Lessons Learned and Patient Partnership in ADAPTABLE

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pcornet

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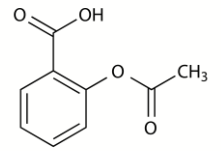
The Aspirin Study

Research Question

In patients with established or pre-existing cardiovascular disease, is a strategy of 81 mg or 325 mg of aspirin better?



Acetylsalicylic acid

Everyday decision for patients (OTC medication)

The correct dose of aspirin may **PREVENT**:

Thousands of deaths / heart attacks

or

Thousands of bleeds

Annually in the United States

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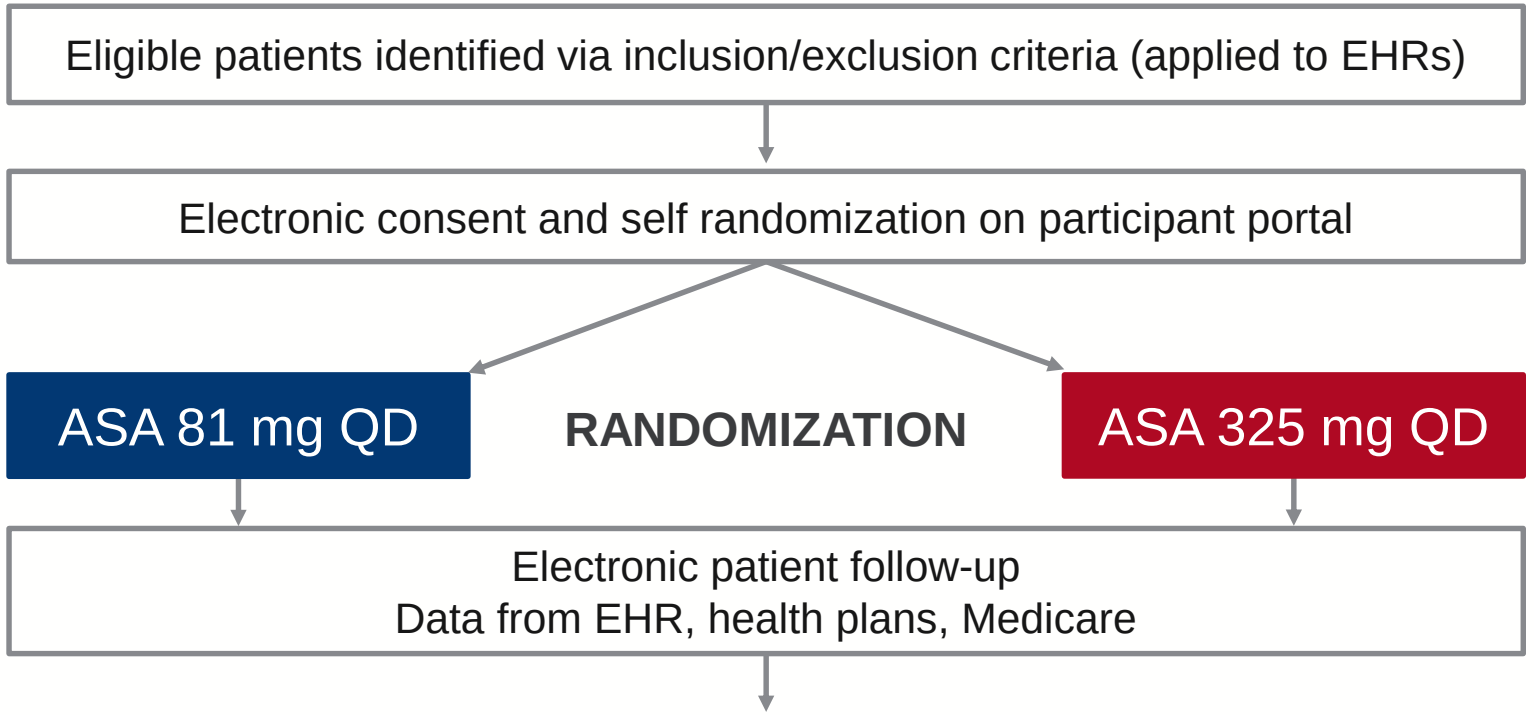
ADAPTABLE Study Design

15,000 patients with known ASCVD + ≥ 1 “enrichment factor”



Primary Endpoint:
Composite of all-cause mortality, hospitalization for MI, or hospitalization for stroke

Primary Safety Endpoint:
Hospitalization for major bleeding

ClinicalTrials.gov: NCT02697916

Direct-to-Participant Research

Screening of CDRN EHR data with computable phenotype

↓

Electronic outreach to potential patients with trial introduction and link to ADAPTABLE web portal

