



SEX AND GENDER DIFFERENCES IN CKD EPIDEMIOLOGY

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DISCLOSURES

- None

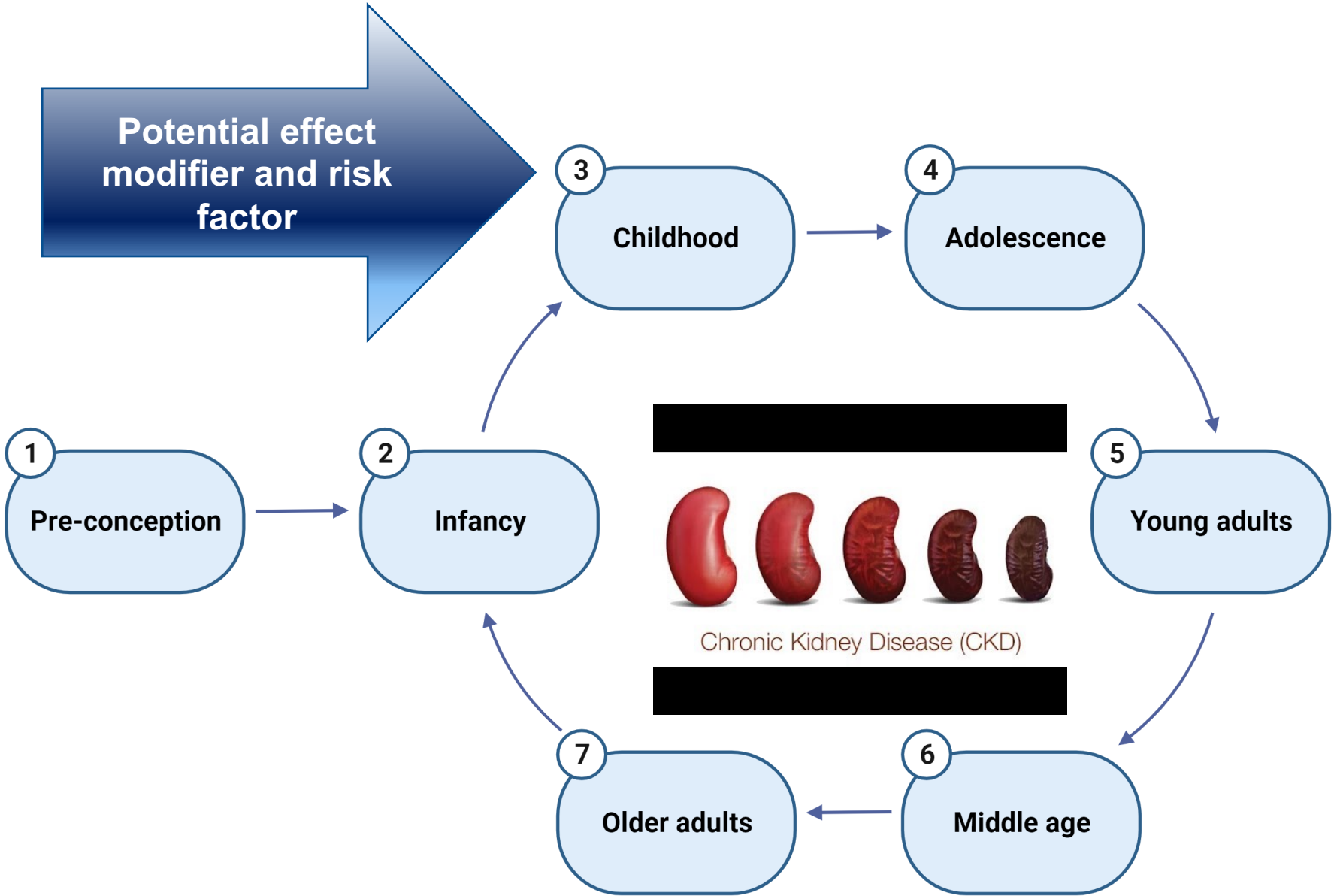
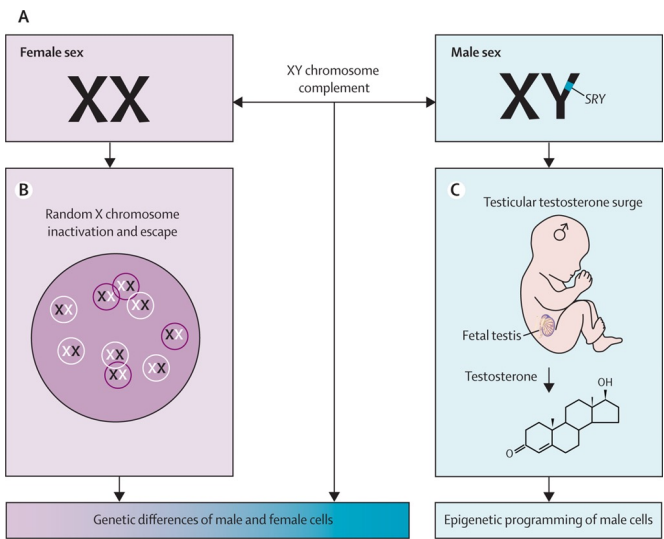
Overview

- Life course approach to sex/gender differences in CKD
- Prevalence of CKD
- Prevalence of kidney failure
- Access to kidney care
- Outcomes of patients with CKD and kidney failure
- Impact of COVID-19

LIFE COURSE APPROACH TO SEX/GENDER DIFFERENCES IN CKD

- **Critical stages, transitions, and settings** where large differences can be made in promoting or restoring health and wellbeing.
- Understand that there are differences in factors that contribute to the gender differences/disparities **over the life span**
- **Changing policies, societal norms, and the environment** can affect the life course trajectory of the sex/gender differences over time

LIFE STAGES



Sex and gender

GENDER

Socially-constructed roles, behaviours, expressions and identities of girls, women, boys, men and gender-diverse people.



SEX

Biological attributes of humans and animals, including physical features, chromosomes, gene expression, hormones and anatomy.



Children and adolescents



Prevalence of CKD in children

- Boys have a higher prevalence of CKD compared to girls, largely due to congenital urinary tract disorders
- Boys also have a higher prevalence of bed-wetting than girls
- Girls have a higher preponderance of autoimmune-related glomerular disease such as Lupus
- Boys are more likely to have advanced stage CKD (KRT and non-KRT dependent).

Advanced stage CKD in children

Advanced chronic kidney disease among UK children

Lucy Plumb ^{1,2}, Winnie Magadi, ¹ Anna Casula, ¹ Ben C Reynolds, ³ Mairead Convery, ⁴ Shuman Haq, ⁵ Shivaram Hegde, ⁶ Andrew Lunn, ⁷ Michal Malina, ^{8,9} Henry Morgan, ¹⁰ Mordi Muorah, ¹¹ Kay Tyerman, ¹² Manish D Sinha ¹³, Dean Wallace, ¹⁴ Carol Inward, ¹⁵ Stephen Marks, ^{16,17} Dorothea Nitsch, ^{1,18} James Medcalf ^{1,19}

Plumb L, et al. Arch Dis Child 2022;107:1043–1045

Table 1 Demographic and clinical characteristics of UK children with advanced CKD, stratified by KRT status (n=1260)

Variable	CKD (not KRT) cohort 0–<16 years (N=199) n (%)		KRT cohort 0–<16 years (N=832) n (%)	
Male sex	128	64.3	518	62.3
Age band (years)				
0–5	57	28.6	143	17.2
6–10	60	30.2	276	33.2
11–15	82	41.2	413	49.6
Ethnicity				
White	114	57.3	570	68.5
Asian	47	23.6	149	17.9
Black	9	4.5	41	4.9
Other	17	8.5	53	6.4
Missing	12	6.0	19	2.3
Area-level deprivation quintile (using country-adjusted indices of multiple deprivation)				
1—least deprived	25	12.6	116	13.9
2	30	15.1	143	17.2
3	34	17.1	155	18.6
4	46	23.1	183	22.0
5—most deprived	61	30.7	226	27.2
Missing	3	1.5	9	1.1

Sex-based differences in CKD progression in children

Sex and Glomerular Filtration Rate Trajectories in Children

Stéphanie Bonnéric,¹ Geeta Karadkhele,² Cécile Couchoud,³ Rachel E. Patzer,^{2,4} Larry A. Greenbaum ⁵ and Julien Hogan ^{1,2}

CJASN 15: 320–329, March, 2020

Table 4. Adjusted associations of clinical characteristics with eGFR trajectory groups in patients with glomerular and nonglomerular primary kidney diseases

Baseline Characteristics	Nonglomerular Diseases ^a		Glomerular Diseases ^b
	OR (95% CI) of Moderate eGFR Decline	OR (95% CI) of Rapid eGFR Decline	OR (95% CI) of Rapid eGFR Decline
Age (per 1-yr increase)	1.01 (0.97 to 1.05)	0.99 (0.82 to 1.20)	1.03 (0.93 to 1.15)
Male sex (versus female)	1.20 (1.00 to 1.44)	2.08 (0.70 to 6.20)	0.61 (0.41 to 0.92)
Baseline GFR (per 10 ml/min per 1.73 m ² increase)	1.08 (0.97 to 1.18)	1.51 (1.10 to 1.92)	1.83 (1.60 to 2.10)
Urine protein-creatinine ratio			
<0.5	Reference	Reference	Reference
0.5–2	0.96 (0.62 to 1.48)	n/a	0.86 (0.42 to 1.78)
≥2	1.89 (1.09 to 3.28)	n/a	1.47 (0.56 to 3.87)

OR, odds ratio; n/a, not applicable.

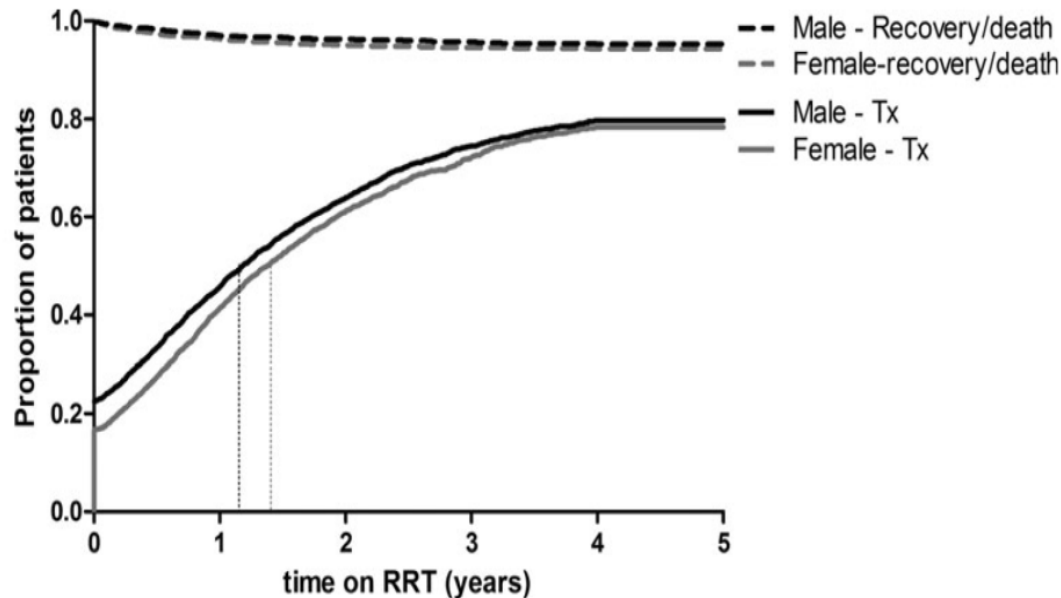
^aReference group for nonglomerular diseases: slow eGFR decline group.

