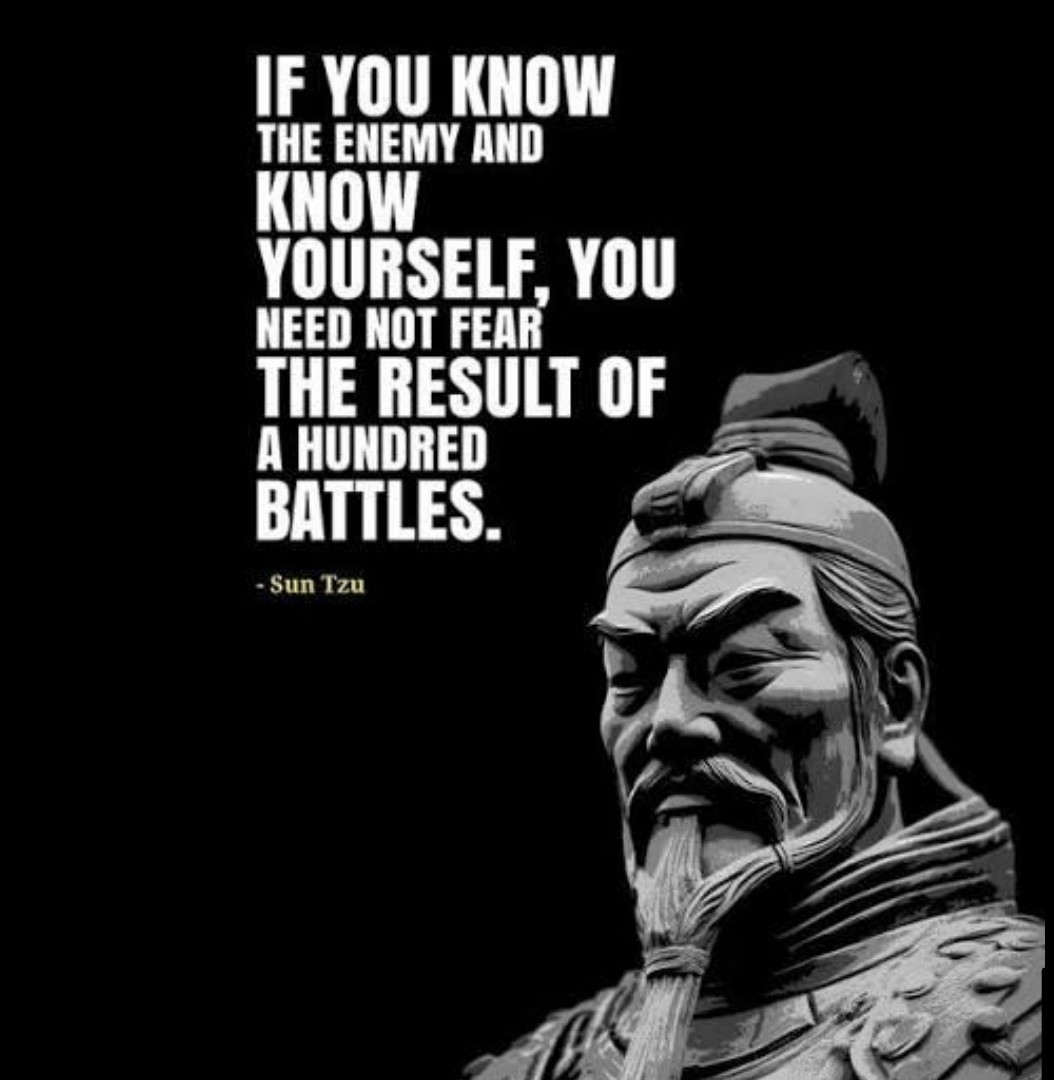
Trombolyse bij CRAO: PRO!

