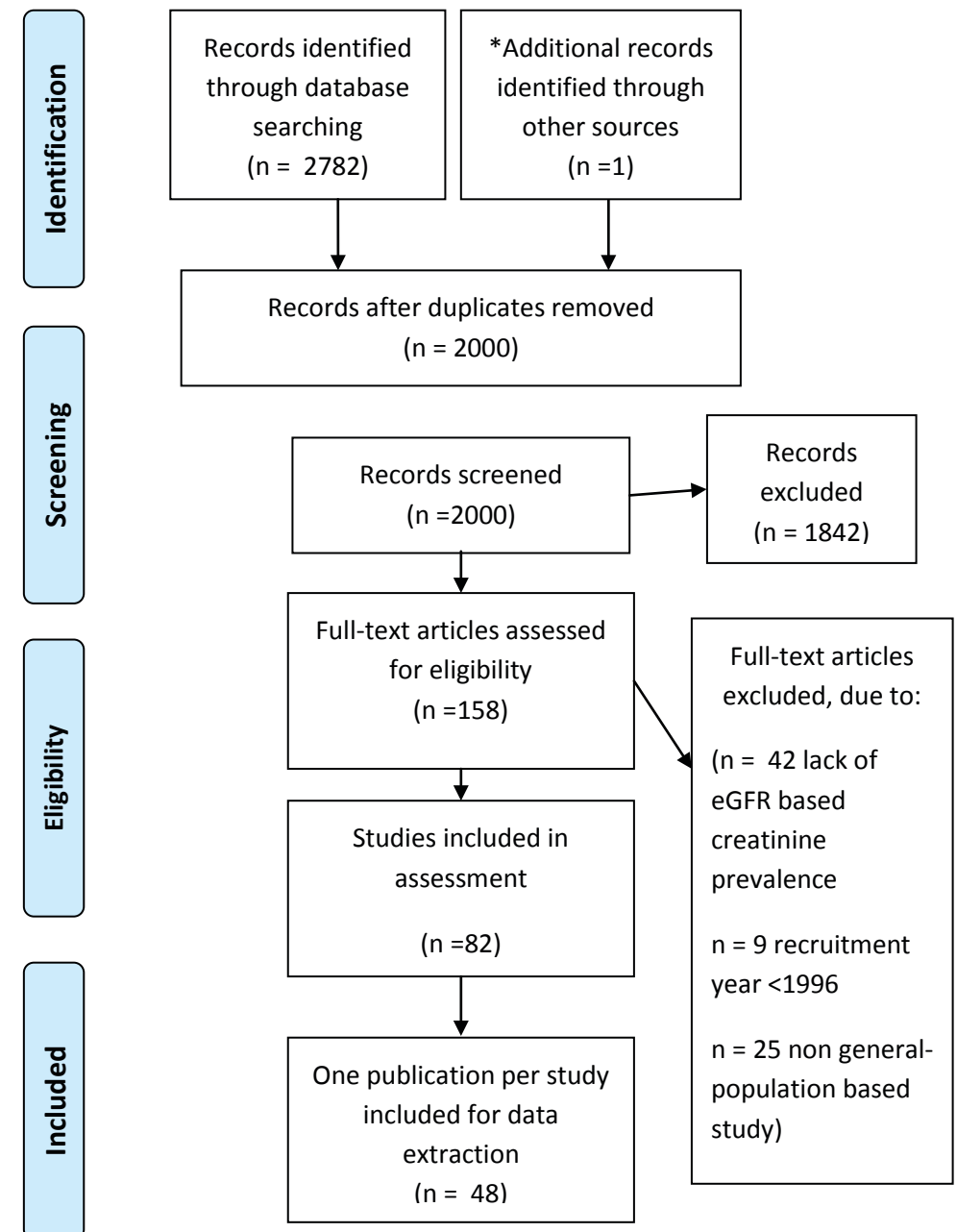
Almost all studies (n=44; 92%) defined CKD as an eGFR below 60 ml/min/1.73m². Eighteen studies (38%) reported CKD prevalence defined as eGFR below 60 ml/min/1.73m² and/or the presence of albuminuria >30mg/g and 15 studies (32%) reported CKD prevalence defined as albuminuria >30mg/g. Although ten studies (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 & Gault equation. Even though both the CKD-EPI and MDRD equation 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 nine 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, these studies presented the CKD prevalence stratified per risk factor, mostly by age (n=24; 50%) and by sex (n=26; 54%).

