Temporal Improvement in Carotid Stent Outcomes: Achievement of AHA Target Goals in Abbott Vascular Post-Marketing Trials

William A. Gray MD, Ronald Fairman MD, Rod Raabe MD, L. Nelson Hopkins MD, Jay S. Yadav MD, Richard Atkinson MD, Mark Wholey MD, Richard Green MD, Stan Barnwell MD.

For the CAPTURE Investigators

Columbia University Medical Center
The Cardiovascular Research Foundation

TCT October 20th, 2007 (Washington D.C.)

CARDIOVASCULAR RESEARCH FOUNDATION

COLUMBIA UNIVERSITY MEDICAL CENTER

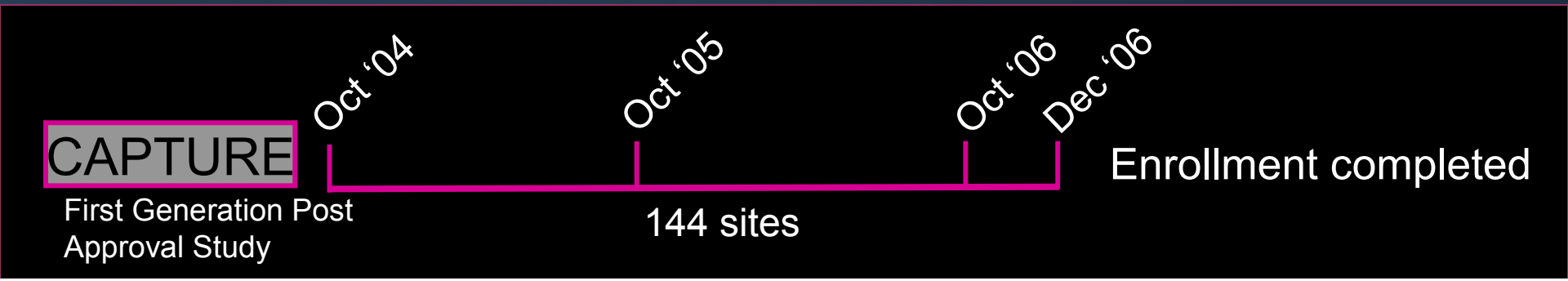
Disclosures

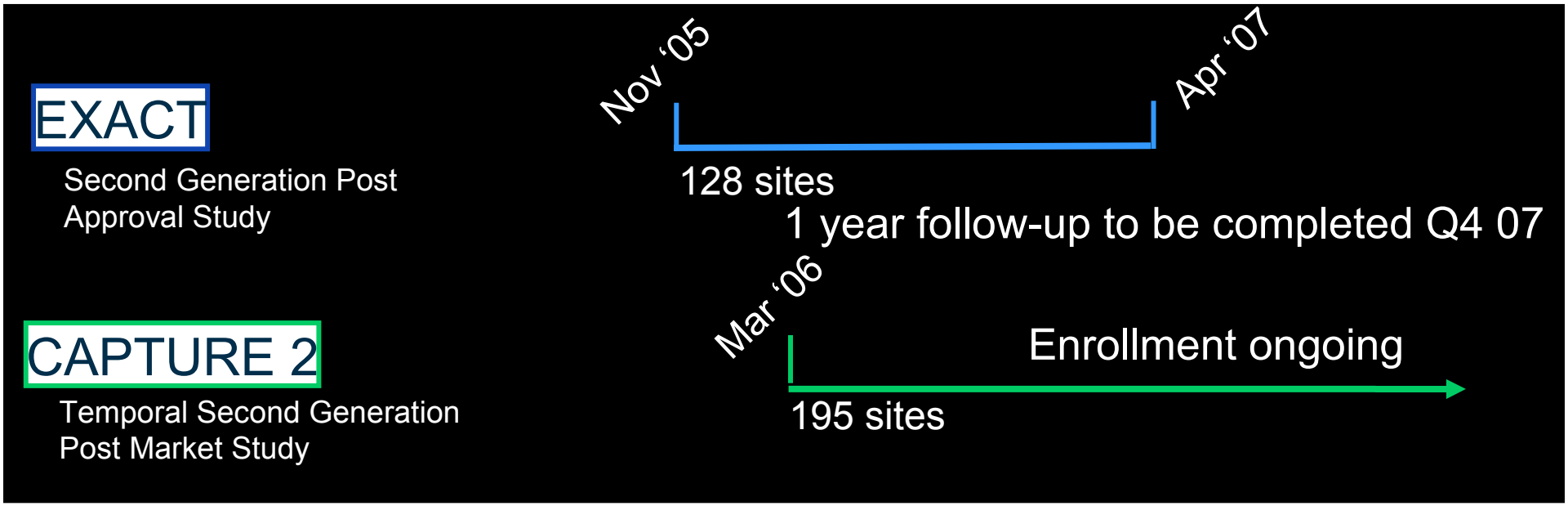
- Consulting Agreement
  - Abbott Vascular
- Clinical Research Support:
  - Abbott Vascular

