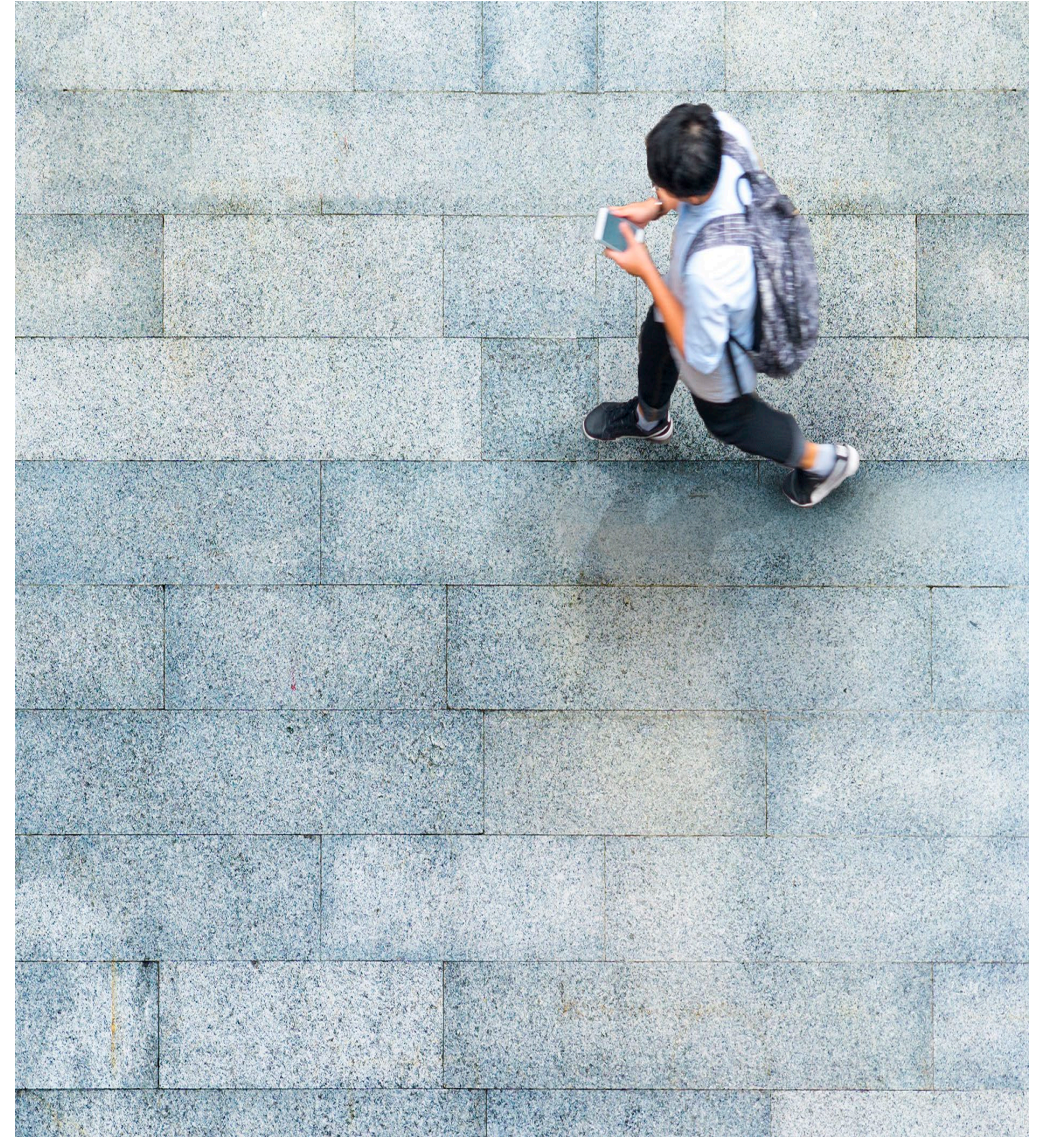# Personalized Patient Data and Behavioral Nudges to Improve Adherence to Chronic Cardiovascular Medications (The Nudge Study)

Grand Rounds, Rethinking Clinical Trials

11/17/2023

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Agenda

- Study introduction
- Initial findings from the UG3 Pilot
- Learning from the opt out consent process
- Findings from the UH3 trial
- Pharmacist-patient interactions
- Patient perspectives of the study
- Lessons learned

Introduction

- Medication non-adherence associated with poor health outcomes, high healthcare costs, and preventable deaths.

- Up to half (50%) of patients with cardiovascular conditions don't take their medications as prescribed.

- Previous adherence interventions have been resource intensive, high-burden, inconsistent, and produced mixed results.

Nudge

What is a Nudge?

- A strategic reminder can help people adopt healthy behaviors

  - Uses principles from behavioral economics and cognitive psychology

    - Behavior commitments
    - Communicating social norms
    - Narrative stories

- Can help patients improve medication adherence by promoting behavioral change through positive reinforcement.

- Should be delivered close to the timing of the desired behavior.

Specific Aims

- **Year 1 (UG3 Phase)**
  - **Aim 1.** Develop and program a nudge message library using iterative N of 1 studies to optimize content for a range of diverse patients.
  - **Aim 2.** Conduct a pilot intervention to demonstrate feasibility of delivering the intervention and preliminary effects in all 3 HCS. Engage patient, provider and health systems stakeholders in designing, refining, and implementing the pilot intervention.

- **Years 2-5 (UH3 Phase)**
  - **Aim 1.** Conduct a pragmatic patient-level randomized intervention across three health care systems (HCS) to improve adherence to chronic CV medications.
  - **Aim 2.** Evaluate the intervention effectiveness using a mixed methods approach and applying the RE-AIM (reach, effectiveness, adoption, implementation, and maintenance) framework.

Patient Population

Inclusion criteria

- Adult patients diagnosed with ≥ 1 cardiovascular condition of interest, prescribed ≥ 1 medication of interest, with a refill gap of at least 7 days

Condition	Classes of medications
Hypertension	Beta-blockers (B-blockers), Calcium Channel Blocker (CCB), Angiotensin converting enzyme inhibitors (ACEi), Angiotensin Receptor Blockers (ARB), Thiazide diuretic
Hyperlipidemia	HMG CoA reductase inhibitor (Statins)
Diabetes	Alpha-glucosidase inhibitors, Biguanides, DPP-4 inhibitors, Sodium glucose transport inhibitor, Meglitinides, Sulfonylureas, Thiazolidinediones, and statins
Coronary artery disease	PGY-2 inhibitor (Clopidogrel, Ticagrelor, Prasugrel, Ticlopidine), B-blockers, ACEi or ARB and statins
Atrial fibrillation	Direct oral anticoagulants, B-blockers, CCB

