



UC Irvine Health



American Heart Association
American Stroke Association
CERTIFICATION
Meets standards for
Comprehensive Stroke Center

Comprehensive Stroke and Cerebrovascular Center

Women and Stroke



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- Level 1 Trauma Center
- Comprehensive Stroke Center by JCM/Provides Telestroke
- HF Certification JCM
- Regional Burn Center
- Magnet



UC Irvine Health

Disclosures:

NONE



Women and Stroke Statistics



- Stroke is the third leading cause of death for women (stroke is the fifth leading cause of death for men).
- ✓ Because in general women live longer than men, stroke will have a more negative impact on their lives.
- By 2030, there will be an estimated 72 million people >65 years old (19% of the population), and women will increasingly outnumber men.
- More likely to live in a long term health care facility after a stroke.
- Have a worse recovery after stroke.



Is There Gender Bias in Stroke Care?

- Male stroke patients are more than twice as likely as female patients to receive tissue plasminogen activator treatment within 30 minutes of hospital arrival.
- Men were 2.2 times more likely than women to get ultrafast treatment; patients arriving by ambulance were 4.7 times more likely to get the fast treatment than stroke patients driven to the hospital; and weekday arrivals were nearly twice as likely as those arriving during the evening or weekends to get ultrafast treatment.

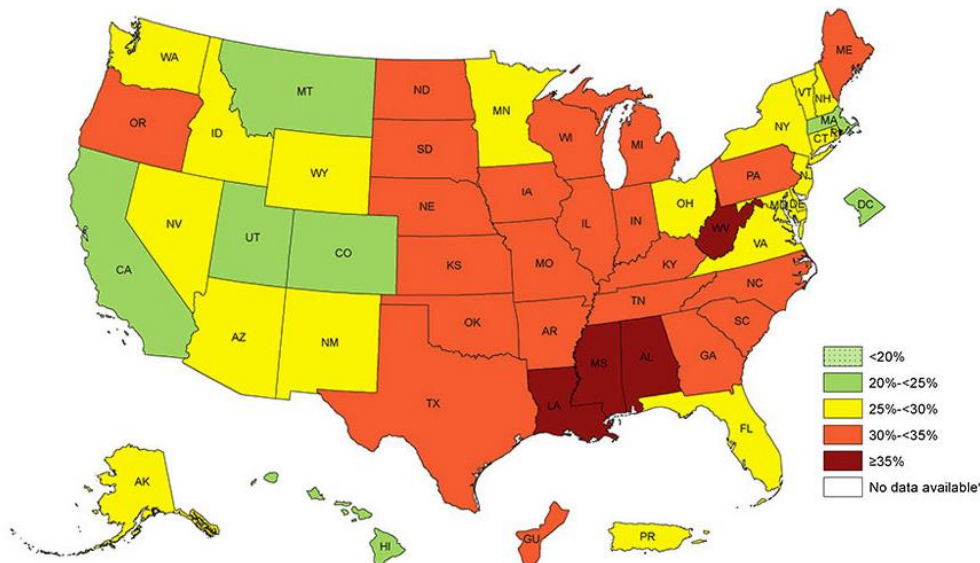


The Ugly Truth

- In the United States, ≈ 1 in 3 individuals is obese. The prevalence of obesity is higher in women than men and is expected to increase over time in both sexes.
- Prospective studies have shown that obesity, abdominal adiposity, and metabolic syndrome are independent risk factors for stroke in both men and women. - Further research is needed to determine whether sex modifies the impact of these conditions on stroke risk and outcomes.

Prevalence[†] of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2015

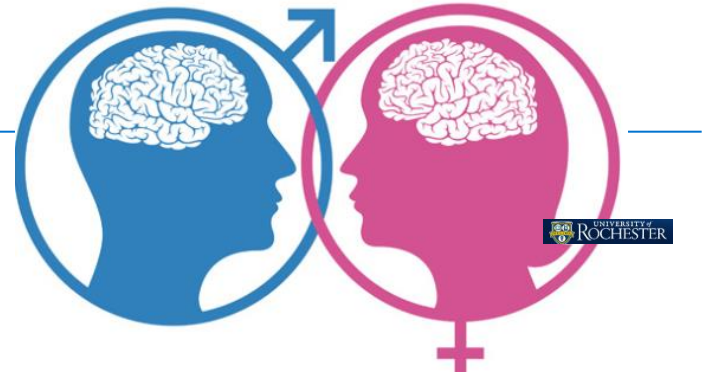
[†]Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.



