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Outline

- ◇ Epidemiology of stroke in select age groups
- ◇ Identify impact of age on stroke care in the US
- ◇ Discuss current challenges in stroke management in select age groups

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Question 1:

- ◇ Which of the following groups has the highest incidence of stroke?
 - A. Age 18-49
 - B. Age 50-70
 - C. Age 70-89
 - D. Age 90+

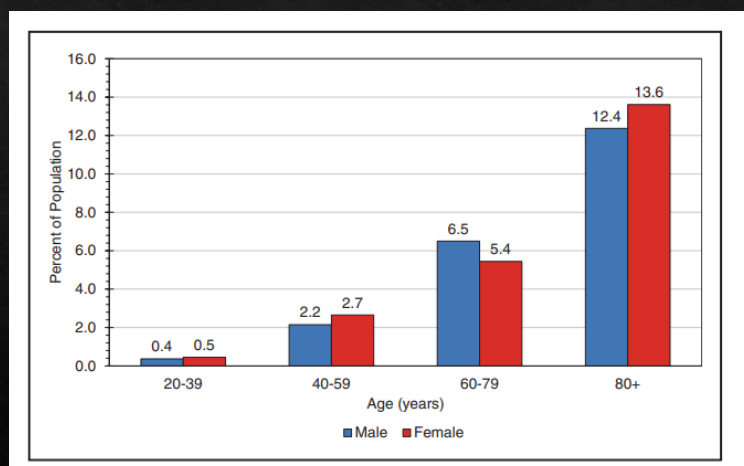
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Question 2:

- ◆ Which of the following is currently the fastest growing segment of the population?
- A. Age 18-49
 - B. Age 50-70
 - C. Age 70-89
 - D. Age 90+

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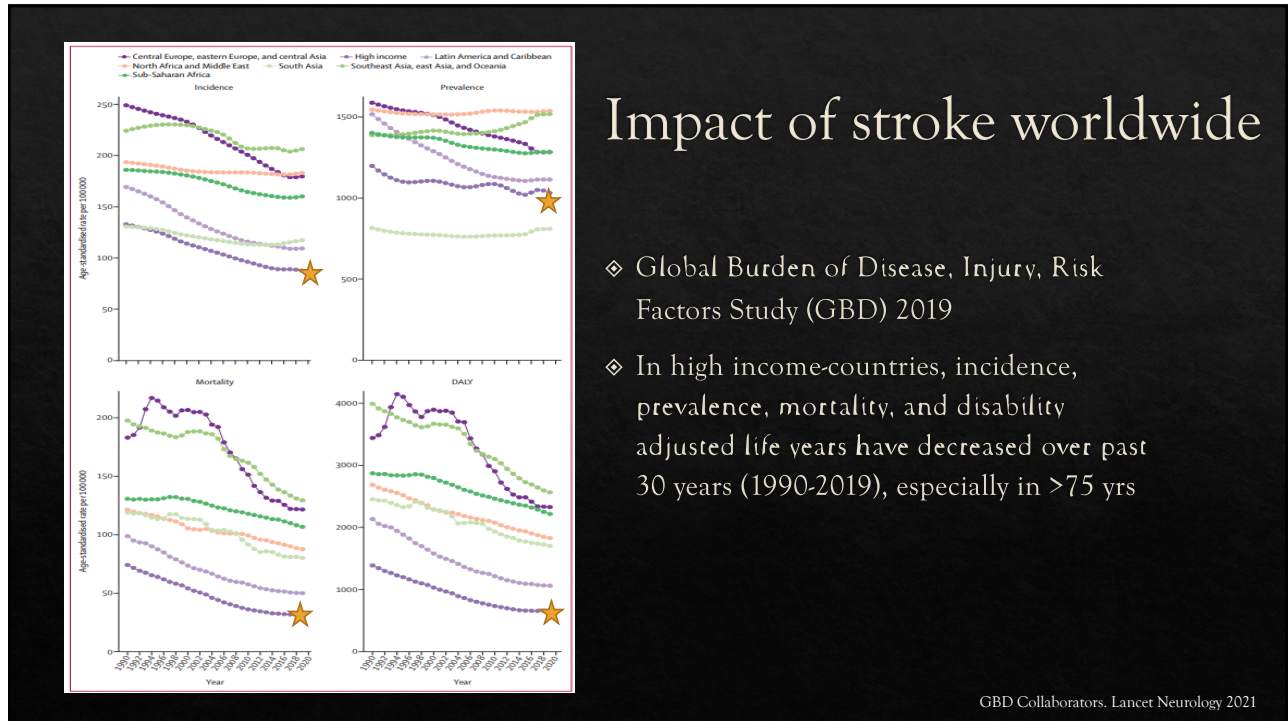
Stroke in the U.S.



