Sex and Gender Differences in Acute Stroke

Tracy E. Madsen, MD, ScM
Division of Sex and Gender, Dept of EM
Alpert Medical School of Brown University
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Presenter Disclosure Information

Tracy E. Madsen, MD, ScM
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Financial Disclosure:
No relevant financial relationship exists

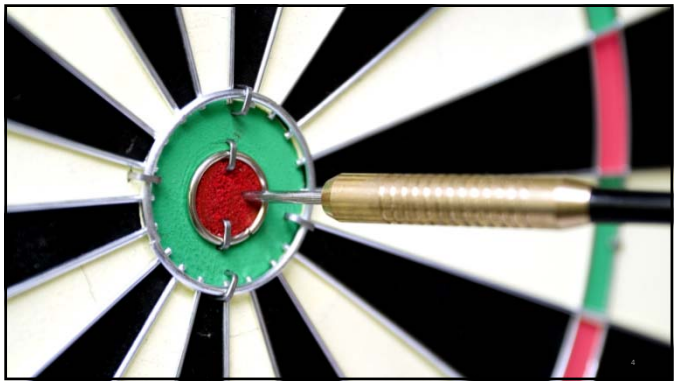
I routinely consider the sex and gender of my stroke patients during diagnosis and/or management.

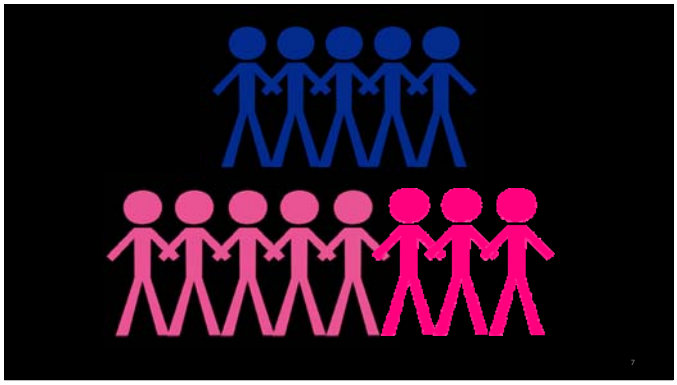
A. Always
B. Almost always
C. Sometimes
D. Rarely
E. Never

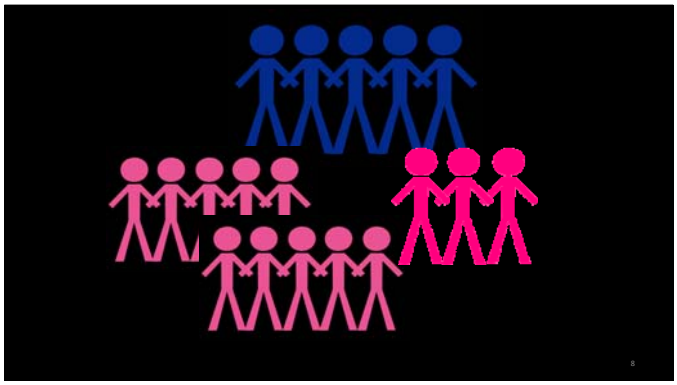
Slide 1

1 Objectives for talk:
1 why should you care- ems, neuro, EM, nursing
imapct on epidemiology
imapct on outcomes
impact on treatment
RFs- Dm, Htn
what can you do?- changes in prevention? advocacy for women being discharged?

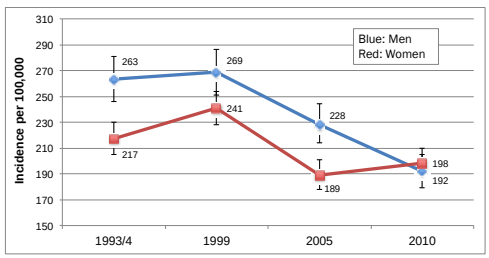
Tracy Madsen, 9/15/2016







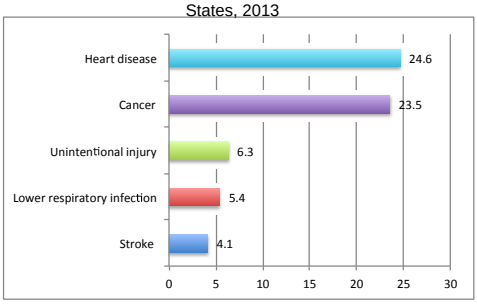
All Stroke, Trends over Time by Sex



Incidence rates and 95% confidence intervals. Incidence rates were adjusted by age and race. Comparisons made between 1993/4 and 2010 were significant in men (p<0.001) but not women (p=0.15). Bonferroni corrections were made for multiple comparisons.