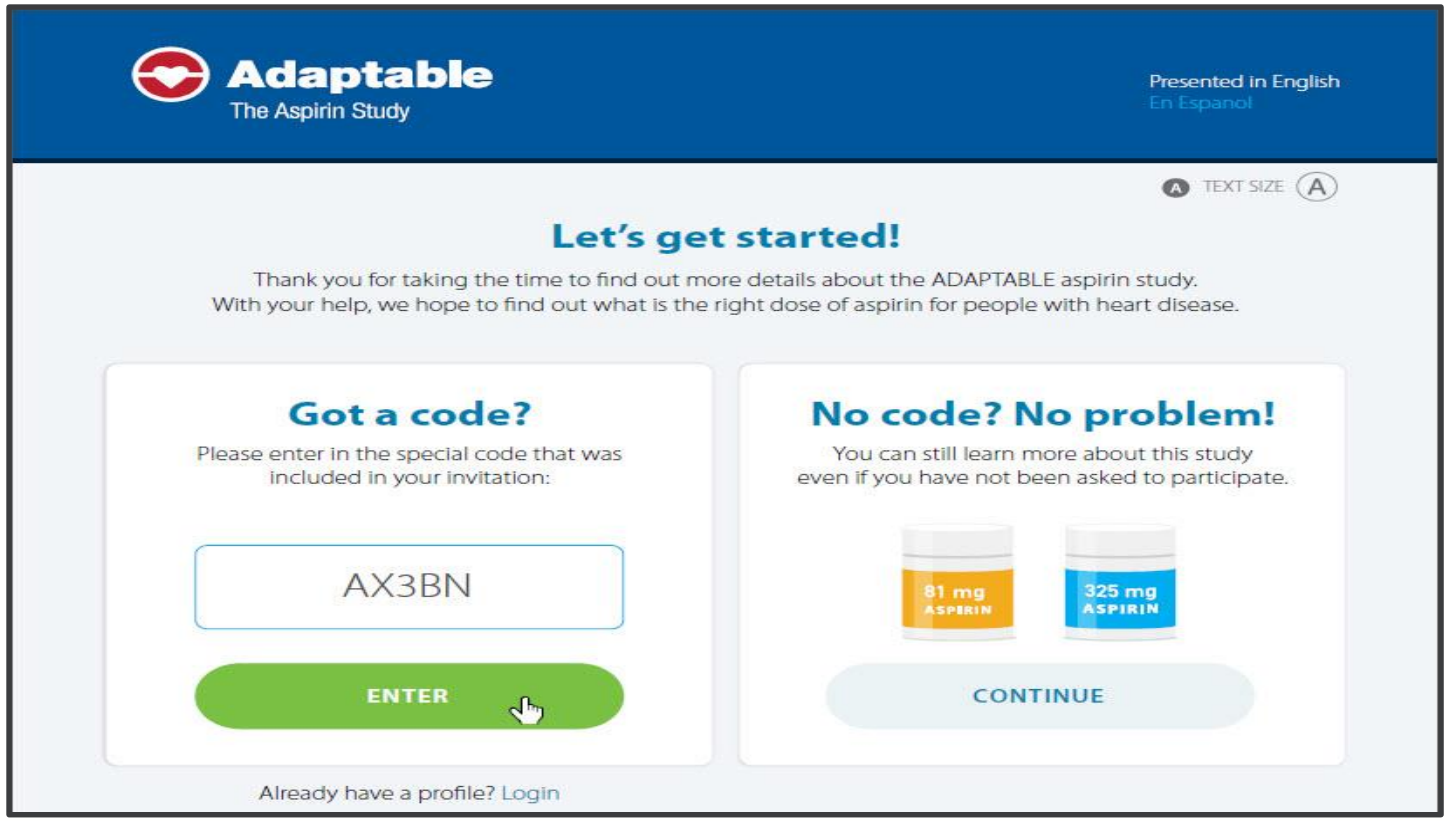
↓

Web-Based, Electronic Informed Consent

- Initial patient contact via web portal ➔ text and video consent options
  Developing a common consent form with selected local adaptations
- Focused questions to confirm patient comprehension for informed consent and eligibility for randomization after consent

↓

Randomization and Aspirin dose assignment



Competing approaches to recruitment

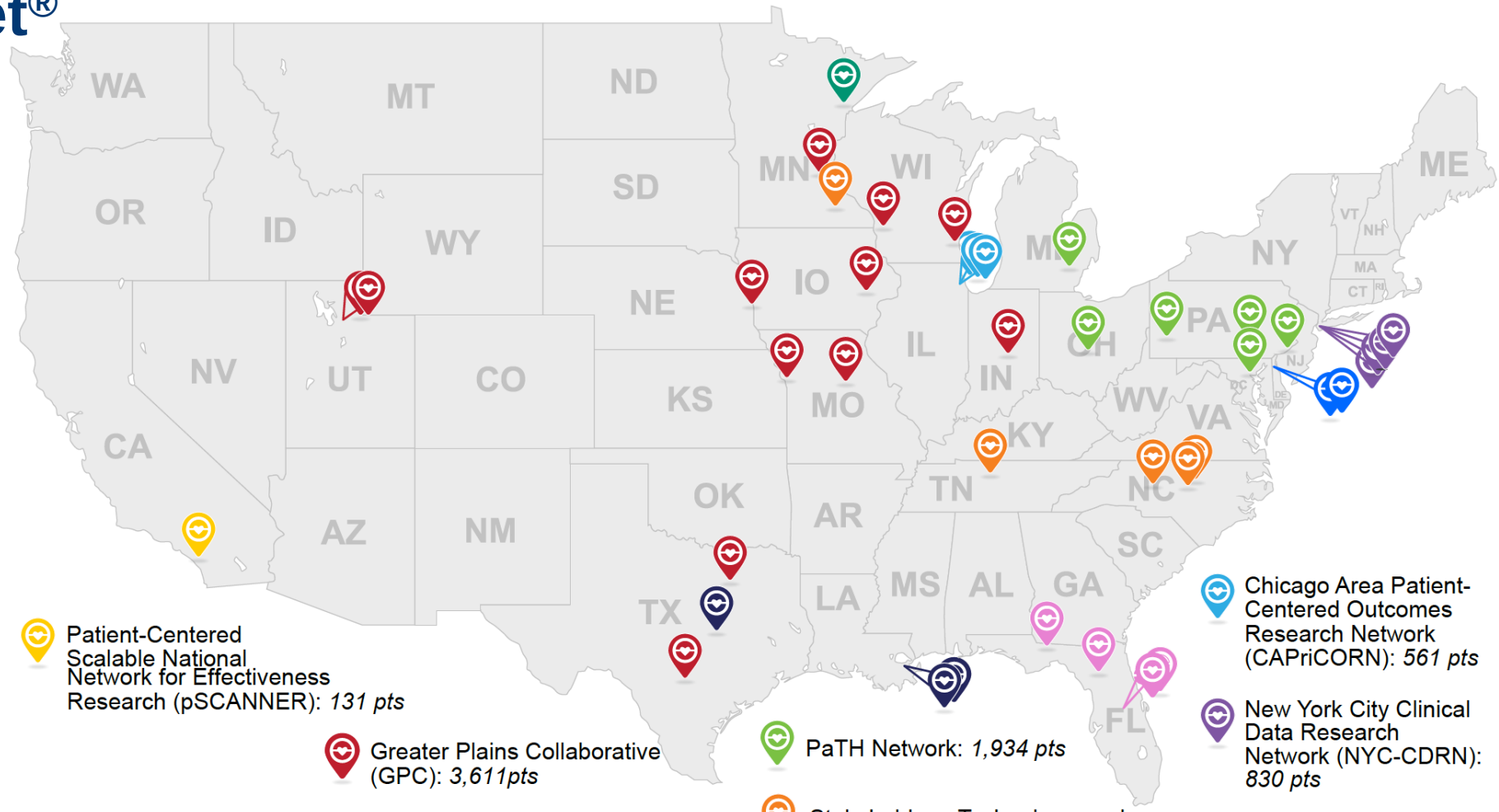
“Pragmatic”

- Broad-based outreach to large pool of eligible patients (email, mail, social media, etc.)
- Lower labor/time intensity
- Lower cost
- Faster pace of contact eligible patients

“Personalized”

