Determinants and burden of chronic kidney disease in the population-based CoLaus study: a cross-sectional analysis*

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ORIGINAL ARTICLE

ABSTRACT

Background. Chronic kidney disease (CKD) represents an increasing health burden. We present the population-based prevalence of CKD and compare the CKD Epidemiology collaboration (CKD-EPI) and modification of diet in renal disease (MDRD) equations to estimate the glomerular filtration rate, using the revised CKD classification with three albuminuria classes. We also explore factors associated with CKD.

Methods. The Swiss population-based, cross-sectional CoLaus study conducted in Lausanne (2003–2006) included 2810 men and 3111 women aged 35–75. CKD prevalence was assessed using CKD-EPI and MDRD equations and albuminuria estimated by the albumin-to-creatinine ratio in spot morning urine. Multivariate logistic regression was used to analyse determinants of CKD.

Results. Prevalence [95% confidence interval (CI)] of all stages CKD was 10.0% (9.2–10.8%) with CKD-EPI and 13.8% (12.9–14.6%) with MDRD. Using the revised CKD classification, the prevalence of low-, medium-, high- and very high-risk groups was 90.0, 8.46, 1.18 and 0.35% with CKD-EPI, respectively. With MDRD, the corresponding values were 86.24, 11.86, 1.55 and 0.35%. Using the revised classification, CKD-EPI systematically reclassified people in a lower risk category than MDRD. Age and obesity were more strongly associated with CKD in men [odds ratio (95% CI): 2.23(1.95; 2.56) per 10 years and 3.05(2.08;4.47), respectively] than in women [1.46 (1.29; 1.65) and 1.78 (1.30;2.44), respectively]. Hypertension, type 2 diabetes, serum homocysteine and uric acid were positively independently associated with CKD in men and women.

Conclusions. One in 10 adults suffers from CKD in the population of Lausanne. CKD-EPI systematically reclassifies people in a lower CKD risk category than MDRD. Serum homocysteine and uric acid levels are associated with CKD independently of classical risk factors such as age, hypertension and diabetes.

INTRODUCTION

Chronic kidney disease (CKD) prevalence is increasing worldwide and the prevalence of end-stage renal disease (ESRD) is expected to rise by 44% from 2000 to 2015 [1]. CKD represents a significant public health problem because of the

high associated morbidity and mortality, mainly attributable to elevated cardiovascular risk [2, 3].

A National Kidney Foundation position statement supports early detection of CKD in asymptomatic individuals at increased risk [4]. Screening for CKD is cost-effective in diabetics and hypertensive patients or in the general population after age 50 [5, 6]. The identification of CKD has been facilitated by the implementation of new equations to estimate the glomerular filtration rate (eGFR) and by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) five-stage classification mainly based on eGFR levels [7].

The simplified four-variable modification of diet in renal disease (MDRD) equation is the most commonly used in clinical practice [8]. However, it was developed in non-diabetic CKD patients (mean age 51 years) [9] and has not been validated for eGFR > 60 mL/min/1.73 m^2 [10]. An alternative equation [CKD-Epidemiology collaboration (EPI)] was developed and validated to reduce the rate of false-positive diagnosis of CKD stage 3 [11]. CKD-EPI has proven to be more accurate than MDRD to estimate eGFR in patients with normal renal function [12] and to predict ESRD, cardiovascular and all-cause mortality [13]. Recently, a revised classification of CKD has been proposed by the Kidney Disease: Improving Global Outcomes (KDIGO) group. This new classification was developed to reflect patient prognosis and includes albuminuria as there is compelling evidence for its prognostic value [14–16].

So far, few large-scale population-based studies estimated the prevalence of CKD comparing CKD-EPI with MDRD [13, 17–22] and very few used the revised classification. The aim of this study was to assess the prevalence of CKD in the general population according to the revised classification to compare the MDRD and CKD-EPI equations and to explore determinants of CKD.

SUBJECTS AND METHODS

Participants

The data from the population-based CoLaus study were analysed for this study. Between 2003 and 2006, 6184 Caucasian participants aged 35–75 were recruited in Lausanne, Switzerland. Details on participant selection, assessment process and clinical data measurements have been described previously [23]. Briefly, recruitment took place in the city of Lausanne in Switzerland, a town of 117 161 inhabitants. The complete list of the Lausanne inhabitants aged 35–75 ($n = 56 694$ in 2003) was provided by the population register. A simple, non-stratified random selection of 35% of the source population was drawn and contacted by letter. Exclusion criteria for this study were to be of non-Caucasian descent and not to be able to provide a written informed consent. The participation rate from the randomly selected population was 41%. The study was approved by the local ethical committee and participants signed written informed consent.

