The ADAPTABLE Study

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

A TRANSLATIONAL SCIENCE BENEFITS MODEL **CASE STUDY**

Project in a Nutshell

Aspirin is a mainstay therapy for patients with atherosclerotic cardiovascular disease, but there are unanswered questions about the best dosage.

ADAPTABLE studied the effectiveness and safety of the two most common aspirin doses.

Significance of the Project

Every year 720,000 Americans have a heart attack, and nearly 380,000 die of atherosclerotic cardiovascular disease (ASCVD), also known as hardening of the arteries. Many patients who survive develop heart failure, stroke, and/or other cardiovascular complications.

These patients often experience chest pain, shortness of breath, and fatigue, which can lead to significant distress and worsening quality of life. Rates of mental health illnesses such as depression are high among both these patients and their caregivers; rates of depression may approach 66% in post-myocardial infarction (MI) patients. Coronary heart disease alone costs the US $108.9 billion each year.

Aspirin, also known as acetylsalicylic acid (ASA), is the most commonly prescribed medication for cardiovascular disease. It significantly reduces outcomes such as heart attack and stroke in patients with previous cardiovascular events and/or atherosclerosis at a cost of less than one cent per day.

However, despite a history of robust evidence generation in patients with cardiovascular disease, there are still critical unanswered question on what dosage of aspirin is most effective and safe. Despite dozens of clinical trials involving more than 200,000 patients, the optimal dose of aspirin has not been determined in direct comparative-effectiveness trials.

Summary of the Project

ADAPTABLE studied the effectiveness and safety of the two most common aspirin doses, and it served as the demonstration project for clinical trials in the Patient-Centered Outcomes Research network (PCORnet), funded by the Patient-Centered Outcomes Research Institute (PCORI).

ADAPTABLE is a pragmatic clinical trial in which 15,076 patients with established ASCVD and at high risk for ischemic events (reduced bloodflow to tissues) were randomized in a 1:1 fashion to receive an aspirin dose of 81 mg/day vs 325 mg/day.

The primary endpoint is a composite of all-cause death, hospitalization for MI, or hospitalization for stroke. The primary safety endpoint is hospitalization for major bleeding with an associated blood product transfusion.

Summary of Results

Results published in May 2021 found no differences in cardiovascular events or major bleeding between patients who took the 81 mg and to those who took 325 mg of aspiring daily.

In addition, this study—as the first demonstration project for pragmatic clinical trials using PCORnet—held important lessons regarding identifying a large cohort of eligible patients; engaging, recruiting, and randomly assigning patients; and performing critical follow-up.

A group of "Adaptors," patient partners who helped design the study and disseminate its results.

Impact of the Project

Clinical

ADAPTABLE answers the question about the most effective and safe dose of aspirin in patients with ASCVD, informing clinical practice guidelines and assisting clinicians who care for patients with ASCVD.

In addition, the methods and processes of ADAPTABLE have informed and changed how research can be done within health systems. The use of a computable phenotype led to the identification of a large potentially eligible population of patients with ASCVD in the study centers. Because aspirin is an over-the-counter medication and the trial is an open label study, direct-to-patient approach strategies were used to initially approach a large group (~450,000) of potential participants.

Utilizing an electronic consent process and web-based patient portal, 15,076 participants were enrolled either virtually or via research coordinator/investigator assistance at a study center. The patient portal was also used for study retention and follow-up, obviating the need for participants to return to the study centers on a routine basis.

The nine Clinical Data Research Networks and their patient partners around the country were involved in every aspect of study design and conduct, including protocol review, design of patient-facing materials and the electronic consent form, and participant newsletters and blogs.

A Patient-Powered Research Network called Health eHeart centered at the University of California, San Francisco was deeply involved in all aspects of our patient engagement plans.

Community

ADAPTABLE has defined the optimal dose of a low-cost drug (ASA) that can enhance health promotion and disease prevention in communities or populations.

Using a low-cost, readily available over-the-counter drug reduces stroke and heart attack risk in patients with ASCVD, improving quality-of-life and life expectancy.

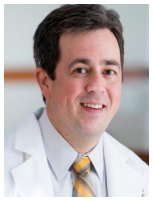
Economic

ASA is a low-cost, over-the-counter option for the treatment of ASCVD and the prevention of heart attacks and stroke in those at high risk.

As such, it can significantly reduce the financial burden of of a chronic disease such as ASCVD.

About the Research Team

Adrian Hernandez, MD - *Principal Investigator*



- Vice Dean and Executive Director, Duke Clinical Research Institute
- Professor of Medicine
- Duke Health Cardiology Professor
- Executive Core Faculty Member, Duke-Margolis Center for Health Policy.