Floris Schreuder
Neuroloog Radboudumc

NeNOS symposium
Vrijdag 9 oktober 2026

Radboudumc



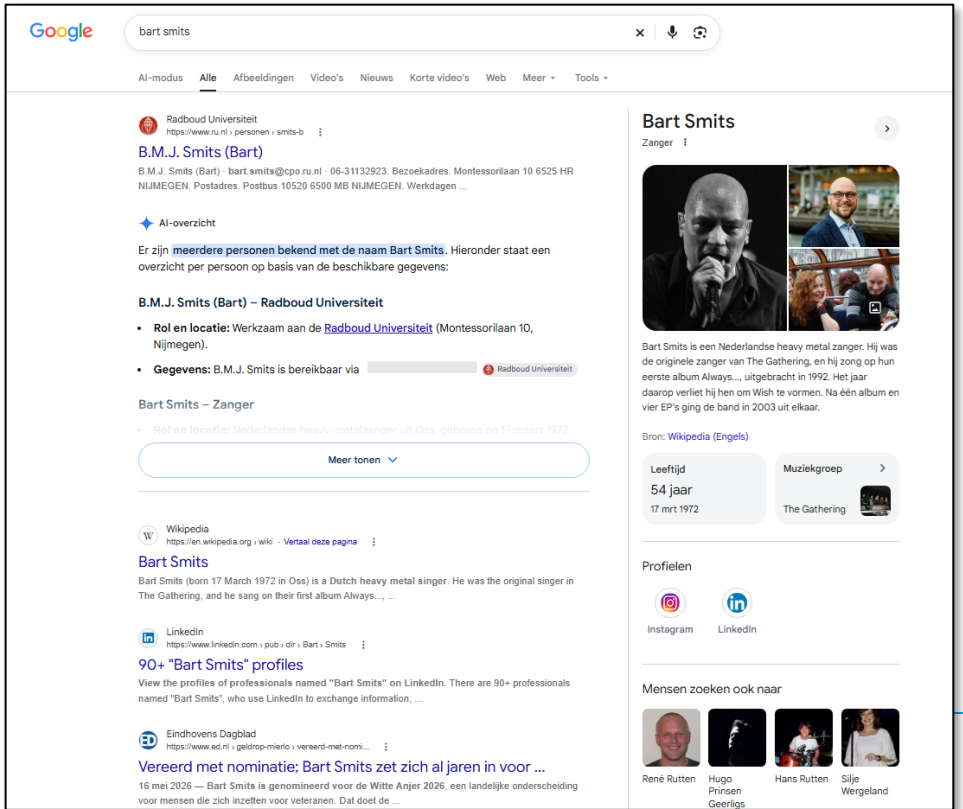
Sun Tzu "*The Art of War*" ~500 BC

Wie is Bart Smits?

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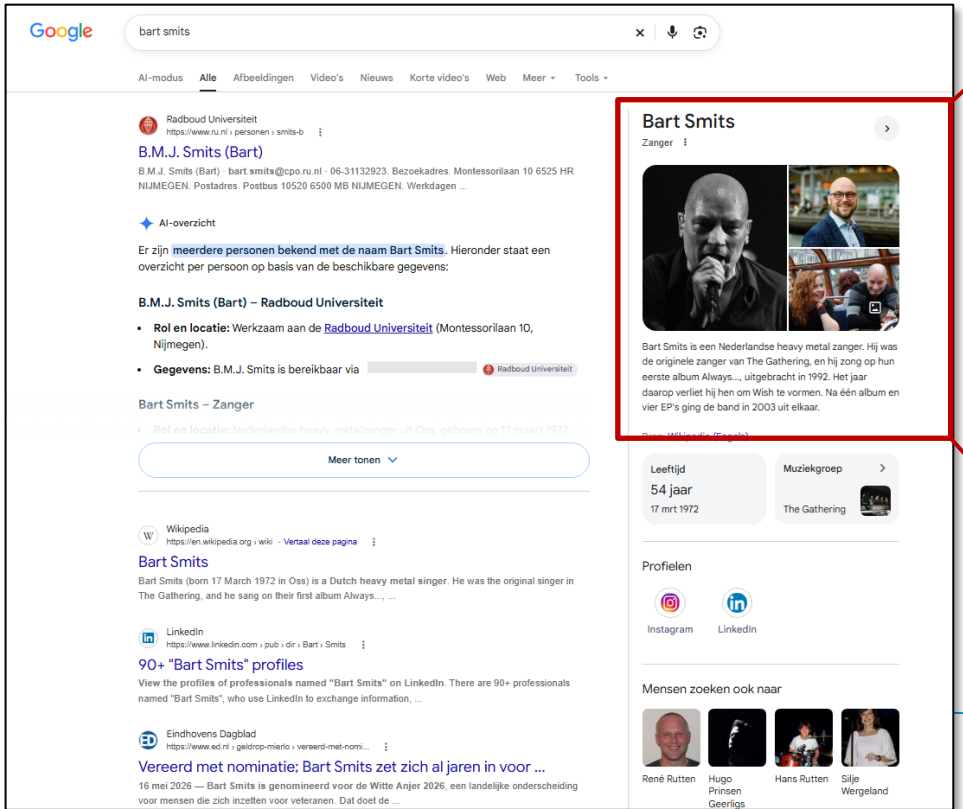


Wie is Bart Smits?



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Wie is Bart Smits?





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Wie is

MAASSTAD ZIEKENHUIS
een santeon ziekenhuis

Menu Zoeken Translate

Artsen en zorgverleners

Smits, Dhr. dr. B.W.

Neuroloog



Even voorstellen

Ik werk graag samen met andere specialismen binnen het ziekenhuis. Mijn aandachtsgebieden liggen dan ook op de grenzen tussen neurologie en andere vakgebieden. Bijvoorbeeld met longziekten (slaapstoornissen), keel neus oor (slaapstoornissen en duizeligheid) en oogheelkunde (neuro-ophthalmologie).

