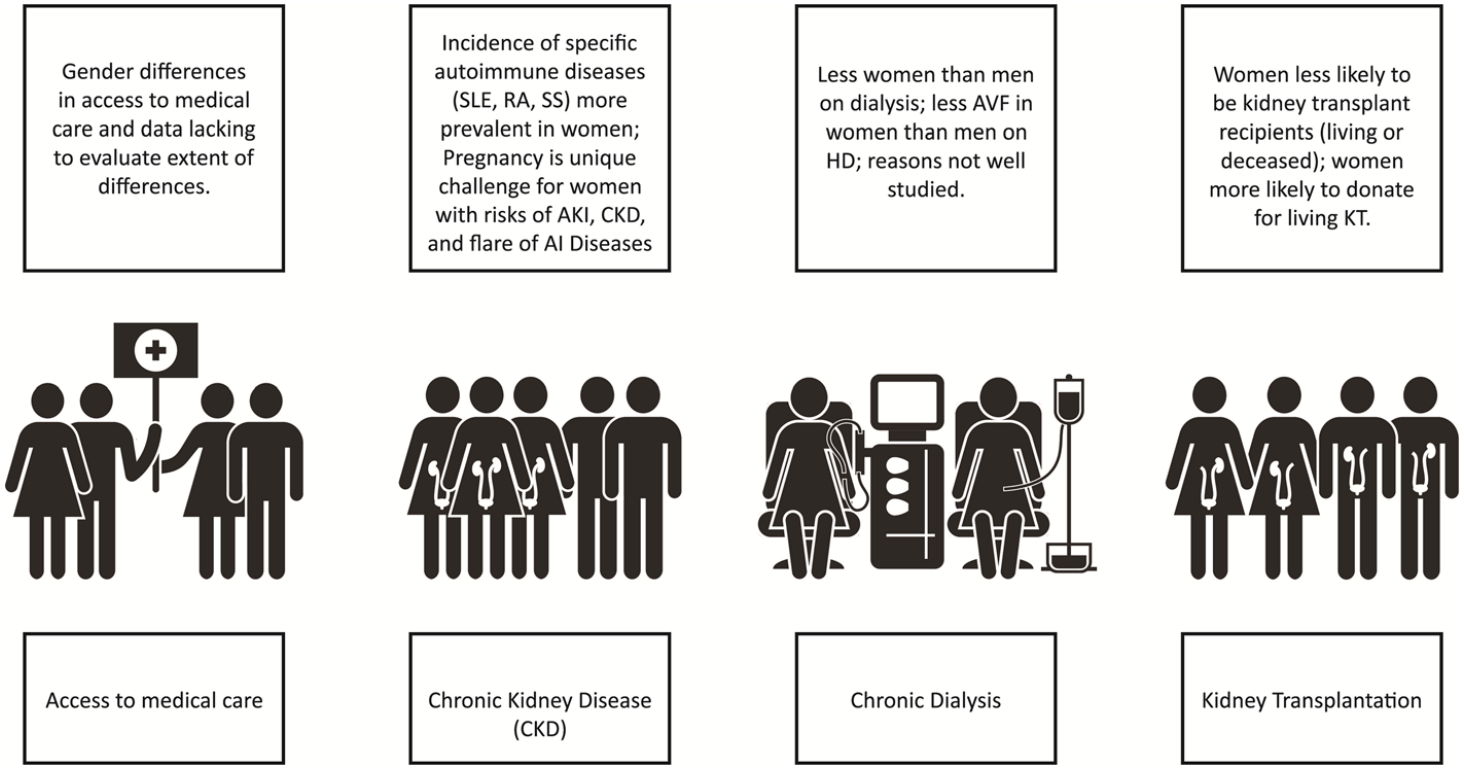
Set of slides for the Factsheet Nephrology

Author(s): PhD, MD, MSs Valerie Luyckx and Prof. Dr. med. Thomas Müller

Take Home Messages

Sex differences throughout the continuum of CKD care

Fig. 1 Sex differences throughout the continuum of CKD care.
SLE = Systemic Lupus Erythematosus;
RA = Rheumatoid Arthritis;
SS = Systemic Scleroderma;
AKI = acute kidney injury;
CKD = chronic kidney disease;
AI = autoimmune;
AVF = arteriovenous fistula;
HD = hemodialysis;
KT = kidney transplant



Sex differences in the prevalence of CKD stages G3-G5 – differences remain unexplained, not only related to limited access to care

Figure 1 | Sex differences in the prevalence of CKD. Findings from population-based studies show differences between geographical regions in the prevalence of chronic kidney disease (CKD) stages G3–G5 (59-<15) as well as sex-specific differences. In most regions, the prevalence of CKD is higher in women than in men, but some countries (for example, Japan and Singapore) show opposite findings, with more men than women being affected by CKD5–27. Prevalences are given as a percent of the population affected. (Häufigkeit)