- Traditional outreach involving personal, one-on-one interface (in-clinic, via phone, etc.)
- Higher labor/time intensity
- Higher cost
- Slower pace of contacting eligible patients

40 Study Centers within PCORnet®



Patient-Centered Scalable National Network for Effectiveness Research (pSCANNER): *131 pts*

Greater Plains Collaborative (GPC): *3,611pts*

Research Action for Health Network (REACHnet): *958 pts*

Essentia: *449 pts*

PaTH Network: *1,934 pts*

Stakeholders, Technology, and Research Clinical Research Network (STAR CRN): *5,466 pts*

Chicago Area Patient-Centered Outcomes Research Network (CAPriCORN): *561 pts*

New York City Clinical Data Research Network (NYC-CDRN): *830 pts*

HealthCore: *357 pts*

OneFlorida: *779 pts*

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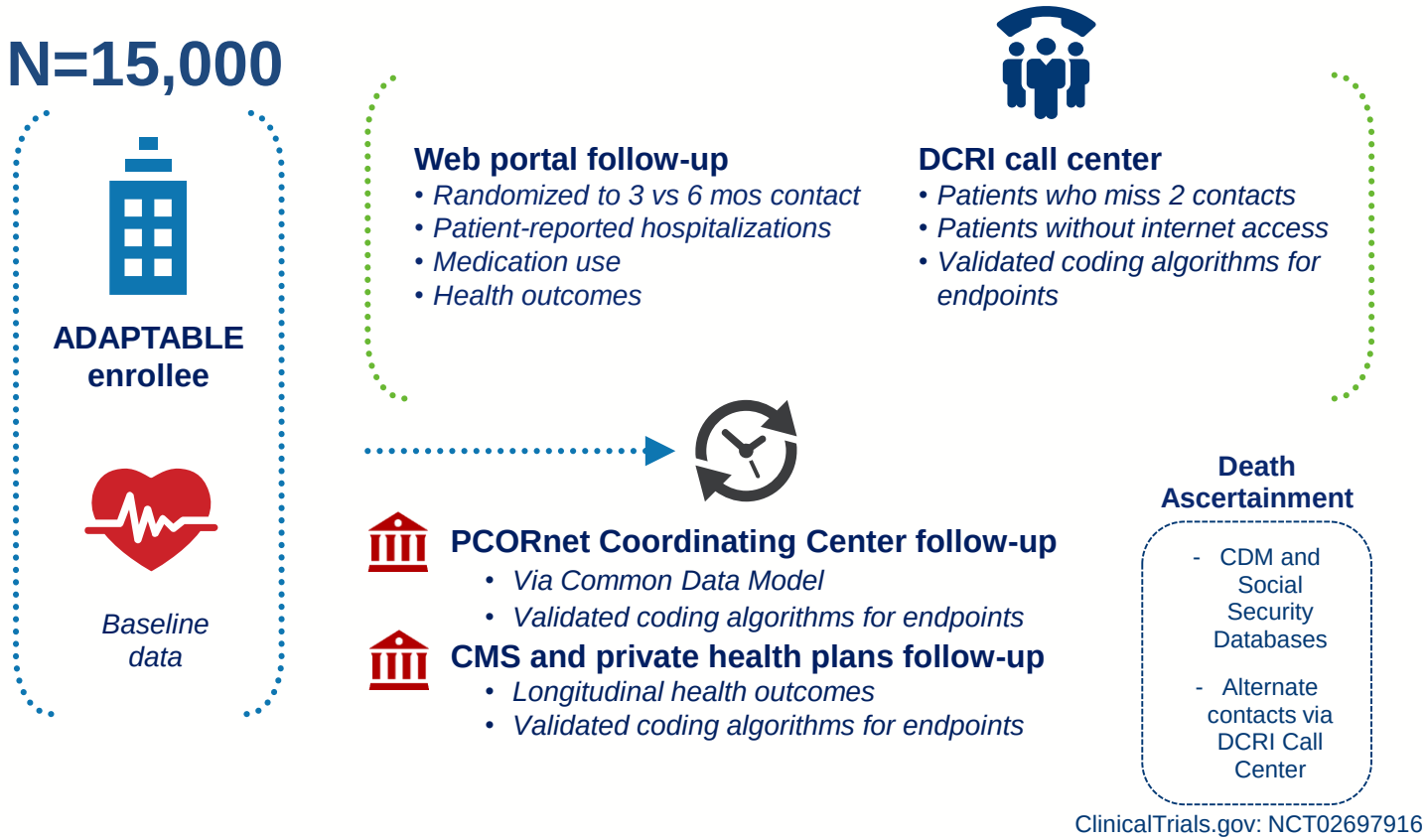
Electronic Data Collection and Follow-Up



ClinicalTrials.gov: NCT02697916

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Many parts of PCORnet were still under construction

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ADAPTBLE Enrolled 15,000!

ADAPTABLE Study
@ADAPTABLEstudy

Congratulations @PCORI #ADAPTABLEstudy team for enrolling the 15,000th participant. Very excited to have reached our enrollment goal! One step closer to finding the best dose of aspirin for people with #heartdisease.

Adrian F. Hernandez @texhern · Jun 25
Congrats all of **@ADAPTABLEstudy** and @PCORnetwork

Robert M Califf @califf001 · Jun 26
Replying to @ADAPTABLEstudy @a_sharlow and 9 others
Great achievement by the ADAPTABLE team: people who volunteered for study; study staff, clinicians, researchers and information scientists. Enrollment completed relatively quickly at a fraction of the cost of traditional, regulated clinical trials. @dukeforge @DCRINews

