Penn Medicine

NIH COLLABORATORY GRAND ROUNDS

Rigorous Testing of Behavior Change Interventions:

Lessons from the BE ACTIVE randomized controlled trial

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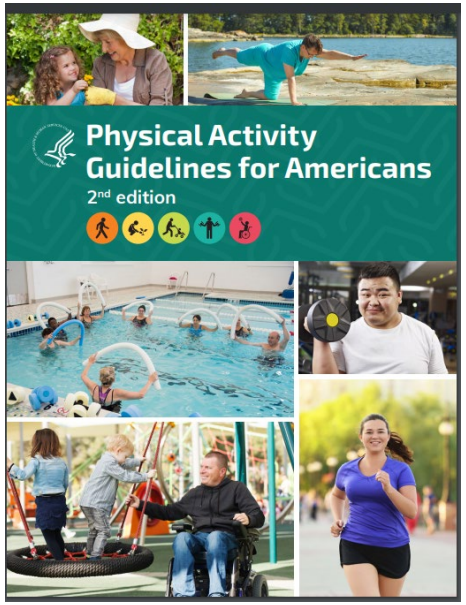
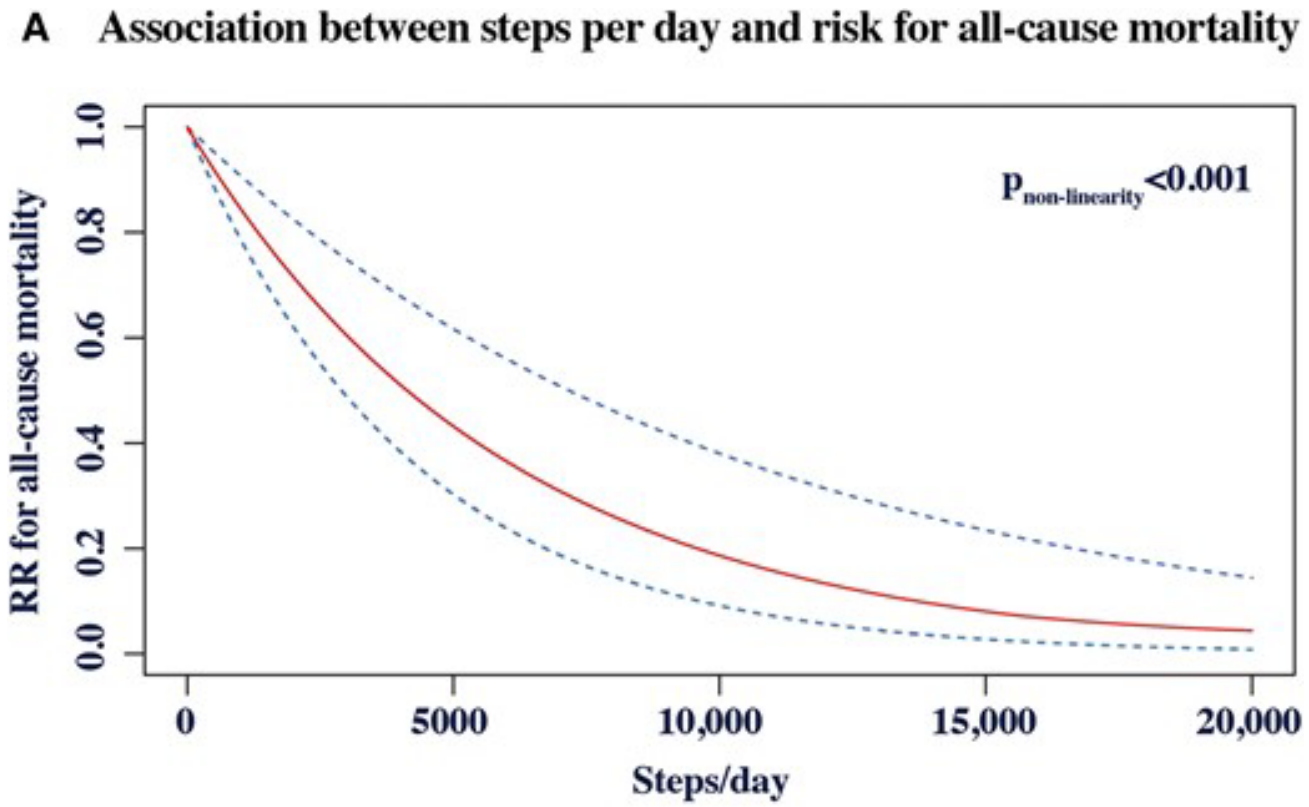
Physical activity



- Many benefits
  - ↓ all cause and CV mortality
  - ↓ risk of heart disease and stroke
  - ↓ risk of hypertension, diabetes, hyperlipidemia
- CDC recommends 150 minutes/week of moderate to vigorous physical activity, but few exercise that much – especially older adults at highest risk for CVD

Move more, sit less

- In observational studies, there is an inverse association between steps per day and outcomes (mortality, CV events)
- Increases in steps of the same size are most helpful for people taking the fewest steps per day at baseline



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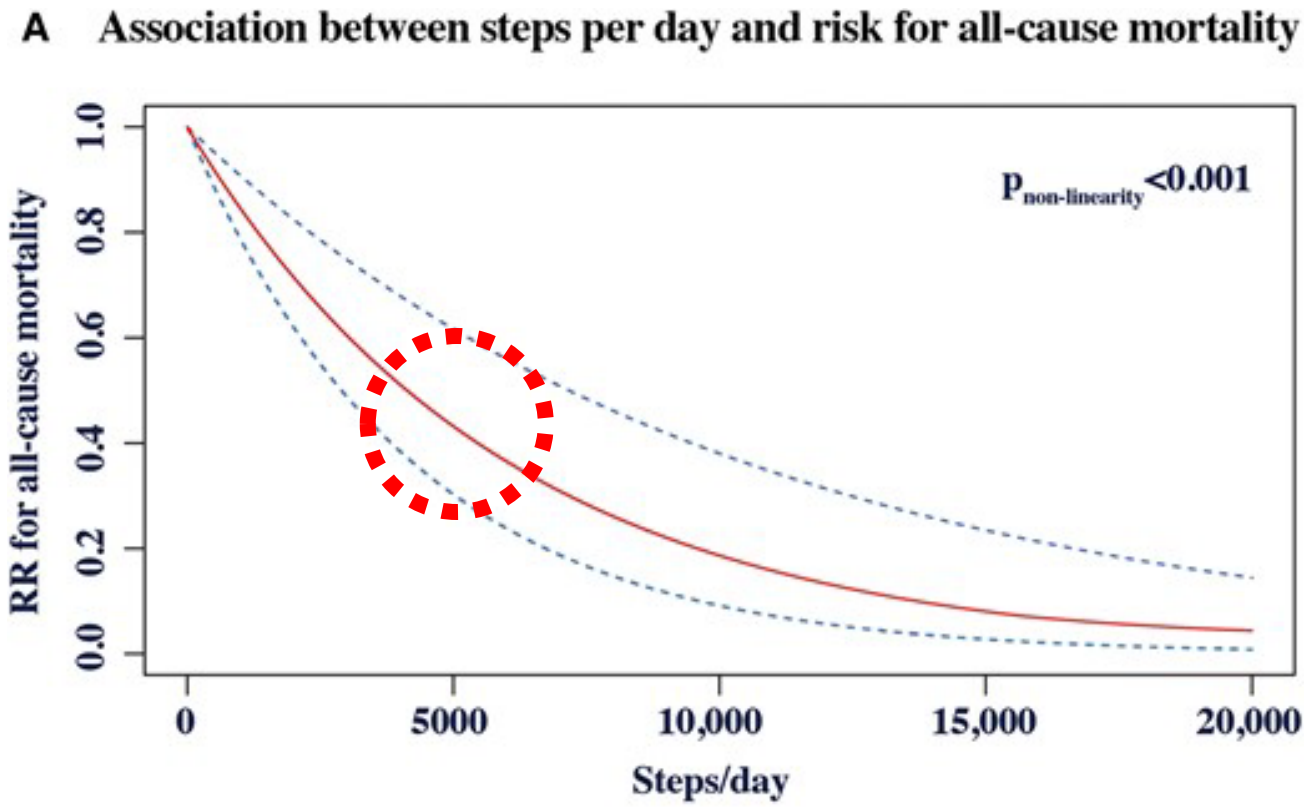
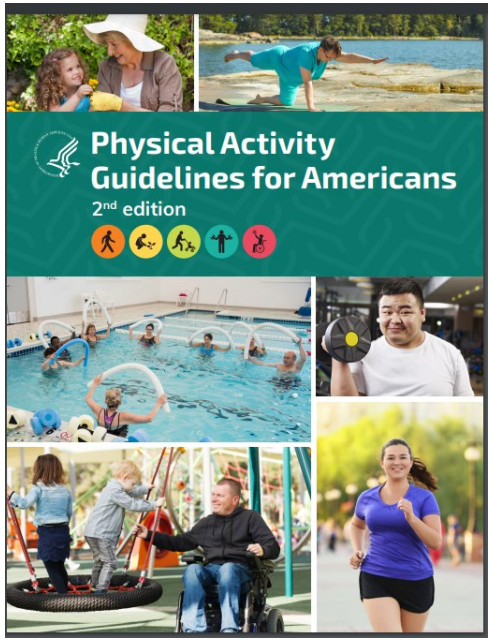
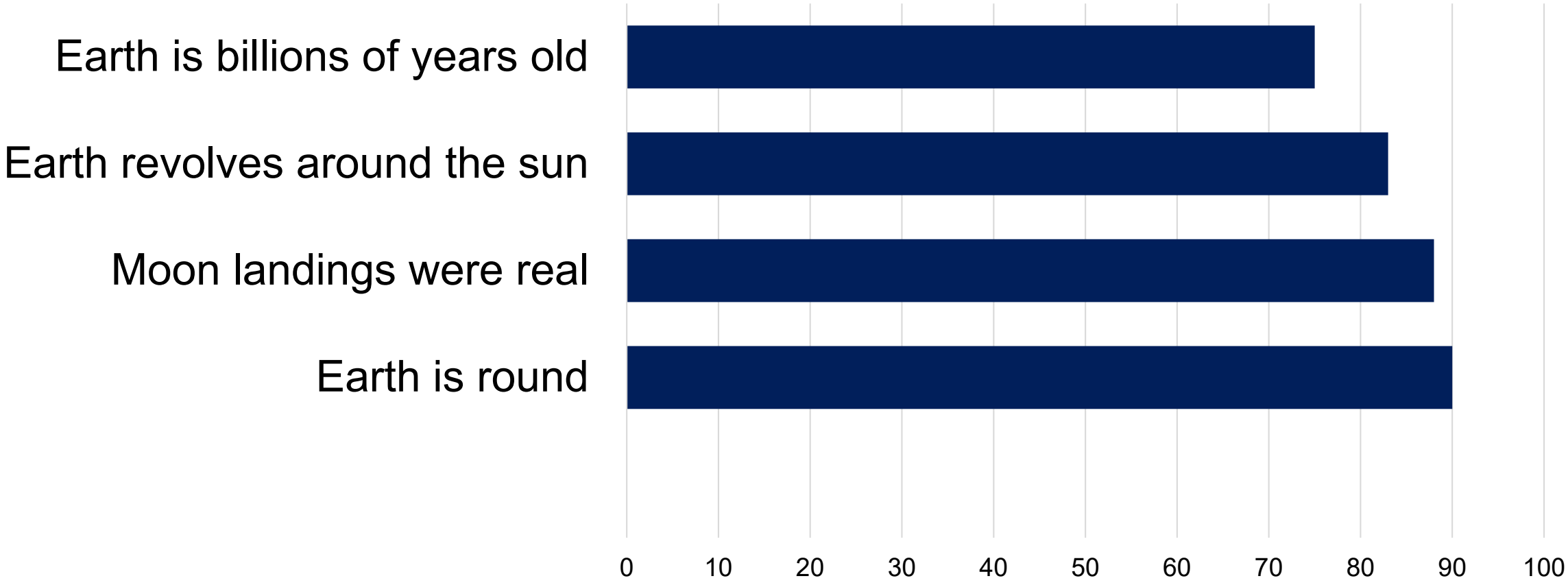


Move More, Sit Less



"Bouts of any length contribute to the health benefits associated with the accumulated volume of physical activity."

Why don’t people exercise?



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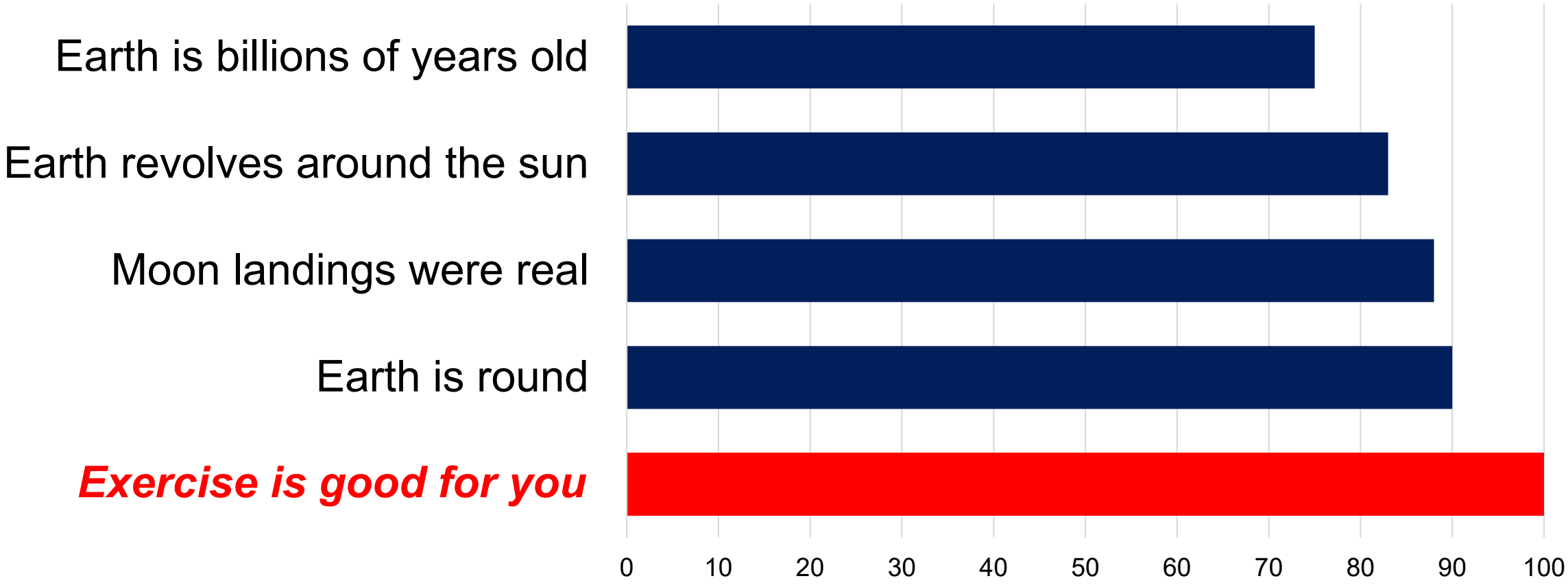
PLOS ONE, 2018; 13 (11): e0207003

Why don’t people exercise?