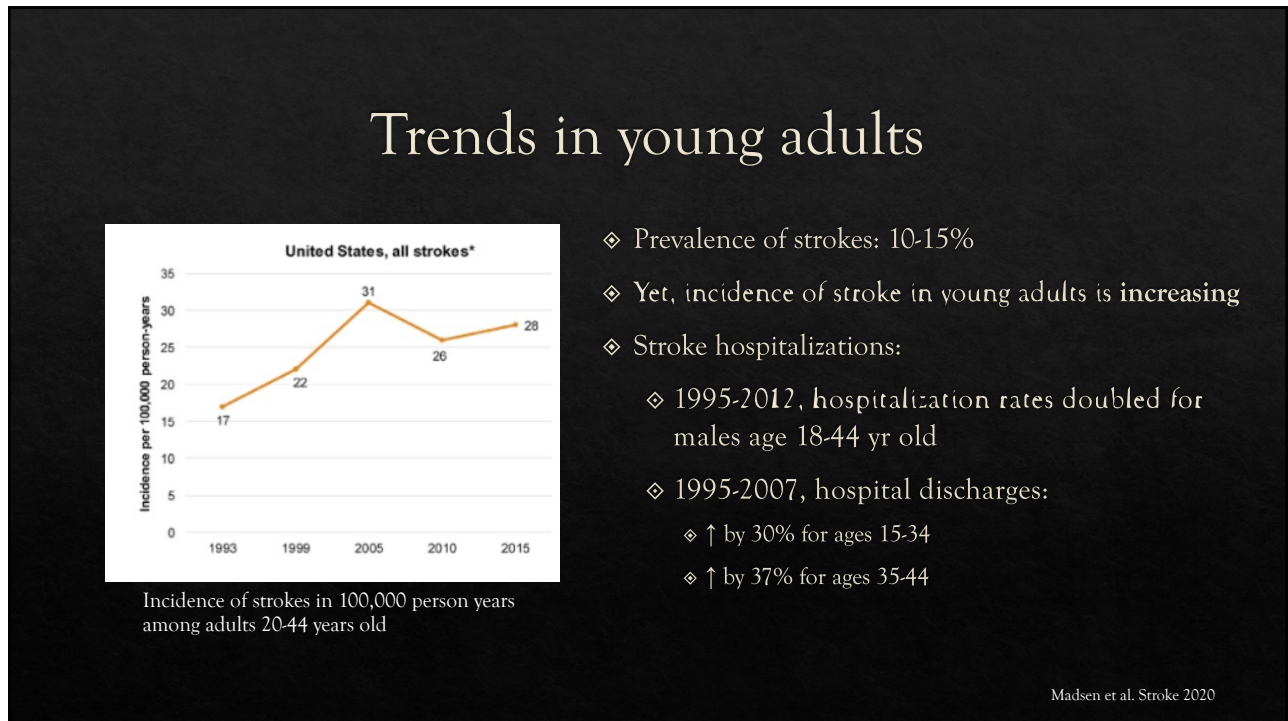
Prevalence of stroke by age and sex from National Health and Nutrition Examination Survey: 2015-2018 (NHANES)

Tsao et al. Circulation. 2022

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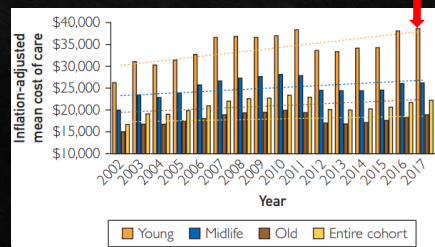
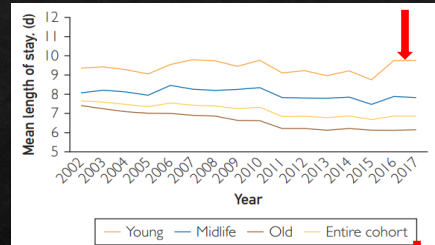
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Challenges with strokes in young adults

- ◆ Total # of years young adults live with disability due to stroke >> elderly patients
- ◆ More likely to be misdiagnosed:
 - ◆ Compared to patients >75 yrs old, young patients have a **7x increase** in being misdiagnosed on initial presentation
 - ◆ In study of 2200 acute stroke patients, younger age was predictor of missed diagnosis
- ◆ Longest hospitalizations and highest cost of stays
 - ◆ US hospitalizations between 2002-2017
 - ◆ 18 - 44 yrs > 45-64 > 65+



Newman-Toker DE. Diagnosis 2014

Khan et al. Mayo Clinic Proc Innov Qual Outcome. 2021.