Carrero JJ et al, Nat Rev Nephrol 2018; n14: 151

Global differences in age-standardized incidence rate of dialysis by gender

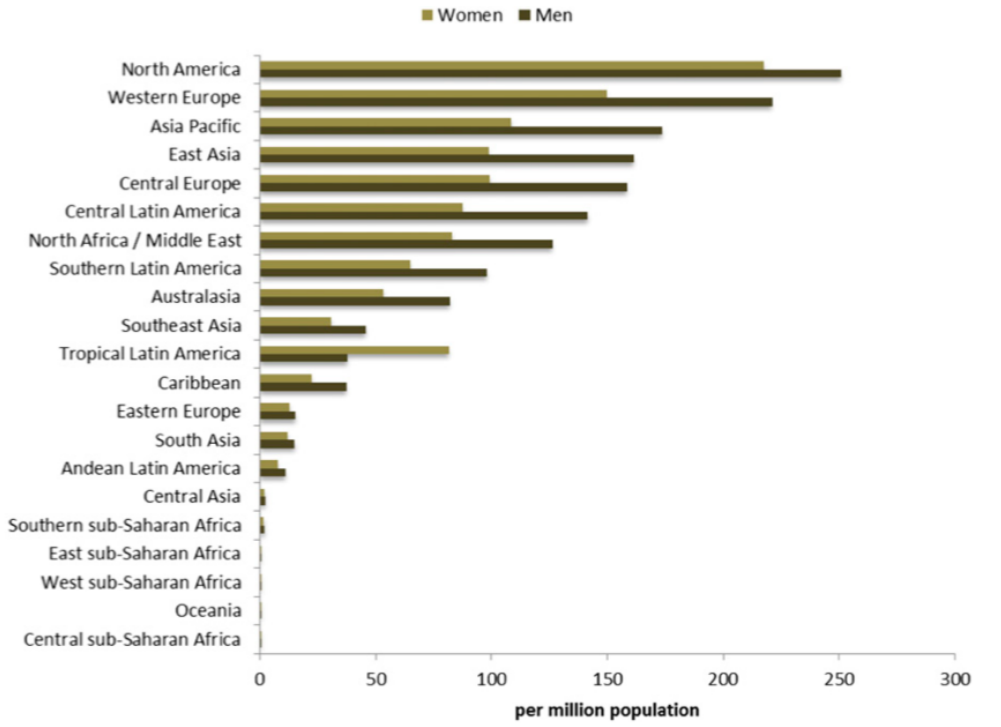


Figure 6. Sex-stratified age-standardized maintenance dialysis incidence rate per million population for 21 world regions in year 2010.

*note huge variability globally in totall access to dialysis – not related to rates of CKD, but to cost dialysis → many die without dialysis

Thomas et al., JASN 26:2621-2633

Sex and gender disparities in the epidemiology and outcomes of CKD

Why the switch here?

- Are women more adherent?
- Women tend to attend screening activities more
- Are women more dialgnosed?
- Are medications e.g. ACEI more effective in women?
- Do pre-and post-menopause play a role?
- Reasons may be different across country income categories
- Risk factors differ e.g. smoking?

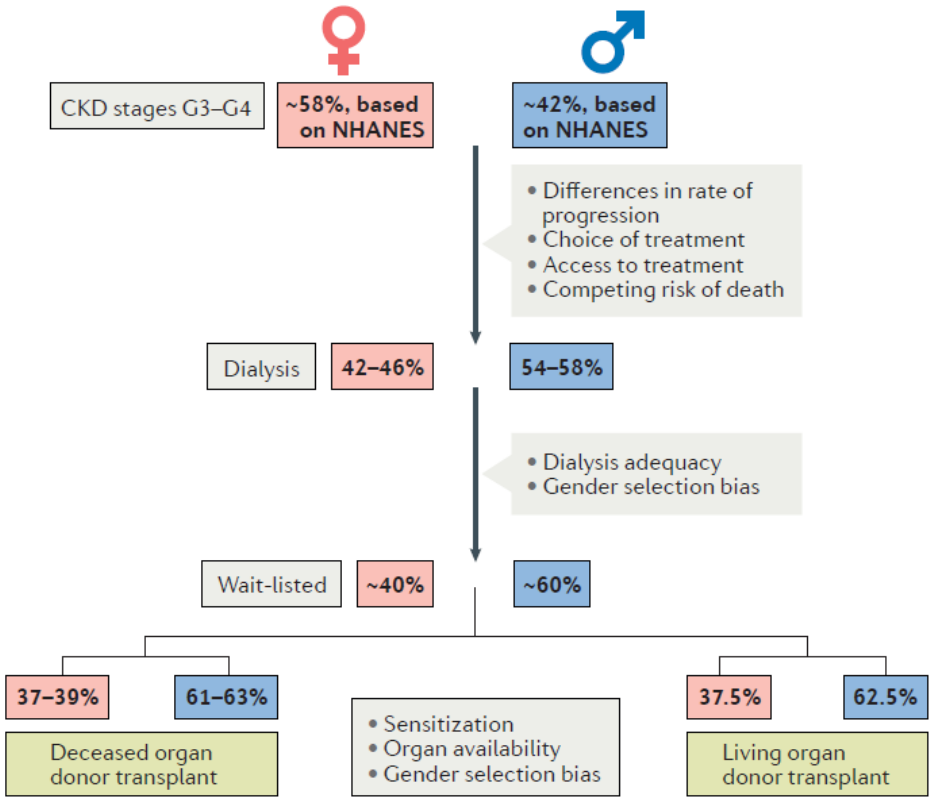


Figure 3 | **Sex and gender disparities in the epidemiology and outcomes of CKD.** Despite more women than men having chronic kidney disease (CKD), more men than women initiate dialysis or undergo transplantation. This discrepancy might in part be attributed to sex (that is, biological) differences, such as in the rate of CKD progression or the effect of sensitization, or to gender (that is, sociocultural) differences, including differences in access to care or differences in attitude towards disease. All percentages in the figure refer to US data. Data are from multiple references9, 45,96,103.

