

A simple long-term stroke risk model for asymptomatic carotid stenosis – will it help us select patients for intervention in the future?

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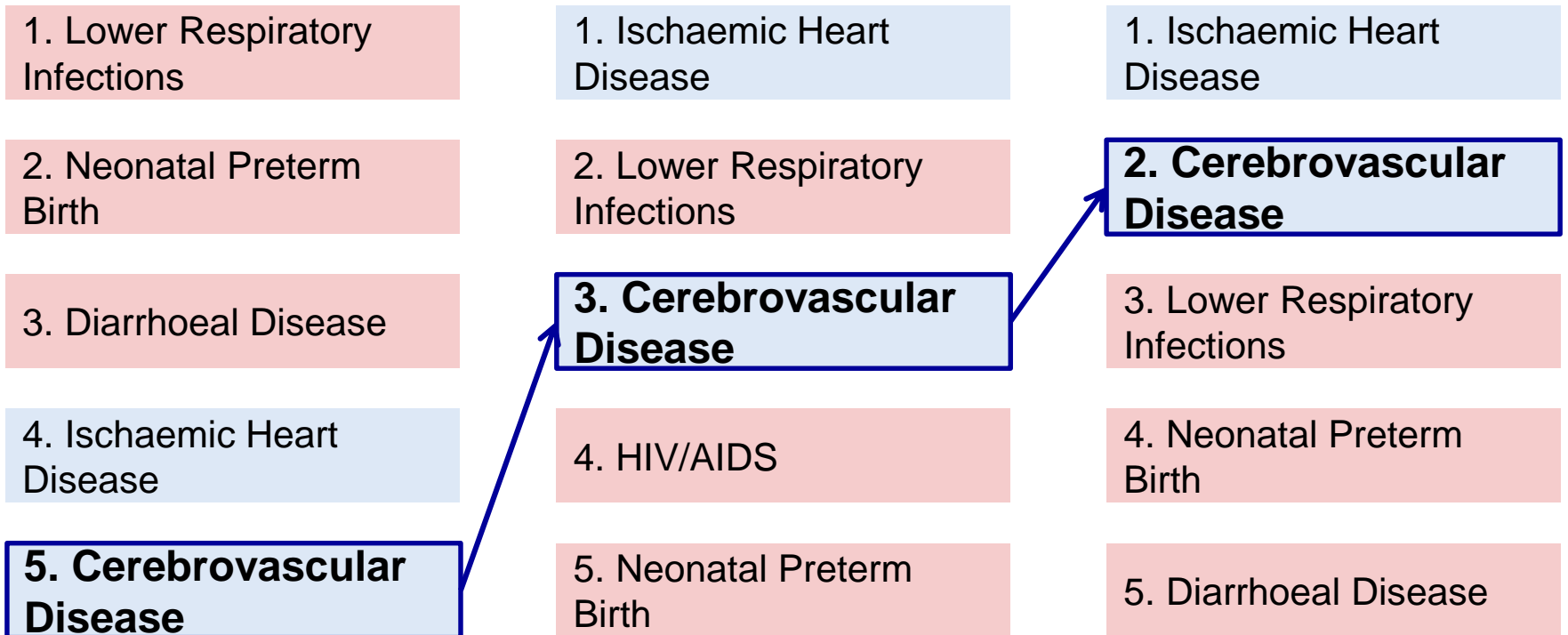
MAC, 09.00 7th December 2017

