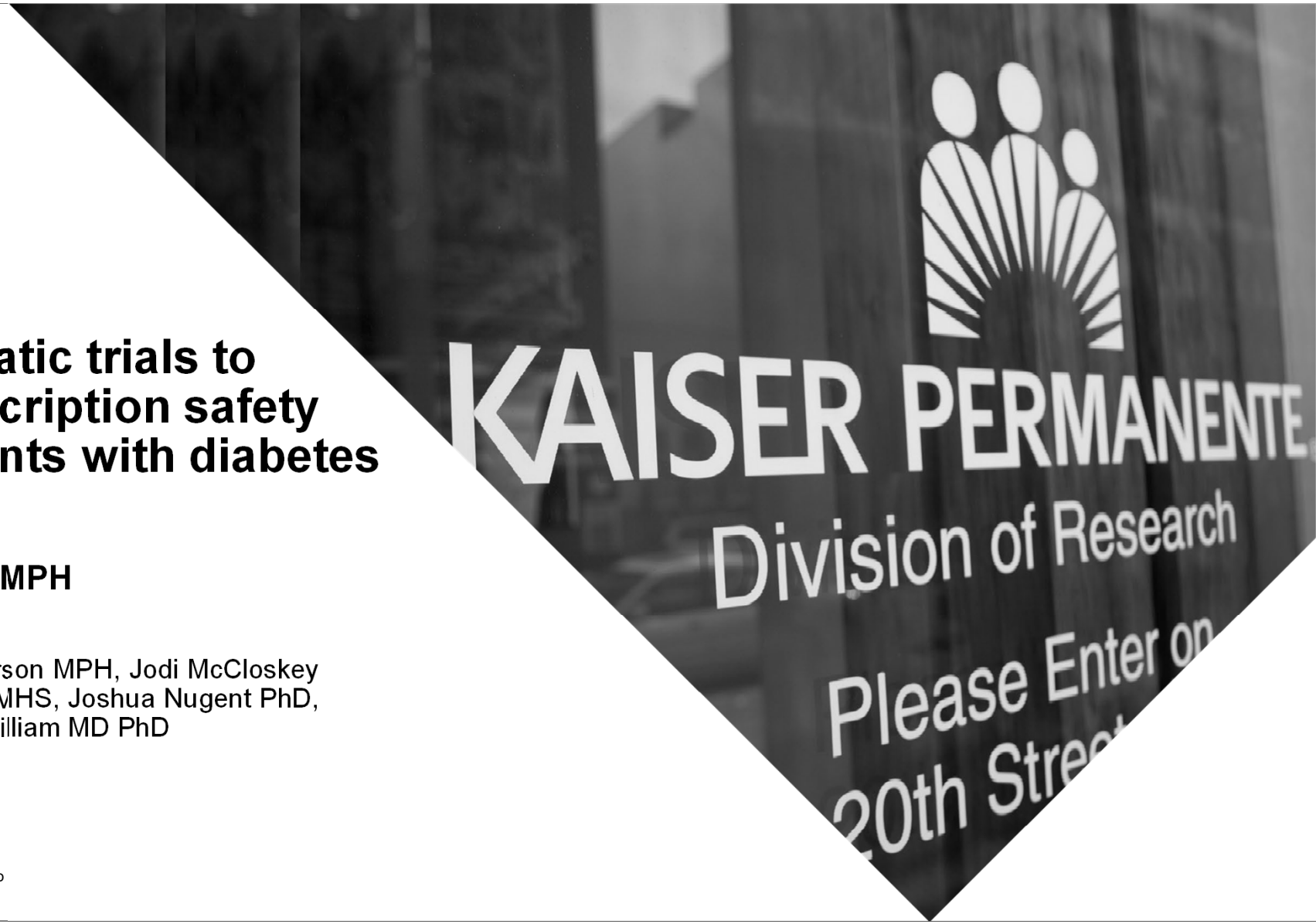
Using pragmatic trials to address prescription safety in older patients with diabetes

