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TRANSFORMING DEMENTIA CARE

Decision Architecture Randomization Trials: Extremely Low-Cost Trials with Preservation of Clinician and Patient Choice

James Flory, MD, MSCE
Assistant Attending Physician, Endocrinology Service, Memorial Sloan Kettering Cancer Center

Housekeeping

- All participants will be muted
- Enter **all questions** in the Zoom **Q&A/chat box** and send to Everyone
- Moderator will review questions from chat box and ask them at the end
- Want to continue the discussion? Associated podcast released about 2 weeks after Grand Rounds
- Visit impactcollaboratory.org
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@IMPACTcollab1 https://www.linkedin.com/company/65346172

No Conflicts of Interest

Learning Objectives

Upon completion of this presentation, you should be able to:

- Define ‘nudges’, ‘decision architecture’, and ‘A/B testing’
- Describe a decision architecture randomization trial (DART)
- Understand how DART relates to other pragmatic clinical trial designs

Randomized Trials are Challenging to Conduct

- Average cost estimated at > $10,000 per patient
- < 30% of phase 3 trials meet accrual goals
- Take up providers' and patients' limited time
- Disrupts routine care
  - Especially if patient prefers treatment A and is randomized to treatment B

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Vickers AJ. Clinical trials in crisis: Four simple methodologic fixes. Clinical trials (London, England).
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Dilts DM, Sandler AB, Baker M, et al. J Clin Oncol. 2006/10/01 2006;24(28):4553-4557.
Speich B, von Niederhäusern B, Schur N, et al. Journal of Clinical Epidemiology. 2018/04/01/ 2018;96:1-11.
Lee SJC, et al. Conceptual Model for Accrual to Cancer Clinical Trials. J Clin Oncol. 2019 Aug 10;37(23):1993-1996.

Pragmatic Designs Help But Are Still Big Undertakings

- Focus on standard of care treatments delivered through normal processes
- Use of routinely collected data
- Cluster randomization

- But, we still need far more high-quality evidence than we can get

https://www.pcori.org/research-results/2015/comparing-two-aspirin-doses-prevent-heart-attacks-and-strokes-people-living-heart-disease-adaptable-study

Bynum JPW et al. J Am Geriatr Soc. 2020 Jul;68 Suppl 2(Suppl 2):S49-S54
Brody A, Durga A, Ford A, Lin SY. Innov Aging. 2022 Dec 20;6(Suppl 1):172.

A/B Testing As a Pragmatic Trial Design

News organizations often randomize to two different versions of a headline

"SOUL-SEARCHING IN BALTIMORE, A YEAR AFTER FREDDIE GRAY'S DEATH"

Vs.

"BALTIMORE AFTER FREDDIE GRAY: THE 'MIND-SET HAS CHANGED'"

https://www.nytimes.com/2016/06/13/insider/which-headlines-attract-most-readers.html

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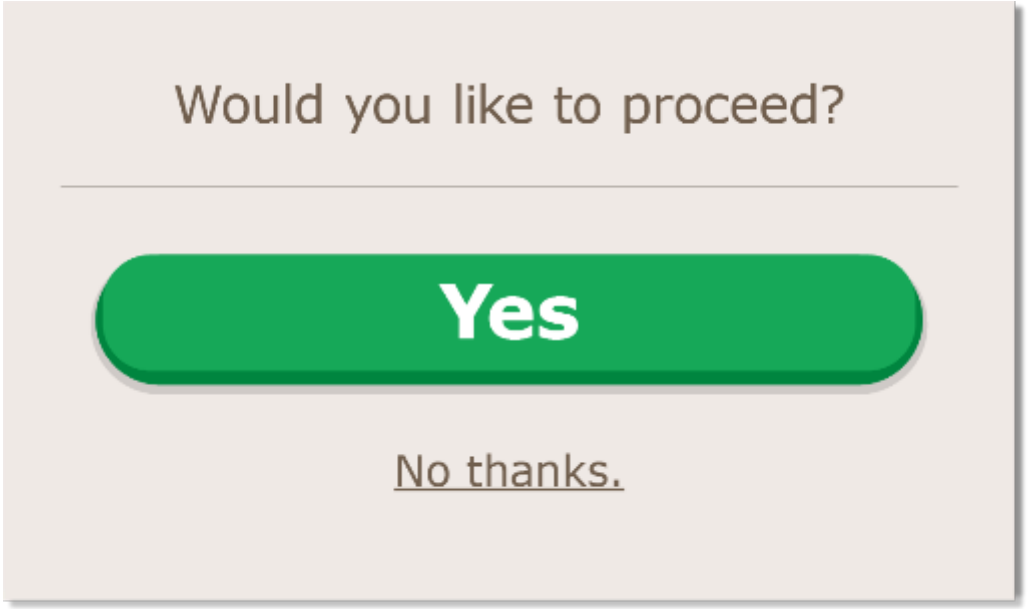
Readership 17 x greater

https://www.nytimes.com/2016/06/13/insider/which-headlines-attract-most-readers.html

Often, A/B Testing is Used to Study Nudges

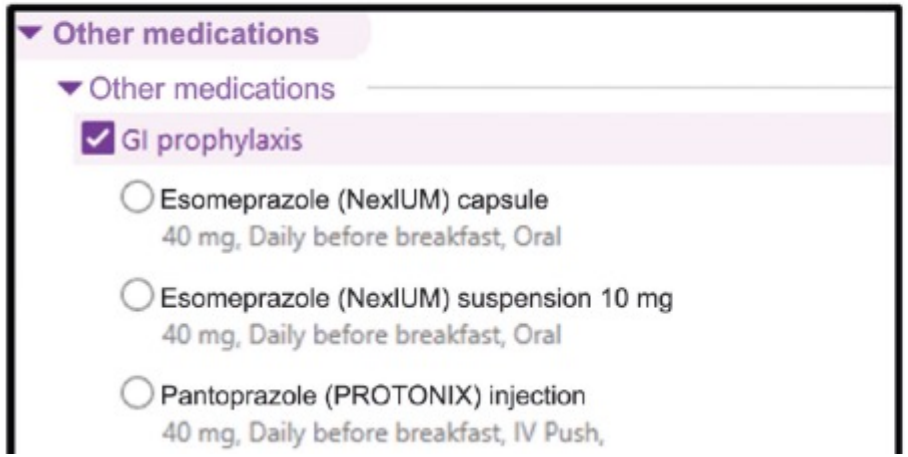
- Nudges make you more likely to do something but don't force you to do it
  - A headline that makes you want to read an article
  - Making one option the 'default'



