

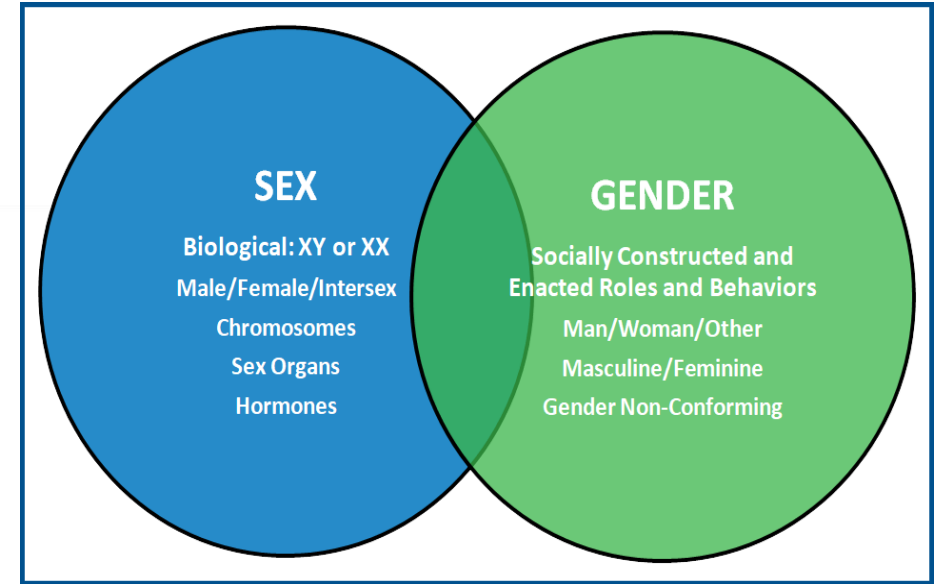
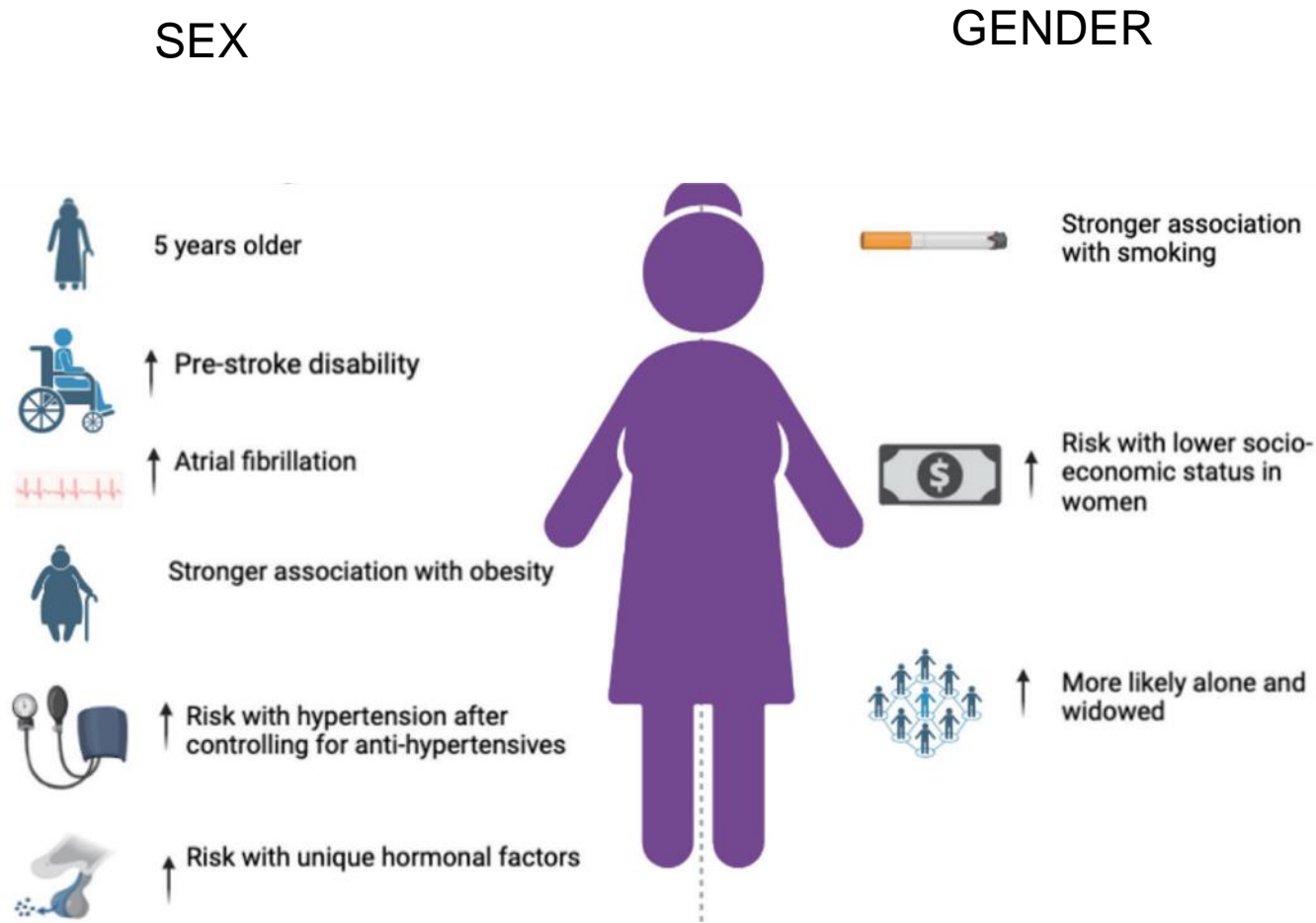
IMPORTANCIA DEL GÉNERO Y EL SEXO EN EL ICTUS

Marta Rubiera
Neuróloga Vascul

Nothing to disclose
(except being a woman)



Sex / Gender - Stroke



AMWA The Vision and Voice of Women in Medicine since 1915
American Medical Women's Association

Sex and Gender Differences in Stroke and Their Practical Implications in Acute Care