CAPTURE and EXACT 2: Clarifications

- Clinical Studies are not directly comparable by methodology presented
- Data from respective studies are presented for educational purposes

Carotid Stenting
Post-Marketing Studies: Temporal relationships





CAPTURE 2 and EXACT: Design, Conduct, Endpoints

- High surgical risk post-approval trials
- Sponsor: Abbott Vascular
- Devices:
  - EXACT: Xact™ Rapid Exchange Carotid Stent System and Emboshield® BareWire™ Embolic Protection Device
  - CAPTURE 2: RX Acculink® Carotid Stent System and RX Accunet™ Embolic Protection System
- Overview
  - Enrollment continues in CAPTURE 2 and follow-up continues in EXACT
    - Analysis cohort includes patients with 30 day follow-up visits or event(s) within 30 days.
  - Pre-enrollment, 24-hour and 30-day neurologic exam performed by an independent neurologist or NIHSS certified specialist
  - Independent adjudication of neurological events
  - All patients return at 30 days for follow-up visit; Subset for EXACT return for 1 year follow-up

Post-Market Multicenter Studies: Quality Independent event adjudication

- Independent CEAC adjudication of all strokes and suspected strokes
- CEAC (Clinical Events Adjudication Committee) composition
  - CAPTURE: two Neurologists on CEAC
  - CAPTURE 2: two Neurologists and at least one IC, IR, or VS
  - EXACT: one Neurologist, one Vascular Surgeon and an Interventionalist

The rate of CEAC adjudicated strokes is ~50% higher than the rate of site reported strokes

- Primary Endpoint: DSMI all cause events at 30 days, including events unrelated to CAS
  - i.e. in ARCHeR, 18 pts had CABG within 30 days, with death/stroke rate of 39%, when excluding these pts, DSMI reduced 1%.

Post-Market Multicenter Study: Quantity
Sample sizes

- EXACT and CAPTURE/CAPTURE 2 were initiated independently by two sponsors (ABT, GDT) and use 2 different device systems (Xact/Emboshield and Acculink/Accunet).

- Large sample size, large # of sites
  - Total patients: 8336
  - 4225 patients/144 sites (CAPTURE),
  - 1987 patients/167 sites (CAPTURE 2),
  - 2124 patients/126 sites (EXACT)

  8334 total patients

Largest prospective, multi-center, neurologically-controlled, independently-adjudicated data set for carotid intervention ever assembled

Prior findings/publication from AV PMS registries

- **Outcomes of CAS in post-approval, non-trial setting**

  Gray WA, Yadav JS, Verta P, Scicli A, Fairman R, Wholey M, Hopkins LN, Atkinson R, Raabe R, Barnwell S, Green R. The CAPTURE registry: results of carotid stenting with embolic protection in the post approval setting. Catheter Cardiovasc Interv. 2007 Feb 15;69(3):341-8.

- **Timing, location, severity, and type of stroke location in CAS**

  Fairman R, Gray WA, Scicli AP, Wilburn O, Verta P, Atkinson R, Yadav JS, Wholey M, Hopkins LN, Raabe R, Barnwell S, Green R; for the CAPTURE Trial Collaborators. The CAPTURE Registry: Analysis of Strokes Resulting From Carotid Artery Stenting in the Post Approval Setting: Timing, Location, Severity, and Type. Ann Surg. 2007 Oct;246(4):551-558.

