Contextualising sex and gender to improve stroke research, policy and practice

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Sex refers to the biological characteristics of individuals including genetic, biologic, and physiological expression.

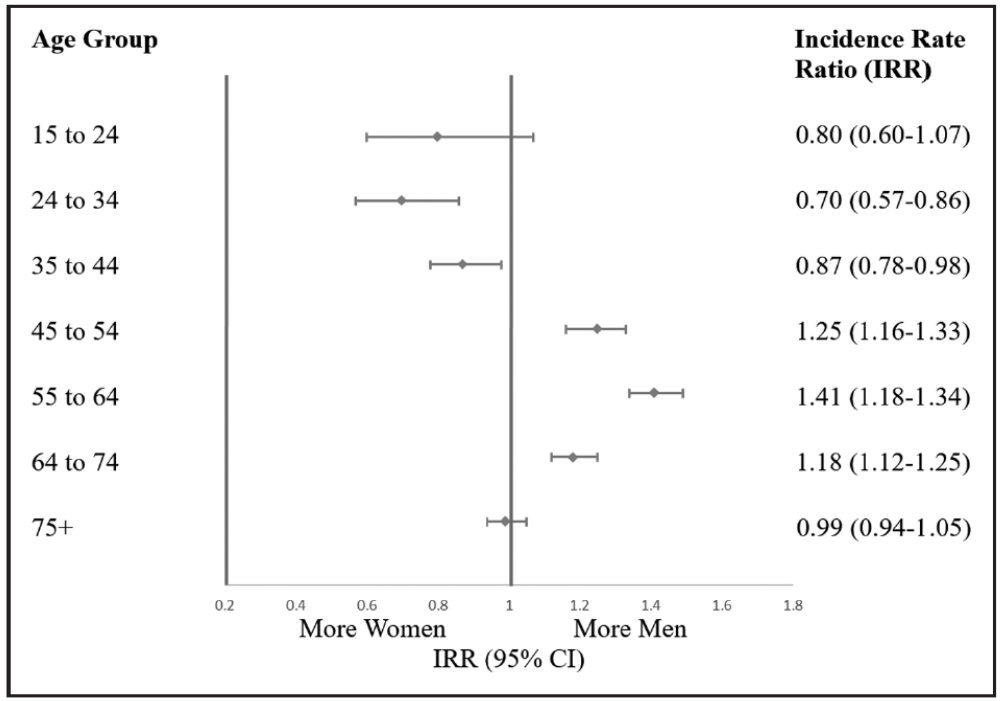
Gender is a social construct that includes gender identity, expression, roles, and stereotypes for female, male, and gender diverse people.

While neither **sex** nor **gender** are binary, most data collection in trials and cohorts have been binary, and sex and gender identity have not been collected separately.

Rexrode Circulation Research 2021

Stroke incidence by sex – across the lifespan

Leppert Stroke 2020

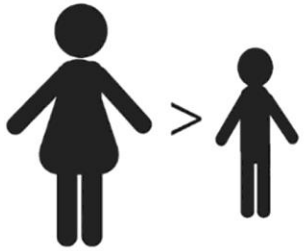


Stroke Risk Factors

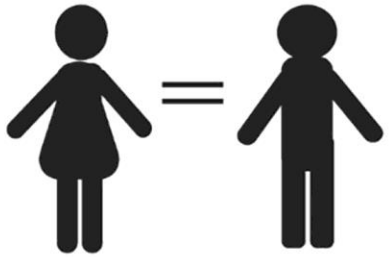
History of APOs:
Pre-term Delivery
Gestational Hypertension
Pre-eclampsia/ Eclampsia
Fetal Growth Restriction

Early/ Late Menarche
Early Menopause
Oral Contraceptives w/ Estrogen
Oral MHT
Parity (≥5 live biths)
GAHT for transwomen