My Fairy Godmother



Women Differ from Men



- Genetic differences in immunity
- Coagulation
- Hormonal factors
- Reproductive factors including pregnancy and childbirth
- Social factors

SIZE OF TREATMENT EFFECT

ESTIMATE OF CERTAINTY (PRECISION) OF TREATMENT EFFECT

	<p>CLASS I <i>Benefit >>> Risk</i> Procedure/Treatment SHOULD be performed/administered</p>	<p>CLASS IIa <i>Benefit >> Risk</i> <i>Additional studies with focused objectives needed</i> IT IS REASONABLE to perform procedure/administer treatment</p>	<p>CLASS IIb <i>Benefit ≥ Risk</i> <i>Additional studies with broad objectives needed; additional registry data would be helpful</i> Procedure/Treatment MAY BE CONSIDERED</p>	<p>CLASS III No Benefit or CLASS III Harm</p> <table border="1"> <thead> <tr> <th></th> <th>Procedure/Test</th> <th>Treatment</th> </tr> </thead> <tbody> <tr> <td>COR III: No benefit</td> <td>Not Helpful</td> <td>No Proven Benefit</td> </tr> <tr> <td>COR III: Harm</td> <td>Excess Cost w/o Benefit or Harmful</td> <td>Harmful to Patients or Harmful</td> </tr> </tbody> </table>		Procedure/Test	Treatment	COR III: No benefit	Not Helpful	No Proven Benefit	COR III: Harm	Excess Cost w/o Benefit or Harmful	Harmful to Patients or Harmful
	Procedure/Test	Treatment											
COR III: No benefit	Not Helpful	No Proven Benefit											
COR III: Harm	Excess Cost w/o Benefit or Harmful	Harmful to Patients or Harmful											
<p>LEVEL A Multiple populations evaluated* Data derived from multiple randomized clinical trials or meta-analyses</p>	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Sufficient evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from multiple randomized trials or meta-analyses 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Sufficient evidence from multiple randomized trials or meta-analyses 									
<p>LEVEL B Limited populations evaluated* Data derived from a single randomized trial or nonrandomized studies</p>	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Some conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Greater conflicting evidence from single randomized trial or nonrandomized studies 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Evidence from single randomized trial or nonrandomized studies 									
<p>LEVEL C Very limited populations evaluated* Only consensus opinion of experts, case studies, or standard of care</p>	<ul style="list-style-type: none"> Recommendation that procedure or treatment is useful/effective Only expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation in favor of treatment or procedure being useful/effective Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation's usefulness/efficacy less well established Only diverging expert opinion, case studies, or standard of care 	<ul style="list-style-type: none"> Recommendation that procedure or treatment is not useful/effective and may be harmful Only expert opinion, case studies, or standard of care 									
Suggested phrases for writing recommendations	should is recommended is indicated is useful/effective/beneficial	is reasonable can be useful/effective/beneficial is probably recommended or indicated	may/might be considered may/might be reasonable usefulness/effectiveness is unknown/unclear/uncertain or not well established	COR III: No Benefit is not recommended is not indicated should not be performed/administered/ other	COR III: Harm potentially harmful causes harm associated with excess morbidity/mortality should not be								
Comparative effectiveness phrases*	treatment/strategy A is recommended/indicated in	treatment/strategy A is probably recommended/indicated in											

