

Update on the BEST-CLI Trial

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BEST-CLI Trial: Overview

- Prospective, randomized, multicenter, open-label superiority trial
- **2100** patients at **160** clinical sites
- Funded by National Institutes of Health

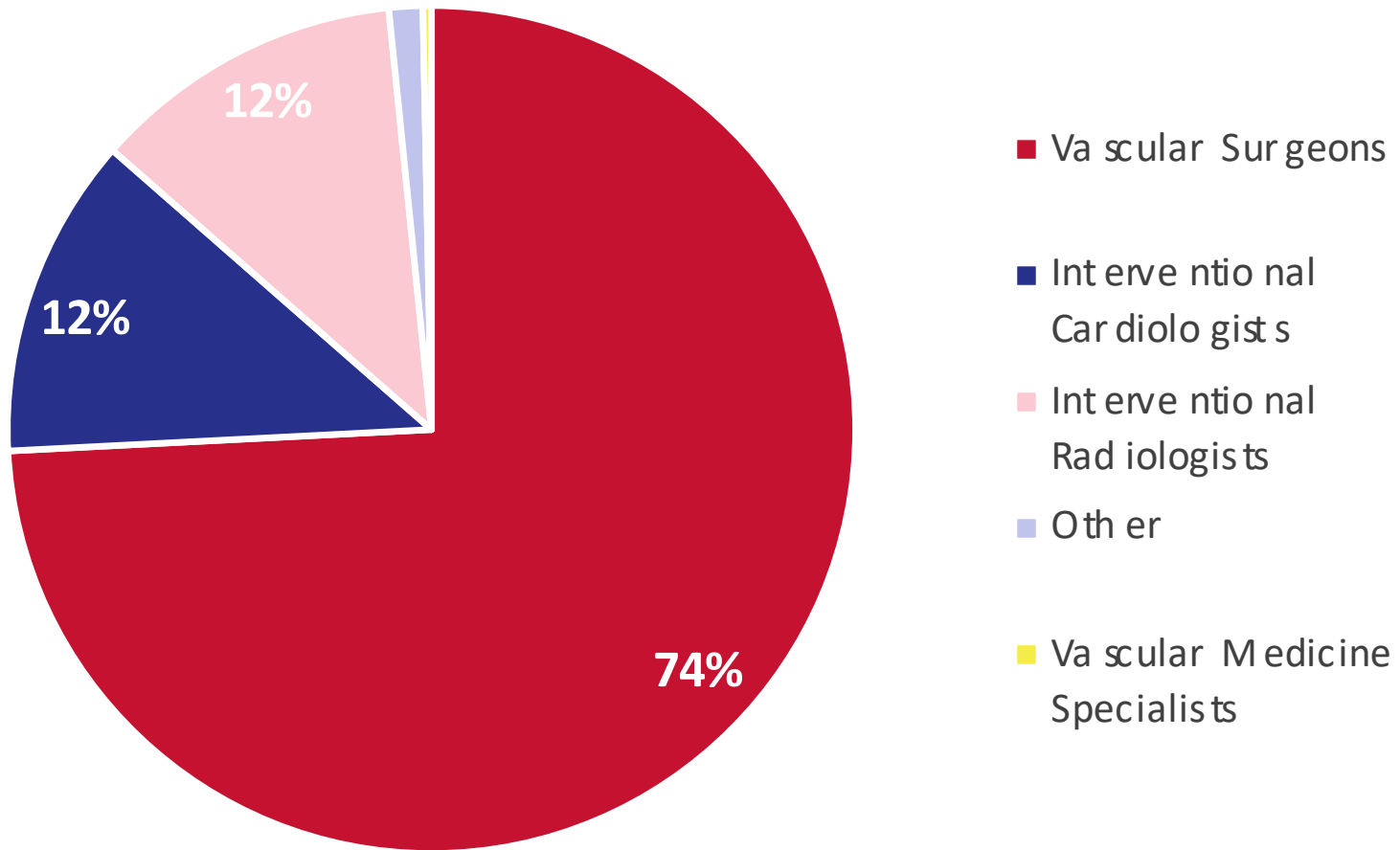
Goal: to assess ***outcomes, quality of life and cost*** in patients who are candidates for both vascular surgery and endovascular therapy