^bReference group for glomerular diseases: moderate eGFR decline group.

Sex-based differences in access to KRT care in children with kidney failure

Gender Disparities in Access to Pediatric Renal Transplantation in Europe: Data From the ESPN/ERA-EDTA Registry

J. Hogan^{1,2}, C. Couchoud¹, M. Bonthuis³,
J. W. Groothoff^{4,5}, K. J. Jager³, F. Schaefer⁶,
and K. J. Van Stralen^{3,*} on behalf of the ESPN/
ERA-EDTA Registry



Patients at risk (N)							
Male	3699	1711	895	443	232	107	
Female	2755	1377	725	364	192	104	

Female gender was associated with a slower access to transplantation compared with **male gender (HR 0.88, 95% confidence interval [CI] 0.83–0.94)** after adjustment for age

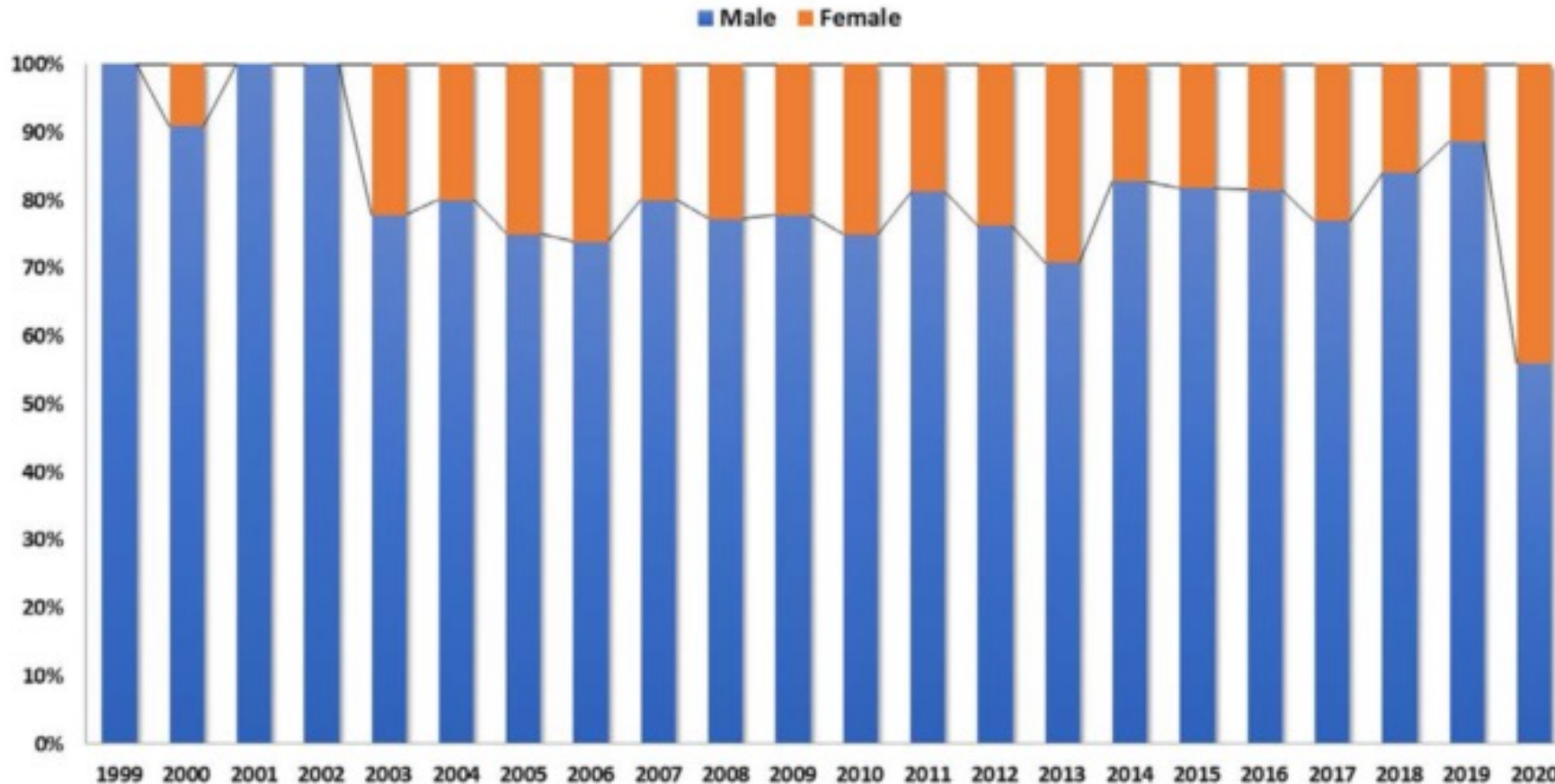
Also less likely to receive pre-emptive transplant ...

Table 3: Likelihood of preemptive transplantation in patient subgroups: females compared with males (logistic hierarchical model)

Patient characteristics	Univariate analysis OR (95% CI)	Multivariate analysis I OR (95% CI) ¹	Multivariate analysis II OR (95% CI) ²
Overall population	0.70 (0.61–0.79)	0.64 (0.56–0.73)	0.77 (0.66–0.88)
Age at RRT (years)			
0 < 1	1.82 (0.36–9.22)	—	1.38 (0.24–7.83)
1 < 2	0.38 (0.15–0.97)	—	0.54 (0.21–1.45)
2 < 6	0.49 (0.34–0.71)	—	0.66 (0.45–0.97)
6 < 10	0.45 (0.32–0.61)	—	0.62 (0.45–0.86)
10 < 14	0.77 (0.60–0.98)	—	0.80 (0.63–1.01)
≥14	0.77 (0.61–0.97)	—	0.86 (0.68–1.09)
Type of donor			
Deceased donor	0.63 (0.50–0.79)	0.59 (0.47–0.74)	0.71 (0.56–0.90)
Living donor	0.70 (0.56–0.87)	0.65 (0.52–0.82)	0.73 (0.58–0.93)
Unknown	0.59 (0.42–0.84)	0.57 (0.40–0.81)	0.72 (0.49–1.06)

Similar patterns are observed in India

Pediatric kidney transplantation by sex



*Kute et al 2022,
Transplantation*

But not in Australia and New Zealand

Sex differences in the likelihood of pre-emptive living donor kidney transplantation, and outcomes after kidney transplantation in children and adolescents

Rowena Lalji^{1,2,3} | Anna Francis^{1,2,3} | Katrina Blazek^{4,5} |
Armando Teixeira-Pinto^{4,5} | Germaine Wong^{4,5,6} | David W. Johnson^{1,3,7}

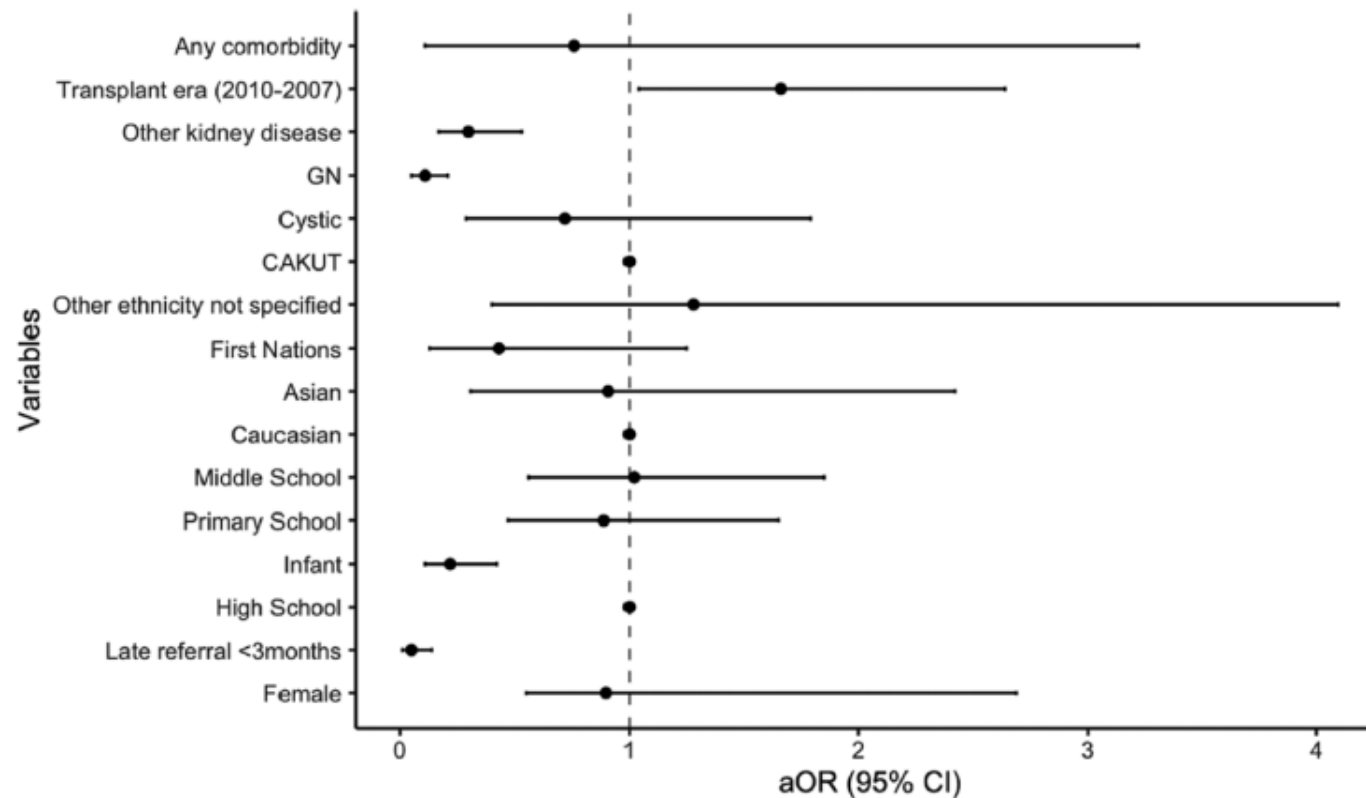


FIGURE 1 Multivariable analysis of the relationship between clinical and sociodemographic variables and the occurrence of pre-emptive live donor kidney transplantation in children and adolescents

