Carotid endarterectomy and stenting

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Disclosures

- Travel, advisory boards, consultancy: Bayer, Amgen, Claret Medical
- Investigator-initiated research grant: AstraZeneca
- Member of the International Carotid Stenting Study Group (**ICSS**)
- Steering Committee Member of the 2nd European Carotid Surgery Trial (**ECST-2**)
- Co-Principal Investigator of the 2nd Asymptomatic Carotid Surgery Trial (**ACST-2**)
- Principal Investigator of the **PRECISE-MRI** Study (ticagrelor versus aspirin in carotid artery stenting)
- Steering Committee Member of the Carotid Stenosis Trialists Collaboration (**CSTC**)

Lecture outline

Epidemiology and pathophysiology of carotid stenosis

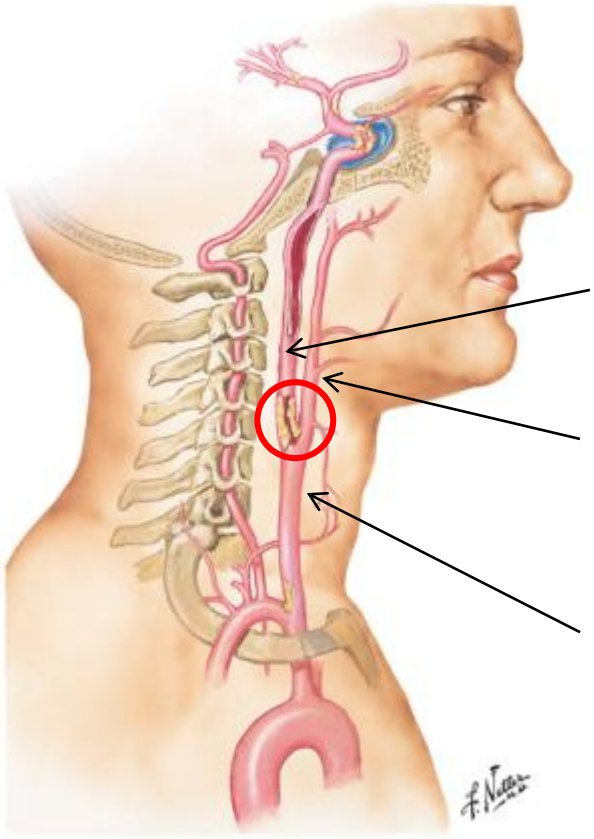
Endarterectomy and stenting for carotid stenosis

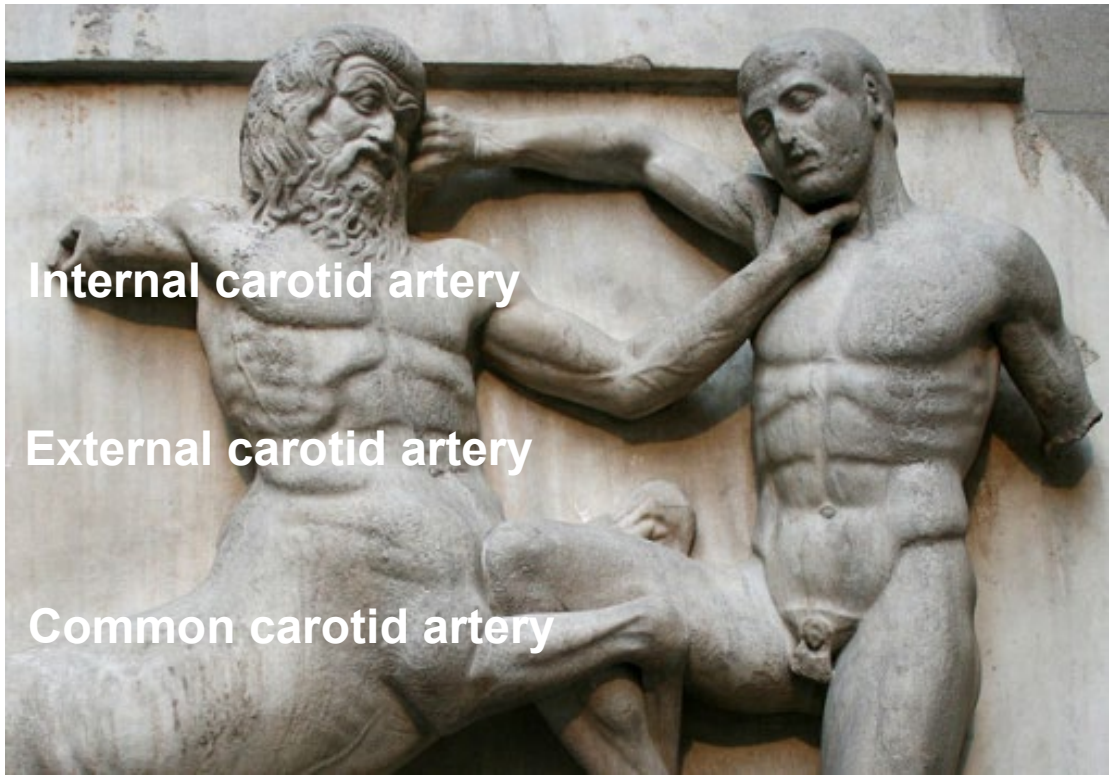
- Symptomatic carotid stenosis
- Asymptomatic carotid stenosis

Patient selection: role of plaque imaging

Management recommendations: ESO Guideline

Parthenon sculptures, 447 – 438 B.C.
The British Museum

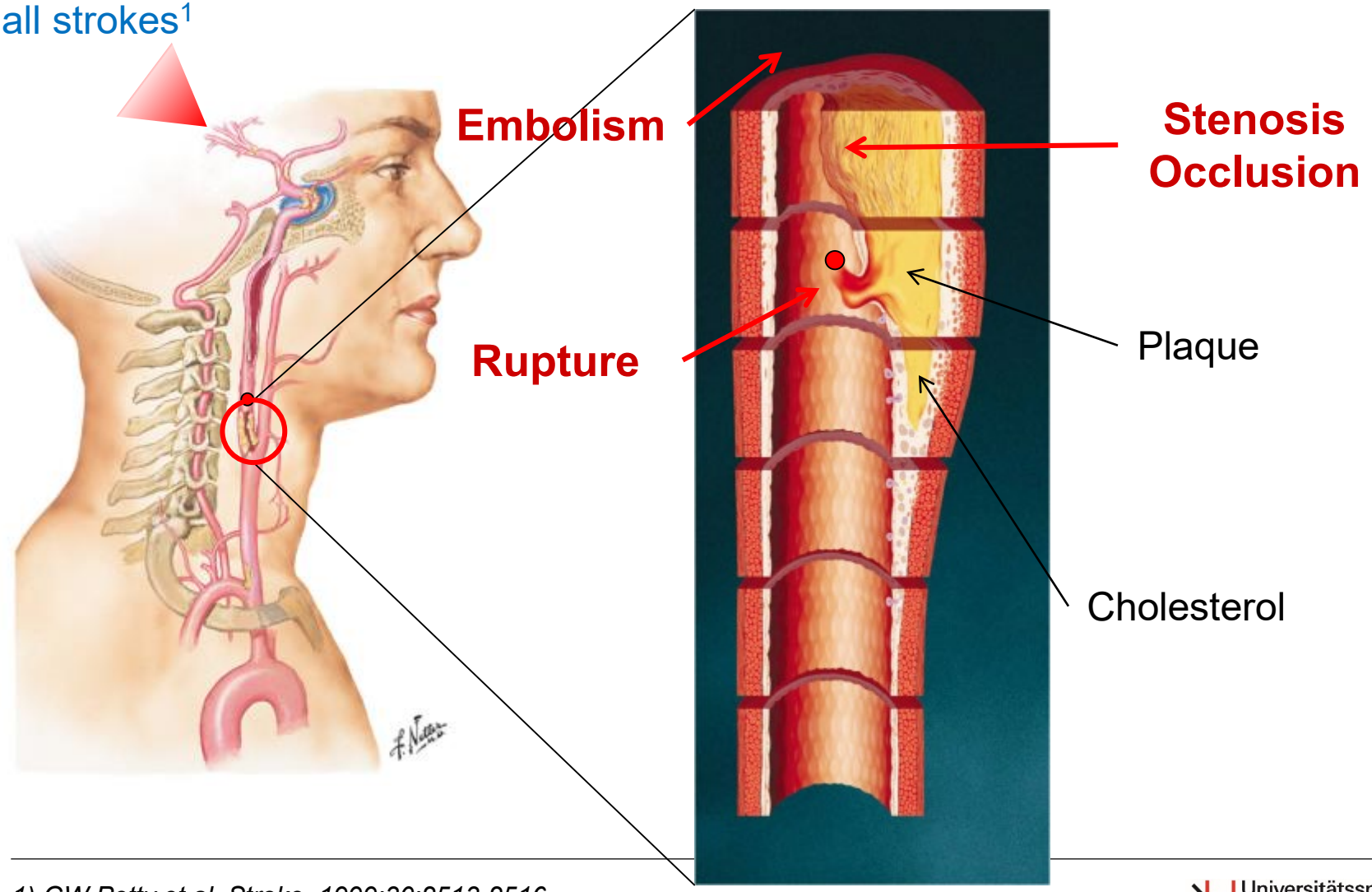




greek καρόω: *to plunge into deep sleep*

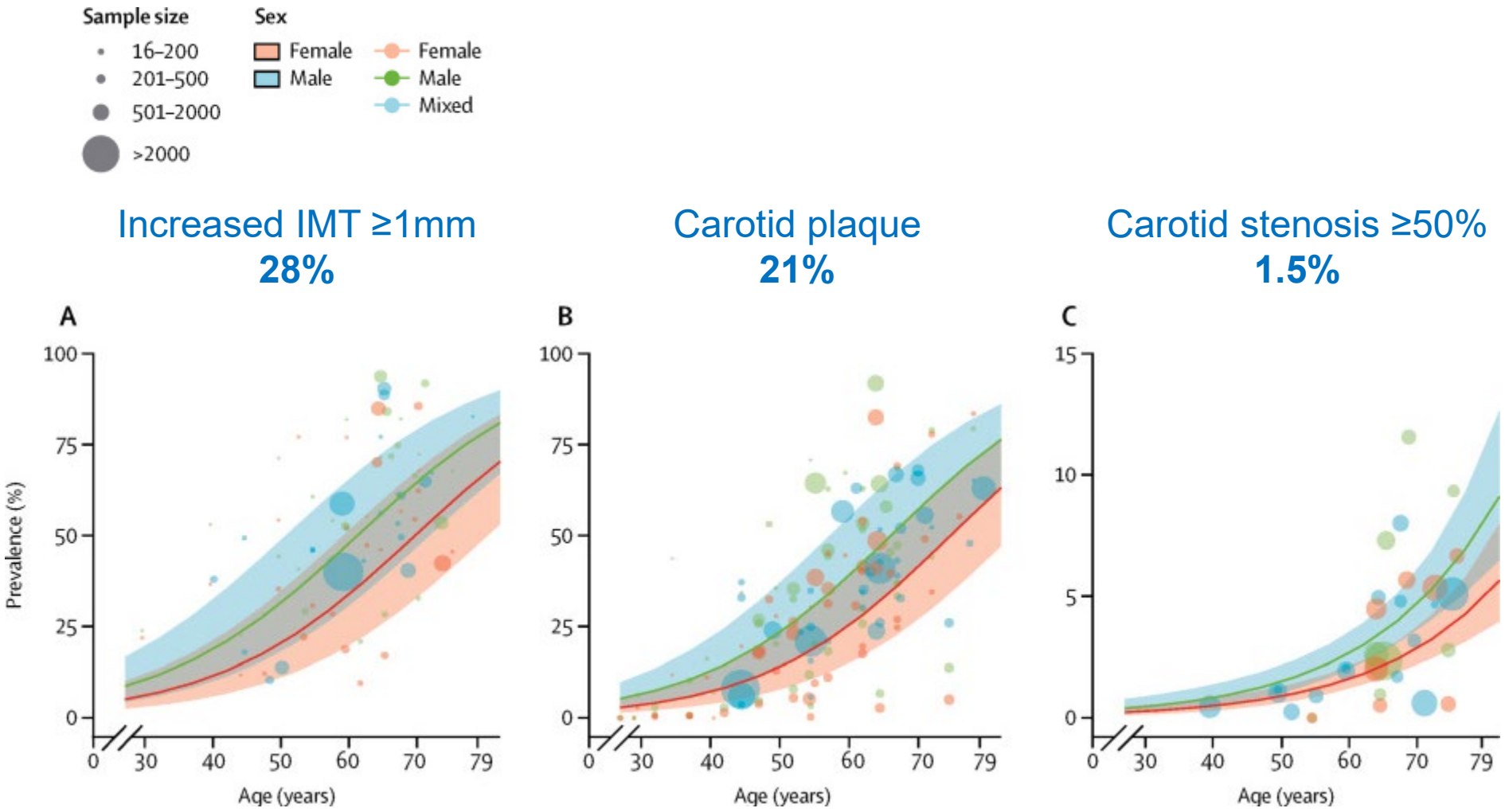
Carotid artery disease: pathophysiology and stroke mechanism

Causes about 15% of all strokes[1]



1) GW Petty et al. Stroke. 1999;30:2513-2516

Global prevalence of carotid disease in people aged 30-79 years



P Song et al., Lancet Glob Health. 2020 May;8(5):e721-e729.

