# Disparities in chronic kidney disease prevalence among males and females in 195 countries: Analysis of the Global Burden of Disease 2016 Study

Boris Bikbov<sup>1</sup>\*, Norberto Perico<sup>1</sup>, Giuseppe Remuzzi<sup>1,2,3</sup>,

on behalf of the GBD Genitourinary Diseases Expert Group

<sup>1</sup> IRCCS - Istituto di Ricerche Farmacologiche Mario Negri, Bergamo, Italy

<sup>2</sup> Unit of Nephrology, Dialysis and Transplantation, Azienda Socio-Sanitaria Territoriale Papa Giovanni XXIII, Bergamo, Italy

<sup>3</sup> L. Sacco Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy

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Corresponding author: Boris Bikbov, MD, Ph.D. IRCCS - Istituto di Ricerche Farmacologiche Mario Negri, Via G.-B. Camozzi 3 – 24020, Ranica, Bergamo, Italy Tel: +39 035 45 35 305 Fax: +39 035 45 35 371 Email: boris.bikbov@marionegri.it

*Background:* Chronic kidney disease (CKD) imposes a substantial burden health care systems. There are some especially vulnerable groups with a high CKD burden, one of which is women. We performed an analysis of gender disparities in the prevalence of all CKD stages and renal replacement therapy (defined as impaired kidney function, IKF) in 195 countries.

*Methods:* We used estimates produced by the Global Burden of Disease Study 2016 revision using a Bayesian-regression analytic tool, DisMoD-MR 2.1. Data on gross domestic product based on purchasing power parity per capita (GDP PPP) was obtained via the World Bank International Comparison Program database. To estimate gender disparities, we calculated the male:female allage prevalence rate ratio for each IKF condition.

*Results:* In 2016, the global number of individuals with IKF reached 752.7 million, including 417.0 million females and 335.7 million males. The most prevalent form of IKF in both groups was albuminuria with preserved glomerular filtration rate. Geospatial analysis shows a very heterogeneous distribution of the male:female ratio for all IKF conditions, with the most prominent contrast found in kidney transplant patients. The median male:female ratio varies substantially according GDP PPP quintiles; however, countries with different economic states could have similar male:female ratios. A strong correlation of GDP PPP with dialysis-to-transplant ratio was found.

*Conclusions:* GBD Study highlights the prominent gender disparities in CKD prevalence among 195 countries. The nature of these disparities, however, is complex and must be interpreted cautiously taken in account all possible circumstances.

Chronic kidney disease (CKD) is one of the most rapidly growing non-communicable diseases (NCD) and imposes a substantial mortality and morbidity burden.[1][2][3] The Global Burden of Disease, Injuries and Risk Factors Study (GBD) is one of the most important projects undertakenin modern epidemiology, and the GBD 2016 revision allowed to produce estimates for the global prevalence of all CKD stages.[1][3] Among the summary estimates for CKD there are some particularly vulnerable groups with high disease prevalence and one of these is women. Notably, CKD in women has profound consequences for global health, since it substantially increases the risk of premature delivery, infants that are small for gestational age and low birth weight,[4] which predispose the next generation to a higher risk for NCD.[5,6] In 2018 the celebration of World Kidney Day is dedicated to women's health,[7] with the major aims being to increase awareness of CKD in the female population and improve kidney health care for women. In this article we explore global gender disparities in CKD prevalence based on data from the GBD 2016 Study.

To retrieve data on CKD prevalence, the Global Burden of Disease Genitourinary Expert Group (GUiDEG) and the Institute of Health Metrics and Evaluations (IHME) performed several rounds of systematic review, covering PubMed and EMBASE, as well as including literature obtained by manual search. Additional data from unpublished data sources, including hospital discharge records, end-stage kidney disease (ESKD) registries, etc. were provided by the geographically distributed GBD 2016 CKD collaborators. Data sources used for CKD burden modelling can be explored in an online data source tool <a href="http://ghdx.healthdata.org/gbd-2016/data-input-sources">http://ghdx.healthdata.org/gbd-2016/data-input-sources</a>. Estimates of CKD prevalence were produced using a Bayesian-regression analytic tool (DisMoD-MR 2.1). More details on GBD methods are described elsewhere.[1][2] Data on gross domestic product based on purchasing power parity per capita (GDP PPP) was obtained via the World Bank International Comparison Program database.[8]

The GBD Study considers six categories of patients with CKD based on albuminuria and glomerular filtration rate (GFR) grades according to the KDIGO classification[9], or receipt of renal replacement therapy (RRT):

- Albuminuria with normal GFR (eGFR ≥60 ml/min/1.73m<sup>2</sup>) refers to KDIGO A2-A3 G1-G2 grades;
- CKD stage 3 (eGFR 30-59 ml/min/1.73m<sup>2</sup>) refers to KDIGO G3 GFR grade independently of albuminuria;
- CKD stage 4 (eGFR 15-29 ml/min/1.73m<sup>2</sup>) refers to KDIGO G4 GFR grade independently of albuminuria;
- CKD stage 5 (eGFR <15ml/min/1.73m<sup>2</sup>) not on renal replacement therapy (RRT) refers to KDIGO G5 GFR grade independently of albuminuria;
- maintenance dialysis;

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- kidney transplantation.

Considering the aforementioned differences between the CKD categories defined in KDIGO and GBD, and the need to map kidney disease as a risk factor for cardiovascular disease, the GBD terminology introduced the term "impaired kidney function" (IKF), with six IKF conditions determined by the above-mentioned categories of CKD patients.

To estimate gender disparities, we calculated the male:female all-age prevalence rate ratio for each IKF condition for 195 countries in all world regions for the year 2016. Taking into account the sensitivity of this ratio in case of small numbers in either numerator or denominator, for the RRT modalities we calculated the male:female ratio both with all country data and separately with countries having substantial numbers of RRT patients.

Differences in continuous variables between groups were compared by Wilcoxon's rank-sum test. Correlations between studied parameters were estimated by the Spearman rho. A P-value less than 0.05 was considered statistically significant. The analyses were performed with R (version 3.4.3).