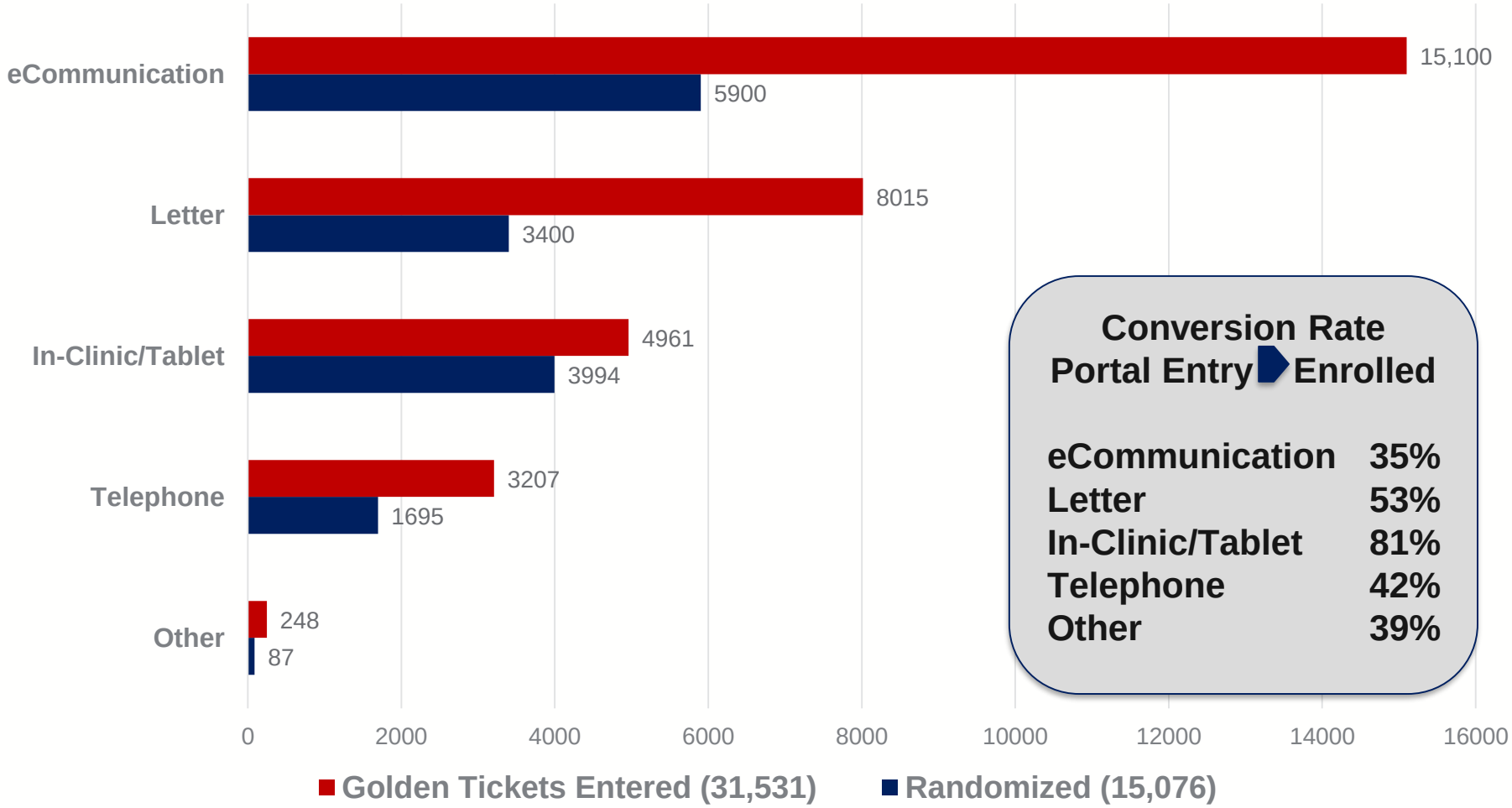
Joe Selby MD, MPH @joevselby · Jun 26
Thanks and congrats to intrepid team @ADAPTABLEstudy - researchers, patients, clinicians, systems are all playing pivotal roles in a ground-breaking study. Millions waiting for the results of this most pragmatic study question. @PCORI @califf001

ADAPTABLE BY THE NUMBERS

- ADAPTABLE is the first large scale pragmatic trial conducted via PCORnet in learning health care systems
- Leverage electronic health records (EHRs) to identify over **650,000** eligible patients across **40** sites
- Developed recruitment strategies leveraging high and low touch methods to approach over **450,000** eligible patients across **3** years of enrollment
- Utilized virtual patient portal where over **31,000** patients used unique access codes to enter the portal and **15,076** enrolled using e-Consent
- Simplified baseline and follow-up data collection through patient-reported outcomes with over **49,000** virtual visits completed to date and queries to multiple data sources

ClinicalTrials.gov: NCT02697916

Invitation Methods
Golden Tickets Entered versus Randomized



Conversion Rate
Portal Entry → Enrolled

eCommunication	35%
Letter	53%
In-Clinic/Tablet	81%
Telephone	42%
Other	39%

Baseline Characteristics

	81 mg group	325 mg group
Age, median, (25th, 75th), years	67.7 (60.7, 73.6)	67.5 (60.7, 73.5)
Female sex, no. (%)	2307 (30.6%)	2417 (32.1%)
Race, Black or African American, no. (%)	664 (8.8%)	647 (8.6%)
Race, White, no. (%)	6014 (79.8%)	5976 (79.3%)
Hispanic ethnicity, no. (%)	249 (3.3%)	232 (3.1%)
Weight, median (25th, 75th), kg	90.0 (78.6, 103.6)	90.0 (78.2, 104.1)
Current Tobacco use, no. (%)	696 (9.2%)	686 (9.1%)
Aspirin use before study		
81 mg	5823/6850 (85.0%)	5724/6687 (85.6%)
162 mg	168/6850 (2.5%)	142/6687 (2.1%)
325 mg	845/6850 (12.3%)	812/6687 (12.1%)
Dual antiplatelet use at baseline	1570 (22.5%)	1511 (22.1%)