Presented at ISC 2016, Los Angeles, CA

Leading causes of death in males, United States, 2013



www.cdc.gov/men/lcod/2013/index.htm

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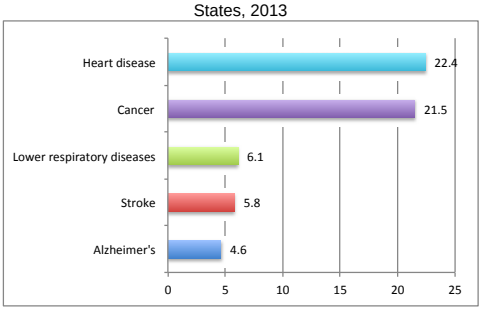
Leading causes of death in females, United States, 2013



www.cdc.gov/women/lcod/2013/index.htm

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Diabetes mellitus → **2.28** → Stroke

Diabetes mellitus → 1.83 → Stroke

Peters SA, Huxley RR, Woodward M. Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775,385 individuals and 12,539 strokes. Lancet 2014;393:1783-80.

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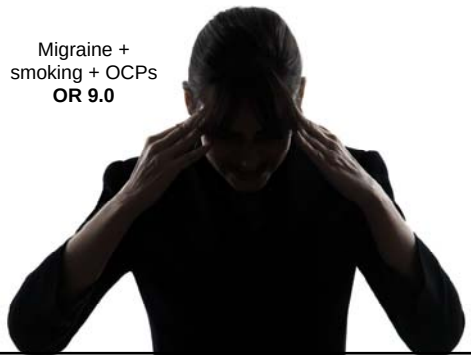
Migraine + smoking + OCPs **OR 9.0**



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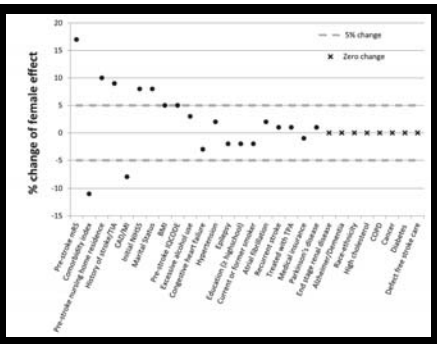
Ischemic: RRR 0.97 (0.79-1.18)
Hemorrhagic RRR 1.17 (1.02-1.34)
SAH

Peters SAE, Huxley RR, Woodward M. Smoking as a risk factor for stroke in women compared with men. Stroke 2013;44:2821-2828.

15



Lisabeth LD, Reeves MJ, Baek J, et al. Factors influencing sex differences in post-stroke functional outcome. *Stroke*. 2015;46:860-863.

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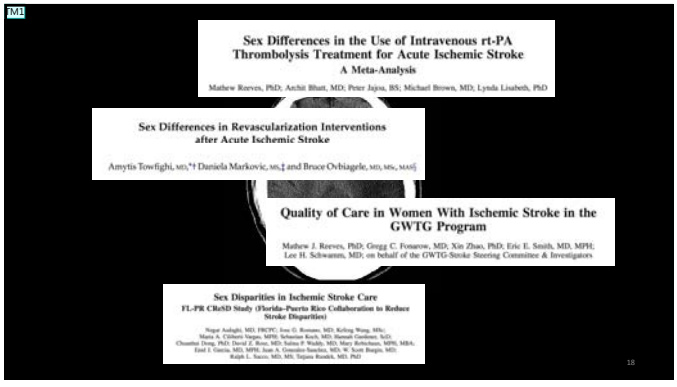

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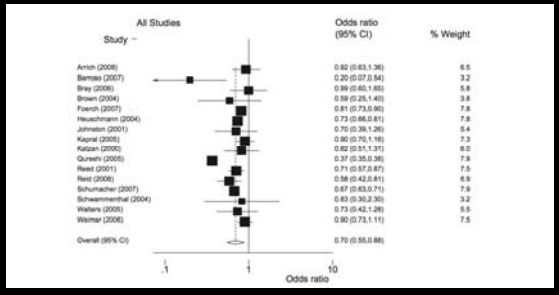
Slide 18

TM1 add other titles to slide
Tracy Madsen, 10/7/2016



Reeves M, Blatt A, Jajou P, et al. Sex differences in the use of Intravenous rt-PA Thrombolysis Treatment for Acute Ischemic Stroke: A Meta-Analysis. Stroke 2009;40:1743-1749.

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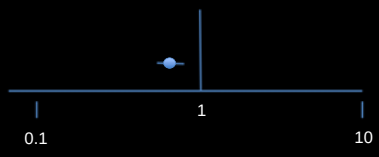

Reeves M, Blatt A, Jajou P, et al. Sex differences in the use of Intravenous rt-PA Thrombolysis Treatment for Acute Ischemic Stroke: A Meta-Analysis. Stroke 2009;40:1743-1749.