### Global estimates

In 2016, the GBD estimates that global number of individuals with impaired kidney function (IKF) accounted for 752.7 million, with 417.0 million females and 335.7 million males(Figure 1). The most prevalent form of IKF in both gender groups was albuminuria with preserved GFR which globally was estimated to affect 260.1 million females (62.4% from IKF in females) and 216.7 million males (64.5% from IKF in males). Another 145.2 million females (34.8% from IKF in females) and 107.6 million males (32.1% from IKF in males) had GFR grade 3. More advanced CKD stages were less prevalent: GFR grade 4 affected 6.8 million females and 6.2 million males (1.6% and 1.8% from IKF, respectively), GFR grade 5 without RRT was estimated to be present in 3.2 million females and 3.2 million males (0.8% and 0.9% from IKF, respectively). Among RRT modalities 1.3 million females and 1.7 million males were treated with dialysis, 0.3 million females and 0.4 million males had a functioning kidney graft.

The male:female all-age prevalence rate ratio significantly differed between IKF conditions (p<0.00005), with values lower than 1 for albuminuria only, GFR grade 3, GFR grade 4, and GFR grade 5 without treatment with RRT, while for dialysis and functioning kidney graft it was higher than 1 (Figure 2). Notably, according to the best available knowledge, RRT was not available or almost inaccessible in many countries. Thus, in 38 countries, the dialysis prevalence rate was less than 20 pmp and in another 15 countries it was between 20 and 100 pmp (19.5% and 7.7% from all world countries, respectively). In 52 countries, kidney transplant recipients were absent or the prevalence rate was less than 10 pmp, and in another 26 countries the prevalence rate was between 10 and 50 pmp (26.7% and 13.3% from all world countries, respectively).

#### Regional and country-level estimates

A very heterogeneous picture emerged during the geospatial analysis (Supplement figures S1-S5). In general, countries in North America and Eastern Europe tended to have a male:female ratio less than 1, while in Southern Asia and in the Middle East this ratio was higher than 1. But even neighbouring countries had highly contrasting male:female ratio values, while it was very similar in other, geographically distant territories. However, there were some prominent examples of extremely high male:female ratios in patients with kidney transplants in Pakistan, India and Nepal (Figure 3), although for them GBD estimates were produced based on the limited data in the absence of national RRT registries.

### Correlation between CKD prevalence and GDP

The median male:female ratio varies substantially according to GDP per capita (Supplement figures S6-S16). However there was no uniform correlation between GDP and this ratio in all IKF conditions, and a similar male:female ratio could be observed for any IFK condition, including dialysis or kidney transplantation, in 195 countries within all ranges of GDP. The male:female ratio for either dialysis or kidney transplantation had no correlation with the GDP (Supplement figures S10, S11). However, for both sexes we found a significant and uniform correlation between GDP and ratio calculated by dividing prevalent counts of dialysis patients with a kidney transplant patients (Figure 4). This correlation underlines the importance of economic development on the availability of kidney transplantation.

GBD results demonstrate the substantial gender disparities in CKD prevalence, which globally was higher in women. Notably, the higher morbidity burden among females was found not only for CKD stages with decreased GFR, but also for albuminuria with normal GFR. Thus, the detected higher CKD prevalence in women is a true phenomenon, and cannot be attributed to the possible discrepancy between measured and estimated GFR (eGFR) due to the limitations of any eGFR equations.[10] The present findings are in line with the previous estimates of global CKD prevalence as reported in a meta-analysis with 44 studies of CKD 1 to 5 [11], which also showed higher CKD prevalence in women than in men. However, the magnitude of this difference is higher in our analysis, that could be attributed to the inclusion of larger number of data sources in the GBD, eventually leading to more refined estimates. It could be also explained by the modeling process in the GBD which assumed possible differences in the age structure of CKD population and general population of the countries. It is noteworthy that the higher prevalence of CKD in women may transfer to to the next generation. Thus, CKD in pregnant women substantially increases the odds of pre-eclampsia, premature delivery, neonates small for gestational age and low birth weight[4], which are associated with low nephron number at birth[6] - conditions that in themselves put a subject at higher risk of developing hypertension, obesity, diabetes and CKD in later life.[5,6] This relationship forms a desperate vicious circle that will increase the global burden of NCD in the future if no public health intervention occurs, and if current and future generations in many countries do not have access to better prevention programs and universal health care. Unfortunately, recent global humanitarian crises forced by wars steal any hope there might be of improving the management of NCD, including CKD, in vast geographical areas in almost all continents.[12][13] Due to this, the already high CKD prevalence in women only amplifies the morbidity burden during the collapse of social order in conflict zones.

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The estimated male:female ratio for CKD we considered reflects complex interactions between many factors, including gender differences in the prevalence of risk factors for CKD development and progression, attention to personal health care, access to medical care, availability of medications and access to RRT.[14][15] The latter represents one of the most sensitive indicators related to the human right for life. Unfortunatelly, on the global scale the projected need for RRT remains 2-4 fold higher than its provision.[16] It is noteworthy that, in many countries, a lack of universal health coverage and high out-of-pocket expenses substantially limit women's access to medical care, due to lower income, resulting in lower solvency.[17] As a consequence, the treatment rate among women is lower compared to men, even in subjects with known CKD (39.6% in women versus. 45.5% in men), as was shown in a cross-sectional study performed in twelve lowand middle-income countries.[18] The data regarding the CKD treatment rate in the general population of high-income countries is not available, but awareness of CKD[19] and a formal diagnosis with referral to a nephrologist[20] was lower in women, a finding that could indicate similar general social mechanisms to the approach to gender roles across low-, middle, and highincome countries. A constellation of extremely challenging economic conditions, as well as women's social roles as non wage-earners in some patriarchal societies may be what leads to the extremely high male: female ratio observed in our analysis regarding dialysis and kidney transplant prevalence rates. However, this cannot be the only explanation for male predominance on RRT, since it occurs all over the world and in all GDP per capita ranges. Biological factors responsible for higher male prevalence rates on dialysis include the protective effects of estrogen in women and damaging effect of testosterone in men,[15] as well as the higher prevalence of NCD risk factors in the general male population [21] [22] and, related to this, faster CKD progression rates in males. [23] The interplay between all factors may be very complex and poorly explained. As a particular example of this complexity, in the USA the prevalence of impaired blood glucose in the general population was higher in men,[21] while among haemodialysis patients diabetes was more

