

Alzheimer's Prevention Initiative Treatment Trials

Jessica Langbaum, PhD
Principal Scientist, Banner Alzheimer's Institute
Associate Director, API



Alzheimer's Prevention Initiative (API): A Program to Accelerate the Evaluation of Preclinical AD Treatments

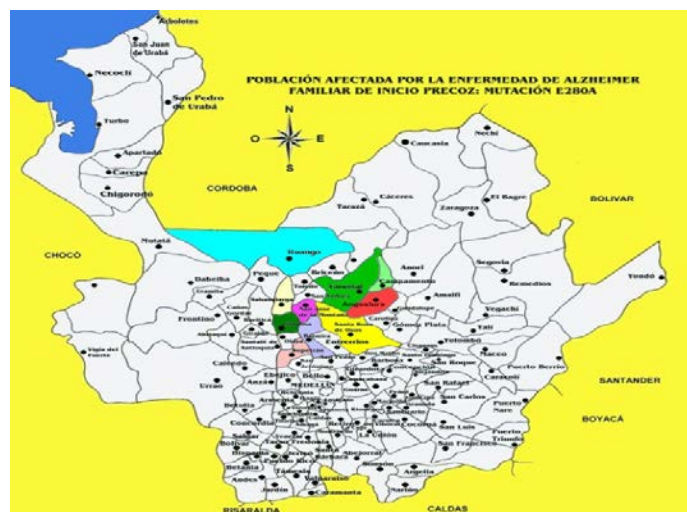
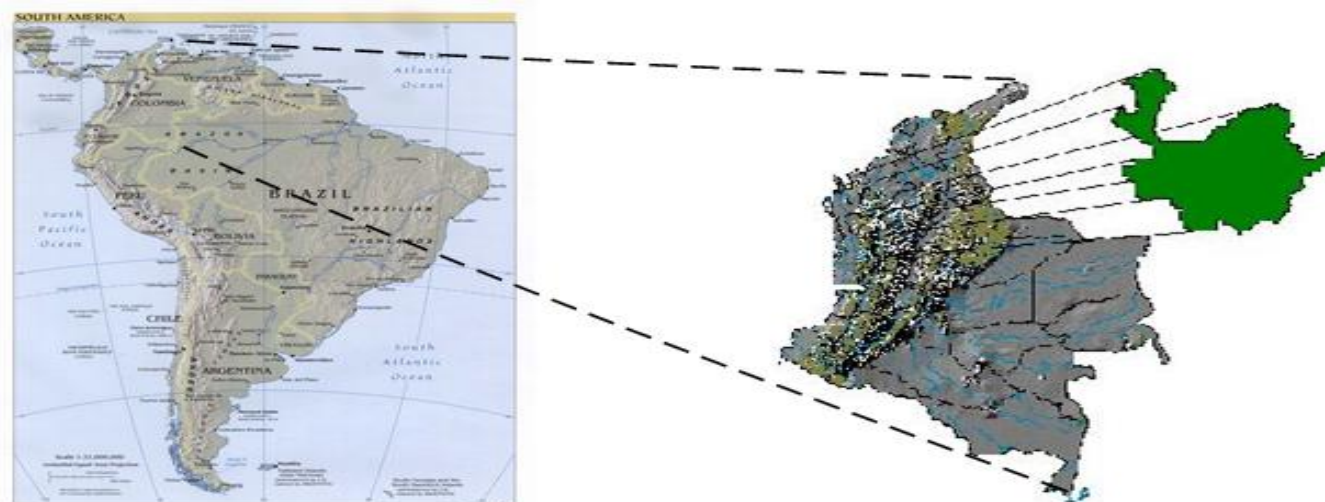
1. Preclinical AD treatment/biomarker development trials in people who, based on their age & genetic background, are at the highest imminent risk of AD symptoms, beginning with:
 - Autosomal dominant AD mutation carriers close to their estimated age at clinical onset
 - *APOE* $\epsilon 4$ homozygotes close to their estimated age at clinical onset
2. Prevention registries to support these & other trials
 - ~3,400 *E280A PSEN1* mutation kindred members in Antioquia, Colombia enrolled in API Colombia Registry
 - ~28,000 people enrolled in web-based Alzheimer's Prevention Registry (www.endALZnow.org)