Global Burden of Stroke

1990

2005

2015



**Age-standardised stroke mortality declining,
but total number rising**

Carotid Artery Disease



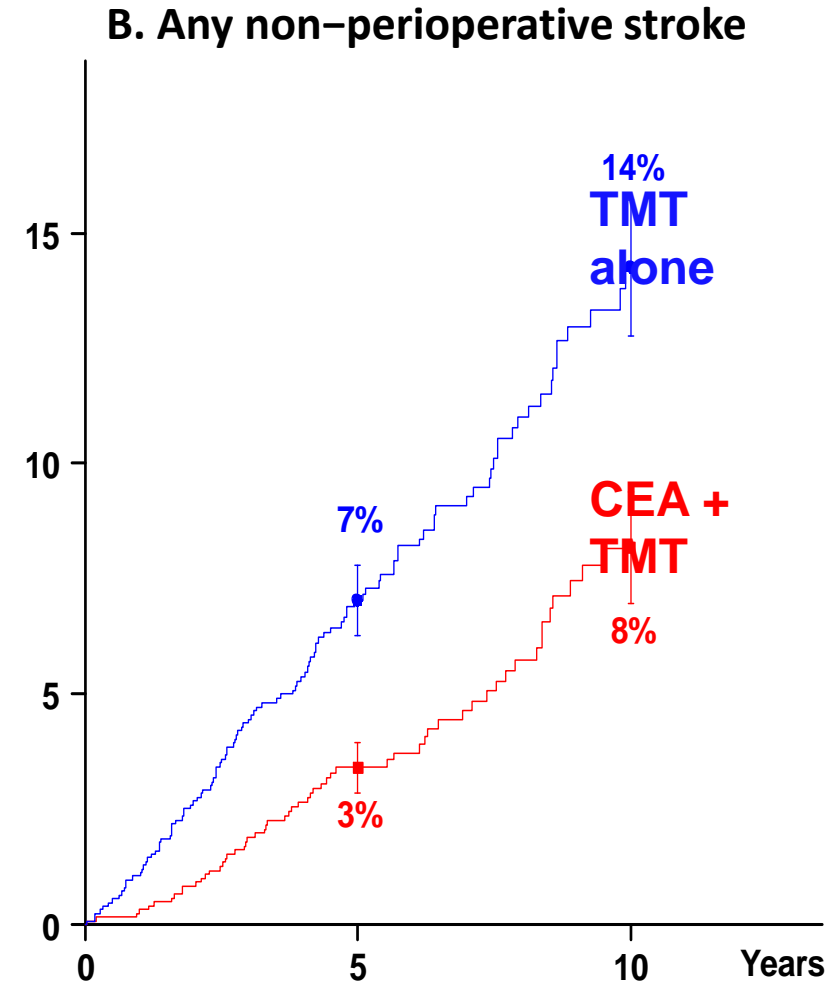
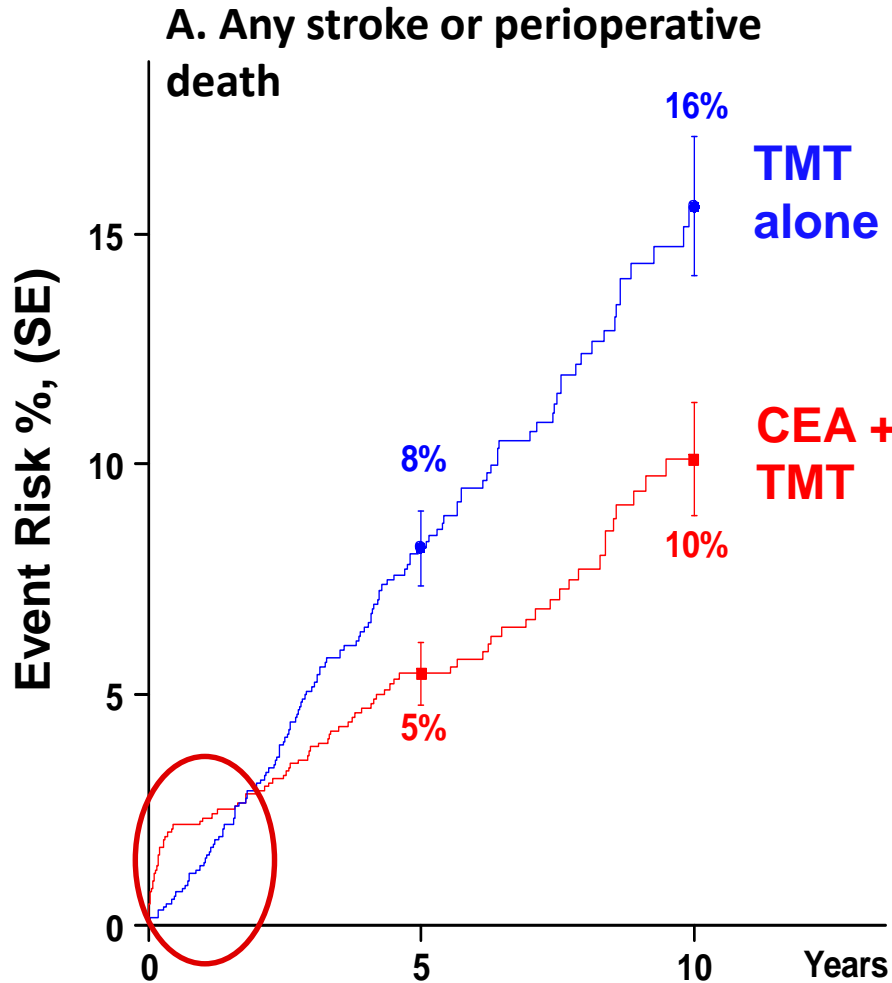
- **Important cause of ischaemic stroke (15-20%)**
- **Most (80%) carotid strokes have no warning symptoms**
- **Asymptomatic stenosis: important long-term stroke risk**
- RCTs confirm **net benefit** of CEA among asymptomatic patients
- Successful CEA **~halves long-term stroke risk**