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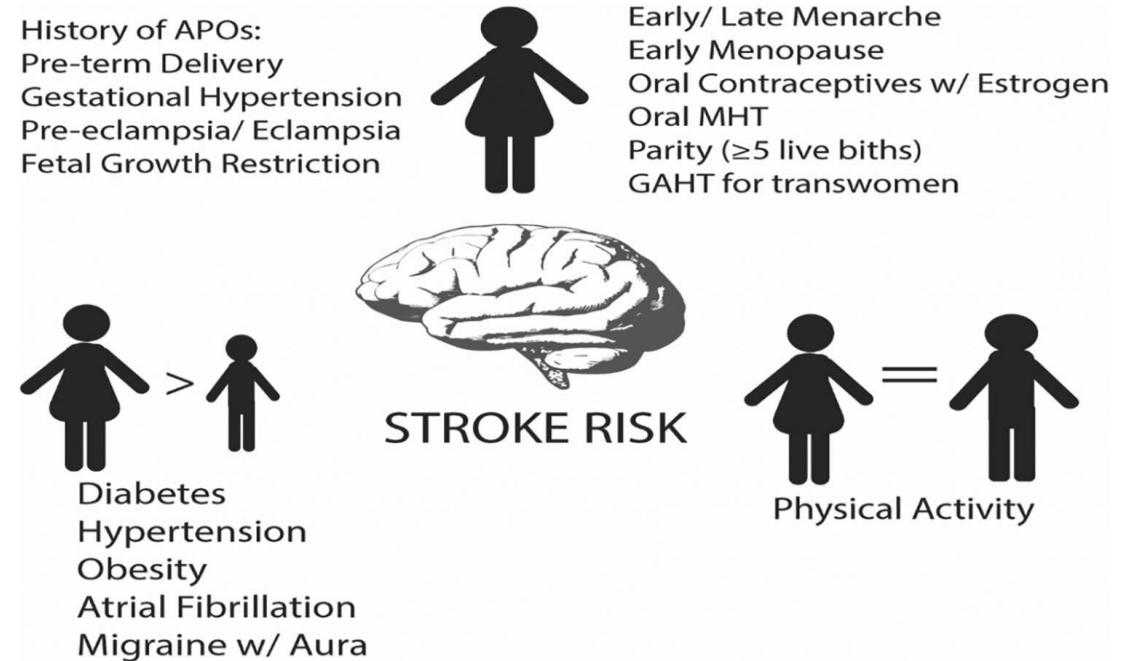
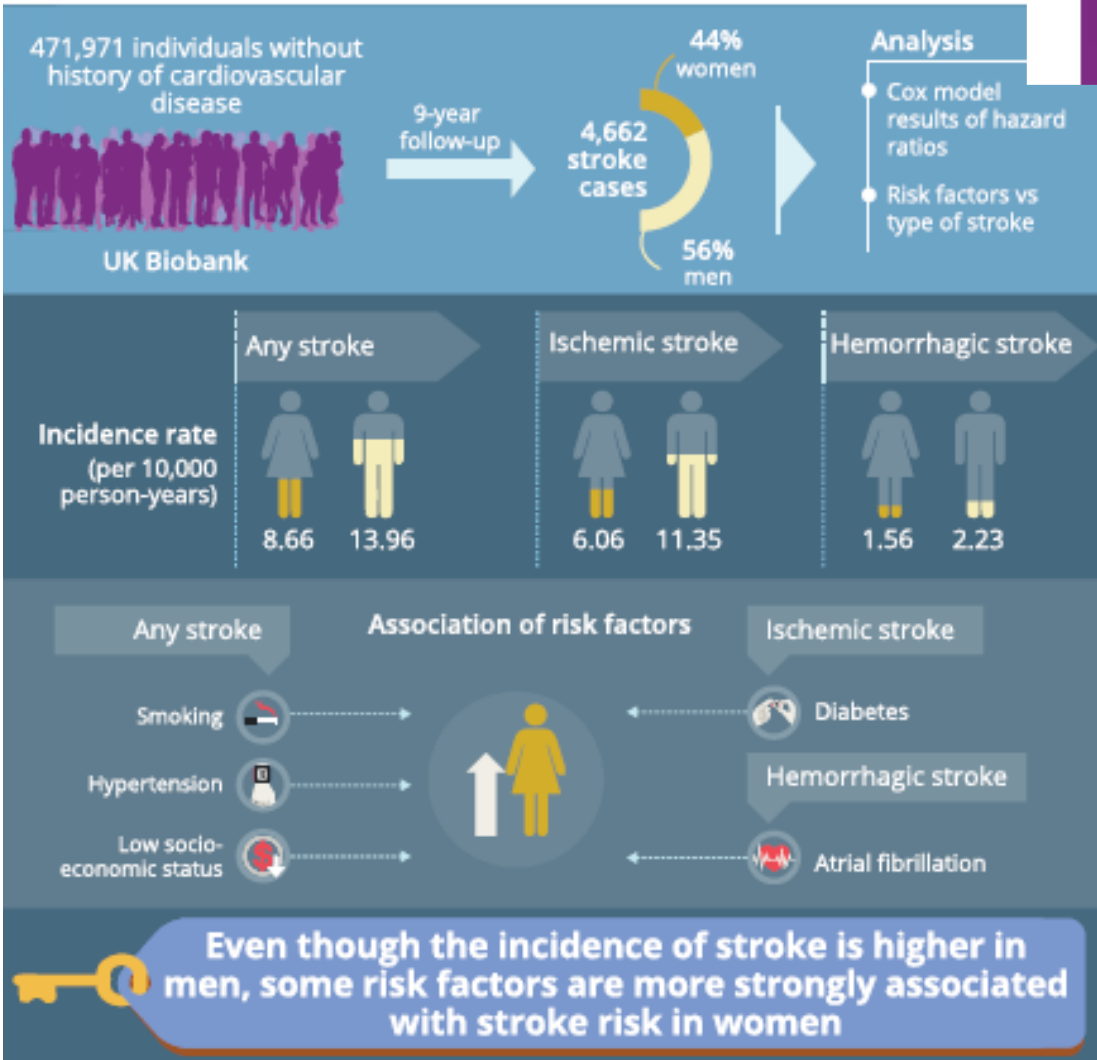
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Journal of Stroke 2023;25(1):16-25
<https://doi.org/10.5853/jos.2022.04077>