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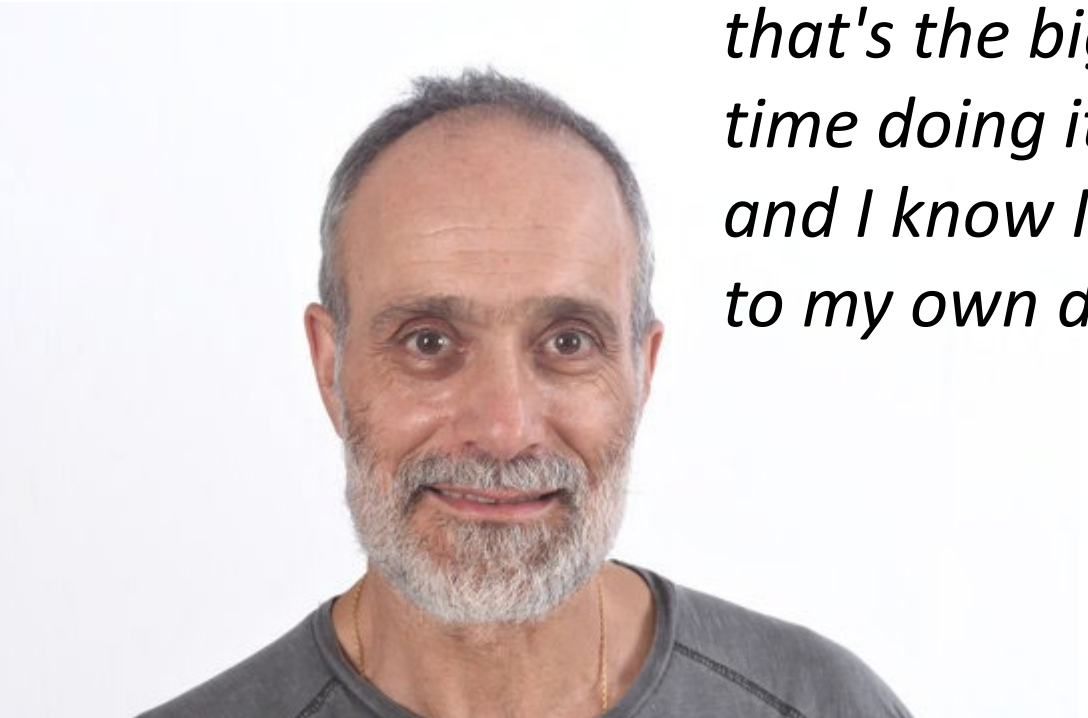
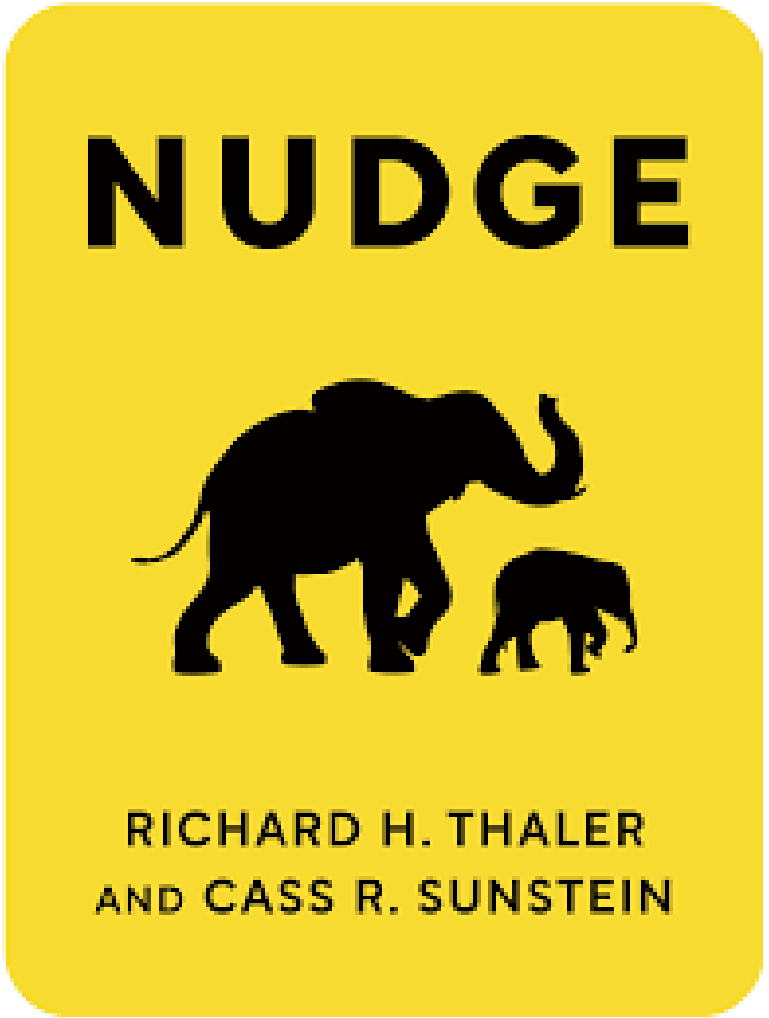
So why *don't* we exercise?

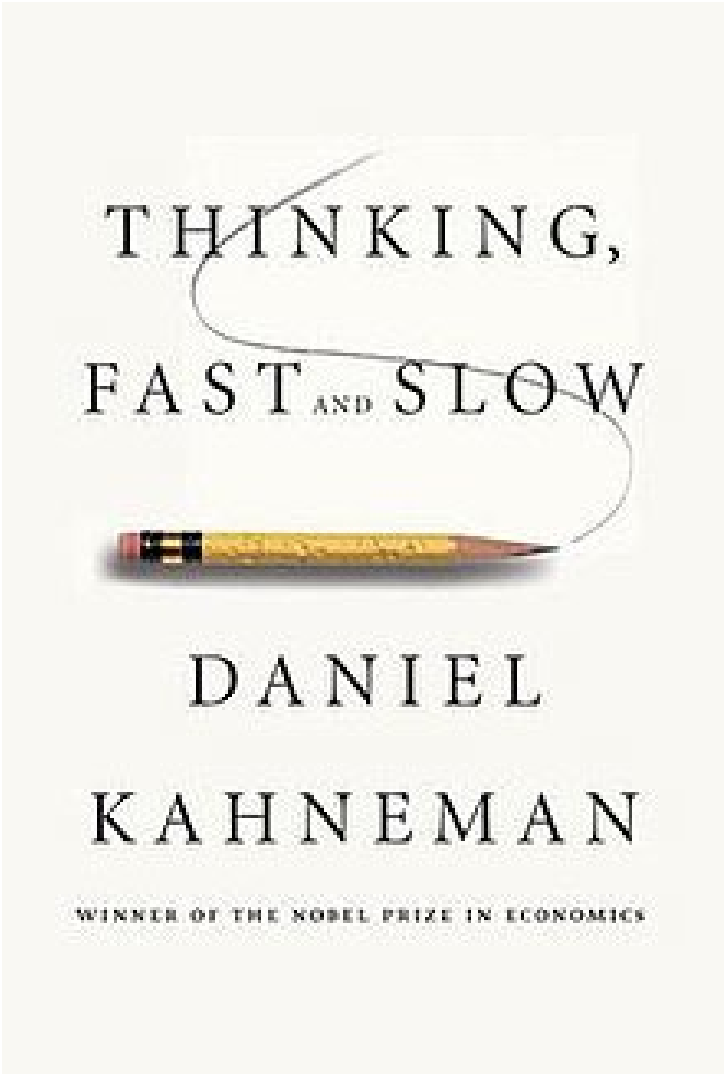


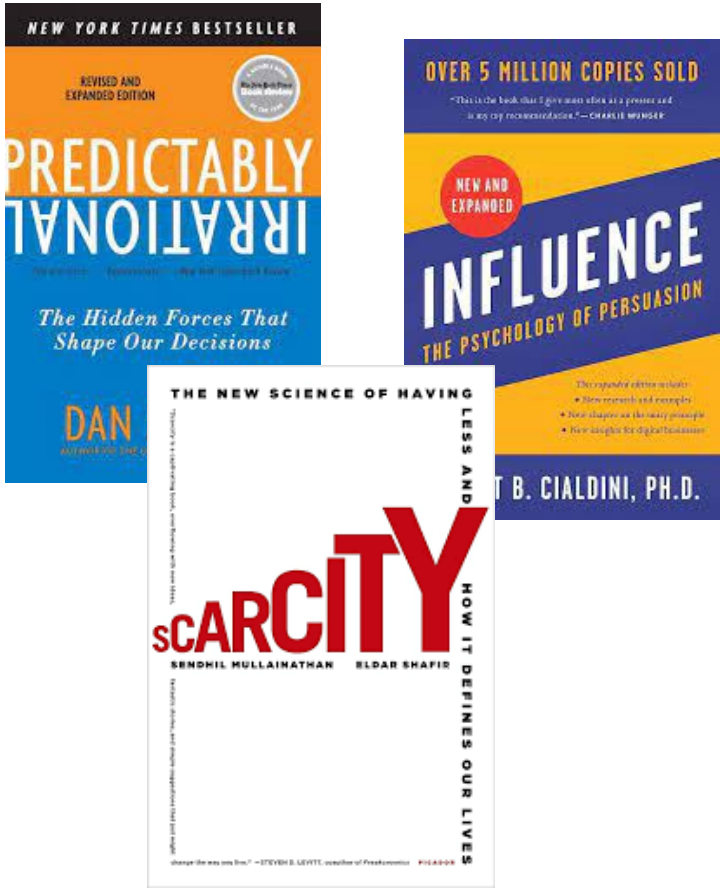
I think my biggest obstacle is, it's hard for me to do it on my own. I'm a bad self-motivator…. On my own, I revert to wanting to just sit on the couch and watch TV when I get home from work. So I think that's the biggest obstacle, is that I have a hard time doing it myself…. Intellectually, I know it's good and I know I should do it, but I find that I don't, left to my own devices.

- A patient, on exercising

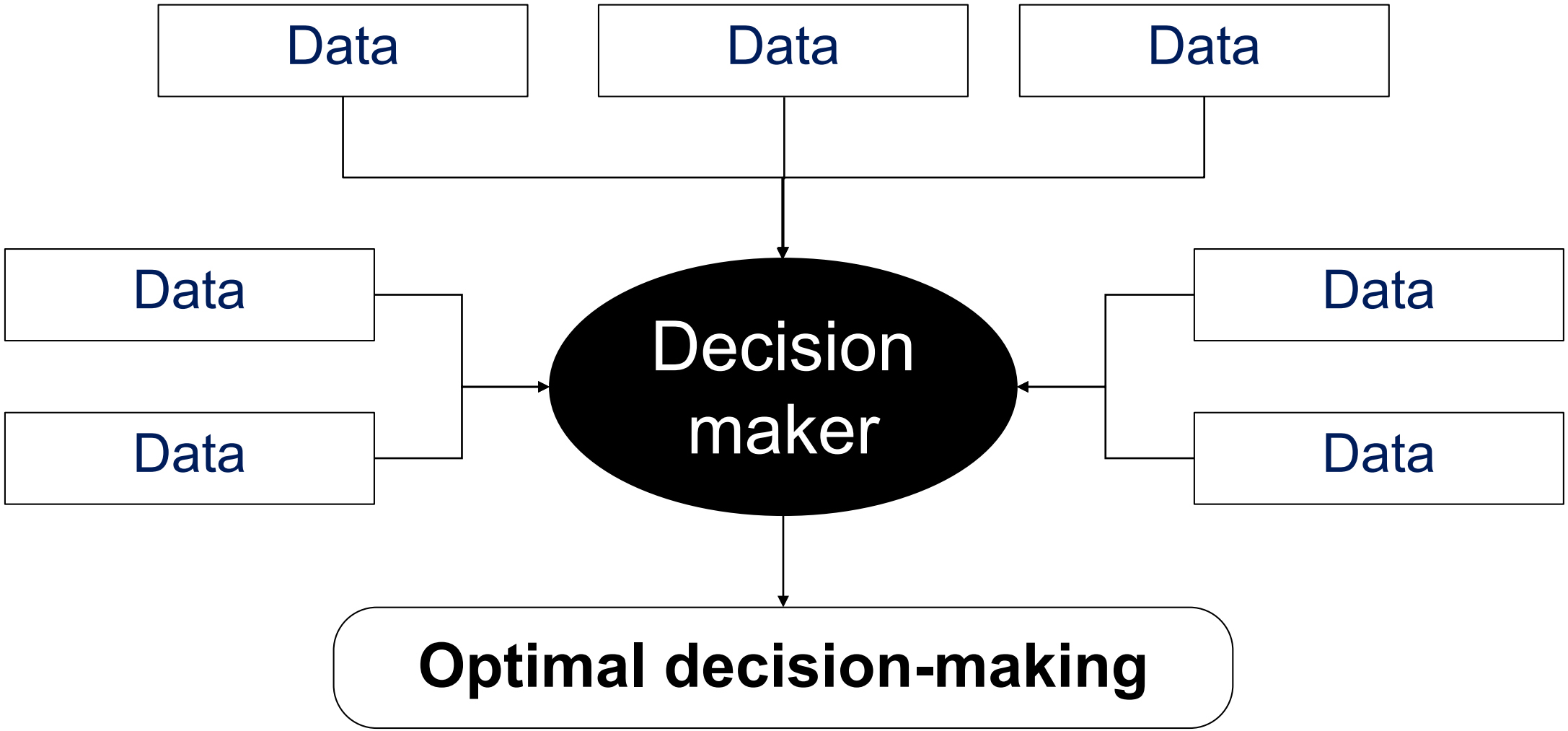
Behavioral economics 101



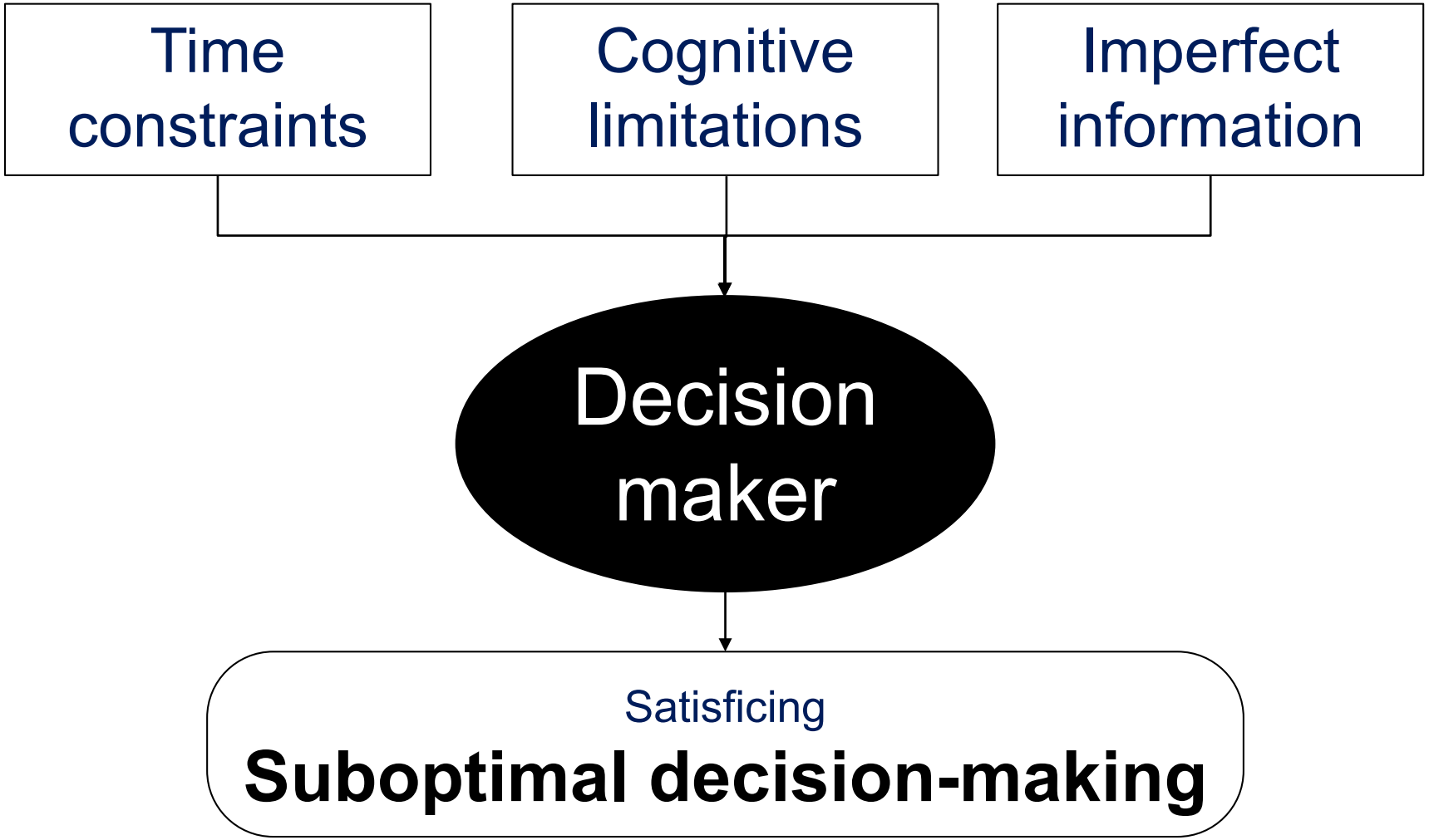




Thinking like an economist



Thinking like a behavioral economist



Thinking like a behavioral economist

- Heuristics guide daily decision-making
  - Immediacy bias
  - Status quo bias
  - Endowment effect
- Disconnect between the planner (who wants to exercise, save for retirement, get their patients on the right medications, etc.) and the doer (who wants to watch TV, spend money, leave clinic on time, etc.)
- “Bounded rationality”
- Cognitive bandwidth is further reduced by scarcity (of resources, time, etc.) leading to even more bounds on rationality