- ***Positioned to provide an Evidence-Based dataset for treatment of CLI***
 - Well powered and designed
 - Real world pragmatic trial
 - Multi-disciplinary – everyone involved
 - Two cohort design
 - SSGSV (optimal conduit) – 1620 patients
 - All conduits are allowed – 480 patients
 - Novel endpoints
 - MALE-free Survival is optimal endpoint
 - Hemodynamic success, clinical success, interventions per limb salvaged
 - Rigorous cost-effectiveness component

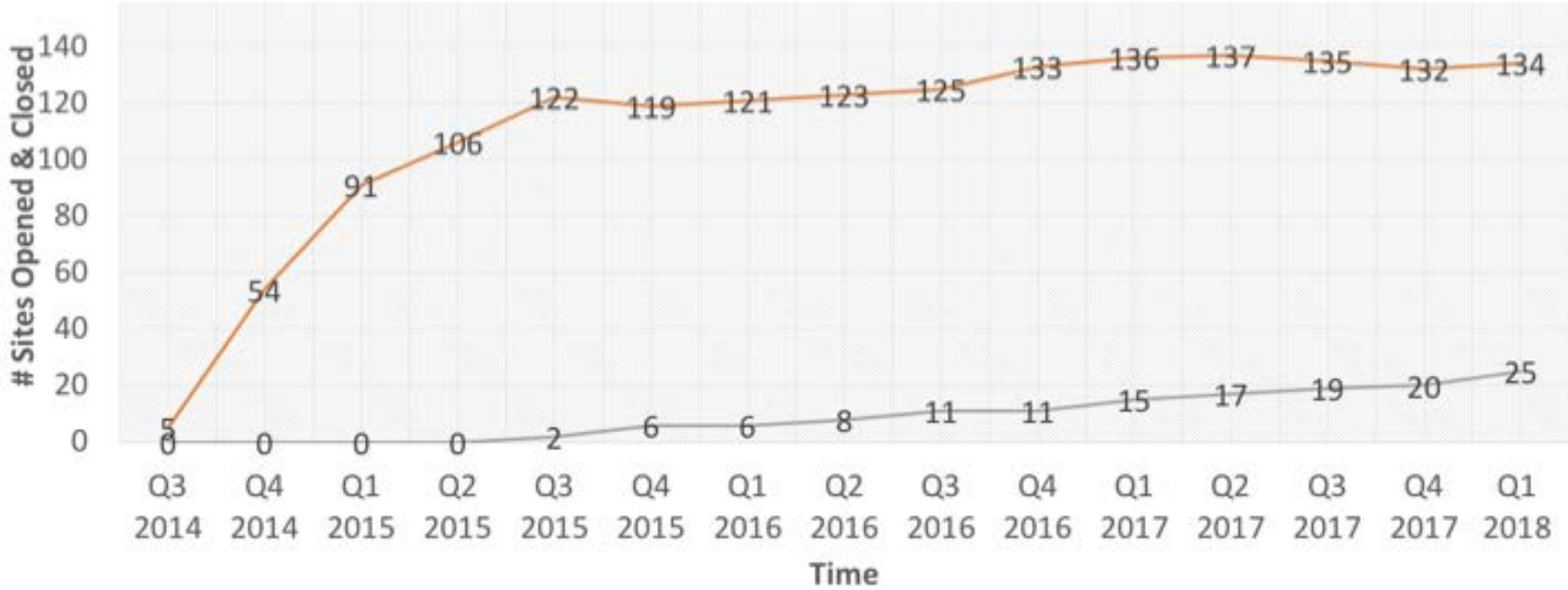
- Investigators, Sites and Enrollment

- 930 Investigators
 - 114 Interventional Cardiologists
 - 111 Interventional Radiologists
 - 3 Vascular Medicine Specialists
 - 690 Vascular Surgeons
 - 12 Other