Carrero JJ et al, Nat Rev Nephrol 2018; n14: 151

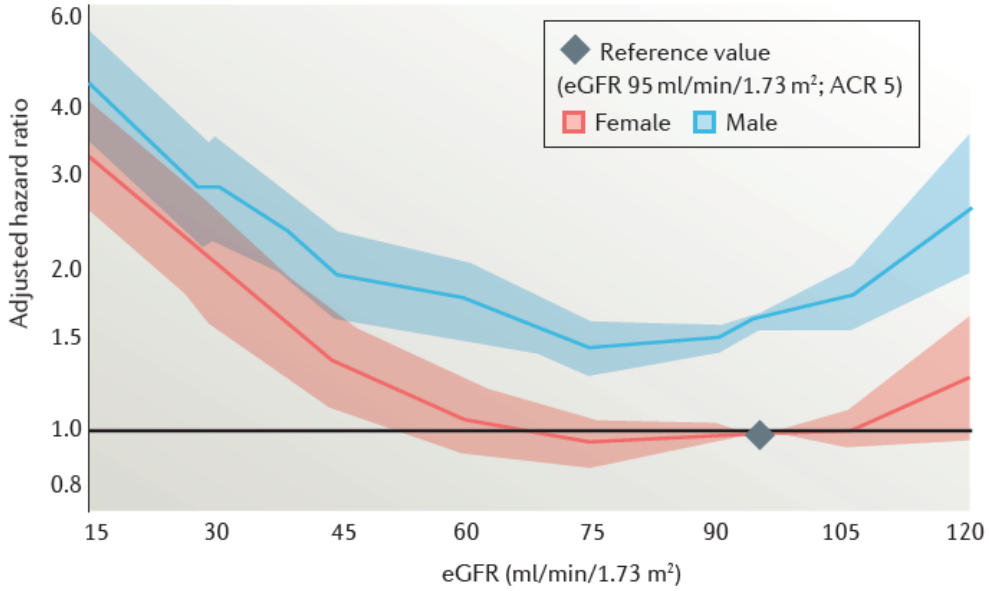
Hazard ratios of all-cause mortality according to estimated glomerular filtration rate by sex - US

Figure 2 | **Hazard ratios of all-cause mortality according to estimated glomerular filtration rate by sex.**

Men have a higher all-cause mortality than women at all levels of estimated glomerular filtration rate (eGFR). The shaded area indicates the 95% CI.

ACR, albumin:creatinine ratio; NHANES, National Health and Nutrition Examination Survey.

Reproduced from Associations of estimated glomerular filtration rate and albuminuria with mortality and renal failure by sex: a meta-analysis, Nitsch, D. et al. BMJ 346, f324 (2013) with permission from BMJ Publishing Group Ltd. (REF 48).



Carrero JJ et al, Nat Rev Nephrol 2018; n14: 151

Causes of death among men and women on dialysis in Europe

- Women in dialysis have similar risk of death as men, whereas lower risk of death in general population → risk of death proportionately higher for women on dialysis
- Are we doing something wrong in dialysis such that women have this higher risk?