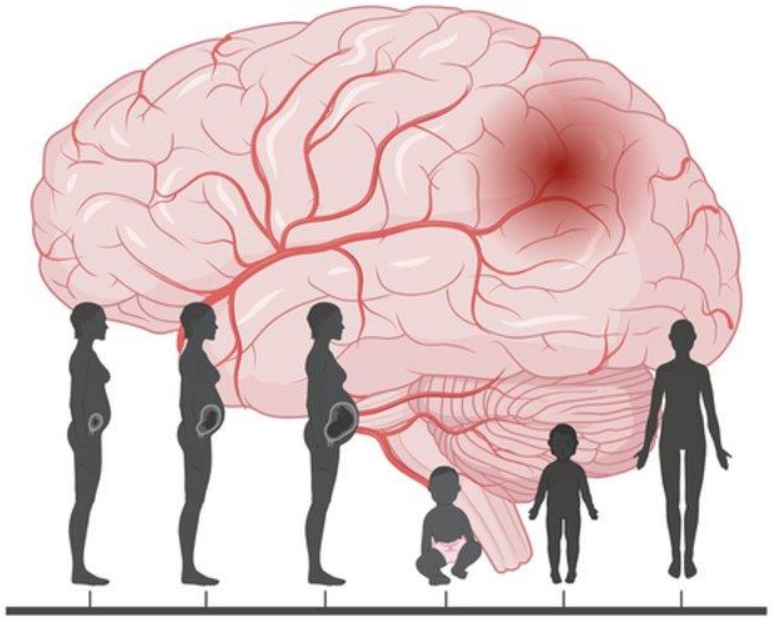
STROKE RISK



Diabetes
Hypertension
Obesity
Atrial Fibrillation
Migraine w/ Aura



Physical Activity



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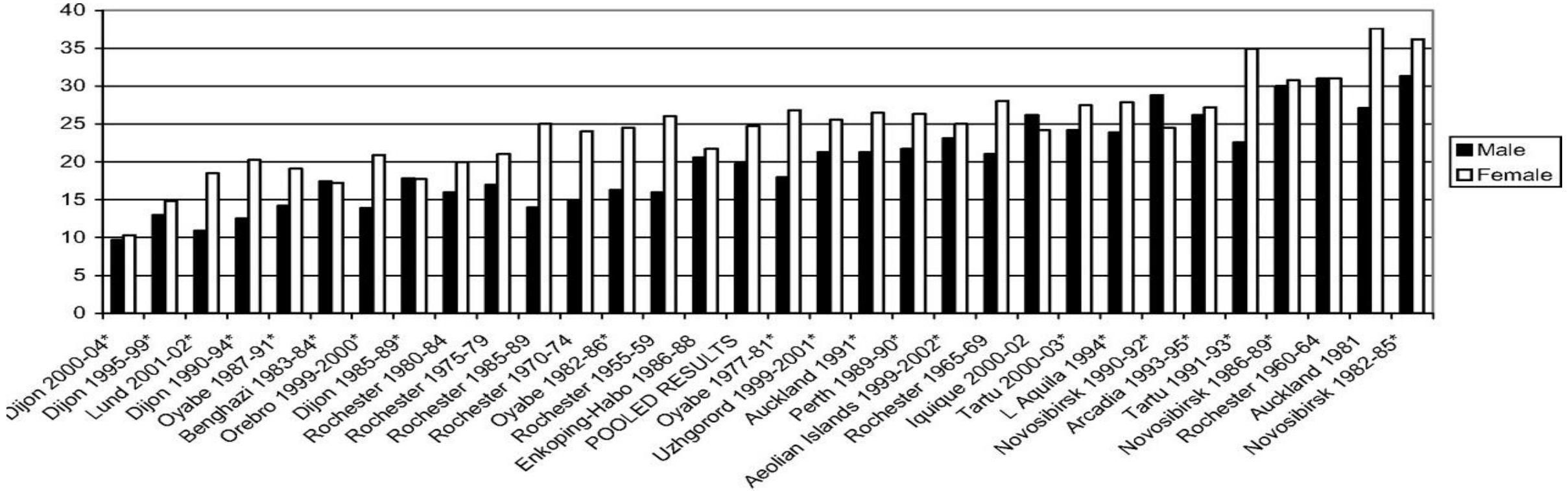
Mortality after stroke