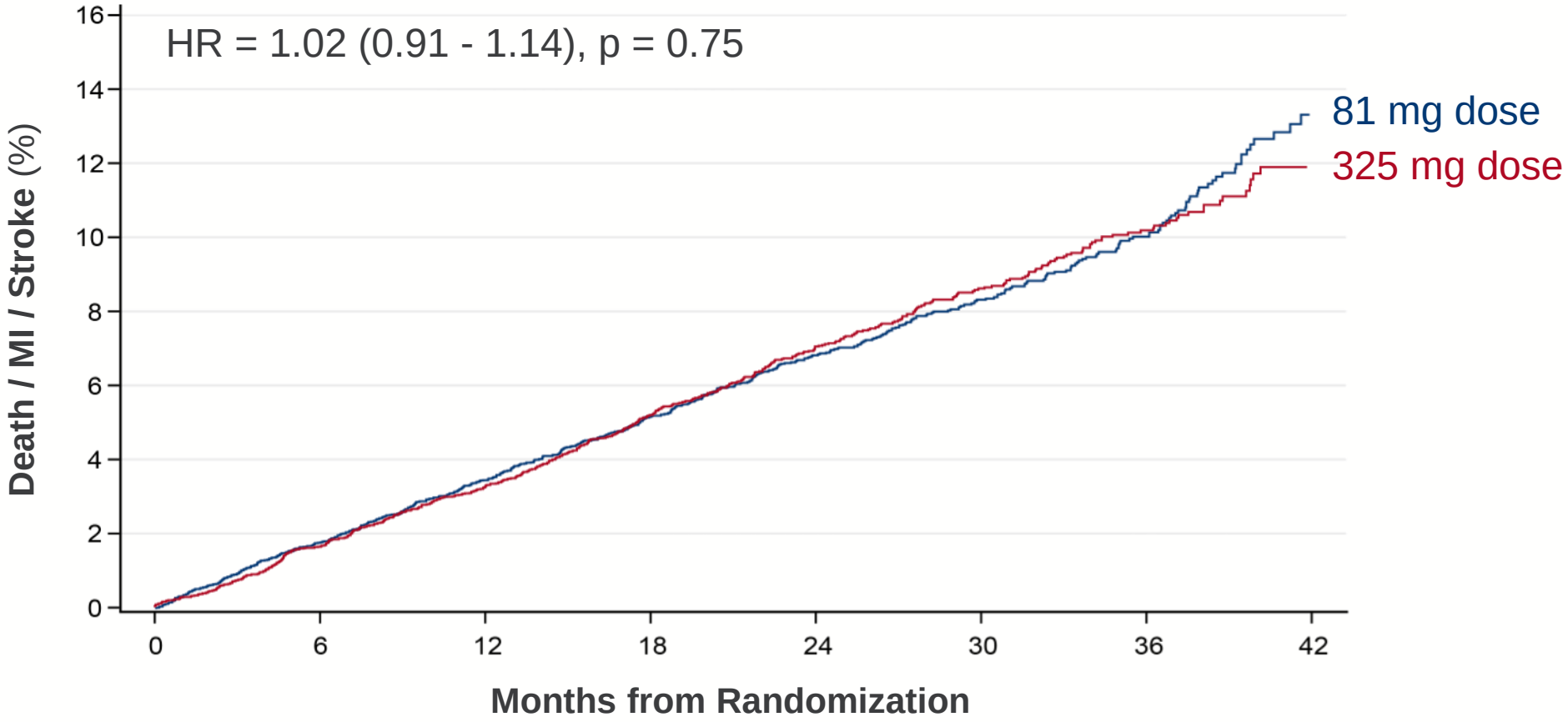
Medical History

	81 mg group	325 mg group
Prior PCI	3005 (40.0%)	2941 (39.1%)
Prior CABG	1786 (23.8%)	1741 (23.2%)
Prior myocardial infarction	2674 (35.6%)	2631 (35.0%)
Hypertension	6264 (83.3%)	6248 (83.1%)
Dyslipidemia	6472 (86.1%)	6474 (86.1%)
Diabetes mellitus	2820 (37.5%)	2856 (38.0%)
Atrial fibrillation	605 (8.0%)	628 (8.4%)
Congestive heart failure	1718 (22.8%)	1786 (23.8%)
Prior GI hemorrhage	455 (6.1%)	495 (6.6%)
Prior intracranial hemorrhage	98 (1.3%)	110 (1.5%)

Medical history was obtained from EHR queries, with look back of 5 years

Primary Effectiveness Endpoint

(All-cause death, hospitalization for MI, or hospitalization for stroke)



At risk								
81 mg dose	7540	7357	7177	5627	4190	2712	1558	636
325 mg dose	7536	7297	7095	5544	4090	2613	1489	592

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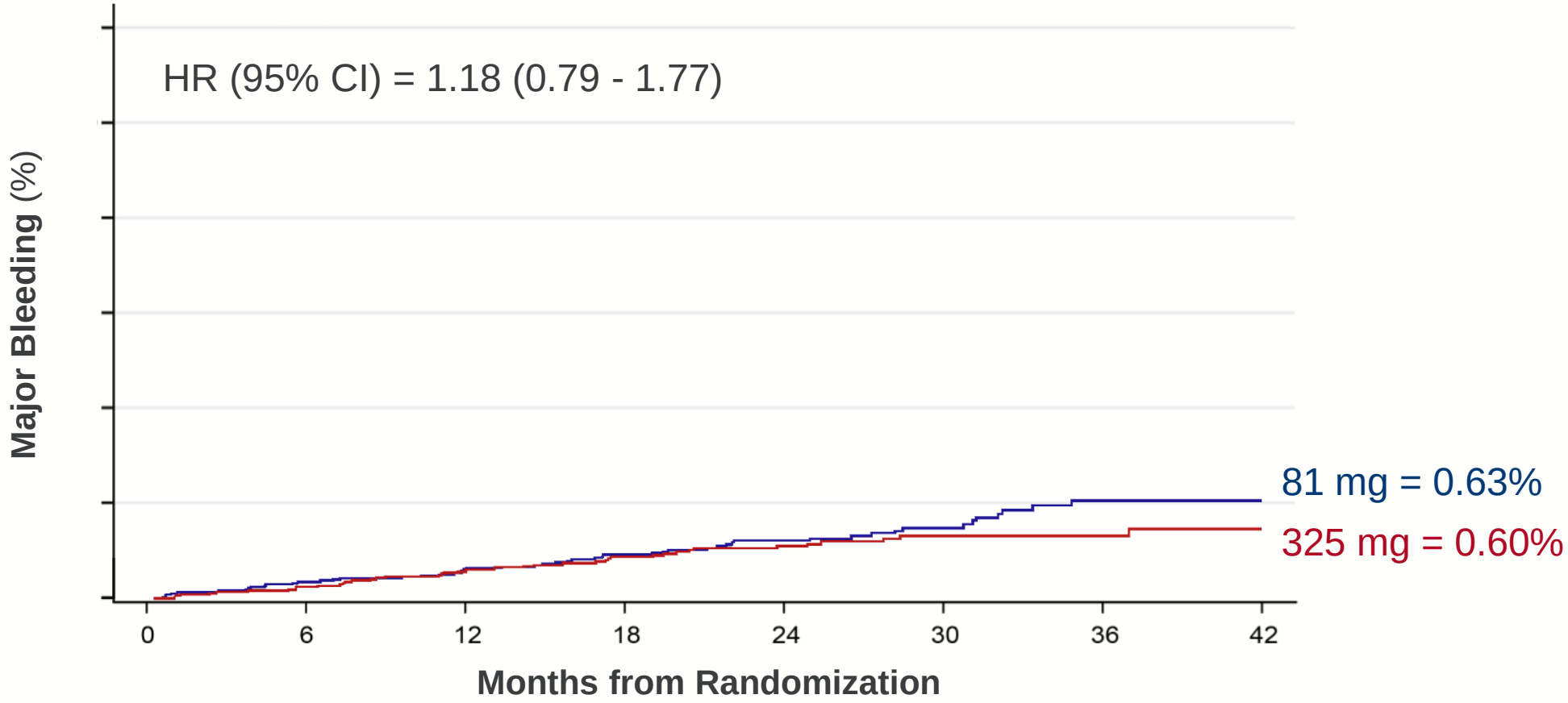
Primary Safety Endpoint