Questionnaire data and clinical measurements

Trained health professionals used standardized questionnaires on socio-demographic characteristics and lifestyle factors, such as tobacco and alcohol consumption as well as treatment. Education was split into <9 versus ≥9 years of school. Physical activity was considered as present if participants reported to be physically active during at least 20 min once a week. For the purpose of the present analyses, smokers were defined as current smokers and non-smokers as never or ex-smokers. Alcohol consumption was considered as present if participants reported to drink alcohol on a daily basis. Menopausal status, hormone replacement therapy and oral contraceptive use were assessed via standardized questionnaire. The body mass index (BMI) was defined as weight in kilograms divided by height in meters squared (kg/m^2) and categorized into normal (<25 kg/m^2), overweight ($25 \leq BMI < 30$ kg/m^2) and obesity (BMI ≥ 30 kg/m^2). Blood pressure (BP) was measured three times on the left arm in the sitting position using a clinically validated automatic oscillometric device [24]. The mean of the last two measures was used to define hypertension status. Hypertension was defined as a mean systolic BP ≥140 mmHg and/or a diastolic BP ≥90 mmHg and/or the presence of antihypertensive drug treatment. Diabetes was defined as a fasting blood glucose ≥7 mmol/L [25] and/or the presence of any antidiabetic drug (including insulin).

Laboratory data

Blood was drawn in all participants after an overnight fast. Clinical chemistry assays were performed by CHUV Clinical Laboratory on fresh blood samples. Serum and urine creatinine were measured using the IDMS-traceable Jaffe kinetic compensated method (Roche Diagnostics, Switzerland, maximum intra- and inter-batch CV: 2.9–0.7%). A single spot urine sample was taken randomly in the morning to assess albuminuria. A quantitative immunonephelometry method was used to quantify albuminuria. Creatinine and albumin were measured to calculate the albumin-to-creatinine ratio (ACR). Uric acid was measured using uricase-PAP (inter- and intra-batch CV: 1.0–0.5%), triglycerides using GPO-PAP (inter- and intra-batch CV: 2.9–1.5%), cholesterol using CHOD-PAP (inter- and intra-batch CV: 1.7–1.6%), homocysteine using high-pressure liquid chromatography following ammonium 7-fluorobenzo-2-oxa-1, 3-diazole -4-sulphonate (SBD-F) derivatization (inter- and intra-batch CV: 3.1–2.9%).

CKD definition

GFR was estimated using the simplified MDRD [8] and the CKD-EPI equations [11]. Given that the CKD-EPI equation more accurately predicts the risk of mortality and ESRD than the MDRD equation [26], CKD-EPI was considered as the gold standard in this study. The simplified MDRD equation adapted for IDMS-traceable serum creatinine was calculated as follows: GFR (mL/min/1.73 m^2) = $175 \times (SCr)^{-1.154} \times (Age)^{-0.203} \times (0.742$ if female), where SCr is serum creatinine concentration in mg/dL and age is in years [8]. Albuminuria was defined as present whenever the ACR was above 30 mg/g, including both micro-albuminuria (ACR 30–299 mg/g) and

macro-albuminuria (ACR ≥ 300 mg/g) [27]. CKD was defined according to K/DOQI guidelines as eGFR < 60 mL/min/1.73 m^2 (stages 3–5) or the presence of albuminuria when eGFR was greater than 60 mL/min/1.73 m^2 (stages 1 and 2). Throughout the manuscript, the term 'CKD' will be used for all stages (1–5).

The distribution of CKD stages was assessed according to the revised classification as proposed by KDIGO, which includes three levels of albuminuria using the ACR (A1 ≤ 10 and 10–29 mg/g; A2 = 30–299 mg/g; A3 = 300–1999 and ≥2000 mg/g) and five stages of eGFR (G1–G5) [16]. This revised classification allows stratifying people into four risk categories: low, medium, high and very high risk. Medium, high and very high risk categories correspond to the traditional K/DOQI CKD stages 1–5. Because of low numbers, we combined the revised high and very high categories in all analyses. The prevalence of CKD according to the revised classification was calculated using the MDRD and CKD-EPI equations.

Statistical analysis

Statistical analyses were conducted using STATA 12.0 (StataCorp, College Station, TX, USA). Quantitative variables were expressed as the mean ± SD or median and interquartile range, and categorical ones as the percentage of participants. We compared continuous and categorical variables in men and women using the t-test and chi-square tests, median tests or Fisher's exact tests whenever appropriate (i.e. expected value in any cell lower than 5).