Ik probeer in mijn vak zoveel mogelijk uit te gaan van samen beslissen. Hiervoor wil ik eerst goed uitvragen wat de klachten van mijn patiënten precies zijn. En wat dit betekent in hun dagelijks leven. Pas als ik dit duidelijk heb, bespreek ik welke onderzoeken we kunnen doen en wat de verschillende behandelingen zijn.

Aandachtsgebieden

Opleiding

- 2012 Afronding promotie onderzoek "Chronic Progressive External Ophthamloplegia: more than meets the eye"
- 2002-2009 Opleiding neurologie in het Radboud UMC Nijmegen
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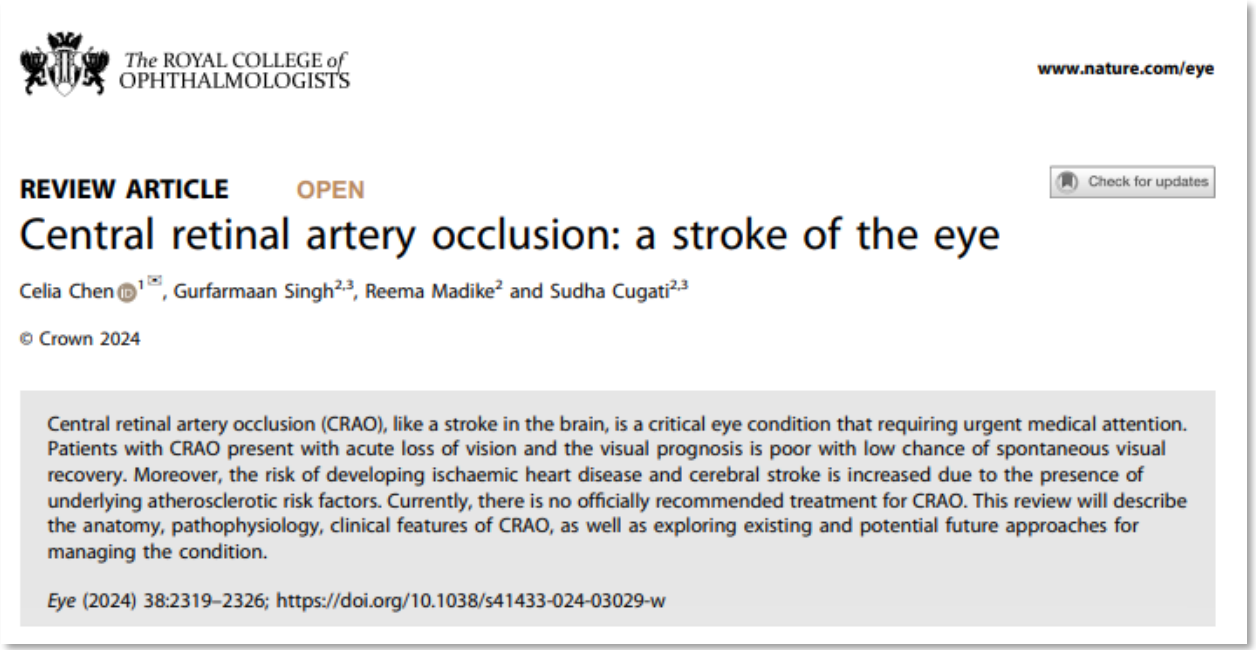
- …?


SAME
EYES
DIFFERENT
MISSIONS
007
INTELLIGENCE
BEYOND
BORDERS
MORE THAN
MEETS THE EYE
BART SMITS IS THE NEW JAMES BOND
EYEWORKS PICTURES PRESENTS A GLOBAL VISION PRODUCTION "MORE THAN MEETS THE EYE"
STARRING BART SMITS MUSIC BY HANS ZIMMER WRITTEN BY IAN FLEMING DIRECTED BY CARY JOJI FUKUNAGA
COMING SOON
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IVT bij CRAO: PRO!



The ROYAL COLLEGE of OPHTHALMOLOGISTS

www.nature.com/eye

REVIEW ARTICLE OPEN

Check for updates

Central retinal artery occlusion: a stroke of the eye

Celia Chen[1], Gurfarmaan Singh[2,3], Reema Madike[2] and Sudha Cugati[2,3]