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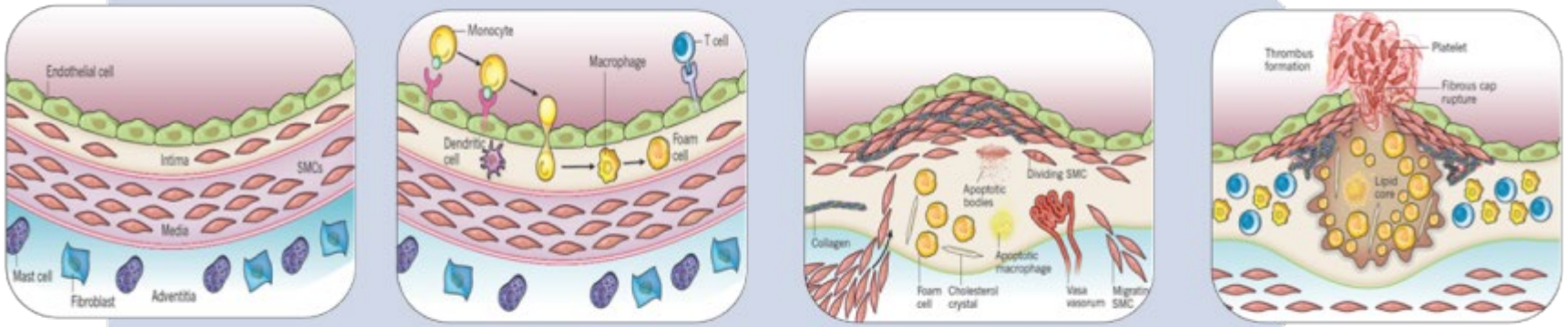
Atherosclerotic disease process

Cholesterol deposition and oxidation

Macrophage and T-cell infiltration

Cytokine and enzyme release

Plaque rupture and thrombo-embolism



Statins

Antiplatelets

Blood pressure lowering

Libby et al, Nature 2002

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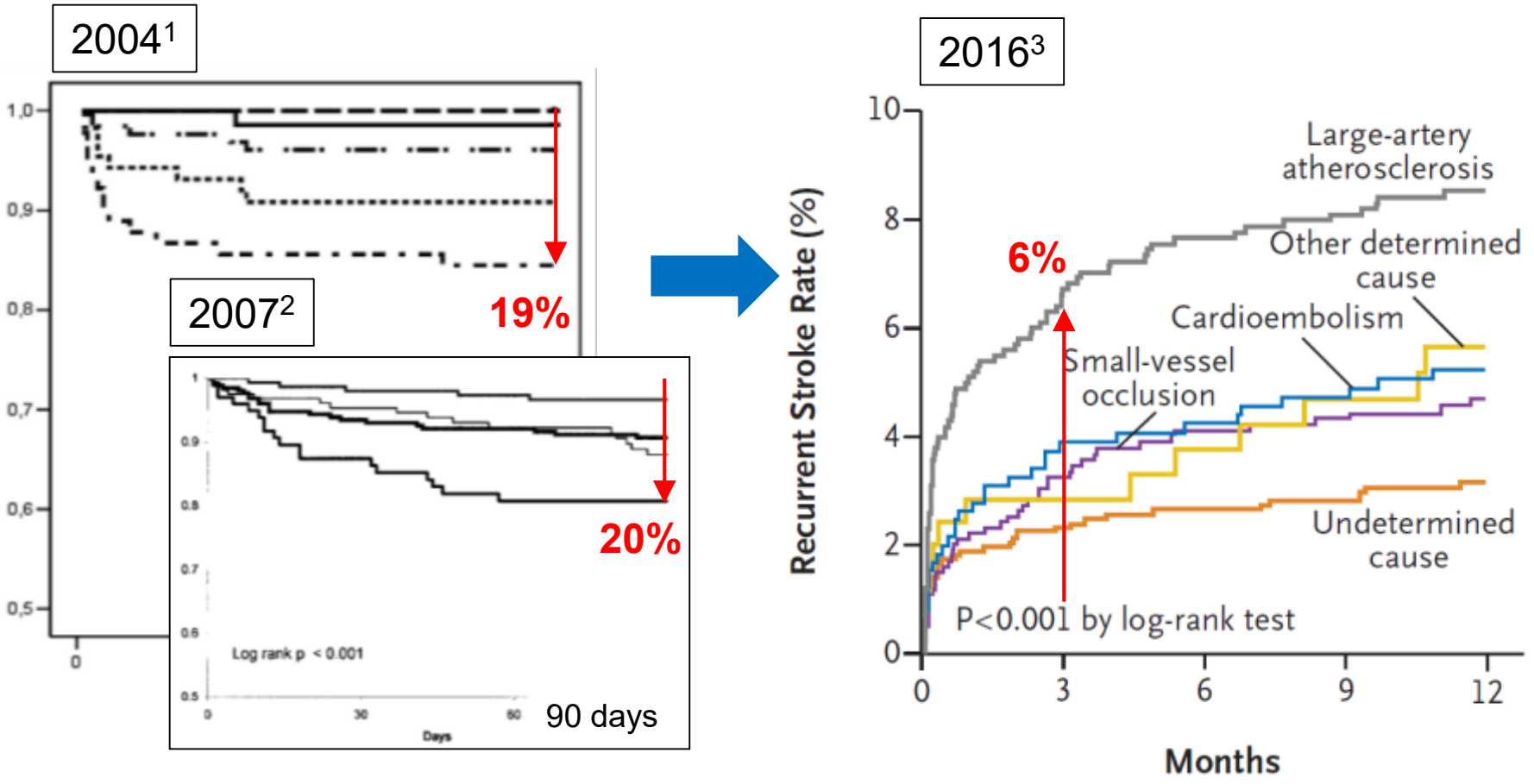
Decrease in stroke risk following TIA due to large artery atherosclerosis



[1]*Lovett et al., Neurology 2004;62:569–573;* [2]*Purroy et al., Stroke. 2007;38:3225-3229; Amarenco et al.,* [3]*TIAregistry, NEJM 374;16*

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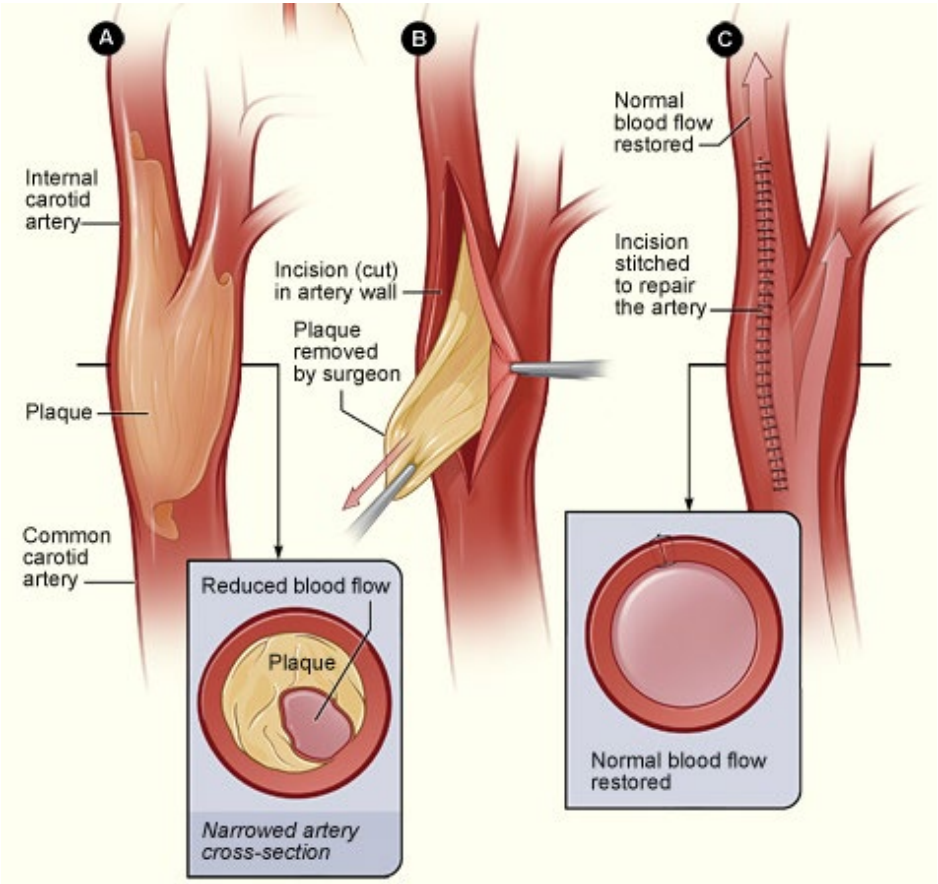
Symptomatic carotid stenosis

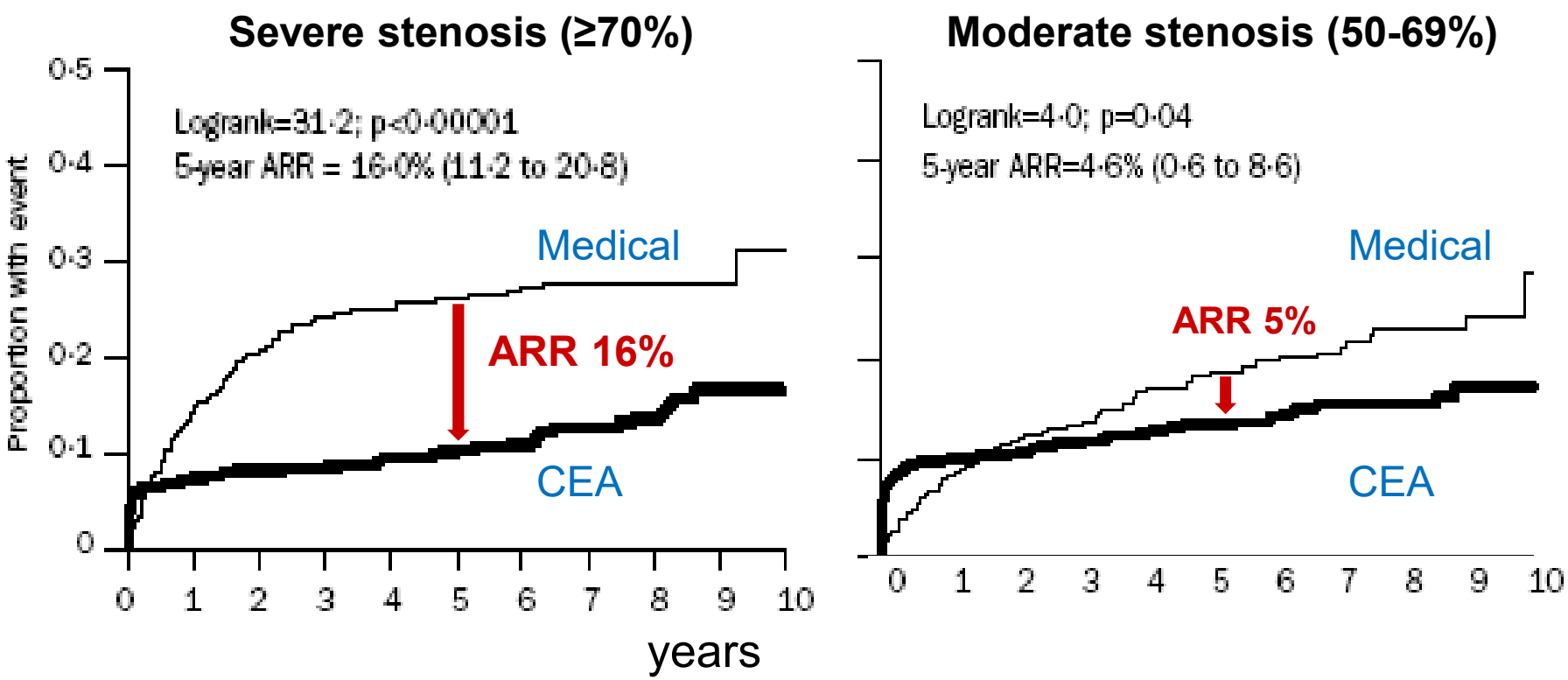
Endarterectomy versus medical therapy

Carotid endarterectomy (CEA)



Symptomatic carotid stenosis: pooled analysis of **NASCET**, **ECST** and **VA** (n=6092)

Perioperative death or stroke, or ipsilateral stroke during follow-up



Rothwell et al., Lancet 2003; 361: 107–16

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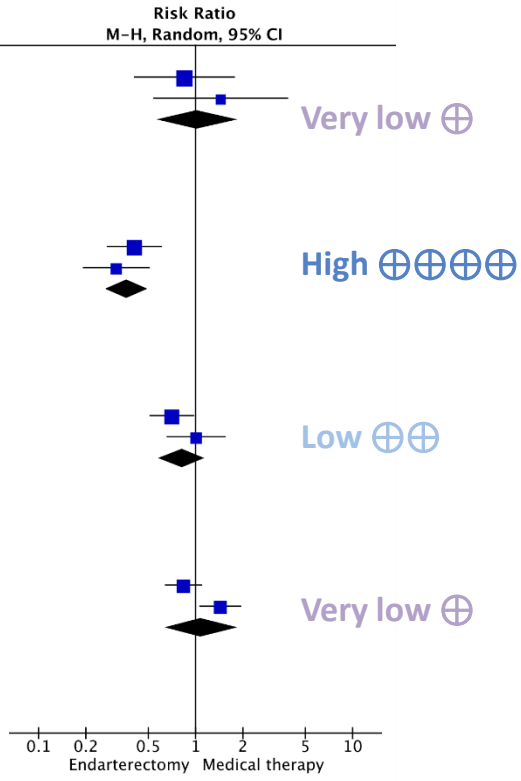
Symptomatic carotid stenosis

Endarterectomy versus medical therapy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 4.1.4)
Subgroup: severity of stenosis

Study or Subgroup	Endarterectomy Events	Endarterectomy Total	Medical therapy Events	Medical therapy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Near occlusion							
NASCET 1991	12	79	12	67	64.2%	0.85 [0.41, 1.76]	1991
ECST 1998	12	78	5	47	35.8%	1.45 [0.54, 3.85]	1998
Subtotal (95% CI)		**157**		**114**	**100.0%**	**1.03 [0.57, 1.84]**	
Total events	24		17				
Heterogeneity: Tau² = 0.00; Chi² = 0.74, df = 1 (P = 0.39); I² = 0%							
Test for overall effect: Z = 0.09 (P = 0.93)							
Severe stenosis (70-99%)							
NASCET 1991	29	261	72	264	59.6%	0.41 [0.27, 0.61]	1991
ECST 1998	21	257	45	172	40.4%	0.31 [0.19, 0.51]	1998
Subtotal (95% CI)		**518**		**436**	**100.0%**	**0.37 [0.27, 0.50]**	
Total events	50		117				
Heterogeneity: Tau² = 0.00; Chi² = 0.70, df = 1 (P = 0.40); I² = 0%							
Test for overall effect: Z = 6.45 (P < 0.00001)							
Moderate stenosis (50-69%)							
NASCET 1991	55	428	78	428	58.0%	0.71 [0.51, 0.97]	1991
ECST 1998	46	380	32	266	42.0%	1.01 [0.66, 1.54]	1998
Subtotal (95% CI)		**808**		**694**	**100.0%**	**0.82 [0.58, 1.15]**	
Total events	101		110				
Heterogeneity: Tau² = 0.03; Chi² = 1.73, df = 1 (P = 0.19); I² = 42%							
Test for overall effect: Z = 1.14 (P = 0.25)							
Mild stenosis (<50%)							
NASCET 1991	87	677	106	690	50.8%	0.84 [0.64, 1.09]	1991
ECST 1998	125	1085	58	723	49.2%	1.44 [1.07, 1.93]	1998
Subtotal (95% CI)		**1762**		**1413**	**100.0%**	**1.09 [0.64, 1.85]**	
Total events	212		164				
Heterogeneity: Tau² = 0.13; Chi² = 7.15, df = 1 (P = 0.007); I² = 86%							
Test for overall effect: Z = 0.32 (P = 0.75)							