Figure 1: Flow chart of publication selection.



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

Table 1: Description of the method of general population sample selection per study. (Part 1)

First author, (ref)	Study	Country	Time period	N	Age range	Sample frame	Sample design	Response
Aumann, (17)	SHIP	Germany	2001-06	2830	25-88	ns	multistage sampling	69%
Bongard, (18)	MONA LISA	France	2006-07	4727	35-75	electoral rolls	age and sex stratified	ns
Browne, (19)	SLAN	Ireland	2007	1098	45+	other (Geo-directory)	multi-stage random sample: by area & region	66%
Capuano, (20)	VIP	Italy	1998-99 2008-09	2400	25-74	electoral rolls	age and sex stratified	ns
Christensson, (21)	GAS	Sweden	2001-04	2815	60-93	census	stratified, age, sex & urban/rural location	60%
Chudek, (22)	PolSenior	Poland	2007-11	3793	65+	ns*	ns*	32%
Cirillo, (23)	Gubbio Pop.	Italy	ns	4574	18-95	ns*	ns*	ns
Codreanu, (24)	**	Moldova	2006-07	973	18-77	ns	ns	ns
De Nicola, (25)	CARHES	Italy	2008	4077	35-79	electoral rolls	age and sex stratified	45%
Delanaye, (26)		Belgium	2008-09	1992	45-75	ns	voluntary nature	ns
Donfrancesco,(27)	MATISS	Italy	1993-96	2924	20-79	random sample	age and sex stratified	60%
Formiga, (28)	Octabaix	Spain	2009	328	85	ns*		ns
Fraser, (29)	HSE	England	2009-10	5799	16+	random 2 stage sample		ns*
Gambaro, (30)	INCIPE	Italy	2006	3629	40+	GP list	random sample	62%

N= Number of subjects with creatinine measurement; ns= not specified. Gubbio Pop.=Gubbio population Study. *authors refer to previous publication. **Early Detection and Intervention Program for Chronic Renal and Cardiovascular Disease in Rep Moldova.

Table 1: (continued).

Gianelli, (31)	InChianti	Italy	1998-2000	676	65+	ns	multistage stratified random sample	ns
Goek, (32)	KORA	Germany	1999-2001	1104	54-75	ns	ns	ns
Gu, (33)	FLEMINGHO	Belgium	2005-10	797	18-89	ns	ns	78%
Guessous, (34)	Swiss Study on	Switzerland	2010-11	1145	15+	other	age and sex stratified random sample	10%
Hallan, (35)	HUNT 2	Norway	1995-97	65181	20+	ns		70%
Hernandez, (36)	IMAP	Spain	2007	2270	18-80	ns*		ns
Juutilainen, (37)	FINRISK	Finland	2002 & 2007	11277	25-74	census	age and sex stratified random sample	74% women 71% men
Lieb, (38)	MONICA/KORA	Germany	ns	1187	25-74	ns	age and sex stratified random sample	71%
Meuwese, (39)	Leiden 85+ study	Netherlands	1997-99	558	85	ns	all in birth cohort	87%
Nitsch, (40)	BWHH	UK	1999-2001	3851	60-79	ns*	random sample	60%
Nitsch, (41)	SAPALDIA 2	Switzerland	1991 & 2002	6317	18+	ns*	rom sample	73%
Otero, (42)	EPIRCE	Spain	2004-08	2746	20+	census	age, sex & region stratified random sample	43%
Pani, (43)	SardinIA study	Italy	2001-	4471	14-102	ns*	ns*	56%
Pattaro, (44)	MICROS	Italy	2002-03	1199	18+	ns*	ns*	ns

N= Number of subjects with creatinine measurement; ns= not specified. *authors refer to previous publication.