Richard Grant MD MPH

Co-Authors: Ilana Peterson MPH, Jodi McCloskey MPH, Kasia Lipska MD MHS, Joshua Nugent PhD, Andy Karter PhD, Lisa Gilliam MD PhD

November 20, 2025



Disclosure Slide

No conflicts to disclose

- Build the nation's capacity to conduct pragmatic clinical trials (ePCTs) of interventions embedded within health care systems

Today's presentation will describe 2 pragmatic RCTs in older adults with type 2 diabetes focused on treatment safety:

1. **Reducing Treatment Risk in Older Adults (RETRO-DM)** – *completed*

2. **Safer Aging with Diabetes Monitoring (SAGE) -** *ongoing*

Consequences of Hypoglycemia in Older Patients with Type 2 Diabetes

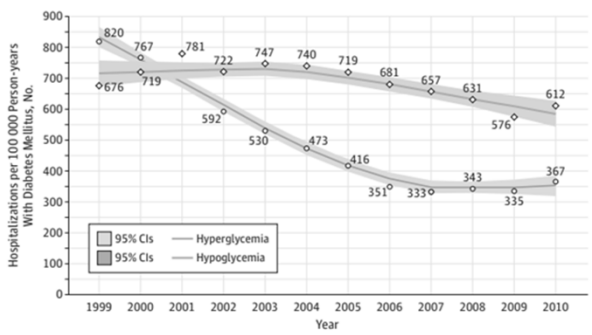
Original Investigation

National Trends in US Hospital Admissions for Hyperglycemia and Hypoglycemia Among Medicare Beneficiaries, 1999 to 2011

Kasia J. Lipska, MD, MHS; Joseph S. Ross, MD; Yun Wang, PhD; Silvio E. Inzucchi, MD; Karl Minges, MPH; Andrew J. Karter, PhD; Elbert S. Huang, MD; Mayur M. Desai, PhD, MPH; Thomas M. Gill, MD; Harlan M. Krumholz, MD, SM

JAMA Internal Medicine July 2014 Volume 174, Number 7

Figure 2. Rates of Estimated Hospital Admissions for Hyperglycemia and Hypoglycemia Among Medicare Beneficiaries With Diabetes Mellitus, 1999 to 2010



Hypoglycemia Associated With Hospitalization and Adverse Events in Older People

Sumit R. Majumdar, MD, MPH[1]
Brenda R. Hemmelgarn, MD, PhD[2]
Meng Lin, MSC[1]
Kerry McBrien, MD, MSC[2]
Braden J. Manns, MD, MSC[2]
Marcello Tonelli, MD, SM[1]

Hospitalized hypoglycemia was independently associated with increased mortality (**60 vs. 19% mortality** for no hypoglycemia), and this increased in a dose-dependent manner (aHR no hypoglycemia = 1.0 vs. one episode = 2.49 vs. one or more = 3.78, P <0.001)

Severe Hypoglycemia and Cognitive Decline in Older People With Type 2 Diabetes: The Edinburgh Type 2 Diabetes Study

Diabetes Care Volume 37, February 2014

"severe hypoglycemia associated with both poorer initial cognitive ability and accelerated cognitive decline"

Association between hypoglycaemic events and fall-related fractures in Medicare-covered patients with type 2 diabetes

S. S. Johnston[1], C. Conner[2,3], M. Aagren[2], K. Ruiz[1] & J. Bouchard[2]

Diabetes, Obesity and Metabolism 14: 634–643, 2012

"Patients with hypoglycemic events had 70% higher regression-adjusted odds of fall-related fractures"

Self-reported hypoglycemia and impact on quality of life and depression among adults with type 2 diabetes mellitus

Andrew J. Green[a], *Kathleen M. Fox*[b,*], *Susan Grandy*[c]

DIABETES RESEARCH AND CLINICAL PRACTICE 96 (2012) 313–318

"Self-reported hypoglycemia was prevalent among individuals with T2DM and associated with lower health-related quality of life, and **greater burden of depression**"

One safety strategy is deprescribing

US Deprescribing Research Network

"**Deprescribing** refers to the thoughtful and systematic process of identifying problematic medications and either reducing the dose or stopping these medications in a manner that is safe, effective, and helps people maximize their wellness and goals of care."