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Prognosis in young adults

- ◆ Stroke recurrence at 5 yrs: up to 9%
- ◆ FUTURE study:
 - ◆ 722 patients age 18-50 with 1st ever ischemic stroke, intracerebral hemorrhage or TIA (1980-2010) in Netherlands, follow up at 9.1 years (mean)
 - ◆ Poor outcome (mRS >2)
 - ◆ 36.5% in ischemic stroke
 - ◆ 49.3% in intracerebral hemorrhage
 - ◆ Dependent (iADL scale <8)
 - ◆ 14.6% in ischemic stroke
 - ◆ 18.2% intracerebral hemorrhage

mRS 0 No symptoms

mRS 1 Nonsignificant disability

mRS 2 Slight disability

mRS 3 Moderate disability

mRS 4 Moderately severe disability

mRS 5 Severe disability

mRS 6 Dead

A. Ability to Use Telephone

- Operate telephone on own initiative; looks up and dials numbers.....1
- Dials a few well-known numbers.....1
- Answers telephone, but does not dial.....1
- Does not use telephone at all.....0

B. Shopping

- Takes care of all shopping needs independently.....1
- Shops independently for small purchases.....0
- Needs to be accompanied on any shopping trip.....0
- Completely unable to shop.....0

C. Food Preparation

- Plans, prepares, and serves adequate meals independently.....1
- Prepares adequate meals if supplied with ingredients.....0
- Heats and serves prepared meals or prepares meals but does not maintain adequate diet.....0
- Needs to have meals prepared and served.....0

D. Housekeeping

- Maintains home alone with occasional assistance (heavy work).....1
- Performs light daily tasks such as dishwashing, bed making.....1
- Performs light daily tasks, but cannot maintain acceptable level of cleanliness.....1
- Needs help with all home maintenance tasks.....1
- Does not participate in any housekeeping tasks.....0

E. Laundry

- Does personal laundry completely.....1
- Launders small items, rines socks, stockings, etc.....1
- All laundry must be done by others.....0

F. Mode of Transportation

- Travels independently on public transportation or drives own car.....1
- Arranges own travel into taxi, but does not otherwise use public transportation.....1
- Travels on public transportation when assisted or accompanied by another.....1
- Travel limited to taxi or automobile with assistance of another.....0
- Does not travel at all.....0

G. Responsibility for Own Medications

- Is responsible for taking medication in correct dosage at correct time.....1
- Takes responsibility if medication is prepared in advance to separate dosages.....1
- Is not capable of dispensing own medication.....0

H. Ability to Handle Finances

- Manages financial matters independently (budgets, writes checks, pays rent and bills, goes to bank); collects and keeps track of income.....1
- Manages day-to-day purchases, but needs help with banking, major purchases, etc.....1
- Incapable of handling money.....0

Scoring: For each category, circle the item description that most closely resembles the client's highest functional level (either 0 or 1).

Putaalaa et al. Ann Neurol. 2010, Synhaeve et al. Stroke 2014

Saver J. Stroke 2021

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Quality of life after stroke

- ◇ European study of 232 pts <50 yrs old, btw 1988-1997:
 - ◇ At 12 yrs follow up, 40% returned to full-time job
 - ◇ High rates of memory impairment, depression, anxiety, sleep disorders
 - ◇ Higher rates of sexual dysfunction, cognitive impairment

Waje-Andreassen et al. Eur. J. Neurol 2013

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Causes of stroke in young adults