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prevalent in women.[24] However, in Russia, Japan and countries in Western Europe, gender differences in the prevalence of NCD risk factors in the general population were directly translated into the male:female ratio in the dialysis population.[22] In cases of functioning kidney grafts, the extremely high male:female ratio in prevalent patients could be attributed to gender inequalities in the country's society with regard to accessing transplantation. However, the almost ubiquitous milder male predominance among kidney transplant patients could be explained by the fact that calculations of kidney transplant rates are performed on the whole population, without taking into account a gender-specific cohort of the population with contraindications to transplantation. Thus, women have a higher prevalence of existing panel-reactive antibodies, and adjustment to this factor could substantially level differences in sex disparities for kidney transplant rates, as shown in the USA.[25]

Our analysis has limitations, with the main shortcoming relating to the absence or low quality of data for many of the countries used to estimate CKD prevalence. This limitation was to some degree balanced by the GBD's advanced methods of statistical modelling, assuming the country-level covariates that allowed to produce estimates even for countries with no primary epidemiologic data.[1][2][3] Moreover, since the male:female ratio is sensitive to extreme values in case of low patient numbers, to avoid this we calculated for RRT modalities the ratio both with all country data and separately with countries with substantial numbers of RRT patients, with both analyses showing similar results.

In conclusion, we demonstrated the existence of prominent gender disparities in CKD prevalence in 195 countries in the GBD Study. However, the nature of these disparities is complex and in some cases hardly explicable. Kidney transplantation could be considered a particularly prominent example of lower female access to renal health care. There is a need for substantial further work to clarify in depth the local causes of the overall gender disparities in CKD prevalence and improve provision of universal and equal access to renal care. This would require joint efforts between the

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scientific community and national health authorities. What we can do as scientists is provide robust data for politicians and national health authorities to act, giving them evidence that their final decisions have an impact on people's health, including that of women, who are at more susceptible due to the unequal access to health care. Moreover, to monitor progress towards equal access in CKD prevention, diagnosis and treatment, health care authorities need clearly defined indicators that could be developed based on wide agreement in the kidney community. Current analysis provides an impact on the construction of the general framework to define such indicators and to reveal the relationships between different factors responsible for the predominance of CKD stages in different populations.

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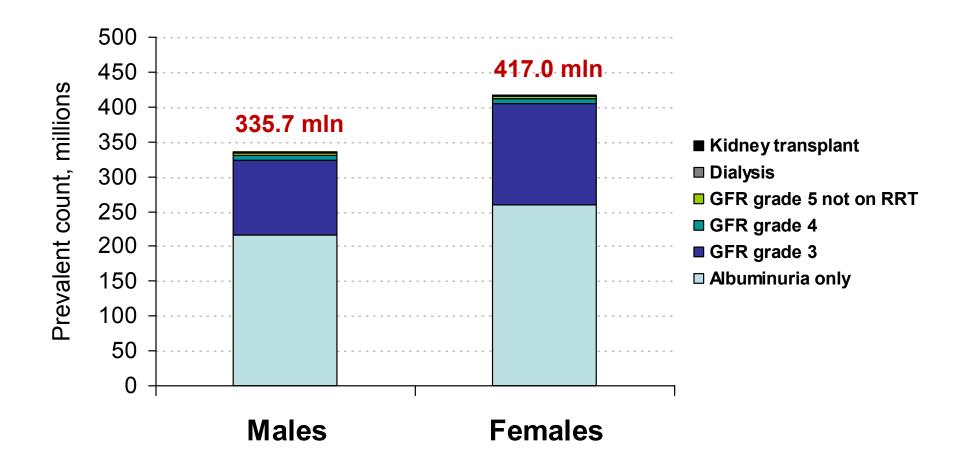
*Figure 1*. Global number of persons with CKD in 2016. CKD – chronic kidney disease. GFR – glomerular filtration rate. RRT – renal replacement therapy.

*Figure 2*. Male:female ratio for each impaired kidney function condition. Each dot in the figure represents a country. For each impaired kidney function condition the? median is indicated by line and numeric value. Alb – albuminuria; CKD – chronic kidney disease; Dial – dialysis; KTx – kidney transplant

*Figure 3*. Male:Female ratio for the kidney transplantation prevalence rate in 120 countries with more than 50 individuals with functioning kidney graft in 2016. Grey filling marks countries with less than 50 individuals with functioning kidney graft for which the ratio is not estimated.

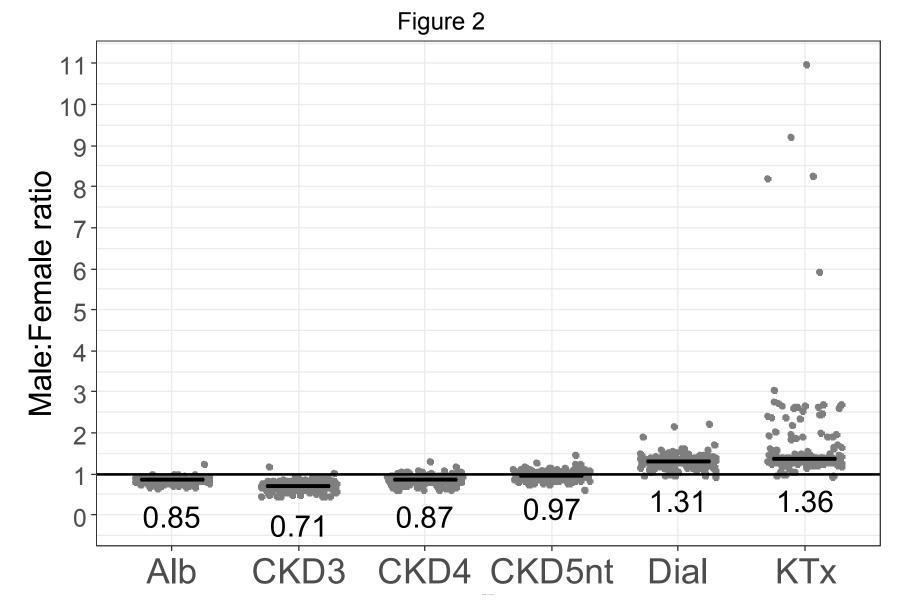
*Figure 4*. Correlation between gross domestic product per capita and ratio of dialysis to kidney transplant prevalence count. Only countries with more than 50 patients on renal replacement therapy were included in the analysis. Each dot in the figure represents a country. GDP PPP – gross domestic product based on purchasing power parity.