© Crown 2024

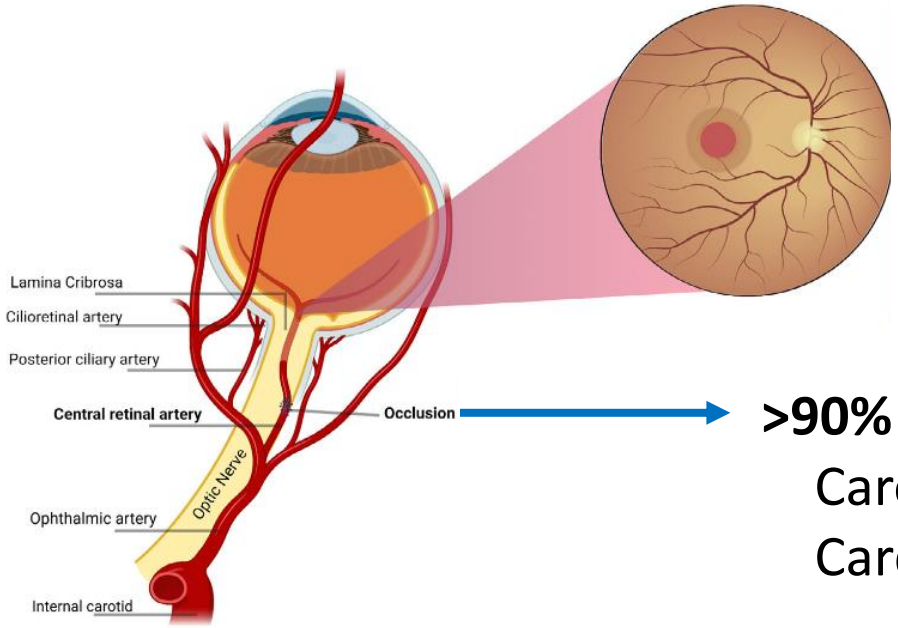
Central retinal artery occlusion (CRAO), like a stroke in the brain, is a critical eye condition that requiring urgent medical attention. Patients with CRAO present with acute loss of vision and the visual prognosis is poor with low chance of spontaneous visual recovery. Moreover, the risk of developing ischaemic heart disease and cerebral stroke is increased due to the presence of underlying atherosclerotic risk factors. Currently, there is no officially recommended treatment for CRAO. This review will describe the anatomy, pathophysiology, clinical features of CRAO, as well as exploring existing and potential future approaches for managing the condition.

Eye (2024) 38:2319–2326; https://doi.org/10.1038/s41433-024-03029-w

Chen e.a. Eye 2024

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PRO: 1) Pathofysiologie

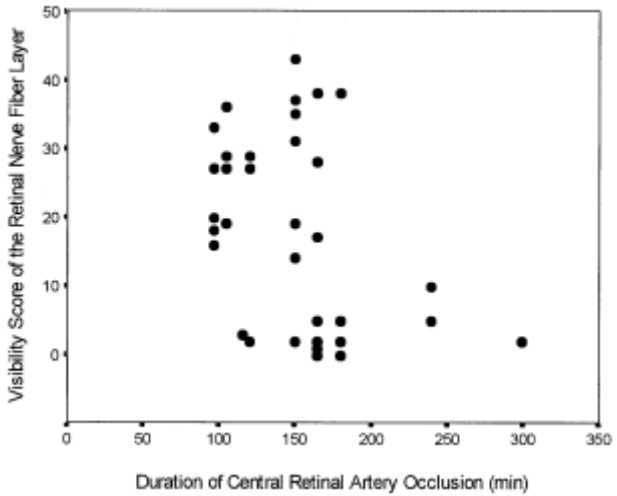


>90% trombo-embolie

Carotis

Cardiaal

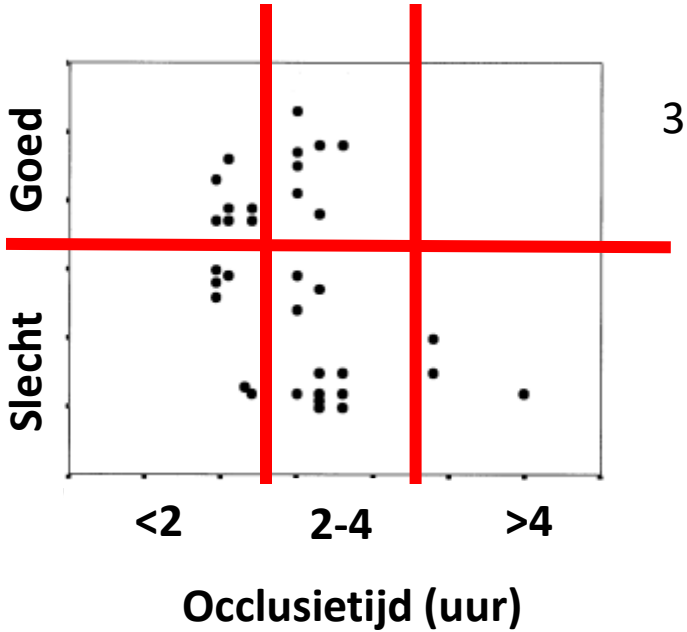
PRO: 2) Time is retina



39 rhesus apen

Hayreh e.a. Am J Ophthalmol 2000

PRO: 2) Time is retina



39 rhesus apen

Hayreh e.a. Am J Ophthalmol 2000

PRO: 3) Ernstige consequenties

Table 2: Initial and final visual acuity by CRAO type

Type of CRAO	Visual acuity	20/15	20/20	20/25	20/30	20/40	20/60	20/70	20/80	20/100	20/200	20/400	CF	HM	LP	NLP	Total*
Non-arteritic CRAO	Initial				1			1			6	13	66	44	28	12	171
	Final			1		1					9	14	43	23	19	12	122