Exclusion criteria

- Patients with neither a landline or cellphone
- Enrolled in hospice or palliative care
- Non-English or Spanish speaking
- Residing out of the state of Colorado.
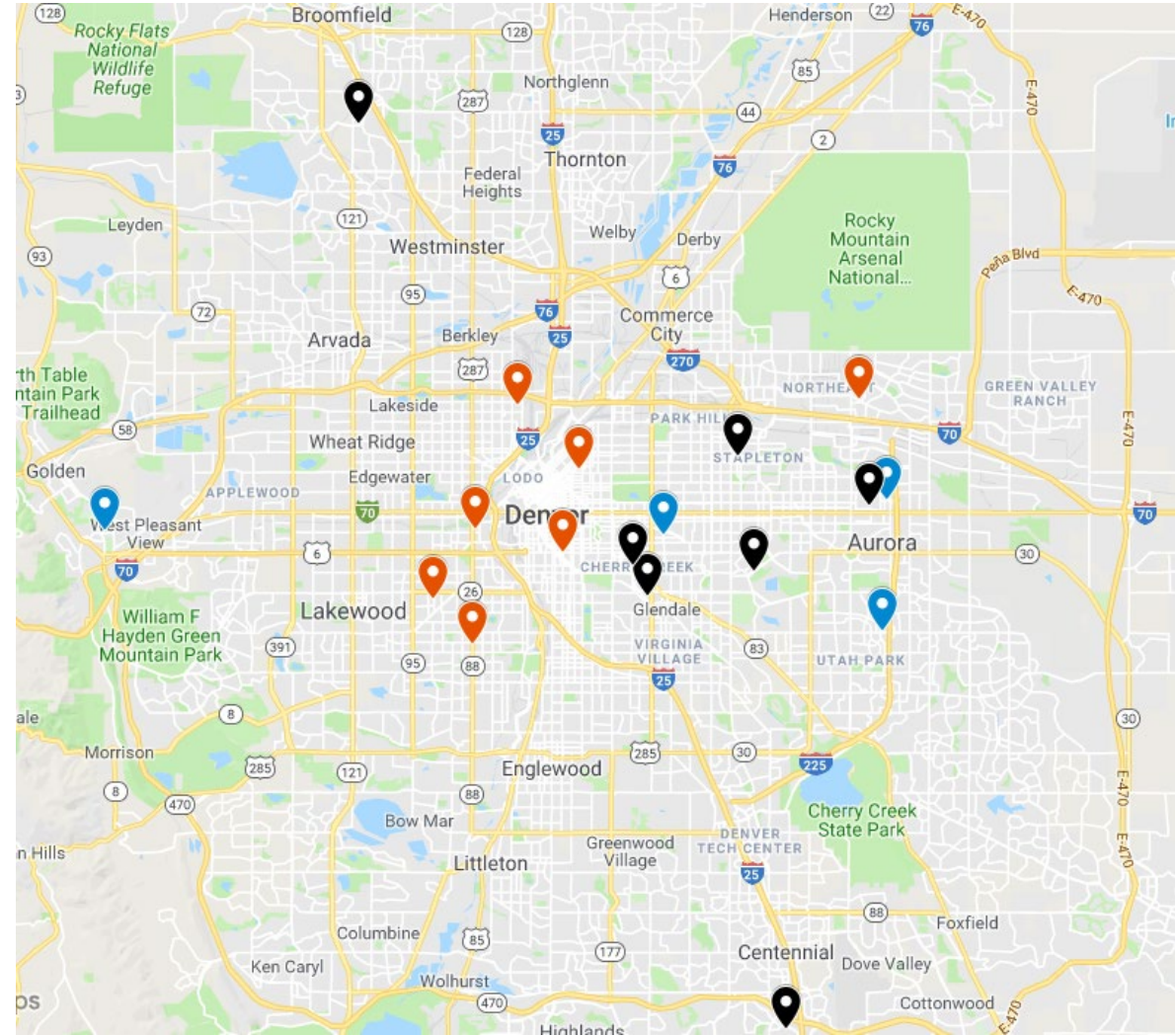
ℕudge

STUDY SETTING

📍 UCHealth Clinics

📍 Denver Health Clinics

📍 VA Eastern Colorado HCS Clinics

Opt out approach

- Opt out approach
  - Low risk intervention
  - Having patients consent may enroll more adherent patients
  - Challenges of consenting large patient population

- Our opt out process included:

  - Mailed packet with information sheet, opt out sheet, and a self addressed stamped envelope

  - Optional survey seeking to understand why patients do not participate in low-risk, opt out studies

  - Materials were signed by Site PI respective to their HCS

  - 4-week deadline to return opt-out form

- A secondary opt-out opportunity was included in subsequent texts
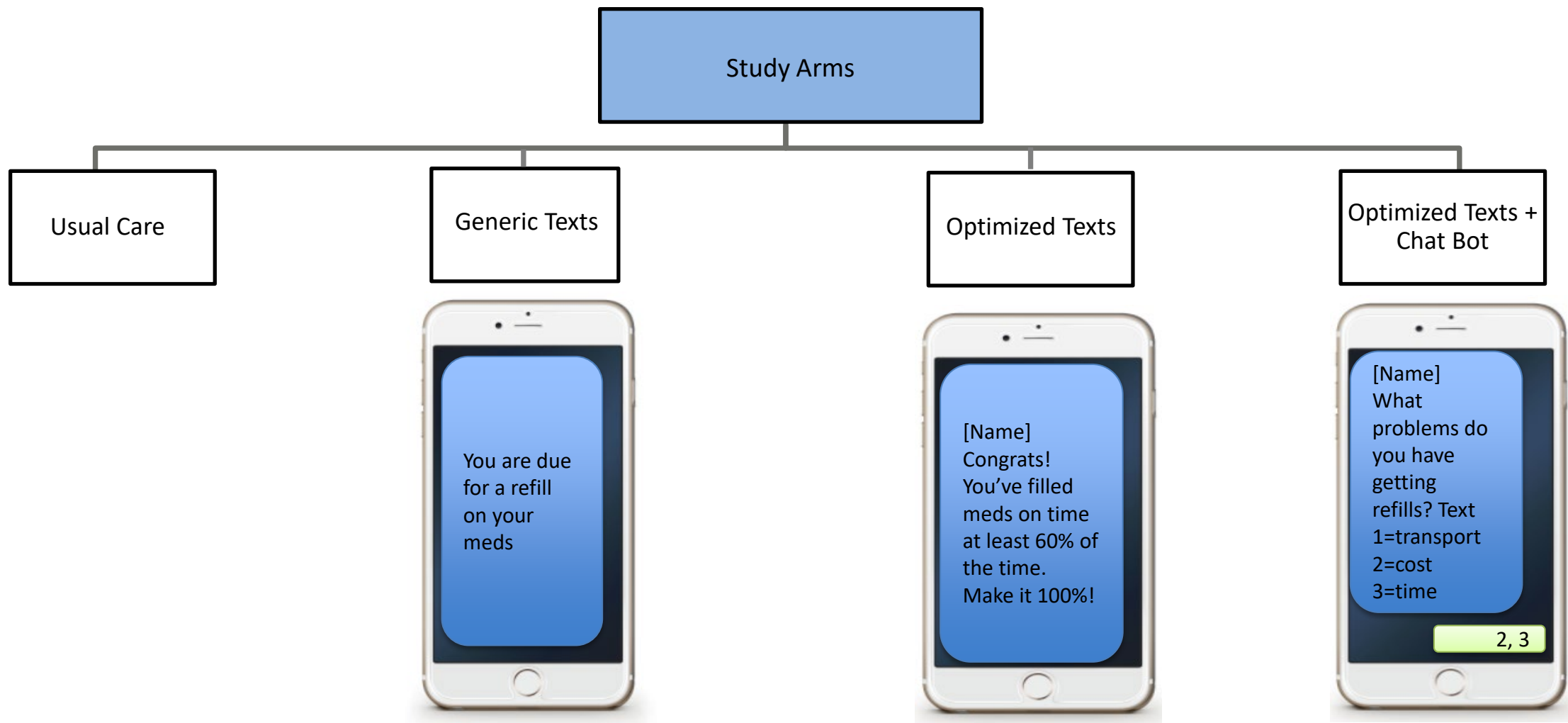
Initial findings from the UG3 Pilot

Nudge

Creation of culturally appropriate nudges

Community Advisory Panel

A Nudge-specific Advisory Panel provided additional input on both the messages and the opt out packets.