Sex / Gender - Stroke

Women Vs Men: Differences in Links Between Major Risk Factors and Risk of Stroke

Associations between various risk factors and the risk of stroke differ between women and men



doi:10.1212/WNL.00000000000010982
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Sex / Gender - Stroke Diagnosis

CÓDIGO ICTUS

ESCALA RACE

PARESIA HEMICUERPO IZQUIERDO		PARESIA HEMICUERPO DERECHO / AFASIA	
Paresia facial izquierda:		Paresia facial derecha:	
Ausente	0	Ausente	0
Ligera	1	Ligera	1
Moderada/Severa	2	Moderada/Severa	2
Paresia del brazo izquierdo:		Paresia del brazo derecho:	
Ausente/Ligera (>10seg)	0	Ausente/Ligera (>10seg)	0
Moderada (<10seg)	1	Moderada (<10seg)	1
Severa (no levanta)	2	Severa (no levanta)	2
Paresia de la pierna izquierda:		Paresia de la pierna derecha:	
Ausente/Ligera (>5seg)	0	Ausente/Ligera (>5seg)	0
Moderada (<5seg)	1	Moderada (<5seg)	1
Severa (no levanta)	2	Severa (no levanta)	2
Desviación oculo-cefálica a la derecha		Desviación oculo-cefálica a la izquierda	
Ausente	0	Ausente	0
Presente	1	Presente	1
Agnosia		Afasia	
Ausente	0	Obedece 2 órdenes	0
Asomatognosia o anosognosia	1	Obedece 1 orden	1
Asomatognosia y anosognosia	2	No obedece ninguna orden	2
TOTAL		TOTAL	

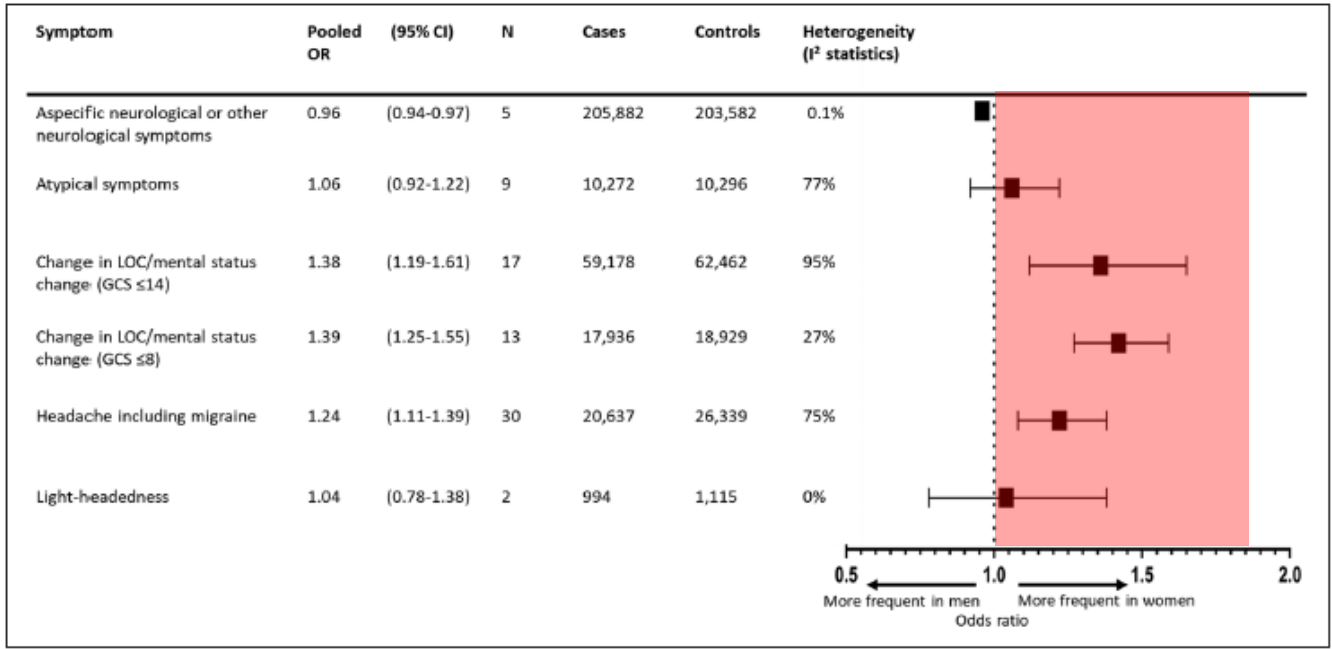
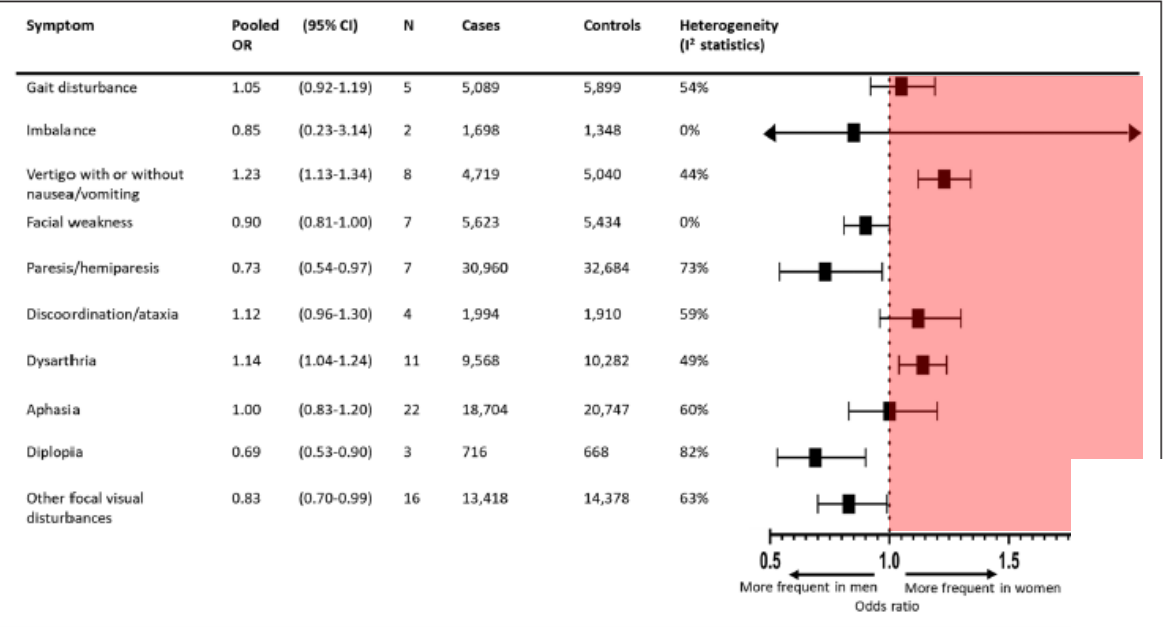