Trial Characteristics – CEA vs not 1983-2008

	VA	ACAS	ACST-1
Recruitment	1983 - 1987	1987 - 1993	1993 - 2003
Participants	444	1 662	3 120
Region	USA	USA	Europe
Follow-up, Median [IQR]	5.7 [4.5- 7.0]	4.8 [3.7- 5.0]	9.0 [6.1- 11.1]

VA, ACAS, ACST-1 Trials

2291 Patients on triple therapy (ie, including statin) before stroke



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Purpose of this Study

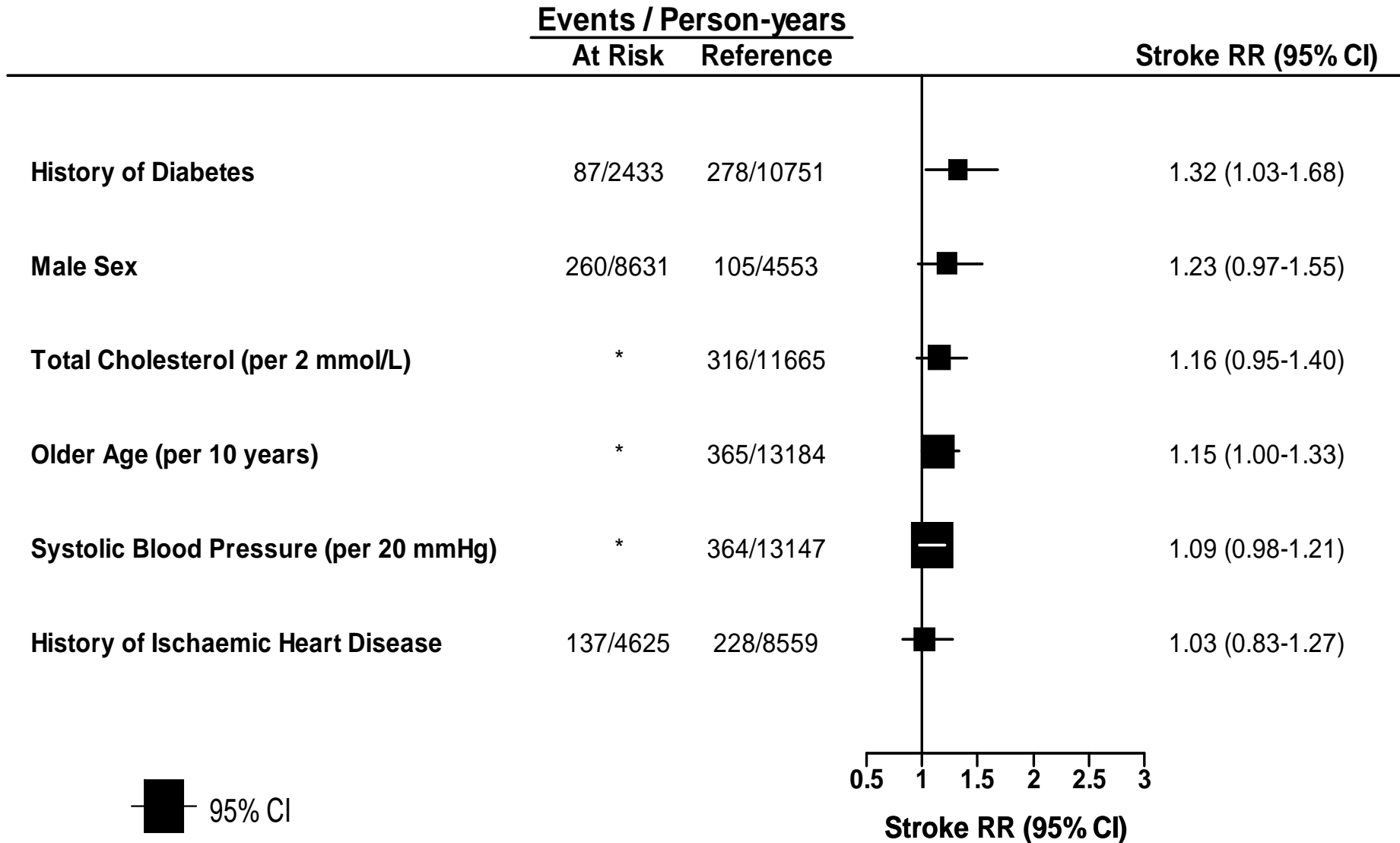
There is uncertainty as to which asymptomatic patients benefit most from carotid intervention

AIM: to develop a simple clinical risk score to identify patients with high risk asymptomatic carotid stenosis

Methods

- IPD of 'medically treatment' patients from all 3 asymptomatic trials
 - VA
 - ACAS
 - ACST-1
- Restricted to those with no CEA prior to stroke (ie, medically managed)
- Stroke risk ratios (RR) from Cox regression
- Most important factors included in risk score (RR >1.3)