Sex-based differences in cardiovascular outcomes among children treated with KRT

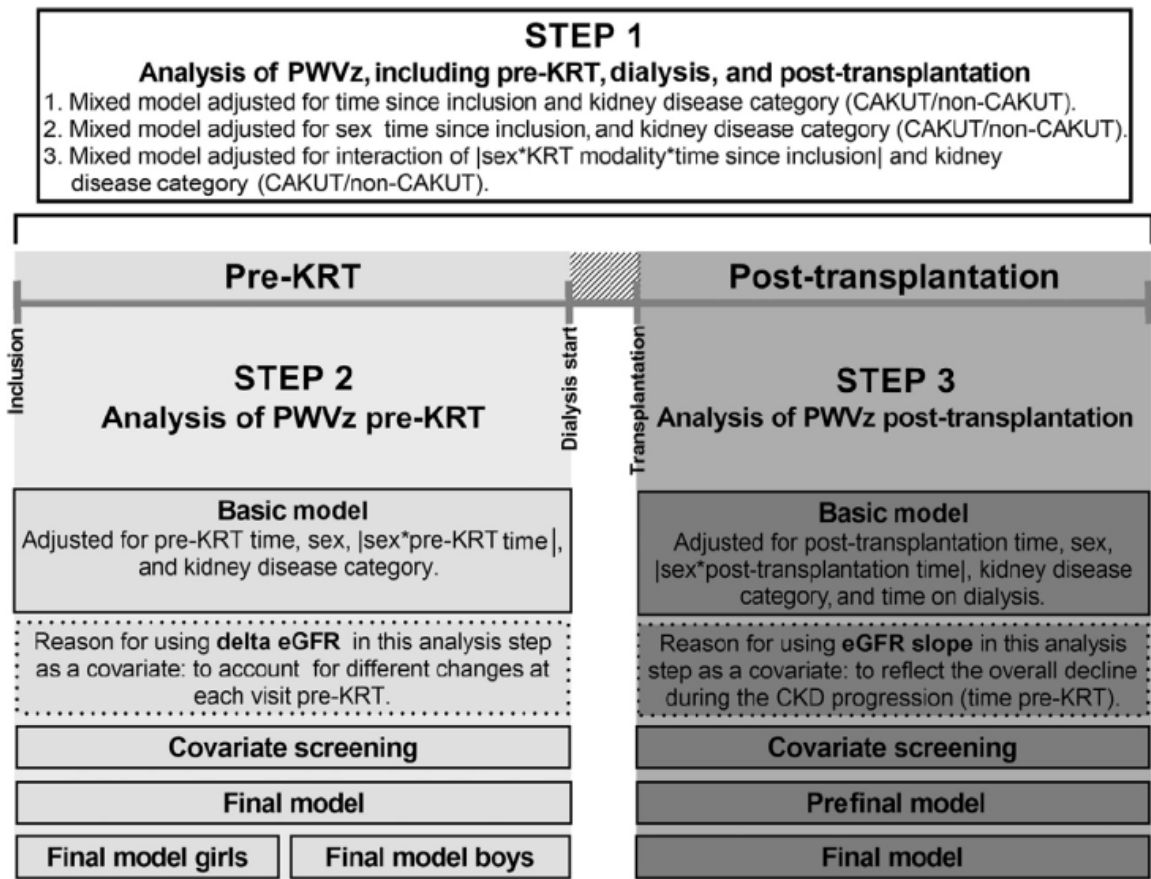
Findings from 4C-T Study demonstrate an increased cardiovascular burden in girls with end stage kidney disease and kidney transplantation

Rizky I. Sugianto¹, Nima Memaran¹, Bernhard M.W. Schmidt², Anke Doyon³, Daniela Thurn-Valsassina^{1,4}, Harika Alpay⁵, Ali Anarat⁶, Klaus Arbeiter⁷, Karolis Azukaitis⁸, Aysun K. Bayazit⁶, Ipek K. Bulut⁹, Salim Caliskan¹⁰, Nur Canpolat¹⁰, Ali Duzova¹¹, Jutta Gellerman¹², Jerome Harambat¹³, Denise Homeyer¹⁴, Mieczyslaw Litwin¹⁵, Francesca Mencarelli¹⁶, Lukasz Obrycki¹⁵, Dusan Paripovic¹⁷, Bruno Ranchin¹⁸, Rukshana Shroff¹⁹, Uwe Tegtbur¹⁴, Jeannine von der Born¹, Ebru Yilmaz²⁰, Uwe Querfeld¹², Elke Wühl³, Franz Schaefer^{3,21} and Anette Melk^{1,21}



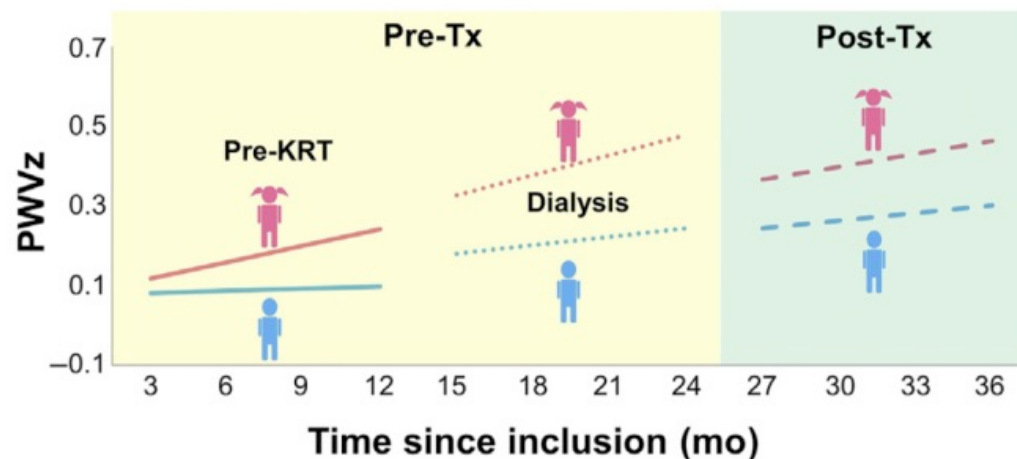
Kidney International (2022) 101, 585–596;

see commentaries on pages 459 and 462
OPEN



Mixed model for PWVz with interaction term between KRT modality, sex, and time since inclusion (yr)
(patients, $n = 235$; observations, $n = 1368$)

Effect	β	SE	P
Intercept	0.076	0.10	0.46
Effect of time since inclusion in:			
Girls pre-KRT (yr)	0.17	0.057	0.004
Girls on dialysis (yr)	0.20	0.073	0.006
Girls post-Tx (yr)	0.13	0.024	<0.0001
Boys pre-KRT (yr)	0.022	0.038	0.56
Boys on dialysis (yr)	0.084	0.053	0.11
Boys post-Tx (yr)	0.075	0.019	<0.0001
Non-CAKUT (ref.: CAKUT)	0.015	0.14	0.92



- Interaction with time, sex and PWVz was observed for girls with CKD.
- Girls in general have higher PYVz scores across all stages of CKD, compared with boys.
- Girls were more likely to experience higher PWVz scores in the pre-KRT, KRT and post-transplant over time. However, the slope of incline appears to decrease post transplant
- This interactive effect with time was not observed in boys except post transplant

Sex based differences in quality of life outcomes in children with CKD

Longitudinal assessment of the health-related quality of life of children and adolescents with chronic kidney disease

Chandana Guha^{1,2}, Anita van Zwieten^{1,2}, Rabia Khalid^{1,2}, Siah Kim^{1,2}, Amanda Walker³, Anna Francis^{4,5,6}, Madeleine Didsbury¹, Armando Teixeira-Pinto^{1,2}, Belinda Barton⁷, Chanel Prestidge⁸, Emily Lancsar⁹, Fiona Mackie^{10,11}, Joseph Kwon¹², Kirsten Howard^{1,13}, Kylie-Ann Mallitt^{1,2}, Martin Howell^{1,2}, Allison Jaure^{1,2}, Alison Hayes¹, Rakhee Raghunandan¹, Stavros Petrou¹², Suncica Lah¹⁴, Steven McTaggart^{4,6}, Jonathan C. Craig^{15,16} and Germaine Wong^{1,2,16}



Kidney International (2023) 103, 357–3

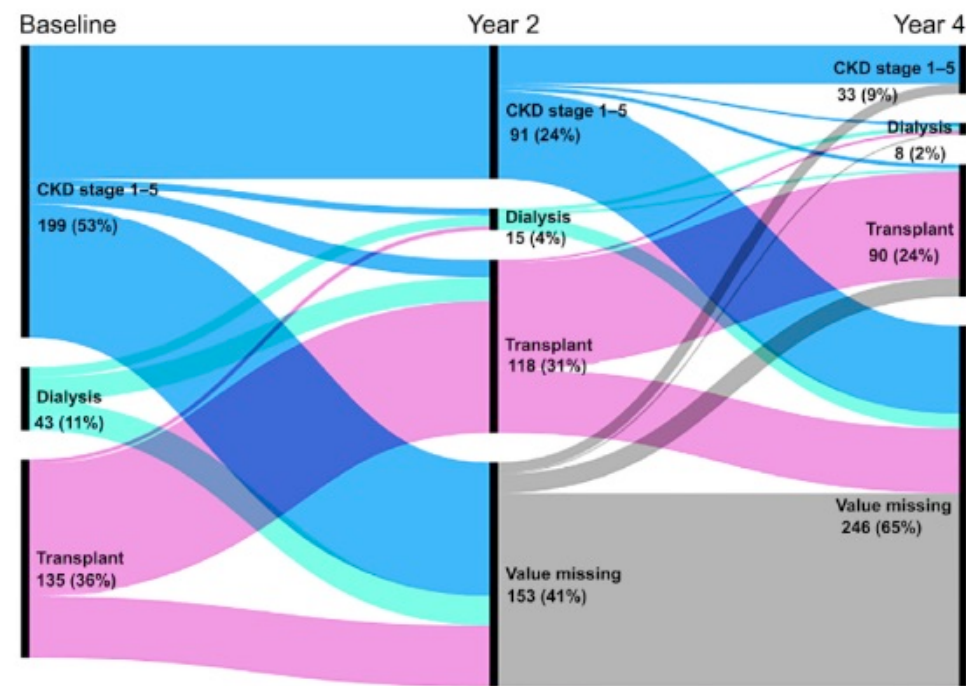


Table 1 | Mixed model for MAU scores with interaction term between baseline CKD stage and follow-up time