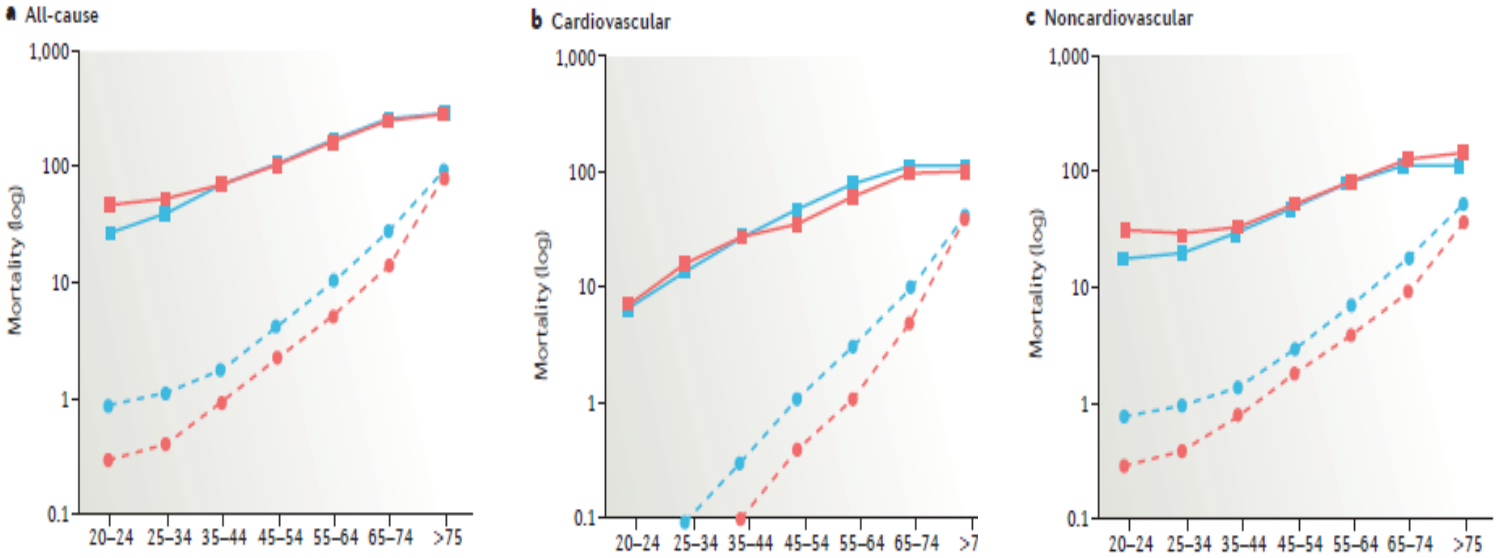


Figure 5 | **Causes of death among men and women on dialysis.**
All-cause (part a), cardiovascular (part b) and noncardiovascular (part c) mortality among men and women from the European general population (GP) and among incident dialysis patients from the European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) Registry. Men and women have similar mortality upon commencement of dialysis, an observation that contradicts the well-acknowledged survival advantage of women versus men in the general population. Analysis of specific causes of death demonstrates lower cardiovascular mortality in women compared with men across all age categories, which is consistent with the lower cardiovascular risk of women versus men in the general population. By contrast, the risk of death due to noncardiovascular causes seems elevated in women compared with men starting dialysis, especially among younger women. Reproduced with permission from REF. 163, Clinical Journal of the American Society of Nephrology.

Carrero JJ et al, Nat Rev Nephrol 2018; n14: 151

The male:female ratio of the incidence of end-stage renal disease across the lifespan in US

Among younger children boys tend to have more severe kidney disease because of the higher rates of congenital abnormaliteis of the urinary tract (CAKUT)

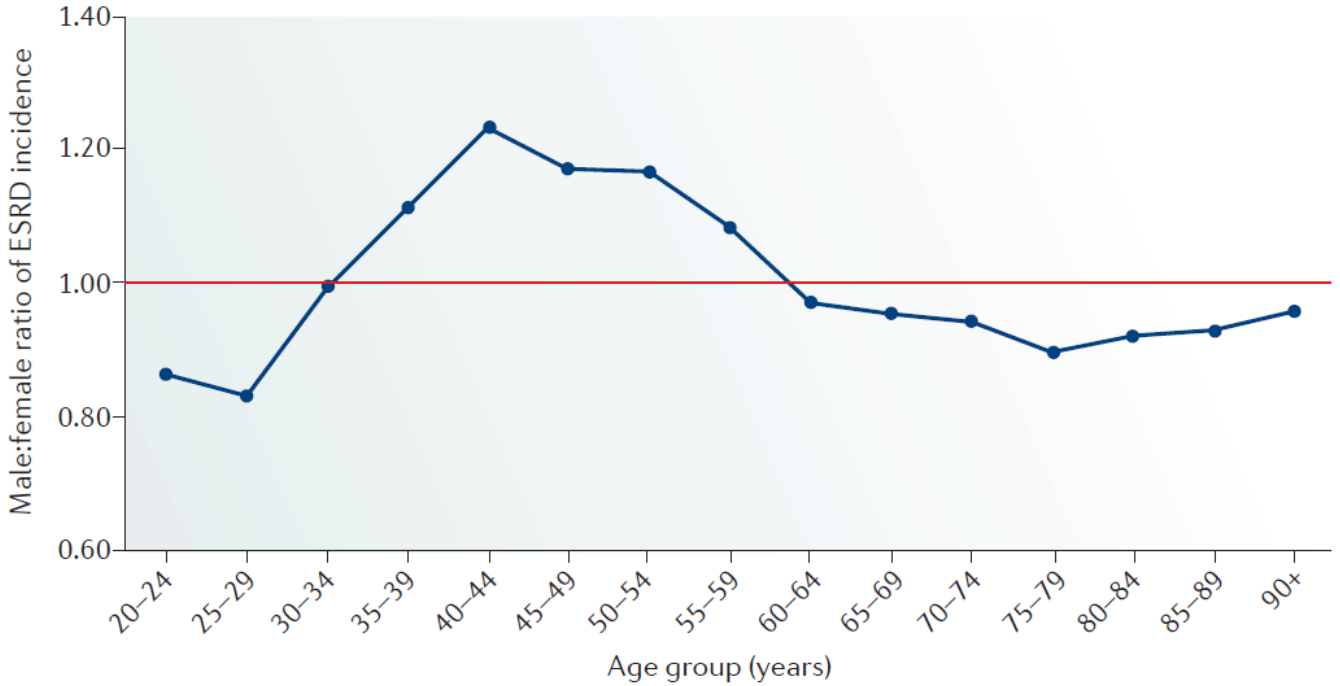
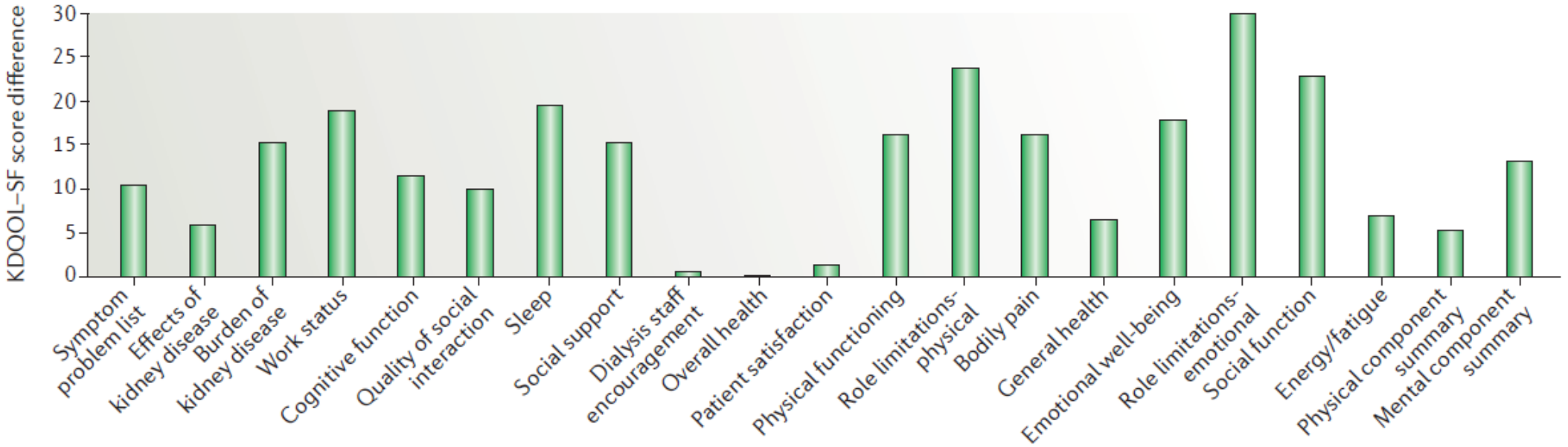