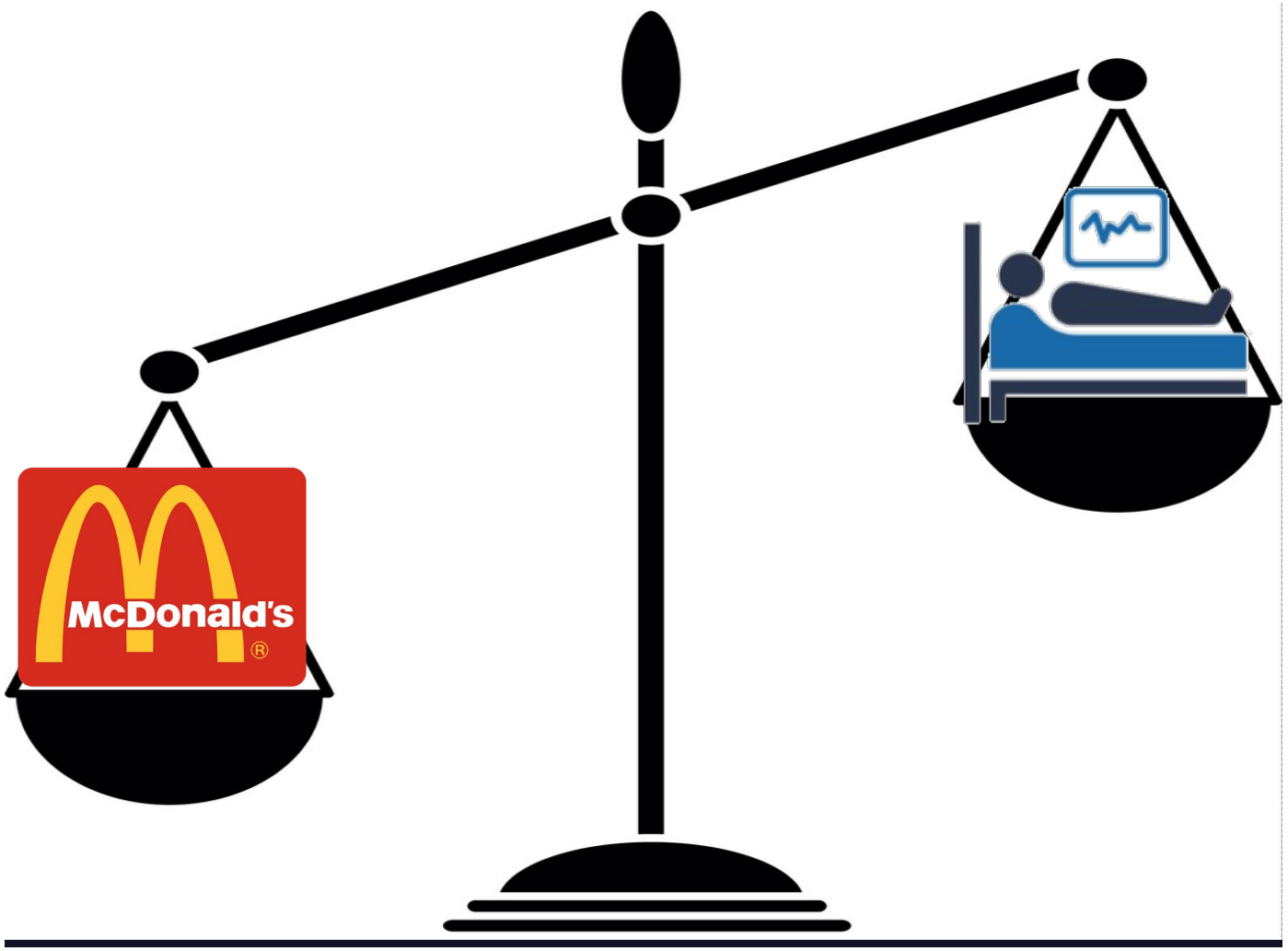
Immediacy bias

$15 now =

$30 in 3 months =

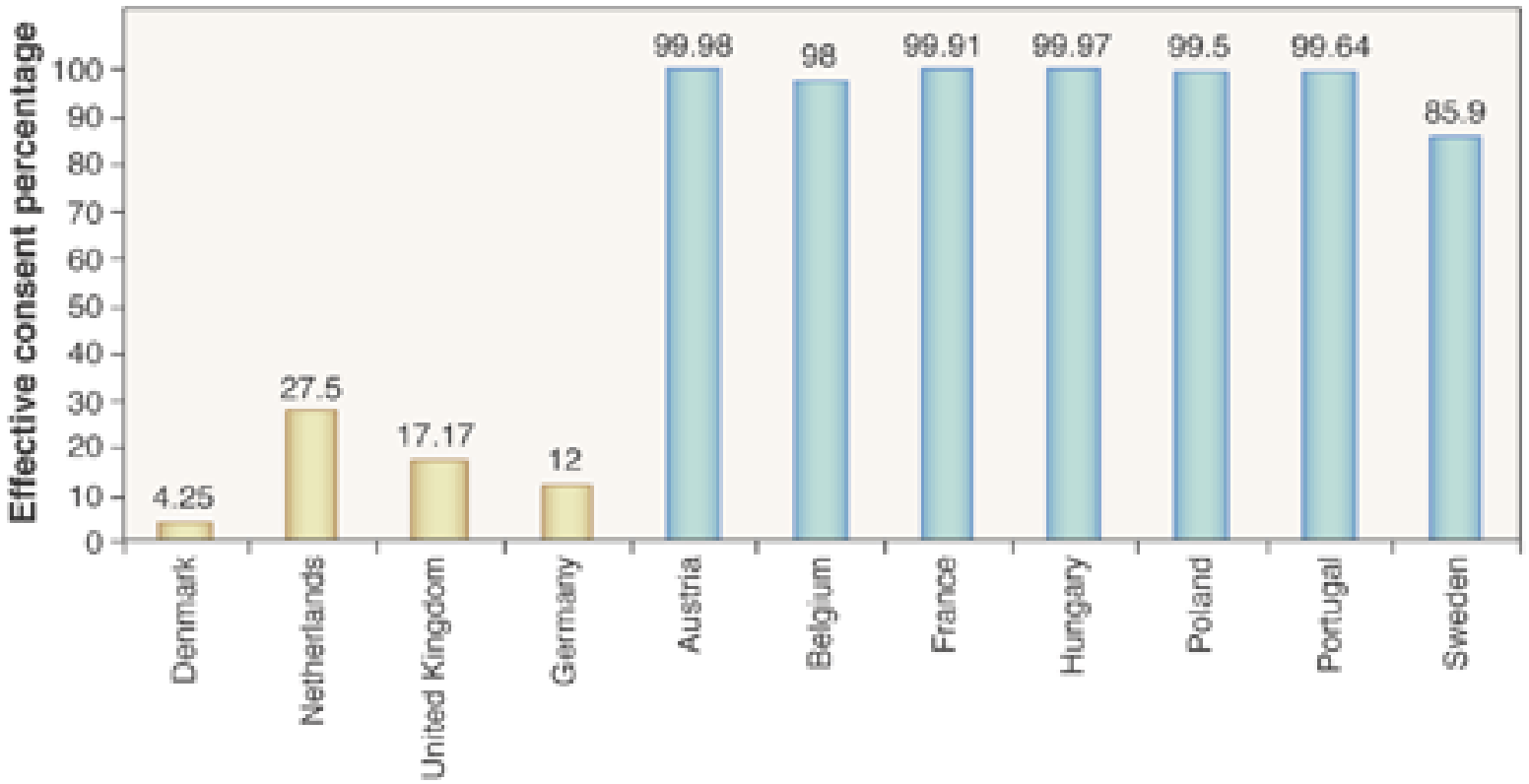
$60 in 1 year =

$100 in 3 years



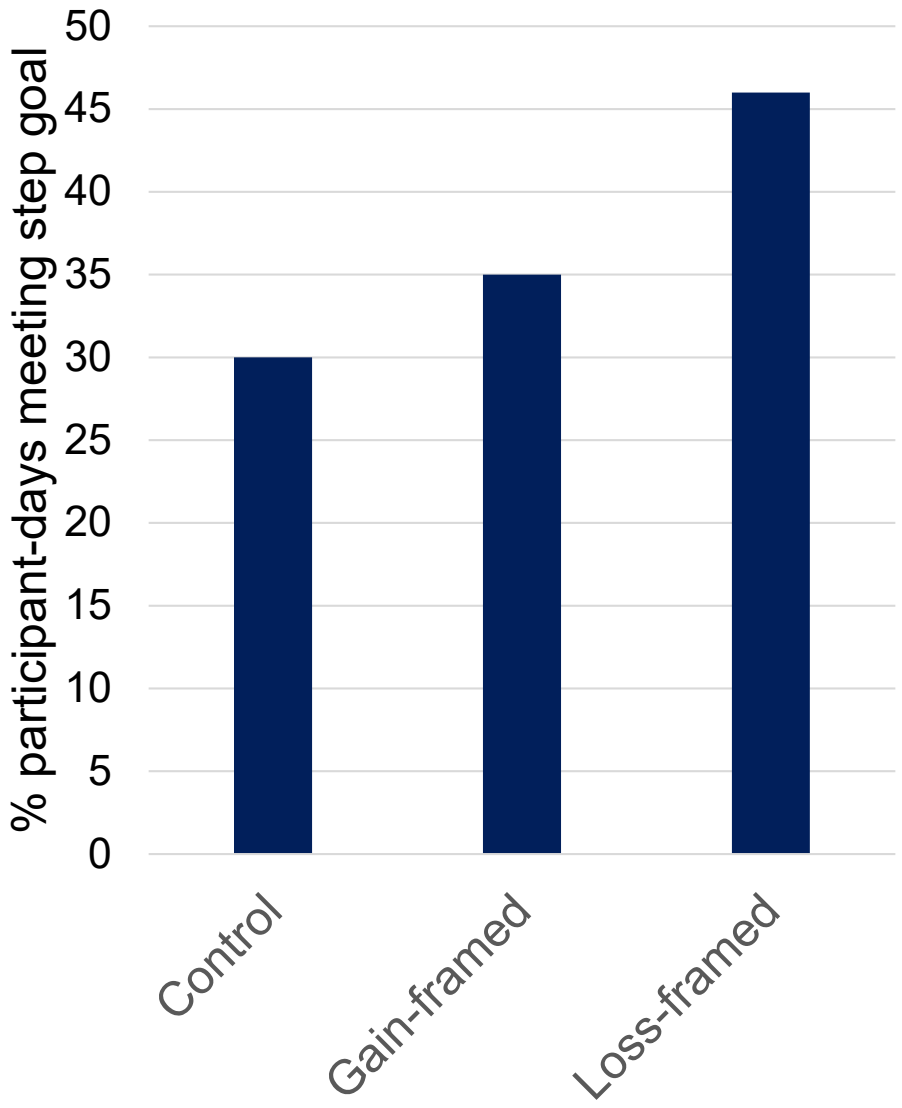
Status quo bias

- People resist change



Endowment effect

- “Ownership increases utility”
- Loss-frame versus gain-frame



Applying behavioral economics to medicine

- Design interventions that make known biases in decision-making work in your favor instead of against you
- Change the decision environment
  - Gamification
  - Financial incentives
- Test interventions developed using state-of-the-art behavioral theory rigorously in randomized controlled trials

Why *else* don’t people exercise?

- The evidence is bad

JAMA | Original Investigation

Levels of Evidence Supporting American College of Cardiology/American Heart Association and European Society of Cardiology Guidelines, 2008-2018

Alexander C. Fanaroff, MD, MHS; Robert M. Califf, MD; Stephan Windecker, MD; Sidney C. Smith Jr, MD; Renato D. Lopes, MD, PhD, MHS

IMPORTANCE Clinical decisions are ideally based on evidence generated from multiple randomized controlled trials (RCTs) evaluating clinical outcomes, but historically, few clinical guideline recommendations have been based entirely on this type of evidence.

OBJECTIVE To determine the class and level of evidence (LOE) supporting current major cardiovascular society guideline recommendations, and changes in LOE over time.

DATA SOURCES Current American College of Cardiology/American Heart Association (ACC/AHA) and European Society of Cardiology (ESC) clinical guideline documents (2008-2018), as identified on cardiovascular society websites, and immediate predecessors to these guideline documents (1999-2014), as referenced in current guideline documents.

STUDY SELECTION Comprehensive guideline documents including recommendations organized by class and LOE.

DATA EXTRACTION AND SYNTHESIS The number of recommendations and the distribution of LOE (A [supported by data from multiple RCTs or a single, large RCT], B [supported by data from observational studies or a single RCT], and C [supported by expert opinion only]) were determined for each guideline document.

MAIN OUTCOMES AND MEASURES The proportion of guideline recommendations supported by evidence from multiple RCTs (LOE A).

RESULTS Across 26 current ACC/AHA guidelines (2930 recommendations; median, 121 recommendations per guideline [25th-75th percentiles, 76-155]), 248 recommendations (8.5%) were classified as LOE A, 1465 (50.0%) as LOE B, and 1217 (41.5%) as LOE C. The median proportion of LOE A recommendations was 7.9% (25th-75th percentiles, 0.9%-15.2%). Across 25 current ESC guideline documents (3399 recommendations; median, 130 recommendations per guideline [25th-75th percentiles, 111-164]), 484 recommendations (14.2%) were classified as LOE A, 1053 (31.0%) as LOE B, and 1862 (54.8%) as LOE C. When comparing current guidelines with prior versions, the proportion of recommendations that were LOE A did not increase in either ACC/AHA (median, 9.0% [current] vs 11.7% [prior]) or ESC guidelines (median, 15.1% [current] vs 17.6% [prior]).