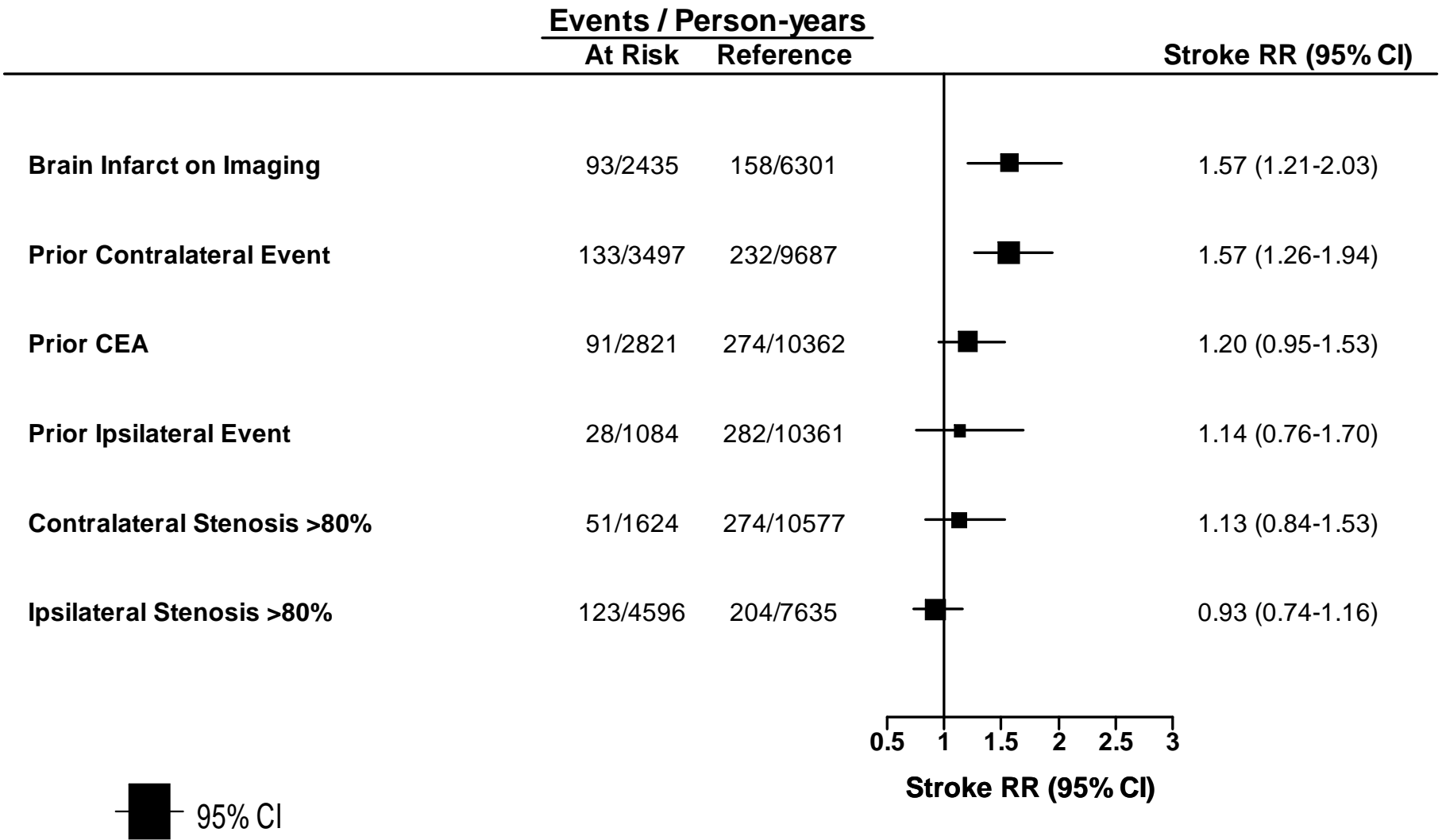
Association of CV Risk Factors with Stroke (among medically managed)