Fig. 1 | **The male:female ratio of the incidence of end-stage renal disease across the lifespan.** The relative risks of end-stage renal disease (ESRD) in men and women change throughout the lifespan. From the age of 60 years, women are at higher risk of developing the disease than men.
Data obtained from the US Renal Data System, 2016 Annual Data Report12. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy or interpretation of the US government.

Harambat Pediatr Nephrol, (2012) 27:363-373
Ashuntantang GE et al, Nat Rev Nephrol 2018

Differences in quality of life (QOL) domains between men and women on dialysis – Men score higher in terms of QOL



Important QOL issues for women

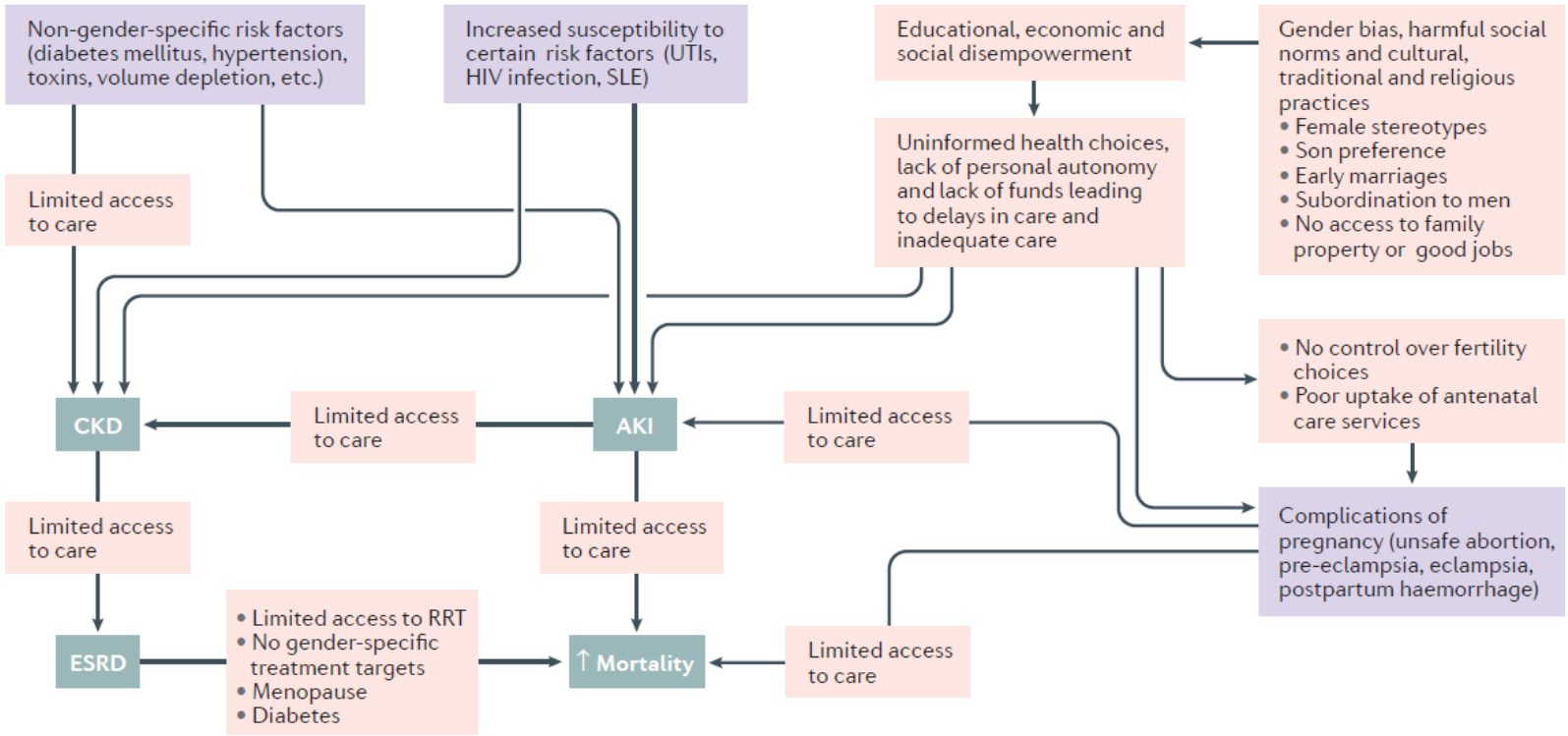
- Body image – many scars
- Loss of fertility → loss of value/status in many cultures

Figure 4 | **Differences in quality of life domains between men and women on dialysis.**
Positive values indicate higher quality of life scores in men than in women across all domains. Self-reported quality of life was assessed 12 months after haemodialysis initiation by use of the kidney disease quality of life short form (KDQOL-SF). Adapted with permission from REF. 136, John Wiley & Sons.