CONCLUSIONS AND RELEVANCE Among recommendations in major cardiovascular society guidelines, only a small percentage were supported by evidence from multiple RCTs or a single, large RCT. This pattern does not appear to have meaningfully improved from 2008 to 2018.

Author Affiliations: Division of Cardiology and Duke Clinical Research Institute, Duke University, Durham, North Carolina (Fanaroff, Lopes); Duke Forge, Duke University School of Medicine, Durham, North Carolina (Califf); Department of Medicine, Stanford University, Stanford, California (Califf); Verily Life Sciences (Alphabet), South San Francisco, California (Califf); Department of Cardiology, Inselspital,

8.5% of ACC/AHA recommendations

14.2% of ESC recommendations

are supported by evidence from RCTs

Fanaroff AC, Lopes RD, et al. JAMA 2019;321:1069

How do we know a recommendation is bad?

1. Not supported by RCT evidence
2. No one follows it because it isn't specific enough to be followed in a useful way
3. Both

I	B	Adults should engage in at least 150 minutes per week of accumulated moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity (or an equivalent combination of moderate and vigorous activity) to reduce ASCVD risk
IIb	C	Decreasing sedentary behavior in adults may be reasonable to reduce ASCVD risk

I	B	Adults should engage in at least 150 minutes per week of accumulated moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity (or an equivalent combination of moderate and vigorous activity) to reduce ASCVD risk
IIb	C	Decreasing sedentary behavior in adults may be reasonable to reduce ASCVD risk

Behavioral interventions to increase activity

- In short-term studies:
  - Gamification increases physical activity
  - Financial incentives increase physical activity
- But it is not certain how long these effects last, or which approach is better
- For any intervention to improve cardiovascular outcomes, it must lead to *sustained* increases in physical activity

BE ACTIVE

- A four-arm pragmatic randomized controlled trial to test the effectiveness of
  - Behaviorally-designed gamification *vs.*
  - Loss-framed financial incentives *vs.*
  - Gamification + financial incentives *vs.*
  - Attention control

for increasing physical activity over a 12-month intervention and 6-month follow-up period

Circulation

DOI: 10.1161/CIRCULATIONAHA.124.069531

Design: Recruitment

- Eligible participants automatically identified via EHR algorithm
  - Age > 18
  - 10-year ASCVD event risk > 7.5% or established vascular disease
- Directly contacted by email or text message with an invitation to participate and link to the Way to Health platform

Way To Health

Evidence Based Patient Engagement

- Automated patient communication
- Device integration
- Clinical Trials
- Behavioral Economics
- Gamification
- Customizable Rules Engine

Way To Health

Evidence Based Patient Engagement

1. Client Layer (Study Participant)

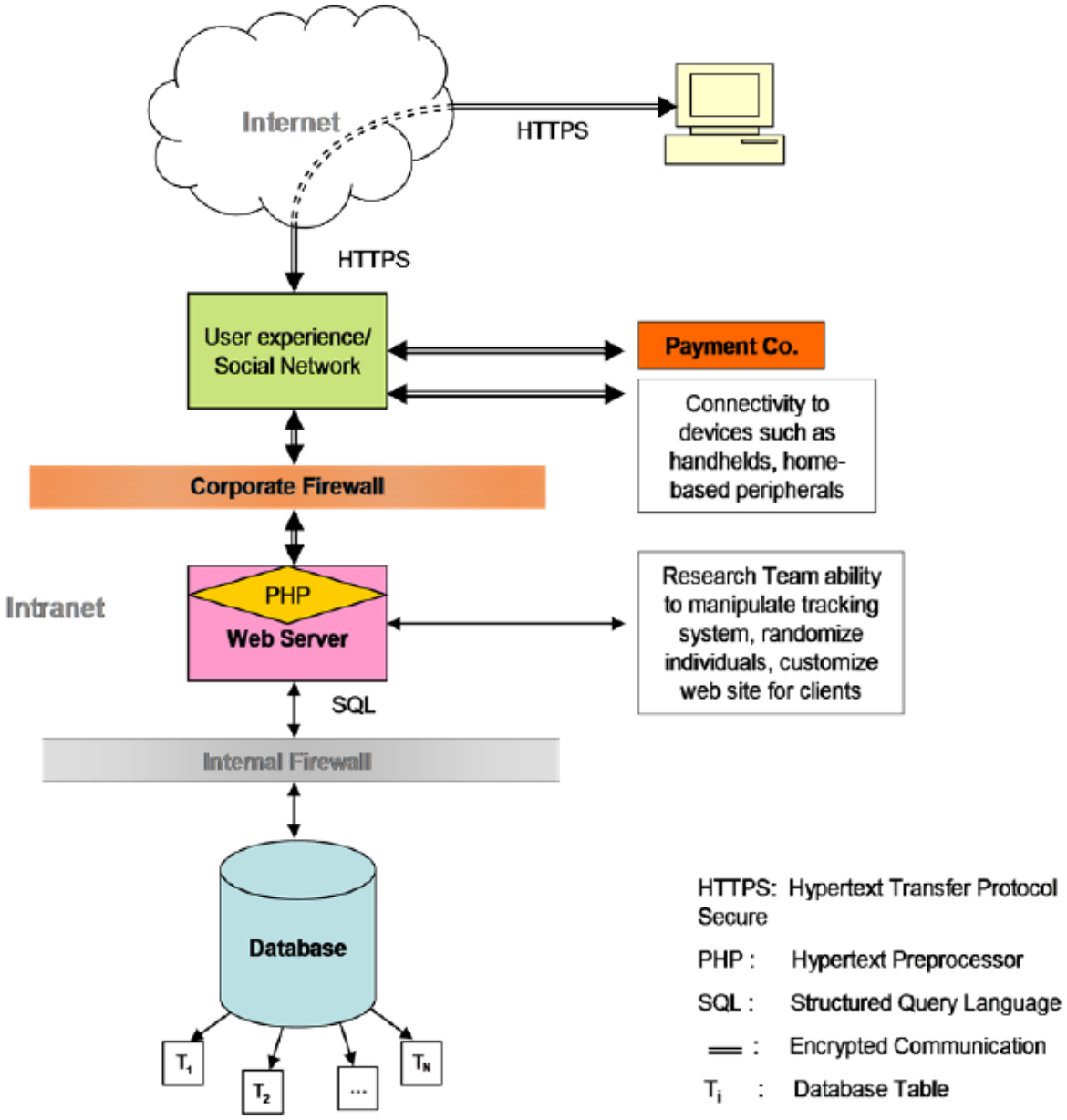
2. Application layer (Web application)

- Social Network Applications +
- Third party development partner (**P'unk Ave**)

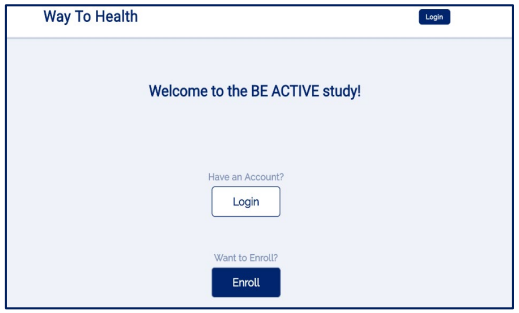
3. Database Layer (Database)

- Hardware maintenance
- System back-up
- Database development & maintenance

Wharton Computing and BMIC



Design: Enrollment and randomization



Patient enrolls in Way to Health

Eligible patients mailed Fitbit

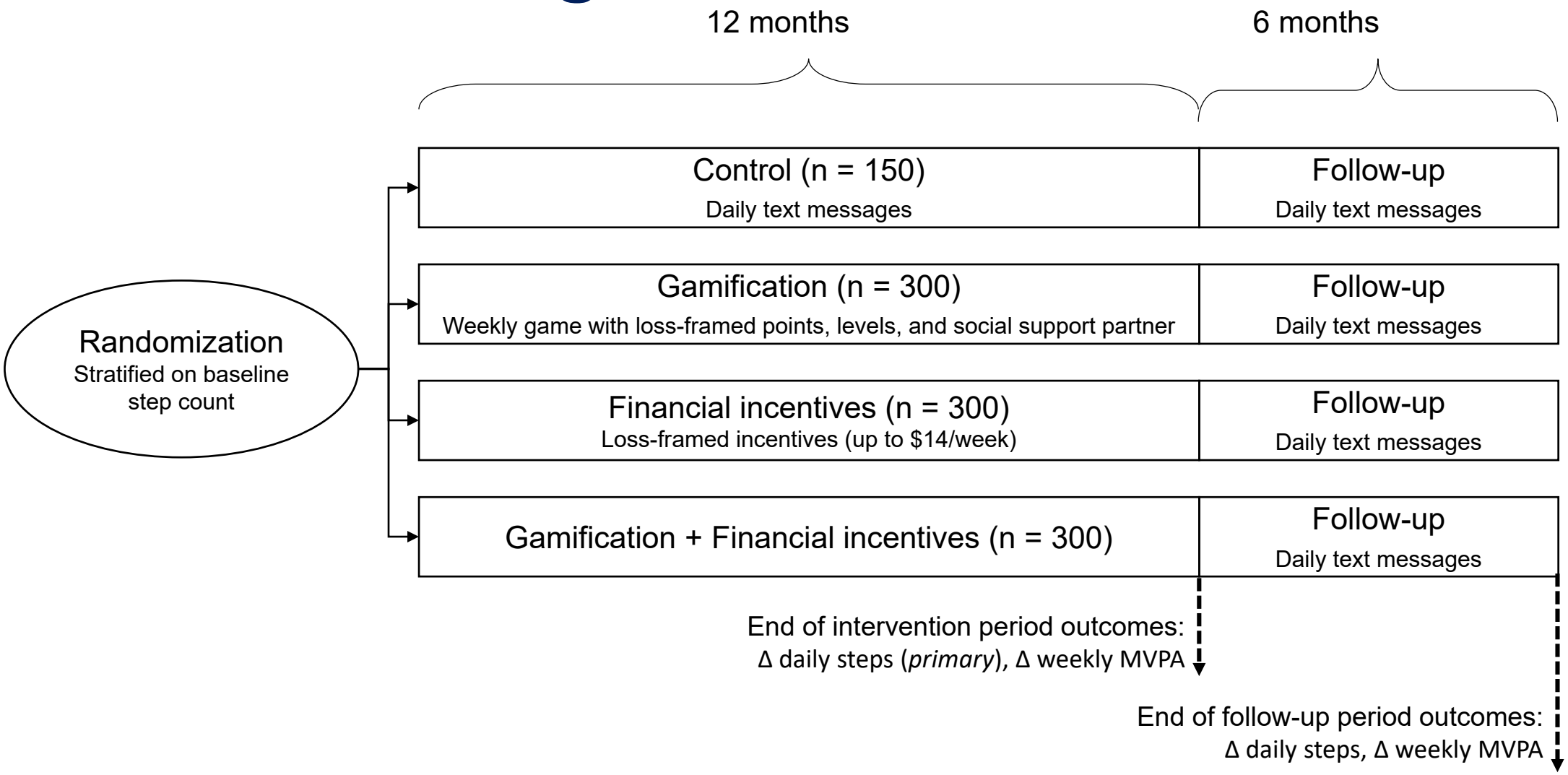
2 week baseline period

Goal selection (self-selected, 33-50% increase)

Randomization

Intervention & follow-up

BE ACTIVE design



Design: attention control

- Daily text messages note how many steps the participant had taken the day before and whether they met their goal
- Isolates the behavioral component of the intervention
- Incorporates goal-setting and social accountability → much stronger than “usual care”

Design: Gamification

- Each week, participants were endowed with 70 points
- Each day a participant did not meet their step goal, they lost 10 points; if they met their goal, they kept their points
- Daily text messages noted whether the participant met their goal the day before, whether they kept or lost points, and how many points they had left for the week
- Weekly text messages noted whether participants have moved up or down a level based on that week's point total (> or < 40)
  - Blue ↔ bronze ↔ **silver** ↔ gold ↔ platinum
- Weekly emails to support partner
- "Fresh start" moves participants in lower levels back to middle

Design: financial incentives

- Each week, $14 was put in the participant's virtual account
- Each day a participant did not meet their step goal, they lost $2; if they met their goal, they kept their money
- Daily text messages noted whether the participant met their goal the day before, whether they kept or lost their money, and how much money they kept that week

Design: Gamification + financial incentives

- Participants received both the gamification and financial incentives interventions
- In all intervention arms, step goal was gradually increased to participant's selected goal over an 8-week ramp-up period

Behavioral economic concepts

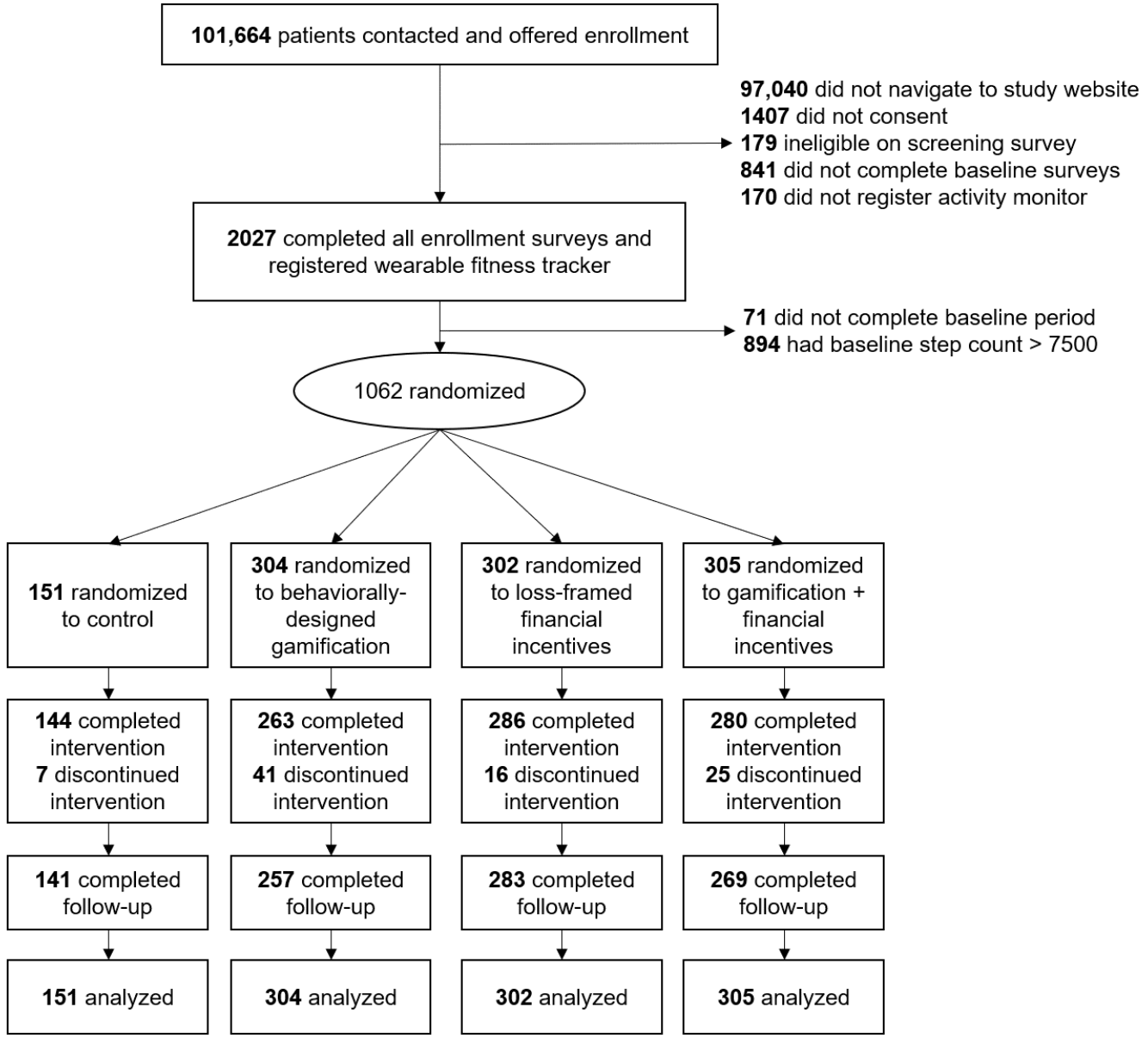
Principle	Explanation	Application in BE ACTIVE
Status quo bias	People favor the path of least resistance and avoid initiating change	Game runs automatically in the background
Immediacy	Immediate rewards are more motivating than future rewards	Points and money awarded daily with daily text message reminders
Loss aversion	People are more impacted when the same situation is framed as a loss rather than a gain	Loss-framed points and financial incentives