API Trials: Aims

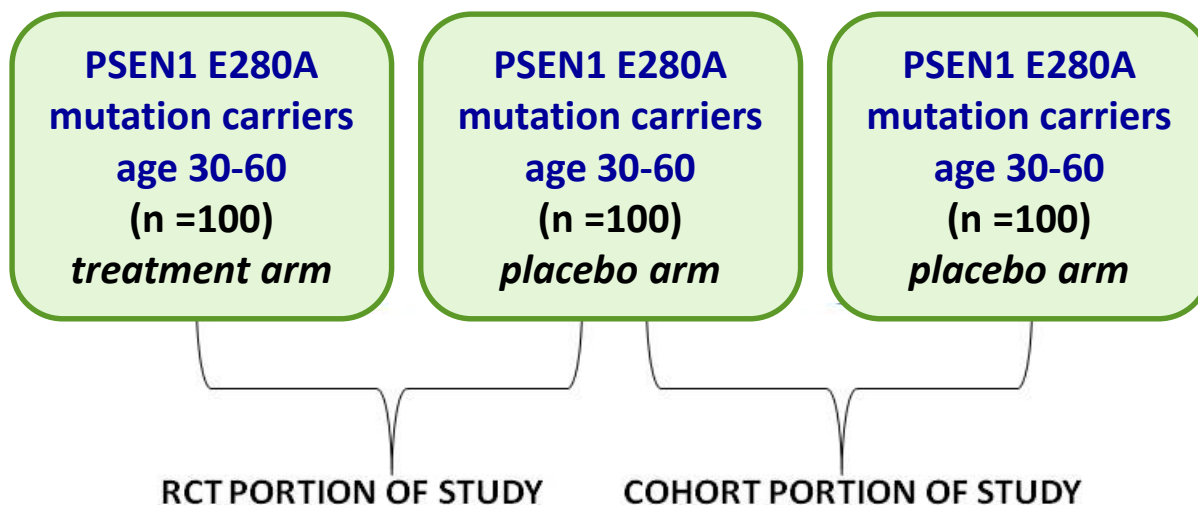
1. Evaluate anti-amyloid therapies in the preclinical treatment of autosomal dominant AD and in people who are *APOE ε4* homozygotes
2. Provide better tests of the amyloid hypothesis
3. Help qualify biomarkers for use as reasonably likely surrogate endpoints in preclinical AD trials
4. Provide a foundation for other preclinical AD trials
5. Complement, support & benefit from other initiatives (including the DIAN & A4 trials)
6. Provide a resource of data & samples to the scientific community after the trial is over
7. Offer persons at highest imminent risk for symptoms of AD access to investigational treatments
8. ...and more trials to come

Antioquia, Colombia: A genetically isolated area with strong founder effect for an autosomal dominant mutation causing early onset AD





API ADAD Trial



Double-blind, placebo-controlled trial for up to 60 months
crenezumab 300 mg SC q 2 weeks