We compared the low-, medium- and high-risk CKD categories between MDRD and CKD-EPI and calculated reclassification percentages. We compared the prevalences of medium- and high-risk categories by hypertension, diabetes and BMI strata using a chi-square test. We used a nonparametric test for trend to compare the low- versus combined medium- and high-risk revised CKD categories across age and BMI strata.

Participant characteristics are presented separately for men and women as all variables except total cholesterol were significantly different (P < 0.001). For this reason, we also systematically explored all two-way interactions with sex for their association with the risk of CKD. We found significant (P < 0.05) sex by age, sex by BMI categories (tested using a likelihood ratio test) and therefore decided to conduct separate etiological models in men and in women.

We used multiple logistic regressions to explore determinants of CKD. We first tested each covariate of interest separately for its association with CKD in the crude analysis (unadjusted model 1). For all covariates in model 1, we then explored the age-adjusted associations (model 2). We then systematically checked the association of each exposure of interest one by one with variables significantly associated with CKD in the model 1 to detect potential confounders. We finally built a model (final model 3) for each exposure factor of interest adjusting for their confounders. Covariates that could lie in the causal pathway (i.e. variable that could be a consequence of the factor of interest and influence the outcome) were not included in the model. For example, hypertension, diabetes, triglycerides and uric acid could be in the causal pathway of the

BMI-CKD association and were excluded from the final model. We also explored whether covariates of interest (e.g. smoking, alcohol consumption, physical activity etc.) not significantly associated with CKD in univariate analyses confounded the association of the other covariates with CKD, but that was not the case. We additionally explored the effects of adding as covariates to models three factors that did not qualify as confounders in our data set but may be argued to represent confounders based on previously published data: no significant changes were observed. We expressed associations as odds ratio (OR) and 95% CIs.

RESULTS

Participant characteristics

Overall, 263 participants had missing data on renal function, serum homocysteine, serum uric acid, alcohol, smoking or on menopausal status and were excluded from the present analyses. We included 5921 subjects (95.7%) with complete information on renal function as assessed by creatinine and albuminuria measurements: 2810 men and 3111 women. Participants' characteristics according to sex are displayed in Table 1. Men were younger than women but had a higher BMI, higher eGFR (CKD-EPI and MDRD) and higher triglycerides, serum uric acid and homocysteine levels. Men also reported higher alcohol intake, higher physical activity and were more educated. Men had the higher prevalence of cardiovascular risk factors such as smoking, diabetes, hypertension and albuminuria.

GFR distribution: comparison between MDRD and CKD-EPI equations

Scatterplots of eGFR versus serum creatinine as well as selected percentiles for eGFR in the adult general population are shown in Figure 1, separately for men and women, according to MDRD and CKD-EPI equations. Compared with the CKD-EPI equation, MDRD underestimated eGFR in all presented percentiles in men and women. The median value for eGFR (CKD-EPI) was higher than for eGFR (MDRD) in men (89 versus 81 mL/min/1.73 m^2, P < 0.001) and women (84 versus 75 mL/min/1.73 m^2, P < 0.001).

Revised CKD classification using the MDRD and CKD-EPI equations

Table 2 shows the percentage of participants in each category of the revised classification for CKD using both the CKD-EPI and MDRD equations. For CKD-EPI, the prevalence in the low-, medium-, high- and very high-risk categories was 90.0, 8.46, 1.18 and 0.35%, respectively. The corresponding values for MDRD were .86.24, 11.86, 1.55 and 0.35%. The prevalence of CKD in our sample was 10.0% [95% confidence interval (CI): 9.2–10.8] for CKD-EPI and 13.8% (95% CI: 12.9–14.6%) for MDRD.

We compared CKD-EPI and MDRD across the low-, medium- and high-risk categories based on the new CKD classification (Supplementary Table S1). We calculated the reclassification that occurred when using the CKD-EPI instead

Table 1. Participants' characteristics by sex (n = 5921)