Carrero JJ et al, Nat Rev Nephrol 2018; n14: 151

Key factors that underlie poor kidney health and adverse outcomes in women – globally limited access to care is a common denominator

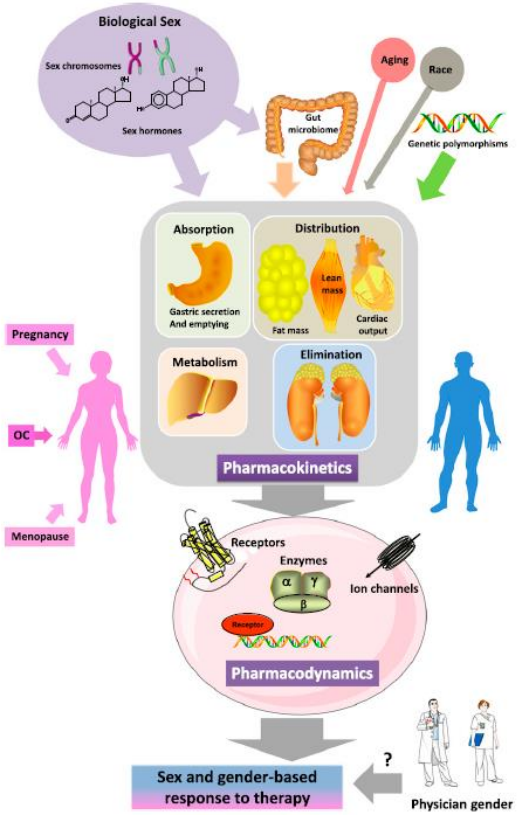
Fig. 2 | Key factors that underlie poor kidney health and adverse outcomes in women. In addition to increased susceptibility to certain risk factors for chronic kidney disease (CKD) and acute kidney injury (AKI) and unique risk factors such as pregnancy complications, social factors such as the disempowerment of women and a lack of access to care make a major contribution to the higher global prevalence of CKD in women than in men and the increased mortality in this population.
ESRD, end-stage renal disease; RRT, renal replacement therapy; SLE, systemic lupus erythematosus; UTI, urinary tract infection.



Summary of sex and gender influences on the pharmacological response to drugs

Summary of sex and gender influences on the pharmacological response to drugs.

- Biologic sex via sex-specific genetic and hormonal influences on cellular systems alters the transcriptome, proteome, and metabolome of all cells and organs as well as the gut microbiome and influences pharmacokinetics (e.g., absorption, distribution, metabolism, and elimination of drugs) and pharmacodynamics (e.g., the effect of drugs on receptors, ion channels, enzymes, and signaling pathways).
- Aging, race, and genetic polymorphism also influence pharmacokinetics and pharmacodynamics parameters in a sex-specific manner.
- In women, the hormonal influences of pregnancy, menopause, and the use of OCs also produce sex differences in the pharmacokinetics and pharmacodynamics of drugs.
- Finally, physician gender could add an additional level of difference in response to treatment.



Mauvais-J et al, Pharmacol Rev 2021; 73:730–62

Possible mechanisms responsible for gender differences in renal disease progression