Investigators by Specialty



BEST-CLI: Open & Closed Sites



Active Sites 167
Open 134
Closed 26

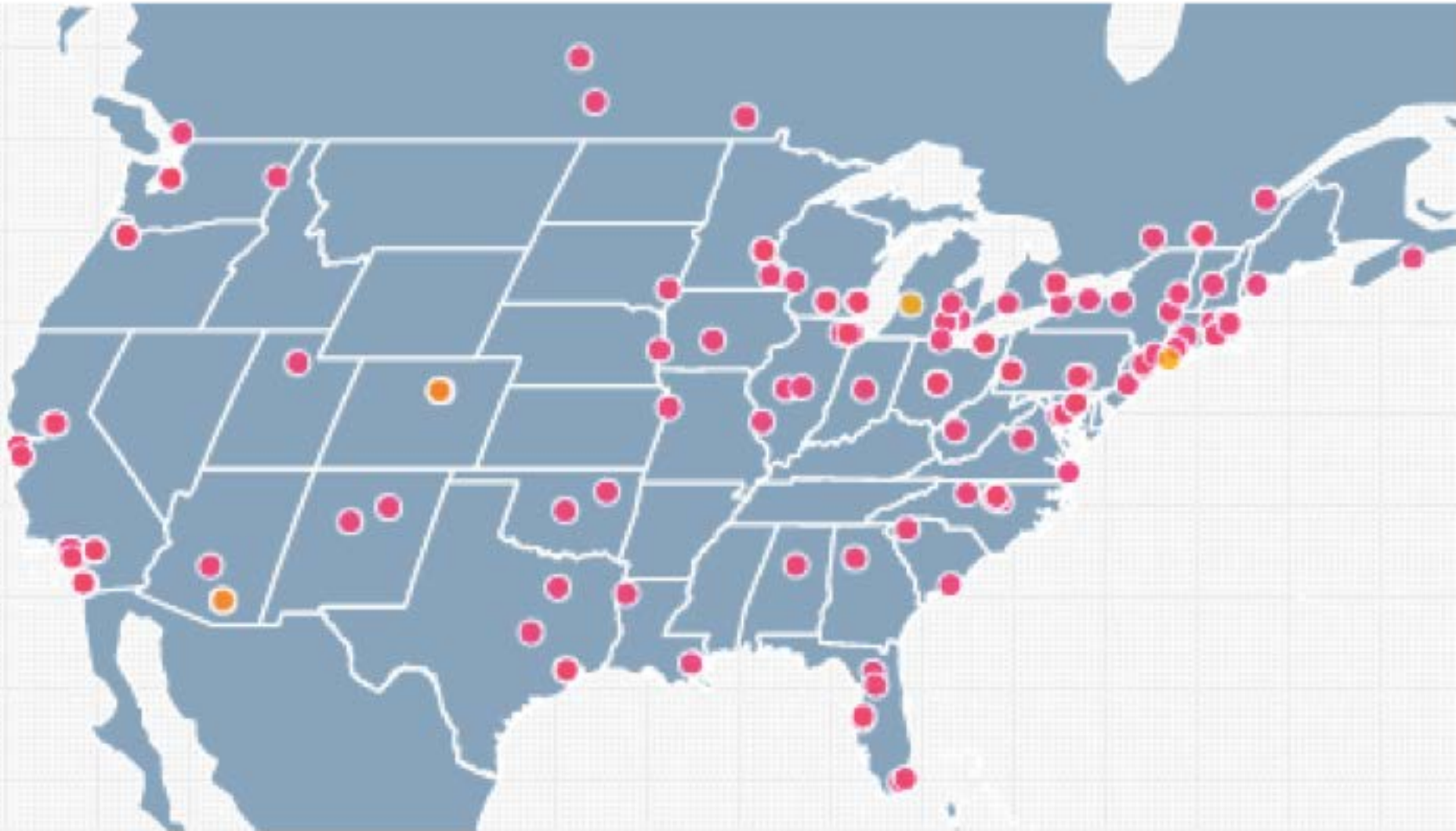
— Sites Opened — Sites Closed

BEST-CLI in North America



North America

130 Active Sites



Europe

Overseas

4 Active Sites

New Zealand

- Wellington Hospital
- Waikato Hospital
- Auckland City Hospital

Finland

- Helsinki University Hospital

Onboarding

Germany

- St. Franziskus Hospital – Muenster

Italy