Test for subgroup differences: Chi² = 21.16, df = 3 (P < 0.0001), I² = 85.8%



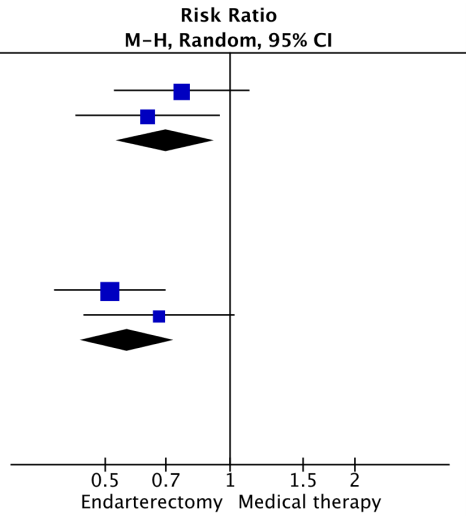
Symptomatic carotid stenosis

Endarterectomy versus medical therapy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 4.1.1)
Subgroup: age

Study or Subgroup	Endarterectomy Events	Endarterectomy Total	Medical therapy Events	Medical therapy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
< 65 years							
NASCET 1991	46	346	48	276	53.2%	0.76 [0.53, 1.11]	1991
ECST 1998	40	385	45	274	46.8%	0.63 [0.43, 0.94]	1998
Subtotal (95% CI)		**731**		**550**	**100.0%**	**0.70 [0.53, 0.92]**	
Total events	86		93				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.47$, df = 1 (P = 0.50); $I^2 = 0\%$							
Test for overall effect: Z = 2.58 (P = 0.010)							
≥ 65 years							
NASCET 1991	50	413	114	483	63.8%	0.51 [0.38, 0.70]	1991
ECST 1998	39	330	37	211	36.2%	0.67 [0.44, 1.02]	1998
Subtotal (95% CI)		**743**		**694**	**100.0%**	**0.57 [0.44, 0.73]**	
Total events	89		151				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 1.08$, df = 1 (P = 0.30); $I^2 = 7\%$							
Test for overall effect: Z = 4.33 (P < 0.0001)							

Test for subgroup differences: $Chi^2 = 1.23$, df = 1 (P = 0.27), $I^2 = 18.6\%$



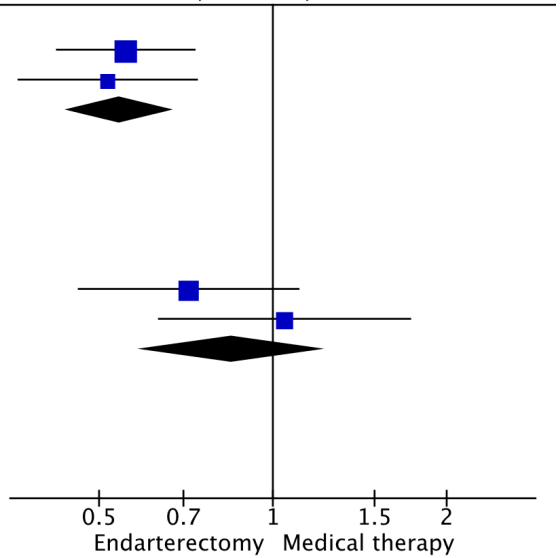
Symptomatic carotid stenosis

Endarterectomy versus medical therapy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 4.1.2)
Subgroup: sex

Study or Subgroup	Endarterectomy Events	Endarterectomy Total	Medical therapy Events	Medical therapy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Men							
NASCET 1991	65	509	124	540	62.7%	0.56 [0.42, 0.73]	1991
ECST 1998	47	504	60	333	37.3%	0.52 [0.36, 0.74]	1998
Subtotal (95% CI)		**1013**		**873**	**100.0%**	**0.54 [0.44, 0.67]**	
Total events	112		184				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.10$, df = 1 (P = 0.75); $I^2 = 0\%$							
Test for overall effect: Z = 5.53 (P < 0.00001)							
Women							
NASCET 1991	31	250	38	219	55.3%	0.71 [0.46, 1.11]	1991
ECST 1998	32	211	22	152	44.7%	1.05 [0.63, 1.73]	1998
Subtotal (95% CI)		**461**		**371**	**100.0%**	**0.85 [0.58, 1.23]**	
Total events	63		60				
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 1.27$, df = 1 (P = 0.26); $I^2 = 21\%$							
Test for overall effect: Z = 0.87 (P = 0.39)							

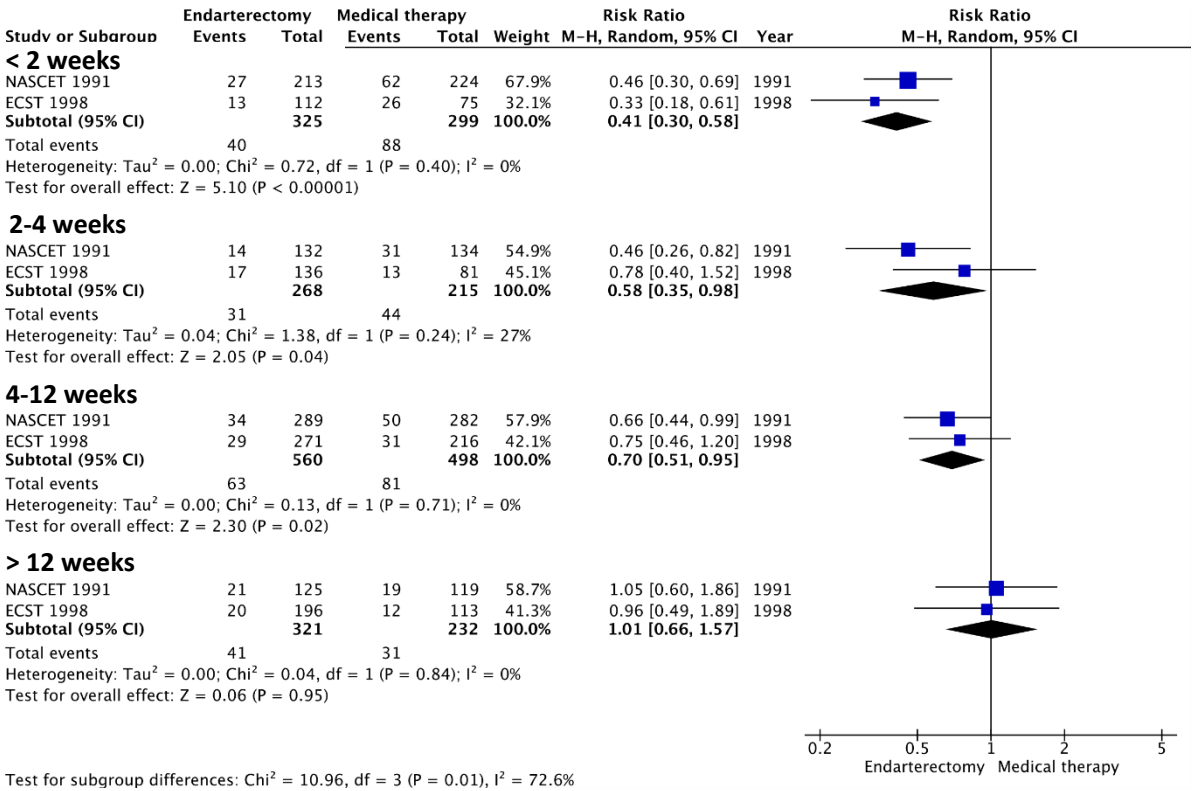
Test for subgroup differences: $Chi^2 = 4.15$, df = 1 (P = 0.04), $I^2 = 75.9\%$



Symptomatic carotid stenosis

Endarterectomy versus medical therapy

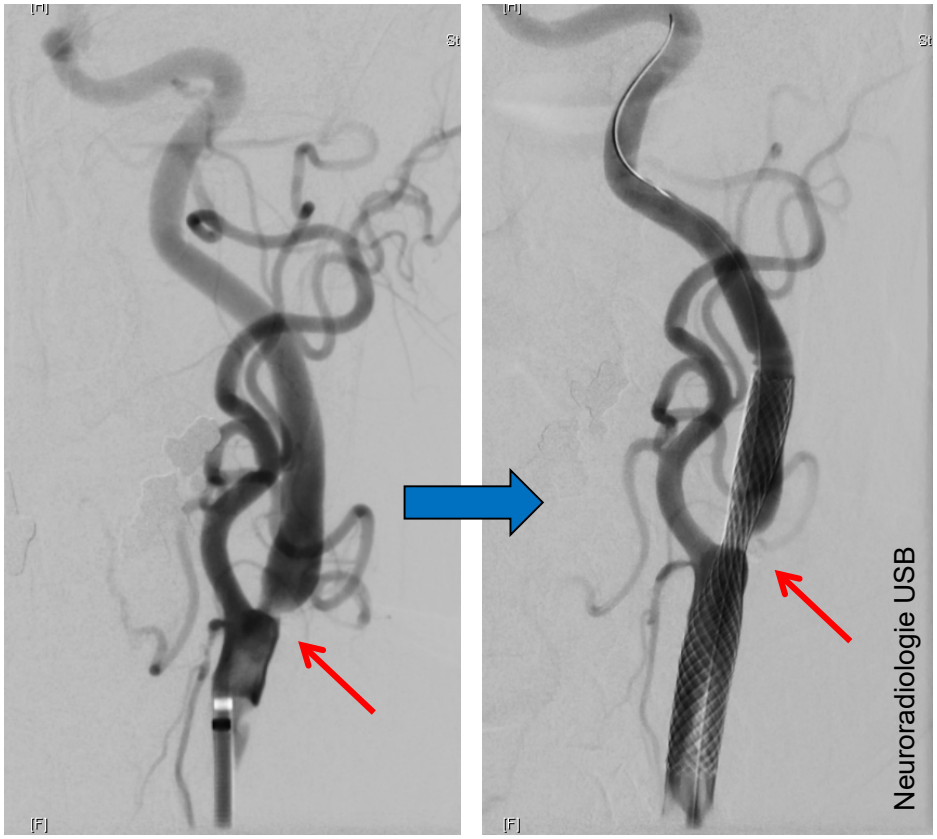
Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 4.1.3)
Subgroup: time since most recent event

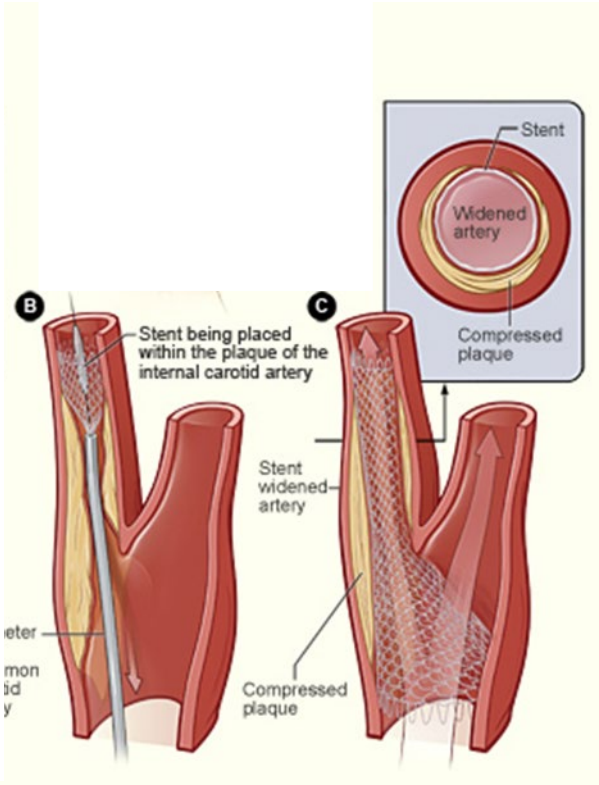


Symptomatic carotid stenosis

Stenting versus endarterectomy

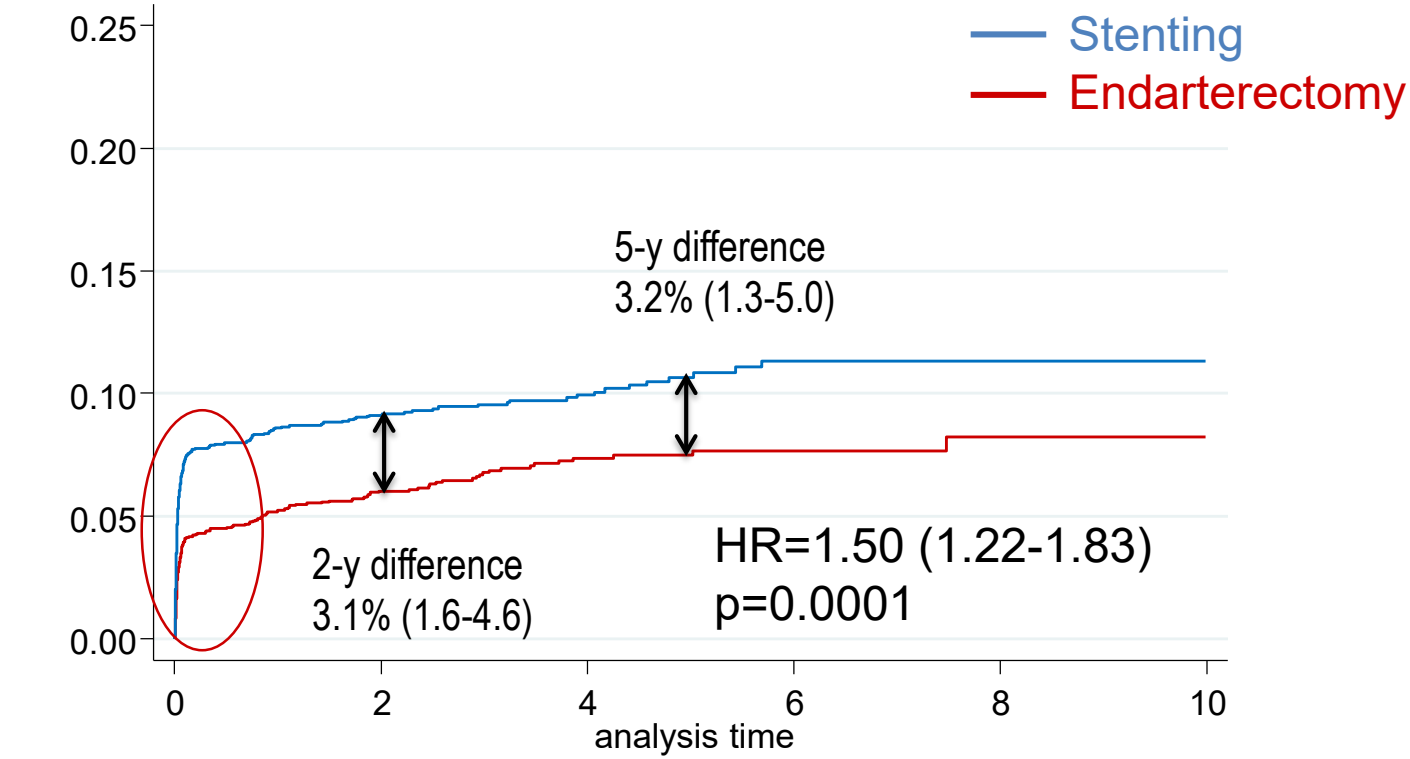
Carotid artery stenting (CAS)