# Figure 1

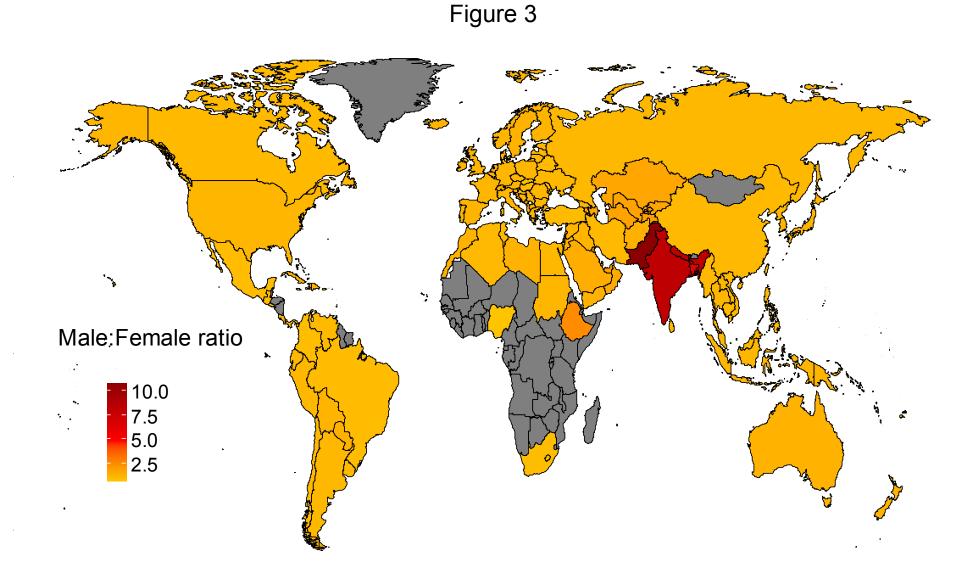


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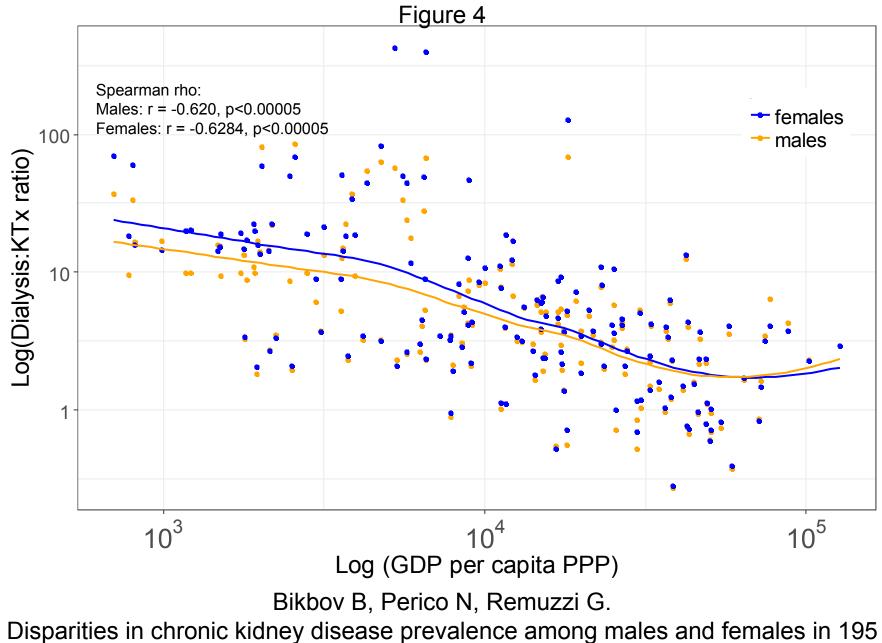
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Analysis of the Global Burden of Disease, Injuries and Risk Factors 2016 Study"

Figure S1. Male:Female ratio for albuminuria prevalence rate in 195 countries in 2016

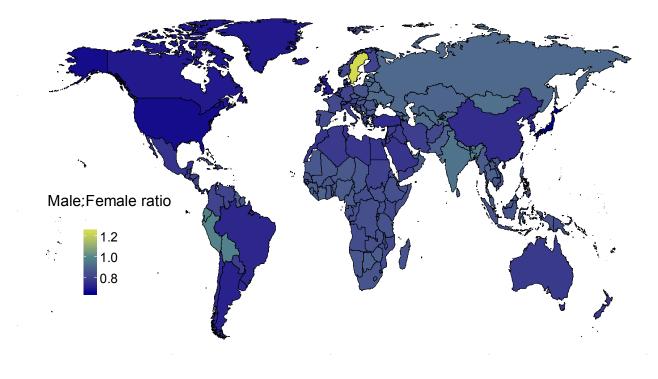


Figure S2. Male:Female ratio for CKD stage 3 prevalence rate in 195 countries in 2016

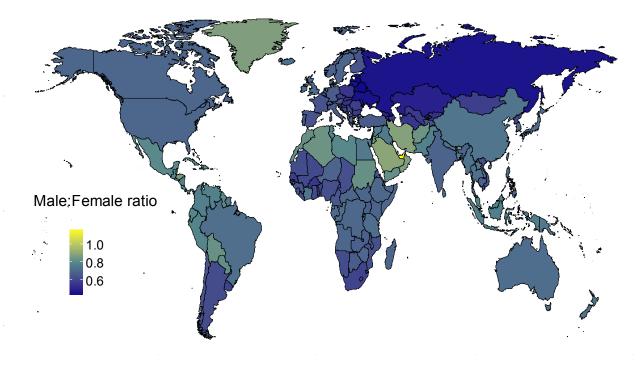


Figure S3. Male:Female ratio for CKD stage 4 prevalence rate in 195 countries in 2016