Table 1: Description of the method of general population sample selection per study. (Part 2)

First author, (ref)	Study	Country	Time period	N	Age range	Sample frame	Sample design	Response
Ponte, (45)	CoLaus	Switzerland	2003-06	5921	35-75	population registry	random sample	41%
Redon, (46)	PREV-ICTUS	Spain	2005	6419	60-	GP lists	random sample	72%
Robles, (47)	HERMEX	Spain	ns	2813	25-79	other	age and sex stratified random sample	83%
Roderick, (48)	MRC	United Kingdom	1994-99	13179	75+	GP list	practices stratified by mortality score & deprivation score	73%
Rothenbacher, (49)	ActiFE Ulm	Germany	2009-10	1471	65+	census	random sample	20%
Rutkowski, (50)	PolNef	Poland	2004-05	2476	ns	other	random sample	26%
Sahin, (51)		Turkey	2005	1079	18-95	ns	age, sex & region stratified	ns
Schaeffner, (52)	BIS	Germany	2011	2072°	70+	ns*	ns*	ns
Scheven, (53)	PREVEND	NL	1997-98	8121	28-75	ns	all inhabitants	48%
Stasevic, (54)		Kosovo & Metohia	2006	423	18+	ns	all inhabitants	43%
Stengel, (55)	3C	France	1991-2001	8705	65 +	electoral rolls	random sample	37%
Suleymanlar, (56)	CREDIT	Turkey	ns	10056	18+	ns	age, sex & region stratified	ns

N= Number of subjects with creatinine measurement, ns= not specified. *authors refer to previous publication. °CKD prevalence was only reported for subgroup (N=570).

Table 1: (continued).

Tavira, (57)	RENASTUR	Spain	2010-12	592	55-85	ns	random sample	ns
Van Pottelbergh, (58)	Crystal	Russia	2009	611	65-91	GP list	all registered on list	66%
Viktorsdottir, (59)	RHS	Iceland	1967-96	19256	33-85	ns	all in birth cohort	ns
Vinhas, (60)	PREVADIAB	Portugal	2008-09	5167	20-79	other	age, sex and region stratified	84%
Wasen, (61)		Finland	1998-99	1246	64-100	ns	all residents born <= 1933	83%
Wetmore, (62)		Iceland	2001-03	1630	18 +	ns	random sample	71%
Zambon, (63)	ProV.A.	Italy	1995-97	3063	65+	other	age & sex stratified random sample	64% women 77% men
Zhang, (64)	ESTHER	Germany	2000-02	9806	50-74	GP list	not specified	ns

N= Number of subjects with creatinine measurement, ns= not specified. *authors refer to previous publication. RHS=Reykjavik Heart Study.

DISCUSSION

We assessed 48 publications, published between 1st of January 2003 and 1st of 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 which 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 (10) which in this case is the entire general population. National census or population registry data are ideal for sampling the general population, for in principal 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 sample design influence the response and non-response bias (10), 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 (10).

Assessment of kidney function

Serum creatinine and albuminuria measurements

There was great variation in the laboratory methods used in studies which 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

(11). In 2006 IDMS standardization has been implemented to reduce the systematic bias in creatinine determination and to increase inter-laboratory comparability (7). The publications which 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 which was published in 2002 (5) and updated by KDIGO in 2012 (12), 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 (13). 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), sample storage conditions (duration of storage, thawing cycles, etc.) should also be reported (14).

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 case of regional prevalence estimates, additionally 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 vs enzymatic) and whether IDMS calibration standardization was used.

Furthermore, a uniform definition of CKD, based on the KDIGO guideline was established (12). CKD was defined as the presence of albuminuria $>30\text{mg/g}$ and/or an eGFR $<60\text{ ml/min/1.73 m}^2$ 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 (15), 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 the 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 etc.)
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, dipstick etc.
IDMS calibration standardization	Describe if IDMS calibration standardization was used (yes/ no)
CKD definition	Use of the same definition of CKD: <u>CKD stage 1-5:</u> eGFR $<60\text{ml/min/1.73m}^2$ calculated by the CKD-EPI equation and /or ACR $> 30\text{mg/g}$ <u>CKD stage 3-5:</u> eGFR $<60\text{ml/min/1.73m}^2$ calculated by the CKD- EPI equation
3.Presentation of results	
CKD prevalence estimate	Report: - unadjusted and adjusted CKD prevalence (e.g. standardized to the EU27 population) - 95% confidence interval
CKD prevalence estimate by strata	Report: - stratified by age group: 20-44, 45-64, 65-74 & 75-84 years - stratified by diabetic, hypertension, and obesity status
Serum creatinine determination	Indicate in tables & figures which studies use: - Jaffe or enzymatic assay - IDMS calibration standardization