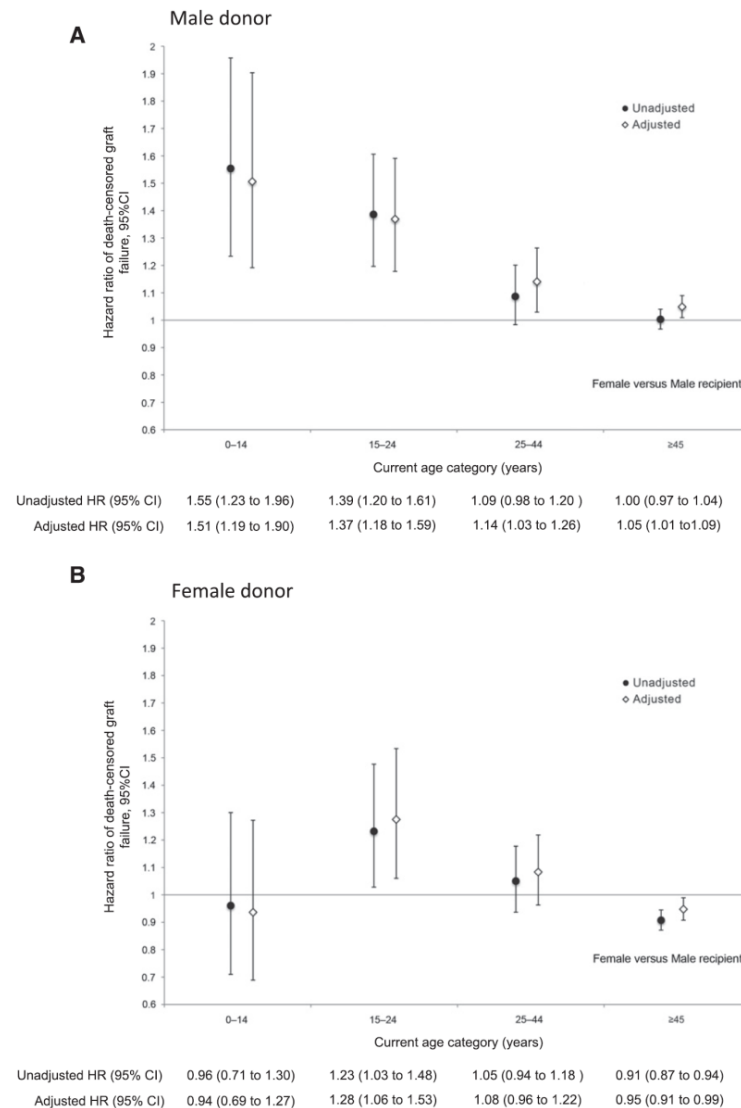
Variable	Estimate	95% CI	P
Intercept	0.77	0.68 to 0.86	<0.001
Time (per year of follow-up)	0.001	−0.01 to 0.02	0.93
Male	0.07	0.01 to 0.13	0.02
CKD stage (ref: transplant)			0.04
1–5	−0.02	−0.08 to 0.05	
Dialysis	−0.14	−0.25 to −0.03	
Global SES index, quartile (ref: SES quartile 4)			0.02
1 (lowest)	−0.13	−0.22 to −0.05	
2	−0.07	−0.15 to 0.01	
3	−0.05	−0.13 to 0.03	
Ethnicity (ref: Caucasian)	−0.02	−0.08 to 0.04	0.52
Time ^a CKD stage			0.01
Effect of time of follow-up on:			
Transplant	ref	ref	
Stages 1–5	−0.003	−0.02 to 0.02	
Dialysis	0.05	0.02 to 0.09	

CI, confidence interval; CKD, chronic kidney disease; MAU; multi-attribute utility; ref, referent; SES, socioeconomic status.

^aAll the CKD stages are at baseline; e.g., the interaction term of time with the dialysis cohort (time*dialysis) refers to the baseline dialysis cohort.



Sex-based differences in post-transplant outcomes



Association of Sex with Risk of Kidney Graft Failure Differs by Age

Fanny Lepeyre,^{*} Mourad Dahhou,[†] Xun Zhang,[†] Julie Boucquemont,^{†‡}
Ruth Sapir-Pichhadze,^{†‡§} Heloise Cardinal,^{*} and Bethany J. Foster^{†‡||}

J Am Soc Nephrol 28: 3014–3023, 2017.

- Three-way interactions between donor sex, recipient sex and recipient age.
- If the donor is male, a higher risk of death-censored allograft loss was observed in younger female transplant recipients. This association was not observed in older female recipients.
- This relationship attenuates when the donor is female.

Differences in kidney graft survival by recipient sex vary by recipient age and by donor-sex

N=438,585 first deceased donor kidney transplant recipients (1988-2019)

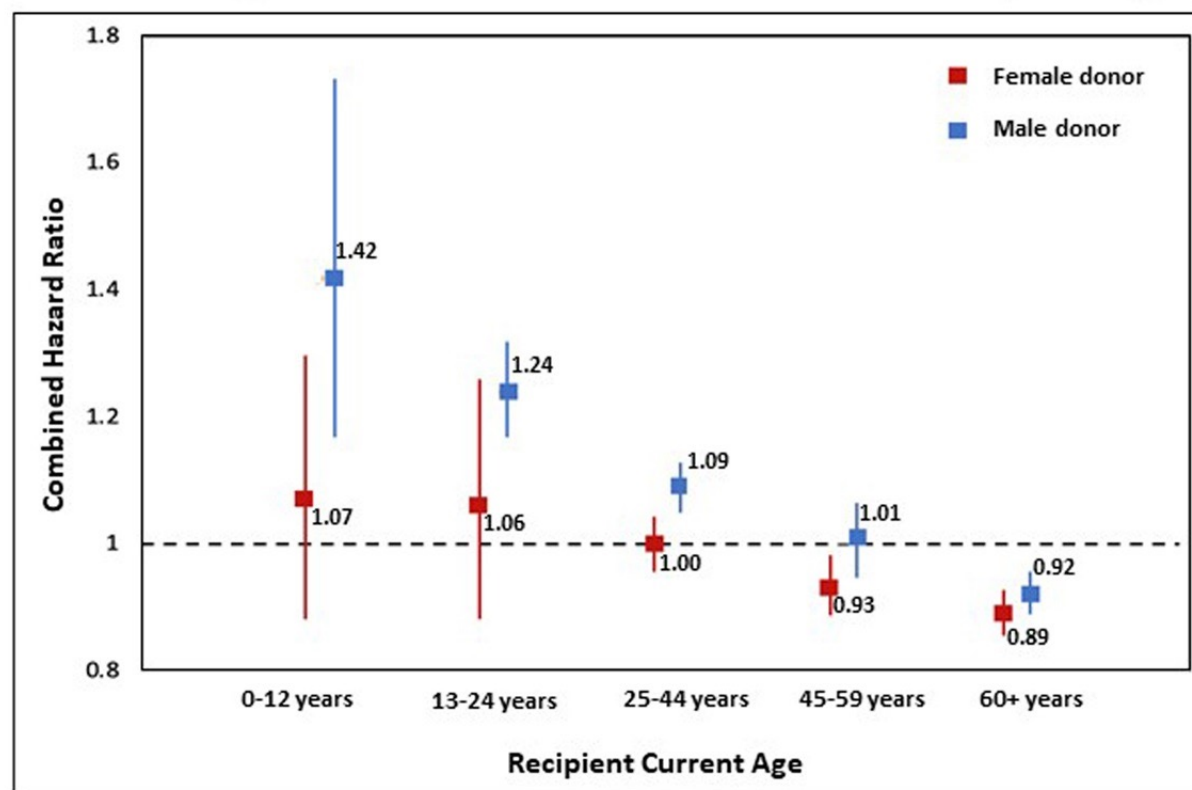
SRTR: Scientific Registry of Transplant Recipients (USA)
N=231,673

CTS: The Collaborative Transplant Study (Europe/International)
N=193,530

ANZDATA: Australia and New Zealand Dialysis and Transplant Registry (Australia/New Zealand)
N=13,382

Multivariable Cox regression analyses in each cohort separately

Individual Patient Data Meta-Analysis: Relative hazards of death-censored graft loss in Female versus Male Kidney Transplant Recipients



When the donor was male, young female recipients had a $\uparrow$ risk of graft loss than young males

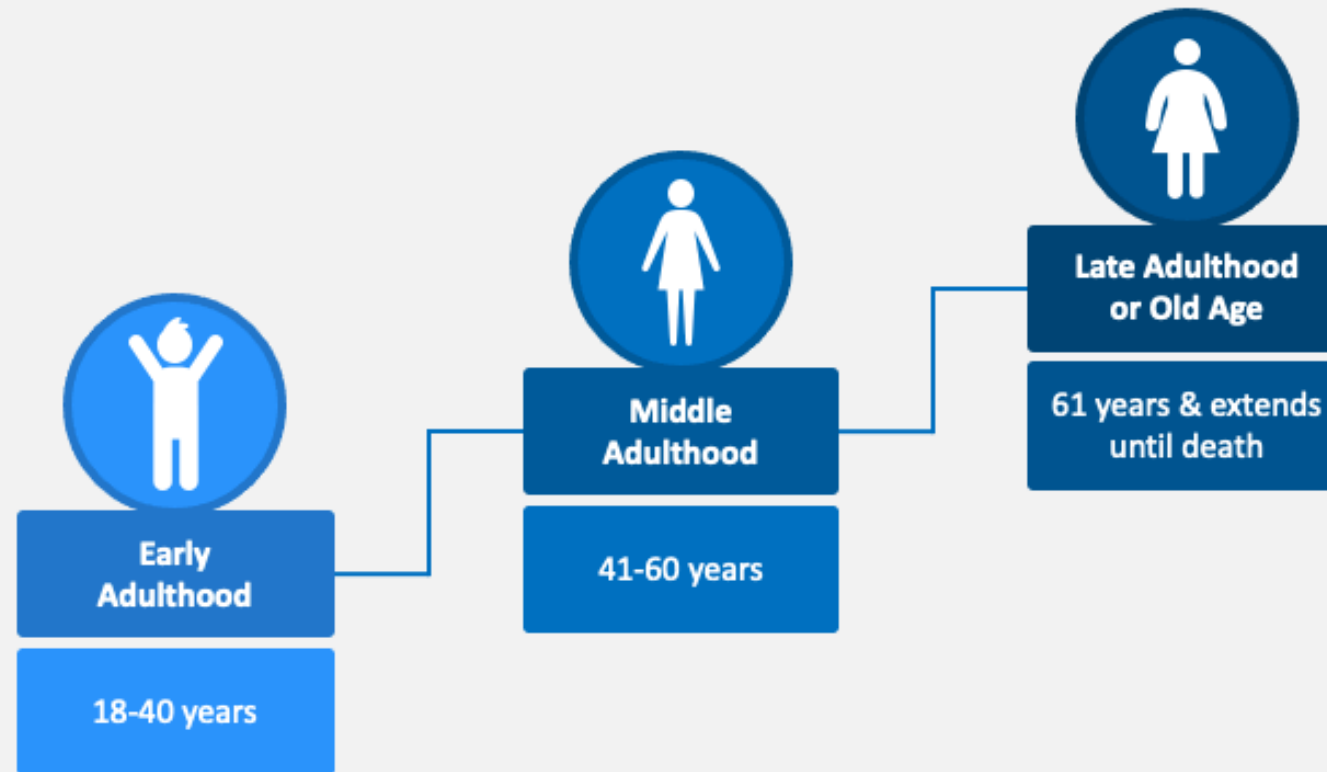
Older female recipients had a $\downarrow$ risk of graft loss than males of the same age