- Panel included patients, providers, health care leaders, and pharmacists
- Panel recommendations led to:

    - Added an option for patients to indicate they had leftover medications (responding "Done")

    - Improved the interactive voice response (IVR) messages by using a robotic voice rather than human voice

    - Provided specific suggestions of way to disseminate findings, including identifying communications platforms at the HCS
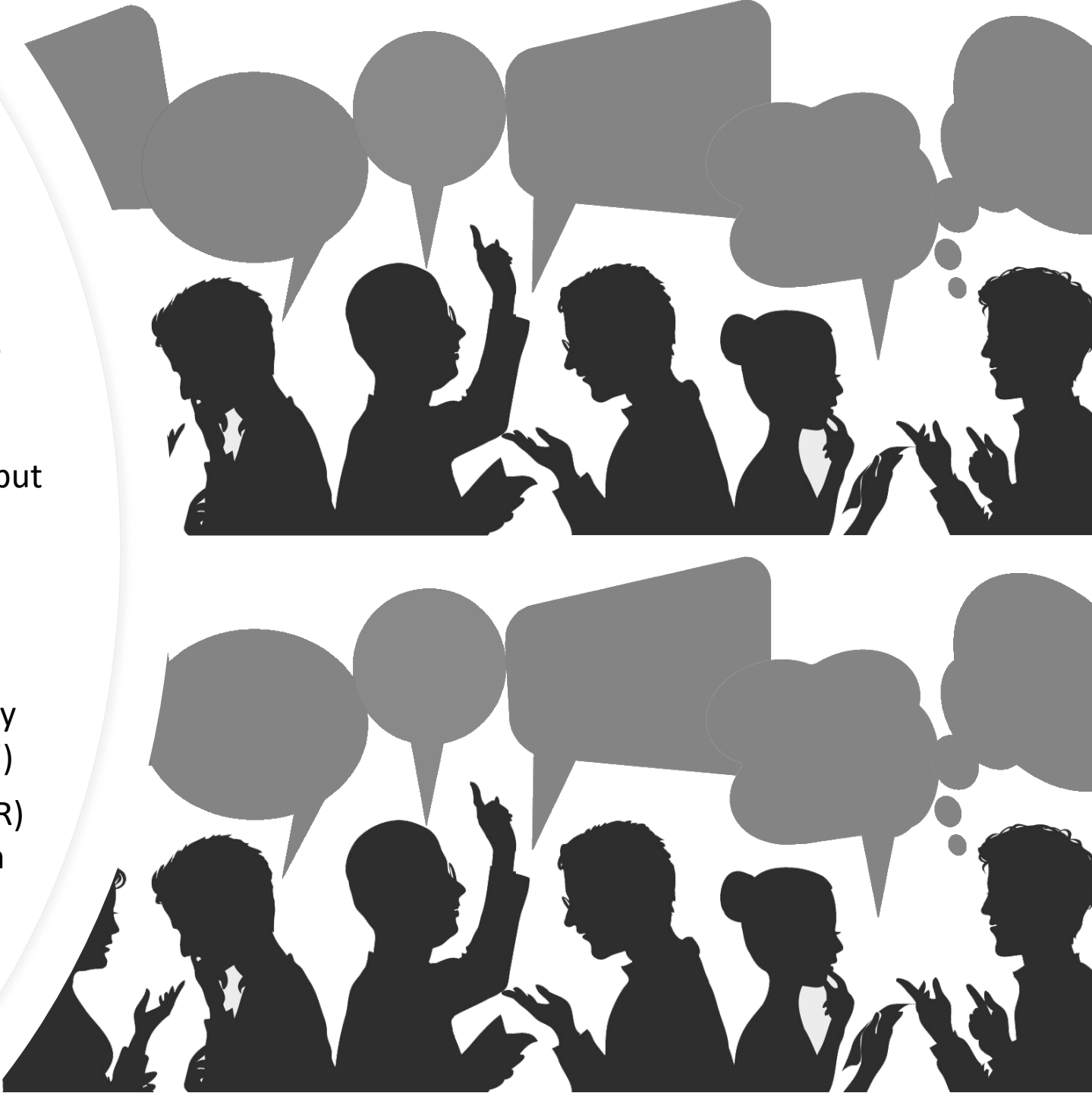
Creation of culturally appropriate nudges

Nof1 interviews

- 35 patients provided their perspectives of our messages, creating an iterative message design process
  - Disliked messages with humor and emojis
  - Preference for direct and simple communications

Example of message evolution

Original	Intermediate	Final
Tell us your best strategy to make getting refills a habit! Text 1 = set my alarm; 2 = rely on my family; 3 = make it part of my weekly routine; 4 = other or unknown.	We noticed you didn't refill some of your meds. Tell us why! Text 1 = too expensive; 2 = I forgot; 3 = I don't like taking them; 4 = Other.	Hi (FIRST NAME) We noticed you haven't refilled your (DRUG NAME). Reply 1 = you'll get them refilled in the next 2 days 2 = I'm still working on a plan to get this done.

UG3 Patient Characteristics

PATIENT CHARACTERISTICS	DENVER HEALTH (N=181)	VA (N=163)
Age, Mean (SD)	57.8 (12.6)	66.0 (8.6)
Male, % (n)	47% (85)	93.3% (152)
Race, % (n)		
Black/African American	17.7% (32)	23.3% (38)
White	11.6% (21)	68.1% (111)
Hispanic	68.5% (124)	9.8% (16)
Other	0	4.3% (7)
Condition, % (n)		
Atrial fibrillation	4.4% (8)	11.0% (18)
Coronary artery disease	14.4% (26)	22.7% (37)
Diabetes	66.9% (121)	38.7% (63)
Hyperlipidemia	43.1% (78)	41.1% (67)
Hypertension	80.1% (145)	78.5% (128)