Carotid Stenosis Trialists Collaboration: symptomatic stenosis **EVA-3S**, **SPACE**, **ICSS** and **CREST** (n=4754)

Procedural stroke or death or ipsilateral stroke during follow-up



No. at risk

CEA	2361	1771	811	313	113	28
CAS	2393	1755	801	323	122	24

Symptomatic carotid stenosis

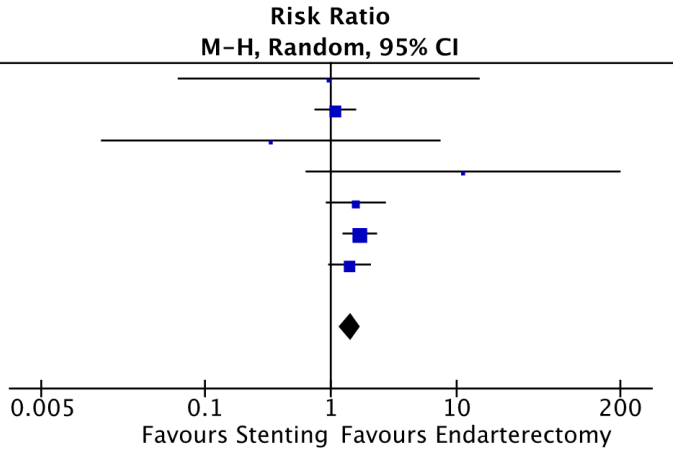
Stenting versus endarterectomy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 6.1)

	Stenting		Endarterectomy			Risk Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
Kentucky 2001	1	53	1	51	0.5%	0.96 [0.06, 14.98]	2001
SPACE 2008	56	607	50	589	25.6%	1.09 [0.76, 1.56]	2008
BACASS 2008	0	10	1	10	0.4%	0.33 [0.02, 7.32]	2008
Regensburg 2008	5	43	0	44	0.5%	11.25 [0.64, 197.44]	2008
EVA-3S 2014	32	265	20	262	13.2%	1.58 [0.93, 2.69]	2014
ICSS 2015	105	853	62	857	35.2%	1.70 [1.26, 2.30]	2015
CREST 2016	62	668	43	653	24.5%	1.41 [0.97, 2.05]	2016
Total (95% CI)		**2499**		**2466**	**100.0%**	**1.43 [1.17, 1.75]**	
Total events	261		177				

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 6.56$, df = 6 (P = 0.36); $I^2 = 8\%$

Test for overall effect: Z = 3.50 (P = 0.0005)



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Symptomatic carotid stenosis

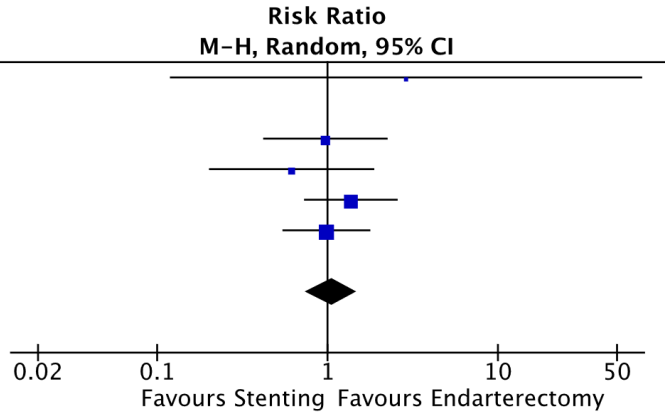
Stenting versus endarterectomy

Post-procedural ipsilateral stroke (PICO 6.2)

Study or Subgroup	Stenting Events	Stenting Total	Endarterectomy Events	Endarterectomy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kentucky 2001	1	53	0	51	1.2%	2.89 [0.12, 69.32]	2001
BACASS 2008	0	9	0	10		Not estimable	2008
SPACE 2008	11	601	11	584	18.4%	0.97 [0.42, 2.22]	2008
EVA-3S 2014	5	263	8	259	10.3%	0.62 [0.20, 1.86]	2014
ICSS 2015	23	842	17	853	32.8%	1.37 [0.74, 2.55]	2015
CREST 2016	22	661	22	651	37.3%	0.98 [0.55, 1.76]	2016
Total (95% CI)		**2429**		**2408**	**100.0%**	**1.06 [0.74, 1.51]**	
Total events	62		58				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.08$, df = 4 (P = 0.72); $I^2 = 0\%$

Test for overall effect: Z = 0.31 (P = 0.76)



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Symptomatic carotid stenosis

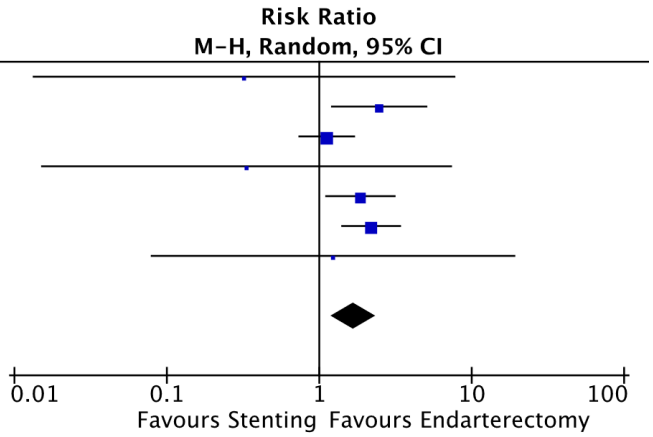
Stenting versus endarterectomy

Peri-procedural stroke or death (PICO 6.9)

Study or Subgroup	Favours Stenting Events	Total	Endarterectomy Events	Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kentucky 2001	0	53	1	51	1.1%	0.32 [0.01, 7.70]	2001
EVA-3S 2006	25	265	10	262	15.5%	2.47 [1.21, 5.04]	2006
SPACE 2006	45	607	39	589	29.5%	1.12 [0.74, 1.69]	2006
BACASS 2008	0	10	1	10	1.1%	0.33 [0.02, 7.32]	2008
CREST 2010	40	668	21	653	23.4%	1.86 [1.11, 3.12]	2010
ICSS 2010	61	853	28	857	28.0%	2.19 [1.41, 3.39]	2010
Ostrava 2014	1	39	1	48	1.4%	1.23 [0.08, 19.05]	2014
Total (95% CI)		**2495**		**2470**	**100.0%**	**1.68 [1.20, 2.34]**	
Total events	172		101				

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 8.52$, df = 6 (P = 0.20); $I^2 = 30\%$

Test for overall effect: Z = 3.05 (P = 0.002)



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Symptomatic carotid stenosis

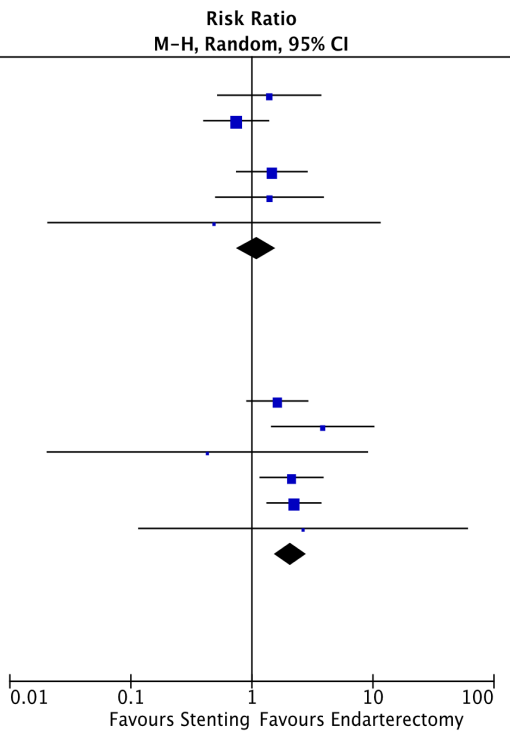
Stenting versus endarterectomy

Peri-procedural stroke or death (PICO 6.9.1)

Subgroup: Age

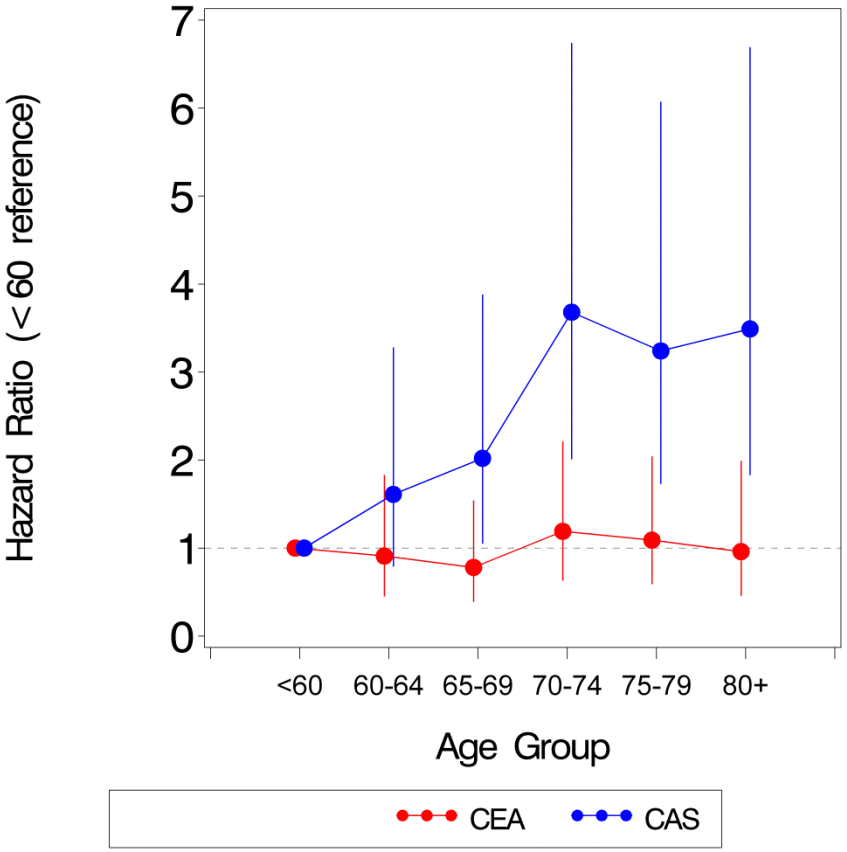
Study or Subgroup	Stenting Events	Stenting Total	Endarterectomy Events	Endarterectomy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
<70 years							
EVA-3S 2006	10	127	6	106	14.9%	1.39 [0.52, 3.70]	2006
SPACE 2006	17	347	22	333	37.9%	0.74 [0.40, 1.37]	2006
BACASS 2008	0	4	0	2		Not estimable	2008
ICSS 2010	20	395	14	404	32.0%	1.46 [0.75, 2.85]	2010
CREST 2010	9	351	6	327	13.7%	1.40 [0.50, 3.88]	2010
Ostrava 2014	0	23	1	34	1.4%	0.49 [0.02, 11.44]	2014
Subtotal (95% CI)		**1247**		**1206**	**100.0%**	**1.10 [0.75, 1.60]**	
Total events	56		49				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.96$, df = 4 (P = 0.56); $I^2 = 0\%$							
Test for overall effect: Z = 0.48 (P = 0.63)							
≥ 70 years							
SPACE 2006	28	260	17	256	27.5%	1.62 [0.91, 2.89]	2006
EVA-3S 2006	17	138	5	156	9.7%	3.84 [1.46, 10.14]	2006
BACASS 2008	0	6	1	8	1.0%	0.43 [0.02, 9.00]	2008
CREST 2010	31	317	15	326	25.7%	2.13 [1.17, 3.86]	2010
ICSS 2010	45	458	20	453	35.2%	2.23 [1.34, 3.71]	2010
Ostrava 2014	1	16	0	14	0.9%	2.65 [0.12, 60.21]	2014
Subtotal (95% CI)		**1195**		**1213**	**100.0%**	**2.10 [1.55, 2.84]**	
Total events	122		58				
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.38$, df = 5 (P = 0.64); $I^2 = 0\%$							
Test for overall effect: Z = 4.79 (P < 0.00001)							

Test for subgroup differences: $Chi^2 = 6.84$, df = 1 (P = 0.009), $I^2 = 85.4\%$

