Secondary Prevention of Stroke in the Very Elderly Patient

Tony Rudd

Emeritus Professor Stroke, Kings College London

Former National Clinical Director for Stroke NHS England

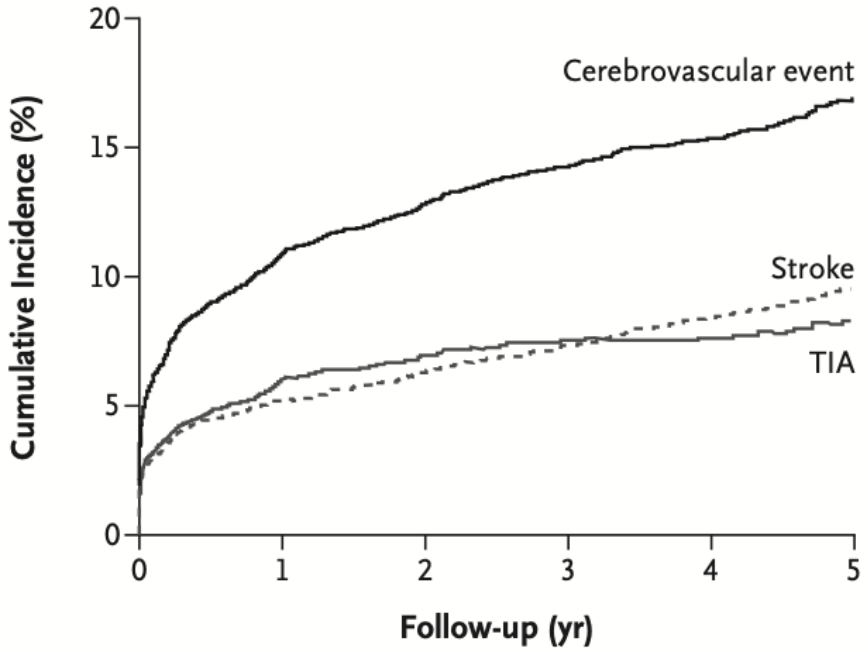
What are the issues?

- The older stroke patient group (over 80) is not homogenous. In fact very diverse - more so than the younger population
- Very little good epidemiological data on the patients in terms of risk factors, natural history stroke type and recurrence rates of different stroke types
- Many trials exclude older patients and especially those with significant comorbidities
- Estimation of benefit using relative benefit may be misleading - relative risk benefit may decline with age but absolute risks increase often leading to similar absolute benefits for old and young

What are the issues?

- Some treatments may take longer to show benefit than life expectancy e.g. statins, carotid endarterectomy
- Risks and side effects of treatment may increase with age and comorbities therefore shifting the balance of risk and benefit
- Issues of polypharmacy
- Lifestyle changes – exercise, dietary adjustments, cessation of smoking may be more difficult
- Importance of considering impact on all outcomes, not just stroke

B **Cerebrovascular Events, Stroke, and TIA**



No. of Patients						
Cerebrovascular event						
Alive and free of event	3847	3291	3028	2825	2664	2066
Event	0	410	481	533	570	621
Death from nonvascular causes	0	54	105	170	231	287
Stroke						
Alive and free of event	3847	3501	3254	3057	2889	2252
Event	0	196	235	271	309	345
Death from nonvascular causes	0	57	114	182	247	303
TIA						
Alive and free of event	3847	3451	3201	3022	2872	2240
Event	0	225	262	280	286	307
Death from nonvascular causes	0	73	138	210	283	350

Cumulative incidence of any cerebrovascular event over 5 years after stroke or TIA (all ages)

Registry of TIA clinics in 21 countries that enrolled 4789 patients with a TIA or minor ischemic stroke from 2009 to 2011. 30% have a cerebrovascular event by 5 years, of which about half TIA.

P. Amarenco et al Five-Year Risk of Stroke after TIA or Minor Ischemic Stroke N Engl J Med 2018;378:2182-90.

Is the risk of stroke recurrence greater in older patients?
Population-based stroke surveillance study that began in 1985; 15,438 residents living in a township in Tianjin, China,

TABLE 2 | Age-adjusted rates of recurrent stroke by subtypes [% (95% CI)].

Groups	Recurrence rate within 1 year	Recurrence rate within 5 years
SEX:		
Men	6.9 (5.1, 8.8)	24.0 (20.4, 27.6)
Women	4.6 (2.7, 6.5)	20.2 (16.0, 24.3)
Total	5.7 (4.4, 6.9)	22.5 (19.7, 25.2)
SUBTYPES OF FIRST-EVER STROKE:		
IS	6.2 (4.7, 7.8)	24.4 (21.2, 27.7)
ICH	6.1 (3.0, 9.2)	19.8 (14.1, 25.5)
Other	0	0
AGE GROUPS:		
<45 years	0	10.6 (1.5, 19.8)
45–64 years	4.9 (3.0, 6.8)	23.8 (19.4, 28.2)
≥65 years	7.4 (5.3, 9.4)	22.6 (18.9, 26.4)

In this cohort recurrence rates greater in those over 65 years

Han J, Mao W, Ni J, et al. Rate and Determinants of Recurrence at 1 Year and 5 Years After Stroke in a Low-Income Population in Rural China. *Front Neurol*. 2020;11:2

Prevalence of modifiable risk factors in stroke patients under 75 years and 75 years and older (Diabetic Chinese population)

Previous history of diseases and risk factors	Younger group	Elderly group	*P*
Hypertension	2,298 (78.6)	515 (74.4)	0.017
Atrial fibrillation	144 (4.9)	94 (13.6)	<0.00001
Artery stenosis	804 (27.5)	186 (26.9)	0.739
Dyslipidemias	1,135 (38.8)	202 (29.2)	<0.001
Obesity	487 (16.7)	130 (18.8)	0.182
Current smoking	1,078 (36.9)	110 (15.9)	<0.001
Alcohol consumption	522 (17.9)	32 (4.6)	<0.001

Long X et al Mortality, Recurrence, and Dependency Rates Are Higher after Acute Ischemic Stroke in Elderly Patients with Diabetes Compared to Younger Patients. Front Aging Neurosci. 2016 Jun 16;8:142..

Outcomes at 12 and 24 months after ischaemic stroke (<75 years and 75 years and over)

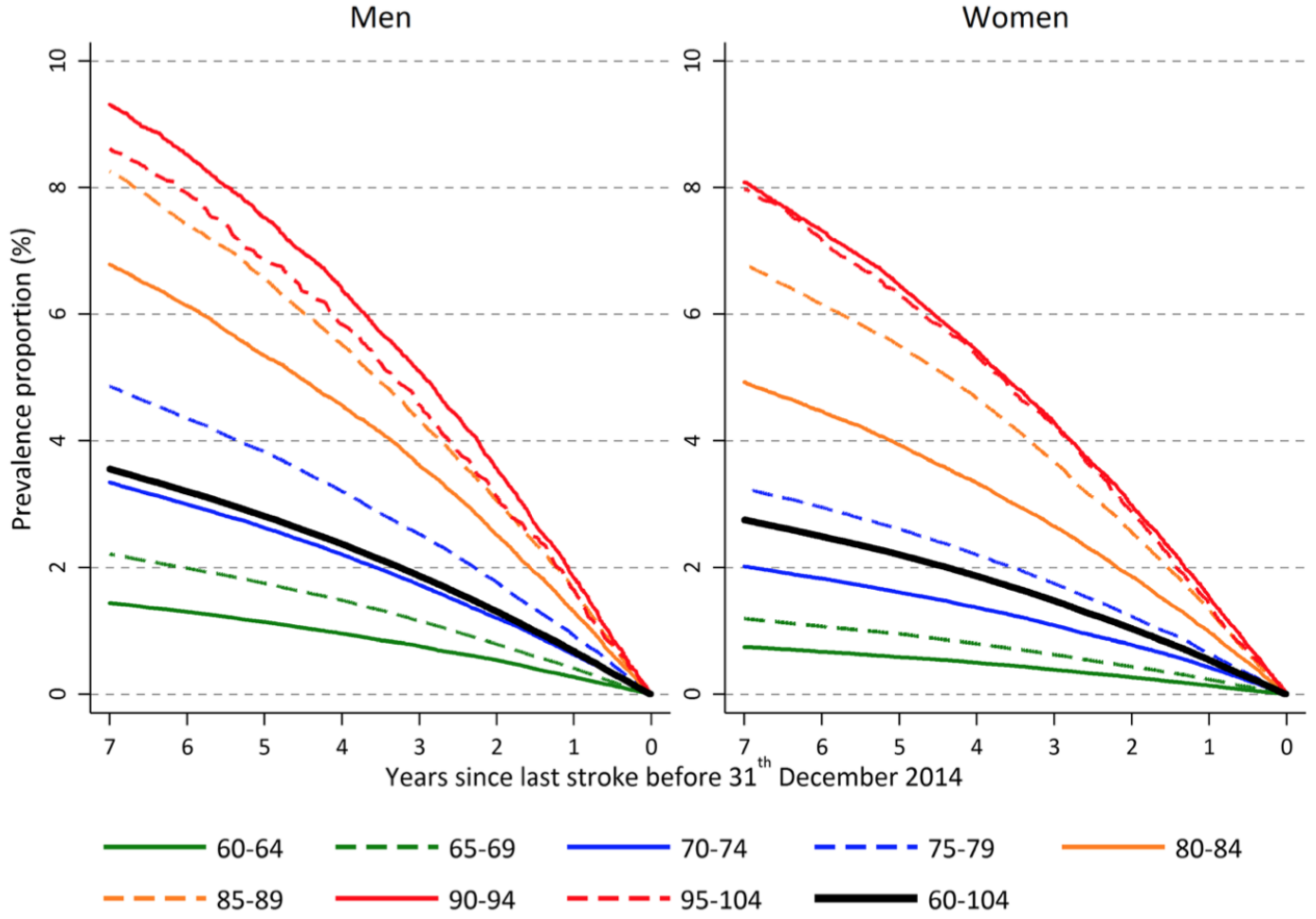
Outcomes	Younger group	Elderly group	Unadjusted		Adjusted†	
			OR (95% CI)	*P*	OR (95% CI)	*P*
12 months:						
Mortality	189 (7.4)	116 (19.0)	2.95 (2.30–3.79)	<0.001	2.18 (1.64–2.89)	<0.001
Dependency	786 (30.7)	296 (48.5)	2.13 (1.78–2.55)	<0.001	1.81 (1.49–2.20)	<0.001
Recurrence	367 (15.4)	102 (20.9)	1.45 (1.14–1.86)	0.003	1.37 (1.06–1.76)	0.016
36 months:						
Mortality	248 (13.7)	151 (35.4)	3.44 (2.70–4.36)	<0.001	3.10 (2.35–4.08)	<0.001
Dependency	1,113 (61.7)	336 (78.7)	2.30 (1.79–2.95)	<0.001	2.04 (1.57–2.64)	<0.001
Recurrence	636 (43.0)	141 (53.8)	1.54 (1.19–2.01)	<0.001	1.40 (1.07–1.85)	0.016

**OR indicated the risks in elderly group reference as younger group. †Indicated adjusted by gender, stroke subtype, severity, and risk factors.*

Higher levels of death, dependency and recurrence in the older cohort

Long X et al Mortality, Recurrence, and Dependency Rates Are Higher after Acute Ischemic Stroke in Elderly Patients with Diabetes Compared to Younger Patients. Front Aging Neurosci. 2016 Jun 16;8:142..