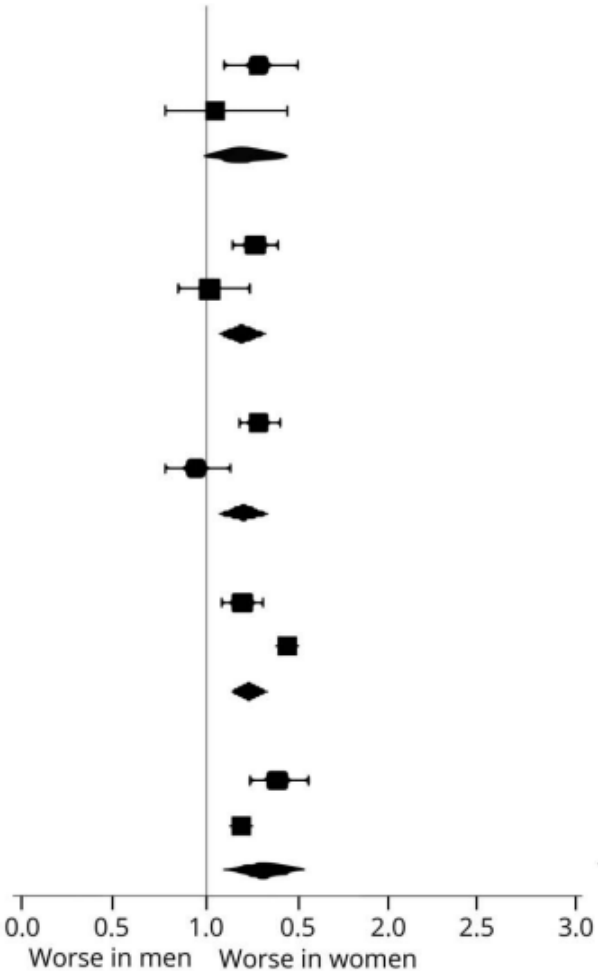
Male and female case fatality percentages at 1 month for different stroke populations