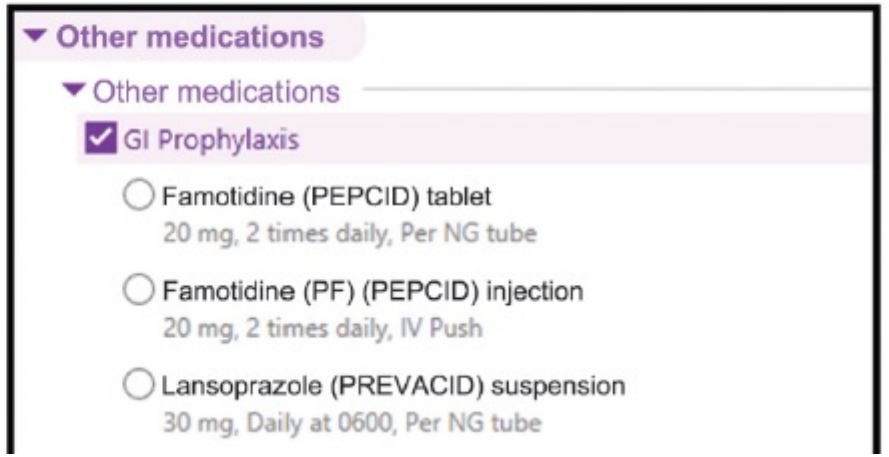
Horwitz LI, Kuznetsova M, Jones SA. Creating a learning health system through rapid-cycle,randomized testing. N Engl J Med 2019;381:1175–9.

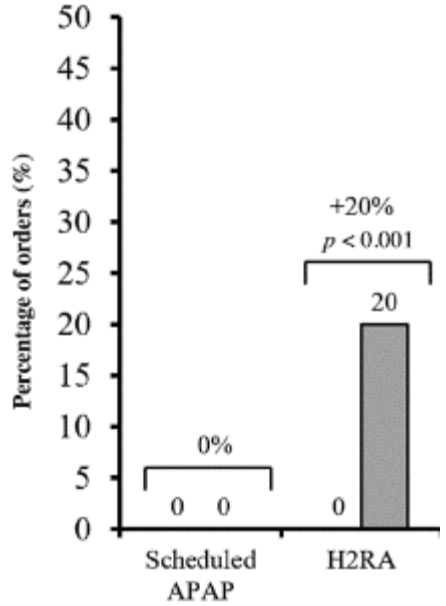
Nudges Can Change Prescribing Decisions

Before
(PPI only option for stress ulcer prophylaxis)



After
(H2RA and PPI are options for stress ulcer prophylaxis)





Adding H2 blockers to an order set increased use by 20%

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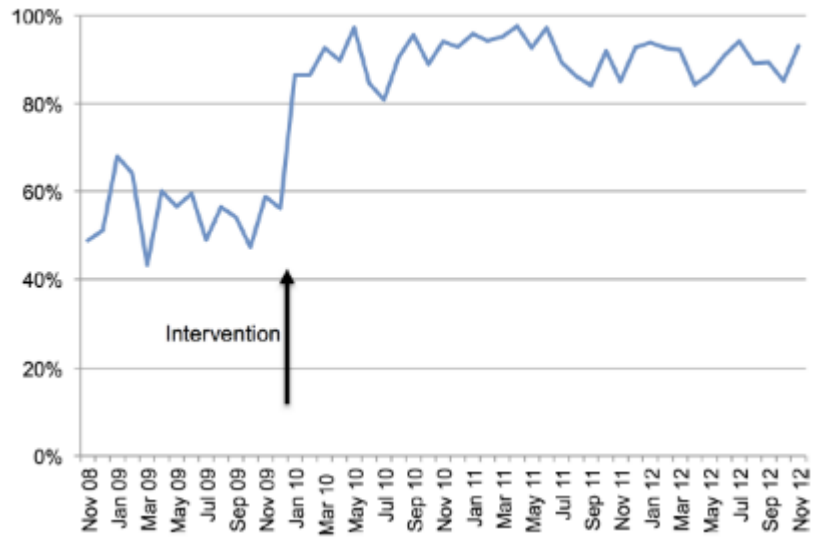
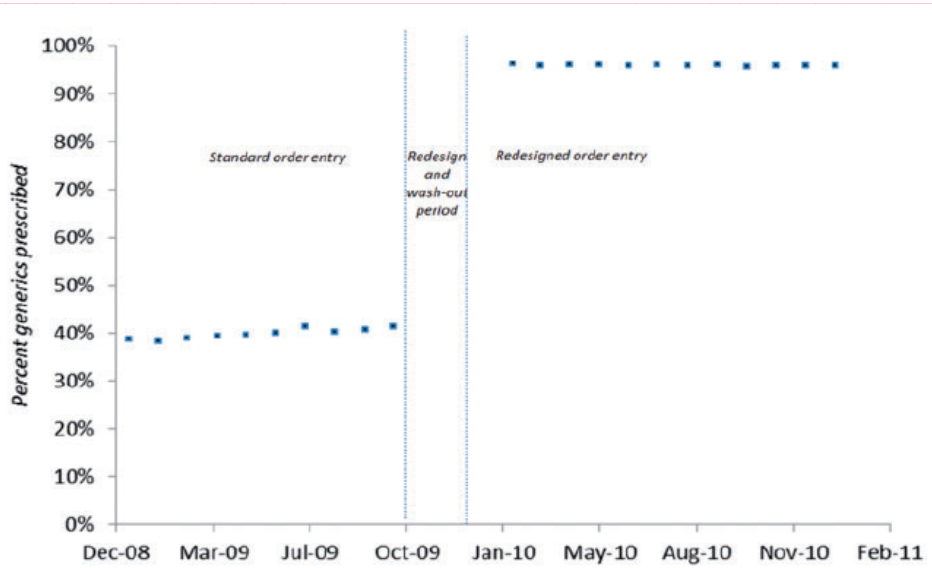
Malhotra S et al. J Am Med Inform Assoc. 2016 Sep;23(5):891-8.
Raban MZ et al. J Am Med Inform Assoc. 2023 Jun 20;30(7):1313-1322.
Bourdeaux CP et al. BMJ Qual Saf 2014; 23 (5): 382–8.
Muniga ET, Walroth TA, Washburn NC. Appl Clin Inform. 2020 Jan;11(1):182-189.

Nudges Can Change Prescribing Decisions



Adding chlorhexidine mouthwash as default to an order set increased use by 35%



Making generic prescribing the default in order entry system increased use of generics by 56%

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Muniga ET, Walroth TA, Washburn NC. Appl Clin Inform. 2020 Jan;11(1):182-189.

Order Sets, Decision Architecture, and Nudges

Vs.