Conclusion: The association between recipient sex and death-censored graft loss is modified by donor sex and recipient age

Adulthood

ADULTHOOD DEVELOPMENT

Classification of Adulthood



Prevalence of CKD in adulthood



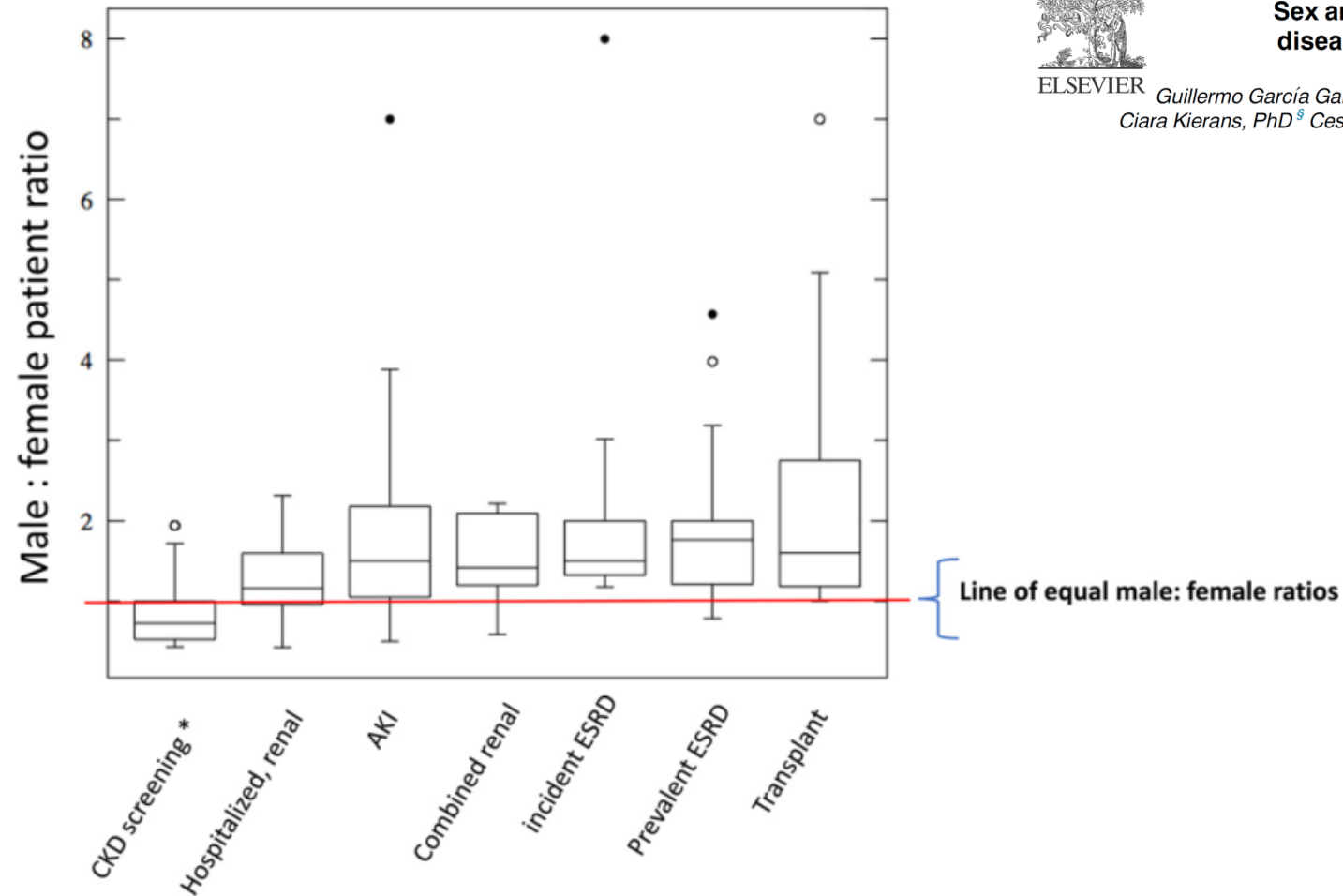
ELSEVIER

Sex and gender differences in chronic kidney disease and access to care around the globe

Guillermo García García, MD* Arpana Iyengar, MD, FPN, FRCP† François Kaze, MD‡
Ciara Kierans, PhD§ Cesar Padilla-Altamira, PhD§|| and Valerie A. Luyckx, MD, MSc, PhD¶, #, **



Prevalence of kidney failure



ELSEVIER

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CKD—Where Have All the Women Gone?



Amy Crosthwaite¹ and Peter G. Kerr²

¹Department of Nephrology, Austin Health, Melbourne, Australia; and ²Department of Nephrology, Monash Health and Monash University, Clayton, Australia

Kidney Int Rep (2022) 7, 375–377; <https://doi.org/10.1016/j.ekir.2021.11.032>

Sex-Specific Differences in Mortality and Incident Dialysis in the Chronic Kidney Disease Outcomes and Practice Patterns Study (CKDopps)



Cohort	At baseline	On follow-up (2.57 yr) hazard ratio in Men vs Women Adjusted for age, black race, diabetes, cardiovascular disease, albuminuria, and eGFR (slope during the first 12 months after enrolment and first eGFR after enrollment)
 CKDopps N = 8237	 eGFR (ml/min/1.73m ²)	
 CKD stage 3-5	 58% Men 28.9 ± 11.5	 Dialysis initiation aHR [95% CI] 1.50 [1.25 – 1.80]
	 42% women 27.0 ± 10.8	 Transplantation aHR [95% CI] 1.53 [0.79 – 2.94]
		 Pre - KRT death aHR [95% CI] 1.15 [0.93 – 1.42]

KRT - kidney replacement therapy

KIREPORTS
Kidney International Reports

Hecking et al, 2022

Visual abstract by:
Divya Bajpai, MD DM

 @divyaa24

Conclusion Men had a higher probability of commencing dialysis before death, unexplained by CKD progression alone. Although the causal mechanisms are uncertain, this finding helps interpret the preponderance of men in the dialysis population



Nephrologists' Perspectives on Gender Disparities in Chronic Kidney Disease and Dialysis

Cohort and Methods



Semi-structured
interviews
conducted



51 nephrologists
(55% women)



22 Countries



October-2019 to
April-2020

Suggestions to address gender disparity

Empowerment in
decision-making



Patient awareness and
education

Accountability



Unconscious
bias in clinicians

Access to clinics,
Communication



Financial support

Results

6 Themes regarding CKD patients

Vigilance and
self-reliance (women)

Primary commitment to
Caregiving (women)

Protecting masculinity (men)

Inequities compounded by
social disadvantage

Stereotyping, stigma and
Judgement (women)

Decisional power and
Ownership (men and women)



Barriers to care for women



Less
social
security



Limited
literacy



Entrenched
Discrimination

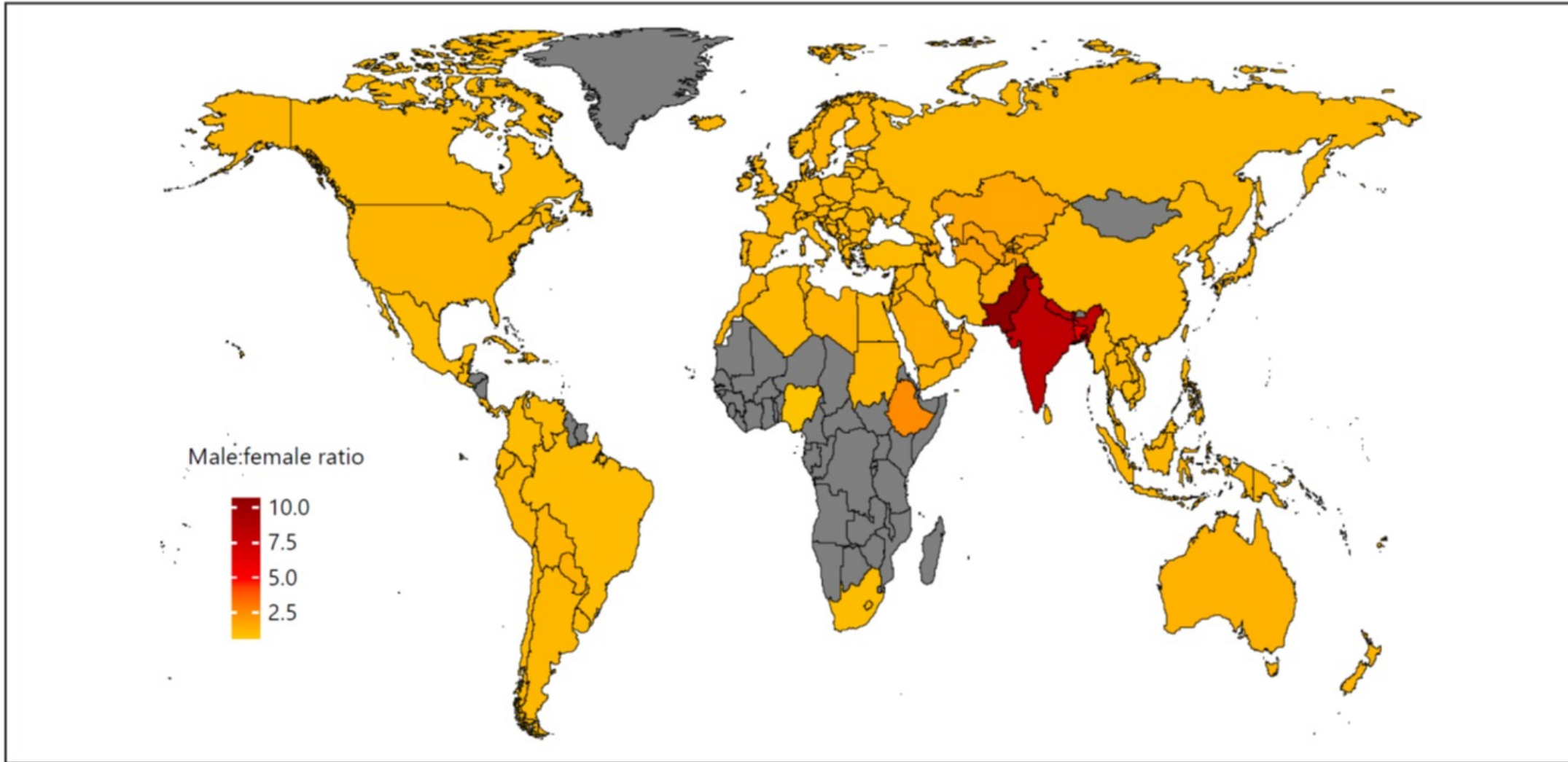


Vulnerability



Financial and
transport
barrier

Male/female ratio and the prevalence rate of kidney transplantation by countries



Gender disparity in Asia-Pacific



“Gender Disparity in Kidney Transplantation in Asia”