Appelros P et al. Stroke 2009

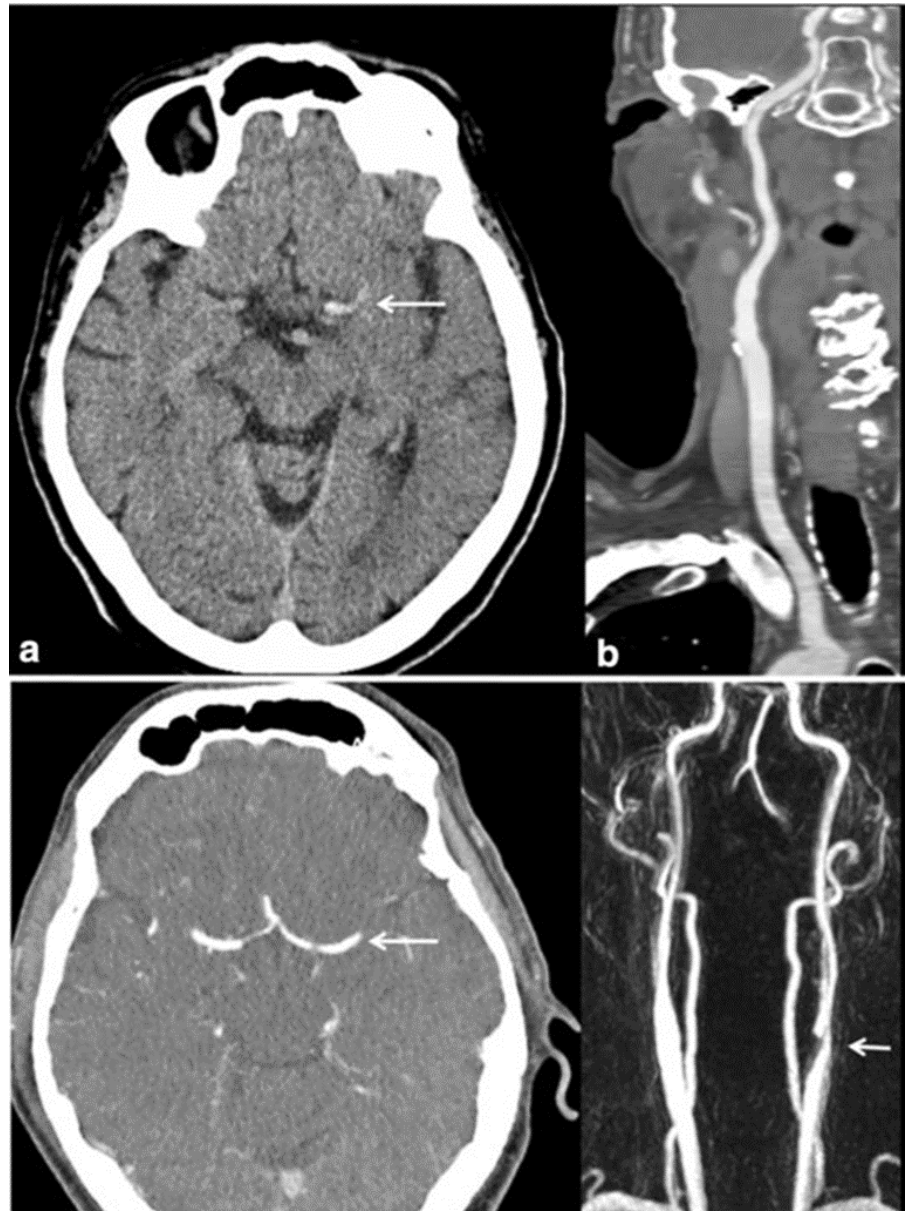
Back to work

Quality of life

Mobility	Women (n/N)	Men (n/N)	OR (95% CI)
Ischemic stroke	2,305/4,680	2,750/7,429	1.30 (1.11–1.51)
Intracerebral hemorrhage	892/1,411	1,377/2,350	1.06 (0.79–1.44)
Total stroke			**1.20 (1.00–1.45)**
Self care			
Ischemic stroke	1,884/4,680	2,227/7,428	1.28 (1.16– 1.40)
Intracerebral hemorrhage	745/1,410	1,044/2,349	1.03 (0.86–1.23)
Total stroke			**1.20 (1.09–1.33)**
Usual activities			
Ischemic stroke	2,567/4,679	3,252/7,428	1.30 (1.19–1.42)
Intracerebral hemorrhage	874/1,411	1,370/2,348	0.95 (0.79–1.14)
Total stroke			**1.21 (1.09–1.34)**
Pain/discomfort			
Ischemic stroke	1,733/4,677	2,178/7,418	1.21 (1.10–1.32)
Intracerebral hemorrhage	637/1,407	893/2,341	1.45 (1.10 –1.91)
Total stroke			**1.25 (1.16–1.35)**
Anxiety/depression			
Ischemic stroke	1,594/4,643	1,843/7,405	1.40 (1.25–1.57)
Intracerebral hemorrhage	533/ 1,406	784/2,330	1.20 (0.86–1.68)
Total stroke			**1.32 (1.11– 1.55)**