Methods

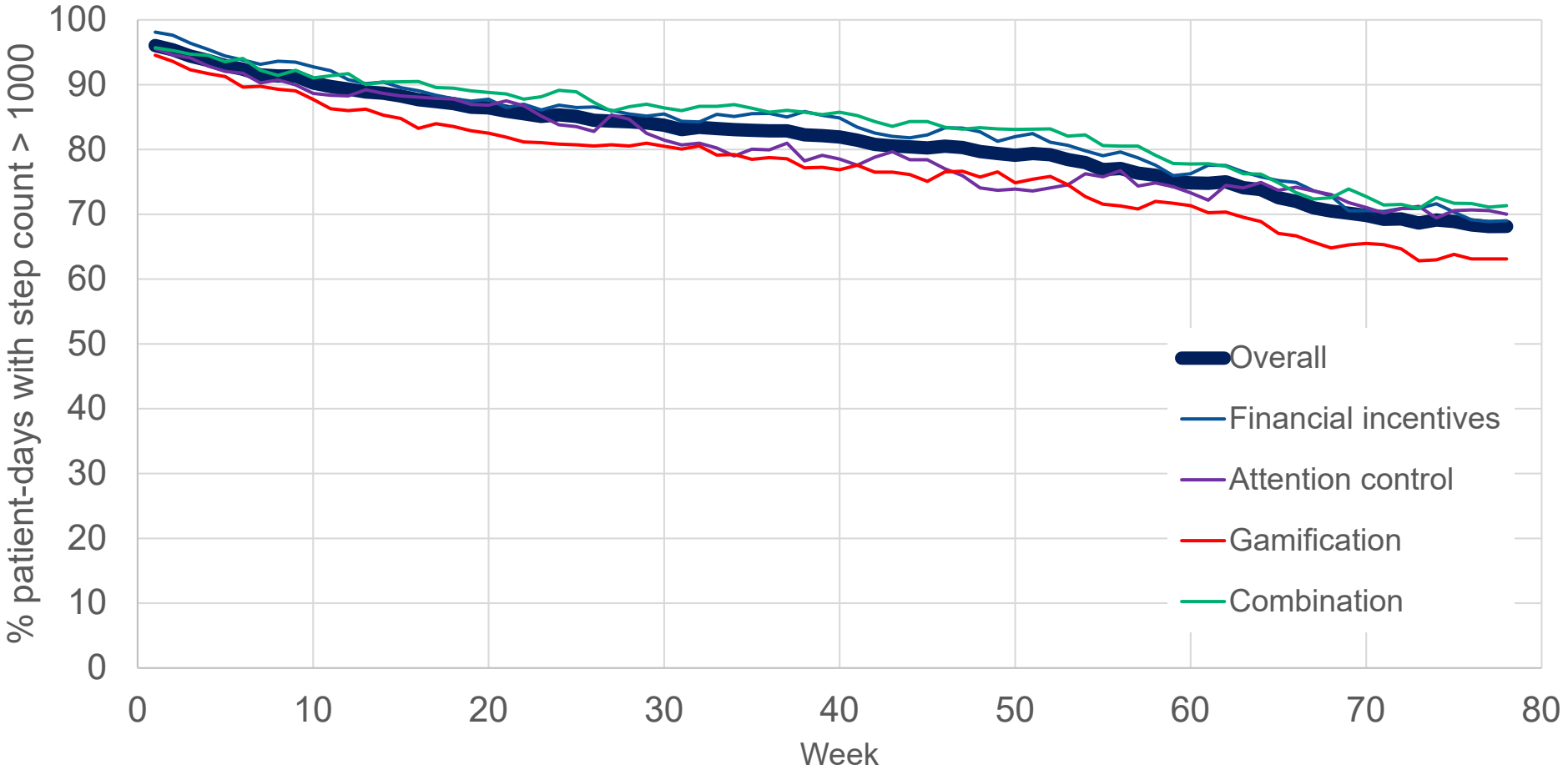
- All randomly assigned patients were included in the intention-to-treat analysis
- Generalized linear mixed effect regression models to evaluate changes from baseline in daily steps and minutes of MVPA
- Multiple imputation for days with missing step count or values < 1000
- Powered to compare all 3 interventions vs. control using Bonferroni adjustment of type 1 error rate with two-sided α = 0.017
  - Intervention arms significant versus control were compared with each other, with same adjustment of type 1 error rate
  - 93% power to detect a difference of 1000 steps and 85% power to detect a difference of 750 steps

Participant flow

- 91.6% (n = 973) completed the 12-month intervention
- 89.4% (n = 950) completed the 18-month study



Longitudinal engagement



- Step count data available for 81.2% of participant-days over 18 month follow-up, including ~ 70% of participant days in the last month of the study

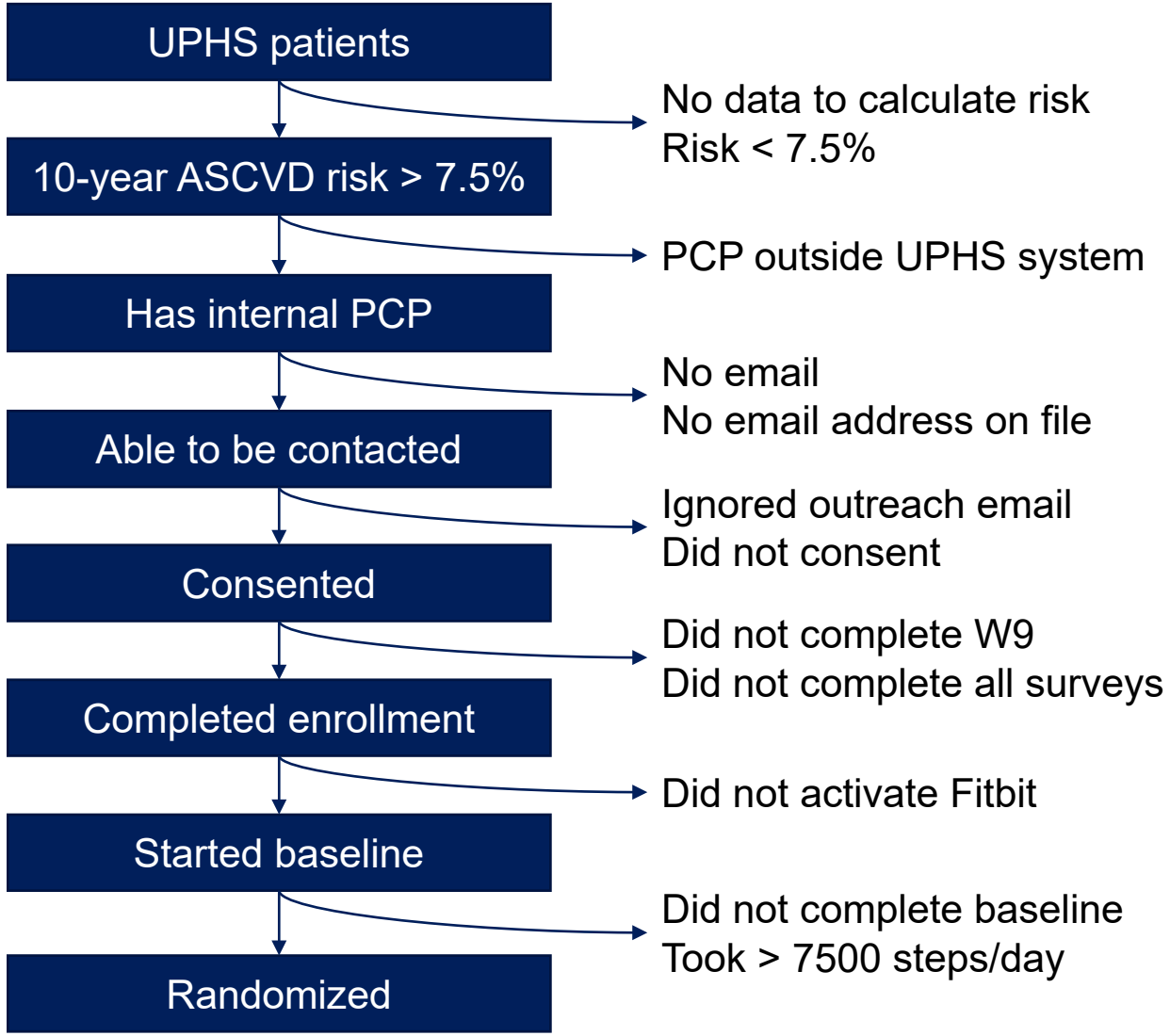
Baseline characteristics

	Overall	Control	Gamification	$ Incentives	Combination
Age	67	67	67	66	67
Black	25%	27%	25%	27%	22%
Annual household income < $50k	23%	32%	20%	24%	20%
Diabetes	23%	25%	21%	22%	25%
Hyperlipidemia	53%	51%	54%	56%	51%
Hypertension	62%	62%	62%	64%	60%
Baseline step count	**5014**	**4980**	**4958**	**5018**	**5081**
Step goal increase	1867	1855	1890	1890	1826

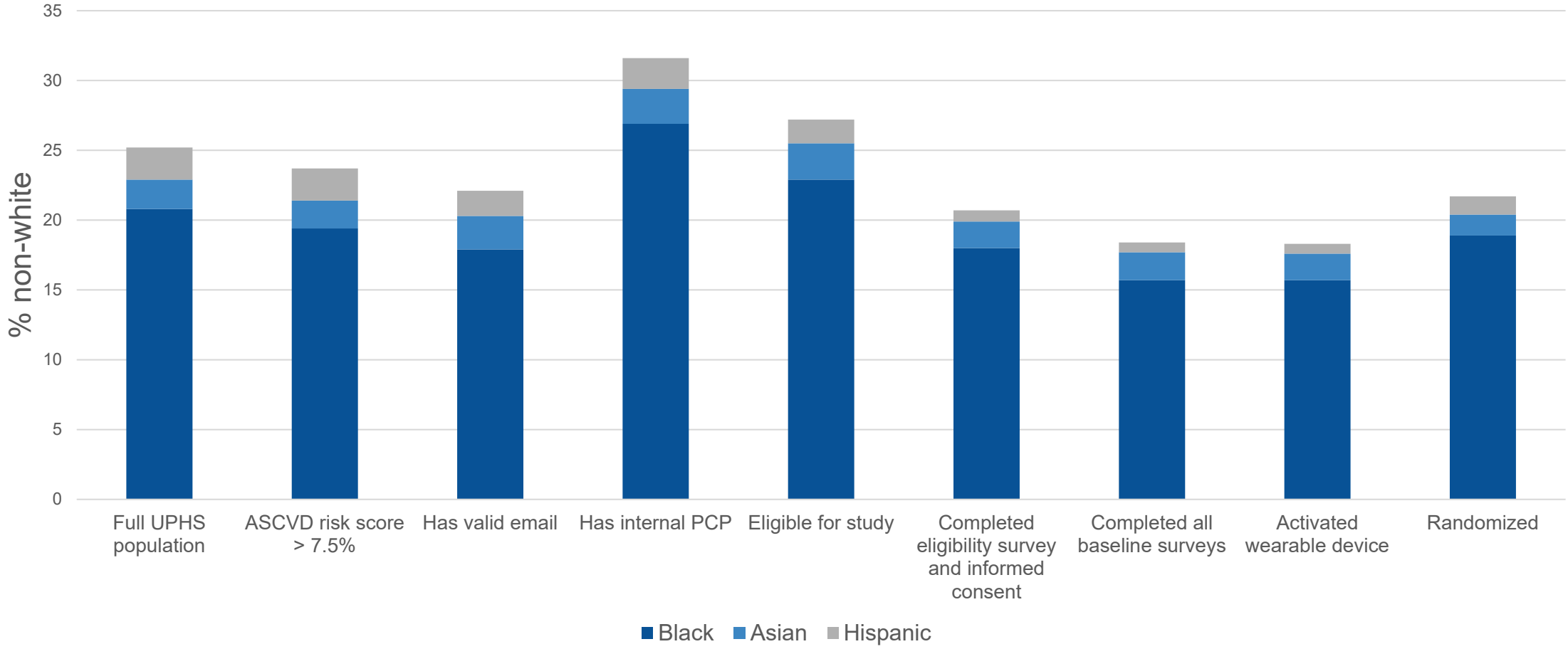
Implications of passive recruitment

- With ~80% of our study population enrolled, 80% of enrolled participants were White, 16% were Black
- We sought to understand where in our process we were losing Black participants

Where is the lesion?