"But **deprescribing isn't easy**. Little is known about how to best identify which medications are prime for deprescribing, how to safely and effectively stop them, and **how to engage patients, clinicians, and the health system** in this process in a seamless and patient-centered manner."

Barriers to Deprescribing in Type 2 Diabetes

A National Survey of Physicians' Views on the Importance and Implementation of Deintensifying Diabetes Medications

Scott J. Pilla, MD, MHS[1,2,3], Rabia Jalalzai, MD, MPH[1], Olive Tang, MD, PhD[4], Nancy L. Schoenborn, MD, MHS[5], Cynthia M. Boyd, MD, MPH[3,4,5], Michael P. Bancks, PhD[6], Nestoras N. Mathioudakis, MD, MHS[7], and Nisa M. Maruthur, MD, MHS[1,2,4]

J Gen Intern Med, Volume 39, 992–1001, (2024)

"While most US physicians viewed deintensifying and switching diabetes medications as important for the care of older adults, they deintensified infrequently. Physicians had **ambivalence about the relative benefits and harms** of deintensification and viewed it as a **potential source of conflict** with their patients. These factors likely contribute to clinical inertia, and studies focused on improving shared decision-making around deintensifying diabetes medications are needed."

Facilitators of and Barriers to Deprescribing Diabetes Medications in Older Adults: A Qualitative Study

Aimee N. Pickering[1] | Sam Richardson[2] | Shari Rogal[3,4,5] | Carolyn T. Thorpe[3,6] | Jennifer Brach[7] | Thomas R. Radomski[1,3]

Journal of the American Geriatrics Society, 2025; 73:2447–2456

"Patient-related facilitators included understanding of **prescriber rationale** and preference to minimize medications, while barriers included fear of negative consequences. Prescriber-related facilitators included trust, perceived investment in care, **perceived expertise**, and collaboration with other prescribers. Medication-related barriers included **perceived benefit** and a lack of side effects impacting quality of life."

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

Question: How can we encourage PCPs and their higher-risk patients to discuss diabetes medication deprescribing?

Patient Eligibility: age 75+ years; T2D on insulin or SU; A1c < 8%

Design: Comparative effectiveness randomized clinical trial (CE-RCT)

Intervention = 2 active comparison arms:

Academic detailing vs. AD + patient pre-visit handout

ClinicalTrials.Gov NCT04585191

pcori PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

Primary Outcome: Deprescribing at 6 months

Definition: Reduction in dose or discontinuation of diabetes medications, switching between high-risk to lower-risk medications, and/or reducing the number of therapeutic classes

Additional Outcomes:

- Patient Self-report: Hypoglycemia, diabetes-related stress
- Structured abstraction: To identify any documentation of diabetes management discussion or medication deprescribing

pcori PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

Safety Outcomes (potential harms of deprescribing):

- Primary emergency department or principal hospital hyperglycemia diagnoses (hyperglycemia, hyperosmolarity with or without coma, or ketoacidosis with or without coma)

- Proportion of patients with HbA_{1c} greater than 8% at 6 and 12 months (controlling for HbA_{1c} level preceding index PCP visit)

- Reversal of deprescribing implemented in the first 6-month period during the second 6-month period

pcori PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

RETRO-DM: Pragmatic Issues for RCT Implementation

- Intervention Design - *How to*:
  - Influence patient-doctor communication with a very light touch
  - Get time with PCPs
  - Engage virtually with older adults