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

First author	Creatinine method	IDMS	Albuminuria method	CKD def.	eGFR equation	Ethnicity	CI	Age & sex stand. prevalence	Stratified prevalence
Aumann	Jaffe	Other	n/a	2	CKD-EPI + Other	Yes	n/a		Yes: Other
Bongard	Jaffe	No	n/a	2	MDRD (old)	No	Yes	Yes to national pop.	No
Browne	Modified Jaffe	Yes	Other	1 + 2	CKD-EPI + new MDRD	Unclear	Yes	Yes to national pop.	Yes: age, sex, & other
Capuano	Modified Jaffe	No	n/a	2	CG	No	No	Yes to national pop.	Yes: age, sex & other
Christensson	Unclear	Other	n/a	Other	CKD-EPI, MDRD (old) & CG	Yes	No	No	Yes: age & sex
Chudek	Jaffe	Unclear	Dipstick - → Immunoassay	1+2+3	CKD-EPI	No	No	No	Yes: age, sex & other
Cirillo	Modified Jaffe	No	Immunoassay	2	MDRD (old)	Yes	N;Yes %;No	Yes to national pop.	Yes: age & sex
Codreanu	Unclear	No	Other	2 + 3	MDRD (old)	No	No	No	Yes: age, sex & other
De Nicola	Enzymatic	Yes	Immunoassay	1+2+3	CKD-EPI	No	Yes	No	No
Delanaye	Compensated Jaffe	Yes	n/a	2	CKD-EPI + new MDRD	Unclear	No	No	Yes: sex
Donfrancesco	Enzymatic	Yes	n/a	2	CKD-EPI	No	No	No	Yes: sex
Formiga	Compensated Jaffe	No	n/a	2	MDRD (old)	No	No	No	No
Fraser	Enzymatic	Yes	ns	1+2+3 +other	CKD-EPI + new MDRD	Yes	No	Unclear	Yes: Other
Gambaro	Modified Jaffe	Other	if Dipstick + → Immunoassay	1+2+3	CKD-EPI	Yes	Yes	Yes to US pop	Yes: age, sex & other

Table 2: (continued).

Gianelli	Modified Jaffe	No	n/a	2	MDRD (old) and CG	No	No	No	No
Goek	Comp Jaffe	Unclear	n/a	2	CKD-EPI	Unclear	n/a	No	No
Gu	Modified Jaffe	Unclear	ns	2	CKD-EPI + MDRD (old)	No	No	No	No
Guessous	Comp Jaffe	Unclear	Unclear	1	CKD-EPI	Yes	n/a	No	No
Hallan	Jaffe	Other	Immunoassay	1+2+3	new MDRD	Yes	Yes	Yes to national pop & US pop	Yes: age, sex & other
Hernandez	ns	Unclear	ns	1&other	CKD-EPI	Yes	n/a	No	Yes: Other
Juutilainen	Enzymatic	Yes	n/a	2&other	CKD-EPI + new MDRD	Unclear	No	No	Yes: age & sex
Lieb	Enzymatic	No	Immunoassay	3	MDRD (old)	Unclear	n/a	No	No
Meuwes	Jaffe	No	n/a	2	CKD-EPI + MDRD (old)	No	n/a	No	No
Nitsch	Modified Jaffe	Other	n/a	2	MDRD (old)	Yes	n/a	No	Yes: Other
Nitsch	Jaffe	Other	n/a	2	MDRD (old) and CG	Yes	Yes	No	Yes: age & sex
Otero	Unclear	Unclear	Unclear	1 + 2	MDRD (old)	Yes	Yes	Yes to national pop.	Yes: age, sex & other
Pani	ns	Other	ns	1+2+3	CKD-EPI + new MDRD	No	Yes	No	Yes: age & sex
Pattaro	Enzymatic	Yes	n/a	2	CKD-EPI, new MDRD + Other	Unclear	Yes	No	Yes: age
Ponte	Comp Jaffe	Yes	Immunoassay	1+2+3	CKD-EPI + new MDRD	Yes	Yes	No	Yes: age & sex

CKD def.= CKD definition 1= CKD stage 1-5; 2= eGFR < 60 ml/min/1.73m²; 3= albuminuria >30mg/g. Ethnicity= 'yes' if collection is reported; 'no' if not reported or not collected. CI= confidence interval given for prevalence estimate, stand.=standardized, CG= Cockcroft and Gault equation, n/a= not applicable.