Visus na 1 week: vingers tellen of slechter bij **97/122 (79%)**

Hayreh. Indian J Ophthalmol 2018

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PRO: 3) Ernstige consequenties

Table 2: Initial and final visual acuity by CRAO type

Type of CRAO	Visual acuity	20/15	20/20	20/25	20/30	20/40	20/60	20/70	20/80	20/100	20/200	20/400	CF	HM	LP	NLP	Total*
Non-arteritic CRAO	Initial				1			1			6	13	66	44	28	12	171
	Final			1		1					9	14	43	23	19	12	122
Non-arteritic CRAO with cilioretinal artery sparing	Initial	1	4	2	3		3	1		1	2			9	2		35
	Final		2		2	3	3				6	2	4	6		1	29
Arteritic CRAO	Initial								1			1	2	2		7	13
	Final										1	1		1		8	11
Transient Non- arteritic CRAO	Initial	2	9	4	2		2	2		1	3	2	10	4			41
	Final	3	8	4	5	3	2	1	1		3	3	5				38

*The differences in the total number of eyes for initial and final visual acuity are due to some patients having only one visit

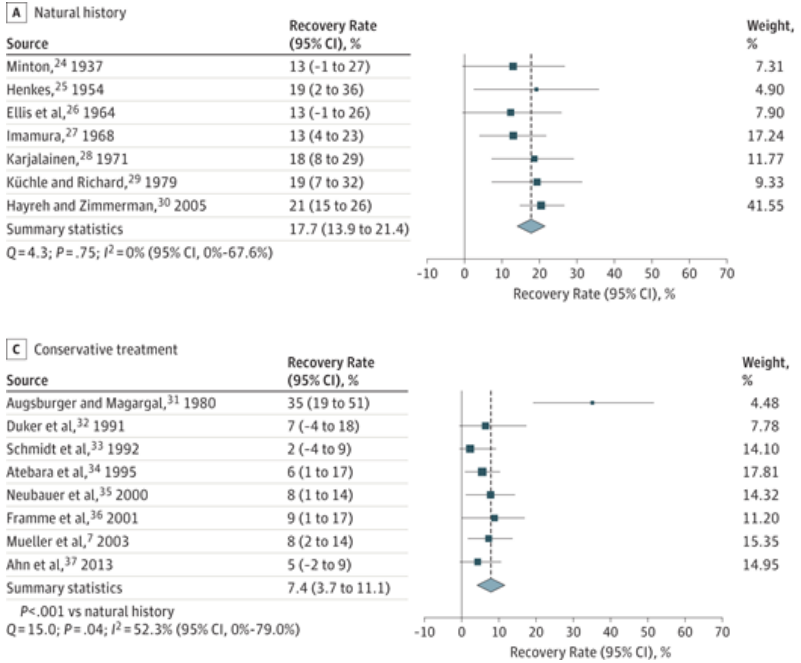
Visus na 1 week: vingers tellen of slechter bij **122/200 (61%)**

Hayreh. Indian J Ophthalmol 2018

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PRO: 4) Géén andere behandelingen

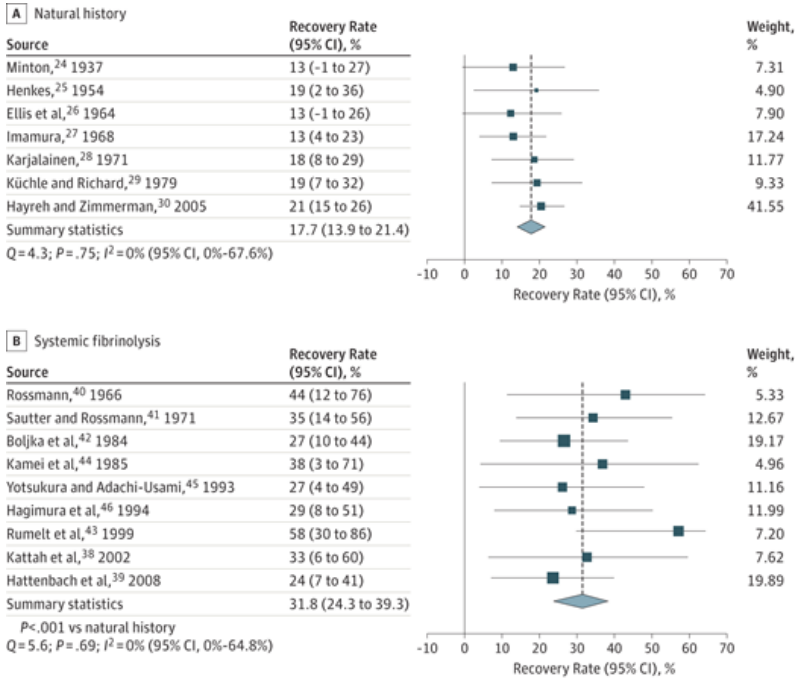
Eight studies[7,31-37] reported visual acuity outcomes in 419 patients after conservative therapies, including ocular massage, anterior chamber paracentesis, and hemodilution. These interventions frequently were used concurrently or in sequence, making it difficult to analyze their effect independently of each other. In the studies using these more aggressive nonfibrinolytic therapies, the recovery rate was substantially lower than in the natural history control group (31 of 419 [7.4%; 95% CI, 3.7%-11.1%] vs 70 of 396 [17.7%; 95% CI, 13.9%-21.4%]; $P < .001$; number needed to harm, 10.0 [95% CI, 6.8-17.4]).