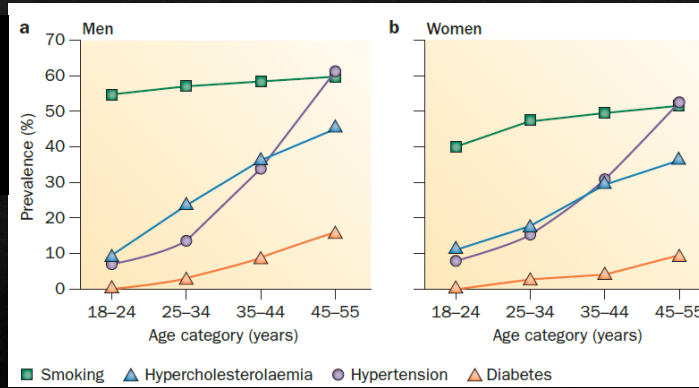
- ◇ Diverse causes
- ◇ Helsinki registry: cohort of 1008 patients with first ever ischemic stroke (15-49 yrs):
 - ◇ Cardioembolism 20%
 - ◇ Cervical arterial dissection 15%
 - ◇ Small vessel disease 14%
 - ◇ Large artery atherosclerosis 8%



Putala. Stroke 2009.

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Increasing role of traditional risk factors



Prevalence of vascular risk factors among men and women with acute ischemic stroke

Maaijwee et al. Nature 2014

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Increasing role of traditional risk factors

Prevalence of risk factors among patients hospitalized with acute ischemic stroke by age and sex.

	HTN	HLD	Diabetes	Tobacco	Obesity	AF	IHD
Males							
18-34 YO							
2003-04	34.0%	14.6%	15.3%	23.1%	6.8%	2.1%	6.4%
2011-12	41.1%*	29.1%*	15.2%	35.7%*	13.3%*	2.9%	5.5%
35-44 YO							
2003-04	54%	29.0%	24.3%	31.3%	7.7%	3.2%	11.1%
2011-12	65.9%*	47.8%*	30.3%*	41.7%*	15.2%*	4.3%	11.2%
Females							
18-34 YO							
2003-04	26.1%	9.6%	11.8%	21.1%	9.1%	1.7%	2.1%
2011-12	30.7%*	21.7%*	15.5%*	26.5%*	15.7%*	1.8%	3.9%
35-44 YO							
2003-04	50.1%	20.8%	24.2%	26.9%	10.9%	1.2%	7.3%
2011-12	57.3%*	37.8%*	31.4%*	35.8%*	21.0%*	2.3%*	7.2%*

National inpatient sample of young adults (18-44) hospitalized with ischemic stroke

The increased incidence in stroke among the young is most likely due to rise in these traditional risk factors

George et al. JAMA Neurology 2017

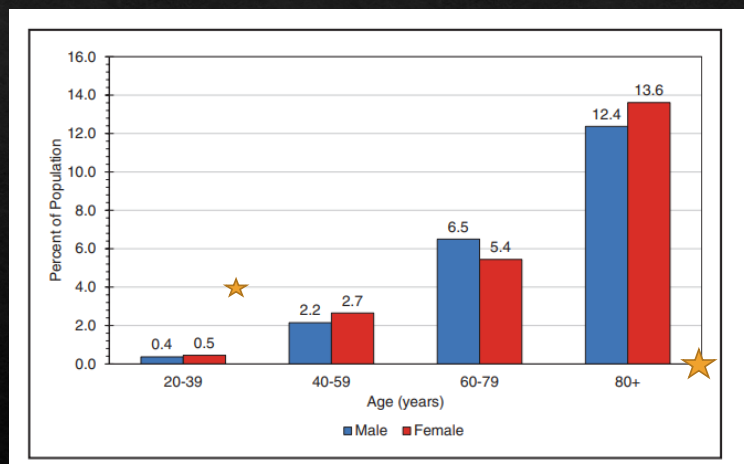
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Switching gears



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Stroke in the U.S.



Prevalence of stroke by age and sex from National Health and Nutrition Examination Survey: 2015-2018 (NHANES)

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The oldest of the old

- ◇ Life expectancy is increasing
- ◇ More people ≥ 90 years old will be affected by ischemic stroke
 - ◇ Number of nonagenarians worldwide
 - ◇ 1995: 6 million
 - ◇ 2010: 12 million
 - ◇ **2050: 71 million projected**
 - ◇ Nonagenarians are the fastest growing group of our population

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Who are the nonagenarians?



The oldest old = the weakest of the weak?
Most dependent?
Highest mortality?

Is this accurate?

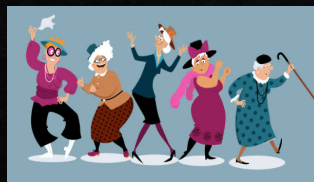
Studies of the nonagenarians:

- Majority are women, live in their own homes
- ~ 50% are independent and require little or no assistance in their daily activities

Currently, in the USA, a 90 yr old person is expected to live another 5 years

Most people 90+ yrs old rated their health as equal/better than 5 years earlier

A special group, those who have succeeded at aging?