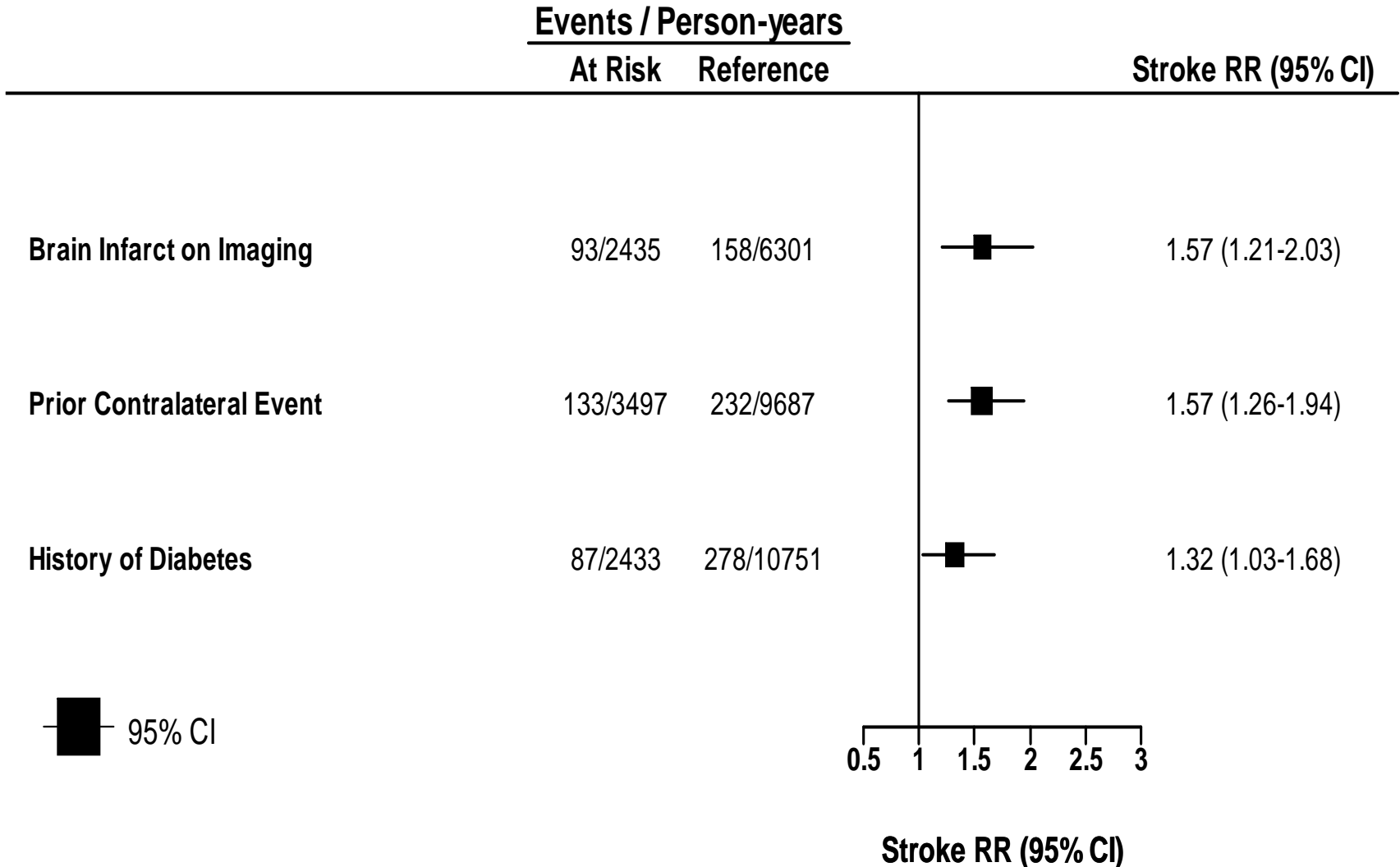
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Association of Cerebrovascular Events with Stroke

(among medically managed)