Thursday, January 28, 2021 & Thursday, February 25, 2021 - 19:00 Seoul / Tokyo time - GMT+9

Meeting Report: First State of the Art Meeting on Gender Disparity in Kidney Transplantation in the Asia-Pacific

Yunmi Kim, MD,¹ Ejaz Ahmed, MD,² Nancy Ascher, MD, PhD,³ Romina Danguilan, MD,⁴ Lai Seong Hooi, MBBChir,⁵ Ni Made Hustrini, MD,⁶ Yeong Hoon Kim, MD,⁷ Vivek Kute, MD,⁸ Rose Marie O. Rosete-Liquete, MD,⁹ Maggie Ma, MD,¹⁰ Roslyn B. Mannon, MD, PhD,¹¹ Yuki Nakagawa, MD,^{12,13} Lkhaakhuu Od-Erdne, MD,¹³ Vasanthi Ramesh, MD,¹⁴ Harun Ur Rashid, MD,¹⁵ Sobhana Thangaraju, MD,¹⁶ Khin Thida Thwin, MD,¹⁷ Anantharaman Vathsala, BS, MD,¹⁸ Lori West, MD, PhD,¹⁹ Khin Khin Win, MD,²⁰ Curie Ahn, MD, PhD,²¹ and Germaine Wong, MBBS, PhD^{22,23}

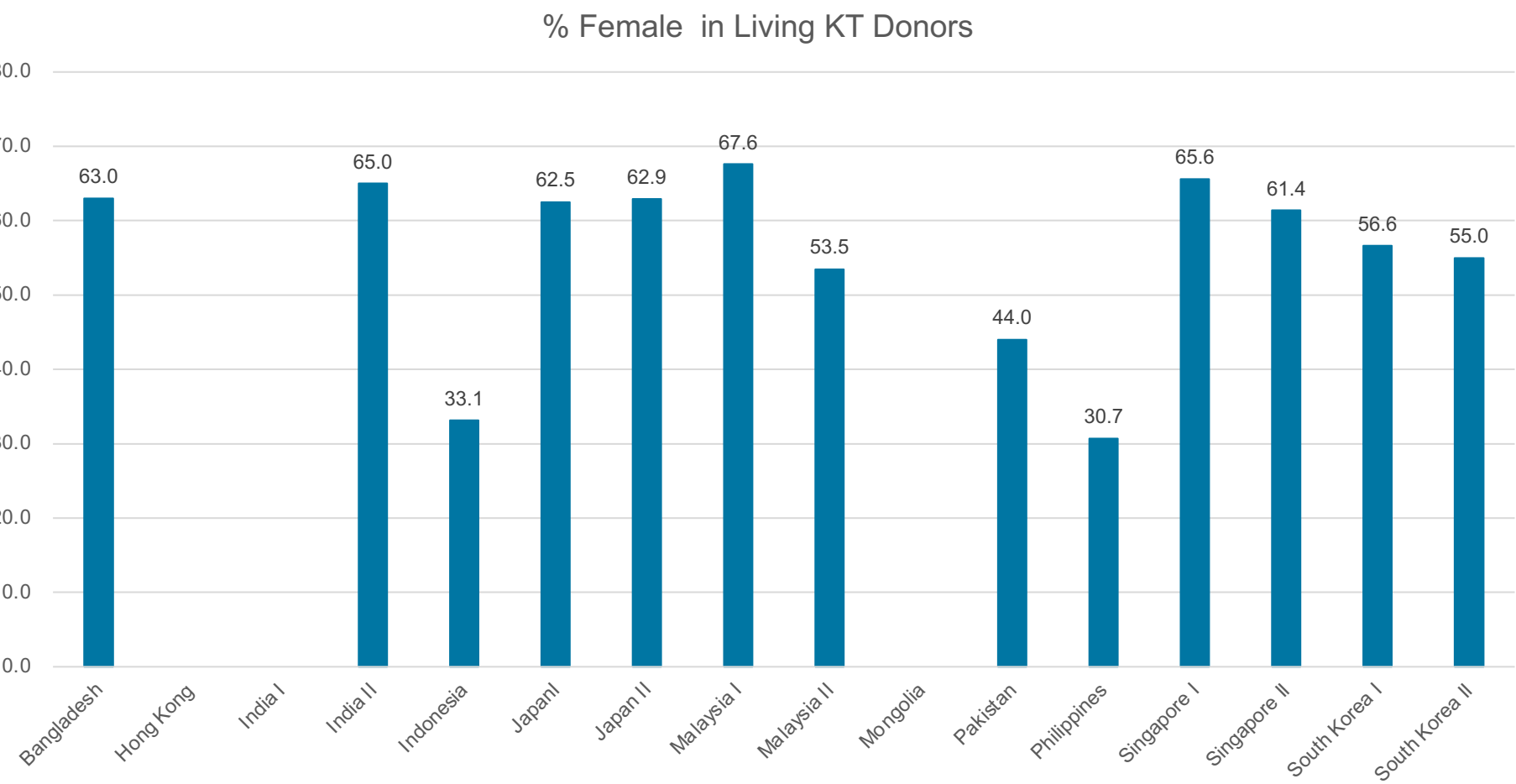


Women in Transplantation



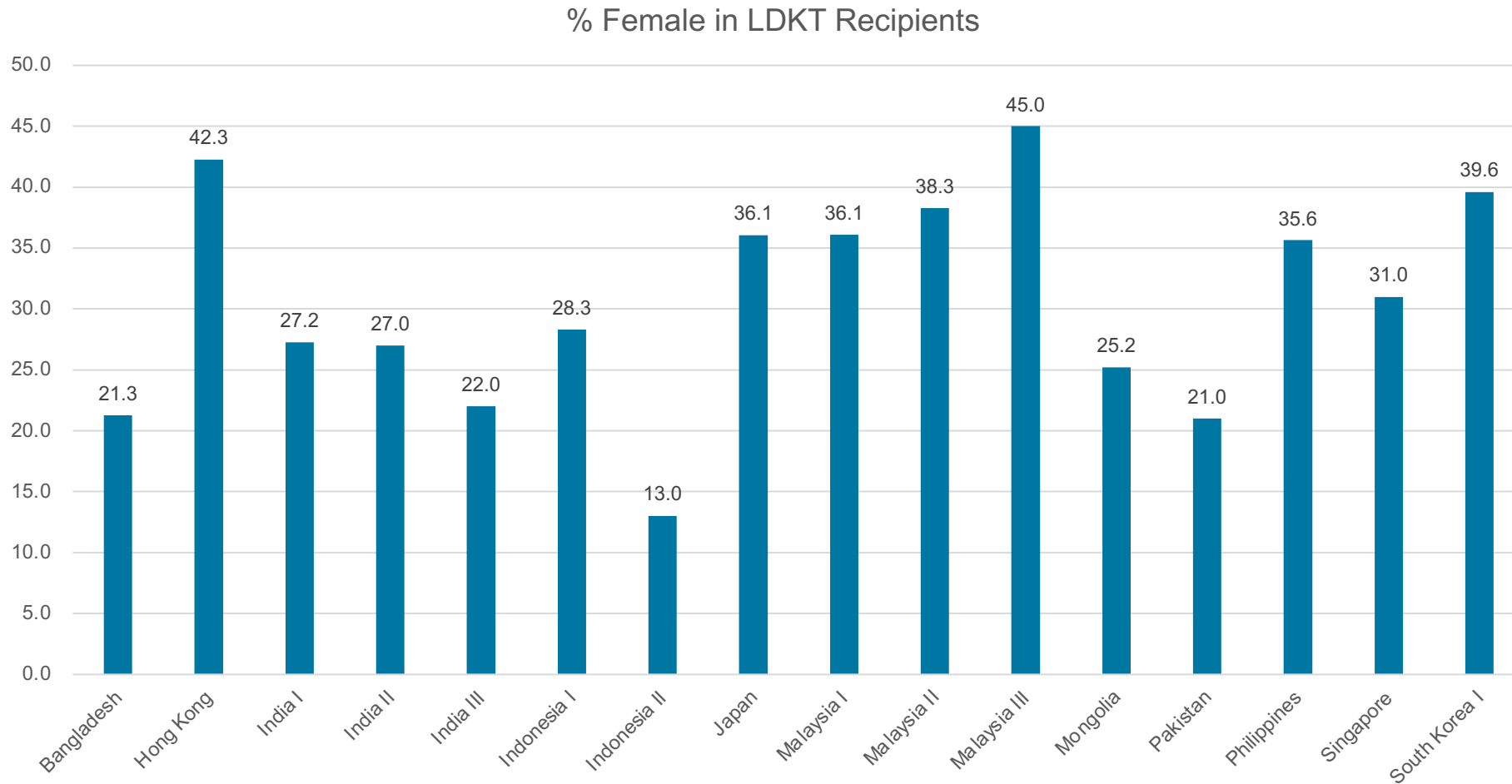
an Initiative of
The Transplantation Society

Gender disparity in living donor kidney transplantation in the Asia-Pacific region



Majority of living donors are females.

Less than 30% of all living donor kidney transplant recipients were women



Global pattern

An analysis by the European Committee on Organ Transplantation of the Council of Europe outlining the international landscape of donors and recipients sex in solid organ transplantation

Background:

The European Committee on Organ Transplantation (CD-P-TO) has committed itself to strive to avoid gender inequities in transplantation.

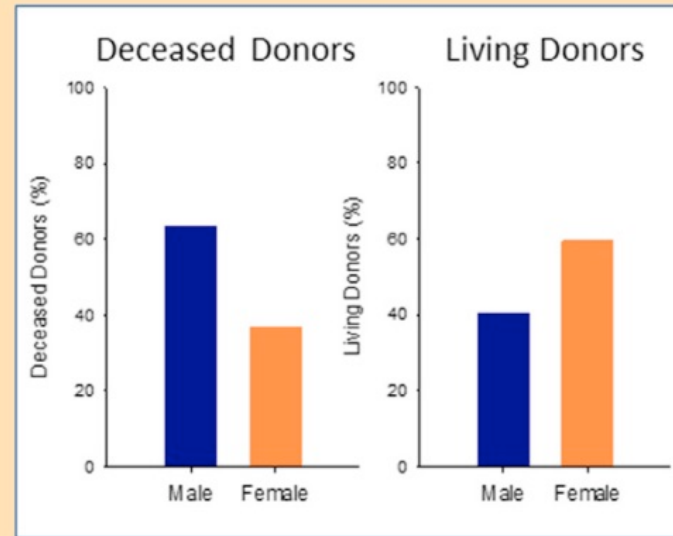
As a first step, we analyzed the distribution by sex among organ donors and recipients in CD-P-TO Member States, observer countries and other States.

Methods:

Data on the sex of solid organ donors and recipients were collected through the national focal points designated by the Ministries of Health at each country. Two data controllers performed QC and data analysis.