Total Swedish population born 1890–1954 living in Sweden from 1987. Using population registers
A total of 19,467,912 person years for men and 23,860,484 person years for women. 282,769 strokes occurred among men and 316,067 among women over the study period 1994 to 2014



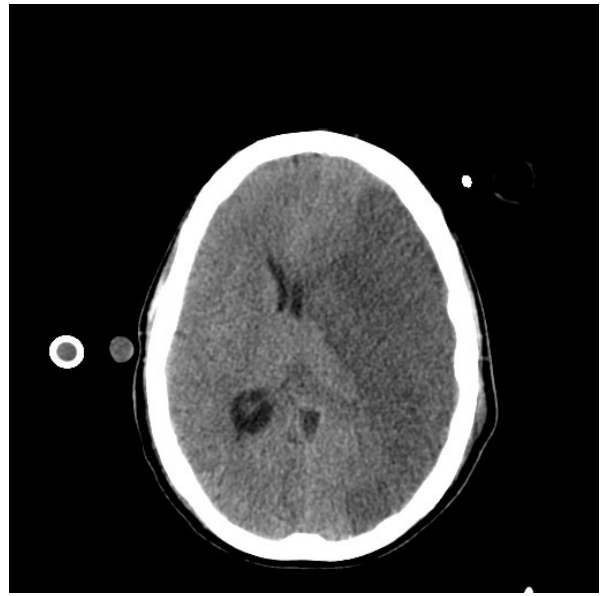
Proportion of patients alive up to 7 years after stroke. Highly age dependent

Fig. 4 Proportion of the population alive 31st of December 2014 with a history of stroke up to 7 years back in time, for different age groups. Men and women

Modig, K., Talbäck, M., Ziegler, L. *et al.* Temporal trends in incidence, recurrence and prevalence of stroke in an era of ageing populations, a longitudinal study of the total Swedish population. *BMC Geriatr* **19,** 31 (2019). https://doi.org/10.1186/s12877-019-1050-1

Case 1

- 89 year old man admitted with left hemisphere infarct leaving him with severe right hemiplegia, dysphasia and some cognitive impairment (MMSE 20)
- Previously living independently. Previous peptic ulcer but no other known comorbidities
- Stroke risk factors identified
  - Hypertension
  - Hyperlipidaemia (total cholesterol 5.5mmol/l)
  - Smoker since teenager of approx. 10/day



What are the risks and benefits of antiplatelets?

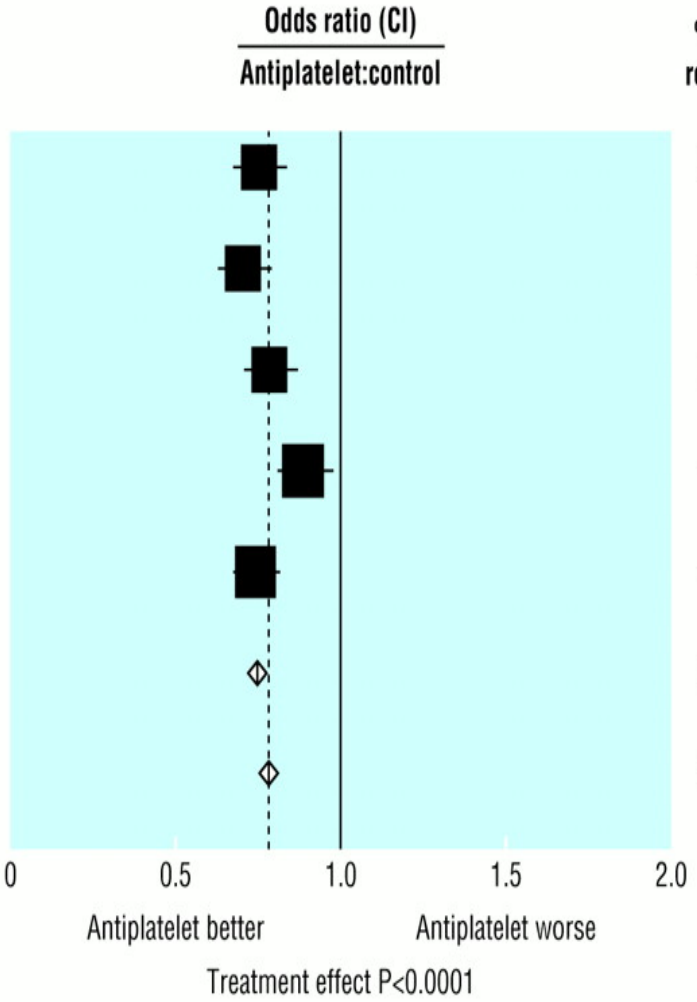
Do we treat the hypertension?

Do we give a statin?

What are the benefits of stopping smoking?

Aspirin is remarkably effective at reducing ischaemic events

Category of trial	No of trials with data	No (%) of vascular events: Allocated antiplatelet	No (%) of vascular events: Adjusted control	Observed-expected	Variance	% Odds reduction (SE)
Previous myocardial infarction	12	1345/9984 (13.5)	1708/10 022 (17.0)	-159.8	567.6	25 (4)
Acute myocardial infarction	15	1007/9658 (10.4)	1370/9644 (14.2)	-181.5	519.2	30 (4)
Previous stroke/transient ischaemic attack	21	2045/11 493 (17.8)	2464/11 527 (21.4)	-152.1	625.8	22 (4)
Acute stroke	7	1670/20 418 (8.2)	1858/20 403 (9.1)	-94.6	795.3	11 (3)
Other high risk	140	1638/20 359 (8.0)	2102/20 543 (10.2)	-222.3	737.0	26 (3)
Subtotal: all except acute stroke	188	6035/51 494 (11.7)	7644/51 736 (14.8)	-715.7	2449.6	25 (2)
All trials	**195**	**7705/71 912 (10.7)**	**9502/72 139 (13.2)**	**-810.3**	**3244.9**	**22 (2)**



Heterogeneity of odds reductions between:

5 categories of trial: χ^2=21.4, df=4; P=0.0003

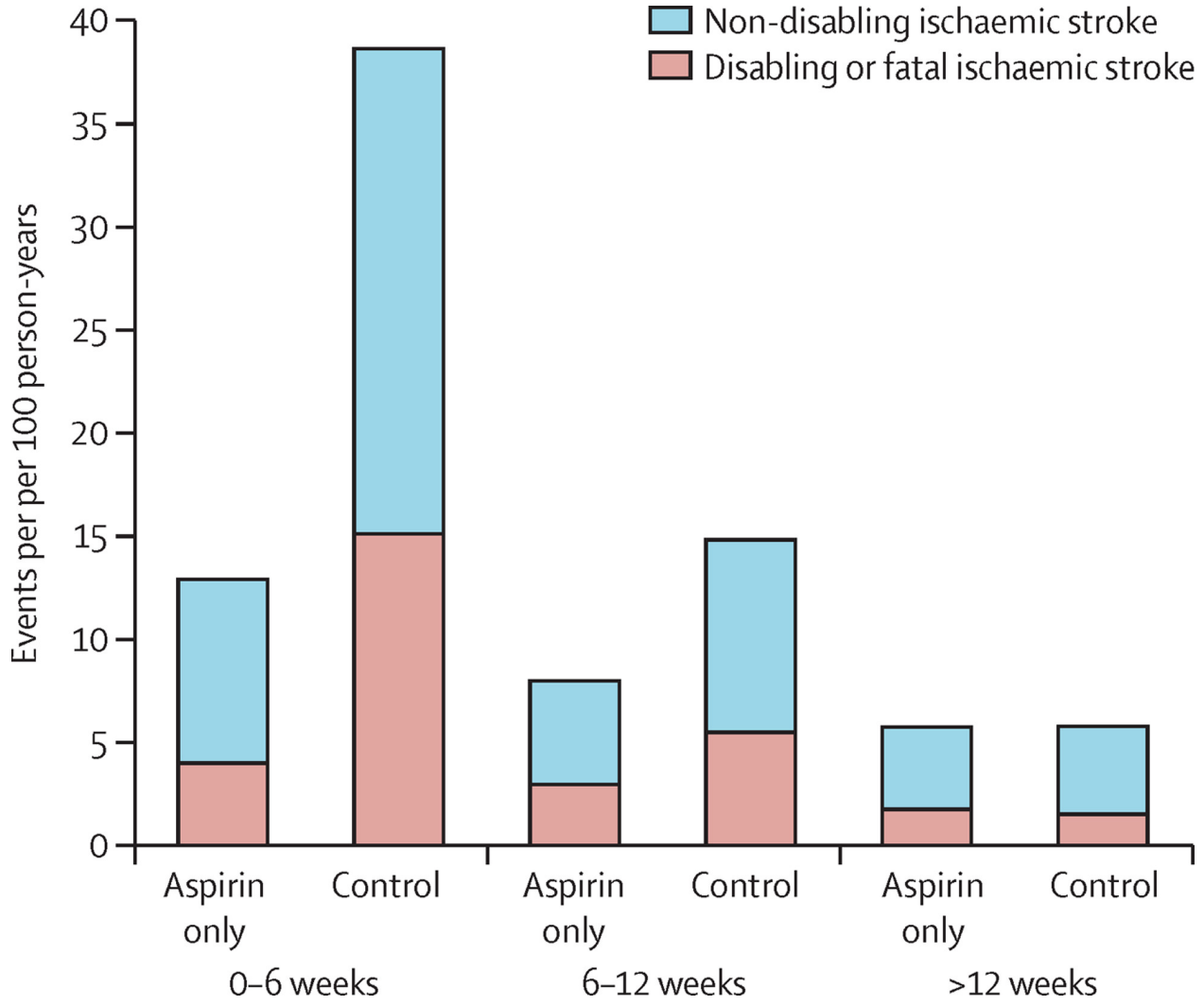
Acute stroke *v* other: χ^2=18.0, df=1; P=0.00002

Anti-thrombotic Trialists Collaboration BMJ 2002;324:71-86

No evidence of of interaction with age (data from CAST and IST)

Benefits of early aspirin (all ages)

15,778 participants from 12 trials of aspirin vs control in secondary prevention. Aspirin reduced the 6 week risk of recurrent ischaemic stroke by about 60% and disabling or fatal ischaemic stroke by about 70% with greatest benefit noted in patients presenting with TIA or minor stroke



Rothwell PM et al Effects of aspirin on risk and severity of early recurrent stroke after transient ischaemic attack and ischaemic stroke: timecourse analysis of randomised trials. Lancet 2016; 388: 365-75.