Odden MC Am J Epidemiol 2019, Hogan, Fung Elby 1999, Bury and Holme 1991, Strauss EV. J Am Geriatr Soc 2000.

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Stroke care in nonagenarians

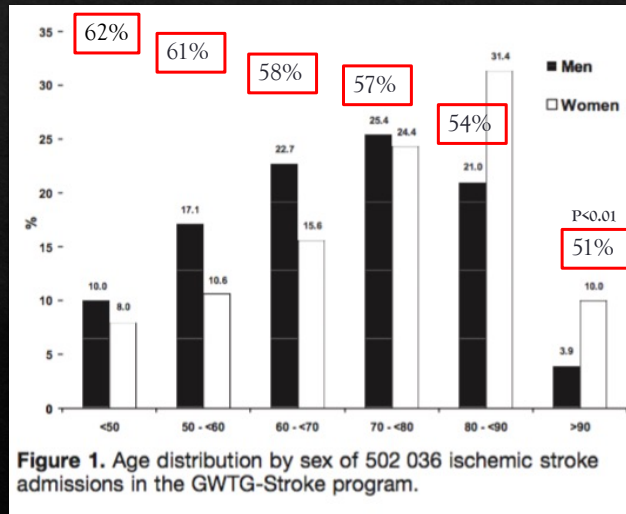
- ◇ Guidelines for acute stroke care for nonagenarians is limited as they were excluded from trials
- ◇ Data suggests acute and chronic treatment of stroke is underused in nonagenarians
 - ◇ IV Alteplase (tPA)
 - ◇ Mechanical thrombectomy
 - ◇ Anticoagulation

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IV-tPA in the elderly

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IV-tPA in the elderly

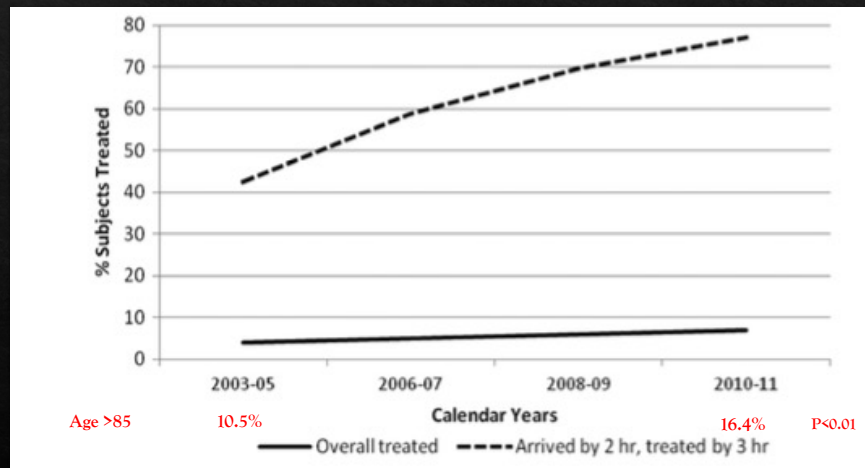


Proportion of eligible patients who received tPA decreases with age, and is lowest in >90 group

Fonarow GC et al. Circulation. 2010

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IV-tPA in the elderly



P<0.01

22

Mechanical thrombectomy in nonagenarians

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Guidelines for mechanical thrombectomy in acute stroke care

3.7. Mechanical Thrombectomy (Continued)	COR	LOE
<p>3. Patients should receive mechanical thrombectomy with a stent retriever if they meet all the following criteria: (1) prestroke mRS score of 0 to 1; (2) causative occlusion of the internal carotid artery or MCA segment 1 (M1); (3) age ≥18 years; (4) NIHSS score of ≥6; (5) ASPECTS of ≥6; and (6) treatment can be initiated (groin puncture) within 6 hours of symptom onset.</p>	I	A