Rexrode Circulation Research 2021


a
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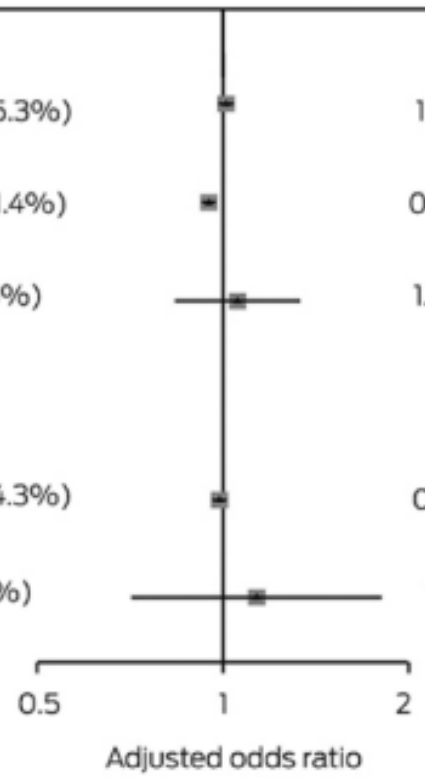
More women than men who had a stroke diagnosis on discharge were interpreted as migraine, headache or anxiety

Xia Wang et al. Med J Aust. 2022

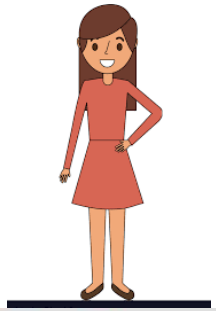
Sandset, E.C. and Ranhoff Hov, M. Med J Aust. 2022

Prehospital care

Outcome	Women (*N* = 51 692)	Men (*N* = 49 665)	Adjusted odds ratio (95% CI)
Management protocol			
Basic patient care	33 941 (65.7%)	32 423 (65.3%)	1.01 (0.99–1.04)
Stroke care	25 580 (49.5%)	25 501 (51.4%)	0.95 (0.92–0.97)
Cardiac arrest	176 (0.3%)	136 (0.3%)	1.06 (0.84–1.33)
Treatment			
Oxygen therapy	17 451 (33.8%)	17 0.32 (34.3%)	0.99 (0.96–1.01)
Ventilation	46 (0.1%)	33 (0.1%)	1.13 (0.71–1.81)



Wang MJA 2022



More frequent in women

Changes in conscious /mental status 1.38 (1.19-1.61)

Coma/stupor 1.39 (1.25-1.55)

Headache 1.24 (1.11-1.39)

Dysarthria 1.14 (1.04-1.24)

Vertigo 1.23 (1.13-1.34)

OUTCOME

Women vs men: OR (95% CI)

60 studies

582,844 patients

50% women

More frequent in men

Aspecific or other neurological symptoms 0.96 (0.94-0.97)

Paresis/ hemiparesis 0.73 (0.54-0.97)

Diplopia 0.69 (0.53-0.90)

Other focal visual disturbances 0.83 (0.70-0.99)

Ali Stroke 2022

Looking forward:
Women in science and gender medicine

WOMEN'S BRAIN PROJECT®

‘Papers with female first and last authors were more likely to report sex’

Factors affecting sex-related reporting in medical research: a cross-disciplinary bibliometric analysis

Cassidy R Sugimoto, Yong-Yeol Ahn, Elise Smith, Benoit Macaluso, Vincent Larivière

Summary

Lancet 2019; 393: 550–59

Background Clinical and preclinical studies have shown that there are sex-based differences at the genetic, cellular,

‘The effect attributable to women’s participation is strongest when women serve as leaders of the author group.’