Nutritional Status

Eating Clear

- (•) Eating
- ( ) Fasting NPO
- ( ) Tube Feeding Continuous

Insulin Dose

Resistant - Use for obese body type, taking steroids Clear

- ( ) Sensitive - Use for Type 1 Diabetes, lean body type, elderly, renal insufficiency, pancreatectomy
- ( ) Average - Use for average or overweight body type
- (•) Resistant - Use for obese body type, taking steroids
- ( ) Custom

Long-Acting Insulin

Insulin detemir (Levemir) Clear

- ( ) None
- (•) Insulin detemir (Levemir)
- ( ) Insulin glargine (Lantus)

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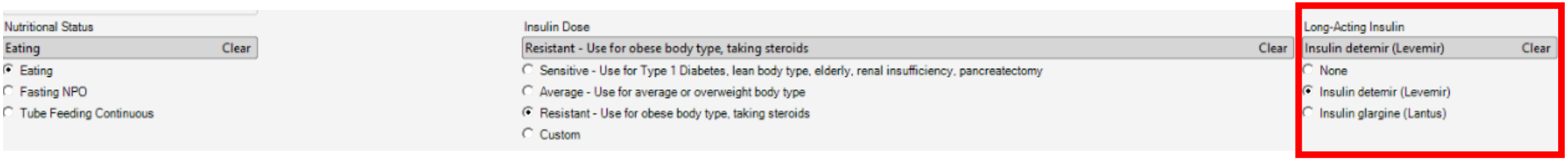
Johnson EJ. The elements of choice: why the way we decide matters. New York: Riverhead Books, an imprint of Penguin Random House LLC, 2021: 390.

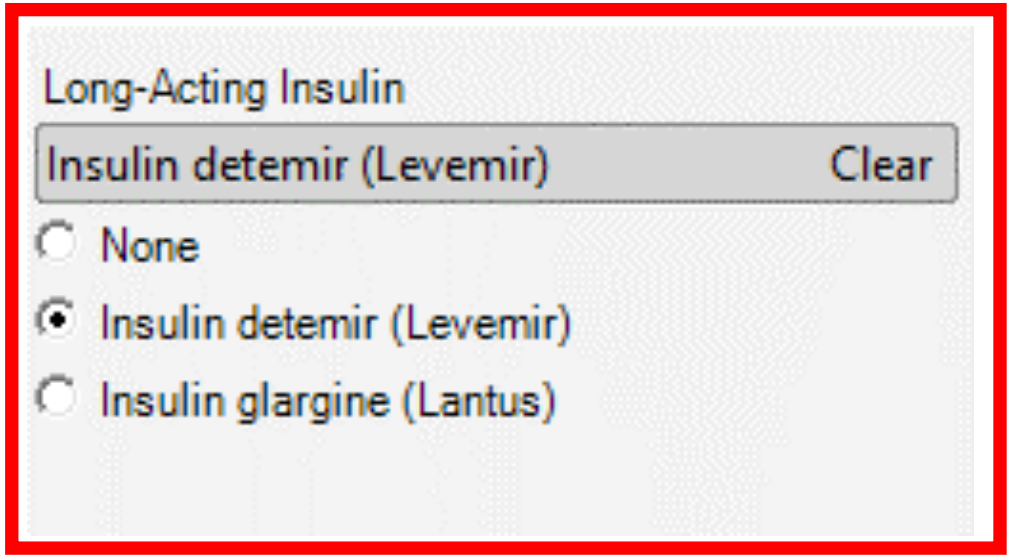
Thaler RH, Sunstein CR. Nudge: the final edition. New Haven: Yale University Press, 2021: 366.

Order Sets, Decision Architecture, and Nudges



Example of a Nudge

- There are two kinds of long-acting insulin at our hospital
- The one that is pre-checked may be more likely to be given



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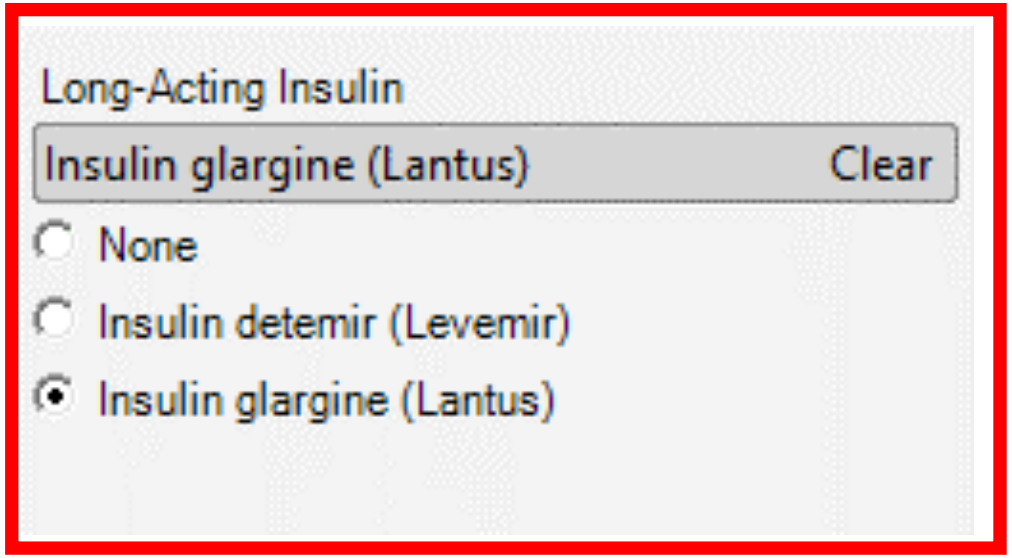
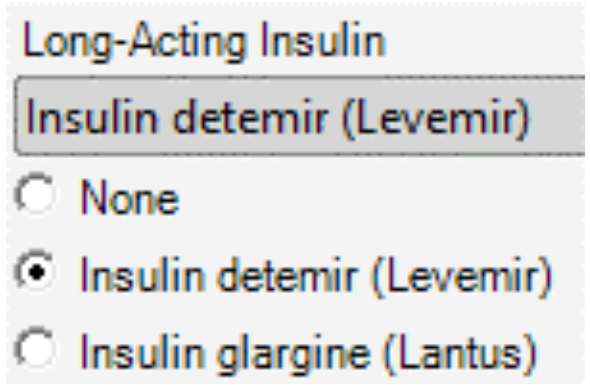


