Multiple Mechanisms to Retain Participants in a Long-Term Randomized Clinical Trial

The Carotid Revascularization Endarterectomy vs. Stenting Trial (CREST)

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Mayo Clinic

32nd Annual Meeting – 2011
Vancouver, British Columbia, Canada
Carotid Revascularization
Endarterectomy vs Stenting Trial

Grant Sponsorship: NIH – US Public Health Service, NINDS, R01 NS 038384
Study Design

- Randomized, controlled trial with blinded endpoint adjudication
- Comparing CEA and CAS in participants with symptomatic and asymptomatic stenosis
- 108 US and 9 Canadian sites
- 2502 patients – average age 70
Patient Retention is required in order to:

• Avoid costly delays

• Achieve pre-specified sample size

• Maintain adequate study power
Challenges to Retention

- Understanding the motivations of patients
- Schedules
- Financial Barriers
- Distance
Why were patients dropping out?

- Patient died
- Patient lost to follow-up
- Patient refused to return for follow-up
  - Bad outcome
  - Dementia and other health problems
  - Did not like the care received
  - Too burdensome/expensive to return
  - Other more important family issues
Structure

CREST Operations Committee

UMDNJ

Statistical and Data Management Center

Mayo Clinic Florida
Multiple Mechanisms to Retain Participants

- Relationship, Relationship, Relationship
- Coordinator training
- Standing agenda item
### Multiple Mechanisms to Retain Participants

**9th Annual CREST Coordinators’ Meeting**  
*May 12, 2011 – Miami, FL*

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Presenter(s)</th>
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<tbody>
<tr>
<td>8:30 am</td>
<td>BREAKFAST</td>
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<tr>
<td>9:00 am</td>
<td>Welcome</td>
<td>Thomas Brott/Linda Flaxman</td>
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<td>9:15 am</td>
<td>Highlights: CREST Progress (May 2010 – May 2011)</td>
<td>Alice Sheffet</td>
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<td>9:25 am</td>
<td>CREST Long Term Follow-up</td>
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<tr>
<td></td>
<td>1) Retention of Participants and Sites</td>
<td>Thomas Brott</td>
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<td>2) Summary Reports</td>
<td>Jenifer Voeks</td>
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<td></td>
<td>• Patients Active, Withdrawals, Deaths</td>
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<td></td>
<td>• Summary of Patient Follow-up Visits</td>
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<td>• Visits Within Targeted Date</td>
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<tr>
<td>3) CREST Site Challenges &amp; Coordinators’ Suggestions for Improvement</td>
<td>Thomas Brott/All</td>
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Advances in medical treatments are made possible by information gained from people such as yourself who choose to get involved in medical research. Thank you for your valuable time and participation in what is now the largest carotid treatment trial to date — anywhere.

As of March 31, 2008, patient enrollment into the randomized phase of CREST totaled 2,337 (1,245 participants with symptoms and 1,092 participants without symptoms). Of the 2,337 enrollees, 35% are women and 9% are minority. It is projected that CREST will reach its goal of 2,500 randomized patients by mid-2008, enrolled from 125 medical centers in the United States and Canada. Results of CREST will be announced after all participants complete follow-up visits and all results are collected and analyzed.

Visits to the doctor and hospital involve time, energy, and sometimes inconvenience. However, follow-up visits are of critical importance to your health. You may not always recognize a symptom reflecting how well your brain is functioning. The CREST follow-up visits are brief, but they do involve evaluations that could pick up a symptom or change of brain function that might otherwise be missed. In addition, risk factors for stroke are monitored during your CREST follow-up visits. Being a participant in CREST is a great opportunity to play an active role in your own health care.

Again, thank you for your participation in CREST and for your valuable contribution in helping to find a better way to prevent strokes.

Next scheduled appointment:
__________________________________________________________________________

Investigator’s Name
__________________________________________________________________________

Coordinator’s Name
Phone: __________________________________________ Email: ______________________

www.CRESTtrial.org
Stroke is a medical emergency. Know these warning signs and teach them to others. Every second counts:

- Sudden weakness or numbness of the face, arm, or leg especially on one side of the body
- Sudden trouble speaking or understanding, or confusion
- Sudden trouble seeing in one or both eyes, or to one side
- Sudden trouble walking, dizziness, loss of balance or coordination
- Sudden, severe headache with no known cause

Call 9-1-1 immediately if you experience symptoms!
Time lost is brain lost!