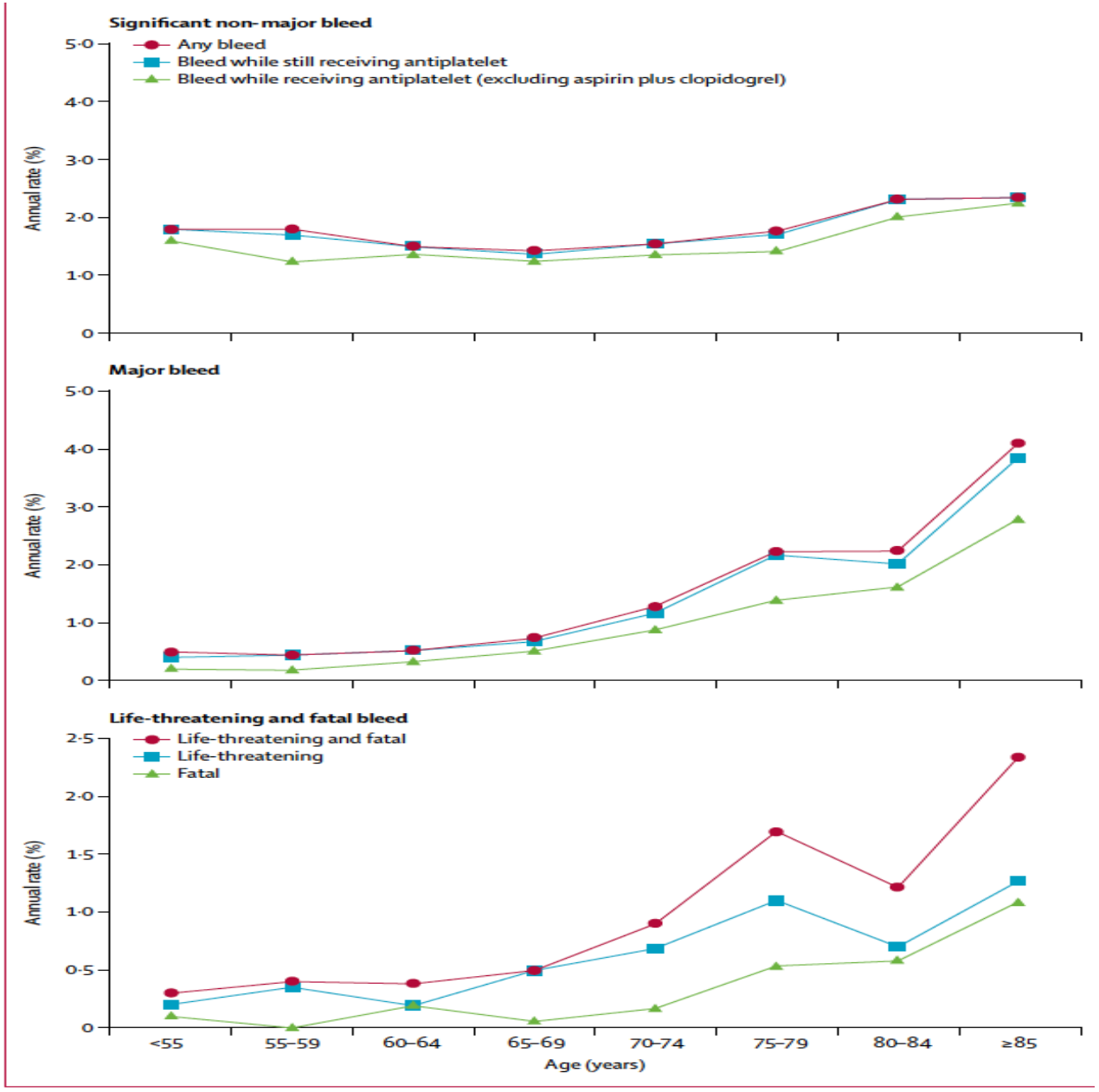


Figure 2: **Age-specific annual rate of bleeding events requiring medical attention**
Stratified by severity and by antiplatelet treatment immediately before the event. Annual rate derived as number per 100 patient-years. We used Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) criteria to define bleeding events as major (substantially disabling with persistent sequelae, intraocular bleeding leading to significant loss of vision, or bleeding requiring transfusion of ≥2 units of blood) and life-threatening or fatal (symptomatic intracranial haemorrhage, fall in haemoglobin of ≥5 g/dL, hypotension requiring intravenous inotropes, or required surgical intervention or transfusion of ≥4 units of blood).

Age specific annual rate of bleeding events by age

- 3166 patients 50% aged ≥75 years.
- 405 first bleeding events (218 gastrointestinal, 45 intracranial, and 142 other) during 13 509 patient-years of follow-up.

Li L, et al Oxford Vascular Study. Age-specific risks, severity, time course, and outcome of bleeding on long-term antiplatelet treatment after vascular events: a population-based cohort study. Lancet. 2017 Jul 29;390:490-499.

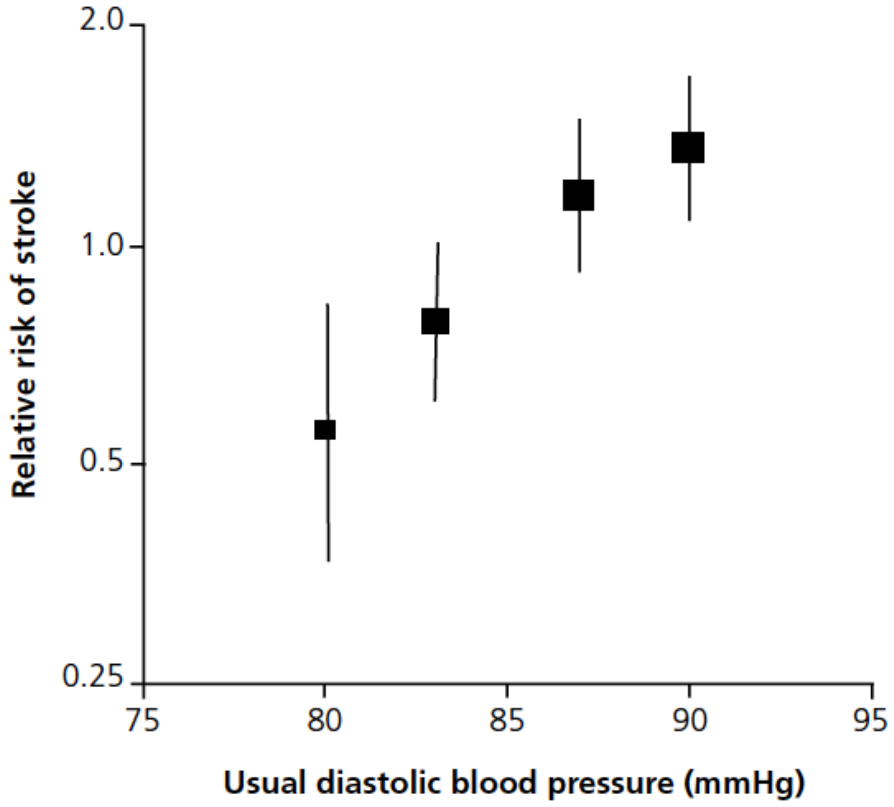
Aspirin complications after vascular events in older patients

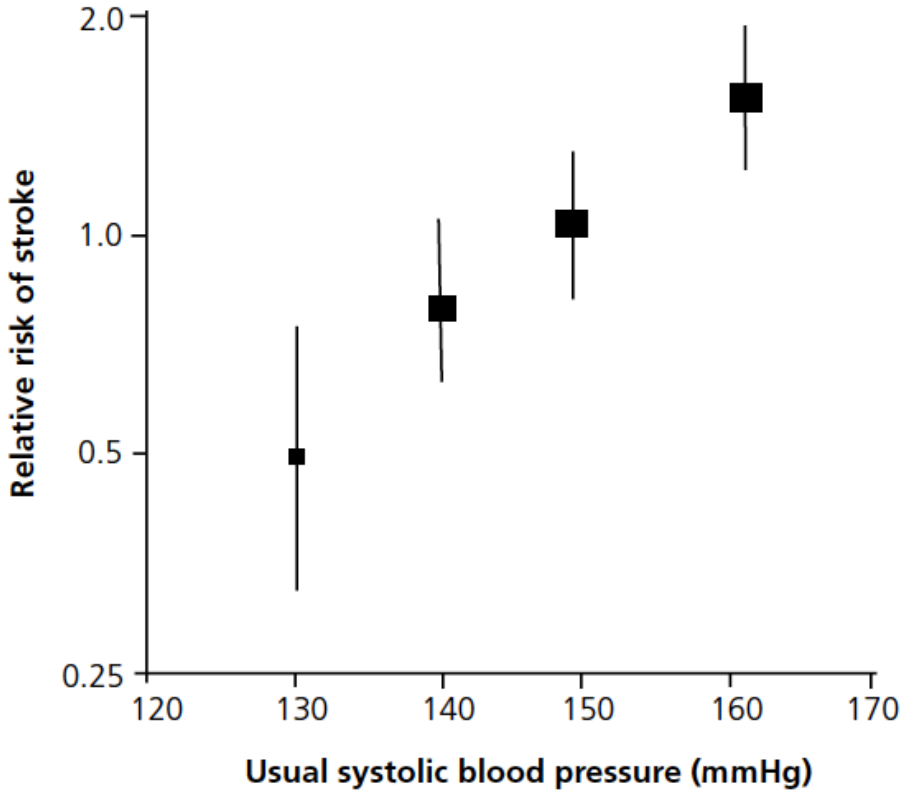
- Risk of non-major bleeding unrelated to age.
- Major bleeding increased steeply with age (≥75 years hazard ratio [HR] 3.10, particularly for fatal bleeds HR 5.53
- The estimated NNT for routine PPI use to prevent one disabling or fatal upper gastrointestinal bleed over 5 years fell from 338 for people <65 years, to 25 for individuals aged 85 years or older.
- Routine PPI use to prevent such bleeds should be encouraged.

Li L, et al Oxford Vascular Study. Age-specific risks, severity, time course, and outcome of bleeding on long-term antiplatelet treatment after vascular events: a population-based cohort study. Lancet. 2017 Jul 29;390:490-499.

Relationship between blood pressure and stroke after TIA or minor stroke

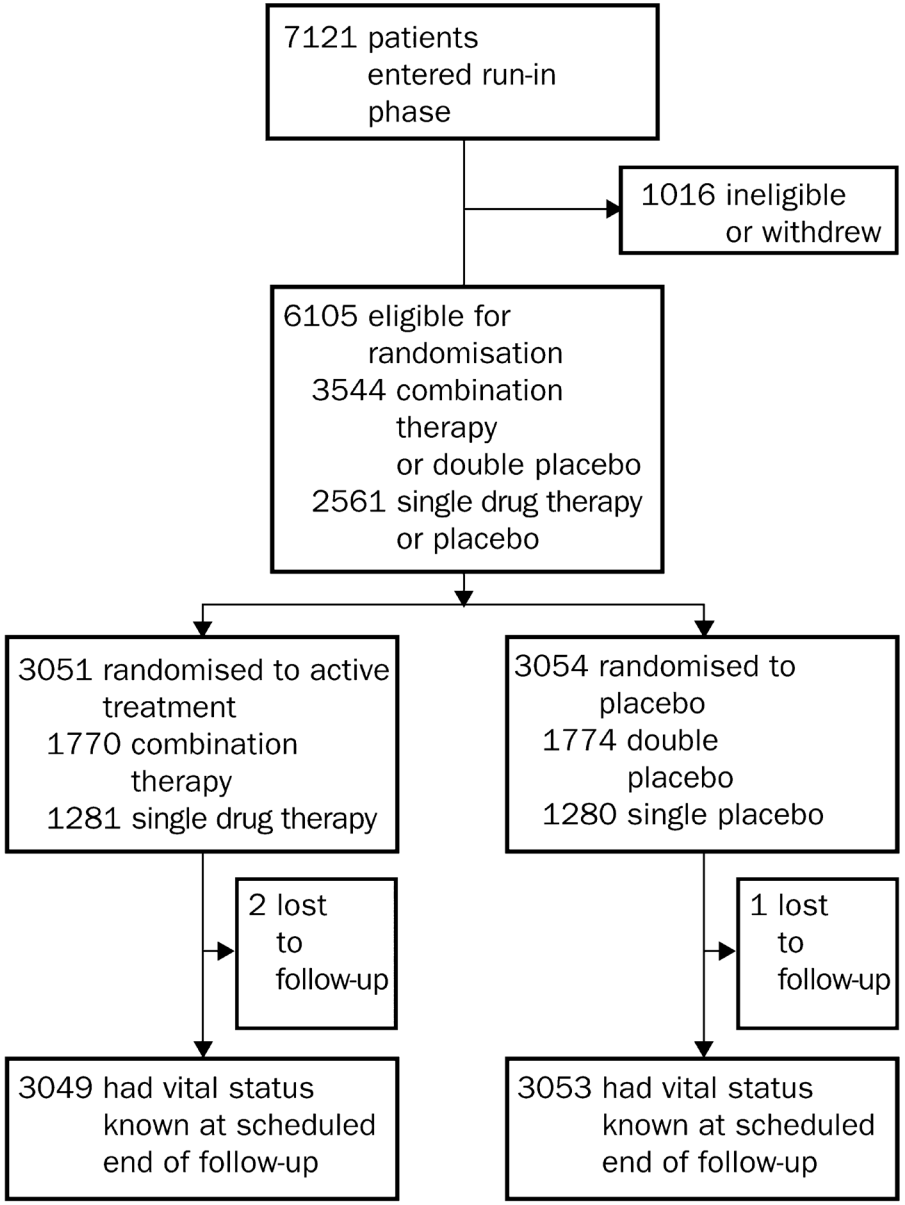
Figure 1 Continuous relationship between usual blood pressure and the risk of stroke in 2435 individuals with a history of transient ischaemic attack (TIA) or minor stroke during 4 years' follow-up in the UK-TIA aspirin trial.





A Rogers. BMJ 1996;313:147.