Figure 2. Summary forest plot for nonfocal symptoms in patients with any type of stroke. Cases: total number of women; controls: total number of men. GCS indicates Glasgow Coma Scale; LOC, level of consciousness; and OR, odds ratio.


Figure 3. Summary forest plot for focal symptoms in patients with any type of stroke. Cases: total number of women; controls: total number of men. OR indicates odds ratio.


Stroke


CLINICAL AND POPULATION SCIENCES

Sex Differences in Presentation of Stroke: A Systematic Review and Meta-Analysis








Mariam Ali, BSc; Hendrikus J.A. van Os, MD; Nelleke van der Weerd, MSc; Jan W. Schoones, MA; Martijn W. Heymans, PhD; Nyika D. Kruyt, MD, PhD; Marieke C. Visser, MD, PhD; Marieke J.H. Wermer, I

60 studies 

582,844 patients 

50% women 

Sex / Gender - Stroke Diagnosis

Risk factors 	Diagnosis 
 <p>Differences in prevalence of risk factors</p>	 <p>Less complete evaluations</p>
 <p>Differences in strength of the risk factors</p>	 <p>More likely diagnosed with stroke mimic</p>
 <p>Sex specific risk factors (APO, early menopause, hormonal factors)</p>	

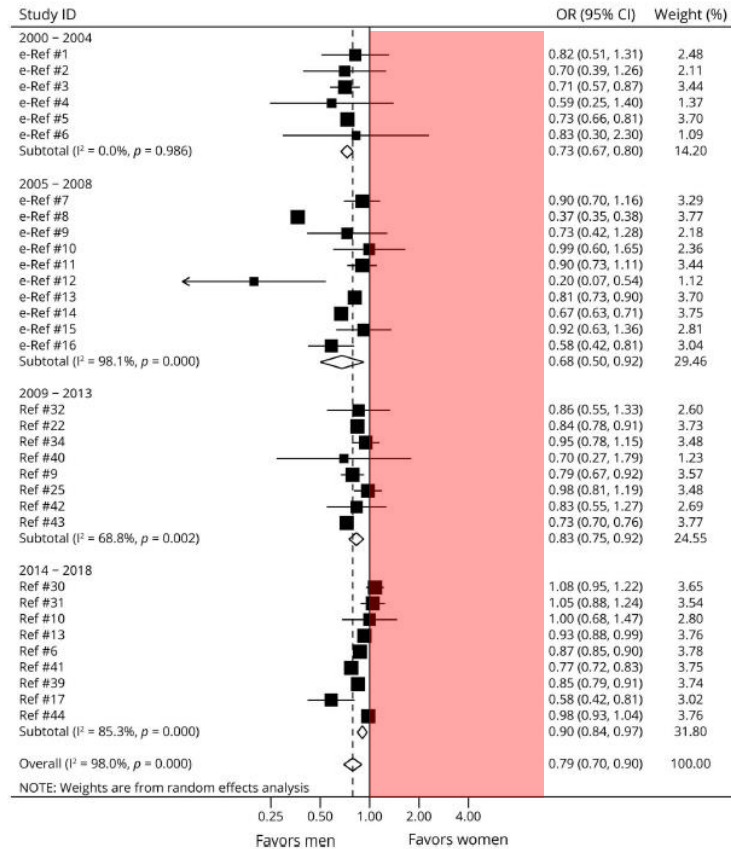
WOMEN AND CARDIOVASCULAR HEALTH COMPENDIUM

The Impact of Sex and Gender on Stroke

Kathryn M. Rexrode , Tracy E. Madsen , Amy Y.X. Yu , Cheryl Carcel , Judith H. Lichtman , Eliza C. Miller 

Sex / Gender - Stroke Treatment

Figure 5 Subgroup analysis by publication date (2000–2004, 2005–2008, 2009–2013, 2014–2018)



Forest plots of the unadjusted odds ratio (OR) of IV recombinant tissue plasminogen activator use in women compared to men in all acute ischemic stroke admissions. Random effects model (n = 33 studies). CI = confidence interval.