- San Giovanni di Dio Hospital



New Zealand



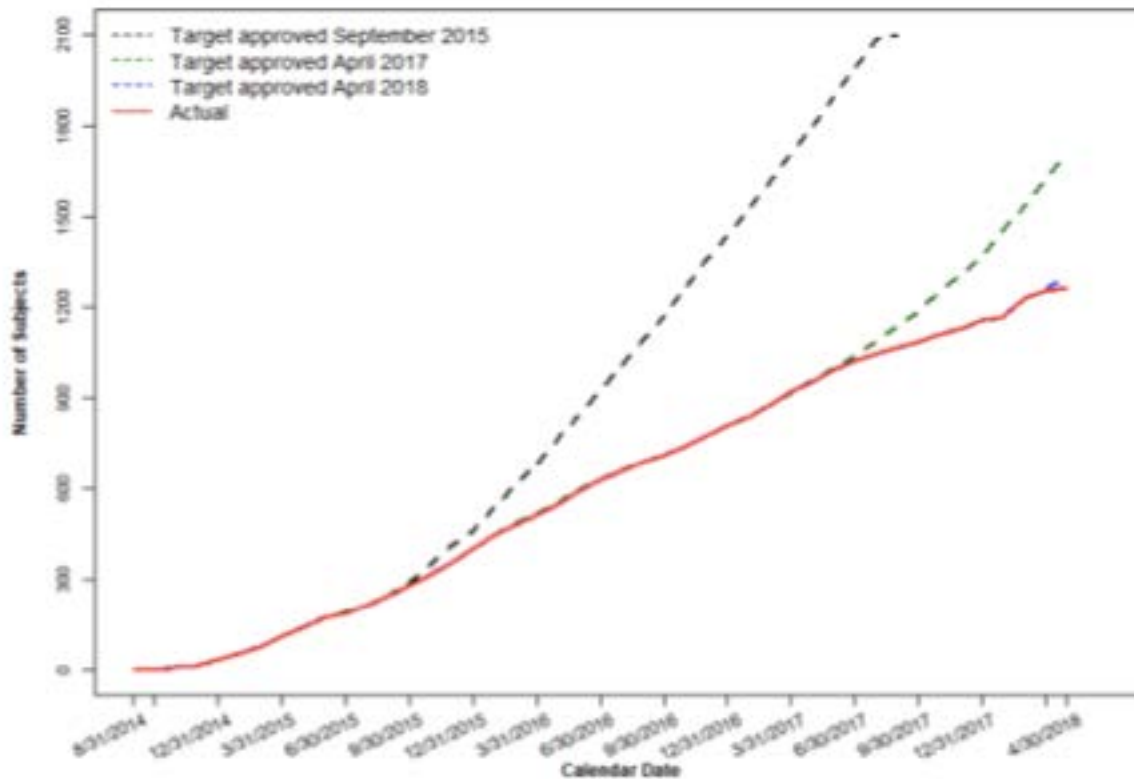
Enrollment Update



1st patient randomized 8/28/2014

As of 6/14/2018

- 1,378 subjects randomized – 722 to go!



**Next Milestone:
1,378 subjects by
June 30, 2018**



Tough Nut to Crack...

Treatment Bias is the Biggest Obstacle



Please get the (Bias) Raccoons out of the Basement!



Highlights



- Sites and Enrollment
- Protocol Amendment is coming!