PROGRESS Trial



Average age 64 years so need caution extrapolating to very elderly

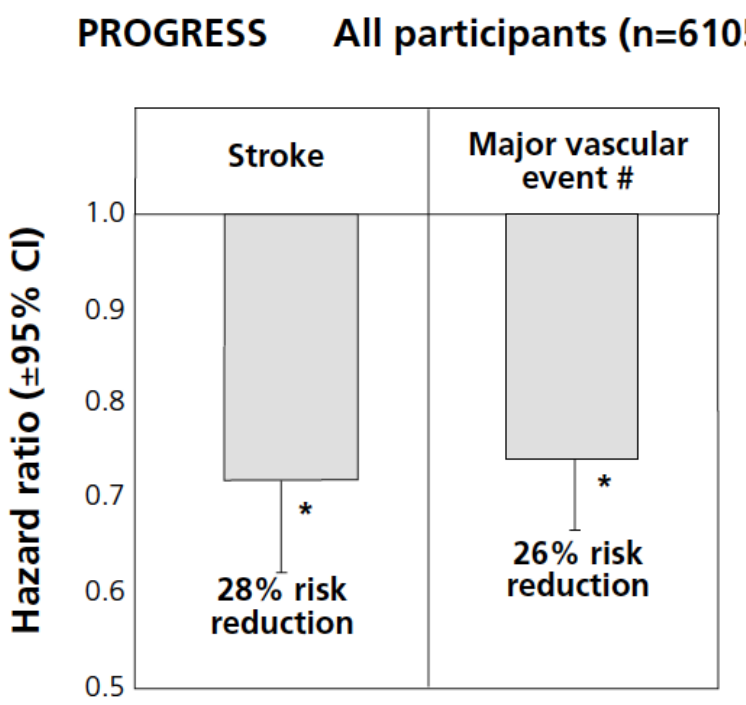
PROGRESS Collaborative Group Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack Lancet 2001;358:1033-1041

PROGRESS Trial

Comparison of placebo vs perindopril or indapamide plus perindopril after stroke or TIA regardless of whether hypertensive or not

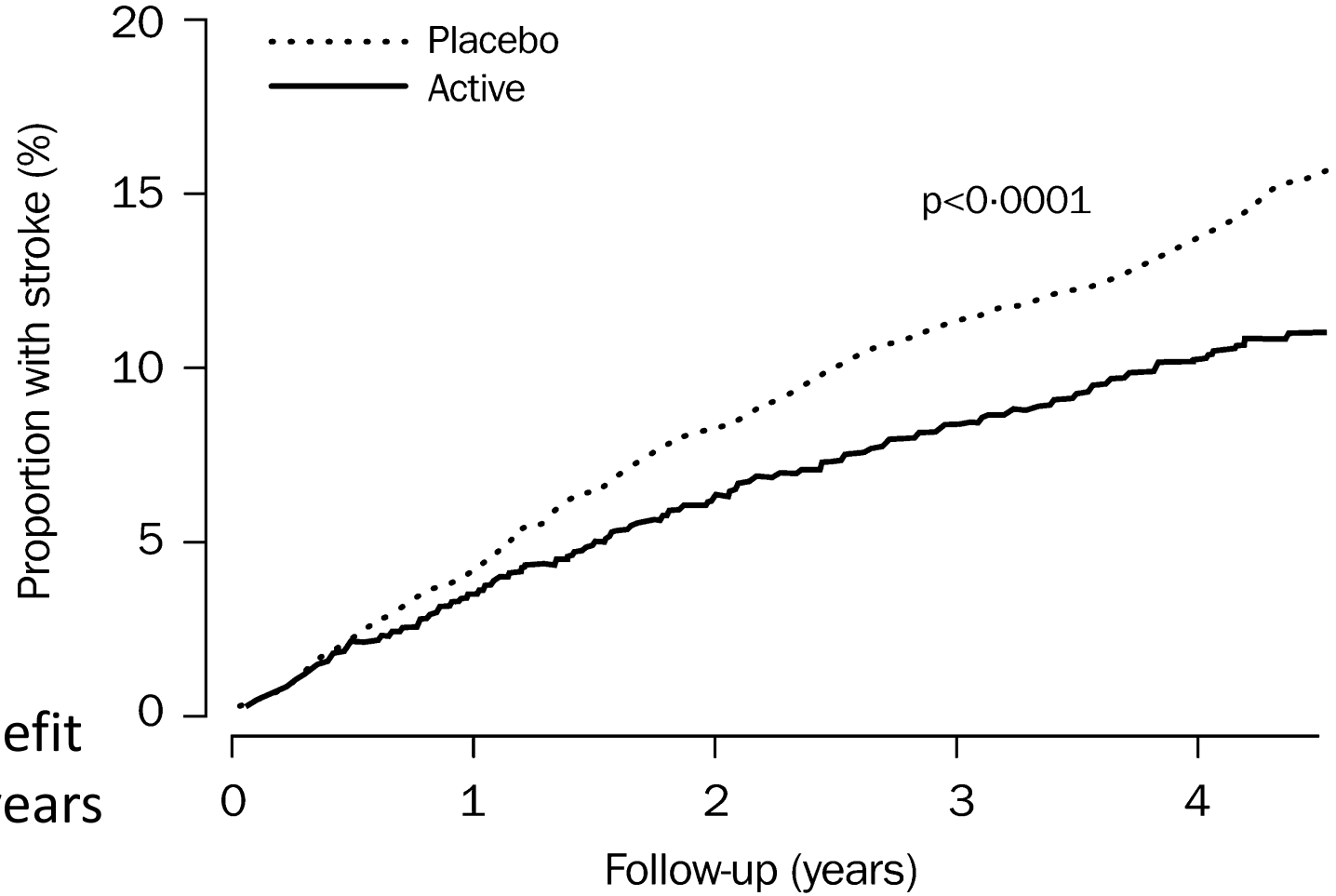
PROGRESS Collaborative Group Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack Lancet 2001;358:1033-1041

Figure 2 Average reduction in the risk of stroke and major vascular events in all participants (n=6105) during 4.2 years' follow-up in the PROGRESS study with active treatment (perindopril ± indapamide) compared with placebo.



* p<0.0001 active treatments *vs.* placebo.
# major vascular events include stroke, heart attack or death from cardiovascular disease.

PROGRESS Trial Results



Numbers at risk

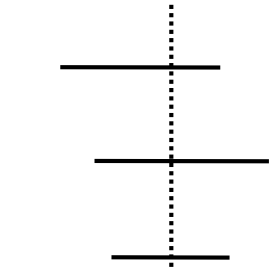
Active	3051	2902	2765	2634	1595
Placebo	3054	2880	2707	2551	1533

Significant benefit after about 2 years treatment

PROGRESS Collaborative Group Randomised trial of a perindopril-based blood-pressure-lowering regimen among 6105 individuals with previous stroke or transient ischaemic attack Lancet 2001;358:1033-1041

PROGRESS Trial Hypertensive and non-hypertensive patient subgroups

	Strokes active	Strokes placebo	Favours active	Favours placebo	Risk reduction (95%CI)
Stroke					
Hypertensive	163	235			32% (17 to 44%)
Non-hypertensive	144	185			27% (8 to 42%)
Total	**307**	**420**			**28% (17 to 38%)**



0.5 1.0 2.0

Standardised hazard ratio

Age-stratified and blood-pressure-stratified effects of blood-pressure-lowering pharmacotherapy for the prevention of cardiovascular disease and death: an individual participant-level data meta-analysis

*The Blood Pressure Lowering Treatment Trialists' Collaboration**

Summary

Background The effects of pharmacological blood-pressure-lowering on cardiovascular outcomes in individuals aged 70 years and older, particularly when blood pressure is not substantially increased, is uncertain. We compared the effects of blood-pressure-lowering treatment on the risk of major cardiovascular events in groups of patients stratified by age and blood pressure at baseline.

Methods We did a meta-analysis using individual participant-level data from randomised controlled trials of pharmacological blood-pressure-lowering versus placebo or other classes of blood-pressure-lowering medications, or between more versus less intensive treatment strategies, which had at least 1000 persons-years of follow-up in each treatment group. Participants with previous history of heart failure were excluded. Data were obtained from the Blood Pressure Lowering Treatment Triallists' Collaboration. We pooled the data and categorised participants into baseline age groups (<55 years, 55–64 years, 65–74 years, 75–84 years, and ≥85 years) and blood pressure categories (in 10 mm Hg increments from <120 mm Hg to ≥170 mm Hg systolic blood pressure and from <70 mm Hg to ≥110 mm Hg diastolic). We used a fixed effects one-stage approach and applied Cox proportional hazard models, stratified by trial, to analyse the data. The primary outcome was defined as either a composite of fatal or non-fatal stroke, fatal or non-fatal myocardial infarction or ischaemic heart disease, or heart failure causing death or requiring hospital admission.

Published Online
August 27, 2021
https://doi.org/10.1016/S0140-6736(21)01921-8

See Online/Comment
https://doi.org/10.1016/S0140-6736(21)01916-4

*Group members listed at the end of the manuscript

Correspondence to:
Prof Kazem Rahimi, Deep Medicine, Nuffield Department of Women's and Reproductive Health, University of Oxford, Oxford OX1 2BQ, UK
kazem.rahimi@wrh.ox.ac.uk

Rate of major cardiovascular events per 5 mm Hg reduction in systolic blood pressure, stratified by treatment allocation and age categories at baseline

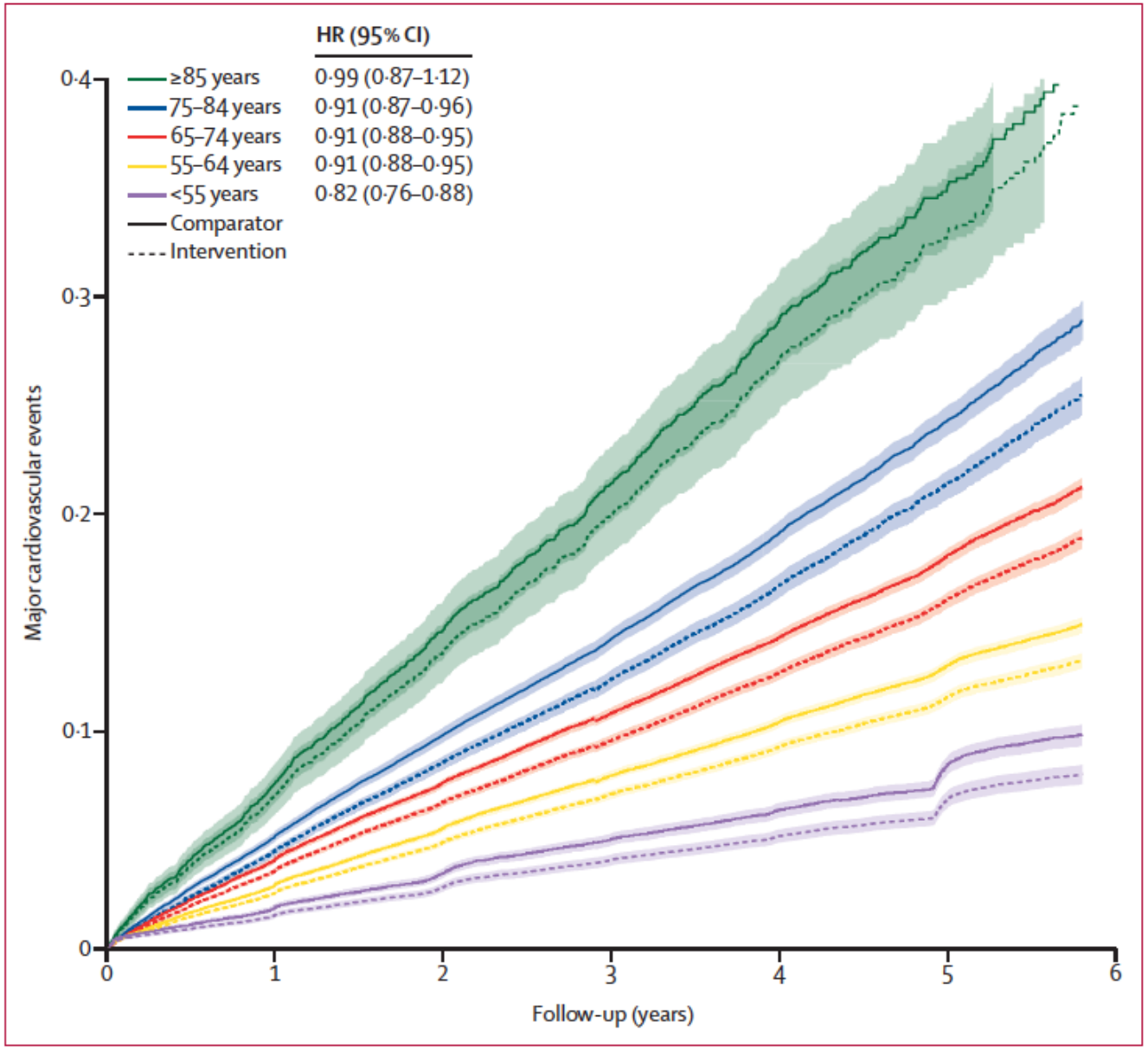


Figure 1: **Rate of major cardiovascular events per 5 mm Hg reduction in systolic blood pressure, stratified by treatment allocation and age categories at baseline**

Major cardiovascular events, defined as a composite of fatal or non-fatal stroke, fatal or non-fatal myocardial infarction or ischaemic heart disease, or heart failure causing death or requiring hospital admission. The shaded area represents the 95% CIs.