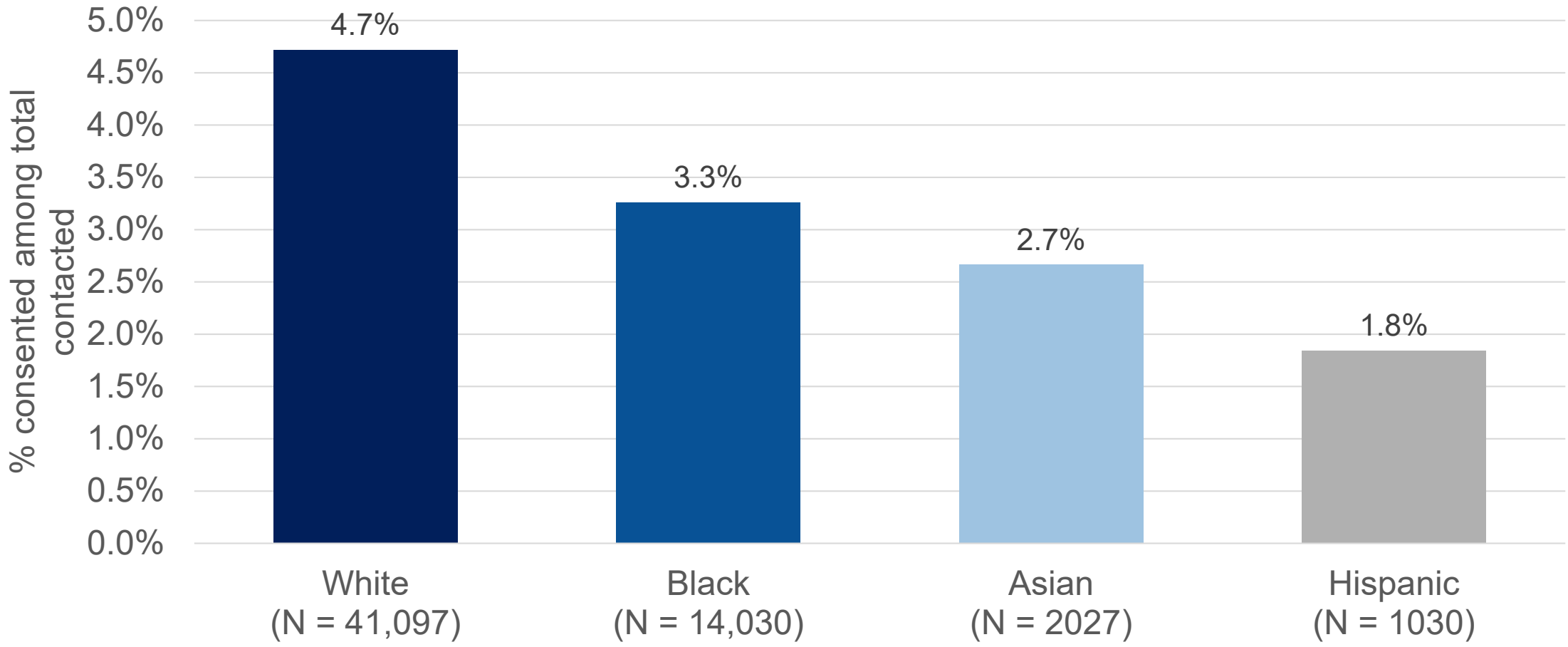


Drop-off in non-white participants

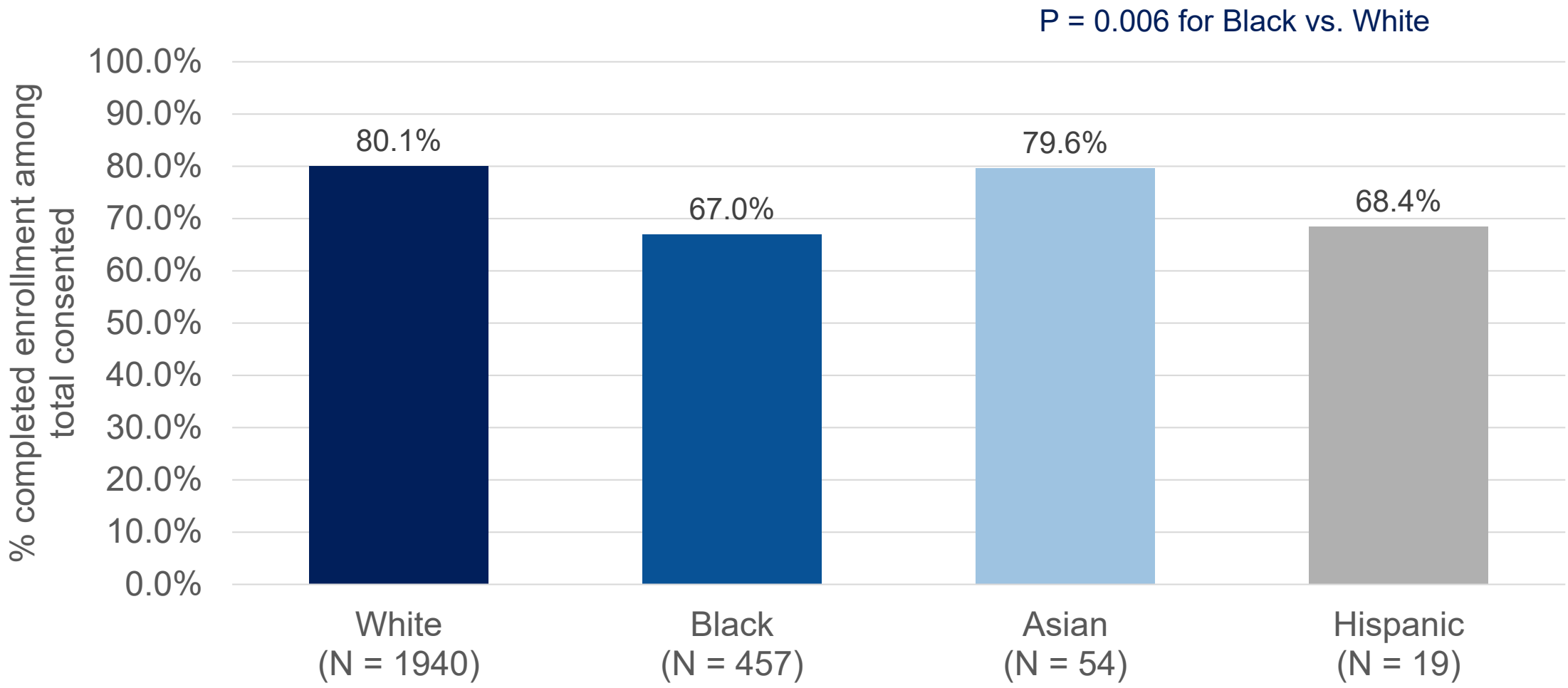


Initial engagement by race

P < 0.0001 for all comparisons vs. White



Retention in enrollment process by race



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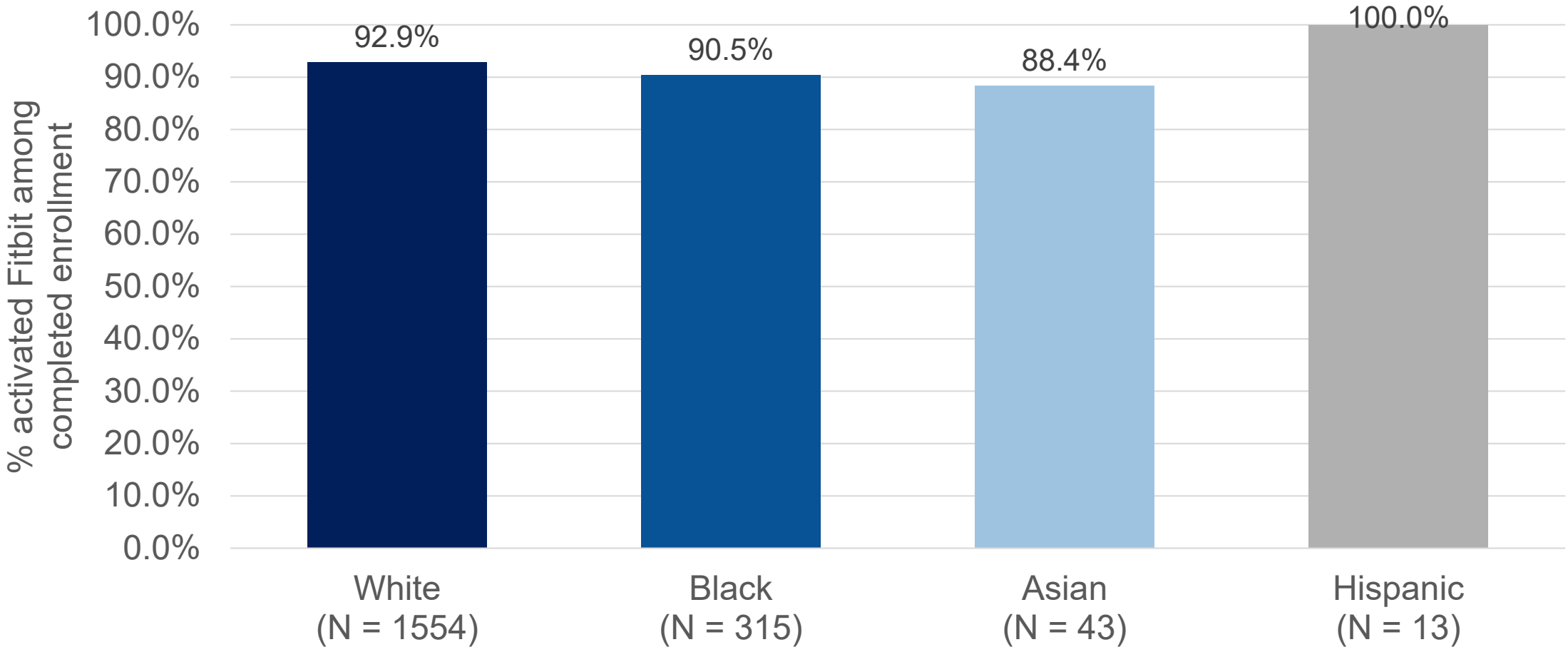

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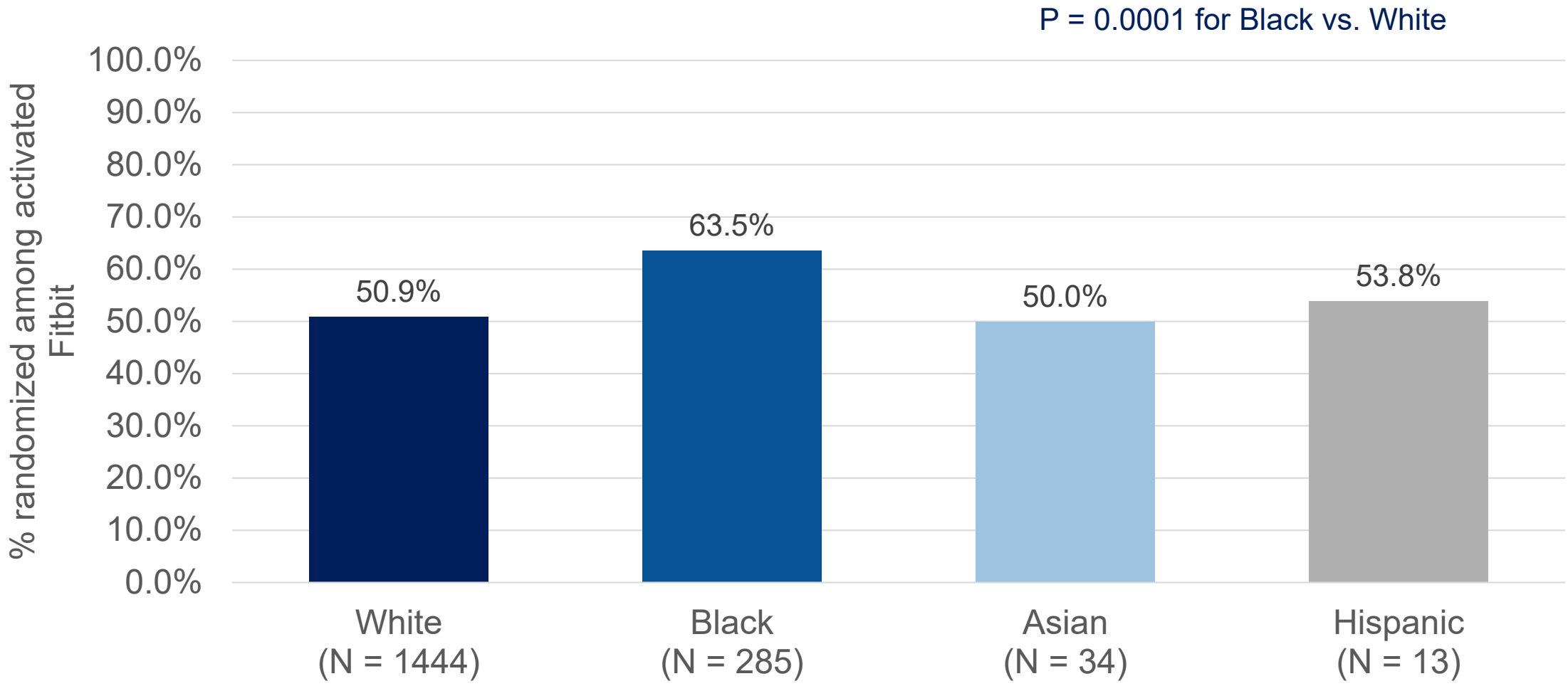
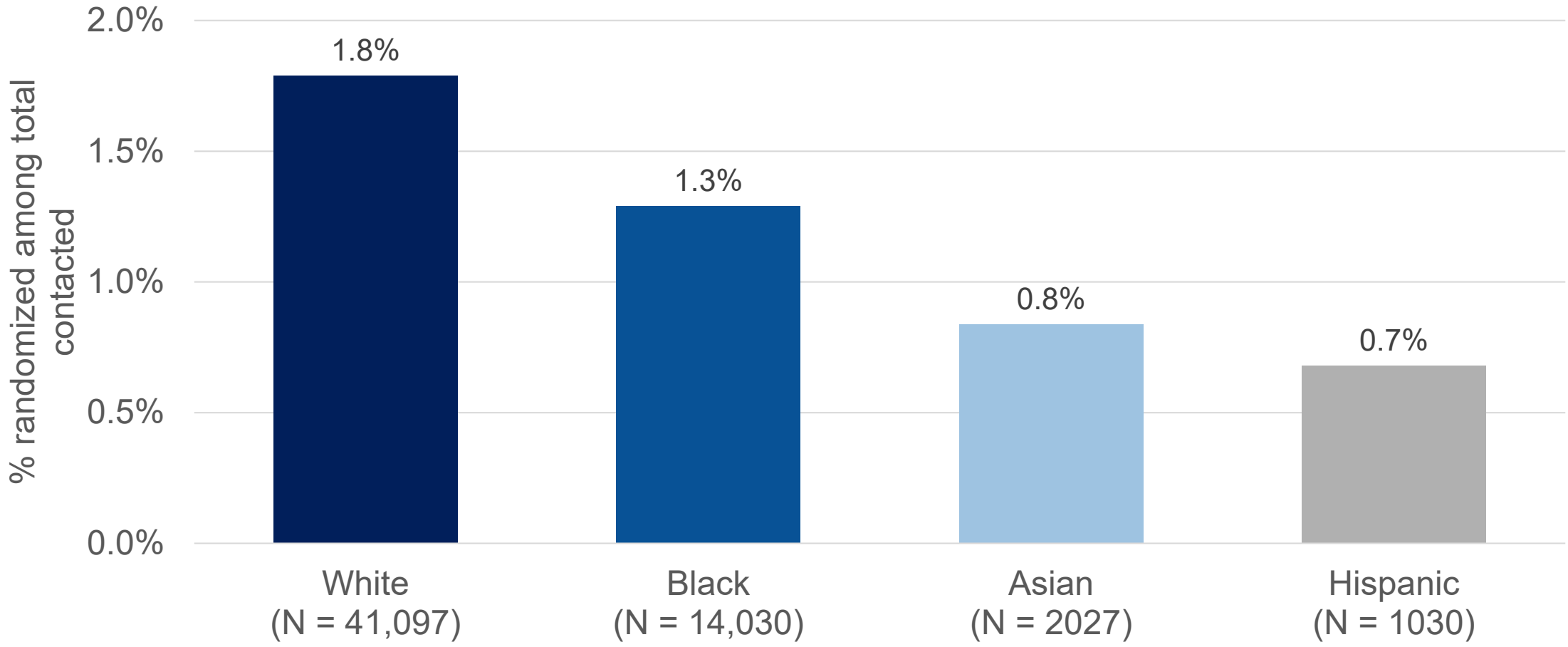