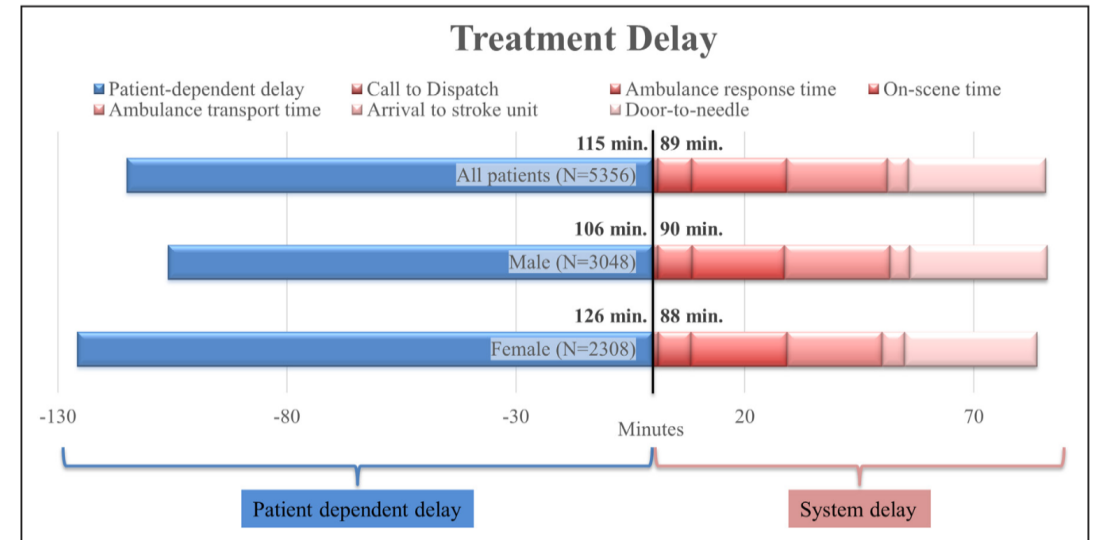
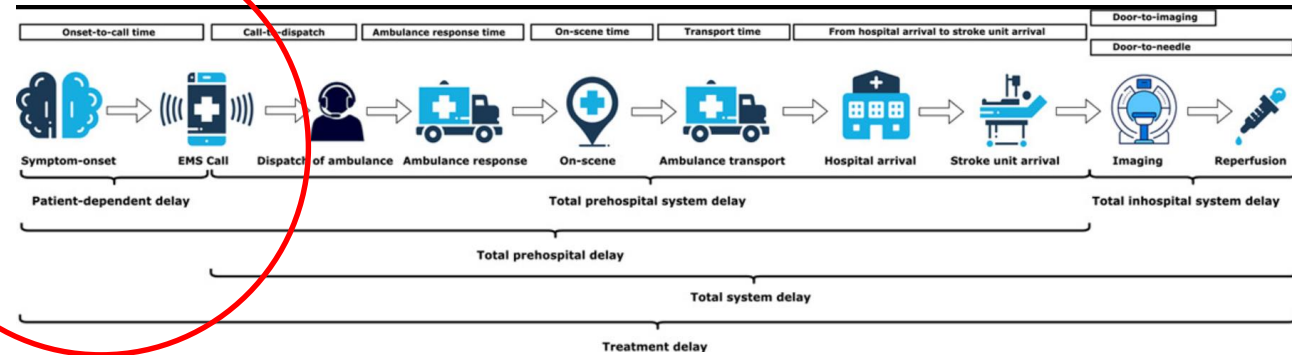
ARTICLE

Sex differences in IV thrombolysis treatment for acute ischemic stroke

A systematic review and meta-analysis

Brent Strong, Lynda D. Usabath, PhD, and Mathew Reeves, PhD
Neurology® 2020;95:e11-e22. doi:10.1212/WNL.00000000000009733

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Disentangling Sex Differences in Use of Reperfusion Therapy in Patients With Acute Ischemic Stroke

Jeppie Mainz, BSc (medicine); Grethe Andersen, MD, DMSc; Jan Brink Valentin, MSc; Martin Faurholt Gude, MD; Søren Paaske Johnsen, MD, PhD

Stroke. 2020;51:2332–2338.



Sex and gender differences in acute stroke care: metrics, access to treatment and outcome. A territorial analysis of the Stroke Code System of Catalonia

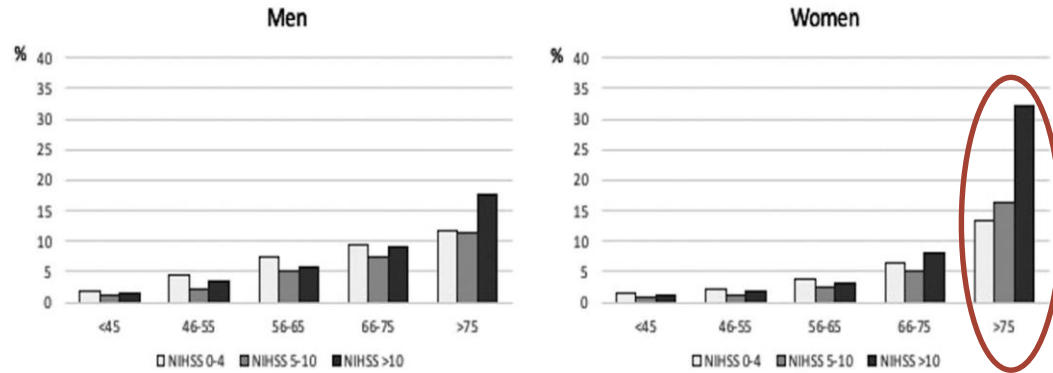


Table 1. Characteristics of stroke code activation by sex: source of stroke activation, prehospital metrics, and final diagnosis.