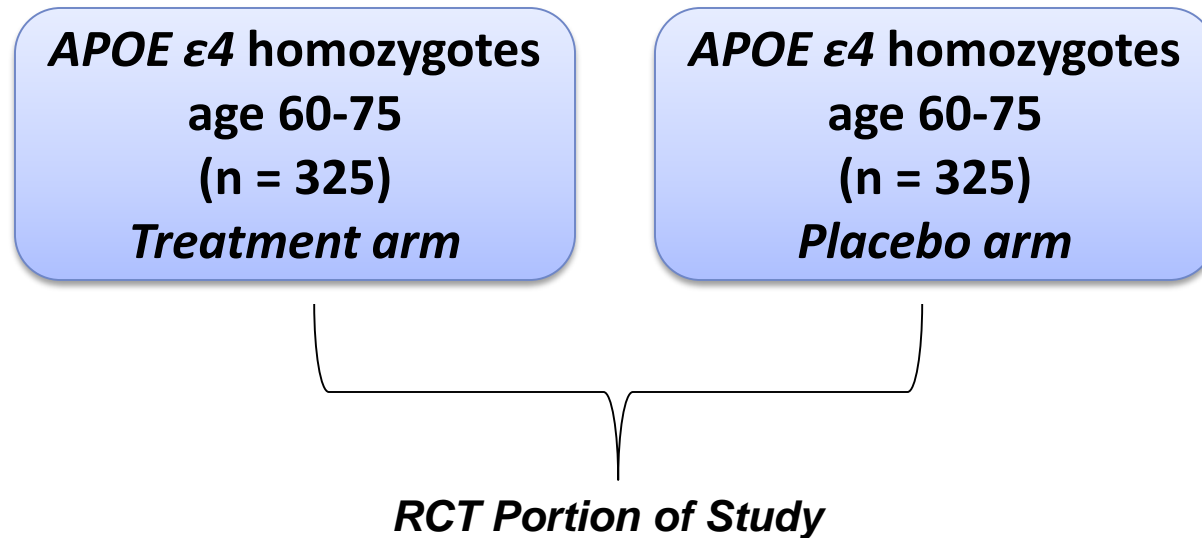
Primary endpoint: change in the API composite cognitive score

24-month interim analysis using several cognitive/clinical endpoints, & florbetapir PET, FDG PET, MRI, CSF

Enrollment began in 2013; Clinicaltrials.gov Identifier: NCT01998841



API APOE4 Trial: Base Case



Double-blind, placebo-controlled trial for up to 60 months; treatment TBD

Primary endpoint: change in the API composite cognitive score

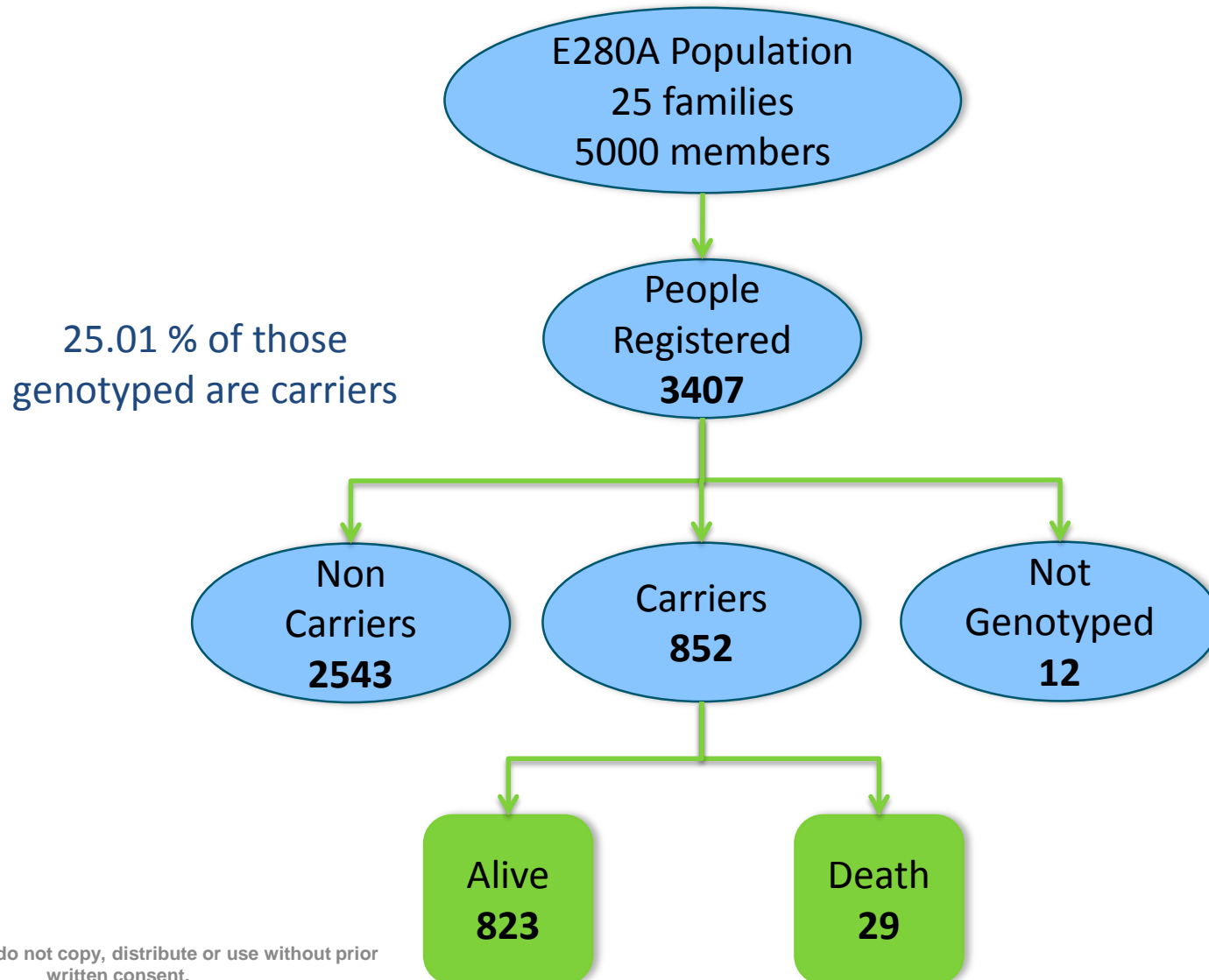
24-month interim analysis using cognitive/clinical endpoints, & amyloid PET, FDG PET, MRI, CSF; tau PET