Proportion of eligible patients randomized

P < 0.001 for all comparisons vs. White



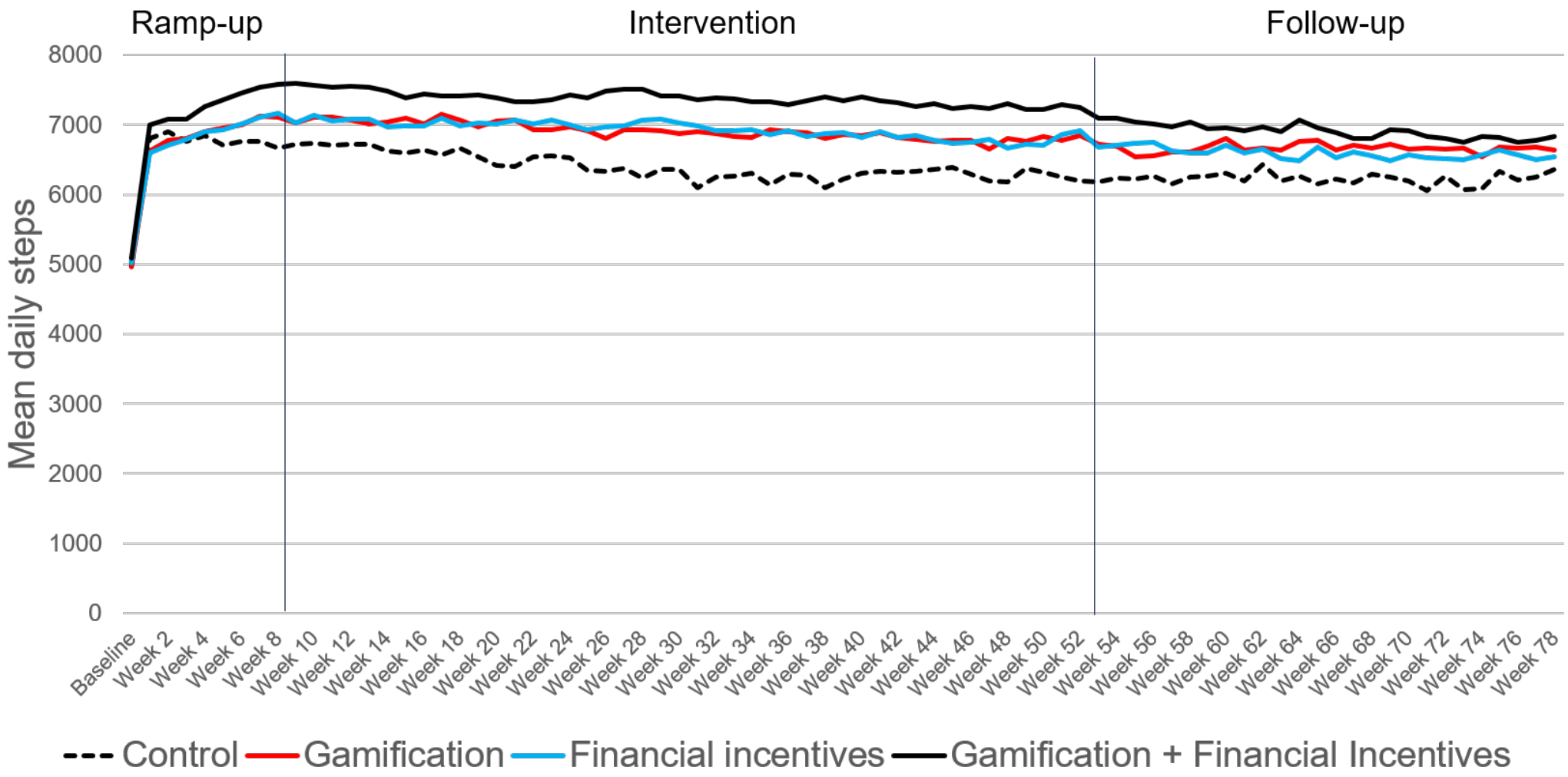
What did we do?

- Stopped recruiting White participants
- Added outreach by text message
- Ultimately enrolled a population representative of the UPHS population

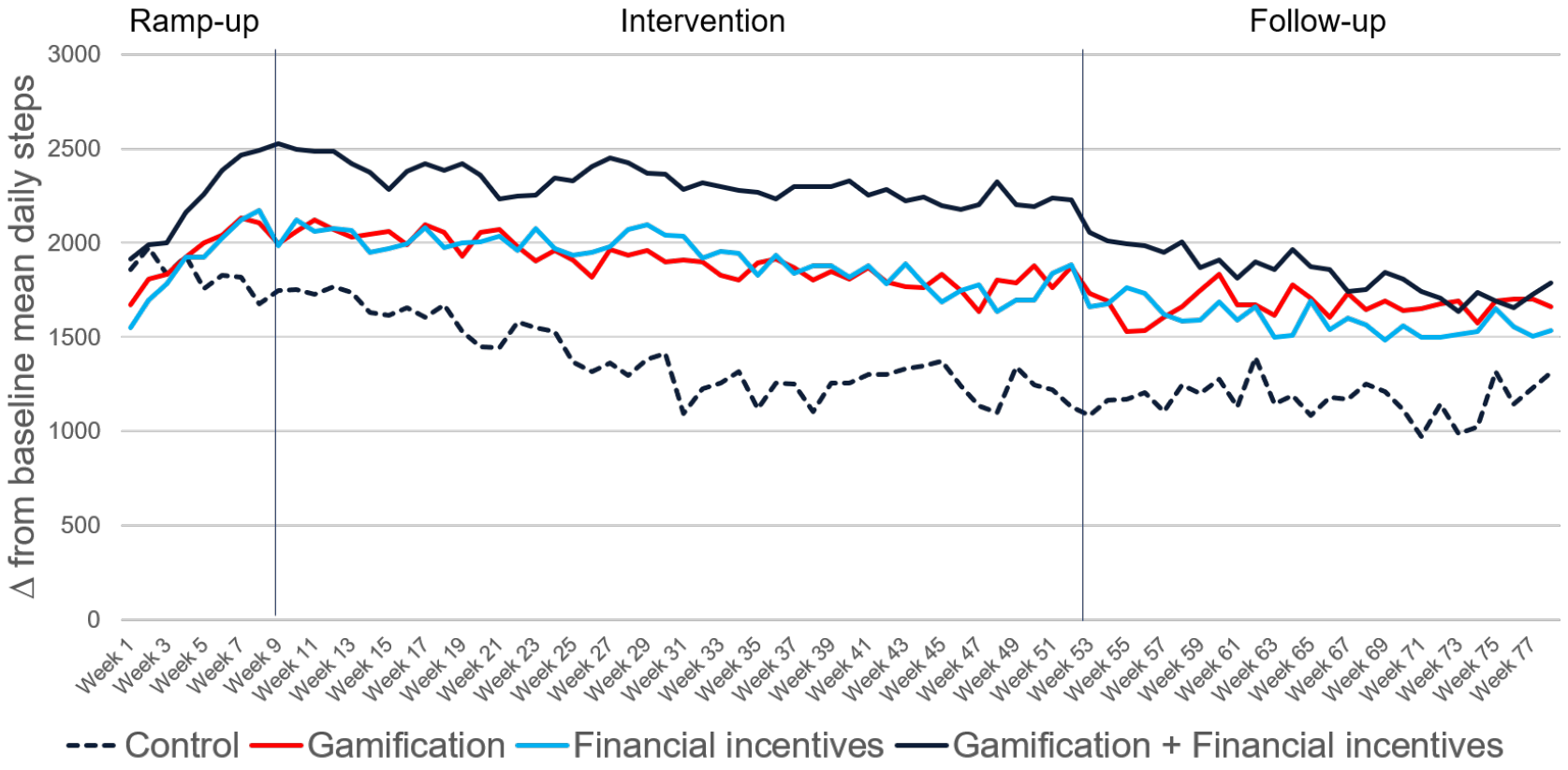
Lessons

- Direct-to-patient recruitment avoids biases related to who physicians invite to clinical trials, but *may introduce* biases related to who trusts researchers enough to join a study
- Ongoing work from our group is trying to understand how we can adjust messaging to enroll more representative populations
  - Email vs. text message
  - Message from study team vs. care team
  - Financial incentives to enroll

Daily steps over time



Change from baseline daily steps



Main intervention period

Control: +1418

from baseline

Gamification +1954

from baseline (+538 over control)*

$ Incentives: +1915

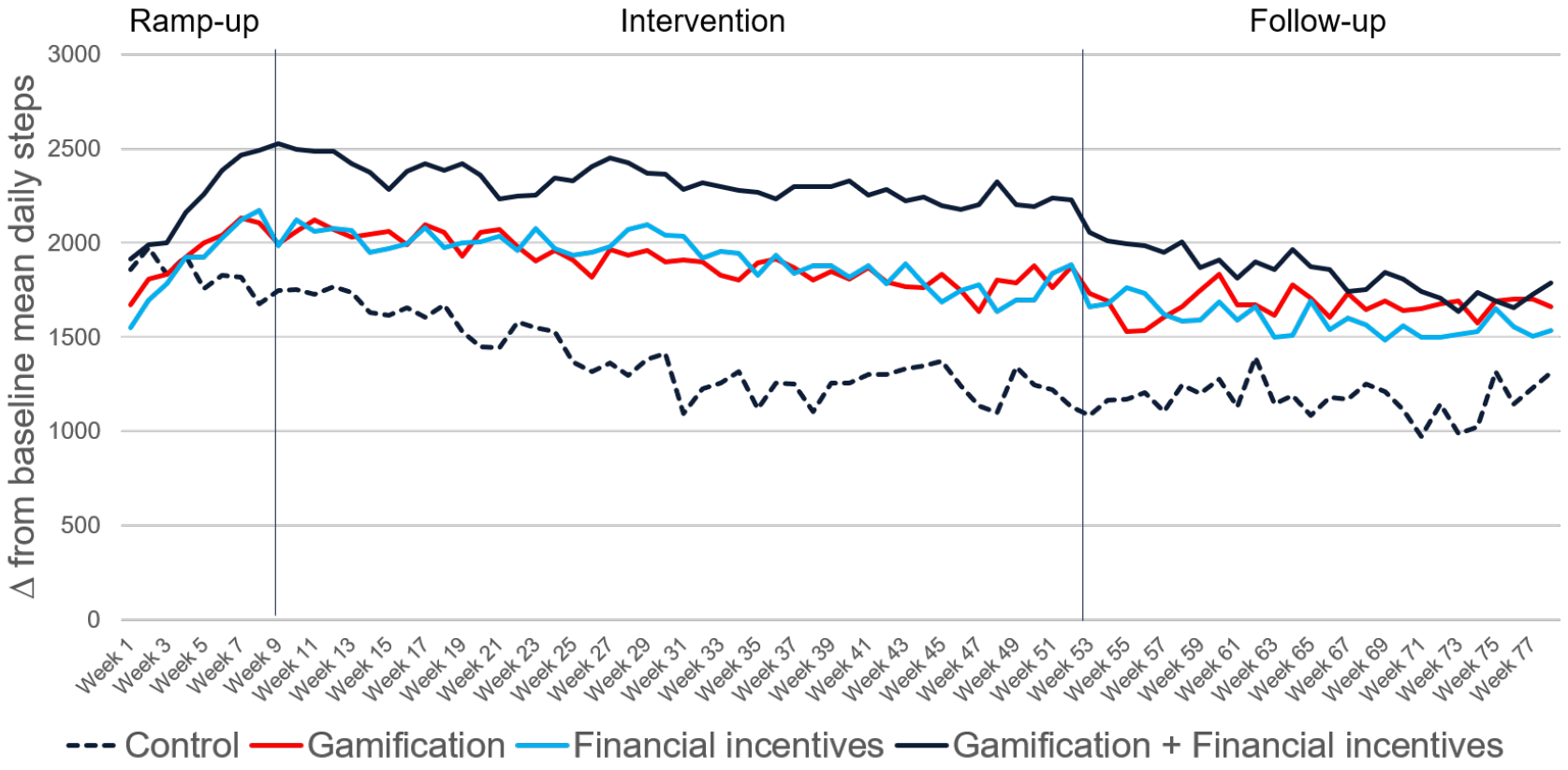
from baseline (+492 over control)*

Combination: +2297

from baseline (+868 over control)*

*, $p < 0.017$ versus control

Change from baseline daily steps



Follow-up period

Control: +1245
from baseline

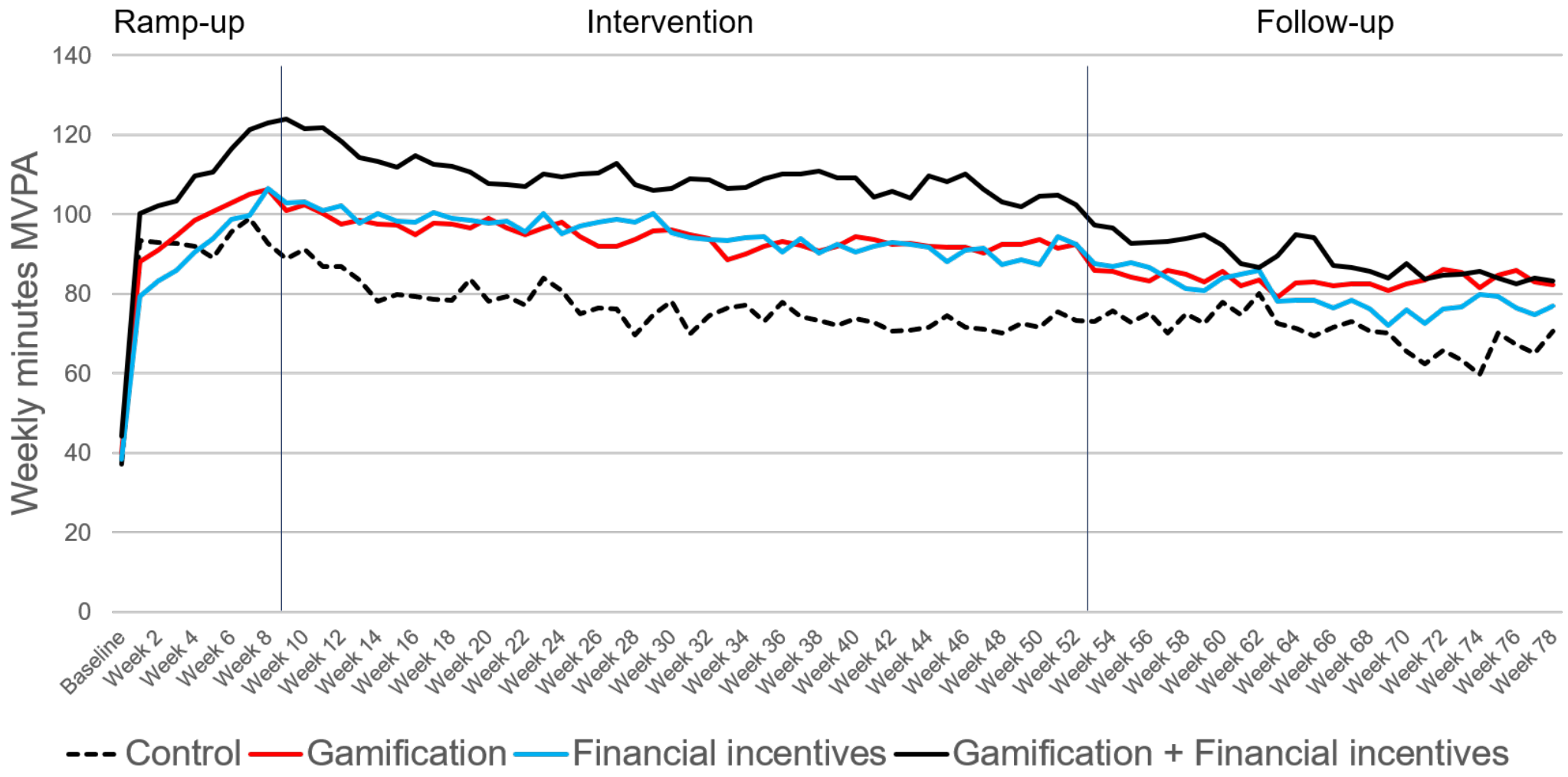
Gamification +1708
from baseline (+460 over control)

$ Incentives: +1576
from baseline (+328 over control)