Nudge

Message responses
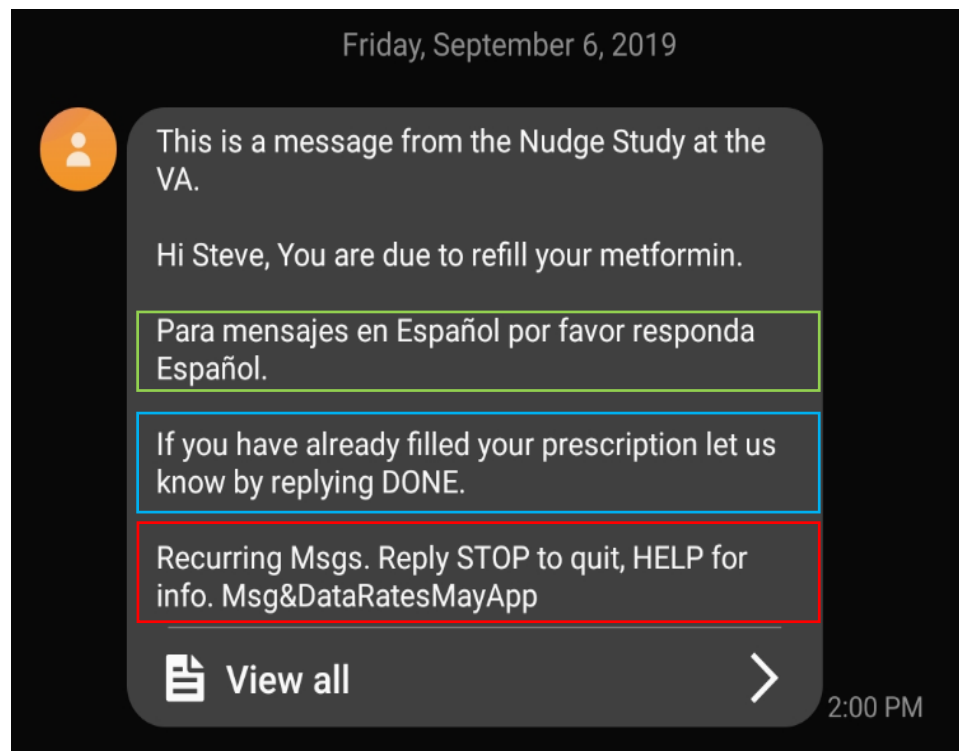
	DH	VA
Patient opt out rate	6.5% (13)	18.5% (37)
Patients with 7-day gap	63.0% (115)	57.7% (94)
Spanish language	11.6% (10)	0
Texted "Done"	15.6% (14)	21.1% (19)
Texted "Stop"	3.3% (3)	1.1% (1)

Medication refill rates

	Arm 1 Usual Care	Arm 2 Generic	Arm 3 Optimized	Arm 4 Optimized + Chatbot
Total N	50	53	52	52
N Medications Gapping at Baseline - Median (IQR)	2 (1, 3)	1 (1, 3)	1 (1, 2)	2 (1, 3)
Filled at Least 1 Gapping Medication - %(n)	18.0% (9)	32.1% (17)	32.7% (17)	26.9% (14)
Filled All Gapping Medications - %(n)	10.0% (5)	17.0% (9)	21.2% (11)	15.4% (8)

Pilot Study Final Conclusions

- Patient feedback important to refine text message content
- Opt-out rates lower than expected
    - Primary opt out rate (12.5%)
    - Secondary opt-out rate (1.2%) (responding with "STOP")
- Real time identification of patients who have not refilled medications is feasible
- Sending text messages is feasible and shows potential for improving refill adherence.

Nudge

Learning from the opt out consent process

Nudge

OPT-OUT STUDY DESIGN

Identify patients with CV disease and prescribed medication

Send opt-out packets to eligible patients

Patients who do not return opt-out form are eligible for enrollment

Monitor for gaps with medication refills

Once gap occurs, patient randomized to a study arm

Secondary opt out option for those receiving texts by replying 'STOP'
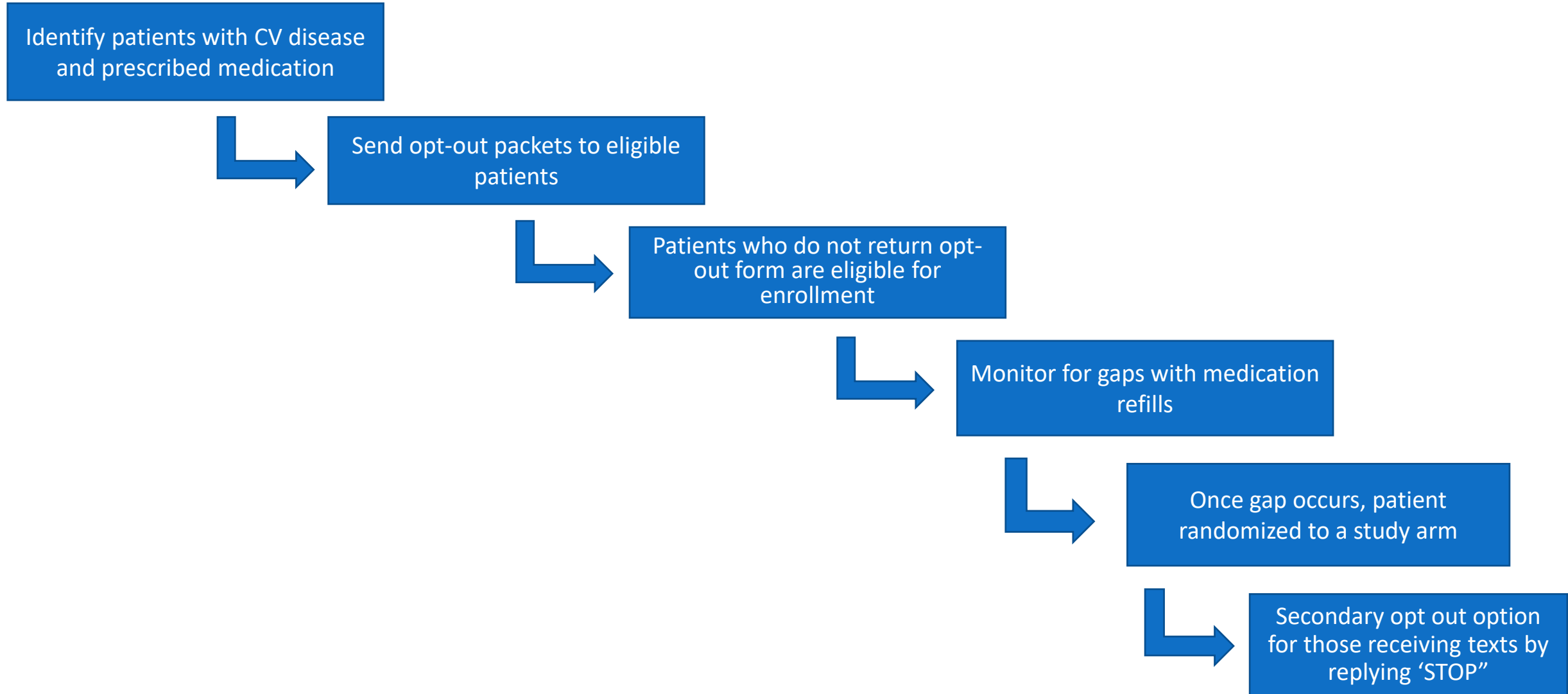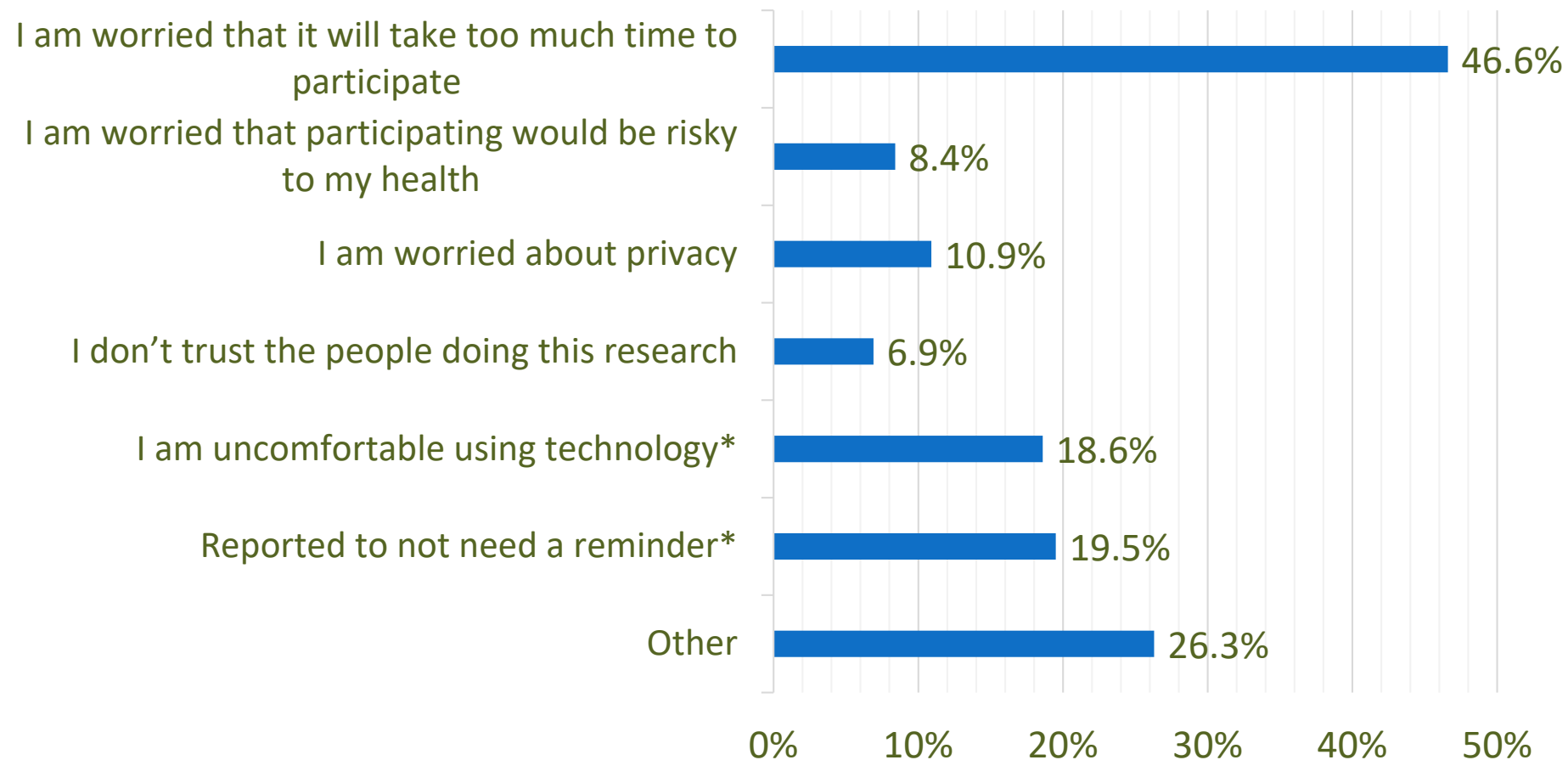
Comparing patients who opt out vs did not opt out