3 Important Stroke Risk Factors



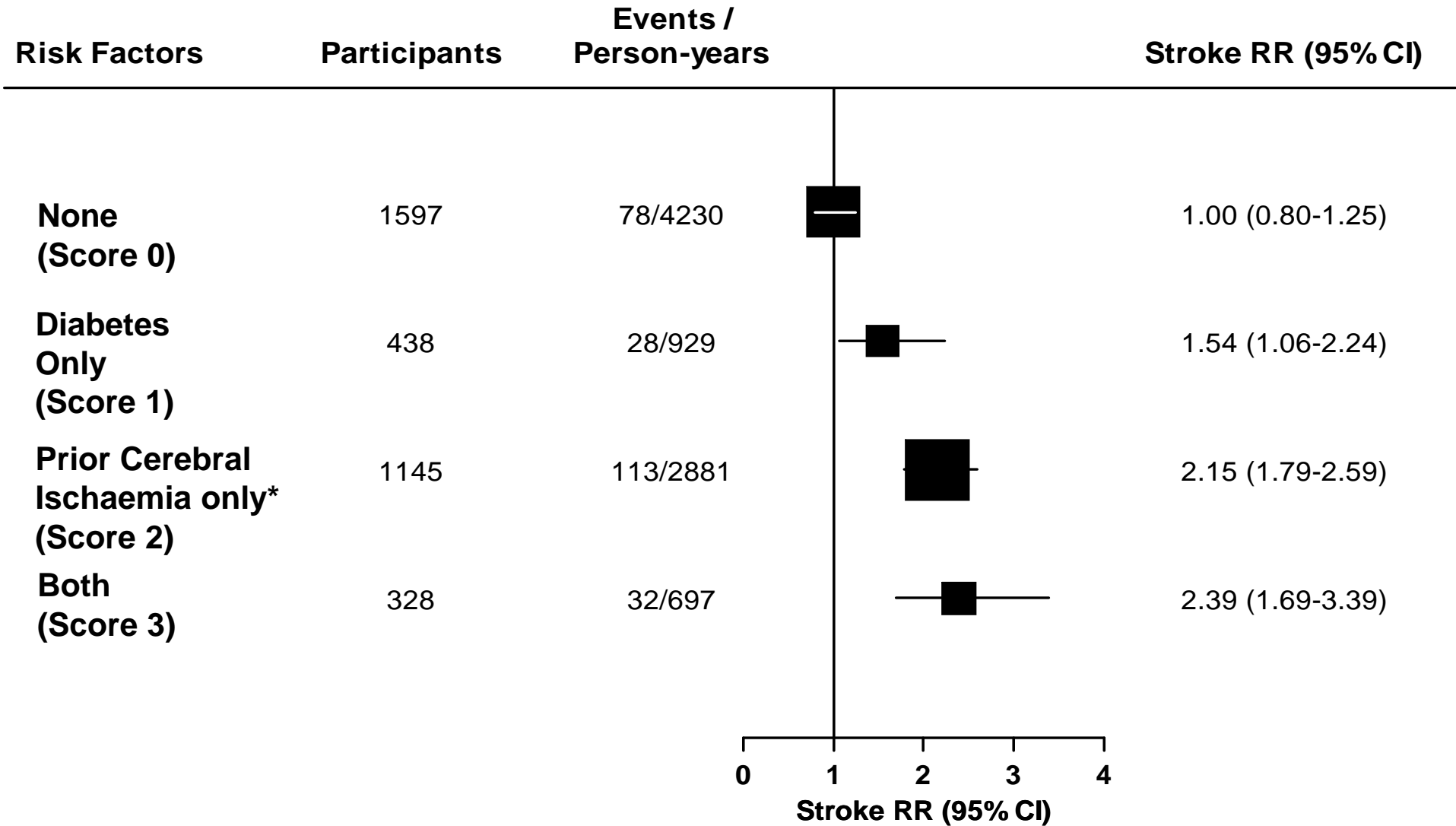
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Summative Risk Score

Risk Factors	Score
None	0
Diabetes only	1
Prior cerebral ischaemia* only	2
Both	3

**Prior contralateral symptoms or brain infarct on imaging*

Risk Prediction



**Prior contralateral symptoms or brain infarct on imaging*

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Risk Prediction

If the 10-year stroke risk is:

9% (no risk factors) **10y Absolute gain from CEA ~5%**

13%* (diabetes) **10y Absolute gain from CEA ~7%**

20% (prior ischaemia) **10y Absolute gain from CEA ~10%**
(*1/3 of trial participants*)

**Stroke risk in medically treated ACST-1 participants taking statins*

Implications

- **Statins work:** With CEA or without CEA, modern statin
~halves stroke risk
- **And CEA works:** With a statin or without a statin, successful CEA ~halves stroke risk
- Risk of stroke ~**double with prior cerebral ischaemia**
- **Those with higher risk scores should derive greater absolute benefit from CEA**

Conclusion

Simple characteristics (diabetes, prior ischaemia)
can be used to **identify high stroke risk patients**
who might benefit most from CEA

ACST-2

Surgery vs Stenting

Asymptomatic patients with tight stenosis requiring intervention:



Which procedure is generally better (in addition to good medical treatment)? :



carotid surgery (CEA)
or
carotid stenting (CAS)?

ACST-2 progress – High Stroke Risk patients

>2731/3600 now recruited, 869 still needed, by end of 2019


30% diabetic

35% previous symptoms or cerebral infarcts


Follow up to date - 3.5 years

Statin treatment is good

2017 ESVS and ESC Guidelines



ACST-2



Go with the Guidelines!

“10-15% of all strokes follow thromboembolism from an asymptomatic ICA stenosis > 50%”
ESVS Guidelines, 2017

Consider for Intervention
IIa B


Asymptomatic 60-90% stenosis at increased risk of late stroke, provided perioperative risk of stroke/death is <3% and life expectancy > 5 yrs

Patients at higher risk of stroke


- History of contralateral TIA/ Stroke
- Silent ipsilateral infection
- Diabetes
- Specific plaque markers/TCl emboli
- Impaired cerebral reserve

“ACST-2 has been randomising asymptomatic patients to CEA or CAS – it is hoped that all surgeons and interventionalists will support these RCTs”
ESVS Guidelines, 2017

Class	Evidence Level
I General Agreement Procedure beneficial/effective	A > 1 RCTs or meta analyses
IIa Conflicting evidence but weight of opinion in favour	B > 1 RCT or large <u>non-randomised studies</u>
IIb Less well established usefulness/efficacy	C Consensus or small studies or registries



ACST-2



Go with the Guidelines!