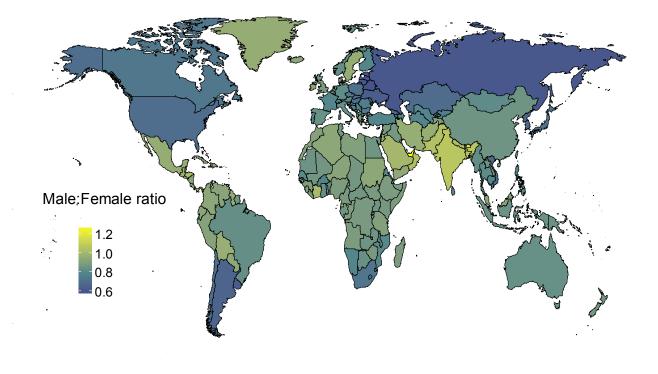


Figure S4. Male:Female ratio for CKD stage 5 not on renal replacement therapy prevalence rate in 195 countries in 2016

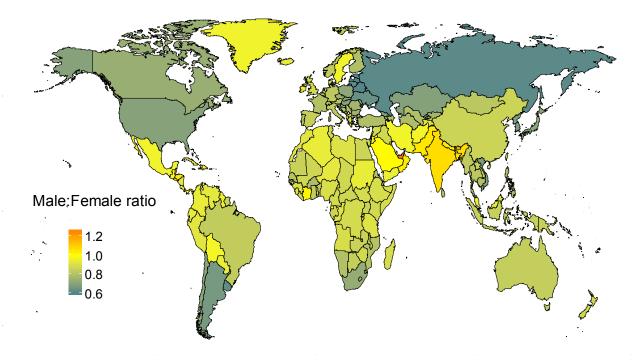


Figure S5. Male:Female ratio for dialysis prevalence rate in 195 countries in 2016 (calculated also for countries with the estimated sporadic number of prevalent dialysis patients)

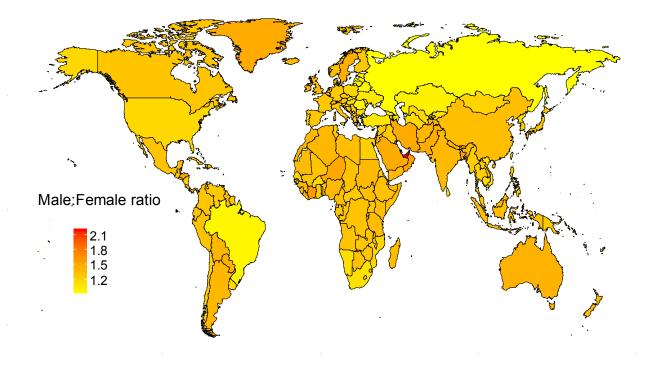


Figure S6. Relationship between gross domestic product per capita and Male:Female ratio for albuminuria prevalence rate in 195 countries in 2016

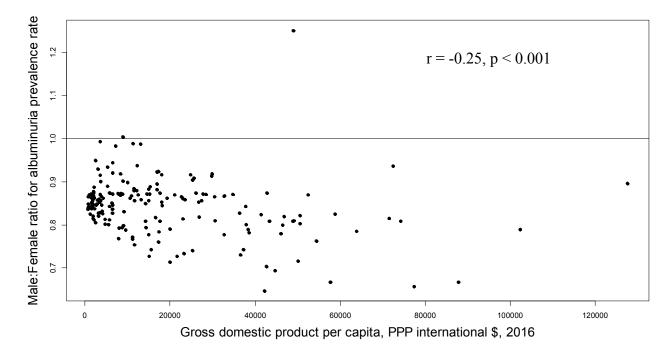


Figure S7. Relationship between gross domestic product per capita and Male:Female ratio for GFR grade 3 prevalence rate in 195 countries in 2016

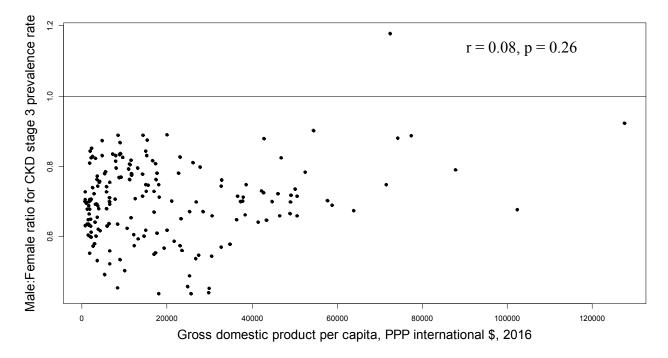


Figure S8. Relationship between gross domestic product per capita and Male:Female ratio for GFR grade 4 prevalence rate in 195 countries in 2016

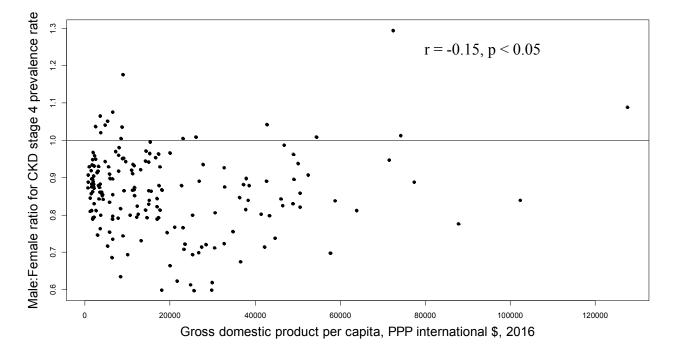


Figure S9. Relationship between gross domestic product per capita and Male:Female ratio for GFR grade 5 without RRT prevalence rate in 195 countries in 2016

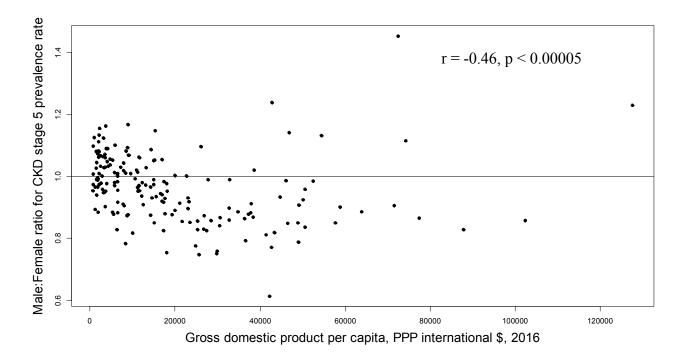


Figure S10. Relationship between gross domestic product per capita and Male:Female ratio for dialysis prevalence rate in 169 countries with more than 20 female persons treated by dialysis in 2016