Suppose we changed this nudge at random

Random Assignment to Orderset

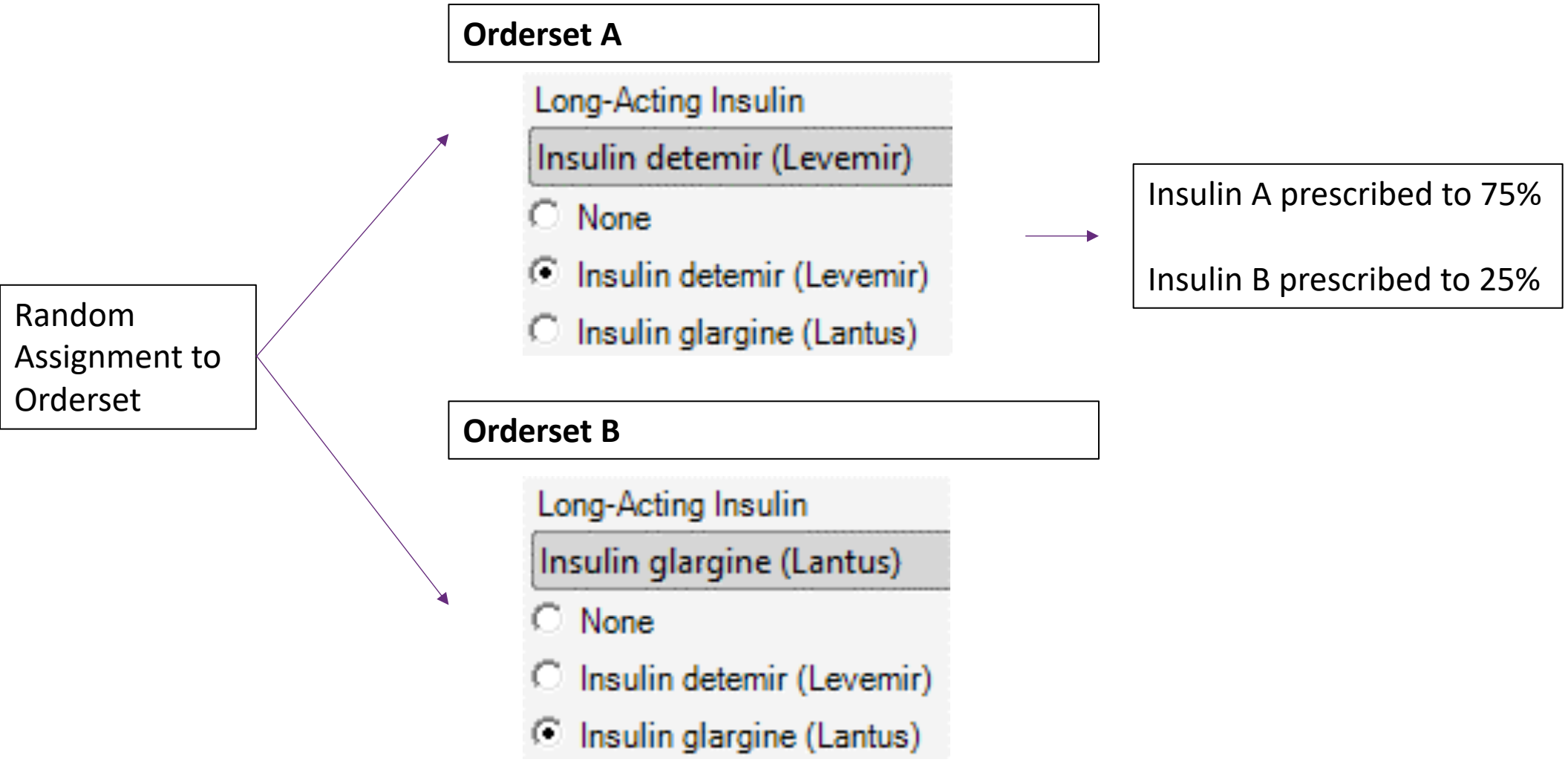
Orderset A



Insulin A prescribed to 75%

Insulin B prescribed to 25%

Suppose we changed this nudge at random



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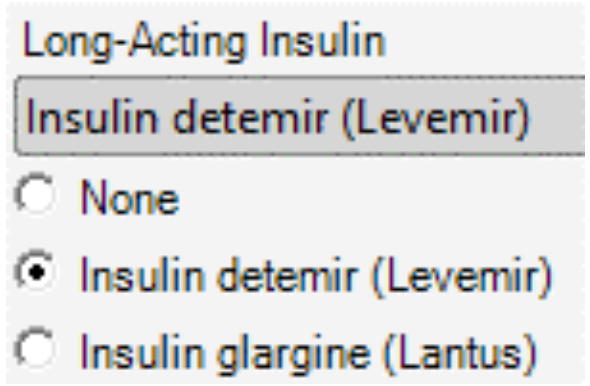

Insulin A prescribed to 75%

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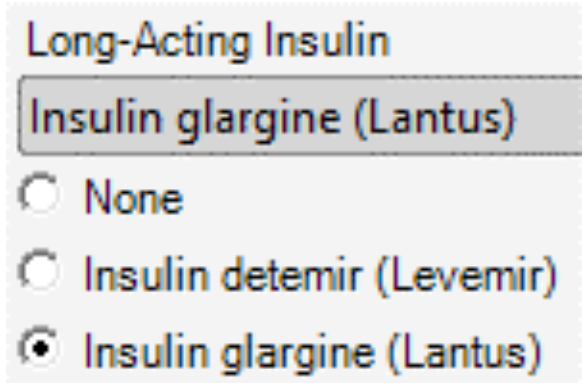
Orderset B



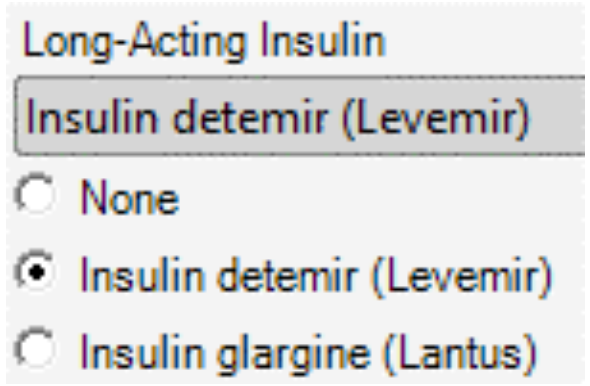
Insulin A prescribed to 25%

Insulin B prescribed to 75%

Suppose we changed this nudge at random

Random Assignment to Orderset

Orderset A



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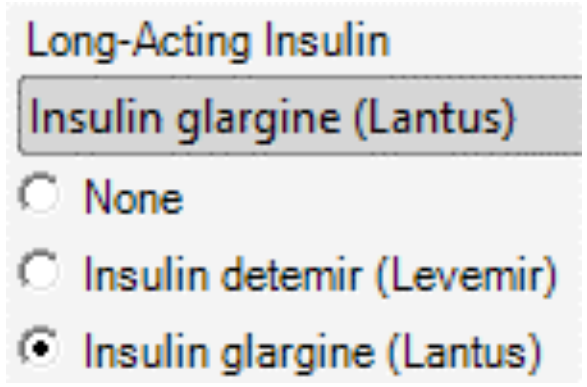


Insulin A prescribed to 25%

Insulin B prescribed to 75%

50% absolute difference between treatment arms

Ethics and Nudges

Routine Care

Patient/Provider Prefer A	→	Patient Receives A
Patient/Provider Have No Preference	→	Patient Receives A or B (based on arbitrary factors)
Patient/Provider Prefers B	→	Patient Receives B

Traditional Randomized Trial

Randomized to A

Patient/Provider Prefer A	→	Patient Receives A
Patient/Provider Have No Preference	→	Patient Receives A
Patient/Provider Prefers B	→	**Patient Receives A**