Schrag e.a. JAMA Neurol 2015

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PRO: 5) Observationele studies



A Natural history

Source	Recovery Rate (95% CI), %	Weight, %
Minton,[24] 1937	13 (-1 to 27)	7.31
Henkes,[25] 1954	19 (2 to 36)	4.90
Ellis et al,[26] 1964	13 (-1 to 26)	7.90
Imamura,[27] 1968	13 (4 to 23)	17.24
Karjalainen,[28] 1971	18 (8 to 29)	11.77
Küchle and Richard,[29] 1979	19 (7 to 32)	9.33
Hayreh and Zimmerman,[30] 2005	21 (15 to 26)	41.55
Summary statistics	17.7 (13.9 to 21.4)	

$Q = 4.3$; $P = .75$; $I^2 = 0\%$ (95% CI, 0%-67.6%)

B Systemic fibrinolysis

Source	Recovery Rate (95% CI), %	Weight, %
Rossmann,[40] 1966	44 (12 to 76)	5.33
Sautter and Rossmann,[41] 1971	35 (14 to 56)	12.67
Boljka et al,[42] 1984	27 (10 to 44)	19.17
Kamei et al,[44] 1985	38 (3 to 71)	4.96
Yotsukura and Adachi-Usami,[45] 1993	27 (4 to 49)	11.16
Hagimura et al,[46] 1994	29 (8 to 51)	11.99
Rumelt et al,[43] 1999	58 (30 to 86)	7.20
Kattah et al,[38] 2002	33 (6 to 60)	7.62
Hattenbach et al,[39] 2008	24 (7 to 41)	19.89
Summary statistics	31.8 (24.3 to 39.3)	

$P < .001$ vs natural history

$Q = 5.6$; $P = .69$; $I^2 = 0\%$ (95% CI, 0%-64.8%)

-10 0 10 20 30 40 50 60 70

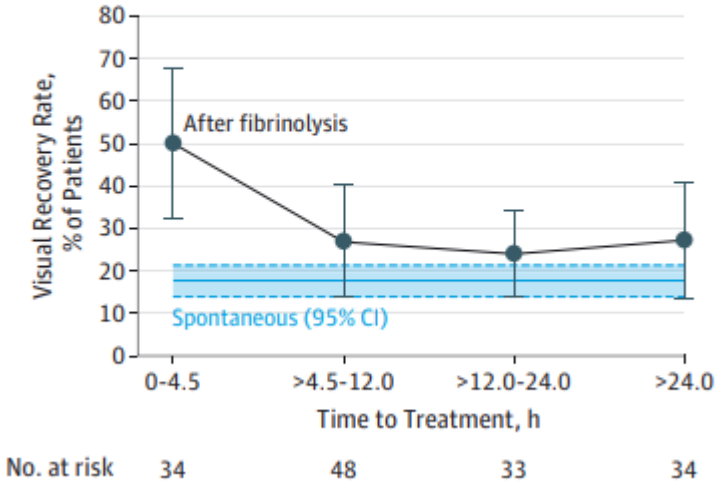
Recovery Rate (95% CI), %

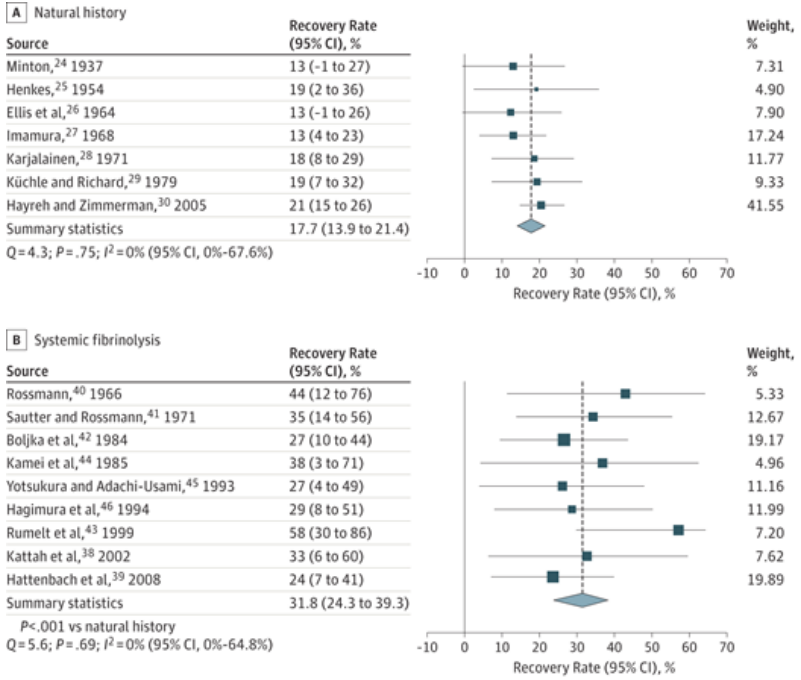
Schrag e.a. JAMA Neurol 2015

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PRO: 5) Observationele studies