- Goal of study was to better understand characteristics of patients who opted out, and reasons for doing so:
    - 9,046 patients receiving packets
        - 906 patients (10.0%) returned opt out forms
        - Of those, 451 (49.8%) returned the opt out survey.
    - Patients who opted out were more likely to be older, white, and non-Hispanic.
    - Those who opted out and completed the opt out survey expressed high levels of trust in their health care providers, research, and system.

Reasons that contributed to patients opting out

Reason	Percentage
I am worried that it will take too much time to participate	46.6%
I am worried that participating would be risky to my health	8.4%
I am worried about privacy	10.9%
I don't trust the people doing this research	6.9%
I am uncomfortable using technology*	18.6%
Reported to not need a reminder*	19.5%
Other	26.3%

Studying patient populations who opted out via replying 'STOP' to text messaging
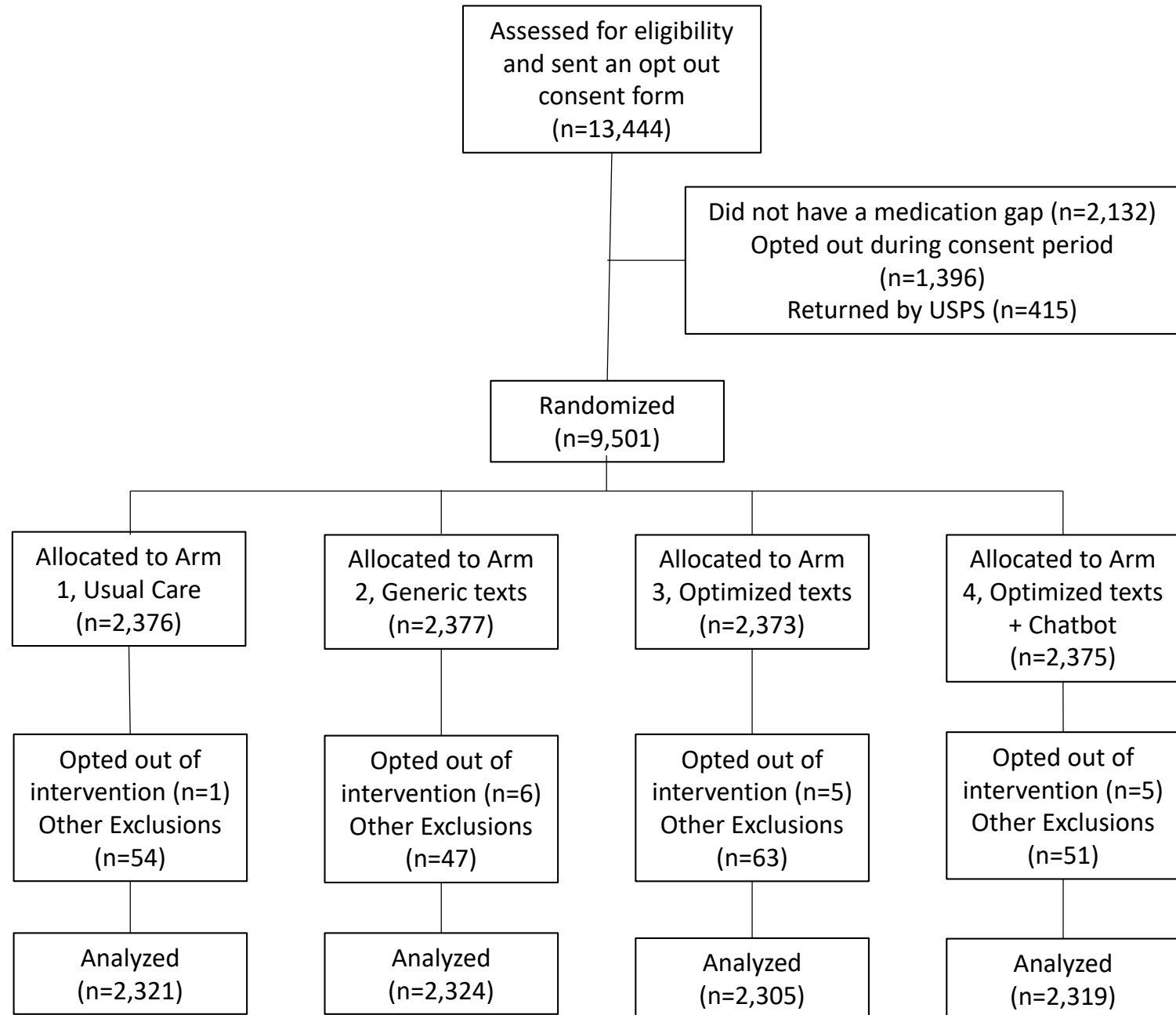
- Of 5,707 patients enrolled, 8.3% opted out by text after receiving a text
  - Median time to opt out was 83 days
  - Black and Hispanic patients, and primary Spanish speakers were less likely to opt out.
  - No significant differences were observed in age, gender, medical condition, or health system between patients remaining in study versus opting out.