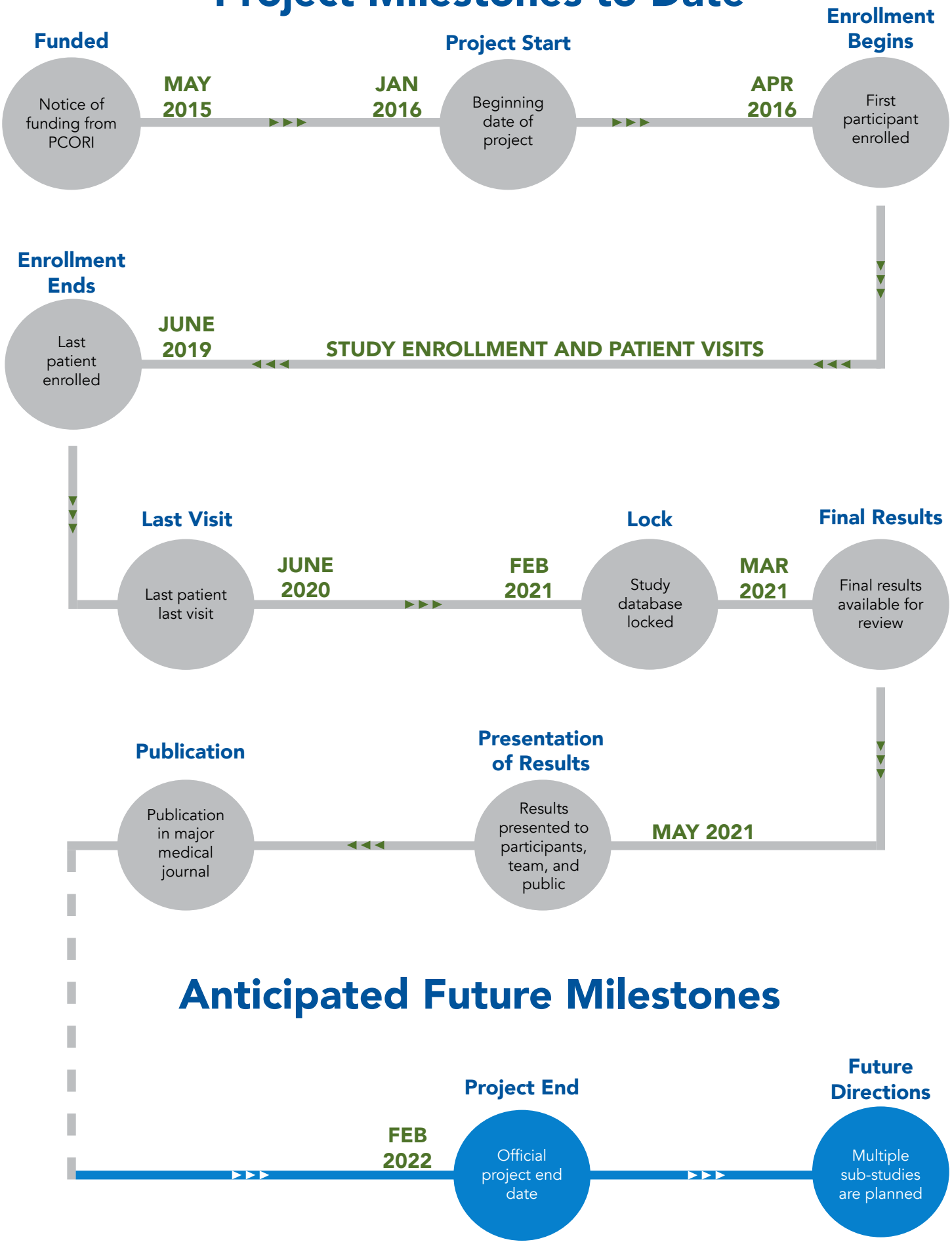
W. Schuyler Jones, MD - *Principal Investigator*

- Assistant Professor of Medicine, Duke School of Medicine
- Associate Professor in Population Health Sciences
- Member of the Duke Clinical Research Institute

Janis Curtis, MSPH

- Associate Director of Clinical Data Research Networks, Duke Clinical & Translational Science Institute

Project Milestones to Date



Anticipated Future Milestones

Translational Science Benefits Summary

CLINICAL

Drugs:
Aspirin to prevent ischemic events in patients with ASCVD at high risk

Guidelines:
Methods and process of ADAPTABLE have changed how research can be done within health systems

Guidelines:
Inform clinical practice guidelines, assisting clinicians who care for patients with ASCVD

ECONOMIC

Cost Savings:
Aspirin is a low-cost option for the treatment of ASCVD and the prevention of ischemic events in those at high risk

Societal & Financial Cost of Illness:
Low-cost medication can significantly reduce the financial burden of a chronic disease (ASCVD)

COMMUNITY

Life Expectancy & Quality of Life:
Using a low-cost, readily-available over-the-counter drug reduces ischemic events and their sequelae in patients with ASCVD improving quality of life and life expectancy

Disease Prevention & Reduction:
Study has defined the optimal dose of a low-cost drug that can enhance health promotion and disease prevention in communities or populations

CTSA Resources Used

Core	Type of Service
Network Capacity Core (Research Networks and Recruitment Innovation)	Expertise and access to Clinical Data Research Networks (STAR Network)
Informatics Core	Facilitated participation in STAR Network
Participant Clinical Interactions Core	Study start-up; participant recruitment; electronic health record expertise

Other Institutional Resources Used

Group	Type of Service
Duke Clinical Research Institute	Part of a broad partnership to lead the way in recruitment activities for ADAPTABLE
Duke Office of Clinical Research & Duke Heart Center CRU	Same as above

For More Information

About Dr. Adrian Hernandez: https://scholars.duke.edu/person/adrian.hernandez

About Dr. Schuyler Jones: https://scholars.duke.edu/person/schuyler.jones

About Duke Clinical & Translational Science Institute: Visit ctsi.duke.edu or email us at DukeCTSI@dm.duke.edu

About the ADAPTABLE Study: https://theaspirinstudy.org/

Translational Science Benefits Model citation:
Institute of Clinical & Translational Sciences at Washington University in St. Louis. Translational Science Benefits Model website. https://translationalsciencebenefits.wustl.edu. Published February 1, 2019. Accessed December 20, 2020.