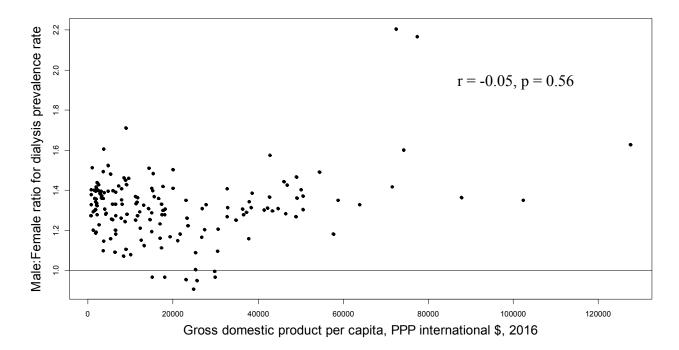
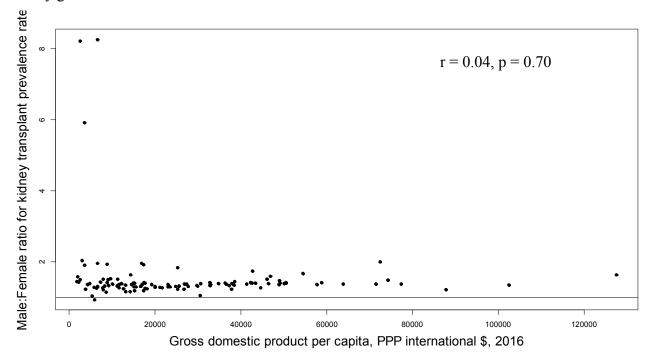
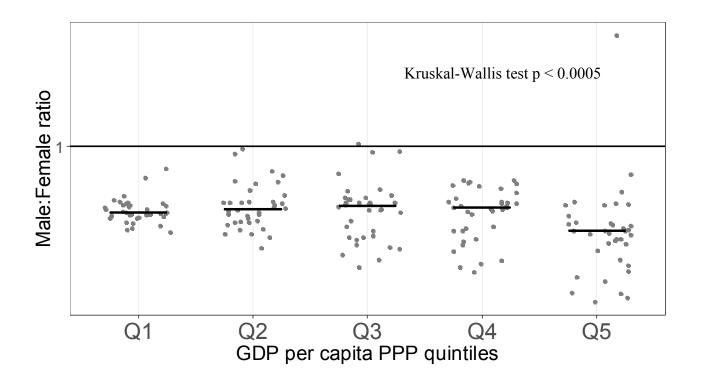


Figure S11. Relationship between gross domestic product per capita and Male:Female ratio for kidney transplantation prevalence rate in 120 countries with more than 20 female persons having kidney graft in 2016

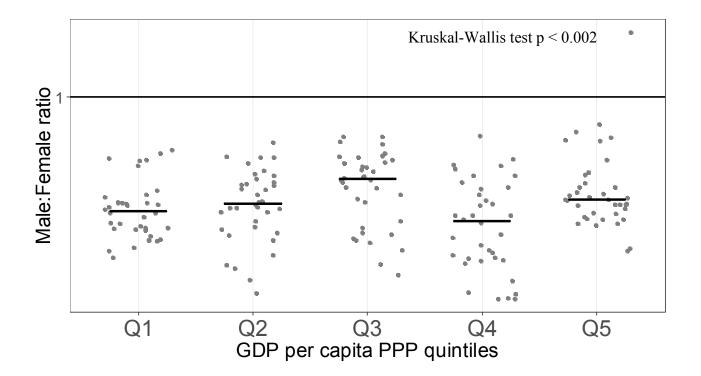


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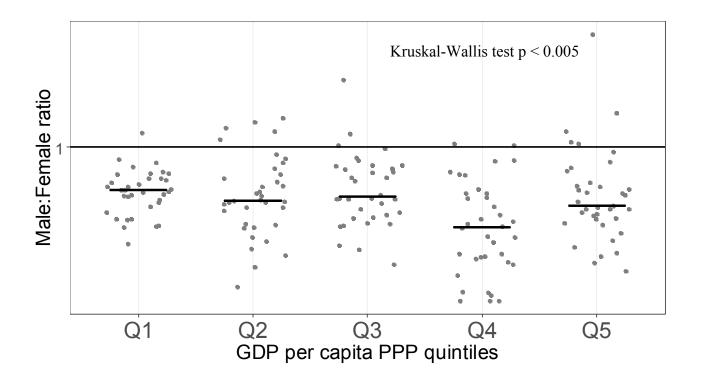
GDP per capita quintile	median	IQR
Q1	0.850	0.840-0.866
Q2	0.858	0.829-0.878
Q3	0.865	0.797-0.881
Q4	0.861	0.809-0.885
Q5	0.808	0.763-0.828

Bikbov B, Perico N, Remuzzi G. Disparities in chronic kidney disease prevalence among males and females in 195 countries: analysis of the Global Burden of Disease 2016 Study. Nephron. 2018. doi: 10.1159/000489897 https://www.karger.com/Article/Abstract/489897 Figure S13. Male:female ratio for GFR grade 3 prevalence rate. Each dot in the figure represents a country. For each GDP category the median male:female ratio is indicated by line, and median and interquartile range (IQR) is mentioned below the figure.