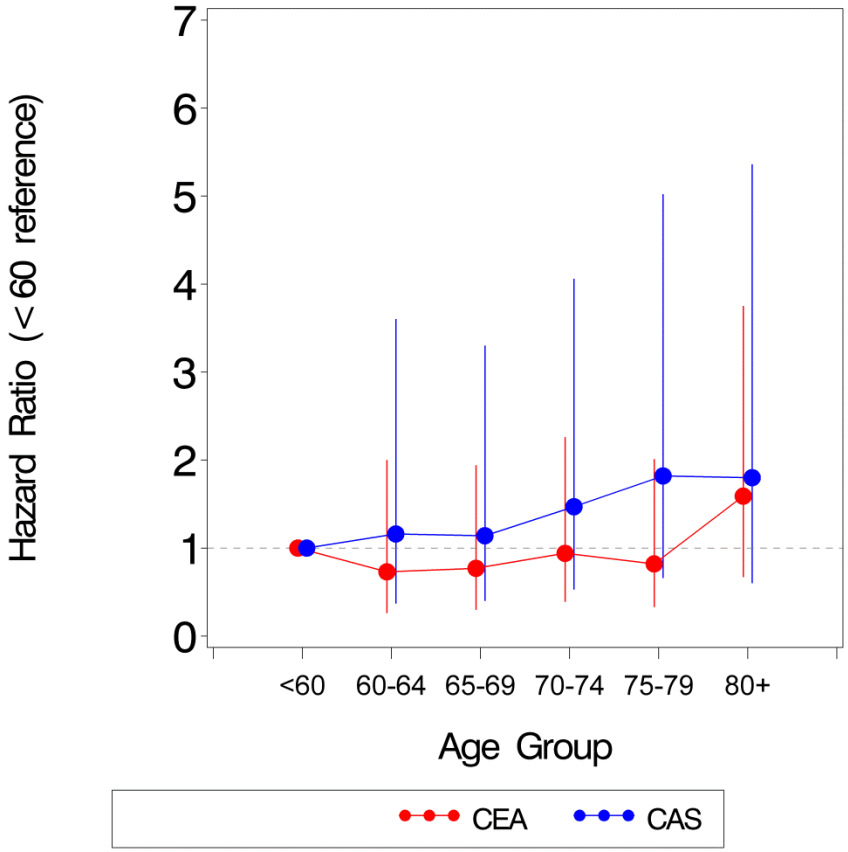


Symptomatic carotid stenosis: impact of **age** in the peri-procedural and post-procedural period (n=4754)

Peri-procedural stroke or death



Post-procedural ipsilateral stroke



G. Howard et al., Carotid Stenosis Trialists' Collaboration. Lancet 2016; 387: 1305–11

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Symptomatic carotid stenosis

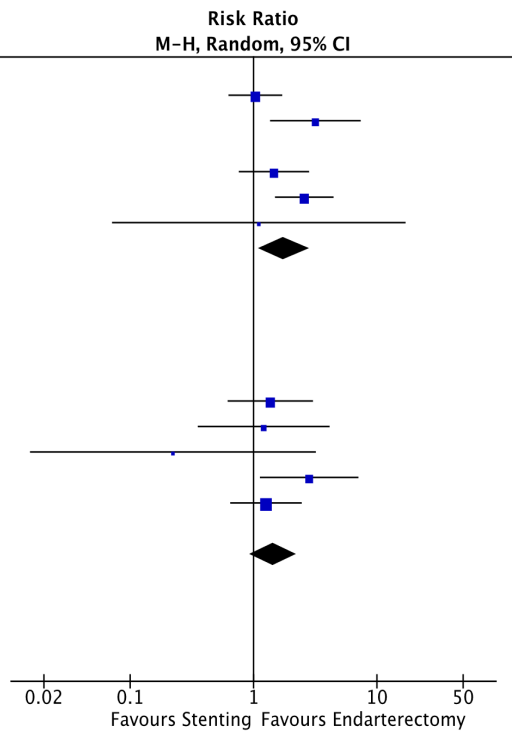
Stenting versus endarterectomy

Peri-procedural stroke or death (PICO 6.9.2)

Subgroup: Sex

Study or Subgroup	Stenting Events	Stenting Total	Endarterectomy Events	Endarterectomy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Men							
SPACE 2006	31	436	29	422	28.5%	1.03 [0.63, 1.69]	2006
EVA-3S 2006	21	193	7	204	18.2%	3.17 [1.38, 7.29]	2006
BACASS 2008	0	8	0	9		Not estimable	2008
CREST 2010	22	428	15	427	23.4%	1.46 [0.77, 2.78]	2010
ICSS 2010	46	601	18	606	27.0%	2.58 [1.51, 4.39]	2010
Ostrava 2014	1	29	1	32	2.9%	1.10 [0.07, 16.85]	2014
Subtotal (95% CI)		**1695**		**1700**	**100.0%**	**1.76 [1.09, 2.85]**	
Total events	121		70				
Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 8.80$, df = 4 (P = 0.07); $I^2 = 55\%$							
Test for overall effect: Z = 2.32 (P = 0.02)							
Women							
SPACE 2006	14	171	10	167	27.2%	1.37 [0.62, 2.99]	2006
EVA-3S 2006	6	72	4	58	12.0%	1.21 [0.36, 4.08]	2006
BACASS 2008	0	2	1	1	2.6%	0.22 [0.02, 3.16]	2008
CREST 2010	18	240	6	226	20.9%	2.83 [1.14, 6.99]	2010
ICSS 2010	19	252	15	251	37.3%	1.26 [0.66, 2.43]	2010
Ostrava 2014	0	10	0	16		Not estimable	2014
Subtotal (95% CI)		**747**		**719**	**100.0%**	**1.45 [0.94, 2.23]**	
Total events	57		36				
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 4.30$, df = 4 (P = 0.37); $I^2 = 7\%$							
Test for overall effect: Z = 1.69 (P = 0.09)							

Test for subgroup differences: $Chi^2 = 0.35$, df = 1 (P = 0.55), $I^2 = 0\%$



Symptomatic carotid stenosis

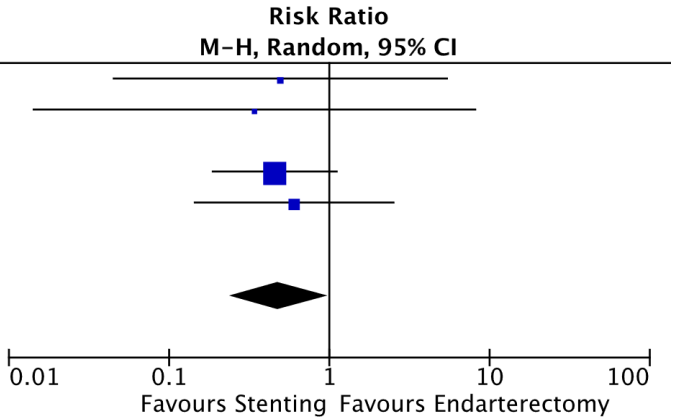
Stenting versus endarterectomy

Peri-procedural myocardial infarction (PICO 6.11)

Study or Subgroup	Stenting Events	Stenting Total	Endarterectomy Events	Endarterectomy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
EVA-3S 2006	1	265	2	262	8.6%	0.49 [0.05, 5.42]	2006
Regensburg 2008	0	43	1	44	4.9%	0.34 [0.01, 8.14]	2008
BACASS 2008	0	10	0	10		Not estimable	2008
CREST 2010	7	668	15	653	62.3%	0.46 [0.19, 1.11]	2010
ICSS 2010	3	853	5	857	24.2%	0.60 [0.14, 2.51]	2010
Ostrava 2014	0	39	0	48		Not estimable	2014
Total (95% CI)		**1878**		**1874**	**100.0%**	**0.48 [0.24, 0.98]**	
Total events	11		23				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.15$, df = 3 (P = 0.98); $I^2 = 0\%$

Test for overall effect: Z = 2.02 (P = 0.04)



Quality: Moderate ⊕⊕⊕
(Indirectness, imprecision)

Symptomatic carotid stenosis

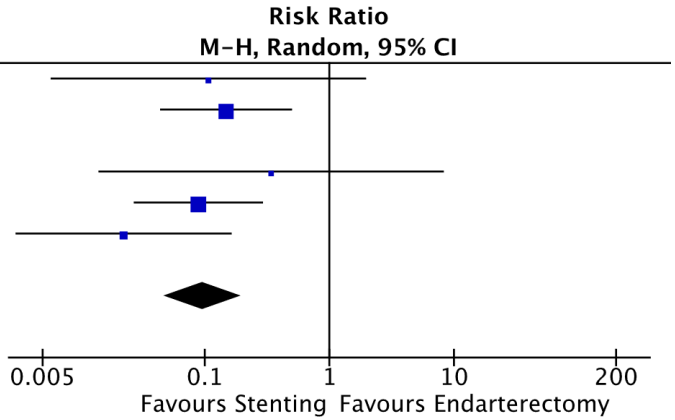
Stenting versus endarterectomy

Peri-procedural cranial nerve injury (PICO 6.12)

Study or Subgroup	Stenting Events	Stenting Total	Endarterectomy Events	Endarterectomy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kentucky 2001	0	53	4	51	6.3%	0.11 [0.01, 1.94]	2001
EVA-3S 2006	3	265	20	262	36.7%	0.15 [0.04, 0.49]	2006
BACASS 2008	0	10	0	10		Not estimable	2008
Regensburg 2008	0	43	1	44	5.3%	0.34 [0.01, 8.14]	2008
CREST 2010	3	668	33	653	38.2%	0.09 [0.03, 0.29]	2010
ICSS 2010	1	853	45	857	13.5%	0.02 [0.00, 0.16]	2010
Total (95% CI)		**1892**		**1877**	**100.0%**	**0.10 [0.05, 0.20]**	
Total events	7		103				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.64$, df = 4 (P = 0.46); $I^2 = 0\%$

Test for overall effect: Z = 6.29 (P < 0.00001)



Quality: High ⊕⊕⊕⊕

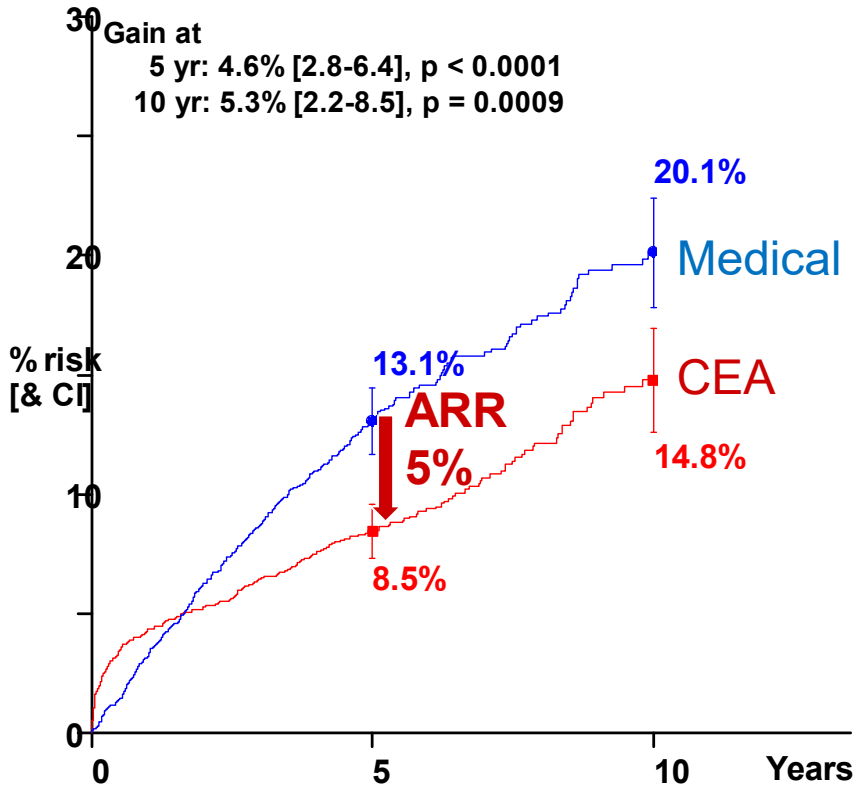
Asymptomatic carotid stenosis

Endarterectomy versus medical therapy

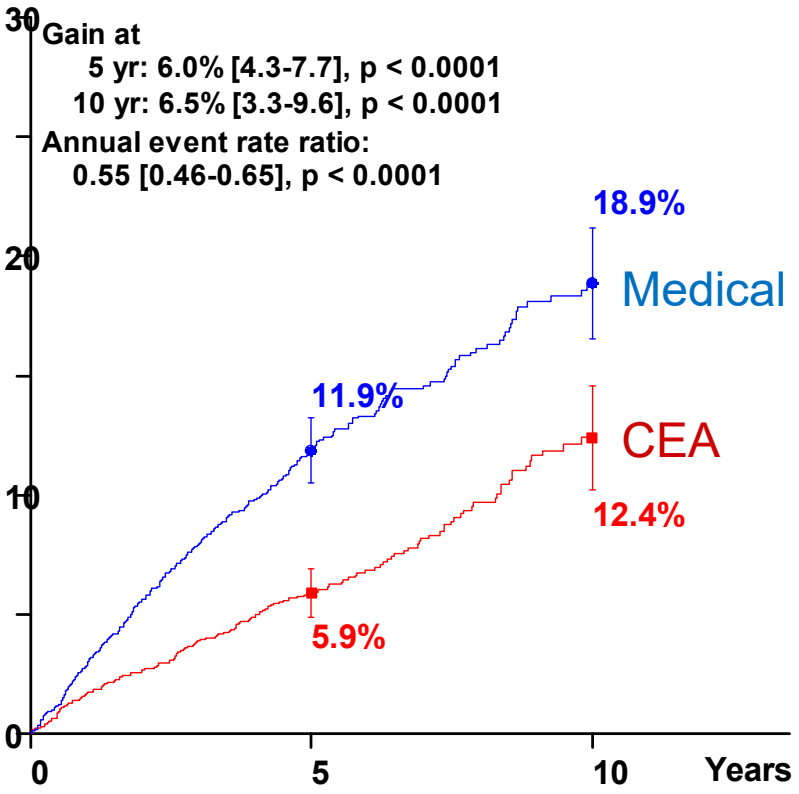
Asymptomatic carotid stenosis: pooled analysis of **VA**, **ACAS** and **ACST** (n=5226)

>60% stenosis

Any stroke or perioperative death



Any non−perioperative stroke



A Halliday et al. Submitted.