Participants are disclosed their *APOE4* genetic status. API exploring potential cohort study of people who learned genetic status (homozygotes and non-homozygotes) and not enrolled in the trial.

Anticipated start date: 2015

Unique Challenge: Recruitment

API Colombia Registry





Alzheimer's Prevention Registry Overview

- Launched in May 2012 to accelerate enrollment into coming prevention studies
- Intended to be a shared resource to the scientific community
- Enrollees provide minimal information at sign-up, receive emails notifying individuals about study opportunities within their communities
- Complements other national efforts (*TrialMatch*) and local registry efforts
- Modeled after other online disease research recruitment registries (Army of Women, Fox Trial Finder)
- Numerous partnerships with academic, government, patient/family advocacy, and corporations



www.endALZnow.org

The screenshot shows the Alzheimer's Prevention Registry website. At the top is a blue header with the logo and navigation links. Below is a light blue section with a three-step sign-up process: 1. SIGN UP to help end Alzheimer's, 2. RECEIVE EMAILS about prevention study opportunities and research news, and 3. PARTICIPATE in studies you choose and qualify for. To the right is a green sign-up box with the text 'JOIN 028640 OTHERS', an email input field with the placeholder 'Enter your email here', and a pink 'Sign up now' button. Below the sign-up box is a privacy notice: 'Your privacy is extremely important! We promise to protect it — [learn more](#).' At the bottom left is a 'WHY NOW' section with the text 'If we do nothing, as many as 16 million people will be diagnosed' and a pink 'LEARN WHAT IT' button. At the bottom right is a section titled 'THE ALZHEIMER'S PREVENTION REGISTRY IS A PARTNERSHIP OF:' followed by logos of partner organizations.