- **Predictors of outcomes in CAS in 3500 patients**

  Gray WA, Yadav JS, Verta P, Scicli A, Fairman R, Wholey M, Hopkins LN, Atkinson R, Raabe R, Barnwell S, Green R for the CAPTURE Trial Collaborators. The CAPTURE Registry: Predictors of Outcomes in Carotid Artery Stenting With Embolic Protection for High Surgical Risk Patients in the Early Post-Approval Setting. Catheter Cardiovasc Interv (in press)

AHA 1998 CEA Guidance Document

Patients With Asymptomatic Carotid Artery Disease

- *For patients with a surgical risk <3% and life expectancy of at least 5 years:*

Surgical endarterectomy has never, to date, demonstrated outcomes consistent with AHA guidelines within a prospective, neurologically-controlled, multi-center, adjudicated critical assessment of high surgical risk patients

Biller J, Feinberg WM, Castaldo JE, Whittemore AD, Harbaugh RE, Dempsey RJ, Caplan LR, Kresowik TF, Matchar DB, Toole JF, Easton JD, Adams HP Jr, Brass LM, Hobson RW 2nd, Brott TG, Sternau L. Guidelines for carotid endarterectomy: a statement for healthcare professionals from a Special Writing Group of the Stroke Council, American Heart Association Circulation. 1998 Feb 10;97(5):501-9.

CAPTURE 2 and EXACT: All Patients

Patient demographics are similar

Characteristic	CAPTURE 2* N=1987	EXACT* N=2124
Mean Age	73	72
Age ≥80	23.4%	23.7%
% Symptomatic	9.9%	9.6%
% Male	61.0%	63.1%
Diabetes Mellitus	34.3%	34.8%
Hypertension	88.9%	89.3%
Hypercholesterolemia	87.8%	74.3%
CHF	17.1%	17.4%
Unfavorable anatomy for CEA	19.2%	9.1%
Current Smoker	23.8%	19.2%
PVD	46.9%	44.9%

*Data not directly comparable; slightly different definitions and data collection

CAPTURE 2: Symptomatic vs Asymptomatic

Patient demographics are similar

Characteristic	CAPTURE 2* symptomatic N=197	CAPTURE 2* asymptomatic N=1788
Mean Age	72	73
Age ≥80	24.4%	23.3%
% Male	65.5%	60.5%
Diabetes Mellitus	34.0%	34.3%
Hypertension	89.3%	88.9%
Hypercholesterolemia	79.4%	88.8%
CHF	17.4%	17.0%
Unfavorable anatomy for CEA	26.8%	18.4%
Current Smoker	26.6%	23.5%
PVD	37.4%	47.9%