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Asymptomatic carotid stenosis

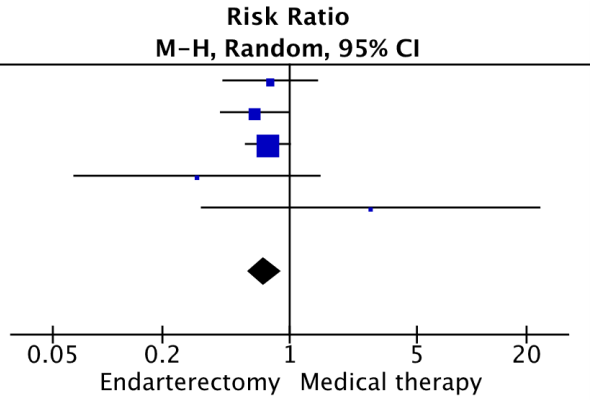
Endarterectomy versus medical therapy

Long-term ipsilateral stroke or peri-procedural stroke or death (PCIO 1.1)

	Endarterectomy		Medical therapy			Risk Ratio	
Study or Subgroup	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**	**Year**
VA 1993	17	211	24	233	13.0%	0.78 [0.43, 1.41]	1993
ACAS 1995	33	825	52	834	25.2%	0.64 [0.42, 0.98]	1995
ACST 1 2010	82	1560	108	1560	58.9%	0.76 [0.57, 1.00]	2010
AMTEC 2015	2	31	5	24	1.9%	0.31 [0.07, 1.46]	2015
SPACE-2 2019	5	203	1	113	1.0%	2.78 [0.33, 23.53]	2020
Total (95% CI)		**2830**		**2764**	**100.0%**	**0.73 [0.59, 0.90]**	
Total events	139		190				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.17$, df = 4 (P = 0.53); $I^2 = 0\%$

Test for overall effect: Z = 2.92 (P = 0.004)



Quality: Moderate ⊕⊕⊕
(Indirectness)

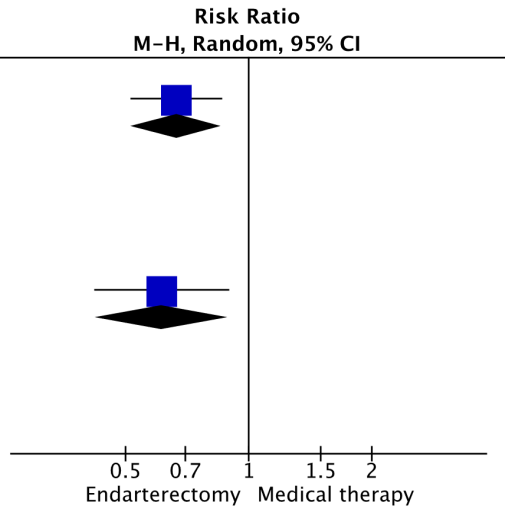
Asymptomatic carotid stenosis

Endarterectomy versus medical therapy

Long-term stroke in <u>any</u> territory or peri-procedural death (PICO 1.2.1)
Subgroup: Sex

Study or Subgroup	Endarterectomy Events	Endarterectomy Total	Medical therapy Events	Medical therapy Total	Weight	Risk Ratio M-H, Random, 95% CI
Men						
ACST 1 2010	89	1021	134	1023	100.0%	0.67 [0.52, 0.86]
Subtotal (95% CI)		**1021**		**1023**	**100.0%**	**0.67 [0.52, 0.86]**
Total events	89		134			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.15 (P = 0.002)						
Women						
ACST 1 2010	40	539	65	537	100.0%	0.61 [0.42, 0.89]
Subtotal (95% CI)		**539**		**537**	**100.0%**	**0.61 [0.42, 0.89]**
Total events	40		65			
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.55 (P = 0.01)						

Test for subgroup differences: $Chi^2 = 0.13$, df = 1 (P = 0.72), $I^2 = 0\%$

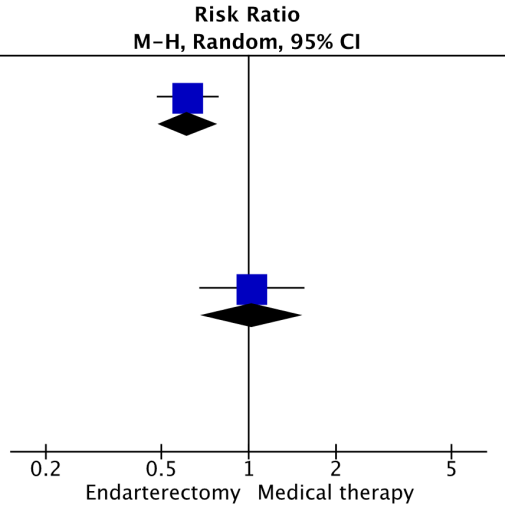


Asymptomatic carotid stenosis

Endarterectomy versus medical therapy

Long-term stroke in any territory or peri-procedural death (PICO 1.2.2)
Subgroup: Age

Study or Subgroup	Endarterectomy Events	Endarterectomy Total	Medical therapy Events	Medical therapy Total	Weight	Risk Ratio M-H, Random, 95% CI
< 75 years						
ACST 1 2010	98	1231	160	1239	100.0%	0.62 [0.49, 0.78]
Subtotal (95% CI)		**1231**		**1239**	**100.0%**	**0.62 [0.49, 0.78]**
Total events	98		160			
Heterogeneity: Not applicable						
Test for overall effect: Z = 3.97 (P < 0.0001)						
≥ 75 years						
ACST 1 2010	41	329	39	321	100.0%	1.03 [0.68, 1.55]
Subtotal (95% CI)		**329**		**321**	**100.0%**	**1.03 [0.68, 1.55]**
Total events	41		39			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.12 (P = 0.90)						



Test for subgroup differences: $Chi^2 = 4.41$, df = 1 (P = 0.04), $I^2 = 77.3\%$

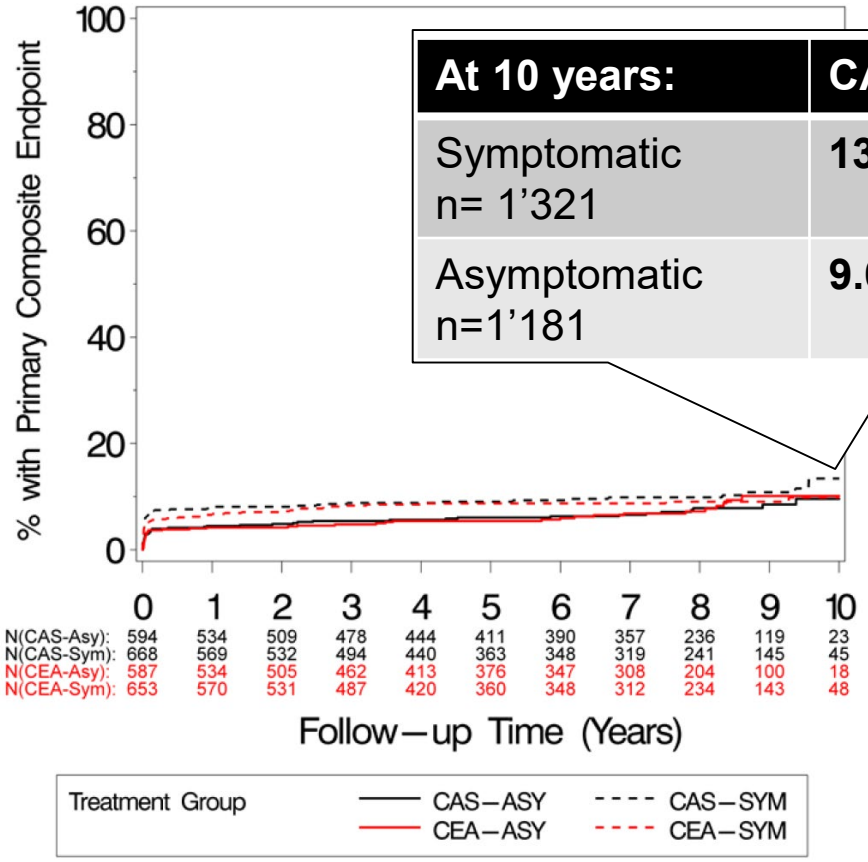
Asymptomatic carotid stenosis

Stenting versus endarterectomy

CREST: stenting versus endarterectomy in patients with symptomatic or asymptomatic carotid stenosis

Any stroke, death or myocardial infarction up to 30 days after treatment or ipsilateral stroke during follow-up

At 10 years:	CAS	CEA	HR (95% CI)
Symptomatic n= 1'321	**13.4%**	**9.8%**	1.17 (0.82 – 1.66) P=0.40
Asymptomatic n=1'181	**9.6%**	**10.1%**	0.99 (0.64 – 1.52) P=0.95



Median duration of follow-up 7.4 years

Brott et al., N Engl J Med 2016; 374:1021-31

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CREST: short-term results according to symptom status

Events within 30 days of treament

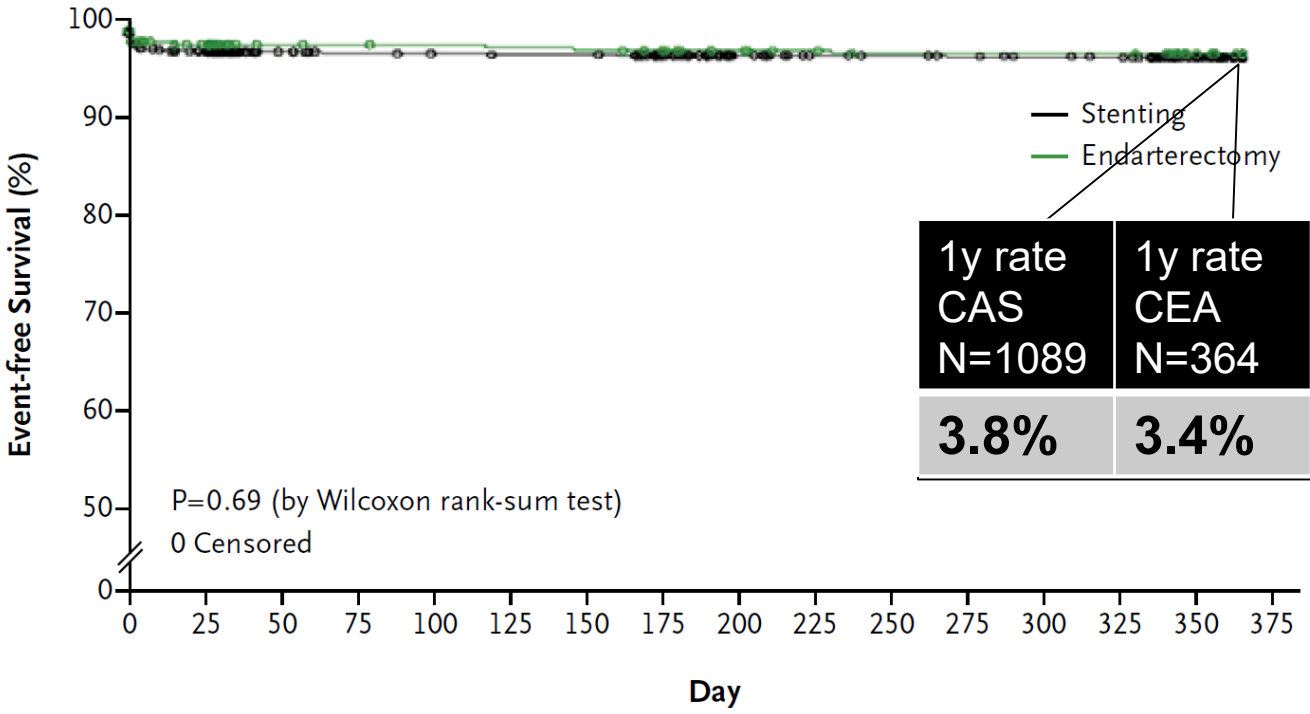
	CAS	CEA	Overall HR (95% CI)
Symptomatic			
Stroke or death	**6.0%**	**3.2%**	1.89 (1.11 - 3.21) P=0.02
Myocardial infarction	**1.0%**	**2.3%**	0.45 (0.18 - 1.11) P=0.08
Asymptomatic			
Stroke or death	**2.5%**	**1.4%**	1.88 (0.79 - 4.42) P=0.15
Myocardial infarction	**1.2%**	**2.2%**	0.55 (0.22 - 1.38) P=0.20

Brott et al., N Engl J Med 2010;363:11-23.

ACT-1: stenting versus endarterectomy in patients with asymptomatic carotid stenosis

3:1 randomisation CAS:CEA
Trial stopped after 1453 patients due to slow enrolment

Any stroke, death or myocardial infarction up to 30 days after treatment or ipsilateral stroke during follow-up



1y rate CAS N=1089	1y rate CEA N=364	Non-inferiority
3.8%	**3.4%**	P = 0.01

Rosenfield et al., N Engl J Med 2016;374:1011-20

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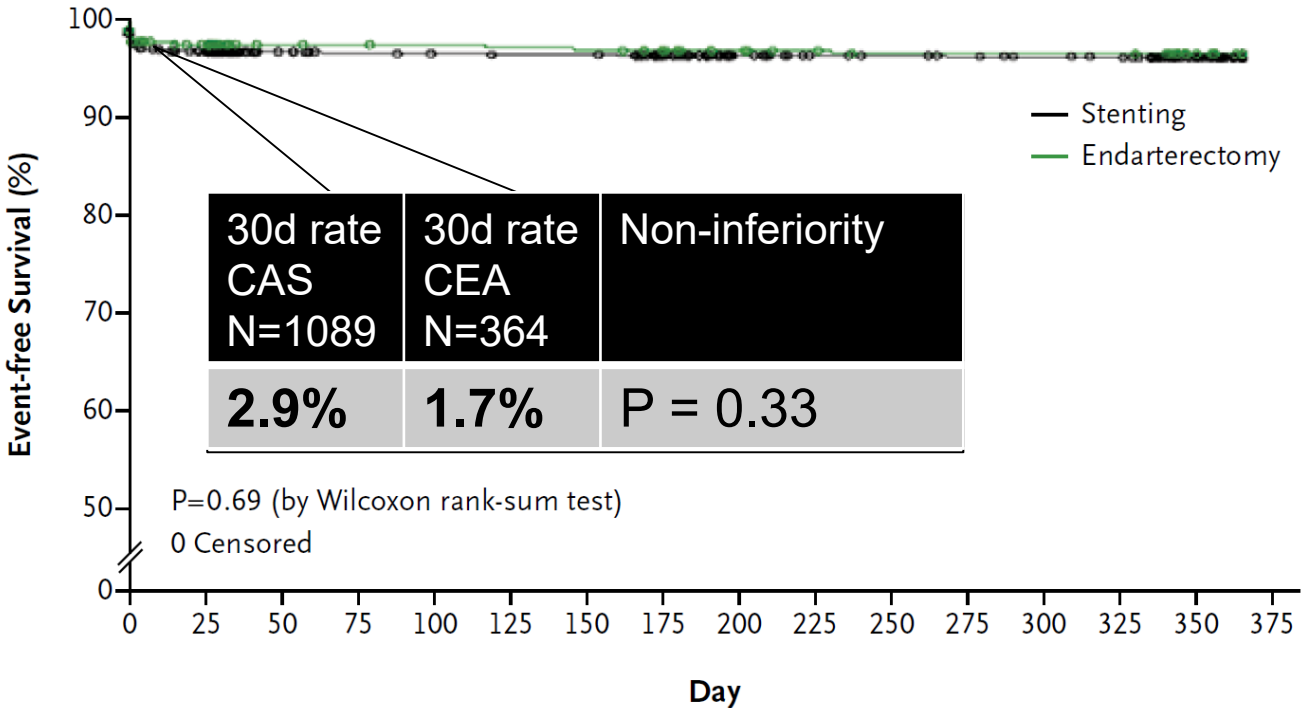
ACT-1: stenting versus endarterectomy in patients with asymptomatic carotid stenosis