Executive Committee

Jessica Langbaum · Marilyn Albert · Meryl Comer · Jeff Cummings
Jennifer Manly · Ron Petersen · Reisa Sperling · Gabrielle Strobel · Michael Weiner
Pierre Tariot · Eric Reiman · Maria Carrillo (ex officio)



Alzheimer's Prevention Registry

Who

- Anyone age 18+

Where

- Anywhere in the world, though initial outreach focused on the United States

What & How

- Provide email address, other demographic & contact information at sign up
- Receive email with study opportunities



National Survey

**Grand-children
of Alzheimer's
Sufferers
(n=252)**

**Adult Children
of Alzheimer's
Sufferers
(n=218)**

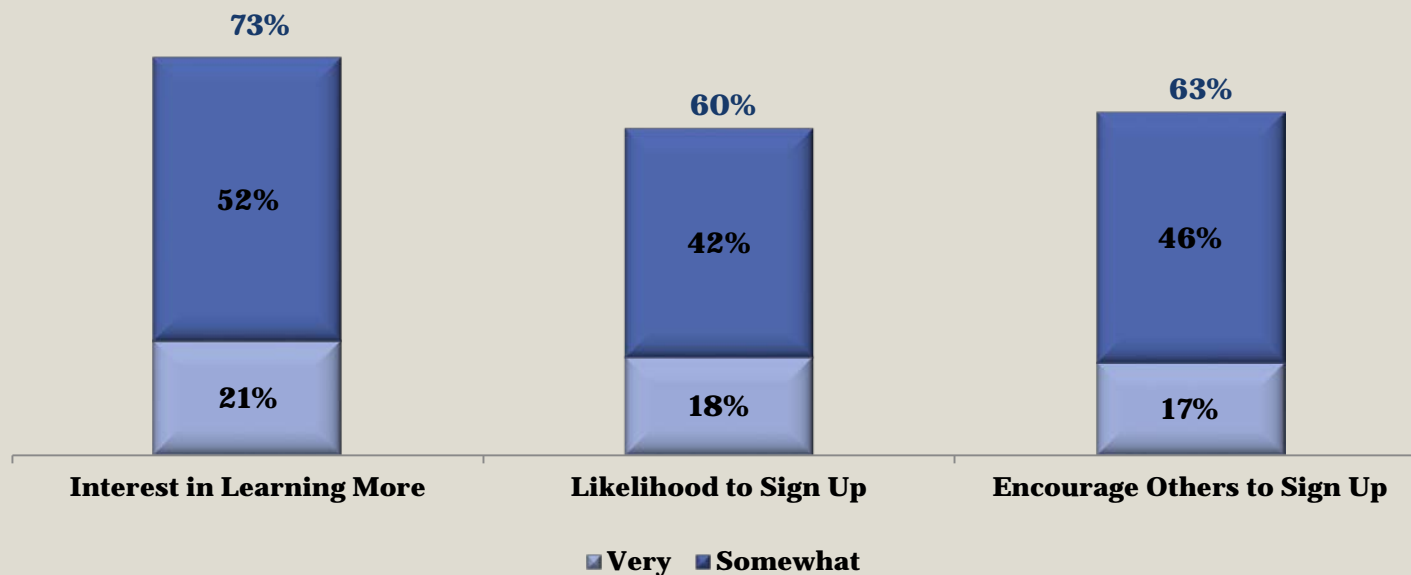
**1,024 US Adults, ages 18-75
Population Representative Distribution
Conducted June 29-July 11, 2012
Margin of error +/- 3.1 percentage points**

**Donors to
Disease-
related
causes
(n=212)**

**Ages 50+ with
Family History
of Alzheimer's
(n=274)**

Perception of the Registry

Interest In Learning More and Likelihood to Sign Up (Base: National Adults)