- In a low-risk intervention, patients who identified as Black, Hispanic, and primary Spanish speakers were more likely to remain in the study

- An opt out approach in the appropriate clinical trial context may be a way to diversify clinical trial populations and improve external validity of results

Patients that remained in study vs opted out

Findings from the UH3 trial

Nudge

Patient flow

Assessed for eligibility and sent an opt out consent form (n=13,444)

Did not have a medication gap (n=2,132)
Opted out during consent period (n=1,396)
Returned by USPS (n=415)

Randomized (n=9,501)

Allocated to Arm 1, Usual Care (n=2,376)

Allocated to Arm 2, Generic texts (n=2,377)

Allocated to Arm 3, Optimized texts (n=2,373)

Allocated to Arm 4, Optimized texts + Chatbot (n=2,375)

Opted out of intervention (n=1)
Other Exclusions (n=54)

Opted out of intervention (n=6)
Other Exclusions (n=47)

Opted out of intervention (n=5)
Other Exclusions (n=63)

Opted out of intervention (n=5)
Other Exclusions (n=51)

Analyzed (n=2,321)

Analyzed (n=2,324)

Analyzed (n=2,305)

Analyzed (n=2,319)

Demographic Characteristics of the Study Population

	All	Usual Care	Generic	Optimized	Optimized + Chatbot	P-Value
	N = 9269	N = 2321	N = 2324	N = 2305	N = 2319	
Age	60.1% (12.7)	60% (12.6)	60% (12.5)	60% (12.9)	60% (12.7)	0.99
Female	47.0% (4351)	47% (1088)	47% (1087)	47% (1075)	47% (1101)	0.94
Race						0.58
White	70% (6460)	69% (1598)	69% (1601)	70% (1615)	71% (1646)	
Black/AA	16% (1517)	17% (392)	17% (391)	16% (378)	15% (356)	
Other	3% (280)	3% (76)	3% (64)	3% (74)	3% (66)	
Ethnicity						0.46
Hispanic	49% (4564)	50% (1149)	47% (1100)	50% (1147)	50% (1168)	
Non-Hispanic	50% (4629)	50% (1150)	52% (1204)	50% (1141)	49% (1134)	
Spanish Speaking	28% (2605)	28% (654)	27% (619)	28% (650)	29% (682)	0.22

HCS & Qualifying conditions

	All	Usual Care	Generic	Optimized	Optimized + Chatbot	P-Value
	N = 9269	N = 2321	N = 2324	N = 2305	N = 2319	
Health Care System						>0.99
Denver Health	77% (7127)	77% (1785)	77% (1786)	77% (1781)	77% (1775)	
UCHealth	10% (939)	10% (235)	10% (239)	10% (225)	10% (240)	
VA	13% (1203)	13% (301)	13% (299)	13% (299)	13% (304)	
QUALIFYING CONDITION(S)						
Atrial fibrillation	6% (548)	6% (134)	6% (132)	7% (152)	6% (130)	0.45
Coronary artery disease	14% (1310)	14% (328)	13% (305)	14% (325)	15% (352)	0.26
Diabetes mellitus	50% (4623)	50% (1149)	50% (1148)	50% (1164)	50% (1162)	0.86
Hyperlipidemia	46% (4267)	45% (1054)	46% (1072)	46% (1052)	47% (1089)	0.73
Hypertension	79% (7351)	80% (1864)	79% (1837)	79% (1829)	79% (1821)	0.5

PDC Difference from Usual Care by Study Month
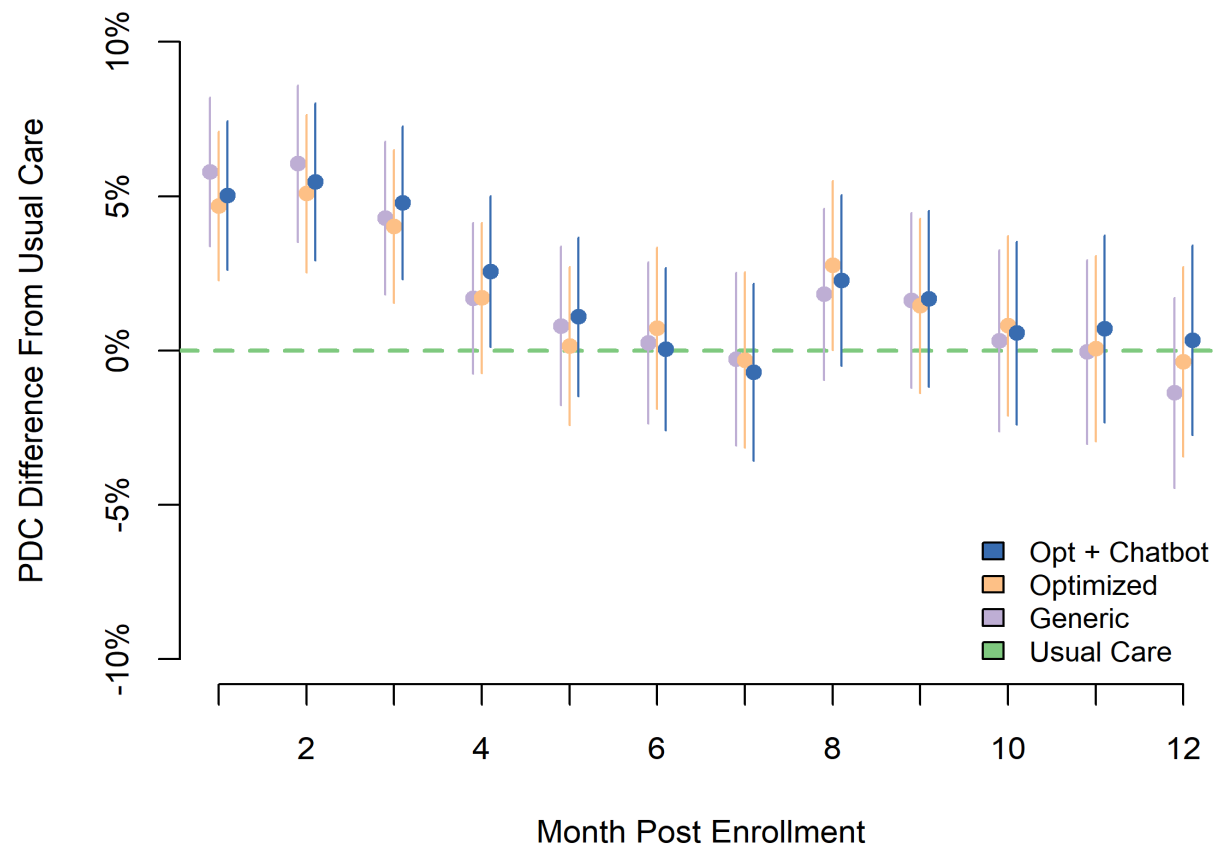
	Usual Care	Generic	Optimized	Opt + Chatbot
PDC at 3 months	56.2%	61.4%	61.1%	61.6%
PDC at 12 months	60.6%	62.0%	62.3%	63.0%