‘Nudge’ Trial

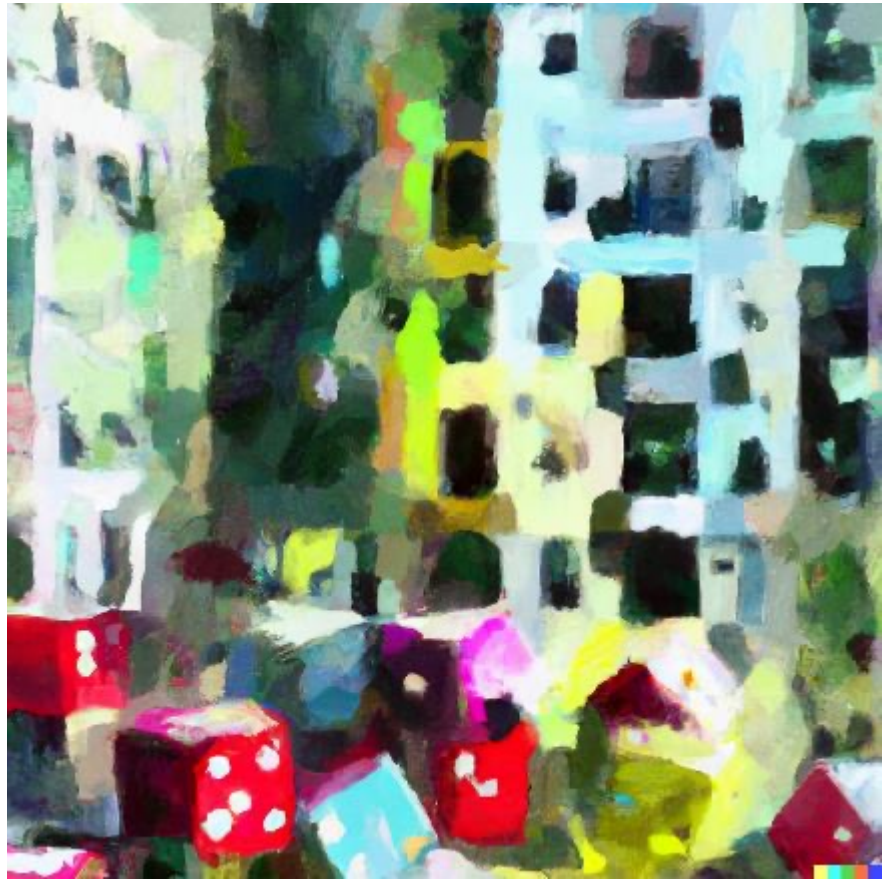
Nudged Towards A

Patient/Provider Prefer A	→	Patient Receives A
Patient/Provider Have No Preference	→	Patient Receives A
Patient/Provider Prefers B	→	**Patient Receives B**

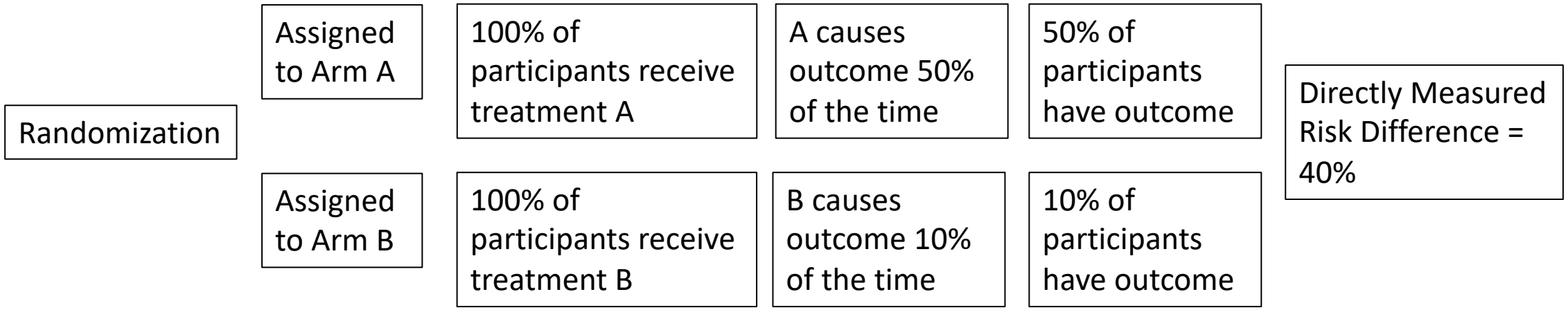
Kim SY, Kimmelman J. Practical steps to identifying the research risk of pragmatic trials. Clin Trials. 2022 Apr;19(2):211-216.

Decision Architecture Randomization Trial

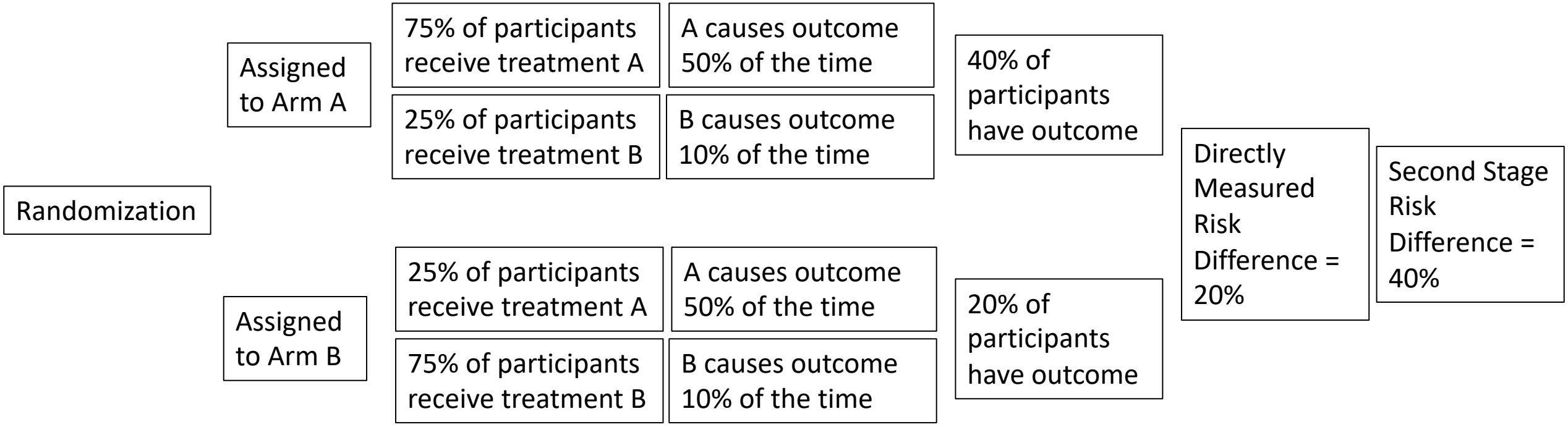
- **Decision architecture**: design choices (e.g., in electronic health records) that affect decision-making
- Decision architecture used to deliver a **nudge**: non-coercive effect making a certain decision more likely
- Use of nudges enables **A/B testing**: unobtrusive, highly scalable randomized trials