The Blood Pressure Lowering Treatment Trialists' CollaborationAge-stratified and blood-pressure-stratified effects of blood-pressure-lowering pharmacotherapy for the prevention of cardiovascular disease and death: an individual participant-level data meta-analysis The Lancet 2021;398:1053-1064

Age-stratified relative risk and absolute risk difference of systolic blood pressure reduction on primary and secondary outcomes

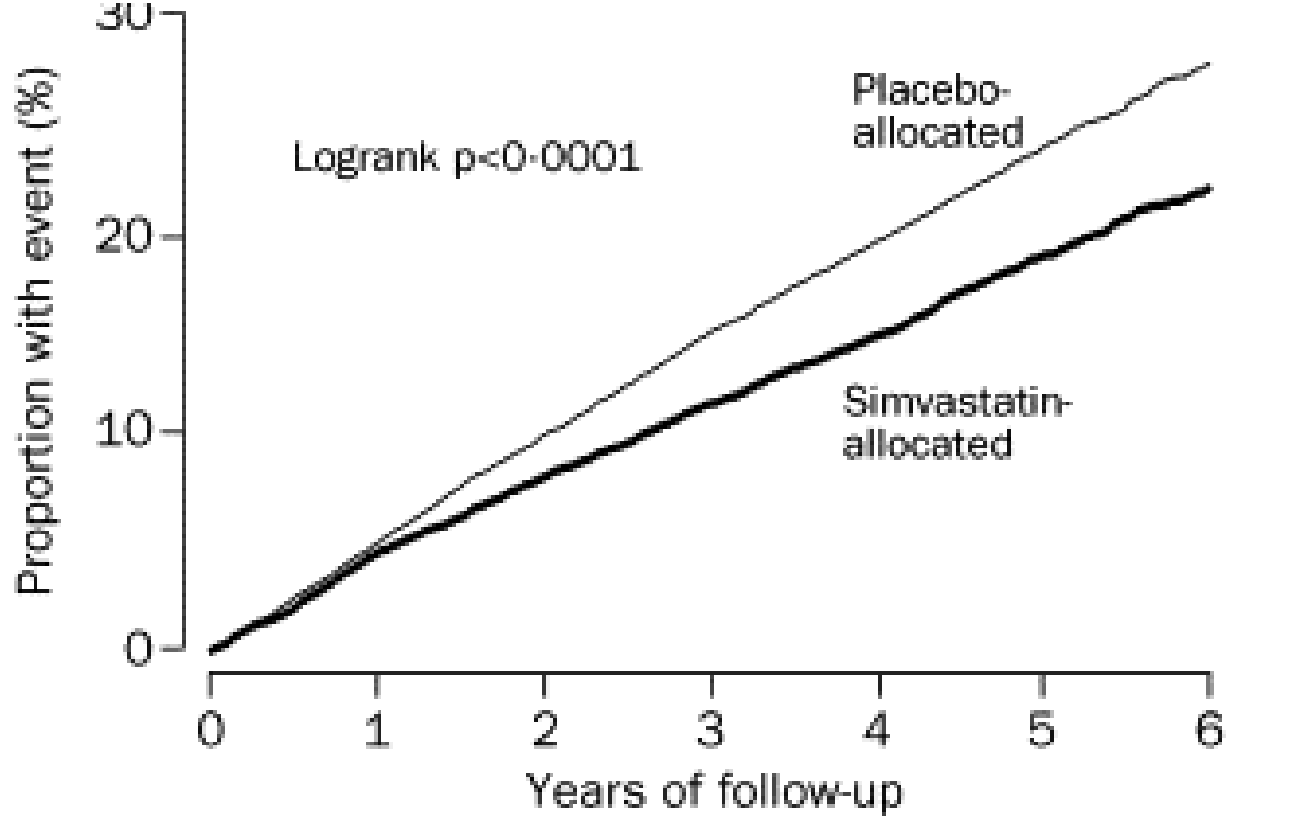
Relative risk reductions are presented with hazard ratios and 95% CIs per 5 mm Hg reduction in systolic blood pressure, separately for each outcome. The absolute risk difference reflects the mean blood pressure reduction for each age category.

	Intervention		Comparator		Hazard ratio (95% CI) per 5 mm Hg reduction in systolic blood pressure	Absolute risk difference (95% CI) between treatment and comparator group
	Events	Total	Events	Total		
Major cardiovascular events						
<55 years	1485	21594	1742	20731	0·82 (0·76 to 0·88)	−0·015 (−0·020 to −0·010)
55–64 years	5636	59649	7080	67526	0·91 (0·88 to 0·95)	−0·010 (−0·014 to −0·007)
65–74 years	7413	59560	9551	67934	0·91 (0·88 to 0·95)	−0·016 (−0·020 to −0·012)
75–84 years	3825	24747	5174	28944	0·91 (0·87 to 0·96)	−0·024 (−0·031 to −0·017)
≥85 years	459	2247	582	2528	0·99 (0·87 to 1·12)	−0·026 (−0·052 to 0·001)
					Adjusted $p_{interaction}$=0·050	Adjusted $p_{interaction}$=0·024
					Unadjusted $p_{interaction}$=0·010	Unadjusted $p_{interaction}$=0·0049
Stroke						
<55 years	476	21599	640	20734	0·71 (0·63 to 0·81)	−0·009 (−0·012 to −0·006)
55–64 years	1763	59704	2200	67569	0·87 (0·82 to 0·93)	−0·003 (−0·005 to −0·001)
65–74 years	2584	59640	3313	68020	0·90 (0·85 to 0·95)	−0·005 (−0·008 to −0·003)
75–84 years	1505	24783	1954	28989	0·92 (0·85 to 0·99)	−0·007 (−0·011 to −0·002)
≥85 years	139	2247	195	2529	0·88 (0·71 to 1·10)	−0·015 (−0·030 to 0·000)
					Adjusted $p_{interaction}$=0·0095	Adjusted $p_{interaction}$=0·093
					Unadjusted $p_{interaction}$=0·0019	Unadjusted $p_{interaction}$=0·019

Interpretation: Pharmacological blood pressure reduction is effective into old age, with no evidence that relative risk reductions for prevention of major cardiovascular events vary by systolic or diastolic blood pressure levels at randomisation, down to less than 120/70 mm Hg. Pharmacological blood pressure reduction should, therefore, be considered an important treatment option regardless of age, with the removal of age-related blood-pressure thresholds from international guidelines.

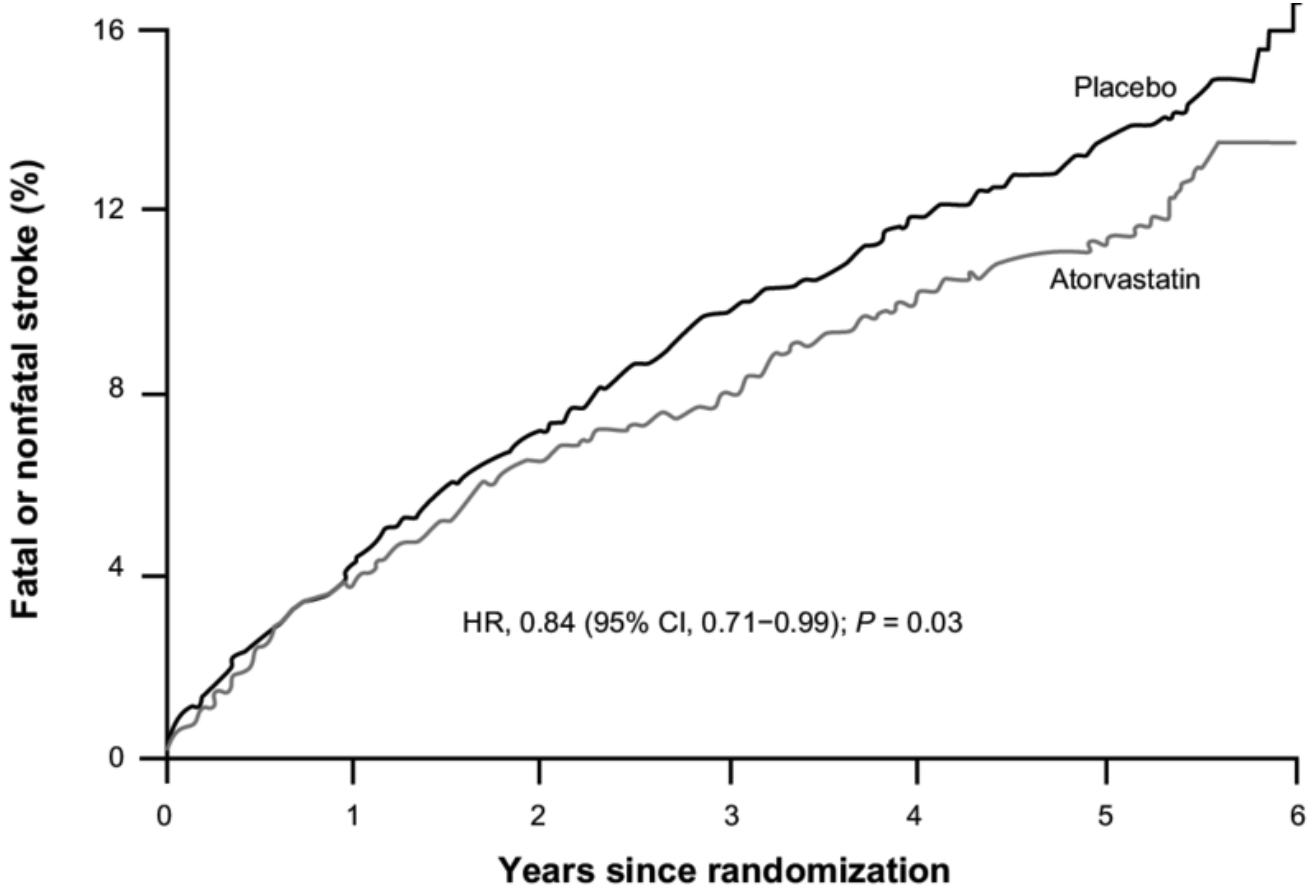
Lipid Lowering after Ischaemic events: Heart Protection Study

10,000 patients receiving simvastatin 40mg and 10,000 placebo after vascular ischaemic event



Heart Protection Study Collaborative Group MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo controlled trial. Lancet 2002;360:7-22

Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) study



No at risk

Atorvastatin	2365	2208	2106	2031	1935	922	126
Placebo	2366	2213	2115	2010	1926	887	137