Results from 6 recent randomized trials of mechanical thrombectomy using predominantly stent retriever devices (MR CLEAN, SWIFT PRIME, EXTEND-IA, ESCAPE, REVASCAT, THRACE) support Class I, LOE A recommendations for a defined group of patients as described in the 2015 guidelines.¹⁰²⁻¹⁰⁷ A pooled, patient-level analysis from 5 of these studies reported by the HERMES collaboration showed treatment effect in the subgroup of 188 patients not treated with IV alteplase (cOR, 2.43; 95% CI, 1.30–4.55); therefore, pretreatment with IV alteplase has been removed from the prior recommendation. The HERMES pooled patient-level data also showed that mechanical thrombectomy had a favorable effect over standard care in patients ≥80 years old (cOR, 3.68; 95% CI, 1.95–6.92).¹⁷² In patient-level data pooled from trials in which the Solitaire was the only or the predominant device used, a prespecified meta-analysis (SEER Collaboration [Safety and Efficacy of Solitaire Stent Thrombectomy–Individual Patient Data Meta-Analysis of Randomized Trials]: SWIFT PRIME, ESCAPE, EXTEND-IA, REVASCAT) showed that mechanical thrombectomy had a favorable effect over standard care in patients ≥80 years old (3.46; 95% CI, 1.58–7.60).¹⁷³ In a meta-analysis of 5 RCTs (MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME, REVASCAT), there was favorable effect with mechanical thrombectomy over standard care without heterogeneity of effect across patient age subgroups (for patient age <70 and ≥70 years: OR, 2.41; 95% CI, 1.51–3.84; and OR, 2.26; 95% CI, 1.20–4.26, respectively).¹⁷⁴ However, the number of patients in these trials who were ≥90 years of age was very small, and the benefit of mechanical thrombectomy over standard care in patients ≥90 years of age is not clear. As with any treatment decision in an elderly patient, consideration of comorbidities and risks should factor into the decision making for mechanical thrombectomy.

Nonagenarians are underrepresented

Table 1 Age as inclusion criterion in past mechanical thrombectomy landmark studies¹

Clinical trials	Sample size	Age as inclusion criterion	Age of enrolled patients
MR CLEAN	500	≥18	Mean 65 (range 23–96)
SWIFT PRIME	196	18–80	Mean 65 (SD 12.5)
EXTEND-IA	70	≥18	Mean 68.6 (SD 12.3; range 18–81)
ESCAPE	315	≥18	Median 71 (IQR 60–81)
REVASCAT	206	18–85	Mean 65.7 (SD 11.3)
THRACE	414	18–80	Median 68 (IQR 54–75)
ASTER	381	≥18	Mean 69.9 (SD 14.3)

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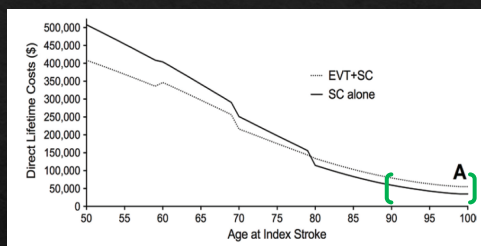
Cost-effectiveness of Endovascular Therapy for Acute Ischemic Stroke: A Systematic Review of the Impact of Patient Age

Wolfgang G. Kunz, MD • Myriam G. Humink, MD, PhD¹ • Konstantinos Dimitriadis, MD, MBA • Thomas Huber, MD • Franziska Dorn, MD • Felix G. Meinel, MD • Bastian O. Sabel, MD • Ahmed E. Othman, MD • Maximilian F. Reiser, MD • Birgit Ertl-Wagner, MD, MHBA • Wieland H. Sommer, MD, MPH • Kolja M. Thierfelder, MD, MSc

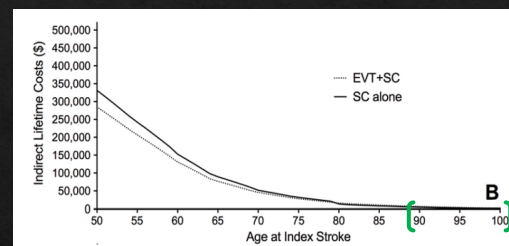
- ◆ Do benefits persist across all ages, even nonagenarians?
- ◆ 2018 cost-effective analysis of mechanical thrombectomy + std care vs. std care alone, in patients ages 50-100 based on MR CLEAN, ESCAPE, EXTEND-IA, SWIFT PRIME, REVASCAT
- ◆ Factored in direct and indirect costs, using US health care model

Kunz W. Radiology 2018

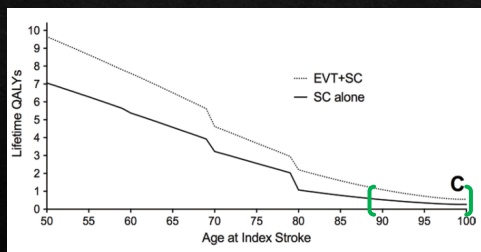
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Small difference in direct costs