Rationale

- Eliminate barriers to enrollment
- Increase subject retention (and Statistical Power)
- Reduce site burden

Diagnostic Angiogram

- Eliminate required diagnostic angiogram
- Allow MRA, CTA, or duplex to randomize at the discretion of the enrolling investigator

Subject Payments

- Increase visit payment to subjects to \$50
- If undue travel burden increase to \$100 (ex. Subject traveling >100mi) on a case by case basis

Lost to follow-up

- Reduce lost to follow-up due to moving away from site by implementing centralized follow-up

■ *Definition of CLI*

- Clarified for Tissue Loss cohort: In certain CLI patients these criteria may not be available or reliably measurable. In recognition of this, the definition of CLI in patients with gangrene or major tissue loss will be left to the discretion of the site CLI team.

- Sites and Enrollment
- Protocol Amendment is coming!
- Central Investigators Meeting

Central Investigators Meeting (CIM)



Washington D.C
Omni Shoreham Hotel
April 12 – April 13, 2018



279 Attendees



44 Speakers



3 Federal Government
Agencies represented
(NHLBI, FDA, CMS)



119 BEST-CLI Sites represented (89% of sites!)

Chu de Quebec Hospital (Canada)

The Ottawa Hospital (Canada)

Sunnybrook Health Sciences (Canada)

Vancouver General Hospital (Canada)

Helsinki University Hospital (Finland)

Waikato Hospital (New Zealand)

Wellington Hospital (New Zealand)



CLI Panel : Defining the Value Proposition



Meet our Panelists



David Goff

NHLBI



Tamara S. Jensen

CMS



Bram Zuckerman

FDA



Niteesh Choudhry

Cost - Effectiveness



Michael Conte



William Hiatt





■ *I thank all of you for what you're doing for your patients, and our country, and really the world, to advance this field of research – what you're doing is so important.*

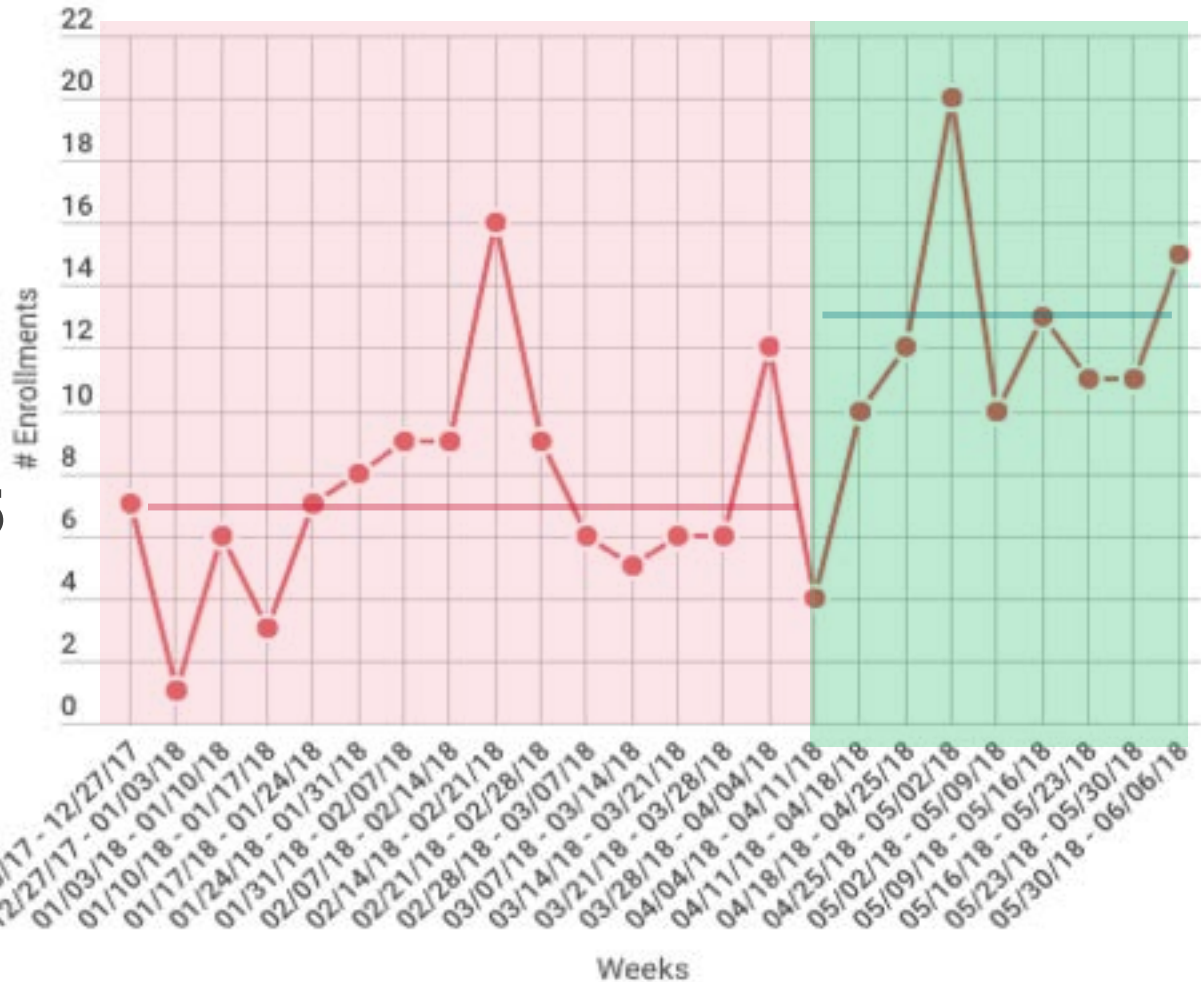
*Dr. David Goff, Director, Division of Cardiovascular Sciences,
National Heart, Lung and Blood Institute*