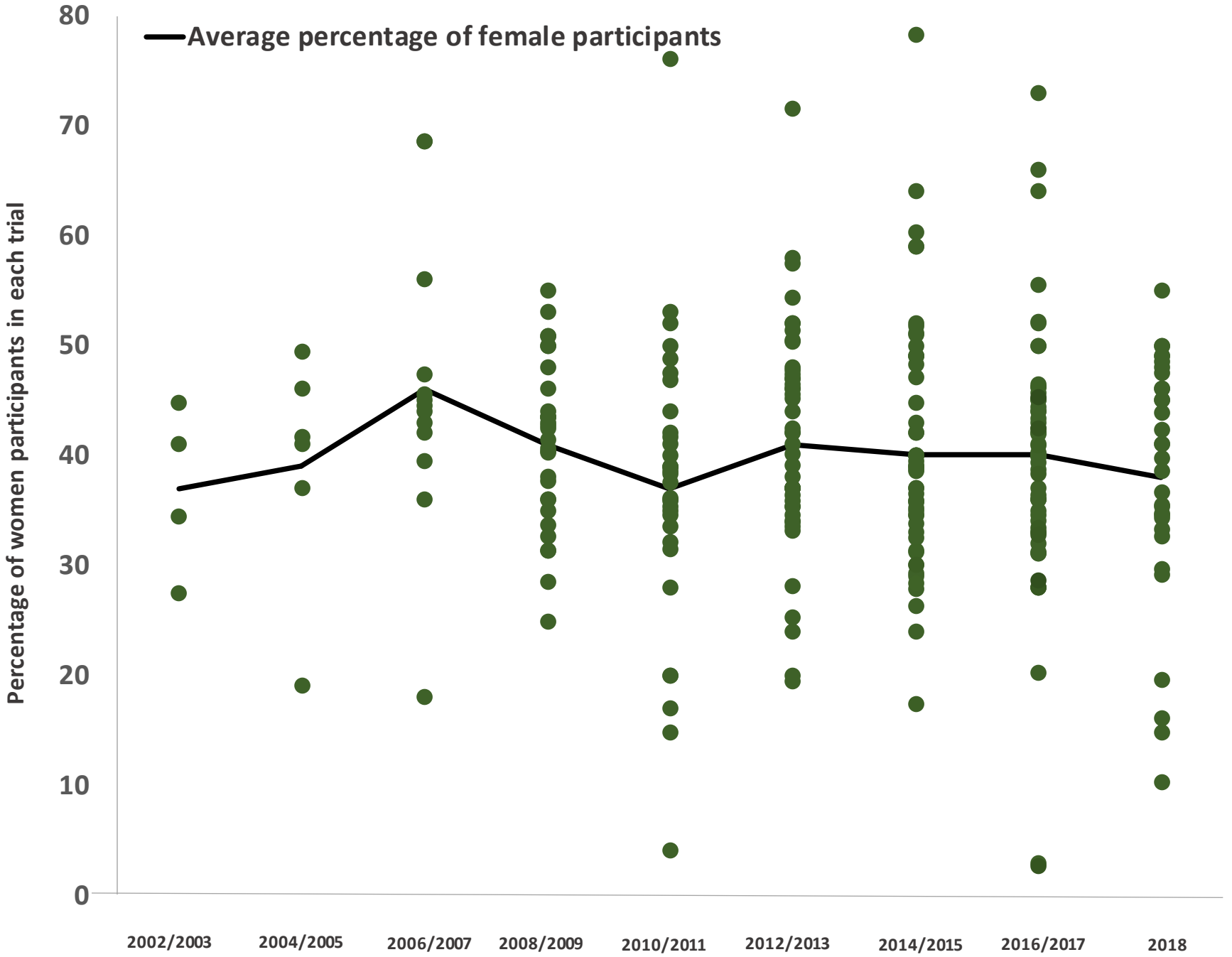
nature human behaviour

LETTERS

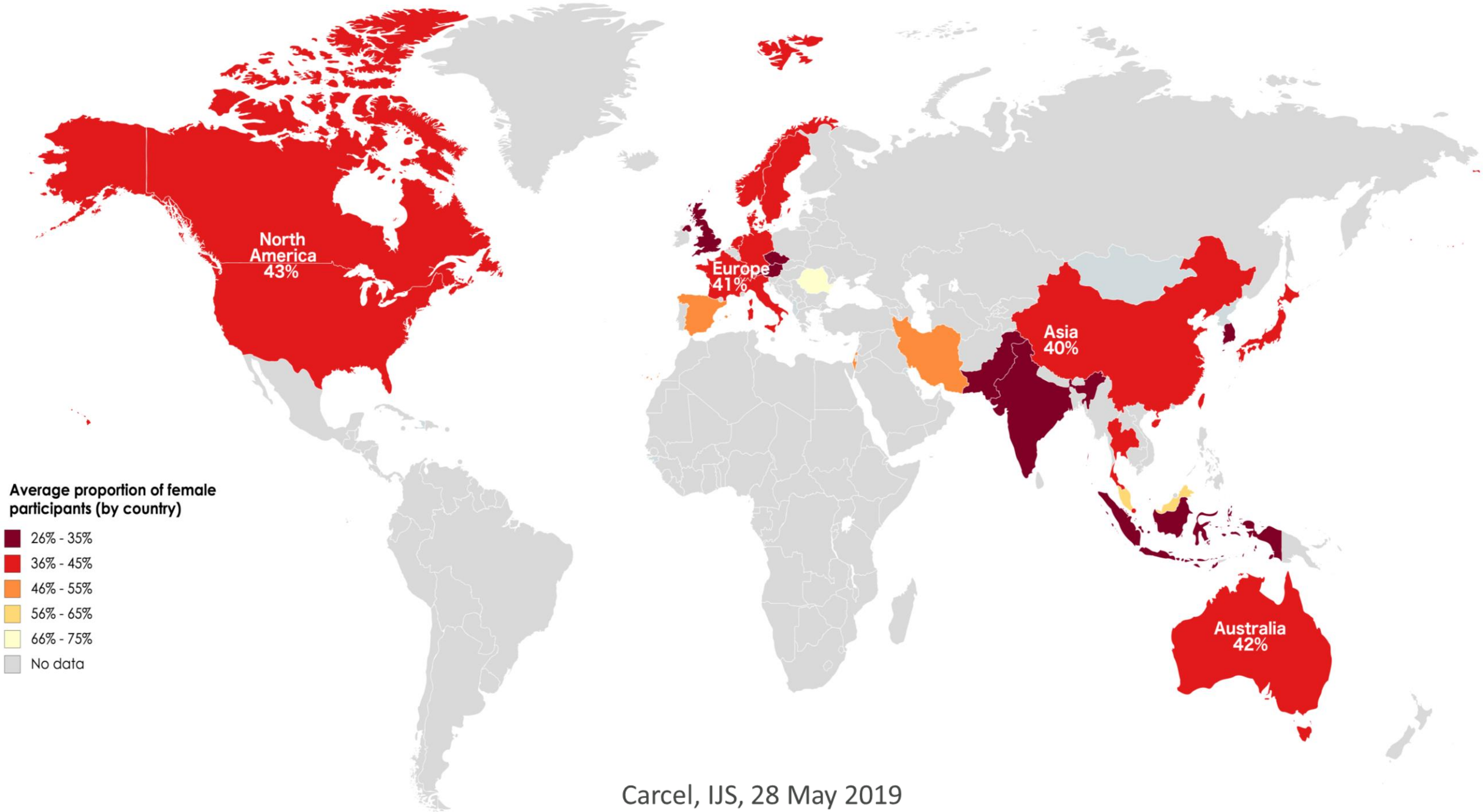
https://doi.org/10.1038/s41562-017-0235-x

One and a half million medical papers reveal a link between author gender and attention to gender and sex analysis

Mathias Wullum Nielsen[1*], Jens Peter Andersen[2], Londa Schiebinger[1] and Jesper W. Schneider[2]



Carcel, IJS, 28 May 2019



Carcel, IJS, 28 May 2019

Participation in trials vs burden of disease

- The prevalence corrected estimates for the participation of women in stroke trials (PPR) were calculated as:

- $$\text{PPR} = \frac{\text{Percentage of women among trial participants}}{\text{Percentage of women among disease population}}$$

- A PPR of 1 indicates the gender composition of the trial approximates the disease population