Critical to Identify Women at Higher Risk for Stroke - Pregnancy

- ~ 3 out of 10,000 pregnant women have a stroke during pregnancy.
- The physiological changes of pregnancy, specifically venous stasis, edema, and hypercoagulability caused by activated protein C resistance, lower levels of protein S, and increased fibrinogen, combine to make pregnancy and the postpartum period a time of increased risk for stroke.
- Pregnancy-related hypertension is the leading cause of both hemorrhagic stroke and IS in pregnant and postpartum women.
- Complications of pregnancy (preeclampsia, gestational diabetes, and pregnancy-induced hypertension) are associated with higher risk for future CVD and stroke beyond the childbearing years than among women without these disorder.
- **2016 ISC:** Pregnancy in older age increases stroke, heart attack risk years later . Pregnancy at age 40 and older increased IS from 2.4 % to 3.8%, hemorrhagic stroke 05.% to 1 %.

Preeclampsia and Pregnancy Recommendations

1. Women with chronic primary or secondary hypertension or previous pregnancy-related hypertension should take low-dose aspirin from the 12th week of gestation until delivery (Class I; Level of Evidence A).
2. Calcium supplementation (of ≥ 1 g/d, orally) should be considered for women with low dietary intake of calcium (<600 mg/d) to prevent preeclampsia (Class I; Level of Evidence A).
3. Severe hypertension in pregnancy should be treated with safe and effective antihypertensive medications, such as methyldopa, labetalol, and nifedipine, with consideration of maternal and fetal side effects (Class I; Level of Evidence A).

Women and Stroke Risk Factors- Oral Contraceptives (OC)

- The risk of stroke is very low in the age group of women who use contraception, but the incidence rises steeply from 3.4 per 100 000 at ages 15 to 19 years to 64.4 per 100 000 in women aged 45 to 49 years.
- Despite the overall low risk of stroke from hormonal contraception, certain subgroups of women, particularly those who are older, smoke cigarettes, or have hypertension, diabetes mellitus, obesity, hypercholesterolemia, or prothrombotic mutations, may be at higher risk for stroke.



OCs Recommendations

1. OCs may be harmful in women with additional risk factors (eg, cigarette smoking, prior thromboembolic events) (Class III; Level of Evidence B).
2. Among OC users, aggressive therapy of stroke risk factors may be reasonable (Class IIb; Level of Evidence C).
3. Routine screening for prothrombotic mutations before initiation of hormonal contraception is not useful (Class III; Level of Evidence A).
4. Measurement of BP before initiation of hormonal contraception is recommended (Class I; Level of Evidence B).

Menopause and Postmenopausal Hormone Therapy

- Results of existing studies of the association between age at menopause or premature or early menopause, whether natural or surgical, and stroke risk appear to suggest increased risk of stroke with earlier onset of menopause, *although the evidence is not entirely consistent*.
- The effects of HRT on stroke may be dose-related and so the lowest effective dose should be prescribed in women who have significant risk factors for stroke.
- Further research is needed to better understand the subgroups of women who may be at risk for stroke associated with HT and to optimize the timing and route of administration, as well as the dose and type of hormone used.
- **2016 ISC:** Women on hormone replacement therapy (HRT) who experience an increase in migraine severity of one grade or more are at increased risk for ischemic stroke- Researchers suggest women with a history of migraines should talk to their doctor about the benefits and risks of hormone replacement, and if they begin hormone replacement, they should monitor migraine severity.-- Rahman HA, Malik A, Saeed O, et al. Abstract WMP 57. Worsening Migraines in Current Hormone Replacement Therapy Users Predicts Higher Risk of Stroke. Presented at: International Stroke Conference; Feb. 16-19, 2016; Los Angeles.

Postmenopausal HT Recommendations

1. HT (conjugated equine estrogen (CEE) with or without medroxyprogesterone) should not be used for primary or secondary prevention of stroke in postmenopausal women (Class III; Level of Evidence A).
2. Selective estrogen receptor modulators, such as raloxifene, tamoxifen, or tibolone, should not be used for primary prevention of stroke (Class III; Level of Evidence A).

Women and Stroke Risk Factors –Atrial fibrillation

- AF is the most common arrhythmia and a major modifiable risk factor for stroke.
 - ✓ The overall number of men and women with AF is similar, but ≈60% of AF patients aged >75 years are women.