Covariate	Men (n = 2810)	Women (n = 3111)	P-value
Age (years)	52.5 (10.7)	53.5 (10.7)	<0.001
Menopause (%)	—	56.1	
More than basic education (>9 years) (%)	82.8	76.2	<0.001
Physical activity (at least 1/week) (%)	10.7	7.52	<0.001
Smoking (%)	29.1	24.9	<0.001
Alcohol consumption (%)	36.1	15.6	<0.001
ACE inhibitor (%)	6.16	4.18	<0.001
ARBs (%)	8.29	6.46	0.007
Lipid-lowering drug (%)	14.3	9.16	<0.001
BMI (Kg/m^2)	26.6 (4.0)	25.1 (4.8)	<0.001
Normal weight (%)	37.4	57.3	
Overweight (%)	45.6	28.4	
Obesity (%)	17.0	14.3	<0.001
Hypertension (%)	42.1	30.1	<0.001
Diabetes (%)	9.32	4.05	<0.001
Serum creatinine (μmol/L)	88.6 (23.3)	72.1 (11.7)	<0.001
eGFR (CKD-EPI) (mL/min/1.73 m^2)	87.7 (15.0)	84.0 (15.0)	<0.001
eGFR (MDRD) (mL/min/1.73 m^2)	81.6 (15.7)	75.9 (14.2)	<0.001
Albuminuria (ACR ≥ 30 mg/g) (%)	9.50	5.24	<0.001
Total cholesterol (mmol/L) [median (IQR)]	5.5 (4.9; 6.2)	5.5 (4.9; 6.3)	0.41
Serum triglycerides (mmol/L) [median (IQR)]	1.3 (0.9; 1.9)	1.0 (0.7; 1.4)	<0.001
Serum uric acid (μmol/L) [median (IQR)]	355 (308; 407)	262 (224; 309)	<0.001
Serum homocysteine (μmol/L) [median (IQR)]	10.4 (8.8; 12.6)	8.8 (7.3; 10.6)	<0.001

Data are the means (SD) unless otherwise specified. eGFR, estimated glomerular filtration rate; ACR, albumin-to-creatinine ratio, IQR, interquartile range.

of the MDRD equation. Compared with MDRD, CKD-EPI reclassified 31.8% from medium to low risk and 19.5% from high to medium risk overall. The corresponding percentages were 16.1 and 12.7% in men and 41.4 and 25.9% in women. All reclassifications were in the direction of a lower risk category.

Factors associated with CKD

The unadjusted prevalence of CKD by age and sex are depicted in Figure 2. Prevalence increased with age mainly in subjects aged ≥55 years, being over 25% after 65 years old. Prevalence of CKD was higher in women compared with men before 55 years old but higher in men over 55 years old.

The unadjusted prevalences of combined medium- and high-risk CKD categories were significantly higher in the presence of diabetes (28.6 versus 8.7% in the absence, P < 0.001) or hypertension (17.4 versus 5.9% in the absence, P < 0.001) as

presented in Supplementary Figure S1. Results were similar in men and women. There was a significant positive trend in the prevalence of combined medium- and high-risk CKD categories across BMI categories (7.1% in normal weight people, 10.8% in overweight people and 17.2% in obese people, P for trend < 0.001) overall. Significant positive trends across BMI categories were also observed when men and women were analysed separately.

In the multivariate analysis, older age, overweight, obesity, hypertension, diabetes as well as serum triglyceride, uric acid and homocysteine levels were independent determinants of CKD in men (Table 3). However, the significant association of triglycerides with CKD was only present when age was included as a covariate in the model. In contrast, overweight and serum triglycerides were not significantly associated with CKD in women, while older age, hypertension, diabetes, serum uric acid and homocysteine levels were (Table 4). Obesity was only
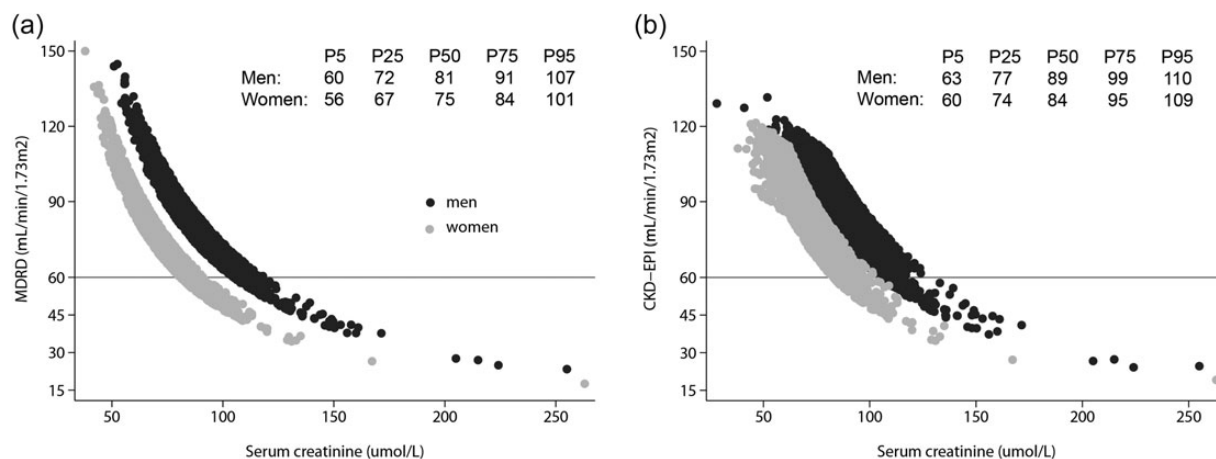
FIGURE 1: Estimated GFR levels versus serum creatinine levels by sex according to MDRD (**a**) and CKD-EPI (**b**) equations. MDRD, modification of diet in renal disease equation; CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration equation. Percentiles 5, 25, 50, 75 and 95 for eGFR in men and women are provided as well.