Any stroke or death within 30 days after treatment



Rosenfield et al., N Engl J Med 2016;374:1011-20

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Asymptomatic carotid stenosis

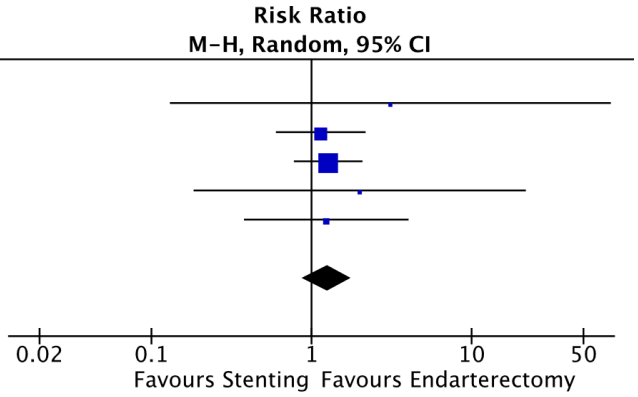
Stenting versus endarterectomy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 3.1)

Study or Subgroup	Stenting Events	Stenting Total	Endarterectomy Events	Endarterectomy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kentucky 2004	0	43	0	42		Not estimable	2004
Houston 2014	1	27	0	28	1.3%	3.11 [0.13, 73.11]	2014
ACT-1 2016	41	1089	12	364	31.9%	1.14 [0.61, 2.15]	2016
CREST 2016	36	594	28	587	55.2%	1.27 [0.79, 2.05]	2016
Carmel Medical Center 2017	2	68	1	68	2.3%	2.00 [0.19, 21.54]	2017
SPACE-2 2019	6	197	5	203	9.3%	1.24 [0.38, 3.99]	2020
Total (95% CI)		**2018**		**1292**	**100.0%**	**1.25 [0.88, 1.79]**	
Total events	86		46				

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.55$, df = 4 (P = 0.97); $I^2 = 0\%$

Test for overall effect: Z = 1.23 (P = 0.22)

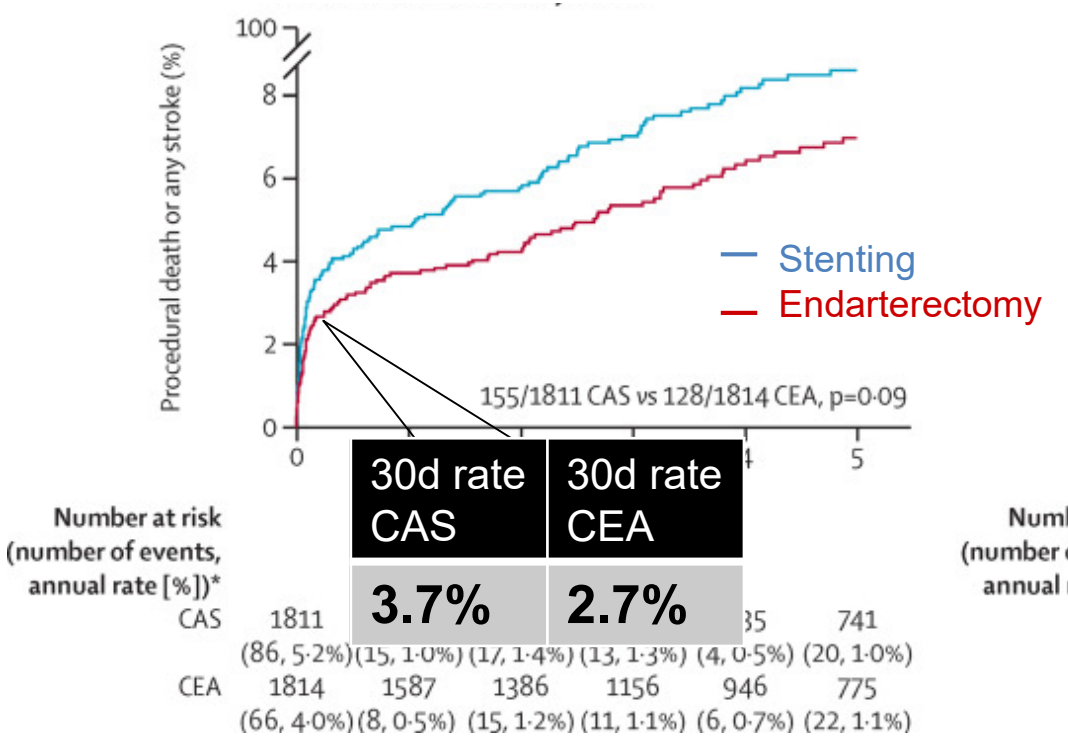


Quality: Moderate ⊕⊕⊕

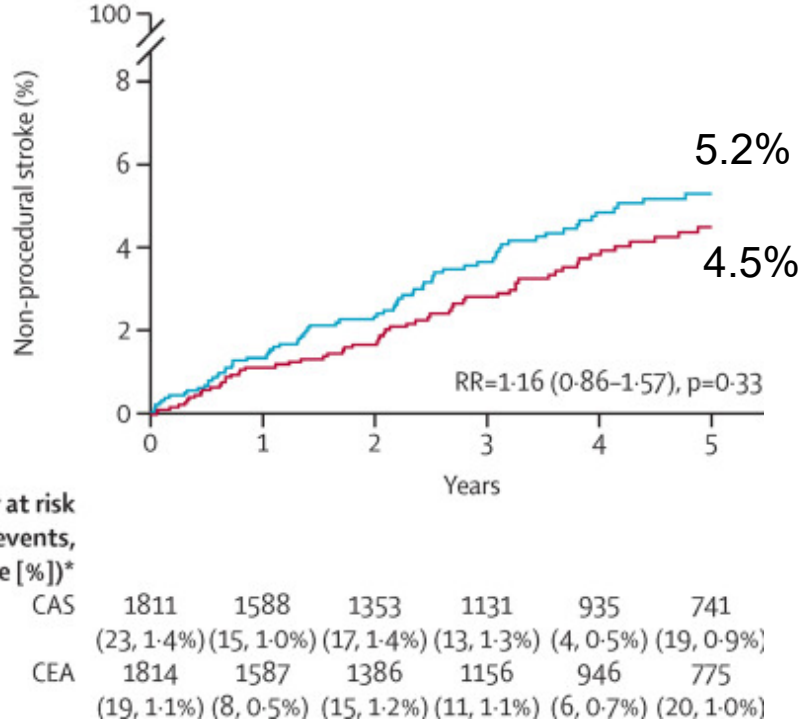
(Imprecision)

ACST-2: stenting versus endarterectomy for asymptomatic carotid stenosis (n=3625)

Any stroke or procedural death



Non-procedural stroke



A. Halliday et al., Lancet. 2021 Sep 18;398(10305):1065-1073

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ACST-2: Severity of worst procedural event & worst non-procedural stroke

	Procedural (<30 days) stroke or death		**Non-procedural** stroke (with mean 5-year FU)	
	Allocated CAS n=1811	Allocated CEA n=1814	Allocated CAS n=1748*	Allocated CEA n=1767*
Disabling or fatal	**15 (0.9%)†**	**18 (1.0%)†**	**44 (2.5%)**	**45 (2.5%)**
Non-disabling	**48 (2.7%)**	**29 (1.6%)**	**47 (2.7%)**	**34 (1.9%)**

* Excludes the 63 CAS vs 47 CEA patients who had a procedural stroke or death

† Includes the 2 CAS vs 6 CEA procedural deaths not involving a stroke

A. Halliday et al., Lancet. 2021 Sep 18;398(10305):1065-1073

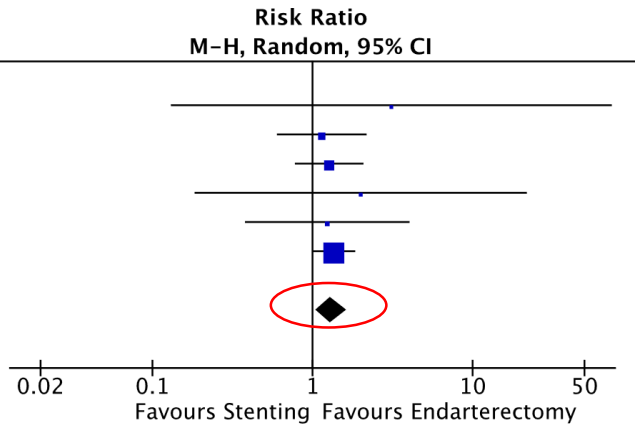
Asymptomatic carotid stenosis

Stenting versus endarterectomy

Long-term ipsilateral stroke or peri-procedural stroke or death (PICO 3.1)
Updated with ACST-2

Study or Subgroup	Stenting Events	Stenting Total	Endarterectomy Events	Endarterectomy Total	Weight	Risk Ratio M-H, Random, 95% CI	Year
Kentucky 2004	0	43	0	42		Not estimable	2004
Houston 2014	1	27	0	28	0.5%	3.11 [0.13, 73.11]	2014
ACT-1 2016	41	1089	12	364	13.0%	1.14 [0.61, 2.15]	2016
CREST 2016	36	594	28	587	22.4%	1.27 [0.79, 2.05]	2016
Carmel Medical Center 2017	2	68	1	68	0.9%	2.00 [0.19, 21.54]	2017
SPACE-2 2019	6	197	5	203	3.8%	1.24 [0.38, 3.99]	2020
ACST-2 2021	99	1811	73	1814	59.4%	1.36 [1.01, 1.83]	2021
Total (95% CI)		**3829**		**3106**	**100.0%**	**1.31 [1.05, 1.65]**	
Total events	185		119				

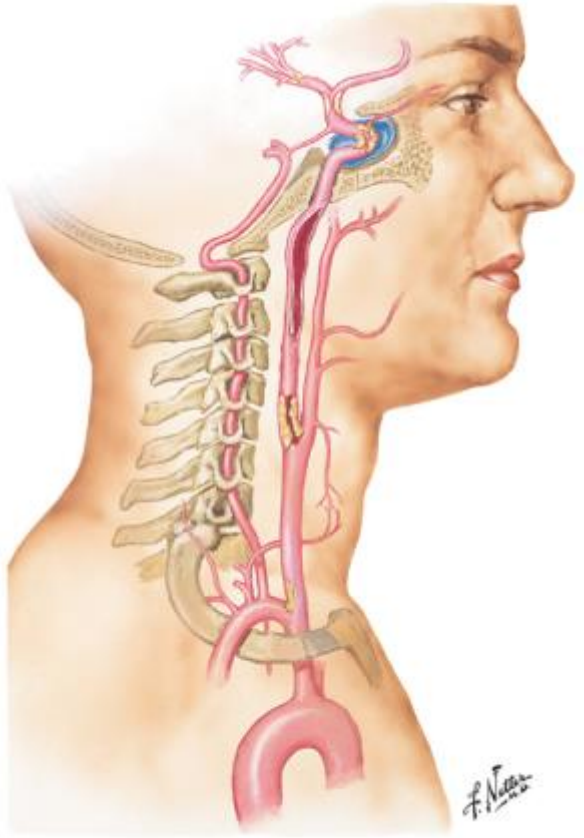
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.67$, df = 5 (P = 0.98); $I^2 = 0\%$
Test for overall effect: Z = 2.35 (P = 0.02)