Analysis of Traditional RCT



Analysis of a DART



Relative Pros and Cons of DART Design

Traditional Randomized Trial	**DART**
Changes process of care	**Imperceptibly integrated into usual care**
Patient & clinician must accept randomly assigned treatment	**Patient & clinician freely choose treatment**
High cost per additional patient accrued	**Potentially no cost per additional patient accrued**
Smaller sample size	Larger sample size

Other Limitations of DART

- Interventions must all be in routine use
- Requires an appropriate nudge that can be randomized
- Assumes baseline characteristics and outcomes can be found in routinely collected data
- Individual patient informed consent likely to be impractical

DART in the Real World

The Great Wave off Kanagawa, Hokusai

DART in the Real World

PCORI Methodology Contract

- Aim 1: Ethics and stakeholder acceptability
- Aim 2: Statistical and technical feasibility
- Aim 3: Pilot DART study

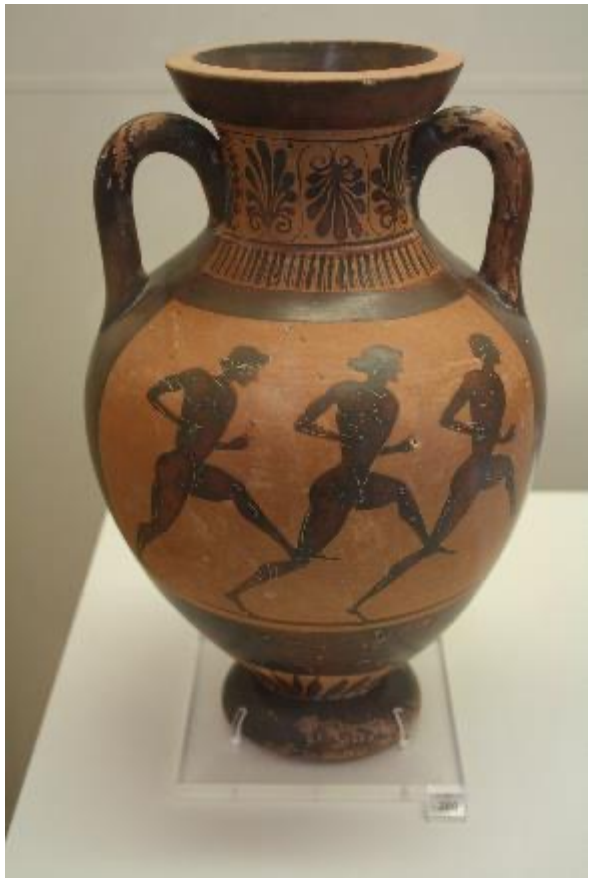
Flory J, Ancker JS, Kim SYH, Kuperman G, Vickers A. Decision architecture randomisation: extremely efficient clinical trials that preserve clinician and patient choice? BMJ Evid Based Med. 2023 Jul 21:bmjebm-2023-112386. doi: 10.1136/bmjebm-2023-112386. Epub ahead of print. PMID: 37479243.

Aim 1: Ethics and Acceptability

- Many DARTs may meet criteria for waiver of traditional informed consent
  - Minimal risk
  - Impracticability with traditional consent
- The scalability of DART should be considered

Moving slowly, not breaking anything

- Facebook used A/B testing to randomize **689,003 people** to positive versus negative emotional content in their feeds
- LinkedIn used A/B testing on over **20 million people** to compare the effectiveness of ‘strong’ and ‘weak’ ties for finding employment
- Both projects were published in high-impact scientific journals
- Both projects attracted concern over research oversight and ethics



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Verma IM. Editorial expression of concern. *Proceedings of the National Academy of Sciences of the United States of America*. 2014;111(29):10779-10779.
Kramer AD, Guillory JE, Hancock JT. Proc Natl Acad Sci U S A. 2014 Jun 17;111(24):8788-90.
https://www.nytimes.com/2022/09/24/business/linkedin-social-experiments.html
Rajkumar K, et al. A causal test of the strength of weak ties. Science. 2022 Sep 16;377(6612):1304-1310.

Stakeholder Engagement

Co-Investigators
- 5 academic researchers
- 3 patient advocates

Diabetes Team
Memorial Sloan Kettering
- 2 MD/DO clinicians
- 2 APP clinicians
- 1 Registered Dietician
- 2 Registered Nurses/Clinical Diabetes Educators

Stakeholder Advisory Board
Coordinated through Vanderbilt and STAR Clinical Research Network
- 3 patient advocates
- 2 clinicians (1 informatician)

Patient and Family Advisory Council for Quality, Memorial Sloan Kettering

Qualitative Research
- 100 members of general public
- 25 institutional review board members
- 25 clinicians

Stakeholder Engagement: Next Steps

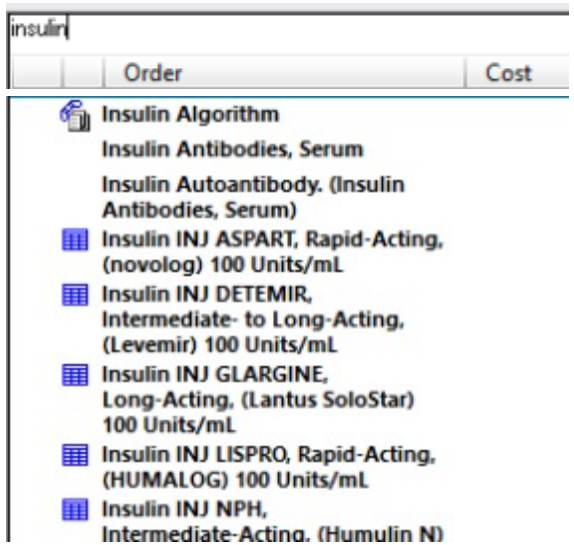
- Moving forward with deliberative democratic sessions with 150 participants
  - Also includes pre-post survey of each participant
- Goals
  - Identify stakeholder concerns about DART
  - Identify potential solutions
    - Including appropriate constraints on how/when DART is done