(Hospitalization for major bleeding with associated blood product transfusion)



At risk								
81 mg dose	7540	7434	7309	5777	4329	2810	1610	674
325 mg dose	7536	7348	7185	5667	4205	2709	1559	624

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Study Medication in ADAPTABLE

	Overall	81 mg	325 mg
Dose switching, % *	24.2%	7.1%	41.6%
Aspirin discontinuation, % **	9.1%	7.0%	11.1%
Median days of exposure, assigned aspirin dose	551 days (139 - 737)	650 days (415 – 922)	434 days (139 – 737)
Median days of exposure, any aspirin dose	658 days (426 - 932)	670 days (439 – 944)	646 days (412 – 922)

** Defined as at least one dose change*

*** Reasons for aspirin discontinuation:*
25% participant did not want to continue
75% doctor's decision or medical condition (e.g., atrial fibrillation, dyspepsia)

Conclusions

- No observed difference in death / MI / stroke in patients assigned to 81 mg vs. 325 mg
- There was a difference in fidelity to the study dose/intervention (more dose switching in 325 mg group)
  - Multiple reasons that patients did not stay on the 325 mg dose
    - Tolerability
    - Medical reasons
    - Participant preferences
    - Clinician practices

Messages to Patients

- **If you are on 81 mg now**, staying (rather than switching) is probably right given the similar study results for the primary endpoint

- **If you are resuming aspirin**, starting a lower dose (81 mg) is probably right due to better tolerability and we did not find conclusive evidence that higher dose is better

- **If you are tolerating 325 mg now**, staying on this dose may be okay and associated with moderate benefit

Patient Partnership

ADAPTOR Patient Investigators

- Patients involved in prioritization of research topic, protocol design, and trial conduct
- ADAPTORS integral to development of participant-centric consent form and comprehension assessment
- ADAPTORS working with health systems on the development of recruitment & retention plans and materials

Patient Advisory Board- ADAPTABLE

- Led by Heart Research Alliance (formerly Health eHeart Alliance) Patient Powered Research Network
  - Heart Patients and Advocacy Organizations (American Heart Association, StopAFib.org & SADS) in conjunction with a Network Facilitator Consultant who led the development of patient-friendly research processes which we leveraged for the ADAPTABLE Patient Advisory Board (PAB)

- Included facilitation strategy and principles to ensure meaningful engagement throughout the research process

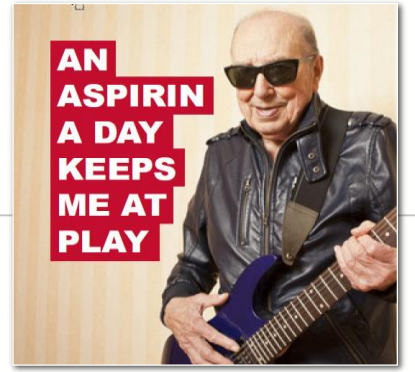
Principles of Patient Engagement

- Trust and Partnership
  - Assume good intent, choose collaboration
- Respect and Listening
  - Make sure to hear all perspectives
- Empower Solutions
  - Hearing patient feedback and brainstorming solutions
- Value and design for the patient experience
  - Give discrete tasks and goals to patient leaders
  - Set our patient leaders up for success

Principles of Patient Engagement

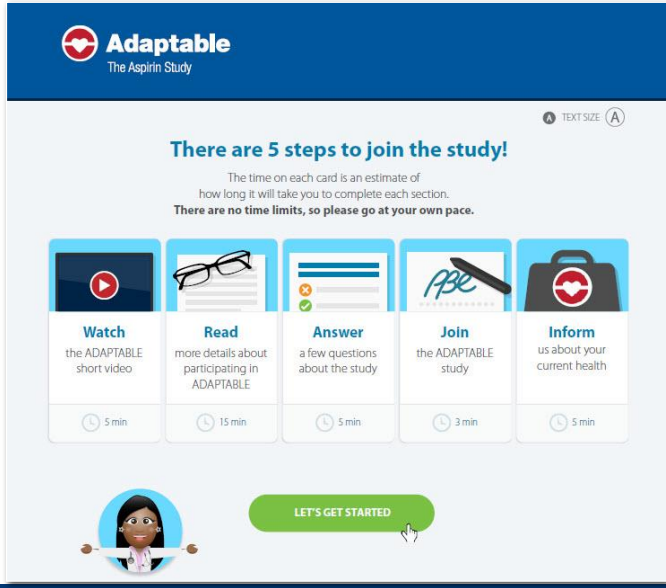
- Important to build capacity in patient leaders by involving them in the process
  - Start up→ Implementation → Results dissemination
- Patients involved in prioritization of the research topic, protocol design, trial conduct, recruitment challenges and plans for results dissemination
- Patients Partners represented in:
  - ADAPTORS PAB (1 patient from each CDRN)
  - Executive Committee (2 patients)
  - Data Safety Monitoring Board (2 patients)
  - Steering Committee (1 patient from each CDRN)

Meaningful engagement of Patient Partners (and Participants!)



- Adaptors collaborated with study team in multiple ways
  - Design public facing webpage
  - Design and approve Newsletters
  - Create mechanism to hear from participants
  - Answer questions from participants
  - Plan for dissemination to participants and the community

- Adaptors reviewed all Patient Facing Materials
  - Consent forms
  - Surveys
  - Recruitment materials, etc



Key Areas of Contribution

- Study Planning
  - Review study portal
  - Design consent process
  - Review surveys (led to shorter questionnaires)

- Study Engagement Tactics
  - Creation of study newsletter
    - Tell your story
    - Ask the team a question
    - Stay involved with the study after Adaptable


Adaptable
The Aspirin Study

February 2018

Welcome to the ADAPTABLE
Participant Community Newsletter

"Celebrating Your Heart and Heart-Health Awareness & American Heart Month"


Welcome to the ADAPTABLE Participant Community Newsletter

October 2017 | Volume: 2

"Better health outcomes for all when patients partner with researchers."