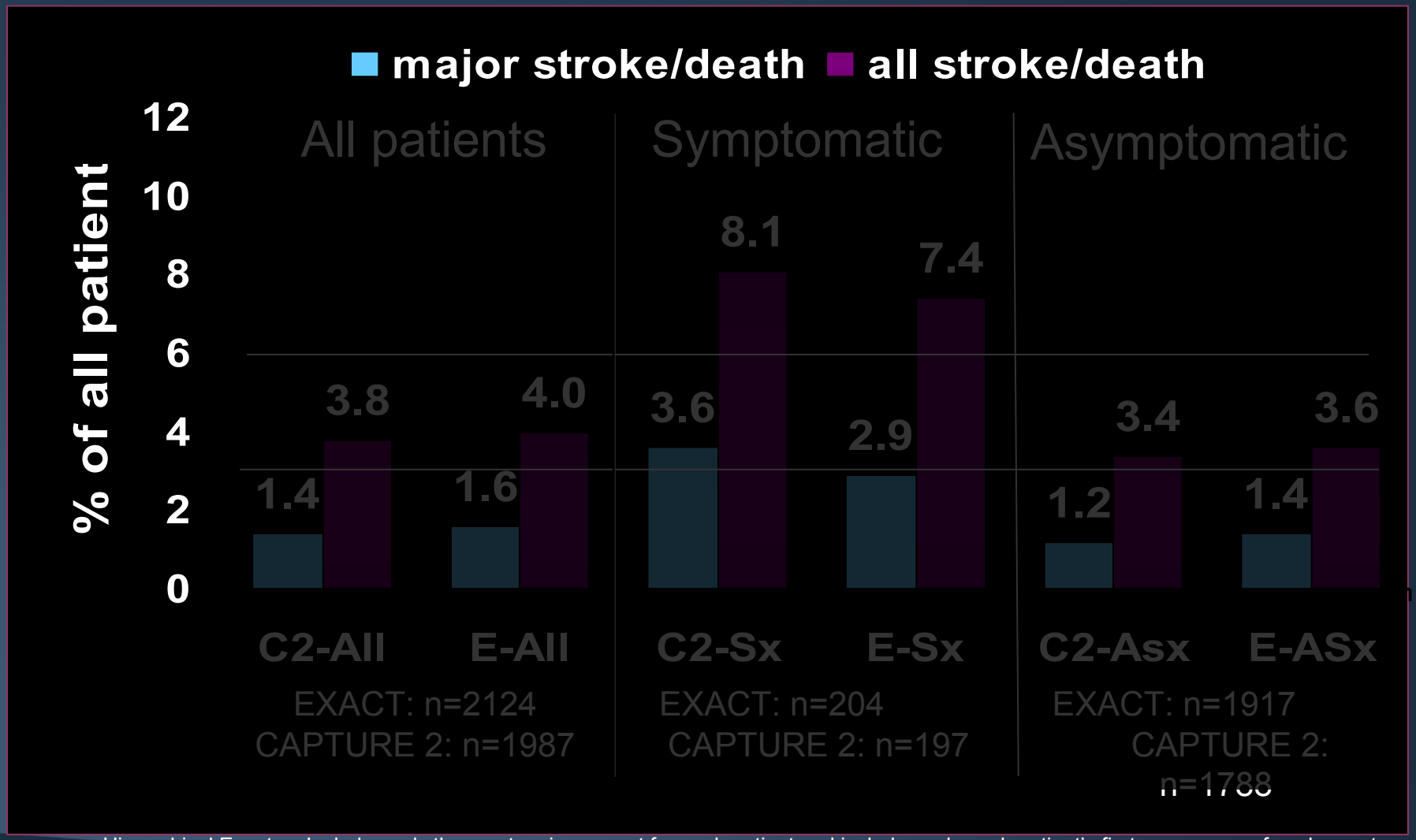
EXACT: Symptomatic vs Asymptomatic

Patient demographics are similar

Characteristic	EXACT* symptomatic N=204	EXACT* asymptomatic N=1917
Mean Age	71	73
Age ≥80	19.1%	24.2%
% Male	66.2%	62.90%
Diabetes Mellitus	33.3%	34.9%
Hypertension	84.7%	89.9%
Hypercholesterolemia	65.6%	75.1%
CHF	13.4%	17.8%
Unfavorable anatomy for CEA	14.6%	8.5%
Current Smoker	25.2%	18.6%
PVD	38.9%	45.6%

CAPTURE 2 and EXACT:

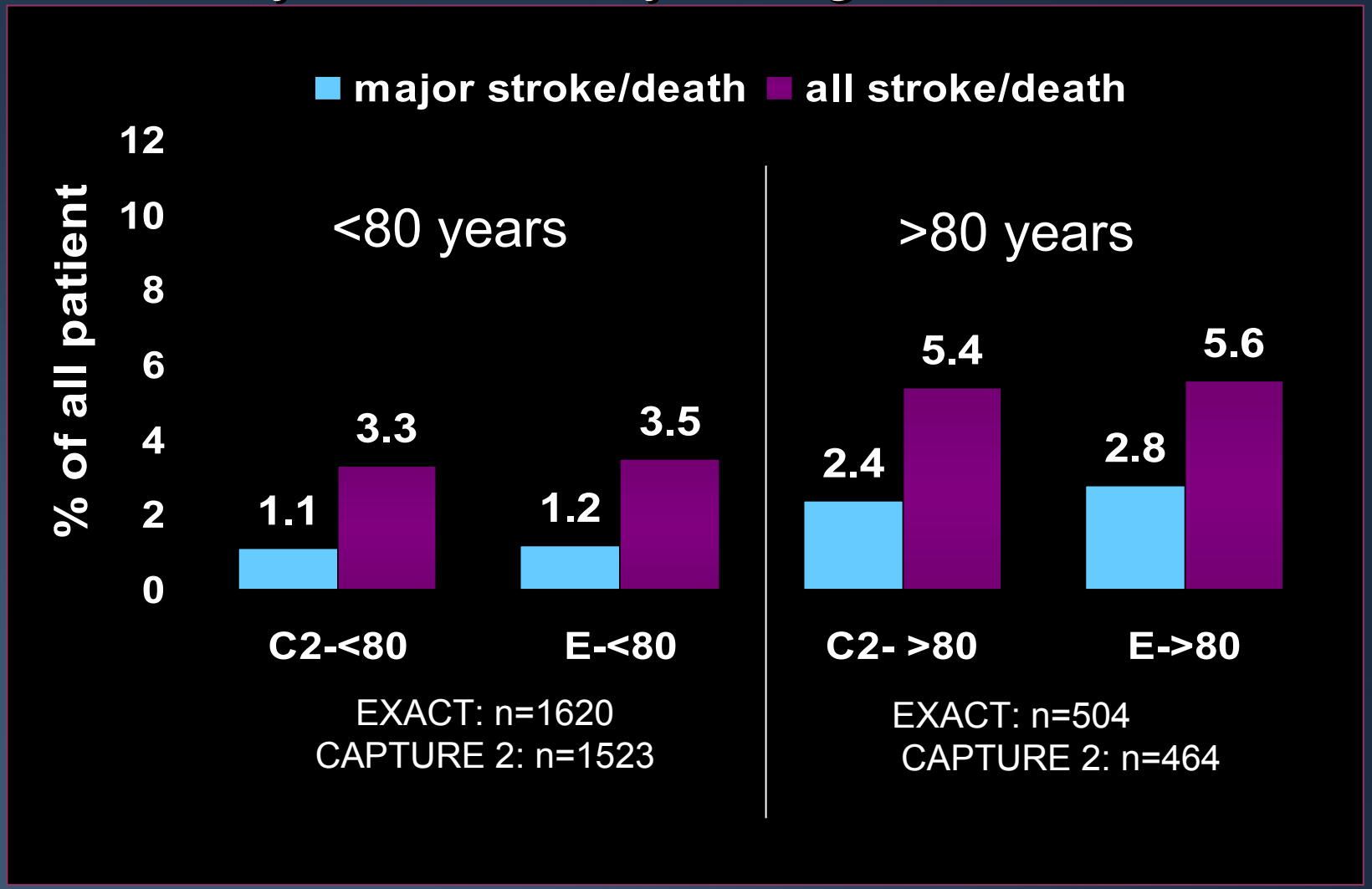
All stroke/death and major stroke/death by symptom status



•Hierarchical Events – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event.
•Clinical Studies are not directly comparable by methodology presented. -Data from respective studies are presented for Educational purposes