Weekly Enrollment Activity (last 6 months)



Before

After



Avg 12.75

Avg 7.125

79%



Bump in Weekly Enrollment

- Sites and Enrollment
- Protocol Amendment is coming!
- Central Investigators Meeting
- DSMB Meeting Next Week!

Patient Characteristics and Trial Compliance

- 1,266 patients
 - Cohort 1: 1004 (79%) – 77% predicted
 - Cohort 2: 262
- Cohort 1
 - Strata
 - Rest pain, no tibial dz 8%
 - Rest pain and tibial dz 12%
 - Tissue loss, no tibial dz 24%
 - Tissue loss and tibial dz 56%

■ Cohort 1

- 29% female – 36% predicted
- 30% non-white race – 27% predicted
- 15% Hispanic – 13% predicted
- Median age: 67 years
- Bilateral CLI: 16%

■ Cohort 1

- HTN: 87%
- DM: 72%
- CAD: 43%
- COPD: 13%
- CVA: 14%
- ESRD: 12%
- Smoking Hx: 76%
 - Current smoking: 34%
- Any previous vascular intervention: 12%
 - Any previous inflow reconstruction: 7%

- Trial compliance
 - *Withdrawal/Loss to follow-up rate: 9%*
 - *Randomized procedure initiated first: 96%*