- AF increases 4- to 5-fold the risk of IS and is associated with higher death and disability.

- Risk stratification tools, such as the CHADS2 and CHA2 DS2 -VASc scores, are useful in guiding the decision making for anticoagulation therapy.

CHADS ₂		CHA ₂ DS ₂ -VASc	
Risk factors	Points	Risk factors	Points
<u>CHF</u>	1	<u>CHF/LVEF ≤ 40%</u>	1
<u>HTN</u>	1	<u>HTN</u>	1
<u>Age ≥ 75</u>	1	<u>Age ≥ 75</u>	2
<u>DM</u>	1	<u>DM</u>	1
<u>Stroke/TIA/embolism</u>	2	<u>Stroke/TIA/embolism</u>	2
	Max 6	<u>Vascular disease (prior MI, PAD, or aortic plaque)</u>	1
		<u>Age 65-74 years</u>	1
		<u>Sex category (Female)</u>	1
			Max 9



AF Recommendations

1. Risk stratification tools in AF that account for age and sex-specific differences in the incidence of stroke are recommended (Class I; Level of Evidence A).
2. Considering the increased prevalence of AF with age and the higher risk of stroke in elderly women with AF, active screening (in particular of women >75 years of age) in primary care settings using pulse taking followed by an ECG as appropriate is recommended (Class I; Level of Evidence B).
3. Oral anticoagulation in women aged ≤ 65 years with AF alone (no other risk factors) is not recommended (Class III; Level of Evidence B). Antiplatelet therapy is a reasonable therapeutic option for selected low-risk women (Class IIa; Level of Evidence B).
4. New oral anticoagulants are a useful alternative to warfarin for the prevention of stroke and systemic thromboembolism in women with paroxysmal or permanent AF and prespecified risk factors (who do not have a prosthetic heart valve or hemodynamically significant valve disease, severe renal failure)



Migraine with Aura



➤ The prevalence of migraine in the population is $\approx 18.5\%$, and for migraine with aura, it is 4.4% .--Women are 4 times more likely to have migraines than men

➤ Migraine with aura is characterized by homonymous hemianopia, weakness, numbness, or tingling of the face, arm, or leg

➤ The association between migraine with aura and stroke is more well established

➤ 2016 ISCO defines migraine with aura as a unilateral, fully formed, and twice as common



presence of unilateral homonymous hemianopia that fully precedes the onset of the headache

men. In women, the risk of stroke increases

have migraine with aura, the risk of ischemic stroke is significantly increased

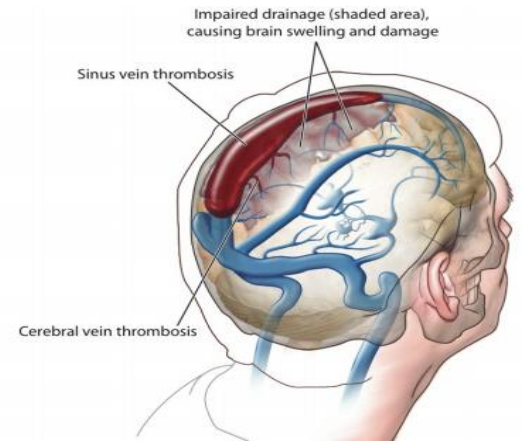
D. Stradling | November 2016 Androulakis XM, Rosamond W, Yim E, et al. Poster T P179. Ischemic Stroke Subtypes and Relationship with Migraine in the Atherosclerosis Risk In Communities Study. Presented at: International Stroke Conference; Feb. 16-19, 2017

Migraine With Aura: Recommendations

1. Because there is an association between higher migraine frequency and stroke risk, treatments to reduce migraine frequency might be reasonable, although evidence is lacking that this treatment reduces the risk of first stroke (Class IIb; Level of Evidence C).
2. Because of the increased stroke risk seen in women with migraine headaches with aura and smoking, it is reasonable to strongly recommend smoking cessation in women with migraine headaches with aura (Class IIa; Level of Evidence B).