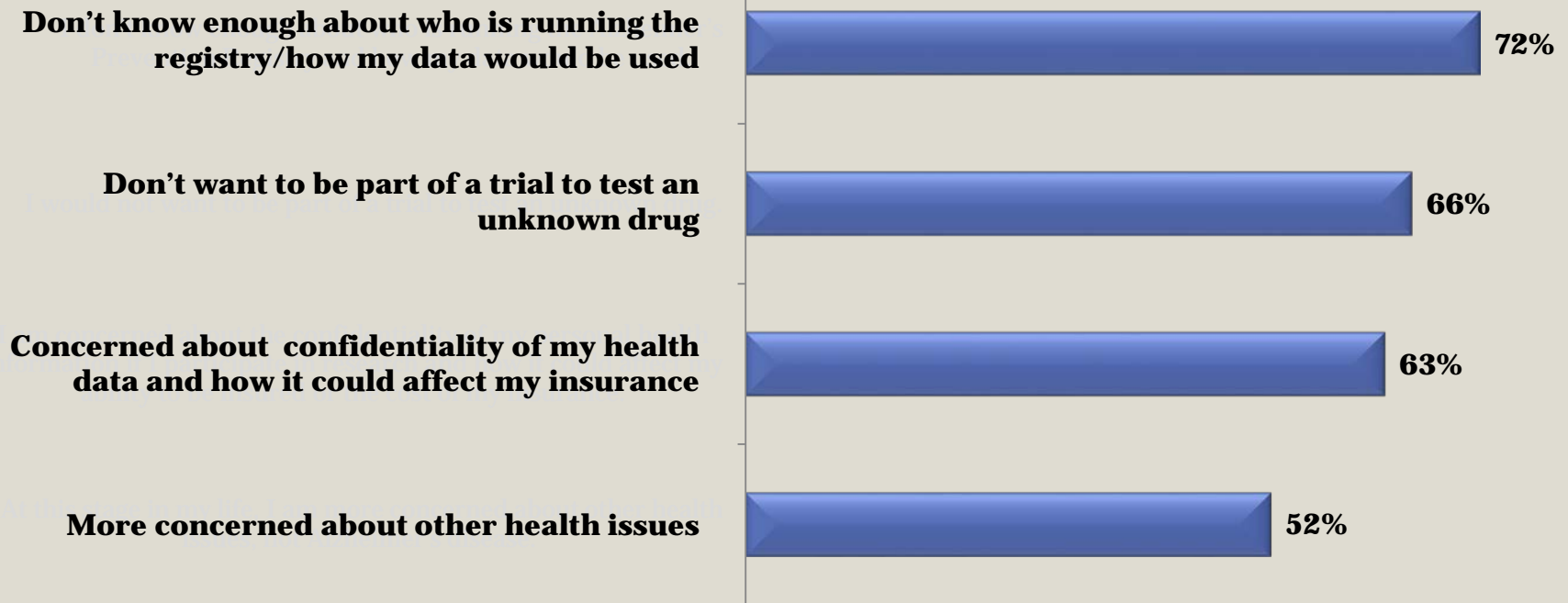
The Registry: Motivators for Joining

% Very/Somewhat Convincing Reason to Join Registry



Barriers To Joining the Registry (Top Tier)

**% Statement Describes My Point of View
About Registry**





Media Coverage Increases Registry Enrollment

The New York Times

AARP BLOG

THE INDIANAPOLIS STAR

THE ARIZONA
REPUBLIC



THE
HUFFINGTON
POST

Detroit Free Press



The New Old Age

Caring and Coping

The Sacramento Bee

The Atlanta
Journal-
Constitution

THE
ENQUIRER
Cincinnati.com



The Record
www.oregonlive.com



Challenges to Increasing Enrollment Numbers (in no particular order!)

- Low awareness about Alzheimer's prevention research
- Uncertainty about participating in research, what it entails
- No reason to join if not able to join a trial TODAY
- Requires email / Internet access
- Needs of minority groups may differ
- Talks, community events result in few signups
- No survivors to tell their story, motivate others (opposite of breast cancer)