Results:

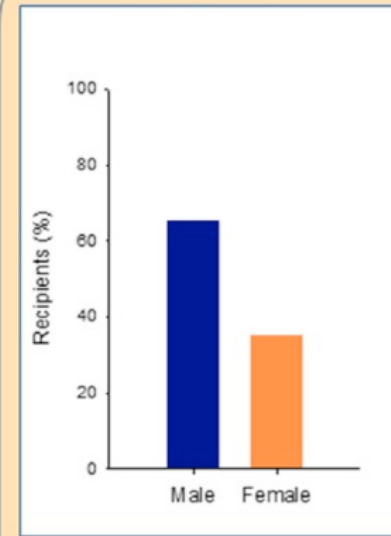
Donors



♂ **Men** are the prevalent source of deceased donors

♀ **Women** are the leading source of organs from living donors

Recipients



♂ Most recovered organs are transplanted into **men**

Conclusions:

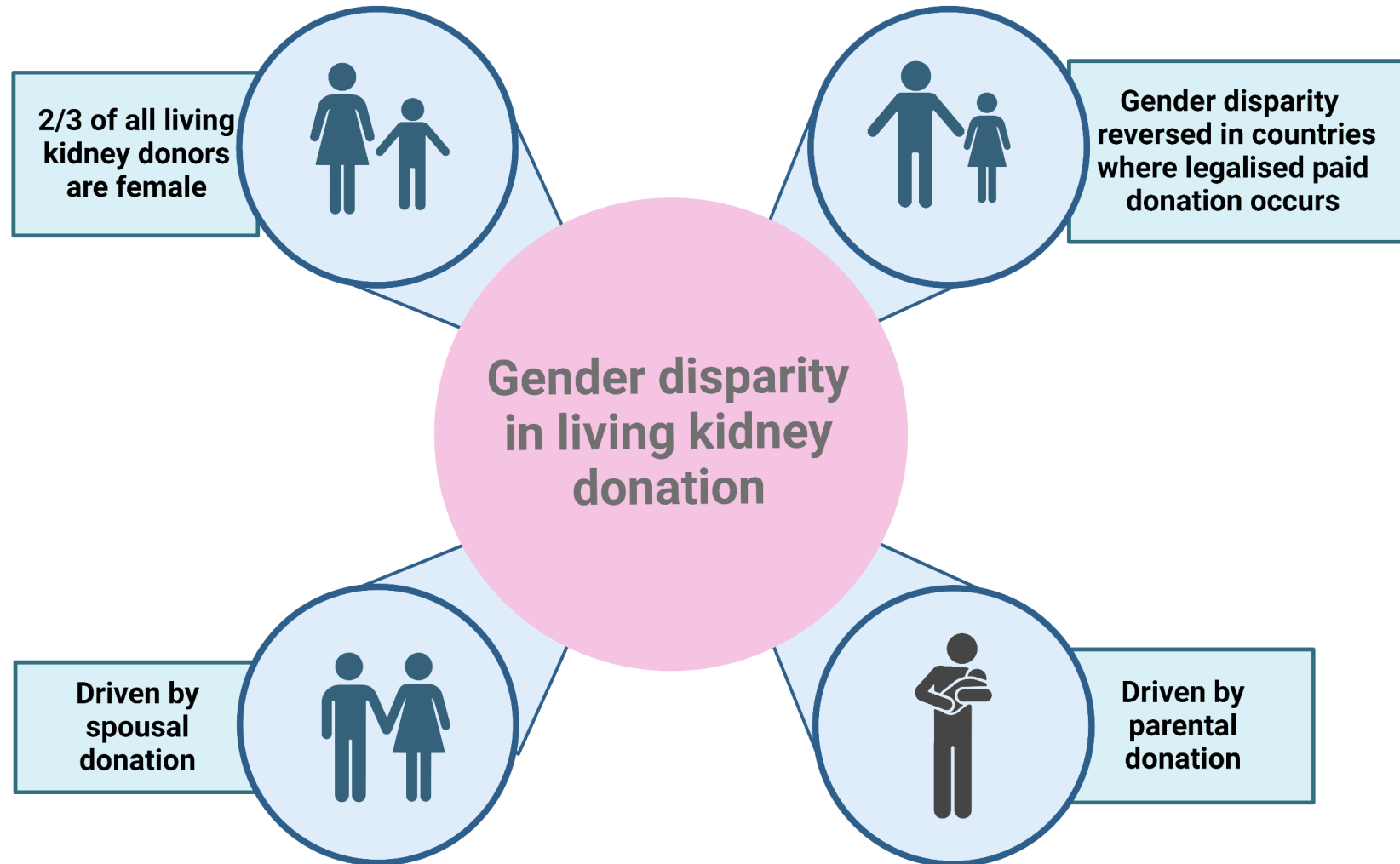
This analysis is an initial step to document differences in donation and transplantation activity among men and women in the CD-P-TO Member States, observer countries and other States.

The collection of data allowing analyses disaggregated by sex represents an important step that may uncover unexpected imbalances, pave the way to more refined investigations on the subject and, where relevant, ultimately act as a trigger for the adaption of national policies.

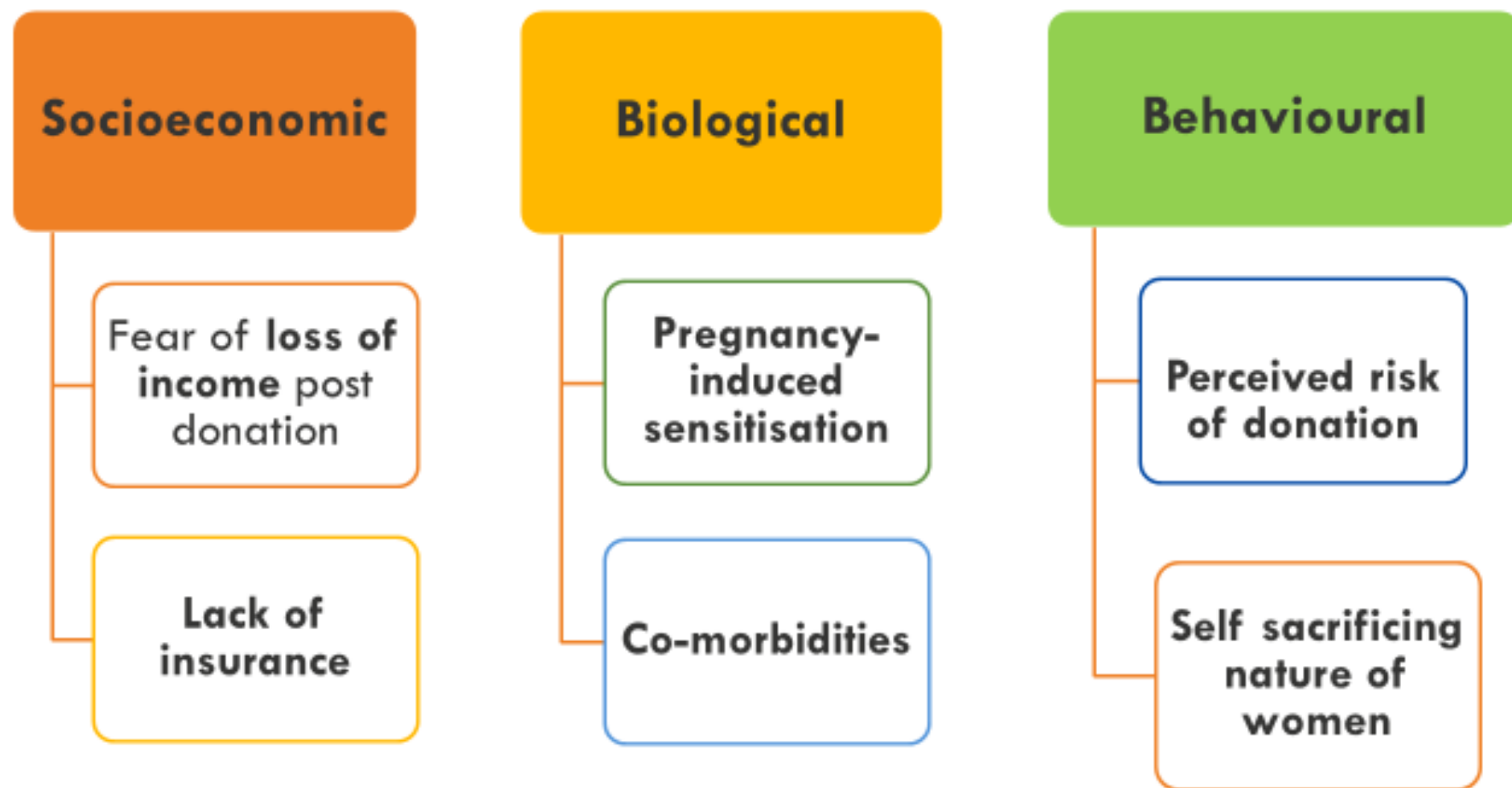
Barriers and facilitators to living donation



Eswari Vilayur



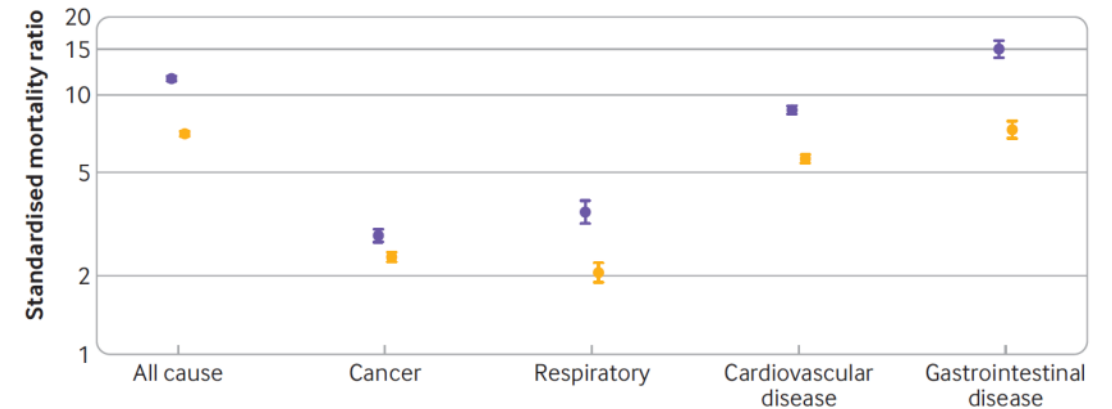
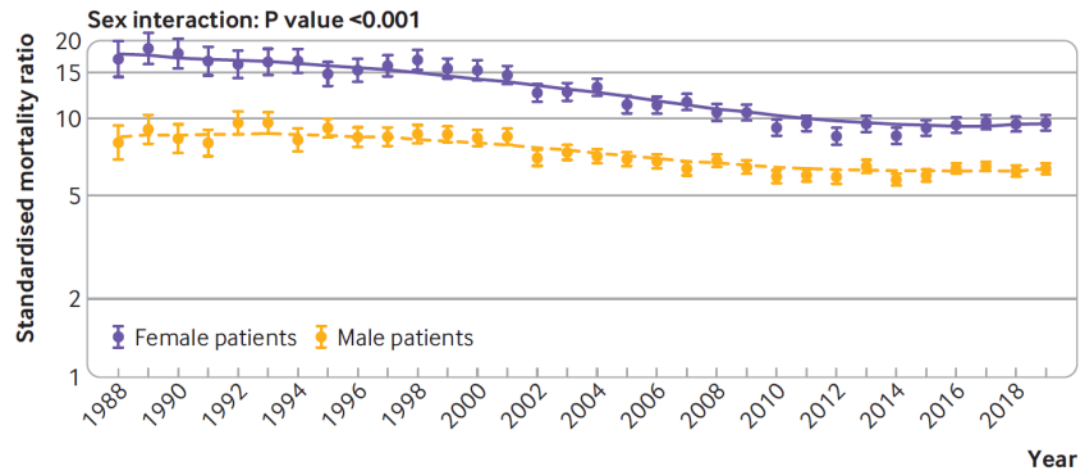
Barriers to kidney donation among men