Mean age at randomisation 63

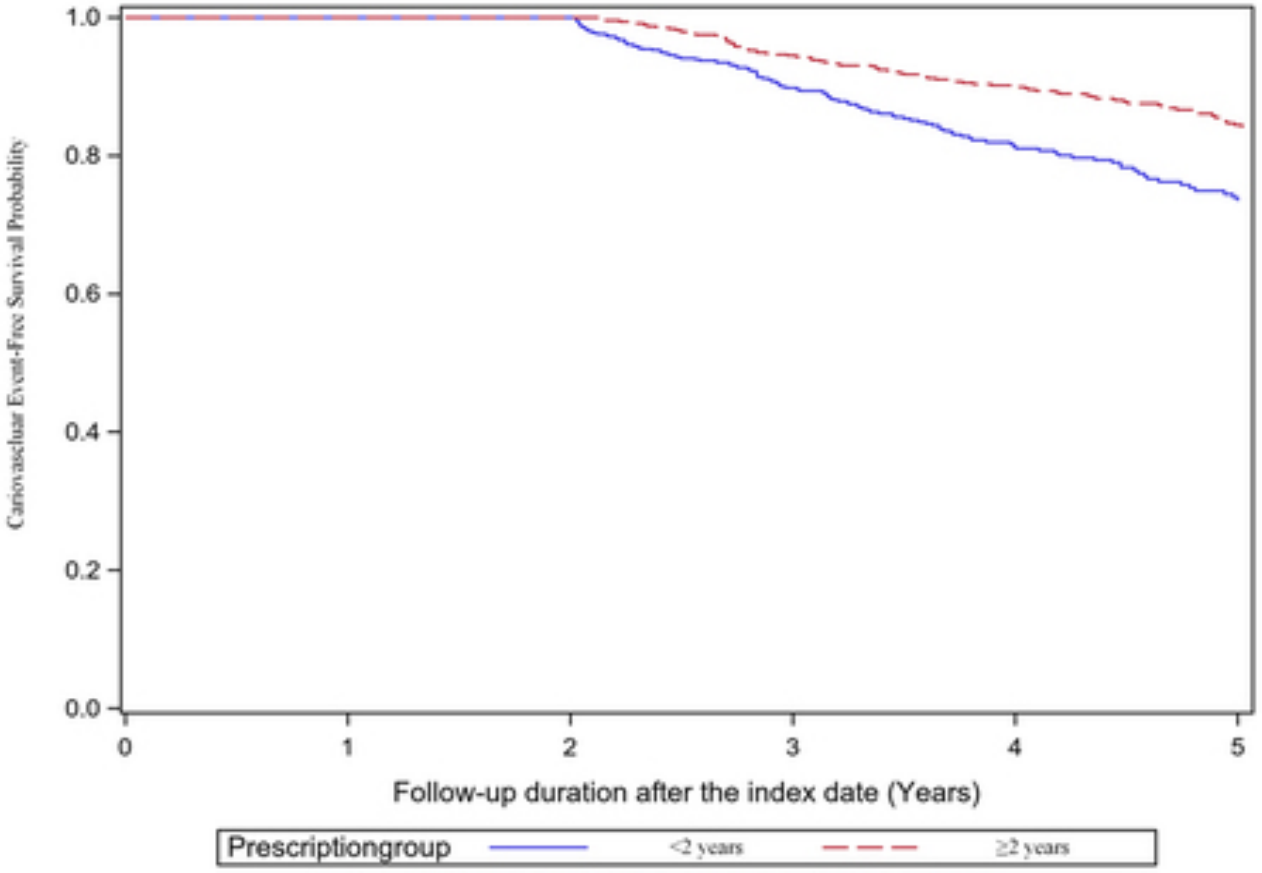
Amarenco P et al , Effects of intense low-density lipoprotein cholesterol reduction in patients with stroke or transient ischemic attack: the Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) trial. Stroke. 2007;38:3198-204.

Kaplan Meier survival curves for older patients after stroke treated with statin for more or less than two years

- 5910 patients >65 yrs included in retrospective cohort study; 3157 aged over 80
- Two years of statin prescription in patients aged 80 years and older resulted in both a lower risk of the composite end point (adjusted hazard ratio, 0.80 [95% CI, 0.62–1.02]) and all-cause mortality (adjusted hazard ratio, 0.67 [95% CI, 0.57–0.80]).

Lefeber GJ et al Statins after ischemic stroke in the oldest. Stroke 2021;52:1244-1252

Statins after Ischemic Stroke in Patients Aged 80 Years and Older, Less than Two Years vs Two Years or More of Statin Prescription



Patients contributing time at year-point + 30 days (crossectional)

	0 + 90 days	1	2	3	4	5
< 2 years	3157	1803	805	355	215	135
≥ 2 years	.	.	458	502	368	258
Total in analysis	3157	1803	1263	857	583	393
Cumulative primary outcome		645	830	968	1067	1144
Cumulative loss to mortality	.	263	449	625	740	839
Cumulative loss to follow-up	.	31	91	157	211	282
Cumulative study end	.	415	524	550	556	499

Is it worth advising quitting smoking after stroke?

- One year after quitting, the added risk of coronary heart disease is half that of a smoker's. Five to 15 years after quitting, a former smoker's stroke risk is reduced to that of a nonsmoker's. *2004 Surgeon General's Report, The Health Consequences of Smoking*
- Two-thirds of older adults said that a healthcare provider advised them to quit smoking, but just over one-third who tried to quit used evidence-based tobacco cessation treatments and only one in 20 successfully quit in the past year *The 2015 National Health Interview Survey*:

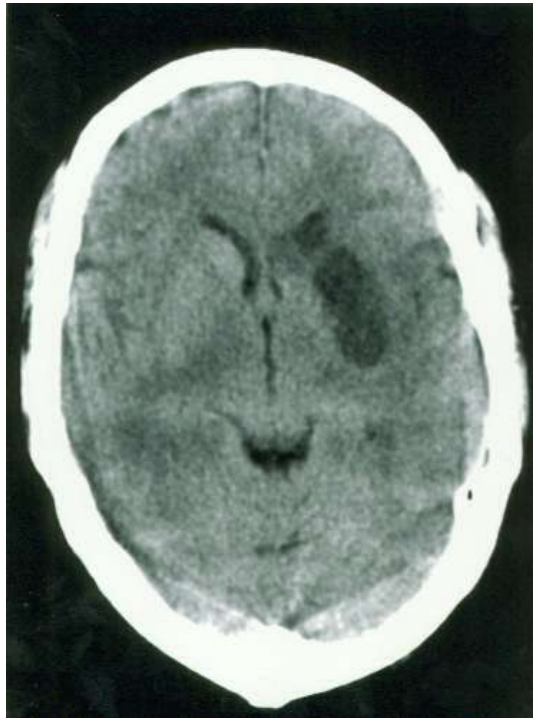
How Would I Manage Case 1?

- Ask the question, is preventing another stroke relevant? Probably yes
- Antiplatelets: Yes, despite previous bleed, clear benefit especially in the early weeks after stroke. I would use clopidogrel with a PPI
- Antihypertensives: Yes to maintain BP below 140/80 and preferably 130
- Cholesterol lowering: ask the question is the patient likely to still be alive after 2 years. If yes then treat with a statin
- Smoking: advise quitting and provide support to do so – pharmacological and psychosocial support. Chances of success low
- Don’t forget diet, exercise advice and support

Case 2

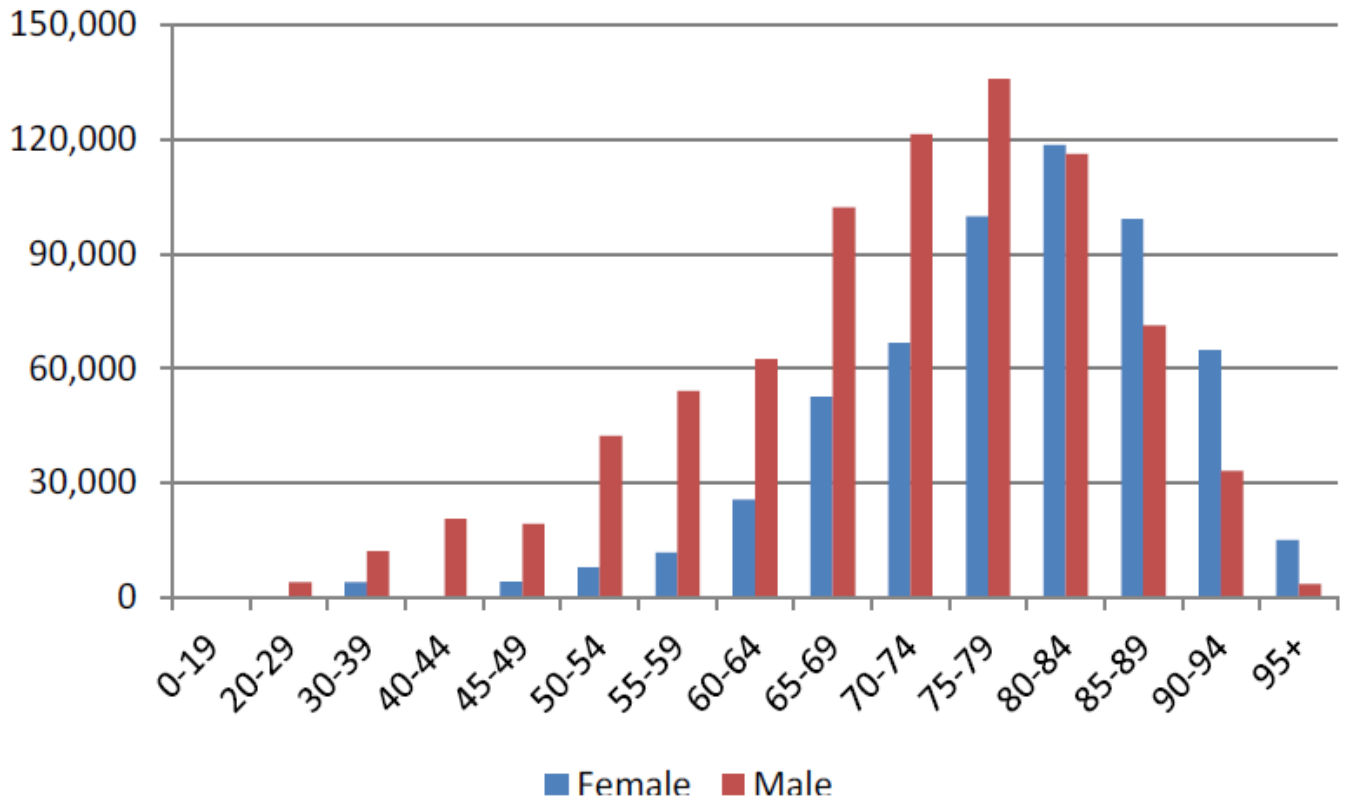
- 88 year old woman with partial left anterior circulation infarct – moderate aphasia and reduced mobility – unsteady gait, susceptible to falling
- Previously known hypertensive. Mild cognitive impairment
- Atrial fibrillation identified as likely cause for the stroke

Do we anticoagulate?



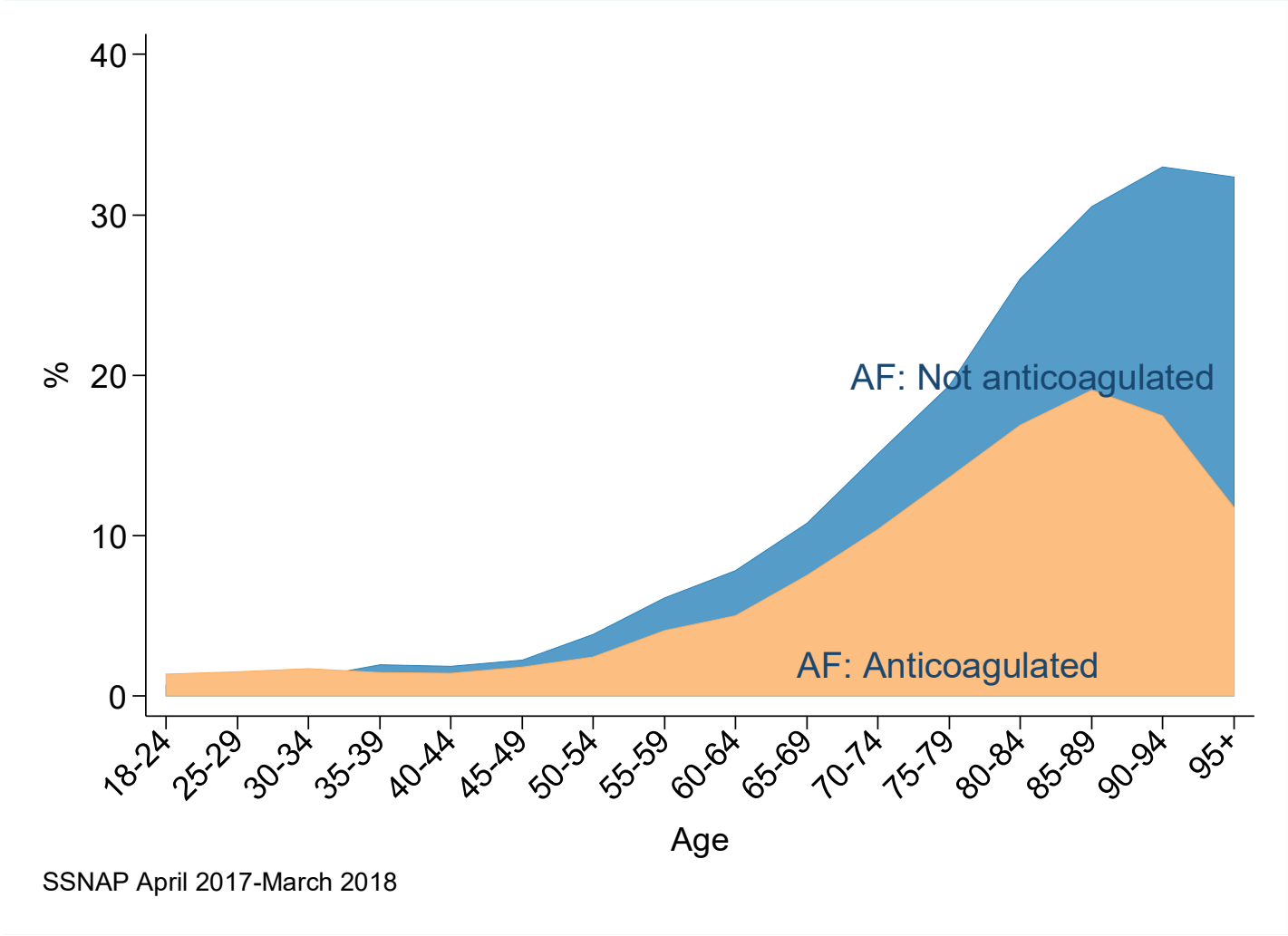
Prevalence AF by Age

Figure 1. Summary of estimated atrial fibrillation prevalence in England, 2014



Unpublished report PHE 2015

Data from National Audit UK – Proportion of people Anticoagulated with known AF when admitted with stroke