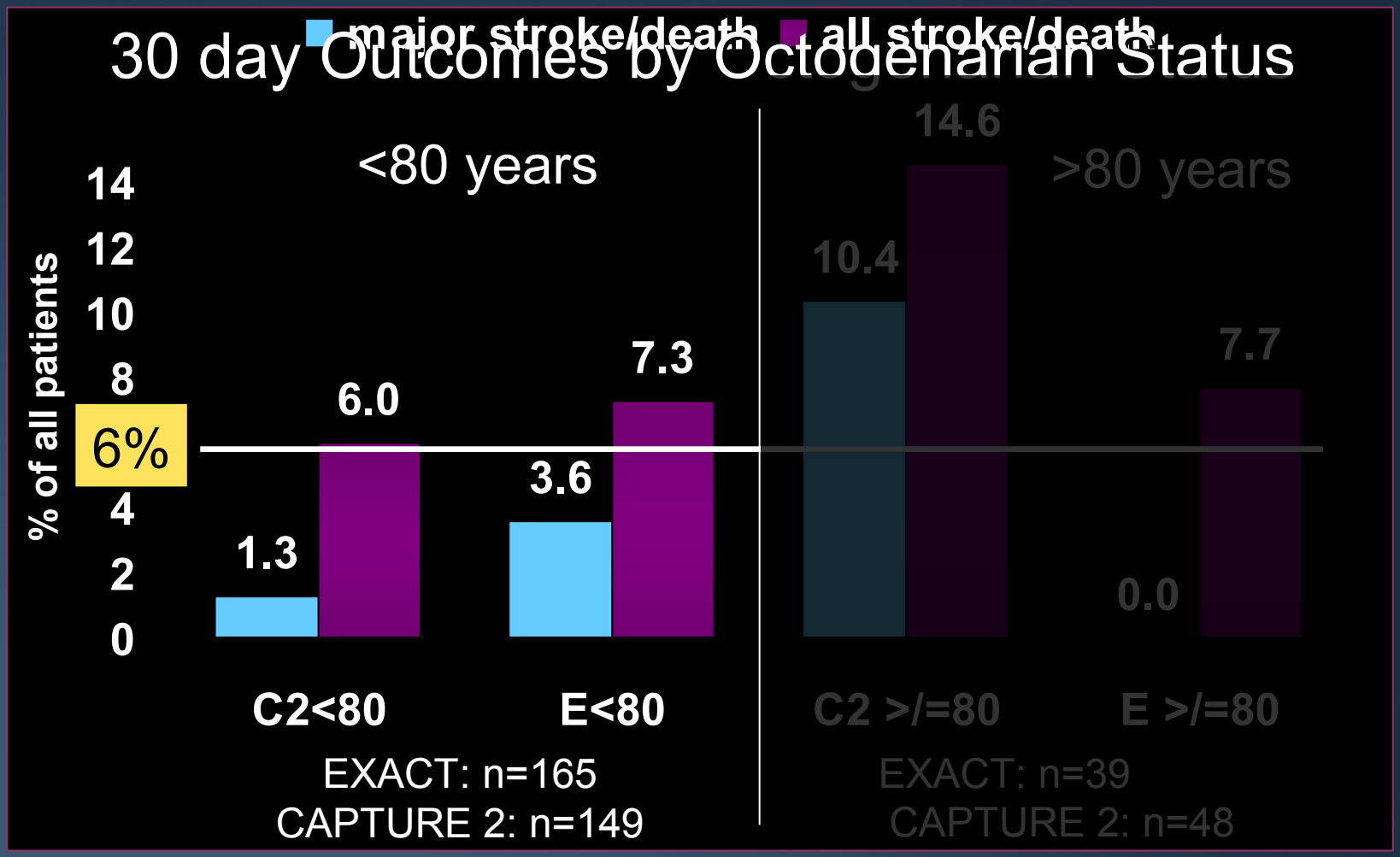
CAPTURE 2 and EXACT: All Patients

30 day outcomes by Octogenarian Status



•Hierarchical Events – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event.
•Clinical Studies are not directly comparable by methodology presented. -Data from respective studies are presented for educational purposes