	Women n = 10,798	Men n = 12,573	p-Value
Age, years (mean ± standard deviation)	73.6 ± 15.2	69.8 ± 13.9	<0.001
mRS pre-stroke 0-2 (n, %)	8683 (80.4%)	11,264 (89.6%)	<0.001
Source of stroke code activation (n, %)			0.001
EMS with pre-notification	6577 (60.9%)	7548 (60.0%)	
EMS without pre-notification	1256 (11.6%)	1310 (10.4%)	
Emergency room of a non-stroke code hospital	1198 (11.1%)	1454 (11.6%)	
Emergency room of a stroke code hospital	1272 (11.8%)	1632 (13.0%)	
In-hospital (admitted for other disease)	495 (4.6%)	629 (5.0%)	
Wake-up stroke (n, %)	2893 (26.8%)	3288 (26.2%)	0.268
Stroke subtype (n, %)			<0.001
Ischemic stroke	6945 (64.3%)	8237 (65.5%)	
Transient ischemic attack	596 (5.5%)	841 (6.7%)	
Intracerebral hemorrhage	1077 (10.0%)	1610 (12.8%)	
Subarachnoid hemorrhage	127 (1.2%)	95 (0.8%)	
Stroke mimic	2053 (19.0%)	1790 (14.2%)	
NIHSS at admission (median (IQR))	9 (4, 18)	7 (3, 16)	<0.001
Etiology of stroke mimic (n, %)			<0.001
Migraine	133 (9.9%)	48 (3.9%)	
Psychiatric disorders	194 (14.4%)	54 (4.4%)	
Seizures	352 (26.1%)	458 (37.2%)	
Metabolic disorders	107 (7.9%)	121 (9.8%)	
Tumor	65 (4.8%)	70 (5.7%)	
Confusional syndrome	59 (4.4%)	61 (5%)	
Syncope	77 (5.7%)	89 (7.2%)	
Nervous system infection	35 (2.6%)	30 (2.4%)	
Time metrics, min (median (IQR))			
Onset-hospital arrival	117 (65, 265)	118 (64, 267)	0.986
Hospital arrival-image	22 (15, 35)	22 (14, 34)	0.020
Hospital arrival-tPA	37 (27, 53)	35 (26, 51)	0.036
Hospital arrival-groin	72 (50, 98)	72 (49, 98)	0.563
Groin-recanalization	48 (28, 75)	48 (29, 75)	0.543



Sex and gender differences in acute stroke care: metrics, access to treatment and outcome. A territorial analysis of the Stroke Code System of Catalonia

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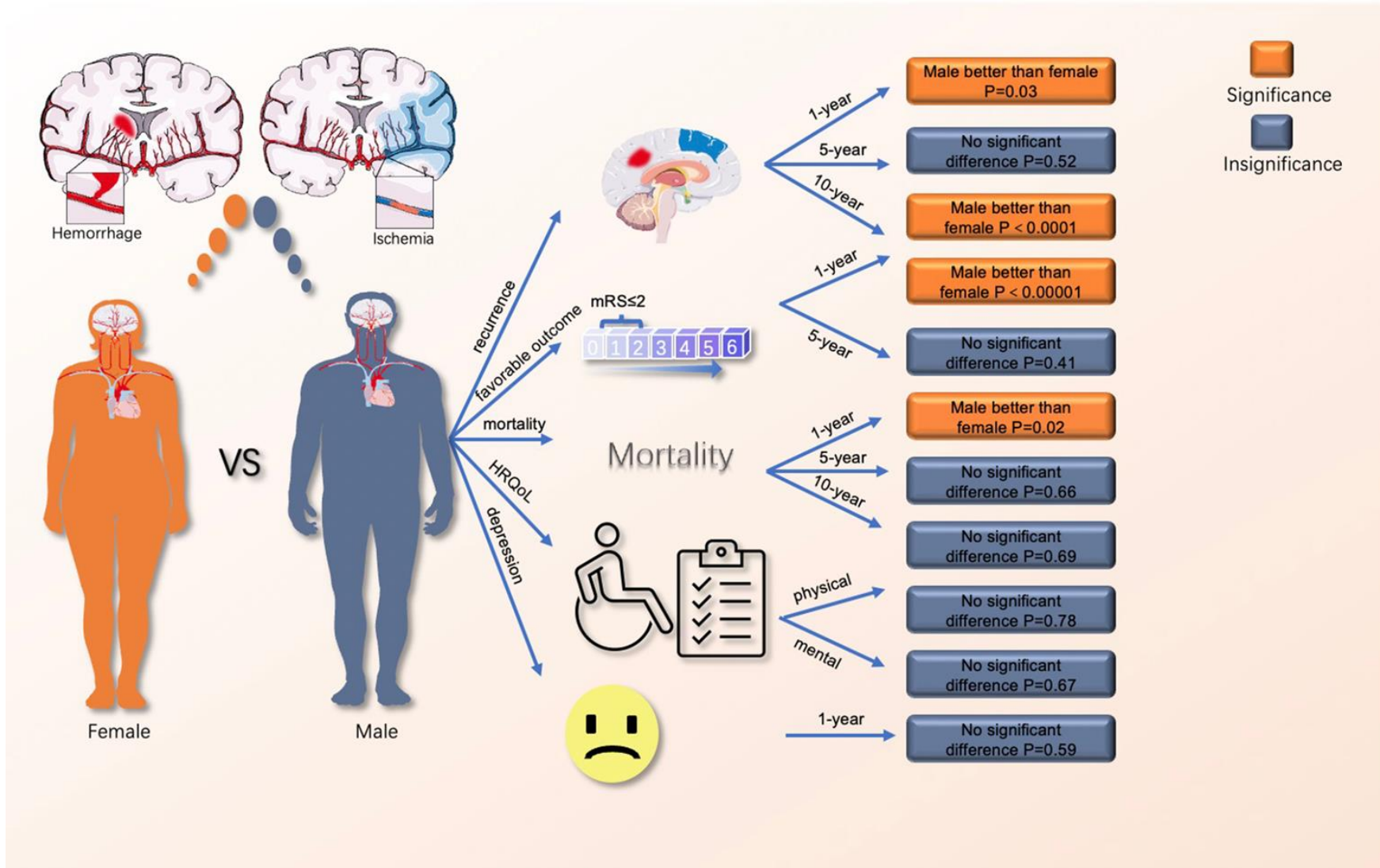
Table 2. Clinical characteristics, metrics, and outcome of patients with ischemic stroke and prior mRS < 3.