Sex-differences in mortality in patients with kidney failure

Sex differences in mortality among binational cohort of people with chronic kidney disease: population based data linkage study

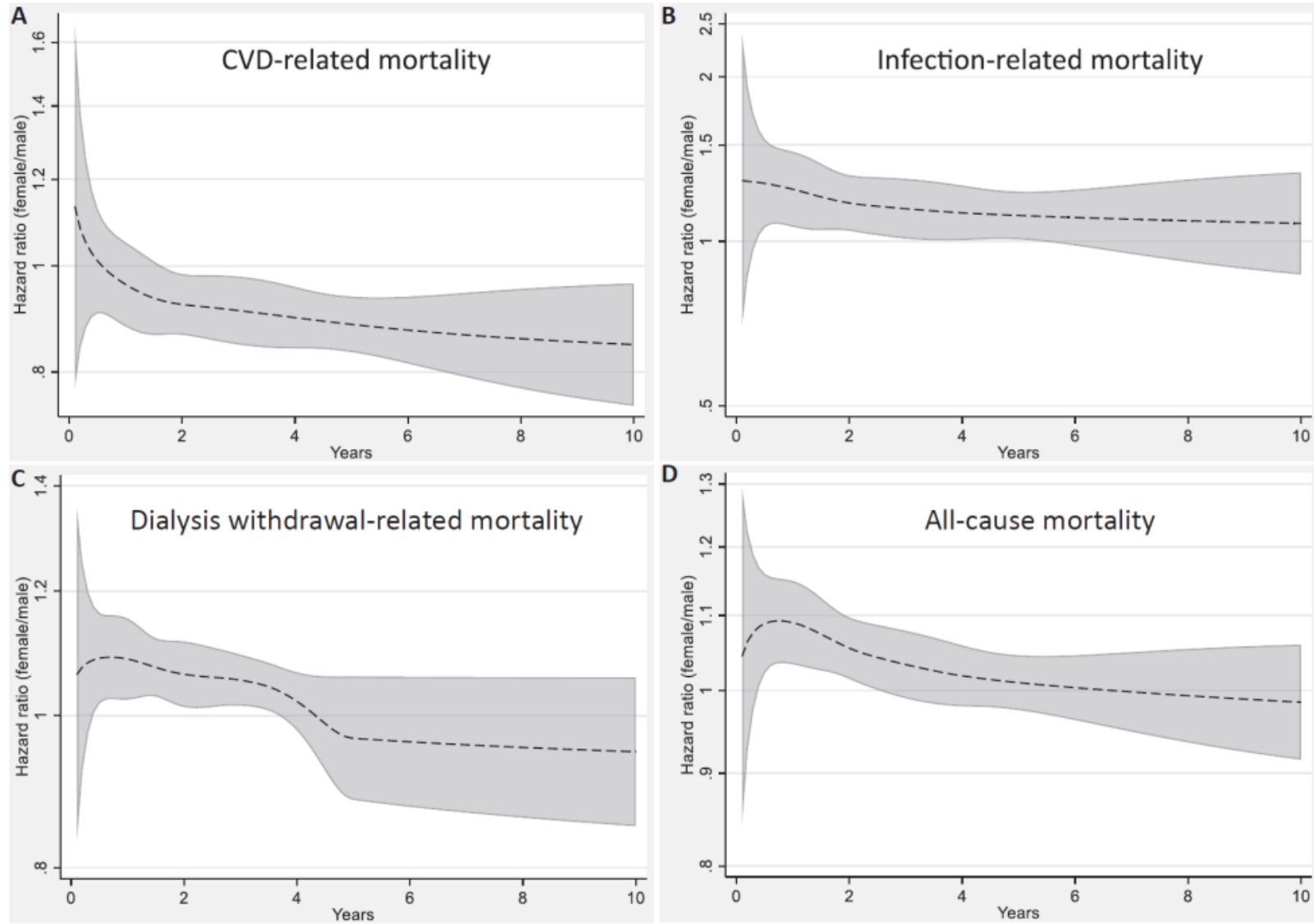
Nicole L De La Mata,¹ Brenda Rosales,¹ Grace MacLeod,^{2,3} Patrick J Kelly,¹ Philip Masson,⁴ Rachael L Morton,⁵ Kate Wyburn,^{3,6} Angela C Webster^{1,7}



Sex Disparity in Cause-Specific and All-Cause Mortality Among Incident Dialysis Patients

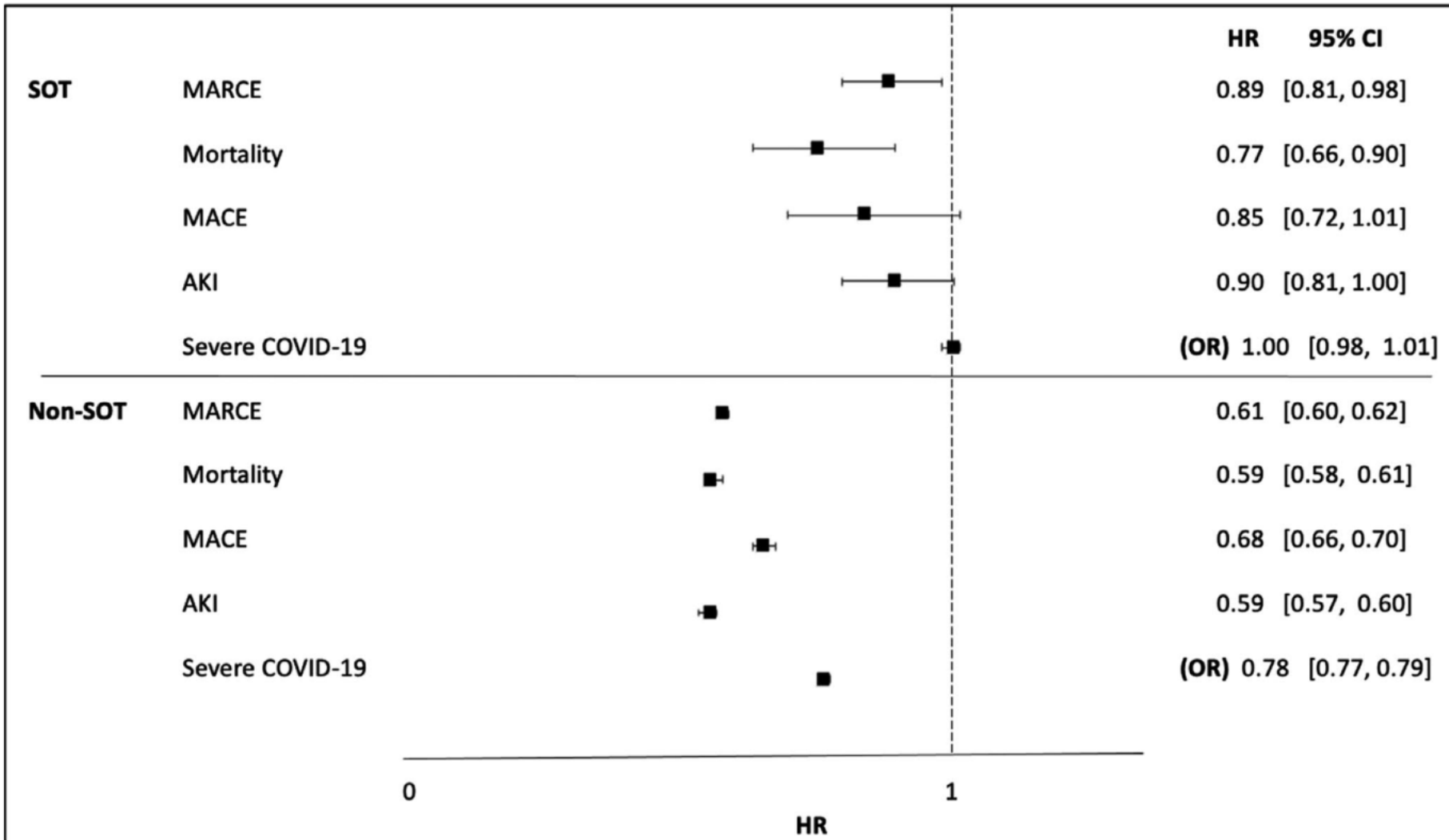


Wai H. Lim, Jenny H.C. Chen, Kimberley Minas, David W. Johnson, Maleeka Ladhani, Esther Ooi, Neil Boudville, Carmel Hawley, Andrea K. Viecelli, Matthew Roberts, Kate Wyburn, Rachael Walker, Monique Borlace, Helen Pilmore, Christopher E. Davies, Charmaine E. Lok, Armando Teixeira-Pinto, and Germaine Wong



Sex and organ-specific risk of major adverse renal or cardiac events in solid organ transplant recipients with COVID-19

Amanda J. Vinson¹  | Ran Dai² | Gaurav Agarwal³ | Alfred J. Anzalone² |
Stephen B. Lee⁴ | Evan French⁵ | Amy L. Olex⁵ | Vithal Madhira⁶ |
Roslyn B. Mannon⁷  | National COVID Cohort Collaborative (N3C) Consortium



Summary

- Prevalence of **CKD is higher in boys than girls**, but **reverse** when they reach **adulthood**
- Prevalence of **men receiving KRT is higher than women**
- Sex disparity in access to KRT care in both dialysis and transplant globally
- **Inequity in access to KRT care** for girls and women are **most marked in lower to middle income countries**
- Compared to boys, girls are at greater risk of CKD progression, CVD disease, lower quality of life
- **Females on KRT** appears to have **very high standardised mortality ratios**
- **Females on dialysis** may have a **higher risk of death** compared to males within the first 5 years of dialysis initiation, attributed to infections-related death and withdrawal
- Recipient sex, donor sex, and recipient age interactions for allograft loss are observed.

Thank you

Steering Committee

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