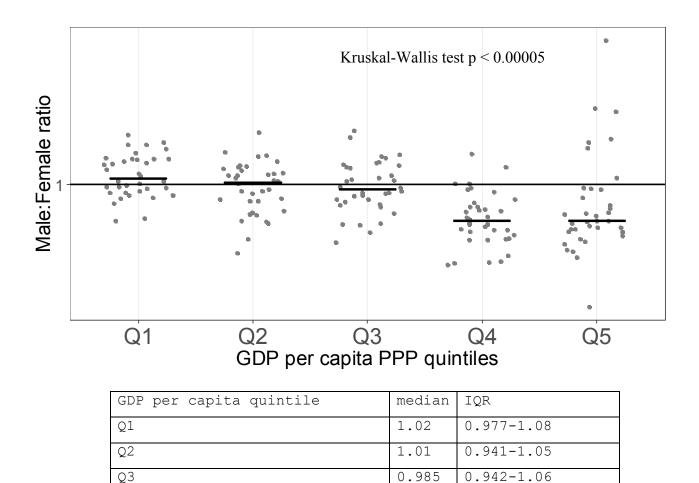
GDP per capita quintile	median	IQR
Q1	0.683	0.633-0.711
Q2	0.704	0.636-0.765
Q3	0.773	0.650-0.820
Q4	0.655	0.549-0.745
Q5	0.715	0.675-0.761

Bikbov B, Perico N, Remuzzi G. Disparities in chronic kidney disease prevalence among males and females in 195 countries: analysis of the Global Burden of Disease 2016 Study. Nephron. 2018. doi: 10.1159/000489897 https://www.karger.com/Article/Abstract/489897 Figure S14. Male:female ratio for GFR grade 4 prevalence rate. Each dot in the figure represents a country. For each GDP category the median male:female ratio is indicated by line, and median and interquartile range (IQR) is mentioned below the figure.



GDP per capita quintile	median	IQR
Q1	0.888	0.854-0.921
Q2	0.861	0.798-0.933
Q3	0.871	0.822-0.946
Q4	0.791	0.706-0.879
Q5	0.847	0.812-0.907

Bikbov B, Perico N, Remuzzi G. Disparities in chronic kidney disease prevalence among males and females in 195 countries: analysis of the Global Burden of Disease 2016 Study. Nephron. 2018. doi: 10.1159/000489897 https://www.karger.com/Article/Abstract/489897 Figure S15. Male:female ratio for GFR grade 5 without RRT prevalence rate. Each dot in the figure represents a country. For each GDP category the median male:female ratio is indicated by line, and median and interquartile range (IQR) is mentioned below the figure.



0.885

0.885

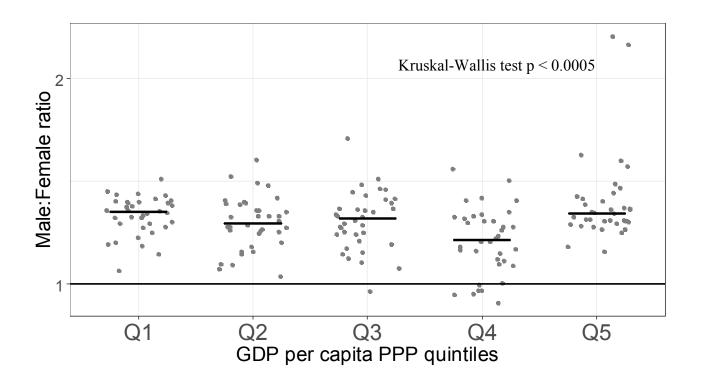
0.838-0.933

0.850-0.985

Q4

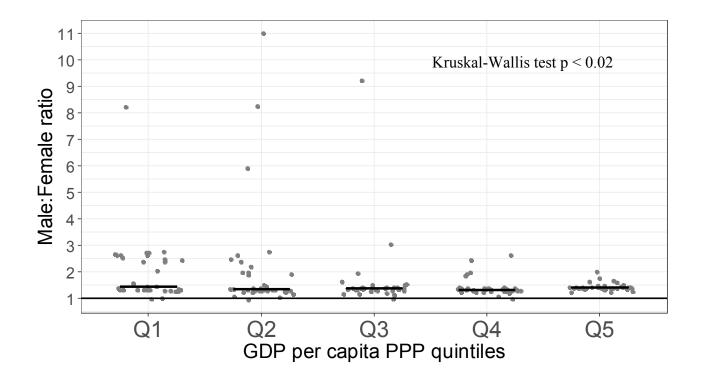
Q5

Bikbov B, Perico N, Remuzzi G. Disparities in chronic kidney disease prevalence among males and females in 195 countries: analysis of the Global Burden of Disease 2016 Study. Nephron. 2018. doi: 10.1159/000489897 https://www.karger.com/Article/Abstract/489897 Figure S16. Male:female ratio for dialysis prevalence rate. Each dot in the figure represents a country. For each GDP category the median male:female ratio is indicated by line, and median and interquartile range (IQR) is mentioned below the figure.



GDP per capita quintile	median	IQR
Q1	1.35	1.29-1.40
Q2	1.30	1.23-1.39
Q3	1.32	1.24-1.40
Q4	1.22	1.11-1.32
Q5	1.34	1.30-1.42

# Bikbov B, Perico N, Remuzzi G. Disparities in chronic kidney disease prevalence among males and females in 195 countries: analysis of the Global Burden of Disease 2016 Study. Nephron. 2018. doi: 10.1159/000489897 https://www.karger.com/Article/Abstract/489897 Figure S17. Male:female ratio for kidney transplant prevalence rate. Each dot in the figure represents a country. For each GDP category the median male:female ratio is indicated by line, and median and interquartile range (IQR) is mentioned below the figure.



GDP per capita quintile	median	IQR
Q1	1.43	1.30-2.55
Q2	1.33	1.28-1.96
Q3	1.36	1.30-1.40
Q4	1.32	1.27-1.37
Q5	1.39	1.36-1.41

Bikbov B, Perico N, Remuzzi G. Disparities in chronic kidney disease prevalence among males and females in 195 countries: analysis of the Global Burden of Disease 2016 Study. Nephron. 2018. doi: 10.1159/000489897 https://www.karger.com/Article/Abstract/489897 Modelling strategy for impaired kidney function prevalence

### Input data

GBD has obtained data from several rounds of systematic review of the CKD prevalence throughout the world conducted in PubMed and EMBASE, and further manual search in the published literature. Additional data were extracted from unpublished data sources covering hospital discharge records, ESKD registries, ISN-KDDC (International Society of Nephrology's Kidney Disease Data Center) database, CKD-PC (Chronic Kidney Disease Prognosis Consortium) online tool database. Data sources can be explored in an data source (http://ghdx.healthdata.org/gbd-2016/data-input-sources).

Condition	Number of sources	Number of countries
Albuminuria	72	31
GFR grade 3	112	47
GFR grade 4	94	40
GFR grade 5	92	38
Maintenance dialysis	534	107
Renal transplantation	430	104

Table S1. Number of data sources used for CKD modeling in GBD 2016 revision.