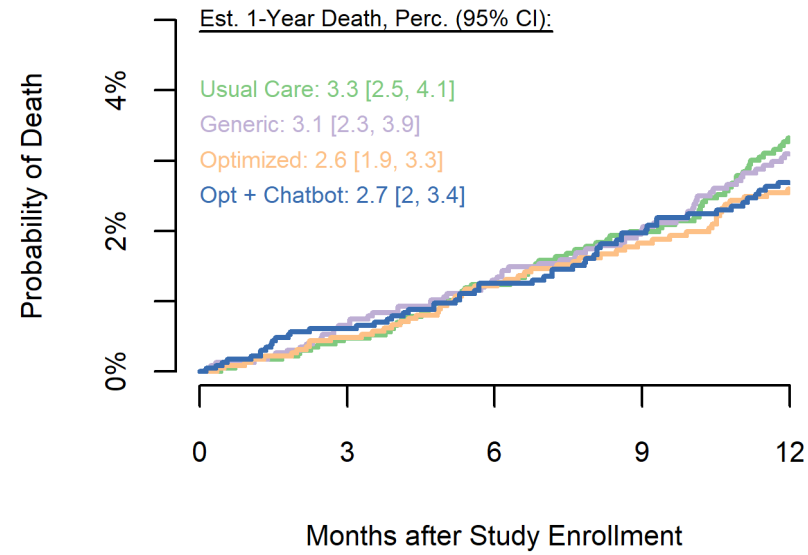# SUBGROUP ANALYSES

Difference in PDC between generic text and usual
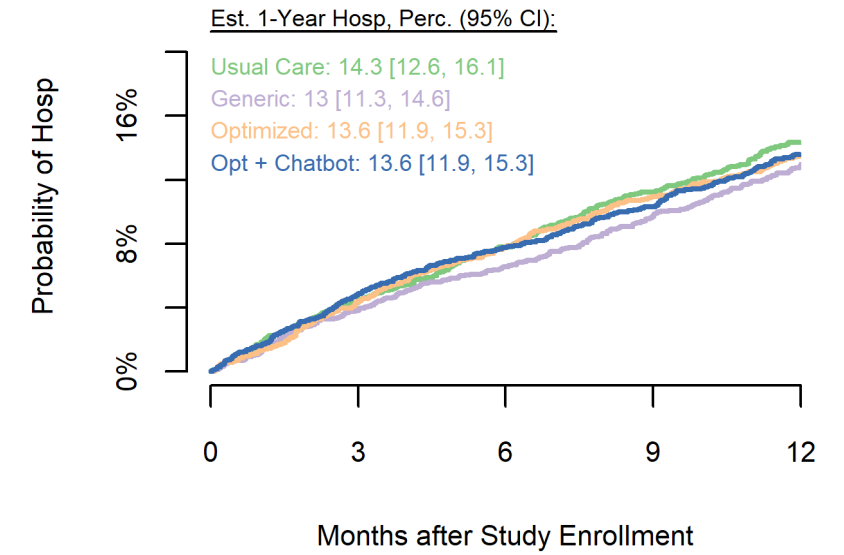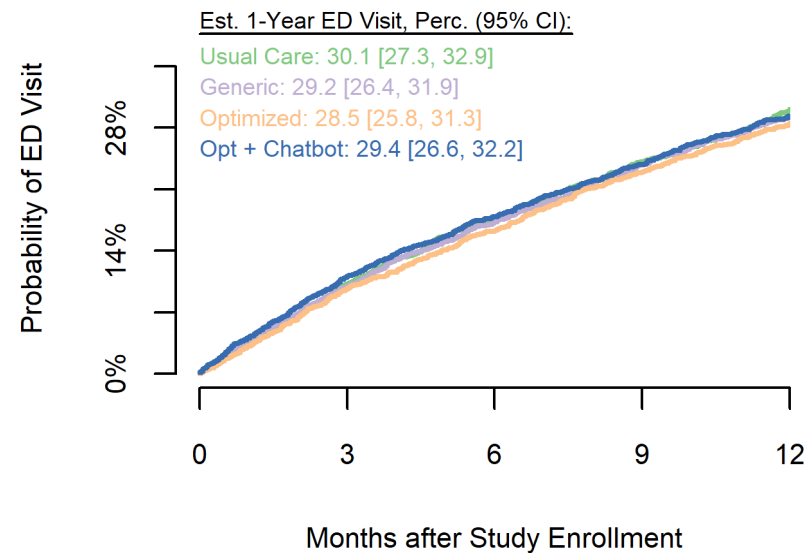care groups at 3-months

Clinical Events

Death

Est. 1-Year Death, Perc. (95% CI):

Usual Care: 3.3 [2.5, 4.1]
Generic: 3.1 [2.3, 3.9]
Optimized: 2.6 [1.9, 3.3]
Opt + Chatbot: 2.7 [2, 3.4]

Probability of Death

Months after Study Enrollment

Hospitalization

Est. 1-Year Hosp, Perc. (95% CI):

Usual Care: 14.3 [12.6, 16.1]
Generic: 13 [11.3, 14.6]
Optimized: 13.6 [11.9, 15.3]
Opt + Chatbot: 13.6 [11.9, 15.3]

Probability of Hosp

Months after Study Enrollment

Emergency Department

Est. 1-Year ED Visit, Perc. (95% CI):

Usual Care: 30.1 [27.3, 32.9]
Generic: 29.2 [26.4, 31.9]
Optimized: 28.5 [25.8, 31.3]
Opt + Chatbot: 29.4 [26.6, 32.2]

Probability of ED Visit

Months after Study Enrollment

Usual Care
Generic
Optimized
Opt + Chatbot

Interactions with Clinical Pharmacists

Nudge

Pharmacist-patient interactions

- Over half of patients receiving messages (52.5%) responded to at least one text. Of those, 305 (9.2%) responded with a question for a clinical pharmacist

- Patient factors associated with sending a text

  - More likely to be enrolled at DHHA

  - More likely to be older (45-64 years, or 65-74 years)

  - Have hypertension

- 20% of patients that had questions for a clinical pharmacist had multiple questions