SSNAP April 2017-March 2018

Risk assessment scores for AF treatment

Annual risk of stroke based on $CHADS_2$ or CHA_2DS_2-VASc score

Score	$CHADS_2$[11]	CHA_2DS_2-VASc[12]
0	1.9%	0.0%
1	2.8%	1.3%
2	4.0%	2.2%
3	5.9%	3.2%
4	8.5%	4.0%
5	12.5%	6.7%
6	18.2%	9.8%
7	—	9.6%
8	—	12.5%
9	—	15.2%

$CHADS_2$: 1 point each for **c**ongestive heart failure, **h**ypertension, **a**ge ≥ 75, **d**iabetes mellitus; 2 points for prior **s**troke or transient ischemic attack.

CHA_2DS_2-VASc: 1 point each for **c**ongestive heart failure, **h**ypertension, **a**ge 65–74, **d**iabetes mellitus, **v**ascular disease (coronary artery disease, peripheral arterial disease, aortic aneurysm), **s**ex **c**ategory female; 2 points for **a**ge ≥ 75 and for prior **s**troke or transient ischemic attack.

HAS-BLED[14]	Points
Hypertension	1
Abnormal renal function	1
Abnormal liver function	1
Stroke	1
Bleeding history	1
Labile INR	1
Elderly (age > 65)	1
Drugs	1
Alcohol	1
Maximum score	9

Hagerty et al Cleveland J Med 2017;85:35-40

ORIGINAL ARTICLE

MAYO CLINIC

Check for updates

Non–Vitamin K Antagonist Oral Anticoagulants in Elderly (≥85 years) Patients With Newly Diagnosed Atrial Fibrillation: Changing Clinical Practice and Outcomes for Stroke Prevention in a Nationwide Cohort Study

Wen-Han Cheng, MD; Chern-En Chiang, MD; Yenn-Jiang Lin, MD; Shih-Lin Chang, MD; Li-Wei Lo, MD; Yu-Feng Hu, MD; Ta-Chuan Tuan, MD; Jo-Nan Liao, MD; Fa-Po Chung, MD; Tzeng-Ji Chen, MD; Gregory Y.H. Lip, MD; Shih-Ann Chen, MD; and Tze-Fan Chao, MD

Abstract

Objective: To investigate the influences of non–vitamin K antagonist oral anticoagulants (NOACs) on rates of initiations of oral anticoagulants (OACs) and outcomes among elderly patients with atrial fibrillation (AF).

Methods: From January 1, 2009, to December 31, 2015, 33,539 newly-diagnosed AF patients older than 85 years old who survived more than 180 days after AF diagnosis were studied. Temporal trends regarding OAC initiation rates after incident AF were analyzed. The 1-year risks of ischemic stroke, intracranial hemorrhage, and mortality of incident AF patients diagnosed each year were compared with that of the year 2009.

Results: Initiation rates of OACs after AF was newly diagnosed in the elderly significantly increased from 9.5% to 34.3%, mainly due to the introduction of NOACs (from 0% to 26.2%). Several clinical factors were associated with OACs underuse, including chronic obstructive pulmonary disease, abnormal renal function, anemia, and history of bleeding. Compared with year 2009 (incidence rate, 5.55%/year), the 1-year risk of ischemic stroke after AF diagnosis decreased in the era of NOACs (incidence rate, 4.20%/year; adjusted hazard ratio [aHR], 0.748 in year 2012; 4.39%/year, aHR, 0.789 in 2014; 2.75%/year; aHR, 0.513 in year 2015; all $P<.01$, except for year 2013, 4.80%/year [$P=.07$]). Also, the risks of mortality were lower in years 2012 to 2015, while the risk of ICH remained unchanged.

Conclusion: Initiation rates of OACs after AF was newly diagnosed in the elderly significantly increased following the introduction of NOACs. A lower risk of ischemic stroke, mortality, and composite adverse events was observed, which was temporally associated with the increasing prescription rates of OACs.

Use and complications associated with anticoagulation for elderly patients with AF

Study of 33,539 patients with AF in Taiwan

Cheng WH, et al Non-Vitamin K Antagonist Oral Anticoagulants in Elderly (≥85 years) Patients With Newly Diagnosed Atrial Fibrillation: Changing Clinical Practice and Outcomes for Stroke Prevention in a Nationwide Cohort Study. Mayo Clin Proc. 2021 Jan;96(1):52-65.

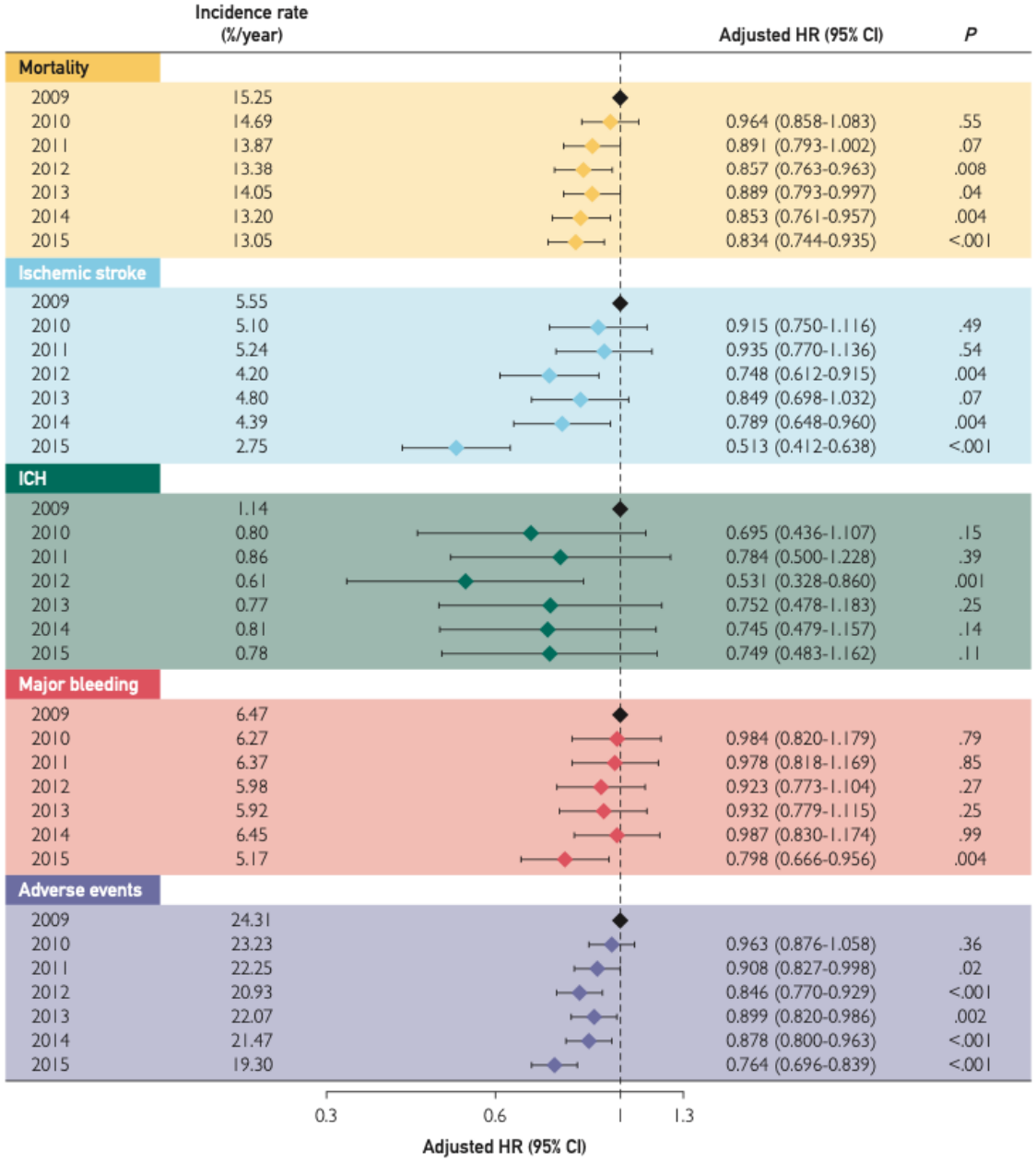


FIGURE 6. Risks and trends of clinical outcomes among elderly newly diagnosed atrial fibrillation (AF) patients from 2009 to 2015. Generally, the risks of ischemic stroke, mortality, and composite adverse events were lower in the era with non–vitamin K oral anticoagulants (NOACs), whereas the risks of ICH and major bleeding did not significantly increase. CHA_2DS_2-VASc = score based on congestive heart failure, hypertension, age, diabetes, previous stroke/transient ischemic attack, vascular disease, female sex; OAC = oral anticoagulant.

Anticoagulant complications between 2009 and 2015 in people >85 years

- Lower mortality
- Fewer ischaemic stroke
- Fewer bleeding complications including ICH
- Overall fewer adverse events

Cheng WH, et al Non-Vitamin K Antagonist Oral Anticoagulants in Elderly (≥85 years) Patients With Newly Diagnosed Atrial Fibrillation: Changing Clinical Practice and Outcomes for Stroke Prevention in a Nationwide Cohort Study. Mayo Clin Proc. 2021 Jan;96(1):52-65.