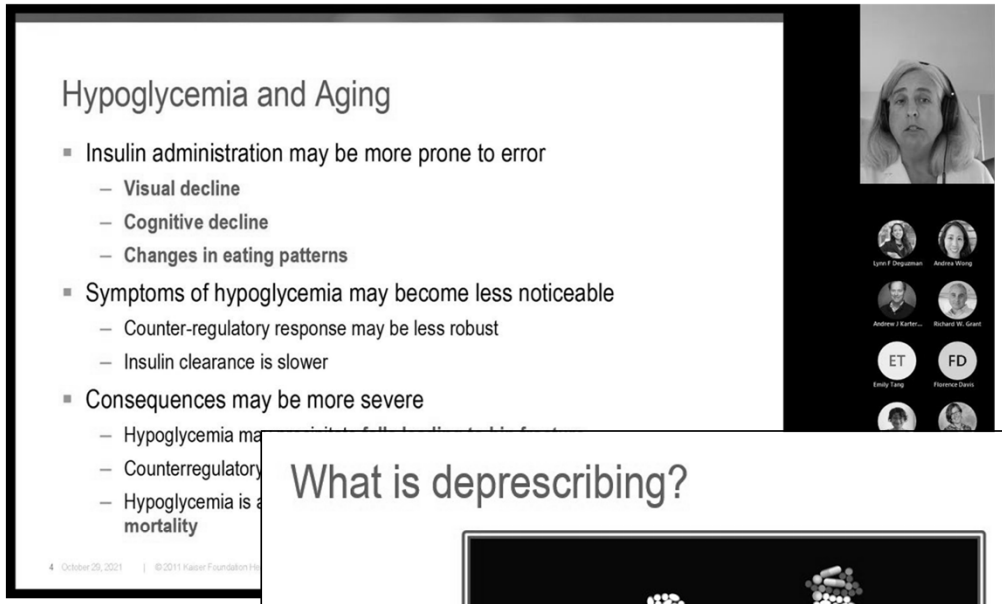
- Questions of consent
  - PCPs
  - Patients

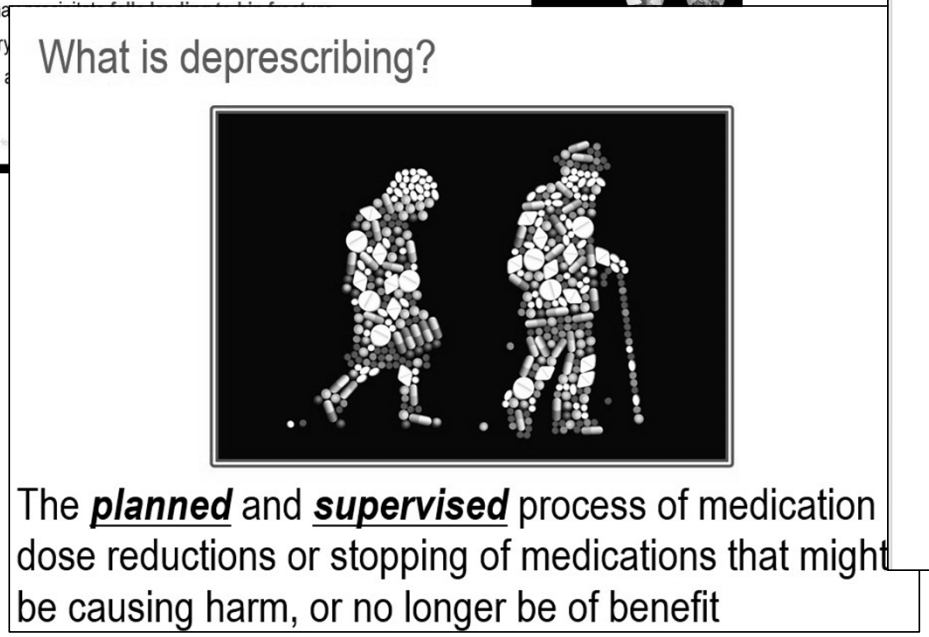
- Outcome Measurement
  - Deprescribing
  - Patient-provider communication