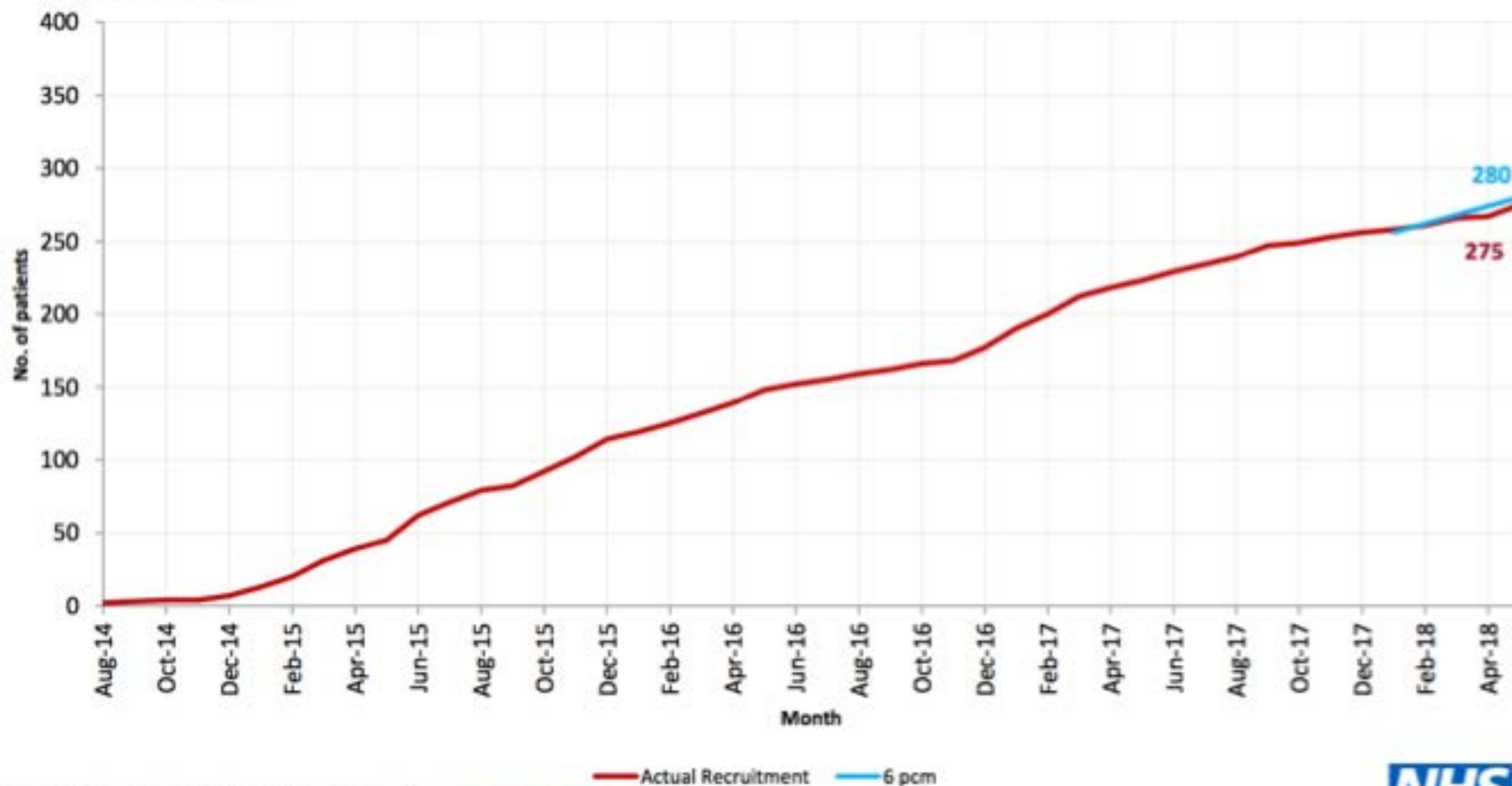
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- **BASIL 2 and 3**



Recruitment Against Projection



Updated 31st May 2018



- VIVA and DCRI coordinating actively with CCC & DCC
- Funding issues - Budget calls for \$9 million
 - Anticipate initiation when \$5 million procured
 - Thus far \$4.0 million committed
 - Approaching approximately 10 other possible supporters who are considering
 - NIH – R01 Application resubmitted
 - (Budget - \$1.5 million direct)

- We are almost 2/3 of the way home!
- Please keep your foot on the gas pedal and continue the drive to enroll patients
- Retention is incredibly important!
 - Please ensure that your patients are getting follow up



SVS VAM

Friday, June 22nd, 3:00-4:00 PM

Hynes Convention Center

Rm 200



Thank you for supporting BEST-CLI!