Changes in anticoagulant usage between 2009 and 2015 in people >85 years

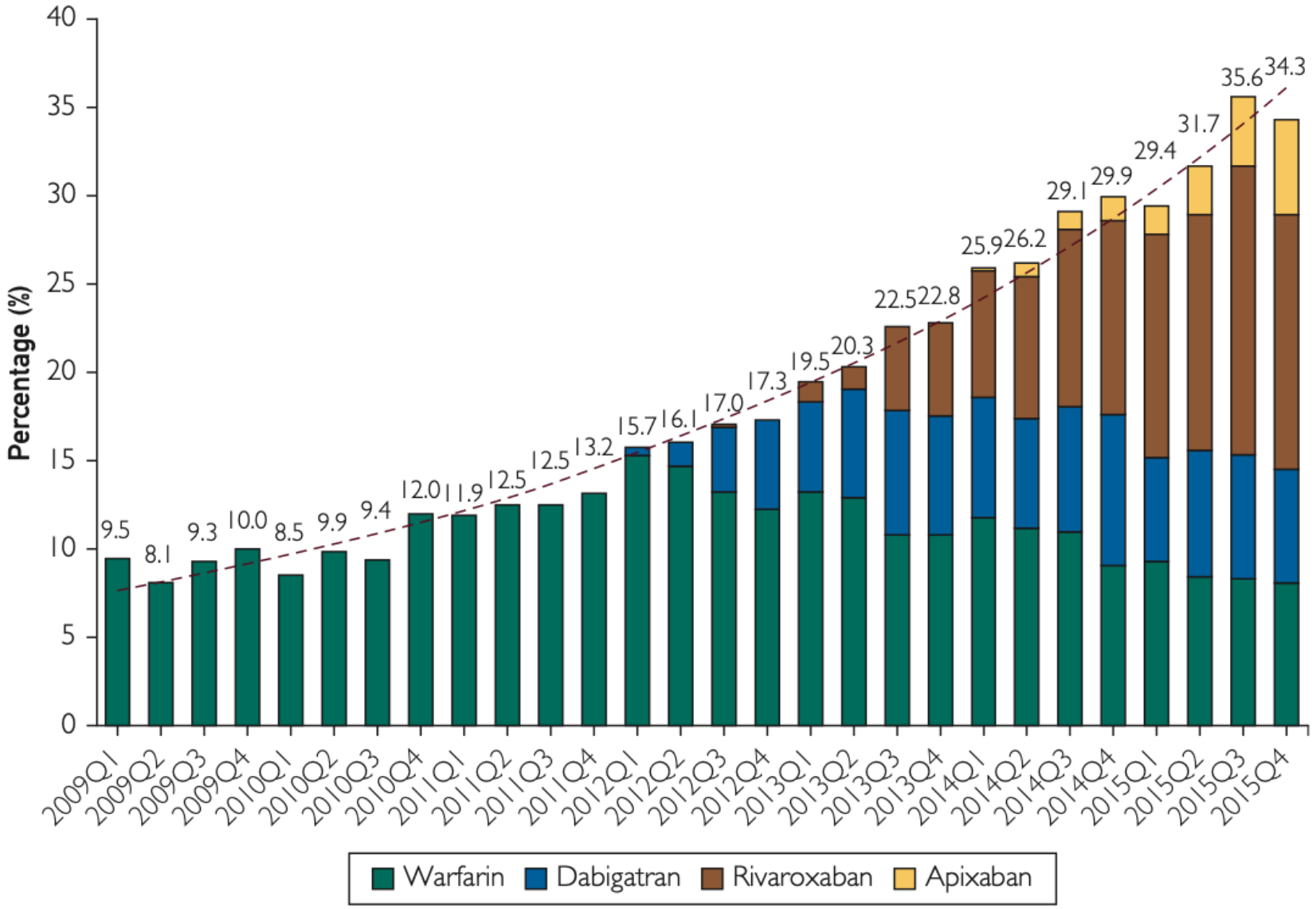


FIGURE 2. Temporal trends of the initiation rates of oral anticoagulants (OACs) among the elderly newly diagnosed atrial fibrillation (AF) patients. The initiation rates of OACs after AF was newly diagnosed in the elderly significantly increased from 9.5% to 34.3%, and is mainly due to the introduction of non–vitamin K antagonist oral anticoagulants (NOACs) (from 0% to 26.2%).

Cheng WH, et al Non-Vitamin K Antagonist Oral Anticoagulants in Elderly (≥85 years) Patients With Newly Diagnosed Atrial Fibrillation: Changing Clinical Practice and Outcomes for Stroke Prevention in a Nationwide Cohort Study. Mayo Clin Proc. 2021 Jan;96(1):52-65.

Balancing the risks of falls and bleeding against the benefits of anticoagulation of patients with AF

- Incidence of falls in community living over 65 yrs 30% in previous year and 50% for nursing home residents
- Older adults with nonvalvular AF and a history of falls 1.9 increased risk of intracranial haemorrhage but no difference between those on antiplatelets, anticoagulants and no treatment. In this analysis, patients with a CHADS2 score of 2 or higher benefited from anticoagulation *Deandrea S, et al Arch Gerontol Geriatr 2013; 56:407–4*
- In another study it was estimated that an individual would have to fall 295 times in 1 year for the risk of fall-related major bleeding to outweigh the benefit of warfarin in reducing the risk of stroke. *Gage BF et al Am J Med 2005; 118:612–617.*

How Would I Manage Case 2?

- Each patient needs an individual assessment; there can be no blanket rule including patient preference
- If severe impairment following previous stroke probably not advise anticoagulation
- I would not anticoagulate if major recent bleed
- Everyone else I would anticoagulate using direct oral anticoagulants regardless of age and falls risk. If high HAS-BLED score I would monitor anticoagulation more carefully but wouldn’t withhold

Case 3

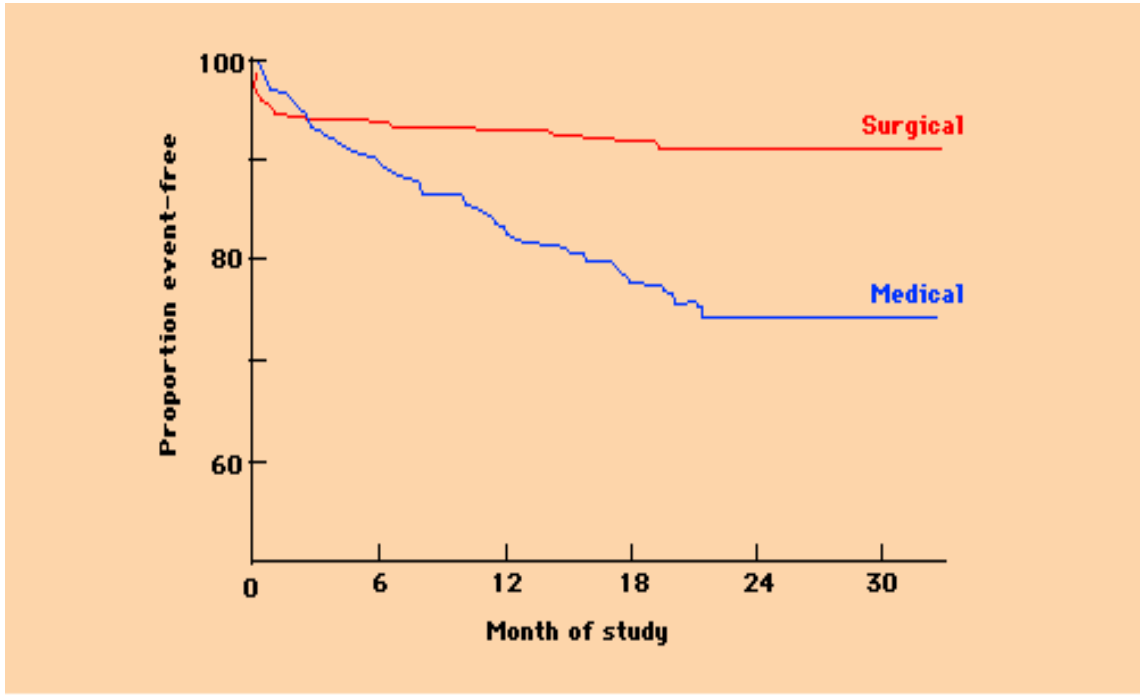
- 90 year old woman with living in a nursing home. Moderate cognitive impairment, frail but mobile with a zimmer frame. Frequent faller
- Transient weakness of right side and dysarthria
- Carotid bruit, hypertensive, total cholesterol 5.0mmol/l

Do we investigate with brain imaging, carotid imaging?

Do we treat with antiplatelets?

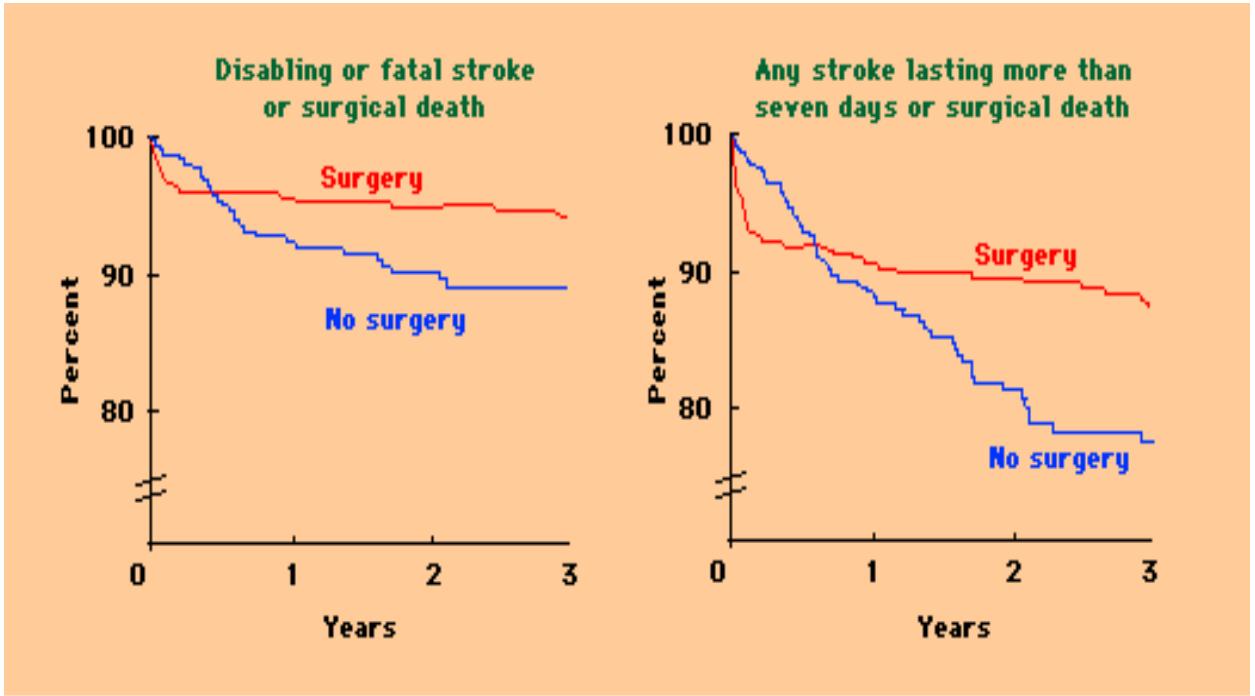
Two major trials of carotid surgery for symptomatic disease

NASCET trial: Cumulative risk of ipsilateral stroke at two years was 26% in medically treated patients and 9% in surgical patients - absolute risk reduction 17%



Ferguson GG et al The North American Symptomatic Carotid Endarterectomy Trial Surgical Results in 1415 Patients Stroke. 1999;30:1751–1758

ECST: Risk of disabling or fatal stroke was reduced in patients treated with CEA



European Carotid Surgery Trialists' Collaborative Group Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). Lancet 1998:351:1379-1387

Carotid endarterectomy or stenting

- The annual risk of stroke in individuals with symptomatic carotid stenosis about 4-12% without carotid intervention.
- Trials of carotid intervention in patients over 70 for symptomatic carotid stenosis consistently show better results for surgery vs stenting
- But risks of surgery high and numerous contraindications
- Carotid surgery trials done before introduction of high intensity medical interventions e.g. high intensity statins so benefits seen in earlier trials maybe attenuated

How Would I Manage Case 3?

- I would not do carotid endarterectomy or stenting. There are very few patients over the age 85 years that I would treat with surgery
- I would image the carotids if I wanted to treat hypertension
- No reason to do brain imaging – history clear and very unlikely to show haemorrhage
- I would treat with a statin and an antiplatelet
- I would treat hypertension very cautiously if carotid stenosis

Summary

- Patients need individual assessment preferably by neurologist working in collaboration with a geriatrician
- Little evidence to suggest that any of the major secondary prevention treatments are less effective in the very elderly
- We do need more evidence to guide management of frail, multimorbid very elderly patients

An excellent summary of the evidence

Stroke
Volume 49, Issue 3, March 2018; Pages 796-802
https://doi.org/10.1161/STROKEAHA.117.017952

TOPICAL REVIEWS

Stroke Prevention in the Very Elderly

Richard I. Lindley, MD

Stroke remains a common cause of death and disability in the very elderly (here defined as those aged 80 years and older), with about a third of all stroke occurring in this age bracket in high-income countries.[1] There is uncertainty on the exact pattern of stroke type in extreme old age, because of potential poor ascertainment of very frail and institutionalized older people in prior studies.