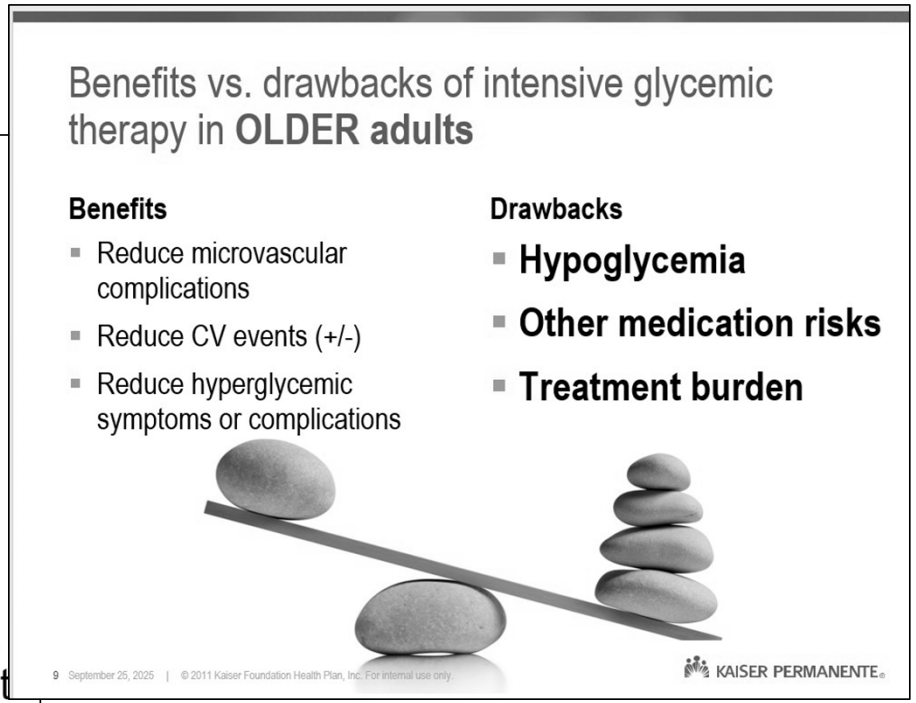
pcori PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Academic Detailing

30-minute virtual presentation conducted during usual primary care practice weekly meetings