# Adjustment of data extracted from different sources

A number of adjustments were applied to extracted data from different sources in order to make the data more consistent and suitable for modelling. Commonly applied adjustments included age-sex splitting, adding study-level covariates, and bias correction. Age-sex splitting was applied to literature data reported by age or sex but not by age and sex assuring that the total number of cases remained as reported. If a source did not report sample size by age or sex, the age-sex distribution of the population for the same location and year was applied to the reported total sample size. The meta-regression component of DisMod-MR 2.1 was applied for most of the bias correction of data for variations in study attributes such as case definitions and measurement method. DisMod-MR 2.1 calculates a single adjustment that is applied regardless of age, sex, or location. If enough data were

Bikbov B, Perico N, Remuzzi G. Disparities in chronic kidney disease prevalence among males and females in 195 countries: analysis of the Global Burden of Disease 2016 Study. Nephron. 2018. doi: 10.1159/000489897 https://www.karger.com/Article/Abstract/489897 available to differentiate these adjustments by age, sex, or location, or if detailed survey data were available to make more precise adjustments between different thresholds on a biochemical measure, the bias corrections to the data before entry into DisMod-MR 2.1 was applied.

### DisMod-MR 2.1 description

DisMod-MR 2.1 is a Bayesian meta-regression model that pool data from different sources, control and adjust for bias in data, and incorporate other types of information such as country level covariates. DisMod-MR 2.1 is a mixed effect model that borrows information across age, time, and locations to synthesise multiple data sources into unified estimates of levels and trends. DisMod-MR organizes the flow of data and settings at each level of the analytical cascade. The sequence of estimation occurs at five levels: global, super-region, region, country and, where applicable, subnational location. The super-region priors are generated at the global level with mixed-effects, nonlinear regression using all available data; the super-region fit, in turn, informs the region fit, and so on down the cascade. The wrapper gives analysts the choice to branch the cascade in terms of time and sex at different levels depending on data density. The default used in most models is to branch by sex after the global fit but to retain all years of data until the lowest level in the cascade. The coefficients for country covariates are re-estimated at each level of the cascade. For a given location, country coefficients are calculated using both data and prior information available for that location. In the absence of data, the coefficient of its parent location is used, in order to utilize the

# *Modelling strategy*

predictive power of our covariates in data sparse situations.

Data sources included in the analysis used different methods for calculating estimated glomerular filtration rate (eGFR) or albuminuria. Due to this the procedure of cross-walking was applied to unify different definitions of eGFR and albuminuria.

For pediatric population eGFR was estimated using the Schwartz equation. For adult population the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was used as a reference standard for eGFR. The GBD modelling crosswalked data reporting eGFR calculated by the Modification of Diet in Renal Disease (MDRD) equation to data reported using the CKD-EPI equation as the GBD reference equation, based on the coefficients figured out in a meta-analysis of

Bikbov B, Perico N, Remuzzi G. Disparities in chronic kidney disease prevalence among males and females in 195 countries: analysis of the Global Burden of Disease 2016 Study. Nephron. 2018. doi: 10.1159/000489897 https://www.karger.com/Article/Abstract/489897 studies reporting prevalence of CKD using both the MDRD and CKD-EPI equations. Exponentiated beta values for this crosswalk are shown in the table below:

Table S2. Coefficients for cross-walking procedure between prevalence estimates produced by MDRD and CKD-EPI equations, for separate eGFR grades.

eGFR calculated by MDRD Equation	Exponentiated beta (95% CI)
eGFR grade 3	1.31 (1.30 to 1.32)
eGFR grade 4	0.99 (0.97 to 1.01)
eGFR grade 5	0.91 (0.87 to 0.97)
eGFR grades 3-5	1.27 (1.26 to 1.28)

Data from sources reporting the prevalence of stage III, IV, and V CKD was aggregated to represent the prevalence of stage III-V CKD. A DisMod-MR 2.1 model was run to produce estimates by age, sex, year, and country for aggregate stage III-V CKD. In order to enforce more consistency between stage models, prevalence of CKD stage III, IV, and V were then scaled to sum to the prevalence and incidence of the stage III-V CKD model, at the gender, age, and country-matched level.

The maintenance dialysis and renal transplant models include bounds on location random effects for East Asia and High-income Asia Pacific. As Taiwan (Province of China) and Japan have rates of renal replacement therapy far out of proportion to other countries in their regions, these bounds prevent renal replacement therapy estimates for surrounding countries lacking data from overinflating. For the modelling purposes GBD assumes the "remission" as one of the principal characteristics of CKD model. In case of dialysis the "remission" refers to the ratio of the incidence of renal transplantation to prevalence of dialysis at the gender, age, and country-matched level.

Albuminuria exposure was modeled using DisMod-MR 2.1 to produce prevalence estimates by age, sex, year, and country. The albuminuria exposure model included country-level covariates indicating prevalence of diabetes mellitus and mean systolic blood pressure. As albuminuria classification is dependent on GFR, this model included a cross-walk adjusting data points obtained using estimating equations other than CKD-EPI to the CKD-EPI equation. GBD also applied a cross-walk to adjust alternate definitions of albuminuria to the reference definition of ACR > 30 mg/g and GFR >=60 ml/min/1.73m<sup>2</sup>. This crosswalk was informed with priors obtained from a linear regression using NHANES data to compare age-standardized prevalence of the alternate

Bikbov B, Perico N, Remuzzi G. Disparities in chronic kidney disease prevalence among males and females in 195 countries: analysis of the Global Burden of Disease 2016 Study. Nephron. 2018. doi: 10.1159/000489897 https://www.karger.com/Article/Abstract/489897 definition to reference definition. Regression outputs were used to adjust prevalence from studies that employ lower cut points than the reference definition to those using the reference cut point.

Table S3. Coefficients for cross-walking procedure between prevalence estimates produced by different thresholds for albuminuria

Definition of ACR	Exponentiated beta (95% CI)
ACR > 17  mg/g	2.084 (1.530 to 2.639)
ACR > 20  mg/g	1.662 (1.220 to 2.103)
ACR > 25 mg/g	1.305 (1.112 to 1.497)

Modelling flowchart for CKD prevalence