This motto crafted by the Adaptors, ADAPTABLE's patient partners, reflects how patient participation in research can help answer health questions that matter most to patients and their doctors. The Adaptors' motto is part of the Hero's Journey Art Project, a touring art exhibit developed by Eli Lilly to honor clinical trial participants and raise awareness of clinical research. Visit the ADAPTABLE website (www.theaspirinstudy.org/news/) to read more about this project.

Key Areas of Contribution

- Recruitment Materials
  - All materials were reviewed and edited prior to recruitment beginning
  - Review of key participant questions prior to consent.
- Linkage with Health Plans
  - Adaptors made significant changes to the letter distributed to participants
  - Significant changes to Consent Language
- Dissemination
  - Dissemination Plan greatly impacted by PAB. Requested that study participants learn about the results at the same time as the scientific community
  - Dissemination in multiple mediums and in patient friendly language. Make sure the value the participants added is front and center!

My Favorite Aspects of ADAPTABLE

Sharing Stories and Local Engagement

VANDERBILT UNIVERSITY MEDICAL CENTER

Institute for Medicine and Public Health

Dear [redacted]

My name is Linda, and I am a Vanderbilt patient with heart disease. Several years ago, I had a stent placed. Since then, I have become interested in learning about and helping out with research. Last year, my doctor told me about the ADAPTABLE aspirin study. This study is trying to figure out the best dose of aspirin for patients with heart disease. The results from ADAPTABLE may help people around the world have fewer heart attacks and strokes. I'm excited about ADAPTABLE and have been serving as a patient advisor.

I'm reaching out to you because our study doctors think you may be a great fit for the ADAPTABLE study. I hope you will consider joining the community of more than 7000 patients who are already taking part in ADAPTABLE. If you want to learn more, I've included a page with more information about the study, including how you can join.

Getting diagnosed with heart disease was hard, but I'm glad I have been able to use my diagnosis to help others like me. Thank you so much for reading my note, and for thinking about ADAPTABLE. Whether or not you join, I wish you the best in your journey to good health.

Sincerely,
Linda
ADAPTABLE Patient Partner

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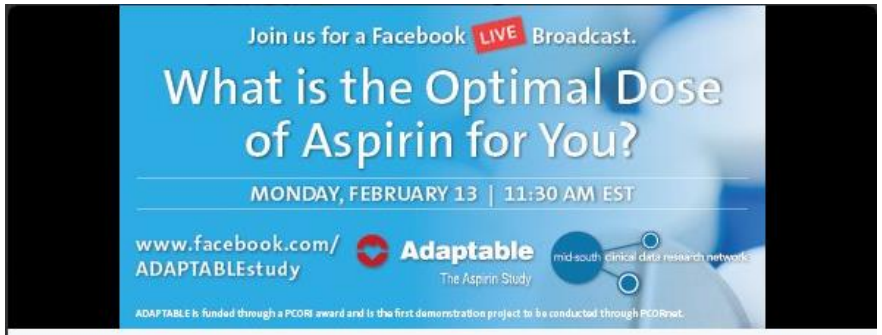

ADAPTABLE Study @ADAPTABLEstudy · Feb 9
#ADAPTABLEstudy will be live on FB on 2/13 at 11:30 AM EST! What questions do you have abt #heartdiseae & #PCOR? bit.ly/2kfm37g pic.twitter.com/TTaQJORgTq

Adaptable
The Aspirin Study

Home | The Optimal Dose of Aspirin | Participate | Meet the Adaptors | The Participant's Voice

ADAPTABLE Study Team Shares Patient Engagement Experiences in CardioSmart Pavilion at American College Cardiology Conference

March 21, 2018

ADAPTABLE Study @ADAPTABLEstudy · Mar 23
From #ACC18: Dan Munoz of @VUMChealth & @MidSouthCDRN describes the key role of patient partners in @PCORI @PCORnetwork #ADAPTABLEstudy: bit.ly/ADPTEACC

"A lot of assumptions that we come in with as researchers and clinicians have been challenged, corrected, and improved upon by our Adaptors, the ADAPTABLE patient partner team."

theaspirinstudy.org

Development of ADAPTABLE Consent Form

- Track record of empirical research to improve informed consent, comprehension
- Determining what information a reasonable person would want to know
  - As opposed to unnecessary detail that may confuse and detract
- What prospective participants find essential may differ from information identified as important by “experts”

ADAPTABLE Consent Team:

- Kevin McKenna, MPH
- Catherine Hammack, JD, MA
- Zach Lampron, MPH
- Martina Bresciani, BA
- Kate Brelsford, PhD, MPH

Messaging to “The Undecided Patient”

- “It is important to know that you will stay on aspirin.”
- “Participating in the ADAPTABLE study will mean that you continue to take a daily aspirin for your heart’s health.”
- “We’re glad that you’ve done well on your dose of ___mg. One of the key questions for patients like you is: what dose of aspirin will permit you to do well into the future? We don’t yet know that answer for patients like you.”

Traditional and Social Media

Patient Blogs

- Monthly guest blog featuring one of our ADAPTORs
- Topics will focus on why patient powered research is important
- Links to ADAPTABLE Study website

Facebook Live

- Facebook *Live* Event at AHA Scientific Session (November 2016)
- First Facebook *Live* event broadcasting about a study during AHA Scientific Sessions
- 20-minute, moderated live Q&A featuring ADAPTABLE leadership and Adaptor

Patient Engagement Pavilion

- CardioSmart Patient Panel at ACC Scientific Sessions 2017 and 2018
- Adaptor & researcher panel presentation at ACC 2017 and 2018 in the CardioSmart Patient engagement pavilion

Connectedness

Shiffen Getabecha, Ken Gregoire, Linda Brown, Jaqueline Alikhaani, Tom McCormick, Desiree Davidson, Bill Larsen, Henry Cruz, Madelaine Faulkner; (Not pictured: Greg Merritt, Kevin Edgeley, Nadine Zemon)

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Lay Summary

THE ADAPTABLE STUDY
Summary of Results

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The Aspirin Study

Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-Term Effectiveness

On behalf of the ADAPTABLE team of patient partners, researchers, and clinicians we would like to thank you for participating in ADAPTABLE. As a research participant, you played a critical role in generating these study results. We truly appreciate your time and commitment to help advance the care of people with heart disease.

WHAT IS THE PURPOSE OF ADAPTABLE?

The purpose of ADAPTABLE is to find the best dose of aspirin, 81 mg or 325 mg, for people with known or existing heart disease to prevent death or another heart attack or stroke.