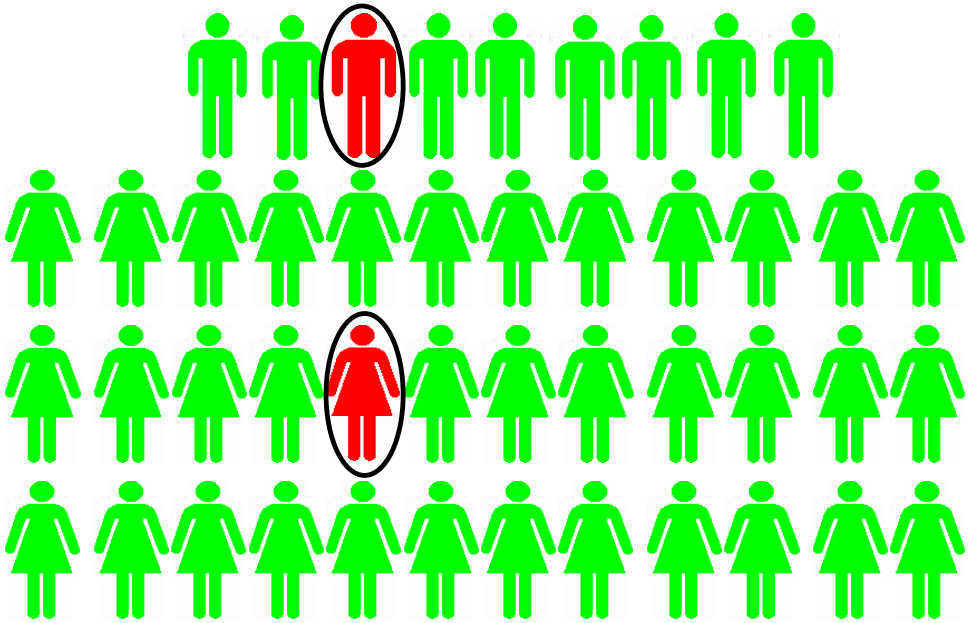


Quality: **High** ⊕⊕⊕⊕

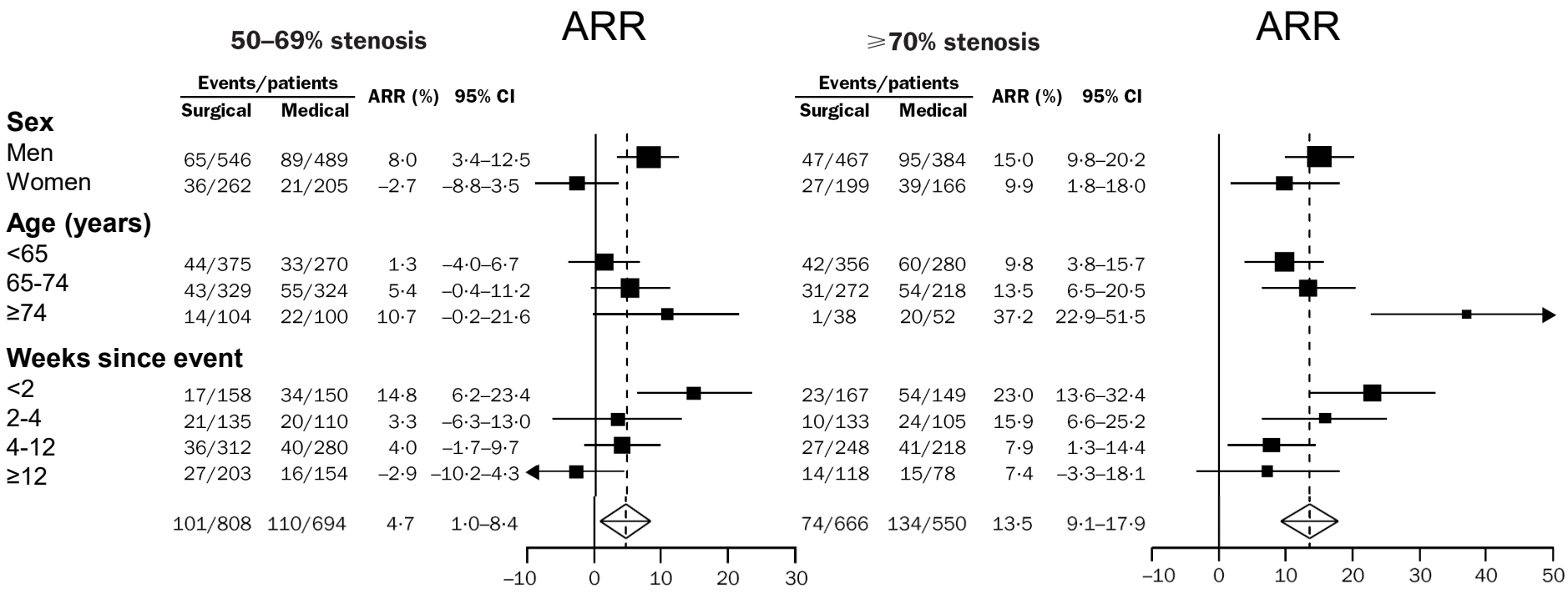
Selection of patients for treatment

Strokes prevented by CEA in patients with
symptomatic 50-99% stenosis after 5 years





Do all patients with symptomatic carotid stenosis benefit equally from surgery?



→ Benefit is highest in men, elderly patients, and if treated within 2 weeks of symptoms

Rothwell et al., Lancet 2004; 363: 915–24

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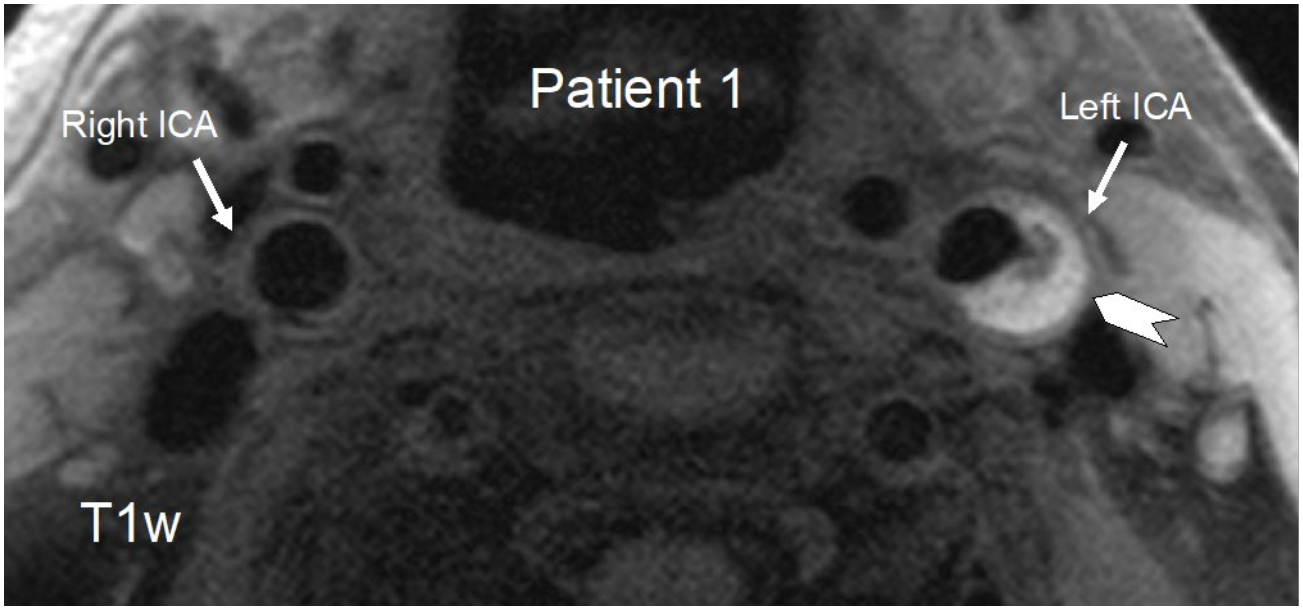
Intra-plaque haemorrhage (IPH) on magnetic resonance imaging

Hyperintense on T1-weighted fat-suppressed sequences



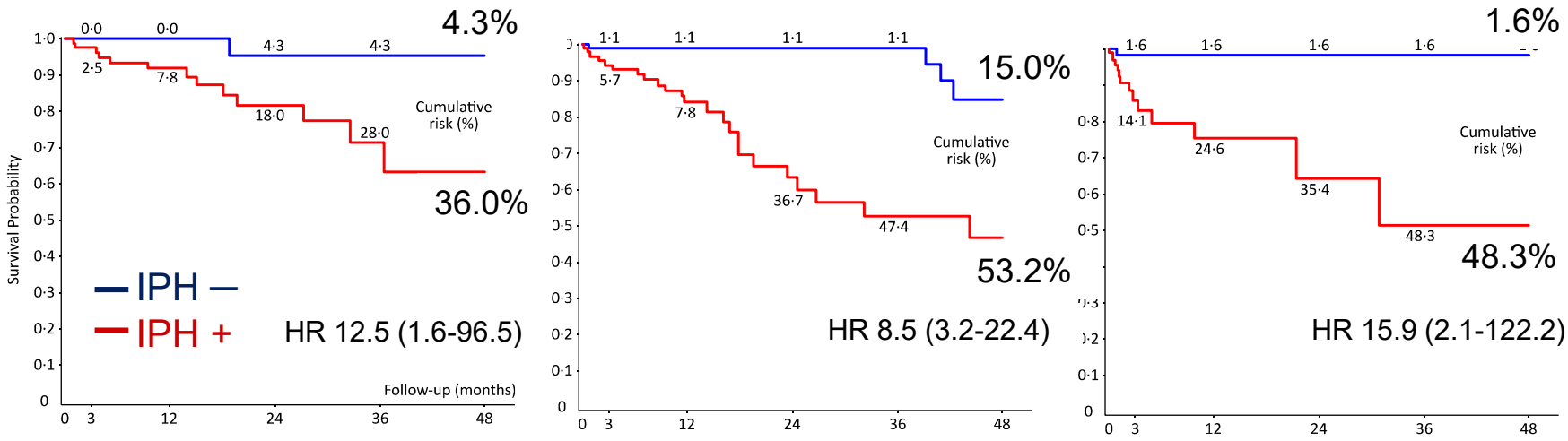
Saam T et al, Dichgans M, Bamberg F et al JACC 2013

IPH increases stroke risk independent of degree of symptomatic carotid stenosis

Minor 30-49% (n=187)

Moderate 50-69% (n=192)

Severe 70-99% (n=181)



Schindler et al., JACC Cardiovasc Imaging. 2020 Feb;13(2 Pt 1):395-406.

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Management recommendations

Recommendations: Medical therapy and risk factor management

- Recently symptomatic carotid stenosis:
  - Early limited-duration dual antiplatelet therapy (aspirin plus clopidogrel or ticagrelor) in patients with recent minor stroke or TIA
- Stable carotid disease (asymptomatic or >1 month after syx):
  - Antiplatelet monotherapy
  - Rivaroxaban 2*2.5 mg + aspirin 100 mg
- High (moderate) intensity statin
  - ideally <1.4 mMol/L LDL-C for symptomatic and asymptomatic patients
  - Add ezetimibe and consider PSCK-9 inhibitors to reach target
- Blood pressure lowering to ≤140/90 mmHg
- Glycaemic control to HbA1c ≤ 6.5%
- Smoking cessation, diet, excercise

European Heart Journal (2011) 32, 2851–2906; Stroke 2011, 42:e420-e463; Circulation. 2014;129:S1-S45; Eur Heart J. 2020 Jan 1;41(1):111-188

EUROPEAN STROKE ORGANISATION

ESO Guideline on Endarterectomy and Stenting for Carotid Artery Stenosis

Leo H Bonati, Stavros Kakkos, Joachim Berkefeld, Gert J. de Borst, Richard Bulbulia, Alison Halliday, Isabelle van Herzeele, Igor Koncar, Dominick J H McCabe, Avtar Lal, Jean-Baptiste Ricco, Peter Ringleb, Martin Taylor-Rowan, Hans-Henning Eckstein

Eur Stroke J. 2021 Jun;6(2):I

Asymptomatic carotid stenosis

Endarterectomy versus medical therapy

Evidence-based recommendation

In patients with ≥60% asymptomatic carotid artery stenosis **considered to be at increased risk of stroke** on best medical therapy alone, **we recommend carotid endarterectomy**.

Quality of evidence: Moderate ⊕⊕⊕

Strength of recommendation: Strong for carotid endarterectomy ↑↑

This recommendation is independent of sex and stenosis severity.

Expert consensus statement

In selected patients 75 years of age or older with ≥60% asymptomatic carotid artery stenosis and an **expected survival of at least five years,** who are considered to be at an increased risk of stroke on best medical therapy alone, **carotid endarterectomy is suggested** after careful consideration of the risks and benefits at a multi-disciplinary team meeting.

Supporting information

Characteristics associated with increased stroke risk:

- Silent infarction on neuroimaging
- High degree or progression of stenosis
- Echolucent plaque on ultrasound
- Intra-plaque haemorrhage on MRI
- Micro-emboli or reduced cerebrovascular reserve on trans-cranial Doppler

L. Bonati et al., Eur Stroke J. 2021 Jun;6(2):I

Asymptomatic carotid stenosis

Stenting versus medical therapy

Evidence-based Recommendation

In patients with asymptomatic carotid stenosis, **we recommend against carotid artery stenting** as a routine alternative to best medical therapy alone.

Quality of evidence: Very low ⊕

Strength of recommendation: Weak against carotid stenting ↓

Supporting information

Carotid artery stenting versus best medical therapy alone are being compared in one of the two parallel study arms in the ongoing *Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial (CREST-2)*

L. Bonati et al., Eur Stroke J. 2021 Jun;6(2):I

Asymptomatic carotid stenosis

Stenting versus endarterectomy *(before publication of ACST-2)*

Evidence-based Recommendation

In patients with asymptomatic carotid stenosis in whom revascularisation is considered to be appropriate, **we suggest endarterectomy as the current treatment of choice**.
Quality of evidence: Moderate ⊕⊕⊕
Strength of recommendation: Weak for carotid endarterectomy ↑

Expert consensus statements

In patients with asymptomatic carotid stenosis in whom revascularisation is considered to be appropriate and **who are less suitable for surgery, stenting may be suggested**. We recommend careful consideration of the risks and benefits at a multi-disciplinary team meeting.

The independently assessed **risk of in-hospital stroke or death** following endarterectomy or stenting for asymptomatic carotid stenosis should be as low as possible, **ideally below 2%**.

L. Bonati et al., Eur Stroke J. 2021 Jun;6(2):I

Symptomatic carotid stenosis

Endarterectomy versus medical therapy

Evidence-based Recommendations

In patients with **severe (70-99%) symptomatic carotid artery stenosis, we recommend carotid endarterectomy**.
Quality of evidence: High ⊕⊕⊕⊕
Strength of recommendation: Strong for carotid endarterectomy ↑↑

In patients with **moderate (50-69%) symptomatic carotid artery stenosis, we suggest carotid endarterectomy**.
Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak for carotid endarterectomy ↑

In patients with **mild (<50%) symptomatic carotid artery stenosis, we recommend against carotid endarterectomy**.
Quality of evidence: Very low ⊕
Strength of recommendation: Strong against carotid endarterectomy ↓↓

In patients with 50-99% symptomatic carotid stenosis in whom surgery is considered appropriate, **we recommend early endarterectomy, ideally within two weeks** of the first neurological event.
Quality of evidence: High ⊕⊕⊕⊕
Strength of recommendation: Strong for carotid endarterectomy ↑↑

These recommendations are independent of sex and age.

Symptomatic carotid stenosis

Stenting versus endarterectomy

Evidence-based Recommendation

In patients with symptomatic carotid artery stenosis requiring revascularisation, **we recommend endarterectomy as the treatment of choice**.
Quality of evidence: Moderate ⊕⊕⊕
Strength of recommendation: Strong for carotid endarterectomy ↑↑

In patients with symptomatic carotid stenosis **<70 years old** requiring revascularisation, we suggest that **stenting may be considered as an alternative to endarterectomy**.
Quality of evidence: Low ⊕⊕
Strength of recommendation: Weak for carotid stenting ↑

Expert consensus statements

The suitability of a patient with symptomatic carotid stenosis for carotid endarterectomy versus stenting should also take into account the **interval** since their last ischaemic cerebrovascular event, as well as **anatomical and morphological features**, including the atherosclerotic burden of the aortic arch.

The independently assessed **risk of in-hospital stroke or death** following endarterectomy or stenting for symptomatic carotid stenosis **should not exceed 4%.**

L. Bonati et al., Eur Stroke J. 2021 Jun;6(2):I

Thank you for your attention

City of Basel