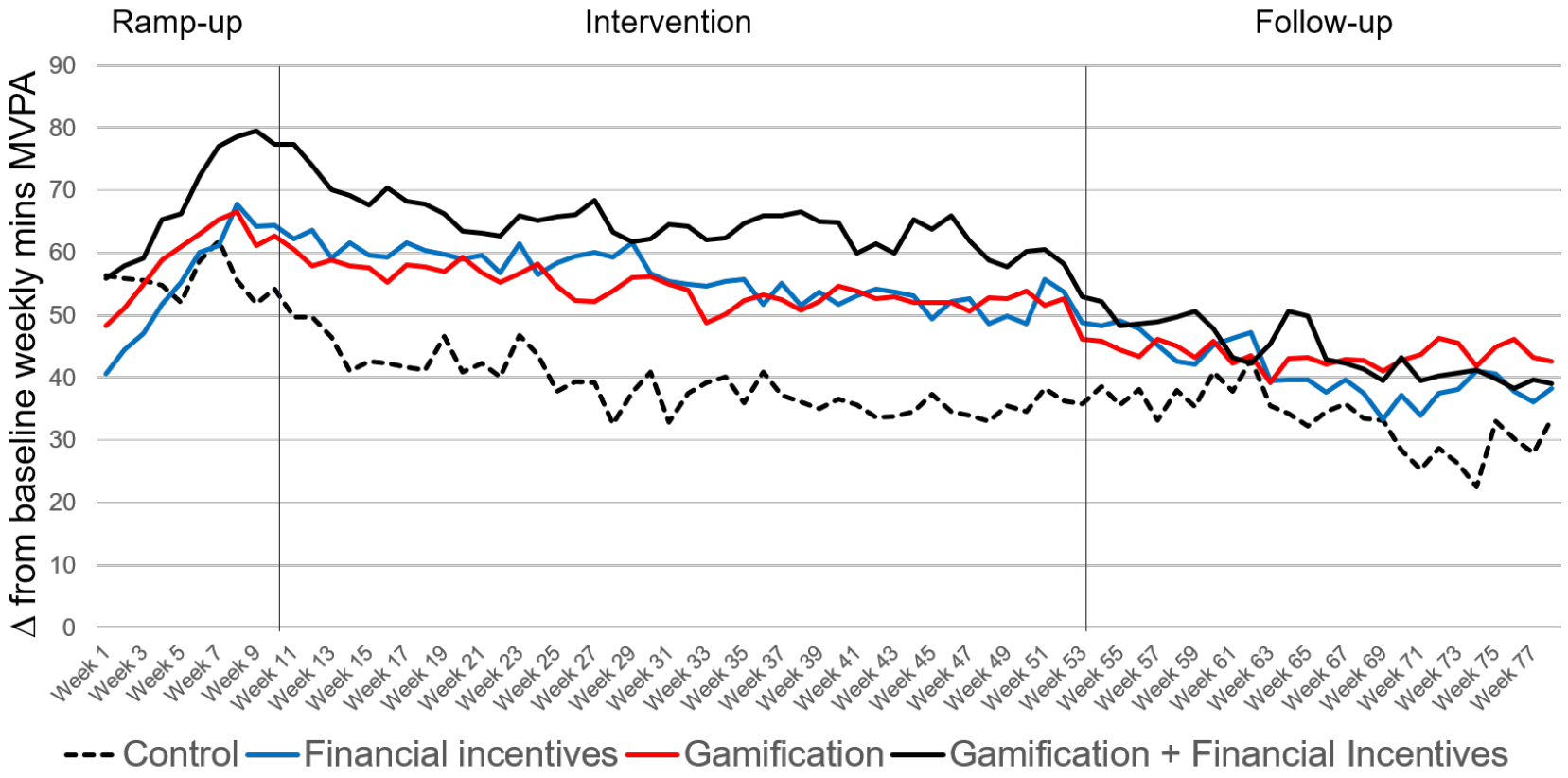
Combination: +1831
from baseline (+576 over control)*

*, $p < 0.017$ versus control

Weekly minutes MVPA over time



Change from baseline weekly minutes MVPA



Main intervention period

Control: +40

from baseline

Gamification +55

from baseline (+15 over control)

$ Incentives: +57

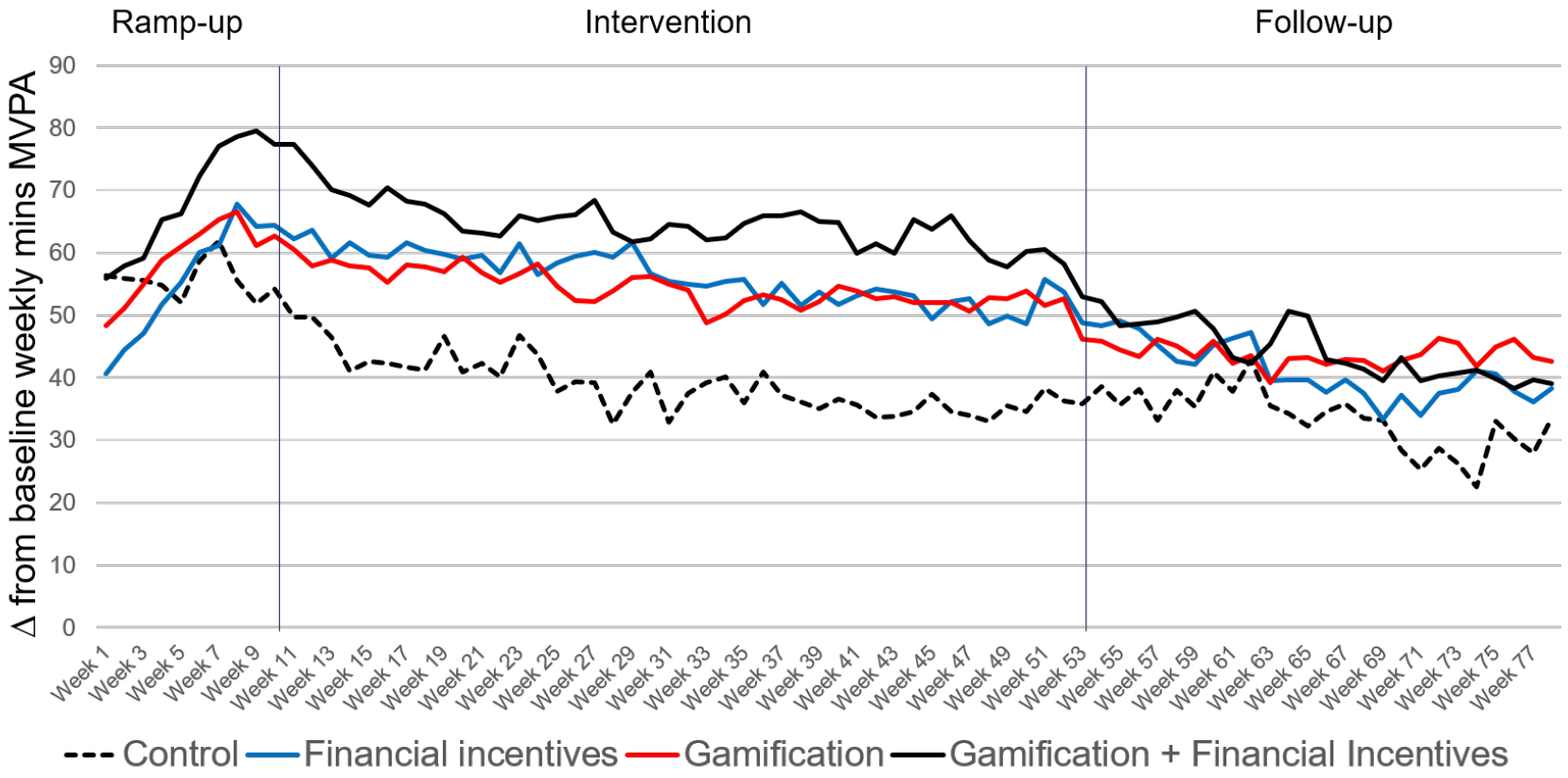
from baseline (+17 over control)

Combination: +65

from baseline (+26 over control)*

*, $p < 0.017$ versus control

Change from baseline weekly minutes MVPA



Follow-up period

Control: +37

from baseline

Gamification +51

from baseline (+11 over control)

$ Incentives: +51

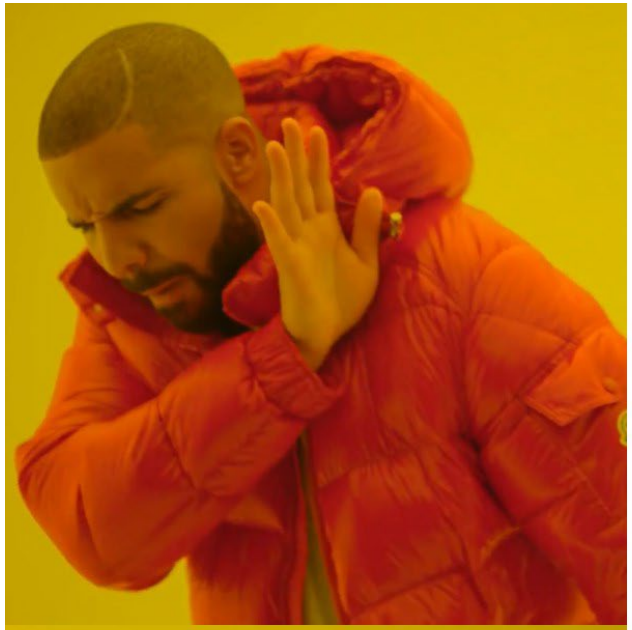
from baseline (+8 over control)

Combination: +58

from baseline (+13 over control)

*, $p < 0.017$ versus control

I	B	Adults should engage in at least 150 minutes per week of accumulated moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity (or an equivalent combination of moderate and vigorous activity) to reduce ASCVD risk
IIb	C	Decreasing sedentary behavior in adults may be reasonable to reduce ASCVD risk

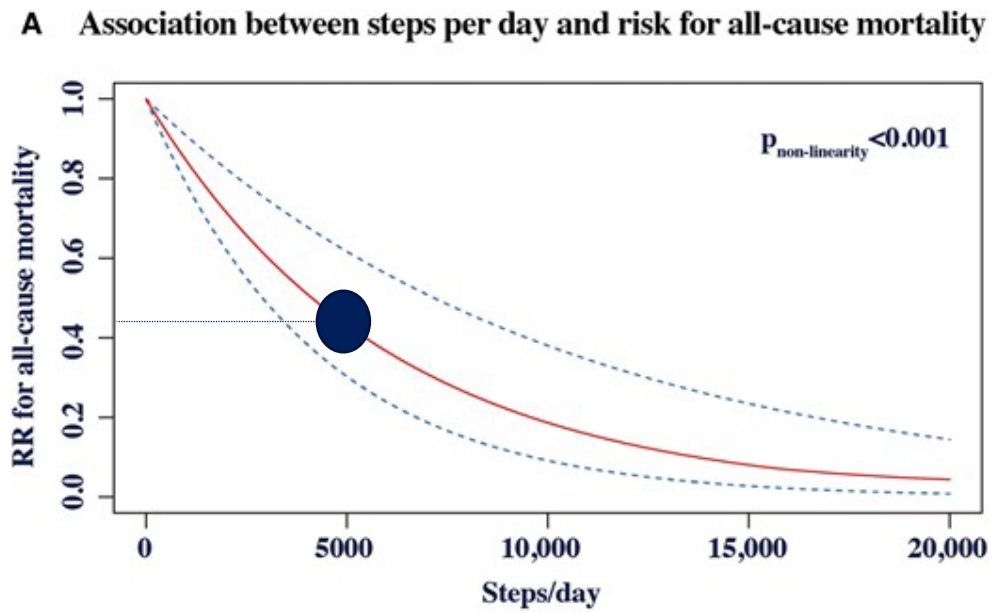


I	B	Adults should engage in at least 150 minutes per week of accumulated moderate-intensity or 75 minutes per week of vigorous-intensity aerobic physical activity (or an equivalent combination of moderate and vigorous activity) to reduce ASCVD risk
IIb	C	Decreasing sedentary behavior in adults may be reasonable to reduce ASCVD risk

	A	Interventions incorporating behaviorally-designed gamification or financial incentives are useful for helping adults increase physical activity

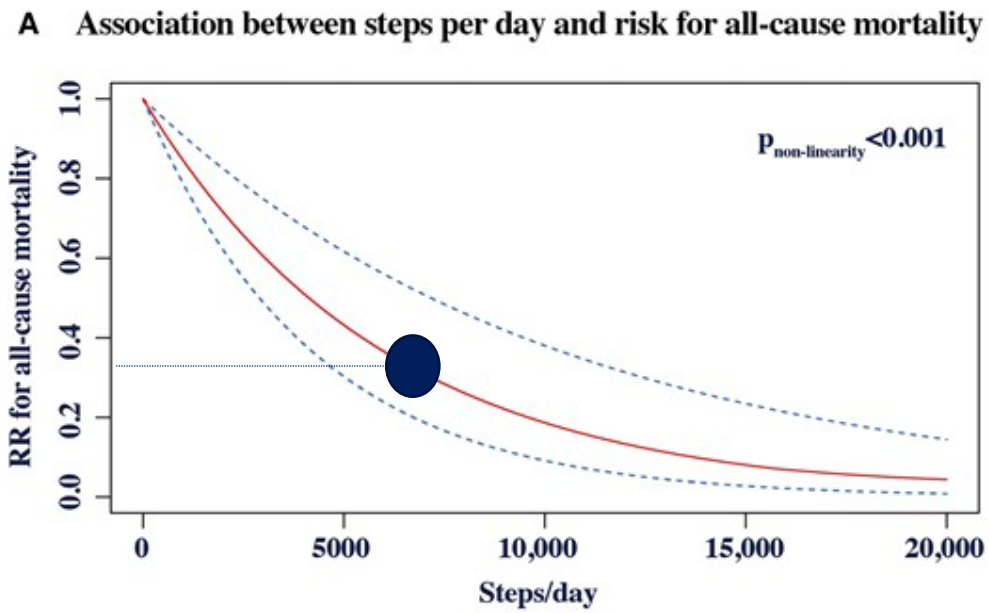
Implications

- In observational studies, there is an inverse association between steps per day and outcomes (mortality, CV events)



Implications

- In observational studies, there is an inverse association between steps per day and outcomes (mortality, CV events)
- From baseline 5000 steps per day:
  - 1700-step increase (gamification vs. baseline) → ~1.2 years longer life expectancy
  - 500-step increase (gamification vs. control) → ~ 0.4 years longer life expectancy



Implications

- Gamification was as effective as financial incentives but is much more scalable.
- Cost to deliver gamification intervention is ~ $450, and could be much lower at scale
  - $150 for Fitbit
  - $100 for technology platform
  - $200 for staff time
- Financial incentives add ~ $400 with no incremental benefit
- Cost-effectiveness analyses pending

Lessons

- Understanding determinants of behavior change help design effective gamification interventions
- Gamification is scalable – drives behavior change without skilled clinical personnel, essentially for the cost of a Fitbit
- Rigorous evaluation of behavior change interventions is possible with the Way to Health platform and necessary if they are to be incorporated into clinical care
- Direct-to-patient recruiting introduces biases that must be considered

Next step

- What is the effect of increasing physical activity on clinical outcomes?
  - For stakeholders to pay for an intervention like this, large scale clinical trials are needed to show improvements in patient-centered outcomes or clinical events

	A	Interventions incorporating behaviorally-designed gamification or financial incentives are useful for helping adults increase physical activity ***and reduce ASCVD risk***

Thank you!

Patients and families

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