Table 2. Prevalence of CKD stages according to the new proposed KDIGO classification [16], based on eGFR calculated with the CKD-EPI or [MDRD] equation

eGFR stages (mL/min/1.73 m^2)		Albuminuria stages[a]				
		A1		A2	A3	
		<10	[10–30[	[30–300[	≥300	All
G1	≥105	8.17 [3.19]	1.77 [1.00]	0.59 [0.32]	0.07 [0.07]	10.61 [4.58]
	[90–105[	23.54 [11.81]	4.95 [2.74]	1.49 [1.01]	0.19 [0.07]	30.16 [15.62]
G2	[75–90[	28.44 [29.39]	4.81 [5.35]	1.82 [1.87]	0.08 [0.15]	35.16 [36.77]
	[60–75[	14.85 [27.73]	3.46 [5.03]	1.22 [1.69]	0.08 [0.14]	19.61 [34.59]
G3a	[45–60[	2.35 [5.12]	1.00 [1.84]	0.47 [0.69]	0.05 [0.03]	3.87 [7.68]
G3b	[30–45[	0.24 [0.35]	0.05 [0.08]	0.14 [0.14]	0.02 [0.03]	0.44 [0.61]
G4	[15–30[	0.03 [0.03]	0.02 [0.02]	0.02 [0.02]	0.03 [0.03]	0.10 [0.10]
G5	<15	0.00 [0.00]	0.00 [0.00]	0.02 [0.02]	0.03 [0.03]	0.05 [0.05]
All		77.62 [77.62]	16.06 [16.06]	5.76 [5.76]	0.56 [0.56]	100 [100]

Low risk (very light grey), medium risk (light grey), high risk (medium grey), very high risk (dark grey). For both CKD-EPI and MDRD, three participants (i.e. 0.05%) belonging to the G5 category have been included in the very high-risk category.
[a]Stages of the ACR in mg/g. $n = 5921$.

found to be associated with CKD in women when serum uric acid was excluded from the model (possible causal pathway). Menopausal status was still associated with the substantially lower risk of CKD in women [OR (95% CI): 0.47 (0.30–0.73)], once adjusted for all confounders including age. Hypertension was associated with an ∼50% higher risk of CKD, and diabetes with a 2-fold higher risk of CKD, in both genders.

DISCUSSION

We report, for the first time in Switzerland, the prevalence of CKD using both eGFR and albuminuria in a population-based sample aged 35–75 years. One in 10 adults suffers from CKD in the city of Lausanne. When using the CKD-EPI equation to estimate, the prevalence in the low-, medium-, high- and very high-risk categories of the revised KDIGO CKD classification [16] was 90.0, 8.46, 1.18 and 0.35%, respectively. These data add to the few population-based estimates of the newly proposed KDIGO CKD risk categories in Europe. A large body of literature confirms that detecting CKD with albuminuria and eGFR is cost effective and better associated with adverse outcomes such as all-cause and cardiovascular mortality and ESRD [14, 15, 28–30]. Those findings justify the use of both the eGFR equation and albuminuria to determine CKD prevalence. In this study, we found lower rates in G1 stages but
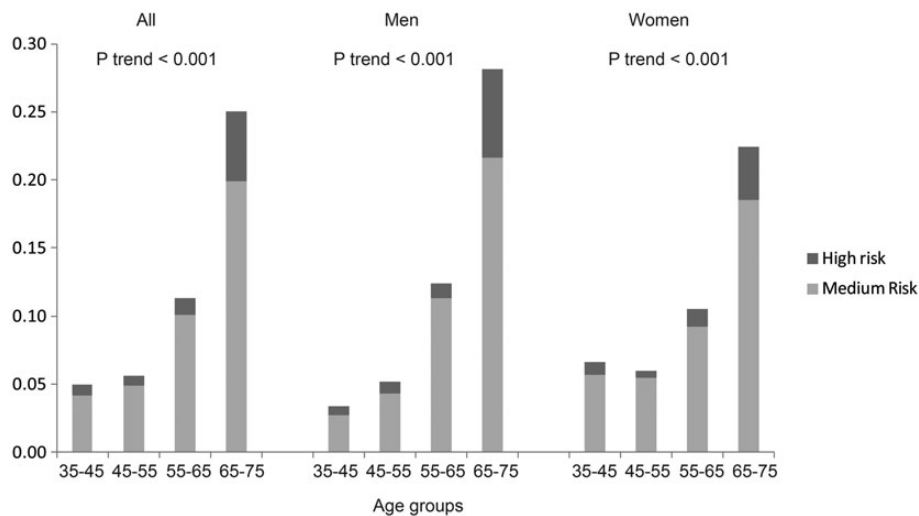
FIGURE 2: Prevalence of medium- and high-risk categories using the revised CKD classification by 10-year age groups and by sex. P-values are from a non-parametric test for trend (nptrend in Stata 12.0) comparing the trend in combined medium- and high-risk categories versus low-risk category across age groups.