Table 2: (continued).

First author	Creatinine method	IDMS	Albuminuria method	CKD def.	eGFR equation	Ethnicity	CI	Age & sex stand. prevalence	Stratified prevalence
Redon	ns	Unclear	n/a	2	CG	No	n/a	No	No
Robles	Jaffe	Yes	Immunoassay	2 + Other	CKD-EPI + new MDRD	Yes	Yes	Yes to EU pop	Yes: age & sex
Roderick	Modified Jaffe & Enzymatic	No	Dipstick	2 + Other	MDRD (old)	No	Yes	No	Yes: age & sex
Rothenbacher	Modified Jaffe	Yes	Immunoassay	1+2+3	CKD-EPI + new MDRD	Unclear	No	No	Yes: age and sex
Rutkowski	Modified Jaffe	No	if Dipstick + → Immunoassay	1+2+3	MDRD (old)	No	No	No	No
Sahin	Modified Jaffe	Unclear	n/a	2	new MDRD	No	No	No	Yes: age, sex & other
Schaeffner	Enzymatic	Yes	ns	2	CKD-EPI + Other	Yes	n/a	No	No
Scheven	Unclear	Unclear	Immunoassay	1+2+3	CKD-EPI	Unclear	n/a	No*	No
Stasevic	Modified Jaffe	Unclear	if Dipstick + → Immunoassay	2 + 3 + Other	MDRD (old)	No	No	No	No
Stengel	Jaffe	Yes ¹	Unclear	1 + 2	CKD-EPI + new MDRD	No	No	No	Yes: age and sex
Suleymanlar	Jaffe	No	Immunoassay	1+2+3	MDRD (old)	Yes	No	Yes to national pop.	Yes: age and sex
Tavira	ns	No	ns	2	MDRD (old)	Yes	n/a	No	No
Van Pottelbergh	Modified Jaffe	No	n/a	2	MDRD (old) and CG	Unclear	No	No	Yes: age and sex
Viktorsdottir	Modified Jaffe	No	Dipstick	1+2+3	MDRD (old) and CG	Yes	No	Yes to global pop	Yes: age and sex

Table 2. (continued).

Vinhas	Modified Jaffe	No	n/a	2	MDRD (old)	Unclear	Yes	Yes to national pop.	Yes: age, sex & other
Wasen	Jaffe	Unclear	Immunoassay	2 + Other	new MDRD and CG	No	No	No	Yes per sex
Wetmore	Unclear	Yes	n/a	2	new MDRD and CG	Yes	No	No	No
Zambon	Jaffe	Other	Dipstick	2 + Other	CKD-EPI and MDRD (old)	Yes	n/a	Yes to national pop.	No
Zhang	Modified Jaffe	No	Immunoassay	2 + Other	MDRD (old)	Unclear	No	No	Yes: age, sex & other

CKD def.= CKD definition 1= CKD stage 1-5; 2= eGFR < 60 ml/min/1.73m²; 3= albuminuria >30mg/g. Ethnicity= 'yes' if collection is reported; 'no' if not reported or not collected. CI= confidence interval given for prevalence estimate. stand.=standardized, CG= Cockcroft and Gault equation, n/a= not applicable.¹ In order to standardize creatinine values, 1720 frozen serum samples were remeasured in a single laboratory with an isotope dilution mass spectrometry (IDMS) traceable enzymatic assay. Hereafter equations relating the Jaffe and IDMS-traceable creatinine were developed to standardized all baseline values as follows: ScrIDMS= 0.86 x ScrJaffe + 4.40. *Population corrected for sampling design (i.e. oversampling of albuminuria).

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 (16). Our recommendations may be used by investigators to optimize both the design and the reporting of future CKD prevalence studies.

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