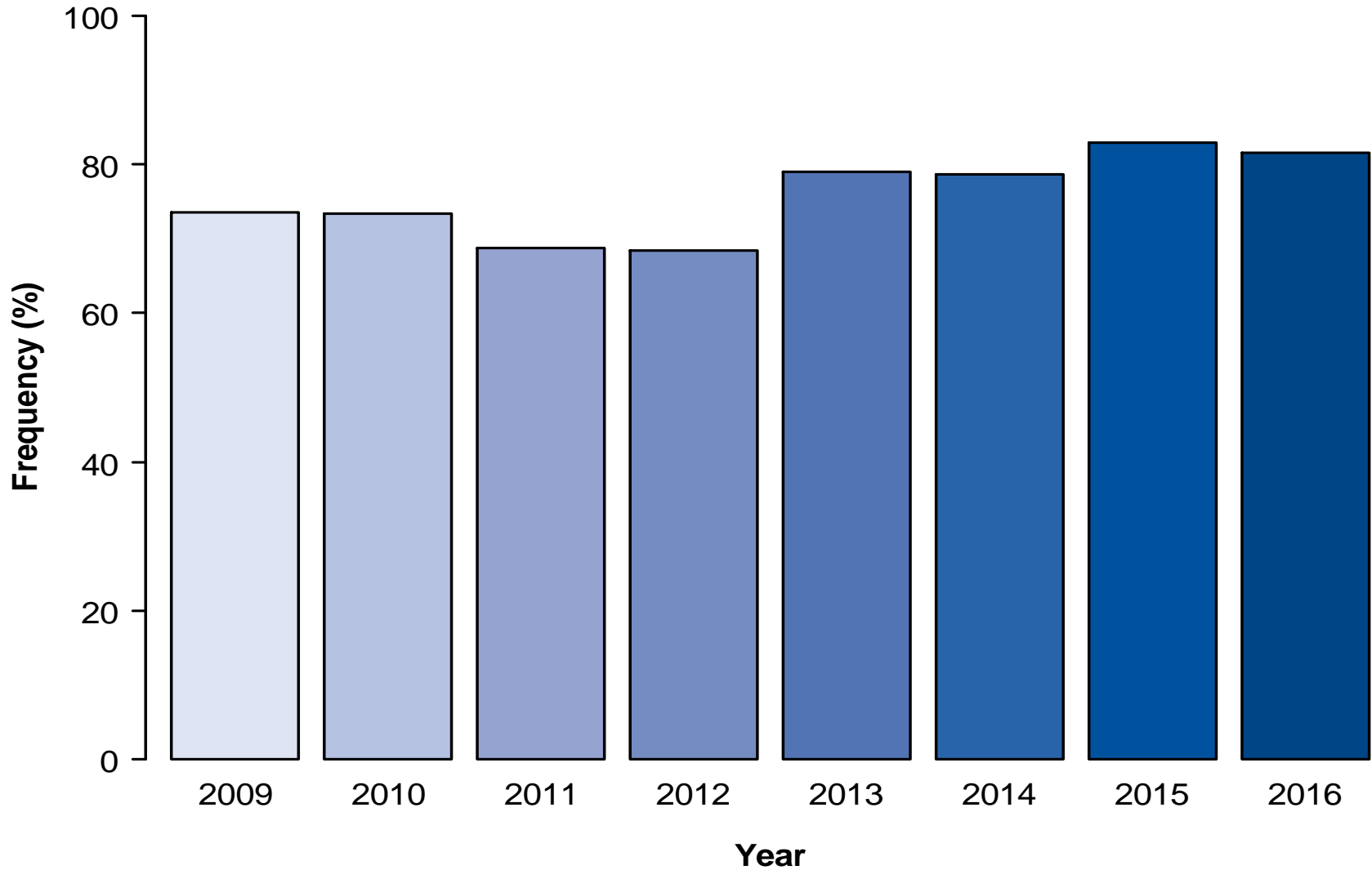
Medical Treatment for all	<ul style="list-style-type: none"> • Longterm single APT (usually aspirin) • Clopidogrel if aspirin intolerant • Statin therapy • BP lowering treatment to maintain BP < 140/90 	I IIa	A C
CEA & CAS	<ul style="list-style-type: none"> • APT periprocedure and longterm • Continue statins • Caution in reducing BP, but avoid uncontrolled hypertension > 180/90 mmHg 	I I II	B B A
CAS only	<ul style="list-style-type: none"> • Consider EPDs • DAPT (aspirin/clopidogrel) for at least 1 month after 	II I	C B
Post procedure	<ul style="list-style-type: none"> • Independent assessment is recommended 	I	C