Cerebral Venous Thrombosis



- CVT is a stroke type that is caused by thrombus formation in ≥ 1 of the venous sinuses and manifests primarily as headache.
- CVT makes up 0.5% to 1% of all strokes but is the stroke type that shows the most prominent differential sex prevalence.
- In adulthood, the majority of affected individuals are women, who represent >70% of cases in most studies.
- Female predominance of CVT has been attributed to hormonal factors (primarily oral contraceptive and pregnancy).
- The use of OCs is associated with an increased risk of CVT, a risk that is increased significantly in women with an underlying hereditary prothrombotic factor, such as factor V Leiden or prothrombin gene mutation.

CVT Recommendations

1. In patients with suspected CVT, routine blood studies consisting of a complete blood count, chemistry panel, prothrombin time, and activated partial thromboplastin time should be performed (Class I; Level of Evidence C).
2. Screening for potential prothrombotic conditions that may predispose a person to CVT (eg, use of contraceptives, underlying inflammatory disease, infectious process) is recommended in the initial clinical assessment (Class I; Level of Evidence C).



Depression and Psychosocial Stress



- In a 12-year Australian study of 10,547 women 47-52 years researchers found that depressed women had a 2.4 times increased risk of stroke compared to those who weren't depressed.
- Even after researchers eliminated several factors that increases stroke risk, depressed women were still 1.9 times more likely to have a stroke.
- More research is needed to understand the mechanisms underlying the association between depression and stroke, as well as to determine which women with depression may be at risk, such as those who are treated versus untreated, and whether self-reported measures are the most accurate to determine stroke risk.

The Take Away

Stroke RISK GOES UP due to ...



PREGNANCY

About 3 out of 10,000 pregnant women have a stroke during pregnancy compared to 2 out of 10,000 young women who are not pregnant.

+



PREECLAMPSIA

This is a term for high blood pressure that develops during pregnancy, and it doubles the risk of stroke later in life.



BIRTH CONTROL PILLS

May double the risk of stroke, especially in women with high blood pressure.



HORMONE REPLACEMENT THERAPY

Once thought to lower stroke risk, this in fact increases the risk.



MIGRAINES WITH AURA + SMOKING

Strokes are more common in women with migraines with aura who also smoke.



ATRIAL FIBRILLATION

Quadruples stroke risk and is more common in women than men after age 75.

LOWER YOUR RISK for stroke by...

Pregnant women with very high blood pressure should be treated with safe blood pressure medications.

Talk to your healthcare provider about whether you should follow the guideline recommendation of low-dose aspirin starting in the second trimester (week 12) to lower preeclampsia risk.

Women should be screened for high blood pressure before taking birth control pills. Women should not smoke, and they should also be aware that smoking and the use of oral contraceptives increases the risk of stroke.

Hormone replacement therapy should not be used to prevent stroke in postmenopausal women.

Smokers who have migraines with aura should quit to avoid higher stroke risk.

All women over age 75 should be screened for atrial fibrillation.

Stroke Signs and Symptoms

01 Sudden confusion, trouble speaking or understanding speech.

02 Sudden numbness or weakness of face, arm or leg. Especially on one side of the body.

03 Sudden trouble seeing in one or Both eyes.

04 Sudden trouble walking, dizziness, loss of balance or coordination.

05 Sudden severe headache with no known cause.

If someone shows any of these symptoms, call 9-1-1 or emergency medical services immediately.

SPOT A STROKE

F FACE DROOPING

A ARM WEAKNESS

S SPEECH DIFFICULTY

T TIME TO CALL 911

Stroke Warning Signs and Symptoms

The graphic features a dark blue background with the title 'SPOT A STROKE' in large white letters. Below the title are four panels, each with a red letter in a white box: 'F' (Face Drooping) showing a woman's face, 'A' (Arm Weakness) showing a man's arm, 'S' (Speech Difficulty) showing a man's mouth, and 'T' (Time to Call 911) showing hands holding a mobile phone. At the bottom, the text 'Stroke Warning Signs and Symptoms' is written in white.

My mom, a stroke survivor



Thank you!

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Questions?



UC Irvine Health