Follow-up Visits:

Date: __________________________
Time: __________________________
Dr.: __________________________
Place: __________________________

Date: __________________________
Time: __________________________
Dr.: __________________________
Place: __________________________

Date: __________________________
Time: __________________________
Dr.: __________________________
Place: __________________________

Coordinator’s Name
Phone: __________________________

Dropping In or Dropping Out

The importance TO YOU for follow-up in CREST

Finding a Better Way to Prevent Strokes

www.CRESTtrial.org
Visits to the doctor and hospital involve:

- inconvenience, but are important to my health
- opportunity to discuss my health
- what specifically gets done for my health

In addition to the risk factors - What about me?

Thank goodness the brain is as complicated as it is. But, as a consequence, I may not always recognize how well my brain is working — and, I may not always be aware of a change in my brain function.

The CREST visits are brief, but they do involve evaluations that could pick up a symptom or change of brain function that might be missed. Research shows that the sooner such symptoms and changes are detected the better.

Bonus Benefits

The risk factors for stroke and heart attack overlap. So do some of the symptoms. The CREST follow-up, therefore, may help me to be heart healthy.

How may the follow-up improve my health?

Risk factors for stroke can be discussed and monitored:

- Blood pressure
- Cholesterol
- Diabetes
- Diet and exercise
- Smoking

Stroke Facts

- Stroke is the third leading cause of death in America and the number one cause of adult disability.
- According to the National Stroke Association, more than 750,000 Americans have a new or recurrent stroke every year, and incidence is on the rise.
- It is estimated that 5.4 million (or 1 in 55) Americans are living with the effects of stroke at any given time.
- After-effects of stroke can appear up to one year later (and sometimes even later than one year).
- Stroke requires emergency treatment.

The above “Stroke Facts” information can be found on the National Stroke Association website. For additional information visit the website at www.stroke.org.
RETENTION UPDATE

It has been 6 months since we debuted the CREST Retention Report (Aug. 2010 Newsletter) to recognize the accomplishments of all CREST centers towards achieving patient re-consenting and retention goals. Since then, we have also utilized this report to provide valuable updates to the NIH, the FDA, and our Site Principal Investigators. Our plan is to continue using this report to track patient status and study progress throughout the CREST long-term follow-up.

There were 2502 subjects in the CREST cohort, of which 213 have since died, 217 have withdrawn and 117 graduated from the study prior to implementation of the long-term follow-up. As per the May 2, 2011 Pragmatic Design CREST has 1046 subjects.

That leaves 340 subjects among our remaining sites for whom Amendment VI status has yet to be determined.

If you have subjects who have not yet been re-consented, please make your best effort to complete this process during their next scheduled contact or sooner!

Special Thanks go out to the CREST teams at the Arkansas VA and Central Baptist for helping to “rescue” several CREST subjects from otherwise being withdrawn by closing sites. When Sandi Brock and Linda Breathitt (RGs at these sites) learned of the potential early study terminations, both...
Summary Reports to Sites

- Future Visits
- Current forms expected, but not overdue
- Missing forms (overdue)
- Retention report
Protocol-based Retention Efforts

- +/- 8 week visit window
- Temporary CPS form
- Vital Status option
- Transfer option
- Decreased contacts in Amendment 6
- Continued evolution
Withdrawal Protocol

- All avenues have been exhausted
- Document attempts
- Seek advice from Mayo, CRAs, UAB
- CONTACT DR. BROTT!!
Results

- **2502** Total patients randomized
  - **213** Deaths
  - **217** Withdrawals
  - **117** Graduates
  - **110** reached 48 month visit – do not wish to continue

1846 patients retained and available for Amendment 6
Yearly Cumulative Rate of Patient Dropouts

- 2005 - 6.7% (41 of 610)
- 2007 - 5.4% (109 of 2022)
- 2009 - 6.4% (159 of 2502)
- 2011 - 8.6% (217 of 2502)
Conclusions:

Multiple mechanisms can be effective in:

- Avoiding timely, cost-effective delays in enrollment
- Sustaining study integrity
- Retaining adequate study power