	Women n=5485	Men n=7419	p-Value
Age, years (mean ± standard deviation)	73.8 ± 13.6	69.4 ± 13.2	<0.001
NIHSS at admission (median (IQR))	8 (3–17)	6 (3–13)	<0.001
Wake-up stroke (n, %)	1584 (28.9%)	2067 (27.9%)	0.204
Large vessel occlusion (n, %)	1909 (35.8%)	2245 (31.1%)	<0.001
Revascularization treatment (n, %)	2645 (48.2%)	3199 (43.1%)	<0.001
IVT	1548 (28.2%)	1983 (26.7%)	
MT	701 (12.8%)	729 (9.8%)	
IVT + MT	396 (7.2%)	487 (6.6%)	
No treatment	2840 (51.8%)	4220 (56.9%)	
Time metrics, min (median (IQR))			
Onset-stroke code activation	122 (60–308)	127 (58–312)	0.750
Onset-hospital arrival	122 (65–290)	124 (65–303)	0.979
Hospital arrival-image	22 (15–34)	22 (15–35)	0.579
Hospital arrival-tPA	36 (26–52)	35 (26–50)	0.158
Hospital arrival-groin	72 (49–97)	71 (49–97)	0.429
Groin-recanalization	48 (28–75)	49 (29–75)	0.669
IVT ^a	n=1548	n=1983	
sICH (n, %)	27/881 (3.1%)	45/1098 (4.1%)	0.222
Mortality 90 days (n, %)	147/1194 (12.3%)	173/1502 (11.5%)	0.527
Good outcome 90 days (n, %)	677/1194 (56.7%)	959/1502 (63.8%)	<0.001
IVT + MT ^b	n=396	n=487	
sICH (n, %)	9/311 (2.9%)	9/366 (2.5%)	0.726
Mortality 90 days (n, %)	41/284 (14.4%)	64/334 (19.2%)	0.119
Good outcome 90 days (n, %)	143/284 (50.4%)	182/334 (54.5%)	0.304
MT ^c	n=701	n=729	
sICH (n, %)	16/531 (3%)	21/540 (3.9%)	0.433
Mortality 90 days (n, %)	108/525 (20.6%)	157/565 (27.8%)	0.006
Good outcome 90 days (n, %)	181/525 (34.5%)	222/565 (39.3%)	0.100

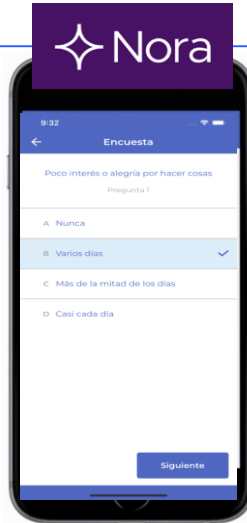
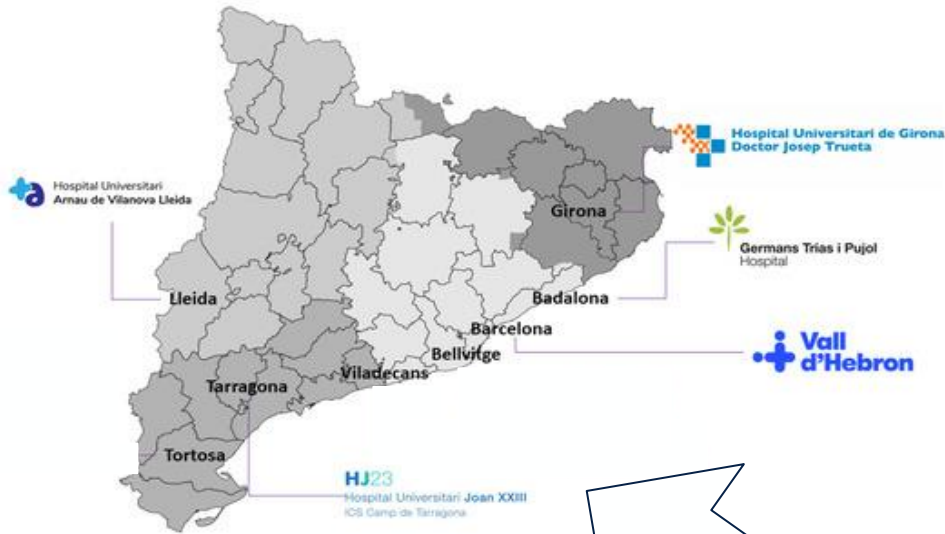
Table 4. Multivariate analysis: factors related to poor outcome (mRS > 2) at 90 days in patients treated with any reperfusion therapy and patients with MT.

	OR	Lower limit of 95% CI	Upper limit of 95% CI	p-Value
Patients treated with any reperfusion therapy (intravenous and/or endovascular)				
Sex (women)	1.071	0.927	1.238	0.275
Age	1.043	1.037	1.049	<0.001
NIHSS at admission	1.101	1.088	1.114	<0.001
Large Vessel Occlusion	1.428	1.211	1.685	<0.001
Patients treated with MT				
Sex (women)	1.028	0.837	1.264	0.791
Age	1.037	1.029	1.045	<0.001
NIHSS at admission	1.077	1.060	1.093	<0.001
Previous iv-tPA	0.487	0.395	0.600	<0.001
General anesthesia	2.227	1.392	3.562	0.001

Sex / Gender - Stroke Outcomes



Guo X, Xiong Y, Huang X, Pan Z, Kang X, et al. (2023) Sex-based differences in long-term outcomes after stroke: A meta-analysis. PLOS ONE 18(4): e0283204. <https://doi.org/10.1371/journal.pone.0283204>
<https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0283204>



7 days

90 days

Please respond to each item by marking the box you chose		Excellent	Very good	Good	Fair	Poor							
Q1	In general, would you say your health is...	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>							
Q2	In general, would you say your quality of life is...	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>							
Q3	In general, how would you rate your physical health?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>							
Q4	In general, how would you rate your mental health, including your mood and your ability to think?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>							
Q5	In general, how would you rate your satisfaction with your social activities and relationships?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>							
Q6	In general, please rate how well you carry out your usual social activities and roles (i.e. relative activities at home, at work and in your community, and responsibilities as a parent, child, spouse, employee, friend, etc.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>							
Q7	It is not clear how you are able to carry out your everyday physical activities such as walking, climbing stairs, carrying groceries, or mowing a lawn?	Completely	Mostly	Moderately	A Little	Not At All							
Q8	In the past 7 days, how often have you been bothered by emotional problems such as feeling anxious, depressed or irritable?	Never	Rarely	Sometimes	Often	Average							
Q9	How would you rate your fatigue on average?	None	Mild	Moderate	Severe	Very Severe							
Q10	How would you rate your pain on average?	No Pain	1	2	3	4	5	6	7	8	9	10	Worst imaginable Pain