Nudge

Questions received by pharmacists

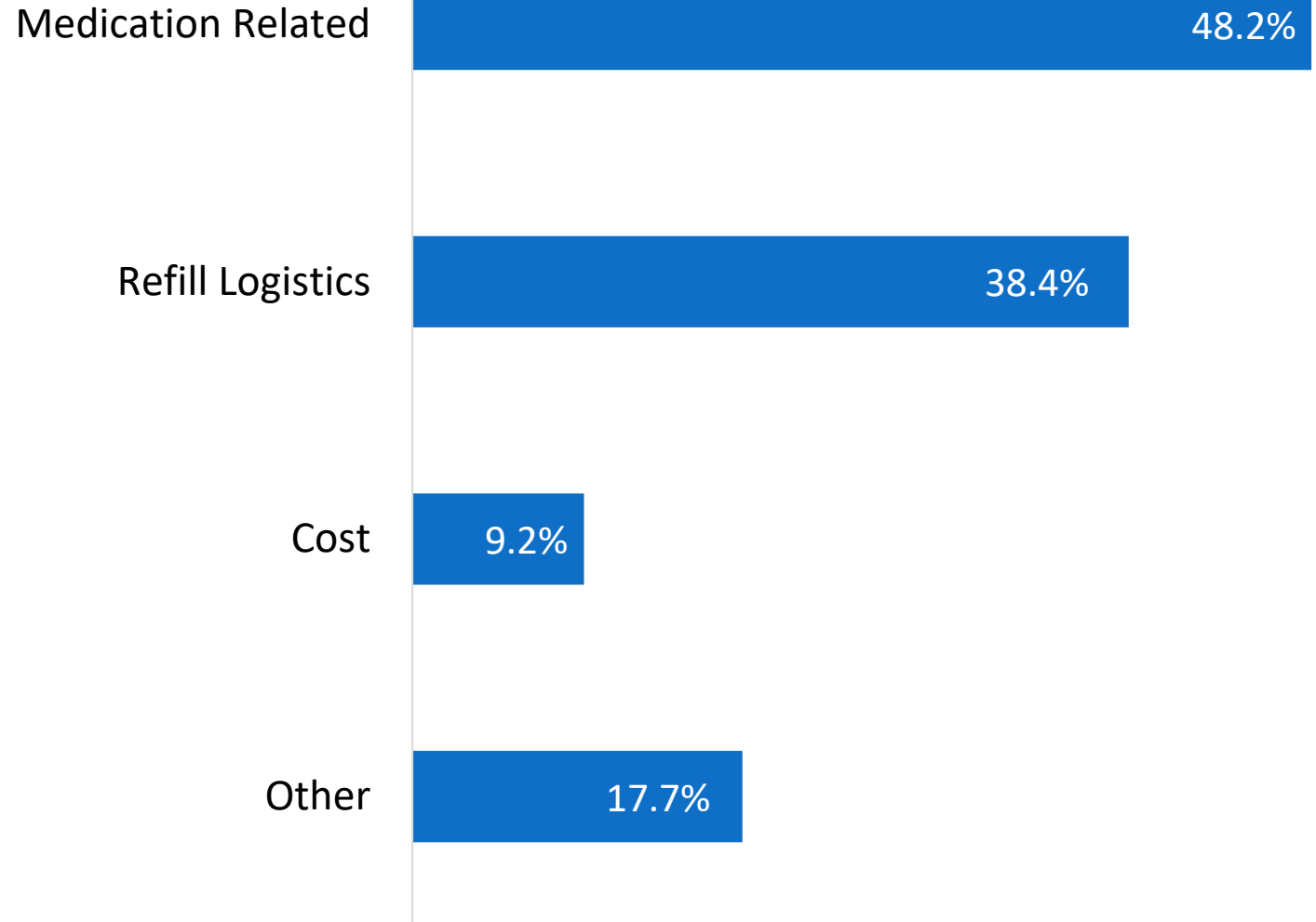Medication Related — 48.2%
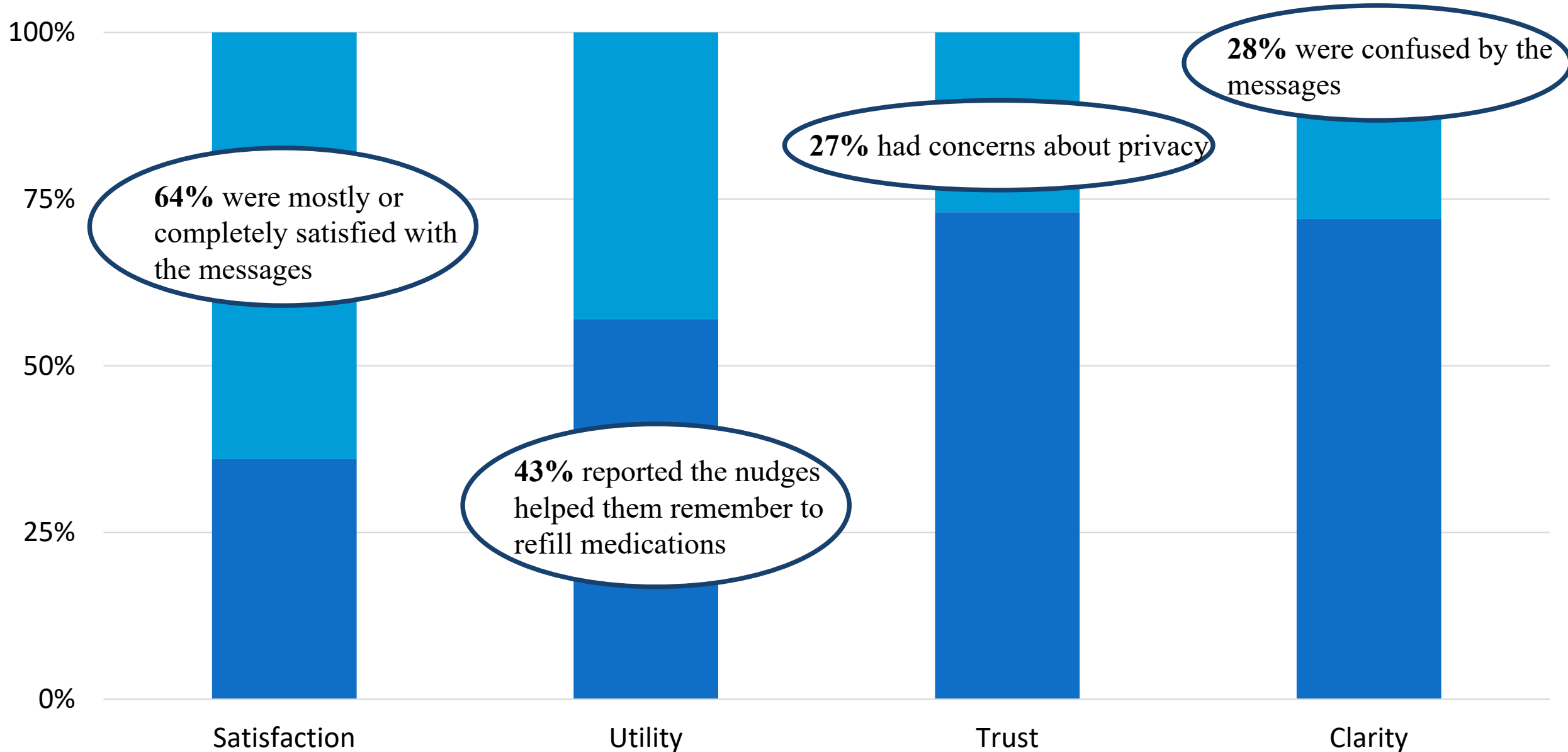Refill Logistics — 38.4%
Cost — 9.2%
Other — 17.7%

Patient satisfaction

Patient satisfaction

- A sample of participants (n=1,526) were sent a post-implementation satisfaction survey via text. We received 100 survey responses (response rate = 6.5%; 76 English speakers and 24 Spanish speakers).
- The survey revealed high levels of satisfaction with the intervention, especially among Spanish speaking populations.
    - Spanish-preferring patients were more likely to rate messages as helpful and to indicate that they would participate in a similar intervention in the future
    - There were no language-based differences in privacy concerns or confusion regarding messages

Patient satisfaction

64% were mostly or completely satisfied with the messages

43% reported the nudges helped them remember to refill medications

27% had concerns about privacy

28% were confused by the messages

Satisfaction	Utility	Trust	Clarity

General lessons learned

- Text message intervention improved medication refill adherence
- Effectiveness consistent regardless of type of message delivered
- Differential impact of intervention across some patient groups
- Opt out approach is feasible and drop out rate was lower than expected
- Patients generally satisfied with text messages
- Patients who identified as non-white and Hispanic were more likely to remain in the study.
- Text messages can be implemented as a low cost intervention to improve medication refill adherence across different HCS with disparate EHR systems