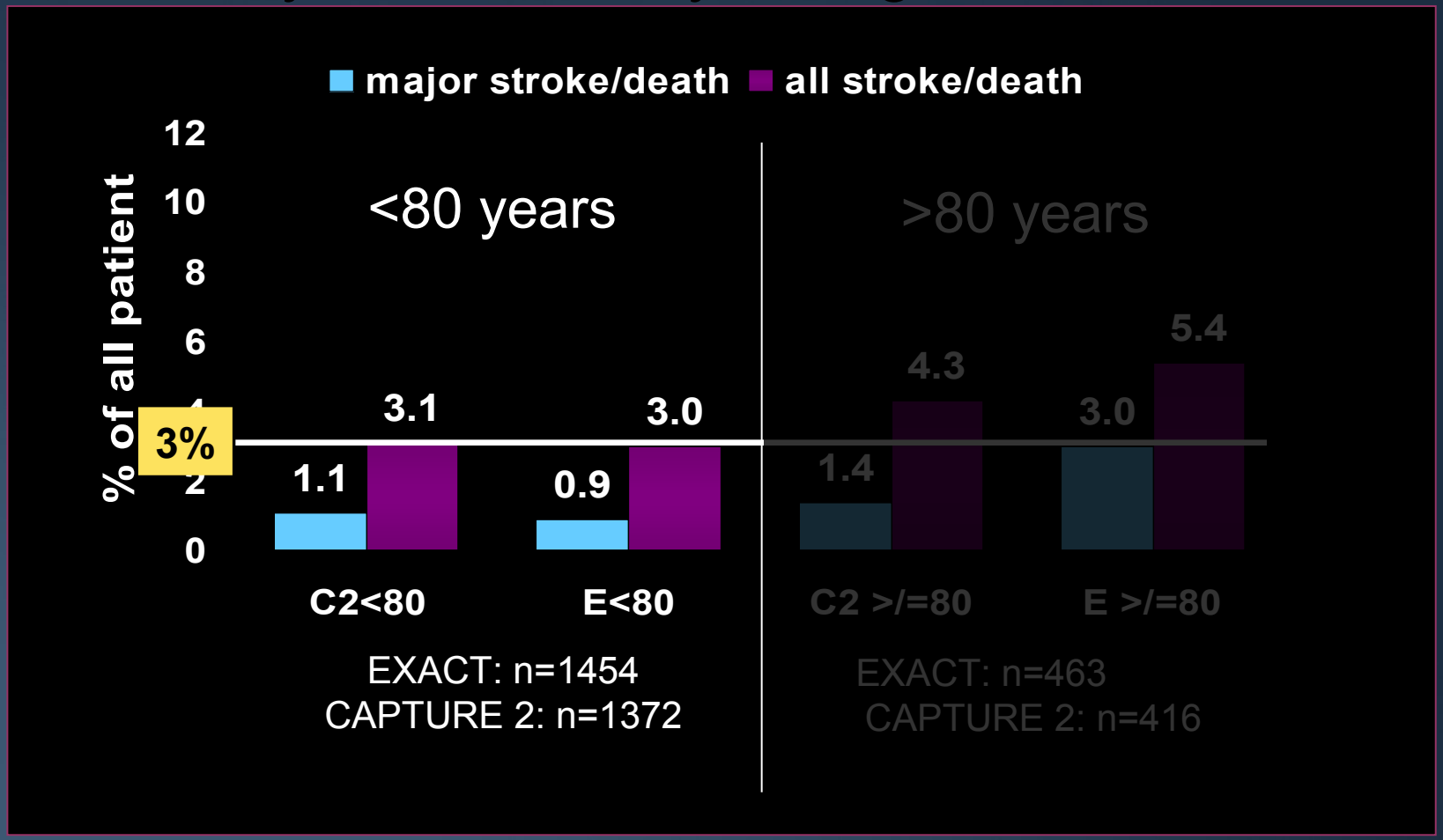
CAPTURE 2 and EXACT: Symptomatics



- Hierarchical Events – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event
- Clinical Studies are not directly comparable by methodology presented. -Data from respective studies are presented for Educational purposes