higher in G2 and G3a than those reported in the USA in NHANES III [16].

The SAPALDIA study previously reported CKD prevalence defined as an eGFR < 60 mL/min/1.73 m^2 in a large Swiss population-based sample but used neither KDOQI stages nor albuminuria in their definition [31]. CKD prevalence strongly varies depending on the inclusion, or omission, of albuminuria in the definition, the studied population and the country. When CKD was solely defined by an eGFR < 60 mL/min/1.73 m^2, the overall prevalence in population-based studies varied between 1.5 and 43.3% [32, 33]. Differences in population sampling, age restriction, number of creatinine samples to define CKD (one versus more) or equation used to estimate eGFR (Cockroft-Gault, MDRD or CKD-EPI) explain some of the observed variability. The different assays used to measure creatinine as well as different standardization methods may also account for some of the observed heterogeneity: although most studies used Jaffe assays, instead of enzymatic ones, those could be compensated or uncompensated, IDMS traceable or not. Studies including elderly participants (>75 years old), patients at high cardiovascular risk, or those using uncompensated Jaffe creatinine assays reported higher CKD prevalences. Studies that combined eGFR < 60 mL/min/1.73 m^2 and proteinuria to define CKD reported a prevalence ranging between 8 and 13.2% [34–41]. Although few population-based studies in Europe have assessed CKD including proteinuria, the prevalence seems to be lower in northern (8–10.2%) [34, 36] than in southern countries (12.7–13.2%) [39, 40]. The overall prevalence of CKD in our study (MDRD: 13.8% (95% CI: 12.9–14.6%) was quite similar to the values reported in Southern European countries, and in the USA [NHANES 1999–2004: 13.1% (12.0–14.1%)] [35].

Most of the previously mentioned studies used MDRD equations. In our study, CKD prevalence was lower using the CKD-EPI than the MDRD equation: 10.0% (95% CI: 9.2–10.8%) instead of 13.8% (95% CI: 12.9–14.6%). CKD-EPI

reclassified 8.2% of people and this was systematically in the direction of a lower-risk category than MDRD. Data on CKD prevalence defined using the CKD-EPI equation are scarce in Europe and only few population-based studies compared CKD-EPI with MDRD equation [13, 18, 20–22]. In those studies, CKD-EPI similarly reclassified individuals, from CKD stages 2 and 3 to a higher eGFR category.

In agreement with previous reports, we found a higher prevalence of CKD in diabetic (30%) and hypertensive (18%) participants [30, 42]. Both hypertension and diabetes were associated with the increased risk of CKD independently of other determinants in a similar way in men and women. In contrast, the associations of age and obesity with CKD significantly differed in men and in women in our study, with a stronger association in men. In both human and animal experiments, the precise underlying causes of sex difference in CKD are unclear and may include diet, kidney size, glomerular haemodynamics and sex hormones [43–45].

We found overweight and obesity as well as triglyceride levels to be associated with CKD in men. In women, only obesity was associated with CKD but the association was smaller than in men. Additionally, in women, this association disappeared when adjusting for serum uric acid potentially due to an over-adjustment for adiposity [46]. In longitudinal studies, obesity was often reported as an independent risk factor for incident CKD, without any mention of sex differences [47, 48]. In a meta-analysis, obesity was a significant independent risk factor for ESRD with a stronger association in men for severe obesity [49]. However, in another meta-analysis, including not only CKD but also ESRD, kidney stones and kidney cancer studies, obesity was a stronger determinant of kidney disease in women than men [50].