No difference in indirect costs



Improved QALY persists across all ages

Mechanical thrombectomy is cost effective across all ages

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Nonagenarians vs 18-69 yr

- ◇ 9/2015-11/2018 at NYU
- ◇ Compared patients with acute stroke undergoing mechanical thrombectomy, 18-69 yr vs ≥90 yrs
- ◇ Included IV-alteplase
- ◇ 3010 stroke patients, 421 (14%) underwent MT

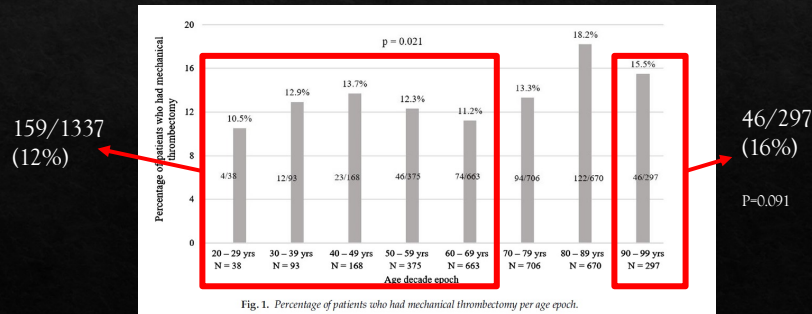


Fig. 1. Percentage of patients who had mechanical thrombectomy per age epoch.

Agarwal A. J Stroke and Cerebrovasc 2020

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Baseline characteristics

	Aged 90-99	Aged ≤69	P
N	39	39	-
DEMOGRAPHICS			
Age, years, median (IQR)	93 (4)	64 (7)	-
Gender, female, n (%)	27 (69.2%)	15 (38.5%)	0.006
Baseline mRS <4, n (%)	32 (82.1%)	34 (87.2%)	0.530
Race			
White, n (%)	24 (61.5%)	16 (41%)	0.069
Comorbidities			
Atrial Fibrillation, n (%)	21 (53.8%)	5 (12.8%)	≤0.001
Coronary Artery Disease, n (%)	7 (17.9%)	9 (23.1%)	0.575
Diabetes mellitus, n (%)	10 (25.6%)	13 (33.3%)	0.456
Hypertension, n (%)	32 (82.1%)	29 (74.4%)	0.411
Smoking, n (%)	0	5 (12.8%)	0.021
Hyperlipidemia, n (%)	10 (25.6%)	13 (33.3%)	0.456
Previous Stroke, n (%)	6 (15.4%)	7 (17.9%)	0.761

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Outcomes

	Aged 90–99 N=39	Aged ≤69 N=39	P
Procedural Outcomes			
Door to Groin puncture time, minutes, median (IQR)	82 (59)*	71 (55)**	0.715
Symptom onset to Reperfusion time, minutes, median (IQR)	569 (1007)¶	372 (384)¶¶	1.000
Groin puncture to Reperfusion time, minutes, median (IQR)	39 (24)¶	24 (25)¶¶	0.632
mTICI grade ≥2b, n (%)	35 (89.7%)	35 (89.7%)	1.000
Primary Outcomes			
Good Discharge Disposition, n (%)	17 (44%)	20 (51%)	0.496
Died during hospitalization, n (%)	4 (10%)	10 (26%)	0.077
Secondary Outcome			
Symptomatic ICH, n (%)	1 (2.6%)	4 (10.3%)	0.165

Good discharge disposition = home or acute rehab

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Conclusion

- ◇ In nonagenarians with good baseline functional status + favorable CT scans who underwent rapid, successful recanalization, there was **NO DIFFERENCE** in clinical outcome compared to matched younger cohort
- ◇ Nearly half were discharged home or to acute rehab
- ◇ Even with high NIHSS (med 22)
- ◇ No difference in tPA administration

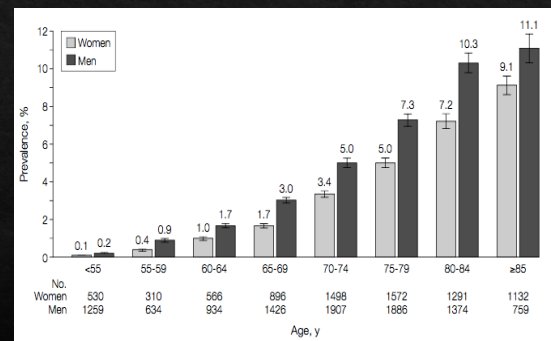
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Anticoagulation in the elderly