WHEN DID ADAPTABLE TAKE PLACE?

The full research study was conducted from May 2015 to May 2021. The first participant enrolled in April 2016, and the last participant enrolled in June 2019.

WHO WAS INVOLVED?

15,076
people with heart disease

clinicians and researchers at

40
large health systems and one health plan across the nation that are part of PCORnet®, The National Patient-Centered Clinical Research Network.

WHY IS THIS RESEARCH IMPORTANT TO PATIENTS, CLINICIANS, AND OTHER RESEARCHERS?

Aspirin can help keep blood flowing. It is recommended for people with heart disease to prevent another heart attack or stroke. However, the best dose for people with heart disease is not known. This is most likely due to the lack of data from clinical trials.

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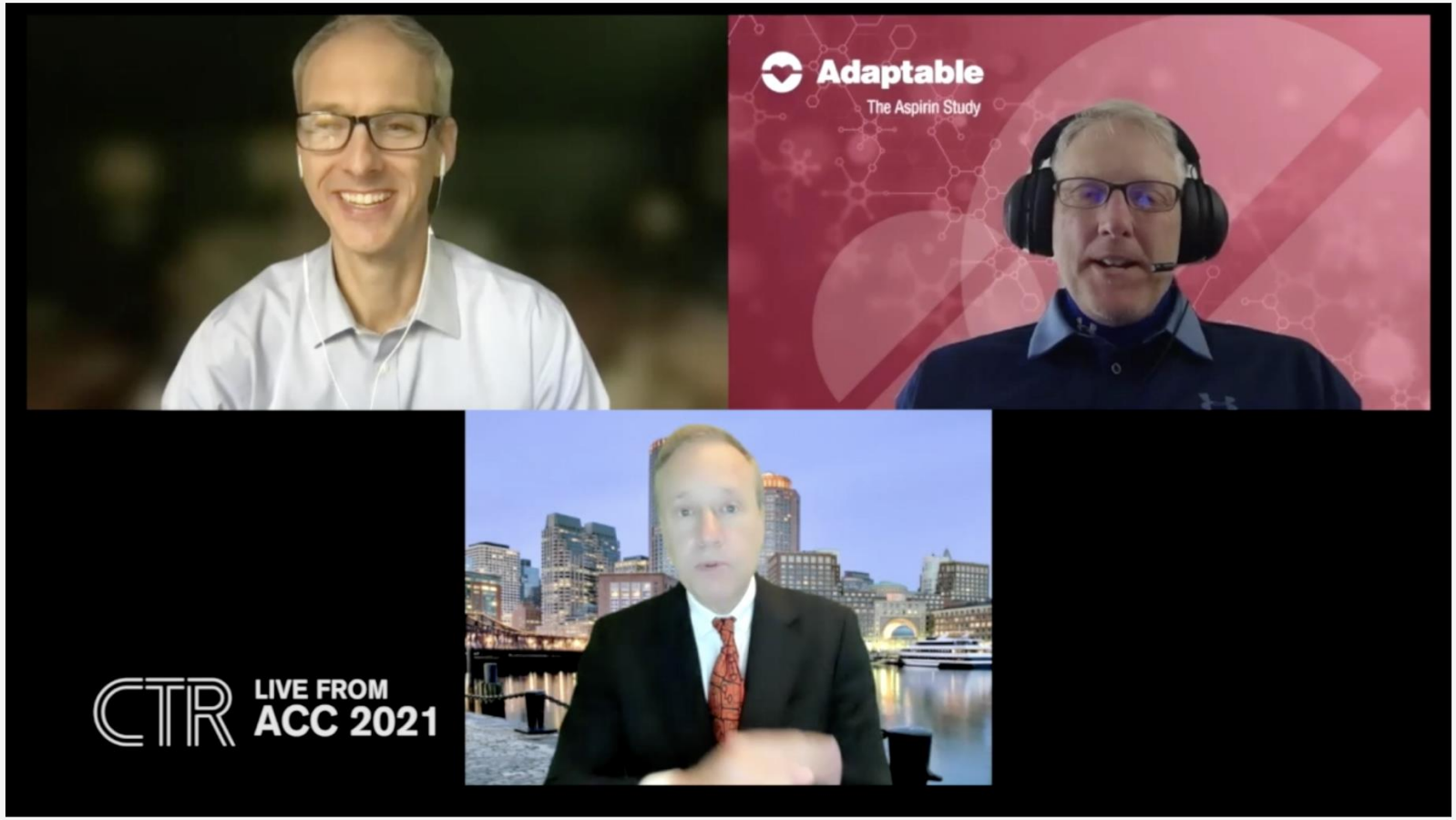
Dissemination

May 15, 2021

2021 | ACC | Cardiology | Trial

Tags: 2021, ACC, Cardiology



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Fully Inclusive Publication – including all ADAPTORS

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparative Effectiveness of Aspirin Dosing in Cardiovascular Disease

W.S. Jones, H. Mulder, L.M. Wruck, M.J. Pencina, S. Kripalani, D. Muñoz, D.L. Crenshaw, M.B. Effron, R.N. Re, K. Gupta, R.D. Anderson, C.J. Pepine, E.M. Handberg, B.R. Manning, S.K. Jain, S. Girotra, D. Riley, D.A. DeWalt, J. Whittle, Y.H. Goldberg, V.L. Roger, R. Hess, C.P. Benziger, P. Farrehi, L. Zhou, D.E. Ford, K. Haynes, J.J. VanWormer, K.U. Knowlton, J.L. Kraschnewski, T.S. Polonsky, D.J. Fintel, F.S. Ahmad, J.C. McClay, J.R. Campbell, D.S. Bell, G.C. Fonarow, S.M. Bradley, A. Paranjape, M.T. Roe, H.R. Robertson, L.H. Curtis, A.G. Sharlow, L.G. Berdan, B.G. Hammill, D.F. Harris, L.G. Qualls, G. Marquis-Gravel, M.F. Modrow, G.M. Marcus, T.W. Carton, E. Nauman, L.R. Waitman, A.M. Kho, E.A. Shenkman, K.M. McTigue, R. Kaushal, F.A. Masoudi, E.M. Antman, D.R. Davidson, K. Edgley, J.G. Merritt, L.S. Brown, D.N. Zemon, T.E. McCormick III, J.D. Alikhaani, K.C. Gregoire, R.L. Rothman, R.A. Harrington, and A.F. Hernandez, for the ADAPTABLE Team*

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Thank you

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