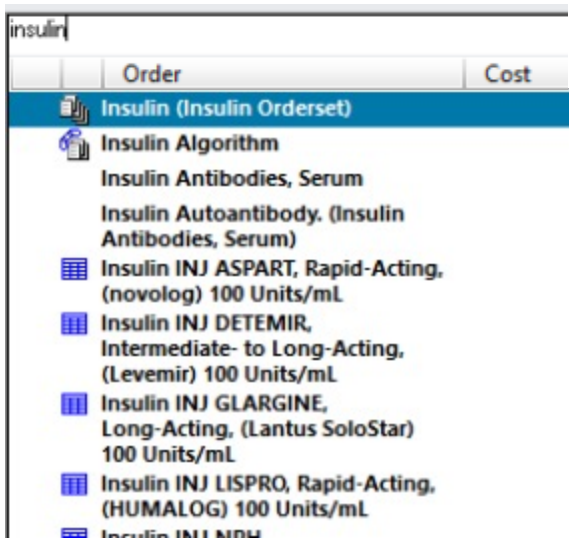
https://commons.wikimedia.org/wiki/File:Assen_Deliberation-Overleg2_Bert_Kiewiet.jpg

Aim 2: Technical Feasibility

Example: Two Insulin Dosing Paradigms

Sliding Scale Only	Fixed + Correction
Give insulin based just on blood sugar	Adds fixed dose before meals
Simpler	More complex
	Preferred by expert guidelines (but little evidence cited)





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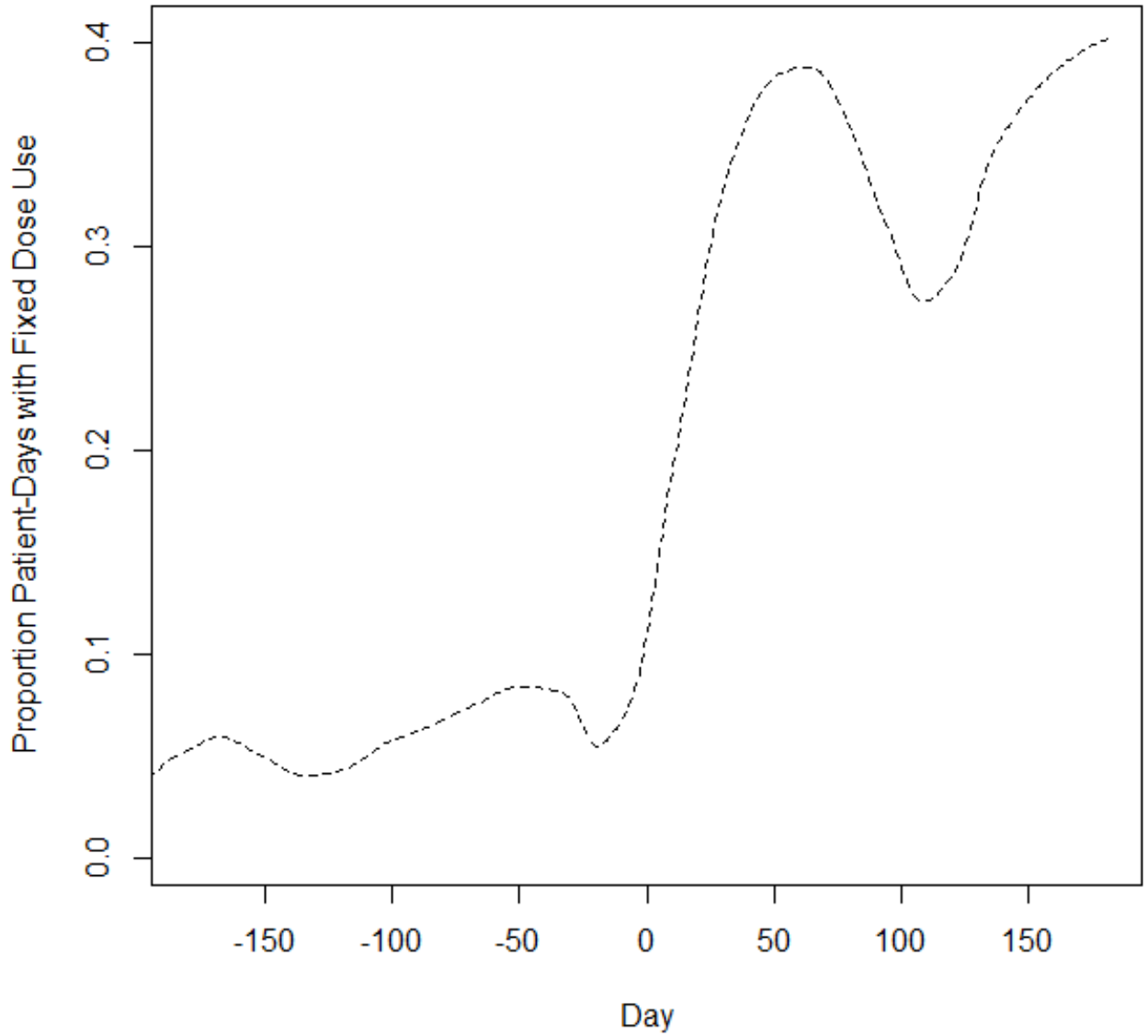
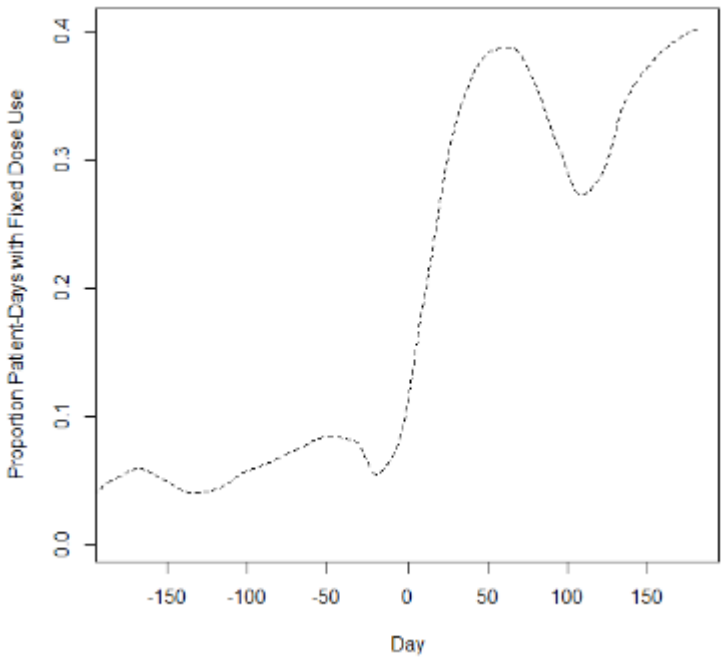
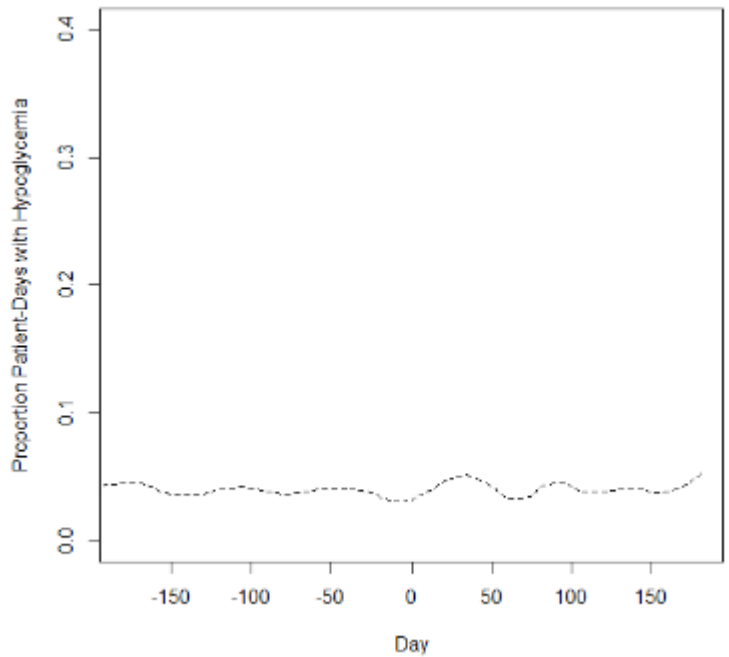
Nuha A. ElSayed, et al; on behalf of the American Diabetes Association, 16. Diabetes Care in the Hospital: *Standards of Care in Diabetes—2023*. *Diabetes Care* 1 January 2023; 46 (Supplement_1): S267–S278.