Figure 2. Effect of Fibrinolysis by Time to Administration





Schrag e.a. JAMA Neurol 2015

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PRO: 6) Randomized trials (1)

NCT	Country	Phase	N (intended)	Intervention	Control	Status
NCT00637468 (**EAGLE**)	Germany	III	84 (200)	IA 5000IU heparin & 50mg alteplase	Conservative*	Prematurely terminated, published[1]
ANZCTR83102	Australia	II	16	IV 0.90mg/kg alteplase	Saline infusion	Published[2]
NCT03197194 (**THEIA**)	France	III	70	IV 0.90mg/kg alteplase + oral placebo	Saline infusion + oral aspirin	Published[3]
NCT04526951 (**TenCRAOS**)	Norway, Sweden, Finland, Lithuania, Denmark, Belgium	III	81	IV 0.25mg/kg tenecteplase + oral placebo	Saline infusion + oral aspirin	Published[4]
NCT05562284	China	?	128	IA 50mg alteplase	Conservative (?)	Unclear
NCT04965038 (**REVISION**)	Germany, Austria, Switzerland	III	127 (422)	IV 0.25mg/kg tenecteplase or 0.90mg/kg alteplase	Placebo	Prematurely terminated, results awaited

**Conservative treatment included hemodilution, ocular massage, topical beta-blocker and i.v. 500mg acetazolamide*

1: Schumacher e.a. Ophthalmol 2010; 2: Chen e.a. Stroke 2011;
3: Preterre e.a. Lancet Neurol 2025; 4: Ryan e.a. NEJM 2026

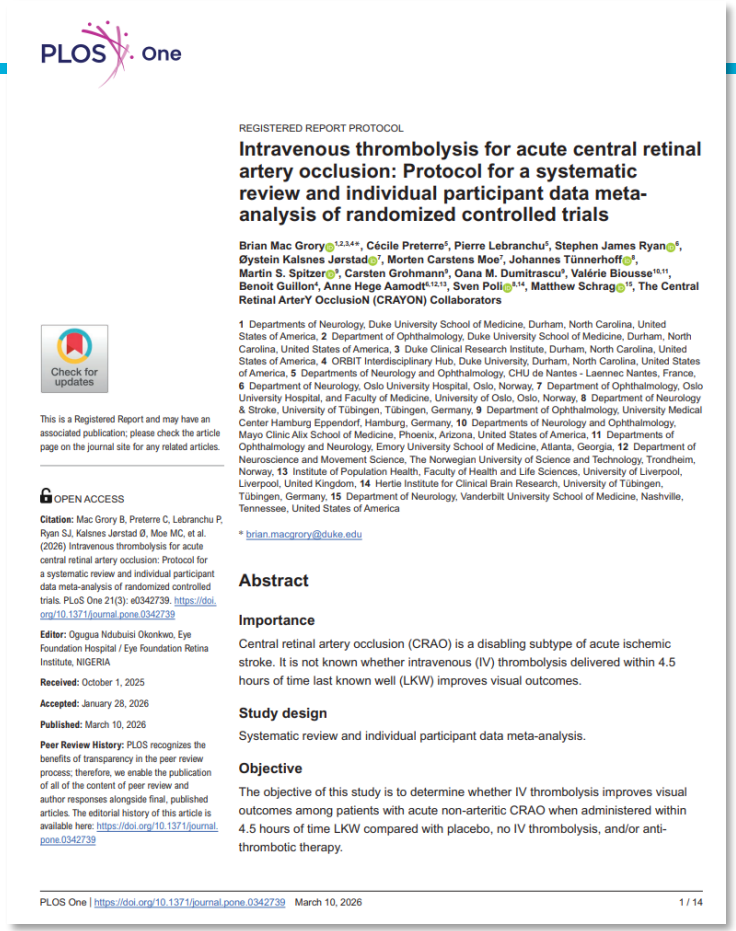
PRO: 6) Randomized trials (2)