Hyperhomocysteinaemia has been previously shown to be a determinant of CKD and albuminuria in the general population [51, 52]. This relation has been confirmed and already discussed in the CoLaus cohort in another manuscript that

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Table 3. Factors associated with CKD in men (*n* = 2810)

	Model 1 unadjusted OR (95% CI)	Model 2: age-adjusted OR (95% CI)	Confounder X	Possible causal pathway	Final model 3: adjusted for X OR (95% CI)	Final model P-value
Age (per 10-year increase)	2.39 (2.10;2.73)	—	Hn OH	BMI HT DM Ura	2.23 (1.95; 2.56)	<0.001
BMI < 25 kg/m^2	1	1	Age	HT DM Tg Ura	1	
BMI 25–30 kg/m^2	2.56 (1.83;3.57)	2.02 (1.44;2.85)			2.02 (1.44; 2.85)	<0.001
BMI ≥30 kg/m^2	4.26 (2.94;6.16)	3.05 (2.08;4.47)			3.05 (2.08; 4.47)	<0.001
Hypertension (presence versus absence)	4.49 (3.40;5.93)	2.48 (1.84;3.35)	All	—	1.66 (1.21; 2.28)	0.002
Type 2 diabetes (presence versus absence)	4.61 (3.40;6.24)	2.99 (2.18;4.11)	Age BMI HT Ura Hn OH	Tg	2.41 (1.70; 3.41)	<0.001
Triglycerides (per 1 mmol/L increase)[a]	1.15 (1.08;1.23)	1.22 (1.13;1.30)	All	—	1.10 (1.02; 1.89)	0.019
Uric acid (per 10 μmol/L increase)[a]	1.08 (1.06;1.09)	1.07 (1.05;1.08)	Age Tg Hn BMI OH	HT DM	1.04 (1.03; 1.06)	<0.001
Homocysteine (per 1 μmol/L increase)[a]	1.09 (1.07;1.11)	1.07 (1.05;1.09)	Age HT DM Tg Ura OH	—	1.05 (1.03–1.08)	<0.001
Alcohol consumption (yes versus no)	1.55 (1.21;1.99)	1.15 (0.89;1.49)	Age HT DM Hn	Tg Ura	1.03 (0.78; 1.4)	0.80
Education level (high versus low)	0.97 (0.70;1.35)	0.95 (0.68; 1.34)	—		—	
Physical activity (regular versus not)	0.89 (0.58;1.34)	1.25 (0.81; 1.93)	—		—	
Smoking (current versus not)	0.89 (0.67;1.17)	1.10 (0.82; 1.47)	—		—	
Total cholesterol (per 1 mmol/L)	0.93 (0.83;1.05)	0.95 (0.84; 1.08)	—		—	

CKD was defined as the presence of stages 1–5 CKD using the CKD-EPI equation. In a model including both men and women, there was a significant age-by-sex interaction (P < 0.001) and age by BMI categories interaction (P = 0.006), so that separate models were built for men and women. BMI, body mass index; HT, hypertension; DM, type 2 diabetes mellitus; Tg, triglycerides; Ura, uric acid; Hn, homocystein; OH, alcohol.
[a]Serum values.

focused on albuminuria [53]. Similarly, several cross-sectional and longitudinal analyses demonstrated an association between serum uric acid and CKD in the general population [38, 54–58]. Homocysteine might lead to endothelial injury through generation of hydrogen peroxide and a decrease in NO [59] and, although mechanisms are not yet clear, uric acid also seems to contribute to endothelial dysfunction through impaired NO production and release [60]. Our results suggest that oxidative stress could be an important determinant of CKD in the general Swiss adult population.

Our study has some limitations. First, we included participants from a single city, which might limit generalizing the findings to the whole country. Second, only Caucasians were included and results might be different in an African or Asian

Table 4. Factors associated with CKD in women (n = 3111)