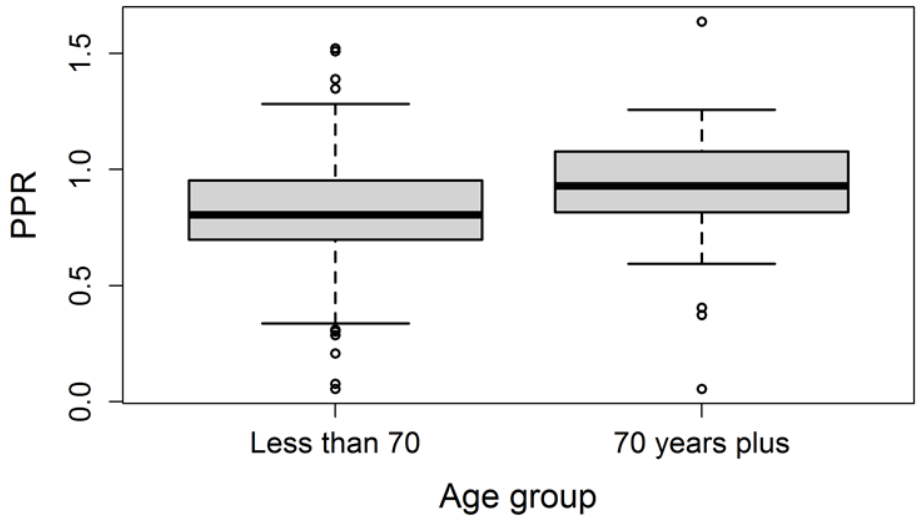
Carcel, Neurology, 2021

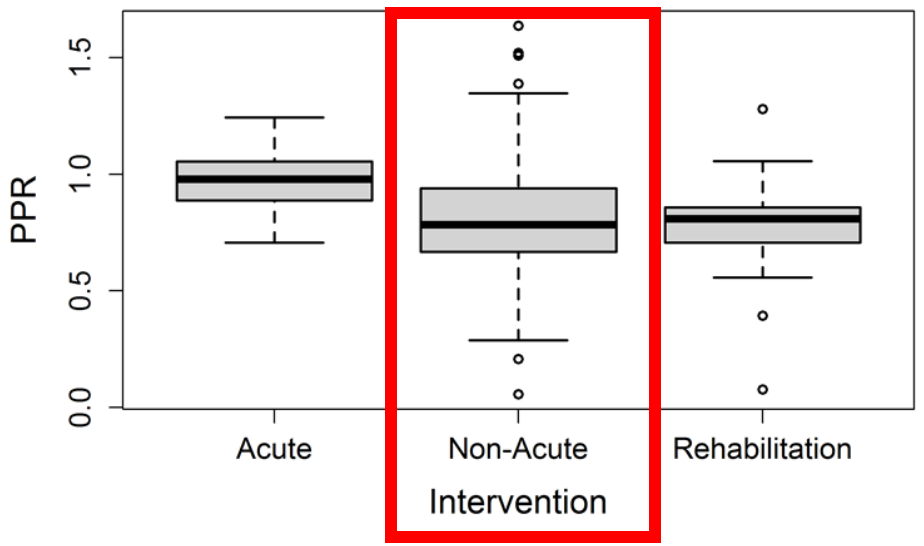
Prevalence corrected estimates of women's in stroke trials

- 281 eligible stroke RCTs with publications from 1 January 1990 to 31 January 2020
  - including 588,887 participants (37.4 % women)
- Prevalence of stroke in women was 48% (range 40% to 56%)
- Participation of women varied per trial (ranging from 3% to 78%) **mean 40%**
- **Overall, the PPR was 0.84**

Carcel, Neurology, 2021

Prevalence corrected estimates of women in stroke trials





Carcel, Neurology, 2021

Take home messages

Be vigilant of differences in symptom presentation in women and men

Identifying **effective strategies to enroll more women** in stroke RCTs are needed

Funders, editors and publishers need a clear sex and gender policy