NCT	Onset-to-treatment time	Primary outcome measure	Intervention	Safety (ICH)
NCT00637468 (**EAGLE**)	< 20h	Change in logMAR from baseline to 30 days	Intervention: -0.443 (0.549) Control: -0.447 (0.545)	Intervention: 2/42 Control: 0/40
ANZCTR83102	< 24h	Change in logMAR from baseline to 180 days	Intervention: 0.10 (0.18) Control: 0.05 (0.14)	Intervention 1/8 Control: 0/8
NCT03197194 (**THEIA**)	< 4.5h	Change in logMAR from baseline to 30 days	Intervention: -0.62 (0.85) Control: -0.44 (0.70)	Intervention: 1/35 Control: 0/35
NCT04526951 (**TenCRAOS**)	< 4.5h	Change in logMAR from baseline to 30 days	Intervention: -0.73 (0.92) Control: -0.60 (0.91)	Intervention: 1/40 Control: 0/38
NCT05562284	< 7 days	MD in Humphrey VFI at 90 days	-	-
NCT04965038 (**REVISION**)	< 4.5h	logMAR <0.5 at 30 days	-	-

1: Schumacher e.a. Ophthalmol 2010; 2: Chen e.a. Stroke 2011;
3: Preterre e.a. Lancet Neurol 2025; 4: Ryan e.a. NEJM 2026

PRO: 6) IPDMA

- Trials zijn underpowered



PLOS One

REGISTERED REPORT PROTOCOL

Intravenous thrombolysis for acute central retinal artery occlusion: Protocol for a systematic review and individual participant data meta-analysis of randomized controlled trials

Brian Mac Grory[1,2,3,4*], Cécile Preterre[5], Pierre Lebranchu[5], Stephen James Ryan[6], Øystein Kalsnes Jørstad[7], Morten Carstens Moe[7], Johannes Tünnerhoff[8], Martin S. Spitzer[9], Carsten Grohmann[9], Oana M. Dumitrascu[8], Valérie Biousse[10,11], Benoit Guillon[4], Anne Hege Aamodt[4,12,13], Sven Poli[8,14], Matthew Schrag[15], The Central Retinal ArterY OccIusioN (CRAYON) Collaborators

1 Departments of Neurology, Duke University School of Medicine, Durham, North Carolina, United States of America, **2** Department of Ophthalmology, Duke University School of Medicine, Durham, North Carolina, United States of America, **3** Duke Clinical Research Institute, Durham, North Carolina, United States of America, **4** ORBIT Interdisciplinary Hub, Duke University, Durham, North Carolina, United States of America, **5** Departments of Neurology and Ophthalmology, CHU de Nantes - Laennec Nantes, France, **6** Department of Neurology, Oslo University Hospital, Oslo, Norway, **7** Department of Ophthalmology, Oslo University Hospital, and Faculty of Medicine, University of Oslo, Oslo, Norway, **8** Department of Neurology & Stroke, University of Tübingen, Tübingen, Germany, **9** Department of Ophthalmology, University Medical Center Hamburg Eppendorf, Hamburg, Germany, **10** Departments of Neurology and Ophthalmology, Mayo Clinic Alix School of Medicine, Phoenix, Arizona, United States of America, **11** Departments of Ophthalmology and Neurology, Emory University School of Medicine, Atlanta, Georgia, **12** Department of Neuroscience and Movement Science, The Norwegian University of Science and Technology, Trondheim, Norway, **13** Institute of Population Health, Faculty of Health and Life Sciences, University of Liverpool, Liverpool, United Kingdom, **14** Hertie Institute for Clinical Brain Research, University of Tübingen, Tübingen, Germany, **15** Department of Neurology, Vanderbilt University School of Medicine, Nashville, Tennessee, United States of America

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OPEN ACCESS

Citation: Mac Grory B, Preterre C, Lebranchu P, Ryan SJ, Kalsnes Jørstad Ø, Moe MC, et al. (2026) Intravenous thrombolysis for acute central retinal artery occlusion: Protocol for a systematic review and individual participant data meta-analysis of randomized controlled trials. PLoS One 21(3): e0342739. https://doi.org/10.1371/journal.pone.0342739

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Abstract

Importance

Central retinal artery occlusion (CRAO) is a disabling subtype of acute ischemic stroke. It is not known whether intravenous (IV) thrombolysis delivered within 4.5 hours of time last known well (LKW) improves visual outcomes.

Study design

Systematic review and individual participant data meta-analysis.

Objective

The objective of this study is to determine whether IV thrombolysis improves visual outcomes among patients with acute non-arteritic CRAO when administered within 4.5 hours of time LKW compared with placebo, no IV thrombolysis, and/or anti-thrombotic therapy.

Mac Grory e.a. Plos One 2026

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IVT bij CRAO: PRO!

- Mechanisme van IVT bij CRAO is plausibel
- CRAO ernstige aandoening
- Géén bewezen alternatieve behandelingen

- Huidige trials zijn té klein om effectiviteit aan te tonen
- ICH bij 5-6% (indien behandeling <4.5h: 2-3%)

- TIME IS RETINA!

IVT bij CRAO: PRO!

- Het woord is aan mijn opponent

- Tot (bijna) bij de borrel!