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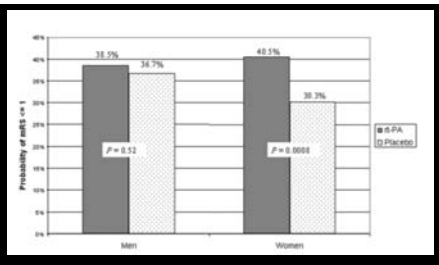
Sex-Based Differences in Response to Recombinant Tissue Plasminogen Activator in Acute Ischemic Stroke : A Pooled Analysis of Randomized Clinical Trials

David M. Kent, Lori Lyn Price, Peter Ringleb, Michael D. Hill and Harry P. Selker



Stroke 2006;36:62-65.

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TABLE 3. Recanalization Status According to TIMI Grades

	MCA+ICA/MCA Occlusion		Isolated MCA Occlusions	
TIMI Grade	Women n=17	Men n=22	Women n=12	Men n=13
TIMI3	10 (59%)	8 (36%)	8 (67%)	7 (54%)
TIMI2	4 (23%)	4 (18%)	3 (25%)	1 (8%)
TIMI1	2 (12)	1 (5%)	1 (8%)	0
TIMI0	1 (6%)	9 (41%)	0	5 (38%)

Savitz S, Schlaug G, Caplan L et al. Arterial Occlusive Lesions Recanalize More Frequently in Women than in Men After Intravenous Tissue Plasminogen Activator for acute stroke. Stroke 2005;36:1447-51.

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Analysis of Tissue Plasminogen Activator Eligibility by Sex in the Greater Cincinnati/Northern Kentucky Stroke Study

Tracy E. Madsen, MD, ScM; Jane C. Khoury, PhD; Kathleen A. Alwell, BSN; Charles J. Moomaw, PhD; Brett M. Kissela, MD, MS; Felipe De Los Rios La Rosa, MD; Daniel Woo, MD, MS; Opeolu Adeoye, MD, MS; Matthew L. Flaherty, MD; Pooja Khatri, MD; Simona Ferioli, MD; Dawn Kleindorfer, MD

SBP > 185 mm Hg or DBP > 110 mm Hg

Females	Males	P-value
17.1% (176)	12.4% (101)	0.02

Stroke 2015;46:717-721.

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NIHSS>25

Females	Males	P-value
2.8% (32)	1.2% (10)	0.01

Stroke 2015;46:717-721.

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Age > 80

Females	Males	P-value
35.0% (358)	17.4% (138)	<0.0001

Stroke 2015;46:717-721.

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Table 3. Overall Eligibility by Sex

Eligible for r-tPA	Overall	Women	Men	*P* Value
Standard criteria	114 (5.9%)	64 (5.7%)	50 (6.1%)	0.70
ECASS III criteria	9 (0.5%)	4 (0.4%)	5 (0.6%)	0.43
Total eligible in 4.5 h	123 (6.4%)	68 (6.1%)	55 (6.8%)	0.55
Absolute criteria in 4.5 h	324 (16.7%)	180 (16.0%)	144 (17.7%)	0.38

Data are reported as raw counts and weighted percentages. Generalized linear models were used for analysis to account for the study design. ECASS indicates European Cooperative Acute Stroke Study; and r-tPA, recombinant tissue-type plasminogen activator.

Stroke 2015;46:717-721.

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Total Eligible

Females	Males	P-value
6.1% (68)	6.8% (55)	<0.55

Stroke 2015;46:717-721.

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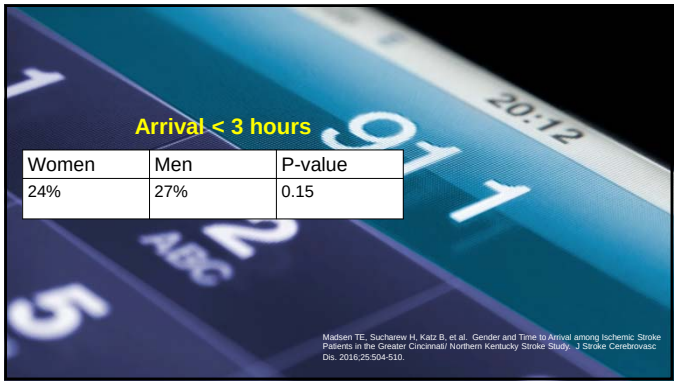

Arrival < 3 hours

Women	Men	P-value
24%	27%	0.15

Madsen TE, Sucharew H, Katz B, et al. Gender and Time to Arrival among Ischemic Stroke Patients in the Greater Cincinnati/ Northern Kentucky Stroke Study. J Stroke Cerebrovasc Dis. 2016;25:504-510.