But also smaller body size
→ might balance out

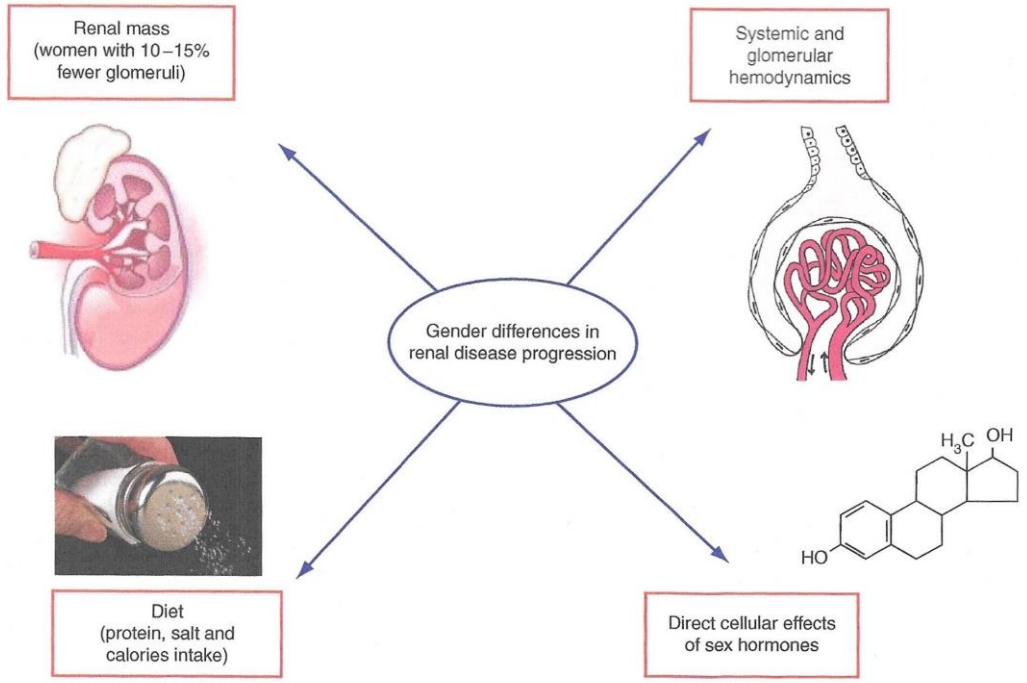
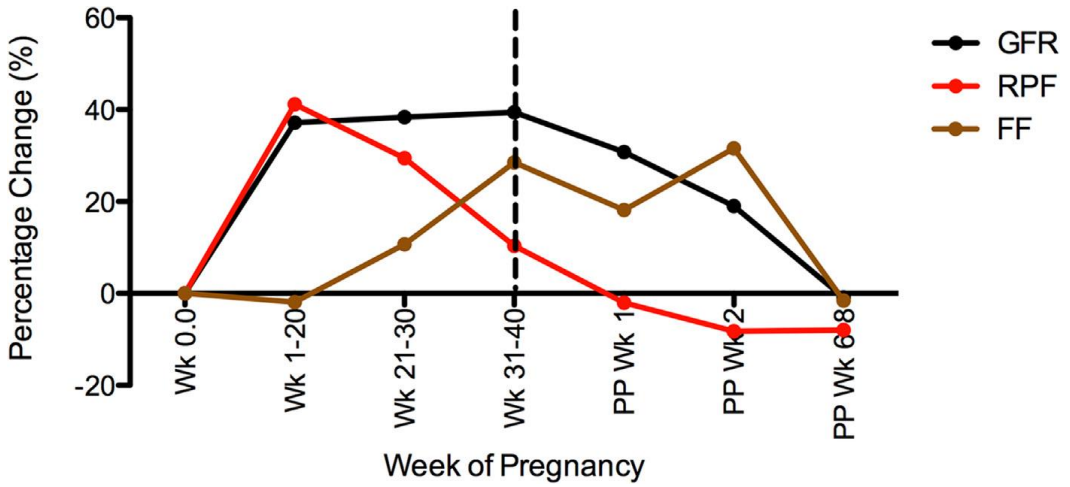


Fig. 7.3 Possible mechanisms responsible for gender differences in renal disease progression

Physiologic changes in kidney function during pregnancy: Increments in GFR, RPF, and FF at different time points during gestation

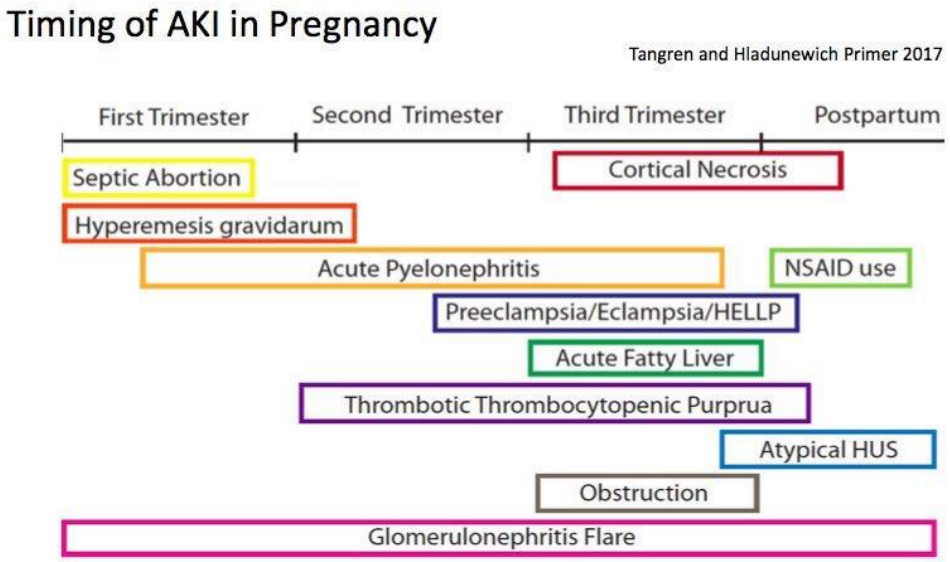
Figure 1. **Increments in GFR, RPF, and filtration fraction (FF) as measured by inulin or iothalamate and p-aminohippurate clearance methodology, respectively, at different time points during gestation.**

(Reprinted with permission from Odutayo and Hladunewich.9)