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Atrial fibrillation (AF)

- ◇ Nonvalvular AF increases risk of stroke by factor of 5
 - ◇ Cardioembolic strokes are *more severe*, carry higher mortality
- ◇ Prevalence of AF increases with age
 - ◇ Among very elderly afib is the single most important cause of stroke
- ◇ Extensive data prove warfarin and DOACS prevent stroke in AF

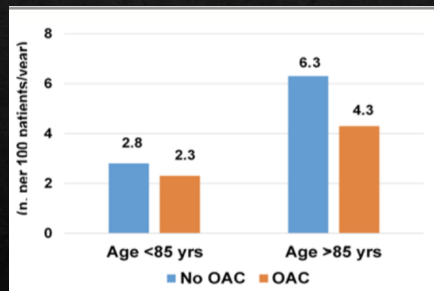


Hylek. NEJM. 2003. Hart. NEJM. 2003. Hart. Ann Int Med. 2007. Go et al. JAMA. 2001.

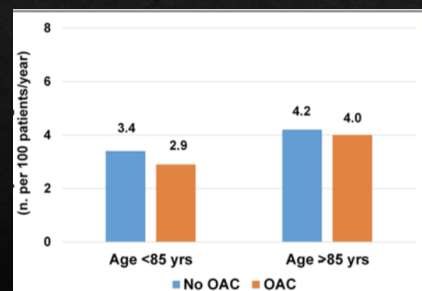
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Registry data

Thromboembolic events



Major bleeding events



Patti et al. JAHA. 2017

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Anticoagulation in the elderly

- ◇ Anticoagulation vastly underused in the elderly
 - ◇ <50% Rx rate for patients *in nursing homes*
 - ◇ Under use of OAC *in high risk AF in most studies from 1998-2008*
 - ◇ Over 2/3 of studies of AF patients with prior stroke, OAC < 60%
- ◇ Risk of fall is one of *most common reasons for withholding*
 - ◇ Estimate that a patient with AF needs to fall **295 times to warrant withholding warfarin**
 - ◇ ICH risk with NOACs is lower



Lip et al. Heart rhythm. 2018.

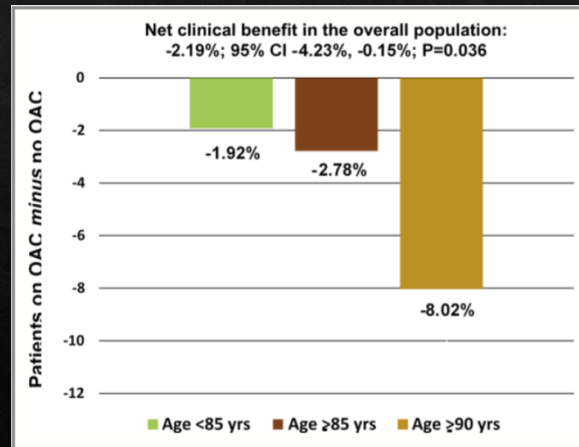
Man-Son-Hing et al. Arch Int Med. 1999.

Ogilvie et al. Am J med. 2010

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AF and anticoagulation in the elderly

- Net clinical benefit of anticoagulation actually *increases* with age due to greater magnitude of increasing ischemic stroke risk



Patti et al. JAHA. 2017

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Answer 1:

- Which of the following groups has the highest incidence of stroke?

- A. Age 18-49
- B. Age 50-70
- C. Age 70-89
- D. Age 90+

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Answer 2:

- ◆ Which of the following is currently the fastest growing segment of the population?
 - A. Age 18-49
 - B. Age 50-70
 - C. Age 70-89
 - D. Age 90+

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Take-away points

- ◆ Incidence of strokes in young adults (18-49) is on the rise
- ◆ This rise is likely due to increased prevalence of traditional vascular risk factors (obesity, hypertension, tobacco)
- ◆ Nonagenarians are the fastest growing segment of our population and their health may be better than expected
- ◆ Anticoagulation for atrial fibrillation after stroke may be underutilized in nonagenarians who stand to gain the most
- ◆ Treating nonagenarians with advanced therapeutics appears to be cost-effective

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