Proportion Patient-Days with Fixed Dose Use
0.0
0.1
0.2
0.3
0.4
-150
-100
-50
0
50
100
150
Day

Rate of Fixed-Dose Use



Rate of Hypoglycemia



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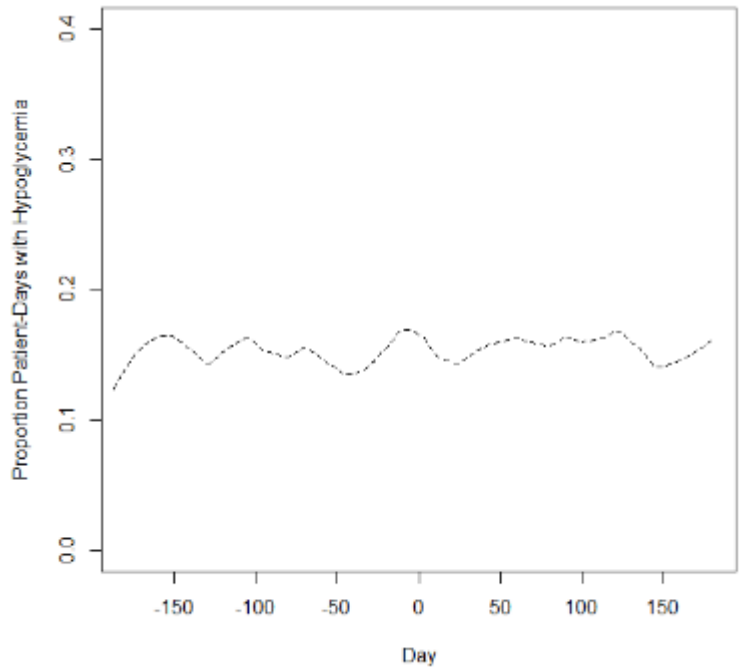
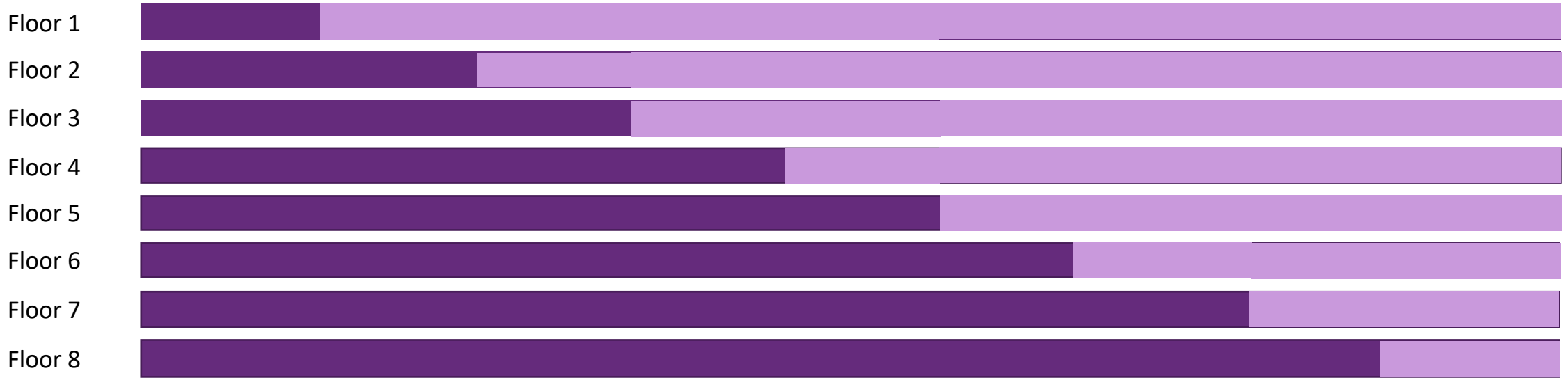


Feasibility: Preliminary Findings

- We can create appropriately strong nudges in our electronic health record
- Close partnership with informatics service is essential
- Randomized or pseudo-randomized deployment of nudges really is needed to draw firm conclusions

Feasibility: Next Steps

- Stepped wedge designs may to be the easiest way to implement DART in many cases
- We are developing approaches to individual patient or provider-level randomization



Aim 3: DARTs Under Development

- **Question:** Which is the better long-acting insulin for hospitalized cancer patients?
- **Nudge:** Default selection in an order set
- **Randomization:** Stepped wedge
- **Outcome:** Glucose control, length of stay

Aim 3: DARTs Under Development

- **Question:** Does tighter glycemic control reduce surgical site infections in colorectal surgery patients?
- **Nudge:** Default selection of correctional insulin in post-surgical order set
- **Randomization:** Individual at level of patient
- **Outcome:** Surgical site infection rate

Aim 3: DARTs Under Development

- **Question:** Does referral to a registered dietician improve outcomes in patients with newly diagnosed type 2 diabetes?
- **Nudge:** One-click option for nutrition service referral in new visit notes
- **Randomization:** Individual at level of provider
- **Outcome:** Glucose control, rate of antidiabetic medication use

Conclusions

- DART is a novel pragmatic trial design intended to:
  - Reduce risk and preserve patient choice
  - Bring the scalability and simplicity of A/B testing to comparative effectiveness research
  - Compare two (or more) standard of care interventions
- Implementation depends on the ability to deliver a randomized nudge (usually through an electronic health record) in a way that is
  - Reasonably strong
  - Not disruptive to care
  - Acceptable to stakeholders

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- Jun Mao
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- Clare Relton
- Jason Karlawish

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- Michele Levy

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Questions?