Unique Challenge: Genetic Disclosure



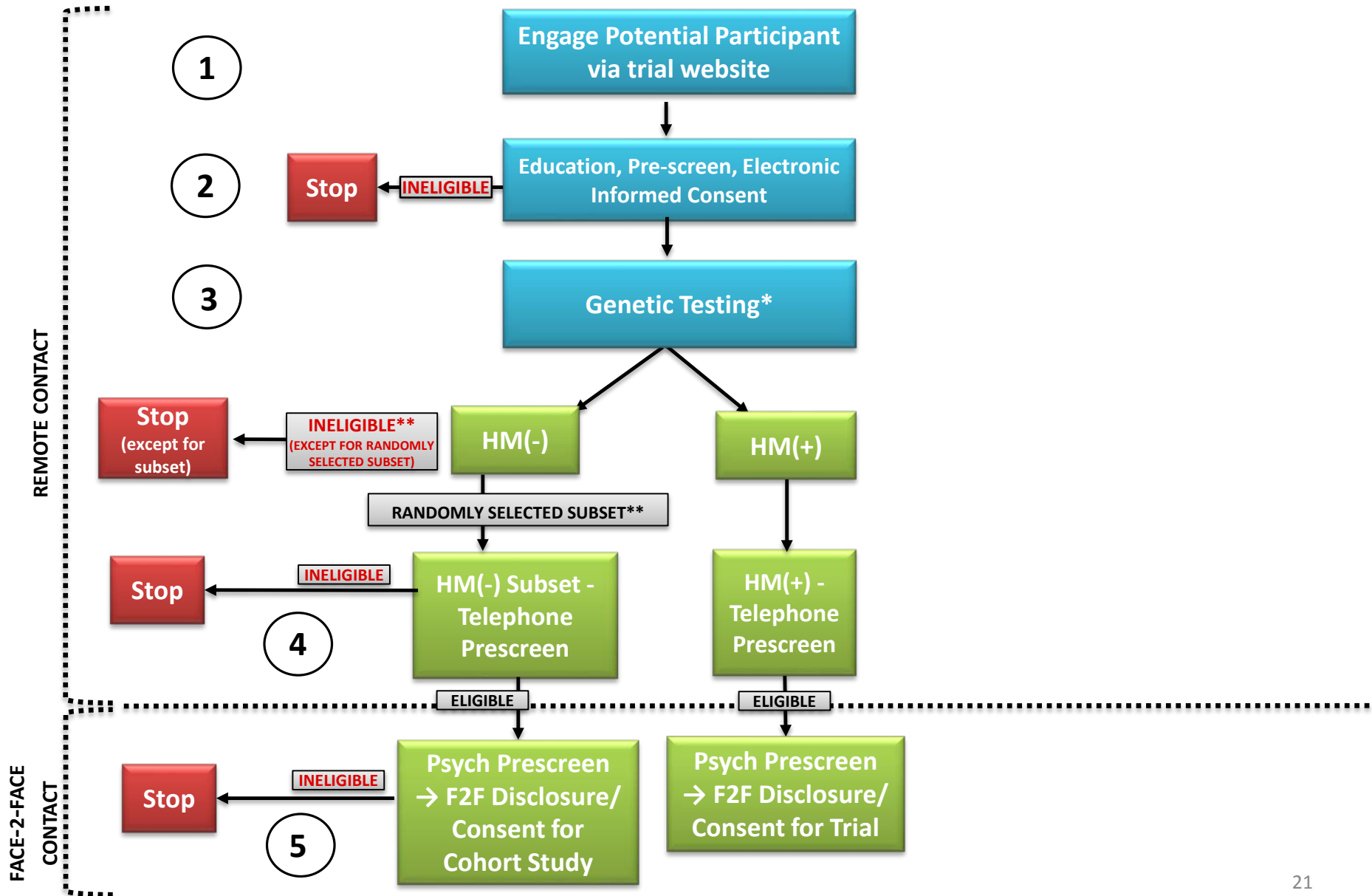
courtesy of the New York Times, with permission



Considerations related to the selection of *APOE* ϵ 4 HMs for the API Trial

- *APOE* ϵ 4 HMs are at the highest known risk for LOAD, but their prevalence is ~2-3%
- We have extensive longitudinal data to help inform the design and power of this trial
- REVEAL suggests disclosure of ApoE4 status is well-tolerated
- How to design a clinical trial that enrolls persons at heightened but not certain genetic risk of AD dementia so that the trial:
 - Minimizes risks to subjects
 - Is valid
 - Is feasible in terms of number of subjects and the resources that are required

API APOE4 Trial Enrollment & Disclosure Proposal





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State of Arizona

Arizona Alzheimer's Consortium

**our colleagues, collaborators, advisors,
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Questions?