	Model 1: unadjusted OR (95%CI)	Model 2: age-adjusted OR (95%CI)	Confounder X	Possible causal pathway	Final model 3: adjusted for X OR (95% CI)	Final model P-value
Age (per 10-year increase)	1.73 (1.54;1.94)	—	Hn S	Mp BMI HT DM Tg Ct Ura	1.46 (1.29; 1.65)	<0.001
Menopause (yes versus no)	2.11 (1.62;2.72)	0.56 (0.36;0.85)	All	—	0.47 (0.30–0.73)	0.001
BMI <25 kg/m^2	1	1	Age Mp Hn S	HT DM Tg Ura Ct	1	
BMI 25–30 kg/m^2	1.19 (0.90;1.57)	0.98 (0.74;1.31)			1.01 (0.76; 1.35)	0.95
BMI ≥30 kg/m^2	2.20 (1.63;2.97)	1.84 (1.35;2.50)			1.78 (1.30; 2.44)	<0.001
Hypertension (presence versus absence)	2.78 (2.20;3.53)	1.91 (1.47;2.47)	All	—	1.56 (1.17; 2.07)	<0.001
Type 2 diabetes (presence versus absence)	3.93 (2.62;5.89)	2.91 (1.92;4.41)	Age Mp BMI HT Ura Hn	Tg	2.10 (1.32; 3.32)	<0.001
Triglycerides (per 1 mmol/L increase)[a]	1.63 (1.39;1.90)	1.41 (1.20;1.67)	Age Mp BMI HT DM Ura Hn	Ct	1.13 (0.92; 1.37)	0.25
Uric acid (per 10 μmol/L increase)[a]	1.09 (1.07;1.11)	1.07 (1.05;1.09)	Age Mp BMI Tg Hn Ct	HT DM	1.06 (1.04; 1.08)	<0.001
Homocysteine (per 1 μmol/L increase)[a]	1.17 (1.13;1.21)	1.13 (1.09;1.17)	All except smoking	—	1.10 (1.06; 1.14)	<0.001
Total cholesterol (per 1 mmol/L)	1.26 (1.13;1.41)	1.05 (0.93;1.19)	Age Mp HT Ura Hn BMI	Tg	1.04 (0.92; 1.18)	0.67
Smoking (current versus not)	0.69 (0.52;0.93)	0.82 (0.60;1.10)	Age Mp BMI HT Ura	—	0.92 (0.67; 1.25)	0.58
Education level (high versus low)	0.86 (0.66;1.13)	1.01 (0.77; 1.33)	—	—	—	
Physical activity (regular versus not)	0.93 (0.59;1.46)	1.24 (0.78; 1.97)	—	—	—	
Alcohol consumption (yes versus no)	1.30 (0.96;1.76)	0.99 (0.72; 1.35)	—	—	—	

Mp, menopause; BMI, body mass index; HT, hypertension; DM, type 2 diabetes mellitus; Tg, triglycerides; Ura, uric acid; Hn, homocystein; Ct, total cholesterol; S, smoking.
CKD was defined as the presence of stages 1–5 CKD using the CKD-EPI equation.
[a]Serum values.

population. Additionally, CKD classification was based on a single measurement of serum creatinine and the ACR, as in most population-based studies. Third, a compensated IDMS-traceable Jaffe method was used and not an enzymatic method. The small bias due to the method is minimized by the use of the appropriate calibrated MDRD equation [61]. Most previous studies reporting CKD prevalences have also used a compensated Jaffe assay (calibrated or not) and not an

enzymatic one. Additionally, the participation rate in the CoLaus study from the original randomly selected sample was 41%. Although the sex distribution of participants and non-participants was similar, participants were under-represented in older age groups compared with non-participants (P < 0.001), which could underestimate CKD prevalence. Furthermore, we cannot exclude a healthy participant bias, which would lead to further underestimate CKD prevalence in this study. In contrast, we expect people with ESRD not to take part in such population-based study. Altogether, we expect the true underlying CKD prevalence to be likely higher than 10%. In this population-based sample, the numbers of participants in the medium-, high- and very high-risk categories (according to the revised KDIGO classification) were too low for us to separately explore their correlates. Finally, the cross-sectional nature of the study limits causal inferences. For instance, some of the factors (e.g. hypertension) that we found to be associated with CKD could either precede or follow the appearance of CKD (unclear temporal sequence). A longitudinal study would be needed to assess whether baseline characteristics are associated with incident CKD.

In conclusion, one in 10 adults suffers from CKD in the population of Lausanne. Age and obesity are more strongly associated with CKD in men than in women, whereas type 2 diabetes, hypertension, serum homocysteine and uric acid levels are independently positively associated with the risk of CKD in both genders.

CONFLICT OF INTEREST STATEMENT

None declared.

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Corticosteroid therapy in IgA nephropathy with minimal change-like lesions: a single-centre cohort study

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ABSTRACT

Background. There is a lack of high-quality evidence that advocates the use of corticosteroids for IgA nephropathy (IgAN) with minimal change-like lesions (also called IgAN with minimal change disease, MCD-IgAN).

Methods. Twenty-seven biopsy-proven adult MCD-IgAN patients were enrolled. Daily single dose of 1 mg/kg (maximum 60 mg/day) prednisone was given until complete remission (CR), followed by gradually decreasing dosage. The clinical data were collected from baseline up to 12 weeks of treatment (Certification No. 2011NLY-006, Clinical trials gov ID. NCT01451710).

Results. The patient cohort consisted of 15 males and 12 females. The mean age of the patients was 29.2 ± 10.8 years (range 18–60 years) at the time when they were subject to renal biopsy. All patients had hypoalbuminaemia (23.7 ± 4.13 g/L) and heavy proteinuria (>3.5 g/24 h). Cumulative CR (proteinuria < 0.4 g/24 h) rates were 3.70, 48.1, 92.6 and 100% after 1, 2, 4 and 8 weeks of treatment, respectively. Two cases relapsed after CR, one at 6 weeks of treatment, likely due to