PROMIS 10

- 0 No symptoms
- 1 No significant disability. Able to carry out all usual activities, despite some symptoms
- 2 Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities
- 3 Moderate disability. Requires some help, but able to walk unassisted
- 4 Moderately severe disability. Unable to attend to own bodily needs without assistance, or unable to walk unassisted
- 5 Severe disability. Requires constant nursing care and attention, bedridden, incontinent
- 6 Dead

mRS

Hospital Anxiety and Depression Scale (HADS)		Anxiety (A)		Depression (D)	
1	I feel tense or "worried"	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2	I feel at the end of my strength	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
13	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
14	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
15	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
17	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
18	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
19	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
20	I feel that I am getting on top of things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

HADs

GHQ 0-100

Consecutive acute stroke patients



To evaluate sex/gender-focused outcomes after acute stroke



HOME



Socio-rehabilitation center



Confounding factors

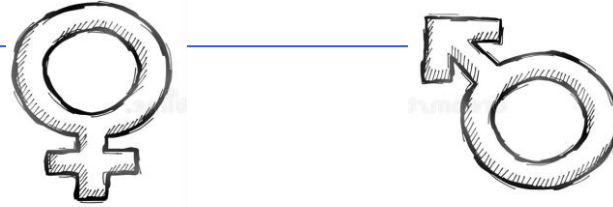
HARMONICS

Harmonising data collection to deliver high value stroke care



	Global (n=2268)	Women (n=964, 42.5%)	Men (n=1304, 57.5%)	p
Age (median, IQR)	74 (63-83)	78 (68-85)	71 (60-80)	<0.001
pre-stroke mRS	0 (0-2)	1 (0-2)	0 (0-1)	<0.001
Baseline NIHSS	4 (1-10)	4 (1-12)	3 (1-8)	0.001
Atrial fibrillation	298 (13.1%)	156 (16.2%)	149 (11.4%)	0.001
Stroke subtype:				0.303
- Ischemic	1701 (75%)	730 (75.8%)	971 (74.5%)	
- TIA	315 (13.9%)	138 (14.3%)	177 (13.6%)	
- Hemorrhagic	248 (10.9%)	92 (9.5%)	156 (12%)	
Discharge NIHSS	1 (0-4)	1 (0-4)	1 (0-4)	0.188
Discharge mRS	2 (1-4)	3 (1-4)	2 (1-4)	<0.001

3 MONTHS OUTCOMES



	Global (n=2268)	Women (n=964, 42.5%)	Men (n=1304, 57.5%)	p
mRS	2 (0-5)	3 (1-5)	2 (0-4.5)	0.026
PROMIS-10 PHY	14 (11-17)	12 (11-15)	15 (12-17)	<0.001
PROMIS-10 MENTAL	12 (10-14)	12 (9-14)	13 (11-15)	<0.001
HADs DEPRESSION	4 (1-8)	5 (2-9)	3 (1-8)	0.004
HADs ANXIETY	4 (2-8)	6 (2.75-9)	4 (2-7)	<0.001
GHQ	70 (50-82)	60.5 (50-80)	71 (50-85)	0.002

* PROMIS and GHQ: higher, better
HADs: lower, better



LOGISTIC REGRESSION ANALYSIS

	Sex (Women)	Discharge mRS	Age
PROMIS-PHY ≥ 13	OR 0.40 (CI 0.27-0.61, $p < 0.001$)	OR 0.64 (CI 0.55-0.76, $p < 0.001$)	0.122
PROMIS-M ≥ 11	OR 0.60 (CI 0.39-0.91, $p = 0.016$)	OR 0.67 (CI 0.57-0.87, $p < 0.001$)	0.057
HADS-ANX < 9	OR 0.43 (CI 0.25-0.72, $p = 0.001$)	OR 0.81 (CI 0.66-0.99, $p = 0.041$)	OR 1.04 (CI 1.02-1.05, $p < 0.001$)
HADS-DEP < 9	0.158	OR 0.63 (CI 0.51-0.76, $p < 0.001$)	0.427
GHQ > 70	OR 0.60 (CI 0.40-0.90, $p = 0.012$)	OR 0.71 (CI 0.60-0.83, $p < 0.001$)	0.201
mRS < 3 or equal to baseline	0.796	OR 0.40 (CI 0.34-0.47, $p < 0.001$)	OR 0.97 (CI 0.95-0.99, $p < 0.001$)





Logistic regression analysis adjusted by age, baseline mRS, stroke severity and discharge mRS



Table. Research Gaps to Eliminate Disparities in Stroke by Sex and Gender

Research area	Research gaps
Stroke epidemiology	Delineation of the separate effects of biologic sex and sociocultural gender
Stroke risk factors	Delineating the separate effects of biologic sex and sociocultural gender
	Prediction models with female-specific risk factors
	CVD prevention for women with a history of adverse pregnancy outcomes: screening and treatment guidelines, as well as understanding biologic mechanisms
Stroke diagnosis	Research on strategies to reduce misdiagnosis in women, as well as in investigation and care
Stroke treatment	Inclusion of women in clinical trials consistent with their stroke incidence
	Increasing the number of women who lead clinical trials
	Presentation of sex-disaggregated data and stratified results from all clinical trials
	Investigation of sex differences in outcomes with endovascular therapy, carotid artery stenting, and carotid endarterectomy
Stroke outcomes	Improved understanding of the factors contributing to worse outcomes after stroke in women
	Interventions to improve outcomes including disability and poststroke depression

TAKE HOME MESSAGES

-  Different baseline, risk factors and stroke related sex/gender specific characteristics
-  Stroke ID and diagnosis more difficult, may delay hospital arrival
-  In Catalonia, no significant delays in stroke workflow nor acute management differences. Adjustment by baseline characteristics and stroke severity dilute sex-influence in mRS at 3 months for reperfusion-treatments
-  Sex/Gender differences in outcomes reported by clinicians and patients were detected in our series, especially PROMS. Whether the differences can be attributed to sex or gender is unknown