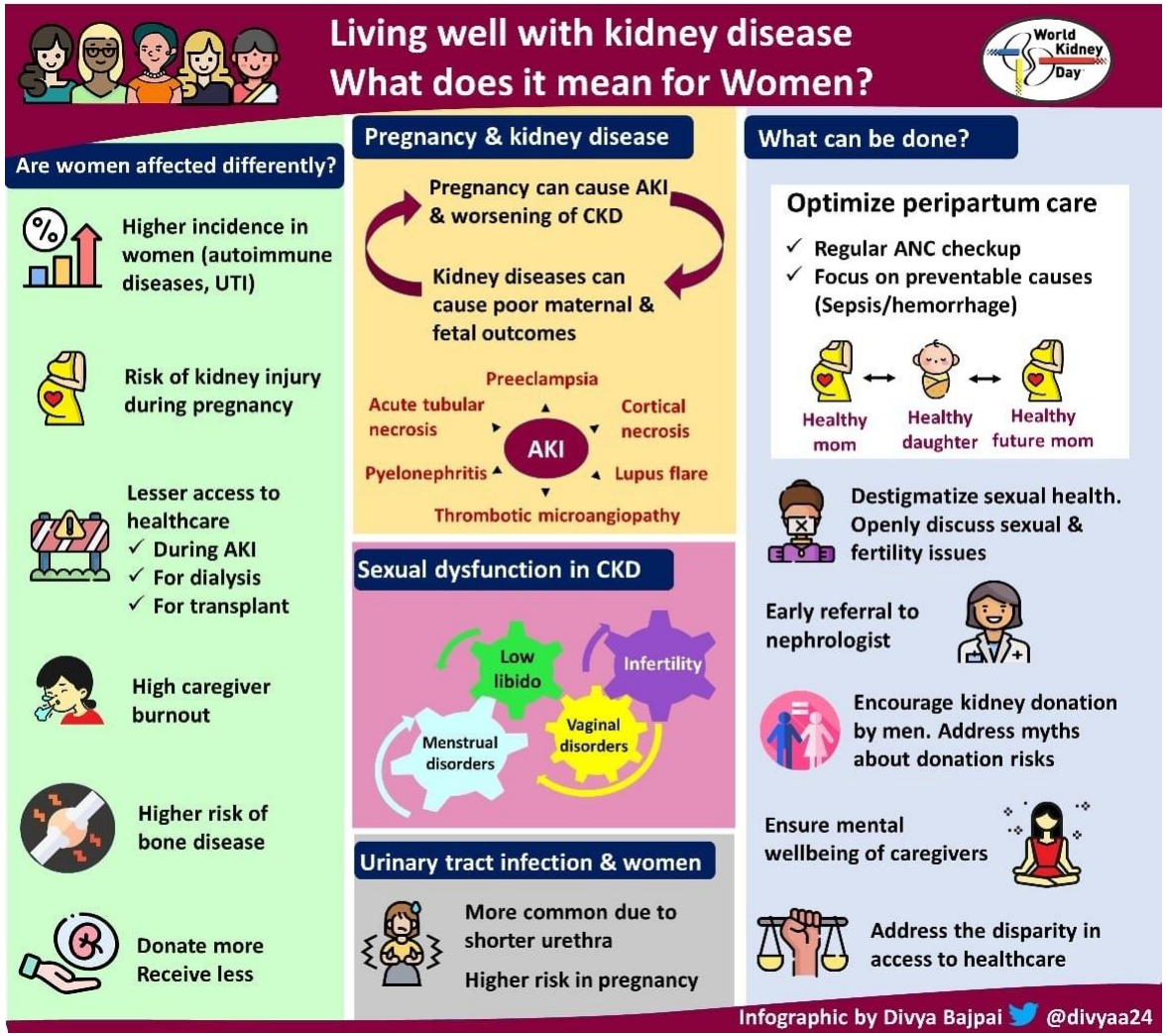


Timing of AKI in Pregnancy

- Pregnancy poses a high risk of #kidney injury due to various etiologies (see pic) which can progress to CKD in the future.
- #Preeclampsia is a definite risk factor for #CKD and #ESKD in mother and also for #cardiovascular disease



Davison et al, Sem Nephrol 2017


Living well with kidney disease
What does it mean for Women?
World Kidney Day
Are women affected differently?
Higher incidence in women (autoimmune diseases, UTI)
Risk of kidney injury during pregnancy
Lesser access to healthcare
✓ During AKI
✓ For dialysis
✓ For transplant
High caregiver burnout
Higher risk of bone disease
Donate more
Receive less
Pregnancy & kidney disease
Pregnancy can cause AKI & worsening of CKD
Kidney diseases can cause poor maternal & fetal outcomes
Preeclampsia
Acute tubular necrosis
Cortical necrosis
AKI
Pyelonephritis
Lupus flare
Thrombotic microangiopathy
Sexual dysfunction in CKD
Low libido
Infertility
Menstrual disorders
Vaginal disorders
Urinary tract infection & women
More common due to shorter urethra
Higher risk in pregnancy
What can be done?
Optimize peripartum care
✓ Regular ANC checkup
✓ Focus on preventable causes (Sepsis/hemorrhage)
Healthy mom
Healthy daughter
Healthy future mom
Destigmatize sexual health. Openly discuss sexual & fertility issues
Early referral to nephrologist
Encourage kidney donation by men. Address myths about donation risks
Ensure mental wellbeing of caregivers
Address the disparity in access to healthcare
Infographic by Divya Bajpai @divyaa24

Male to female subject distribution of renal patients in sub-Saharan Africa by medical service location/treatment group

Figure 2. Male to female subject distribution of renal patients in sub-Saharan Africa by medical service location/treatment group, data published between 1990 and 2015. The ratio of men to women increases as the cost of kidney care increases.

*Screening data were obtained from a systematic review reported by Stanifer et al.90 This Figure was presented previously at the World Congress of Nephrology, 2015, by Osafo et al based on systematic reviews reported by

Olowu et al. and Ashuntantang et al.