ESC/ESVS Algorithm for Treatment of Asymptomatic Carotid Stenosis

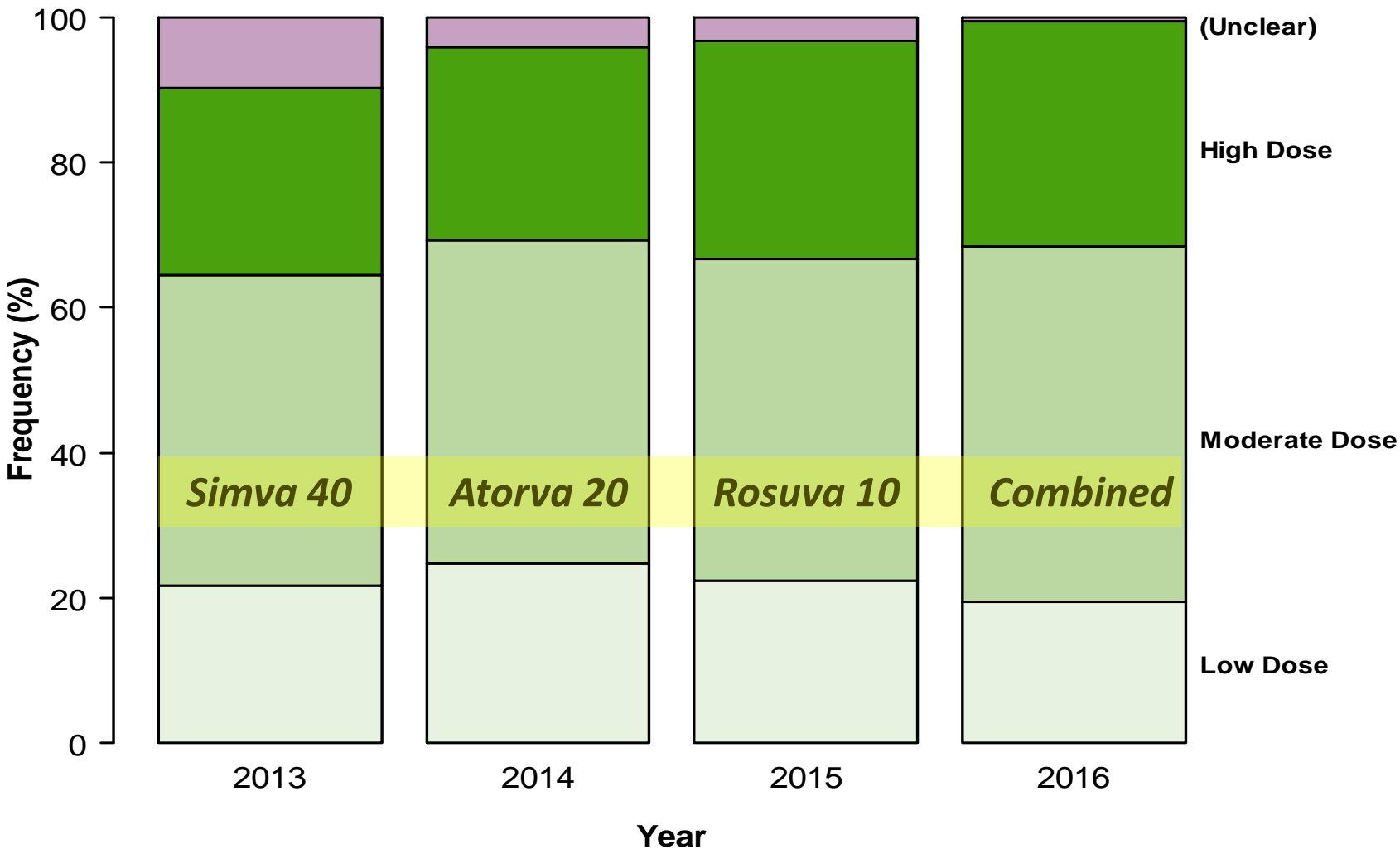
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    graph TD
      A["60-99% stenosis  
No recent TIA/stroke  
Symptoms ipsilaterally"] --> B["Life expectancy >5 yrs?  
Favourable anatomy?  
Higher stroke risk on BMT?"]
      B -- Yes --> C["Consider CEA +BMT  
IIa B  
Within ACST-2  
Consider CAS + BMT  
IIb B"]
      B -- No --> D["BMT  
I A"]
    
```

ACST-2: Long-term statin use >80%



ACST-2: >75% on good (or very good) statin regimens



Acknowledgements

ACST, ACAS, VA Trialists and
to the participants who took
part

ACST-2 information
website acst-2.org