CAPTURE 2 and EXACT: Asymptomatics

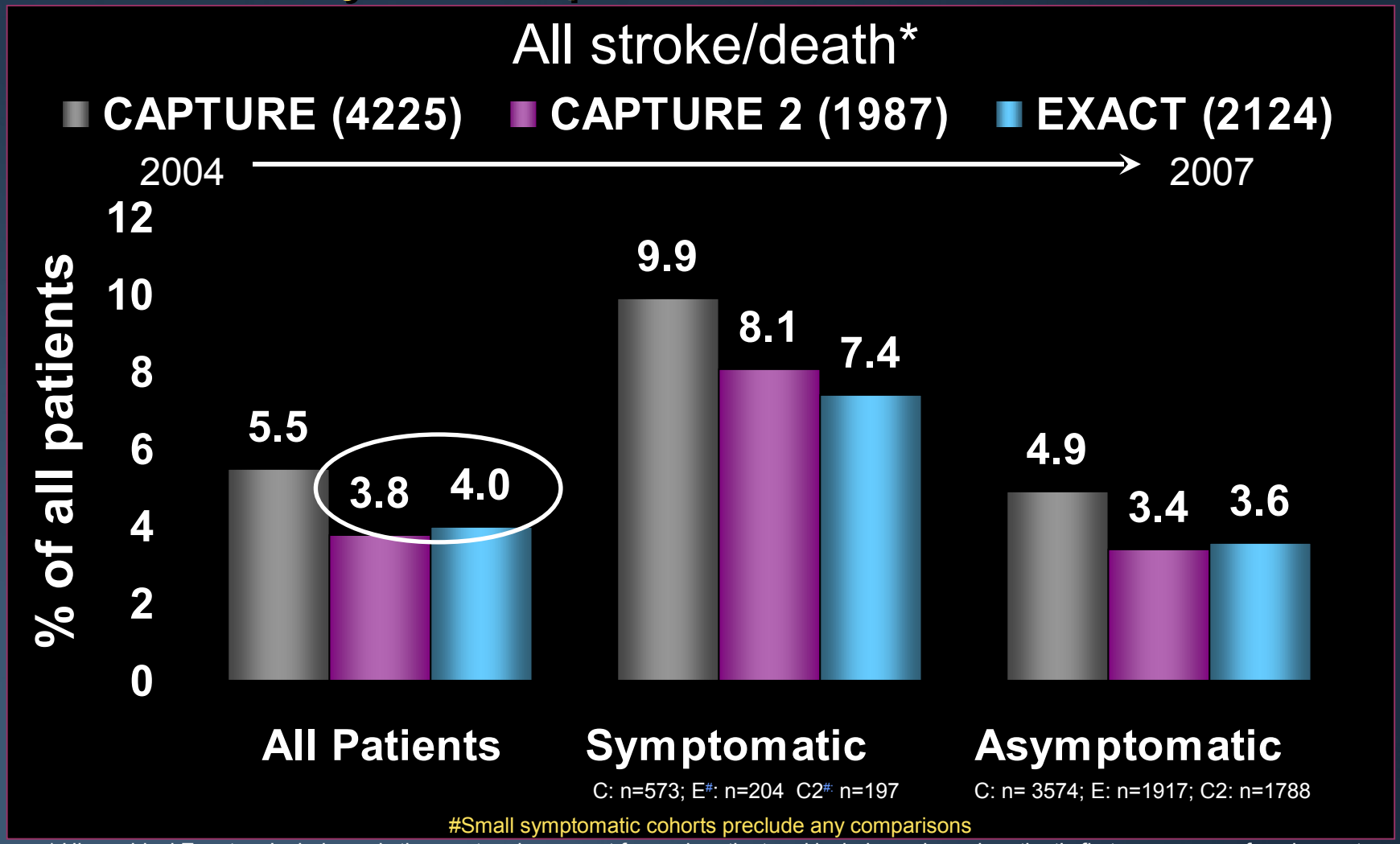
30 day Outcomes by Octogenarian Status



- Hierarchical Events – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event
- Clinical Studies are not directly comparable by methodology presented. -Data from respective studies are presented for educational purposes

CAPTURE and CAPTURE 2 and EXACT:

3 year improvement in outcomes



#Small symptomatic cohorts preclude any comparisons

* Hierarchical Events – Includes only the most serious event for each patient and includes only each patient's first occurrence of each event

CAPTURE 2 and EXACT:
Strengths and limitations of this analysis

Limitations of Analysis:

- Clinical Studies are not directly comparable
- Interim results: analysis is on-going
  - EXACT reporting on 2124 patients
  - CAPTURE 2 reporting on 1987 patients
  - Small symptomatic cohorts preclude any comparisons

- Strengths:
  - Large sample size
  - Large number of sites and clinicians
  - Diverse experience levels
  - Neurological evaluation requirement
  - Independently adjudicated

CAPTURE 2 and EXACT: Conclusions

- Post Approval Studies continue to compare favorably to landmark trial results.
  - EXACT stroke/death rate of 4.0% and CAPTURE 2 stroke/death rate 3.8% includes various levels of experience and high risk anatomical and co-morbid conditions
- Second generation post market trials CAPTURE 2 and EXACT suggest improving outcomes compared to the first generation study.
- No apparent differences are observed between open-cell based system (Acculink and Accunet) and closed cell based system (Xact and Emboshield) as exemplified in this cohort in excess of 4000 patients.

CAPTURE 2 and EXACT: Conclusions

- Ongoing improvement in outcomes in <80 symptomatics, approaching AHA guidelines
  - Conclusions are limited by small numbers

- Ongoing improvement in outcomes in <80 asymptomatics, approaching/achieving AHA guidelines

First-ever demonstration of carotid revascularization in high surgical risk patients with outcomes consistent with AHA guidelines