Predictors of Stroke Knowledge by Gender

Table 3. *Factors associated with a low score on Stroke Symptoms Knowledge Scale*

Variable	Adjusted odds ratio	95% Confidence interval
Male gender	1.36	1.28-1.45
Race		
White	1.0	Ref
Black	1.54	1.41-1.68
Other	2.04	1.72-2.41
Hispanic ethnicity	1.13	.91-1.41
Age, y		
18-34	1.20	1.1-1.31
35-54	1.0	Ref
55-74	1.04	.97-1.10
>75	2.43	2.25-2.62
Income		
Less than $20,000	2.87	2.59-3.18
$20,000-<$35,000	2.19	1.99-2.41
$35,000-<$50,000	1.62	1.45-1.81
$50,000-<$75,000	1.31	1.18-1.45
Over $75,000	1.0	Ref
Don't know/refused	2.55	2.29-2.84
Primary medical doctor	1.33	1.22-1.45

Madsen TE, Baird KA, Silver B et al. Analysis of Gender Differences in Knowledge of Stroke Warning Signs. J Stroke Cerebrovasc Dis. 2015;24:1540-1547.

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Males were 1.36 times more likely to have a low score on **knowledge of stroke symptoms.**

Madsen TE, Baird KA, Silver B et al. Analysis of Gender Differences in Knowledge of Stroke Warning Signs. J Stroke Cerebrovasc Dis. 2015;24:1540-1547.

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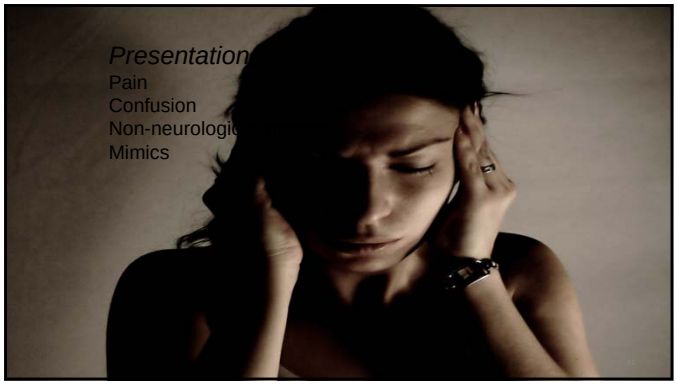

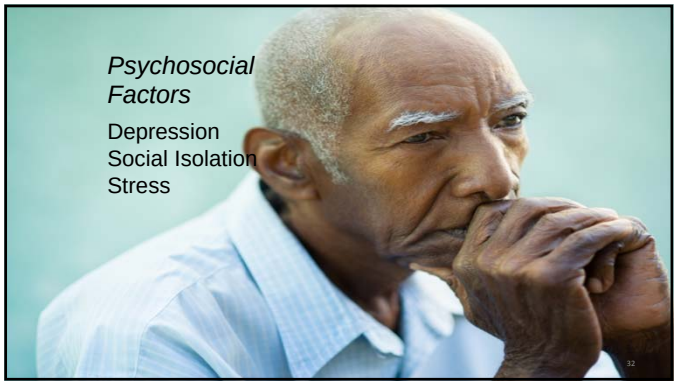

Future Directions

Stroke **pathophysiology**
Stroke **prevention** strategies
Stroke **preparedness** strategies
Planning sex and gender-specific research

A 36 year-old woman with a history of tobacco use, obesity, anxiety, and hypertension presents with severe headaches, right sided facial numbness, right arm numbness, and right arm weakness. Her NIHSS score is 4. As you consider stroke as a possible cause of this patient's symptoms.

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Which of the following is *not* true?

- You should ask this patient about a history of pregnancy complications including pre-eclampsia.
- Another pertinent historical factor that will change this patient's stroke risk is the use of oral contraceptives.
- If this patient has a history of migraines with aura, her risk of ischemic stroke is also elevated.
- There may be significant overlap between the symptoms of stroke and the symptoms of atypical migraine.
- You should not consider tPA in this patient as this is likely a stroke mimic, and giving tPA has a high likelihood of leading to symptomatic intracerebral hemorrhage.

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Based on known sex and gender differences in stroke, what steps could be taken to optimize outcomes for stroke patients?

- When caring for women who are at risk for stroke or have had a stroke, providers should take into account sex and gender specific risk factors.
- Providers working in the acute care setting should be aware of potential treatment disparities in the use of IV tPA.
- Stroke should be on the differential of patients with pain, altered mental status, and other "atypical" symptoms.
- Following stroke, psychosocial factors including depression and social isolation should be considered and addressed to improve outcomes.
- All of the above.

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