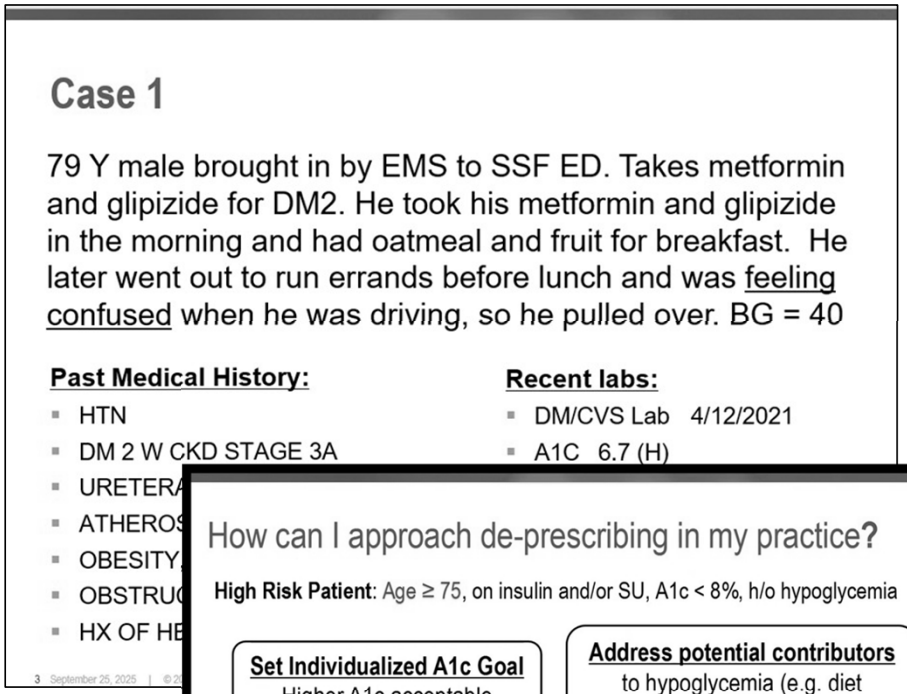


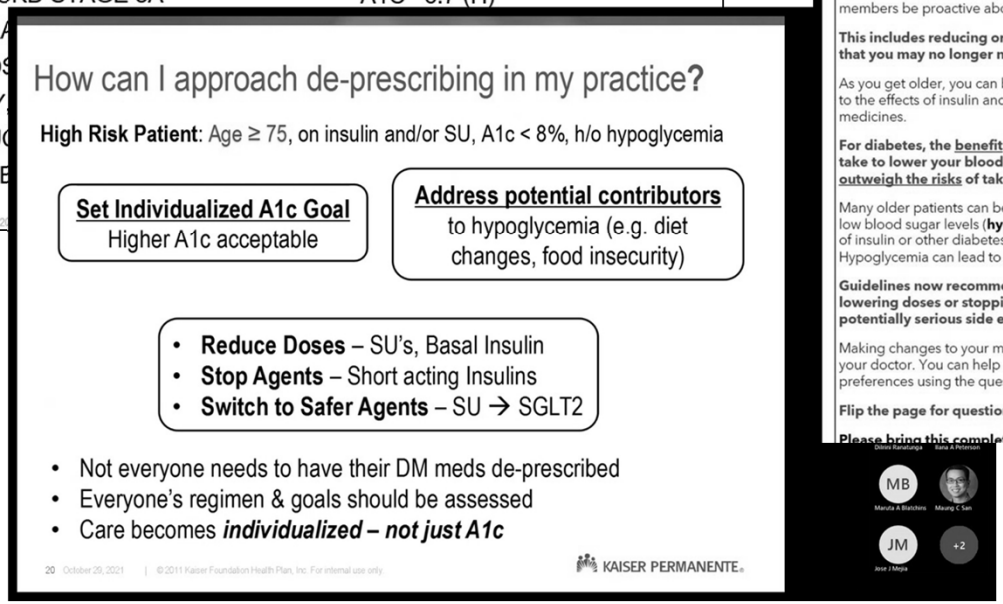


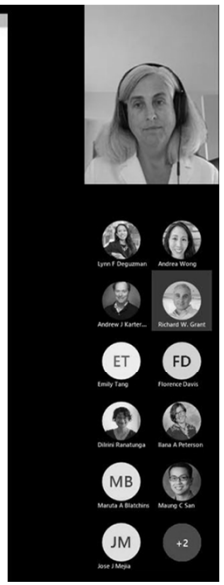


Academic Detailing

Evidence-based presentation with illustrative cases and opportunity for questions about specific patients







Talking to Your Doctor about Diabetes:

Are My Current Medicines Still Right for Me?

Get Ready for Your Visit

At Kaiser Permanente, we believe in helping our members be proactive about their health care.

This includes reducing or stopping medicines that you may no longer need.

As you get older, you can become more sensitive to the effects of insulin and other diabetes medicines.

For diabetes, the benefit of the medicines you take to lower your blood sugar should outweigh the risks of taking these medicines.

Many older patients can be at increased risk for low blood sugar levels (**hypoglycemia**) even if they are taking the same doses of insulin or other diabetes medicines that they took when they were younger. Hypoglycemia can lead to dizziness, falls, and emergency care.

Guidelines now recommend easing up on blood sugar targets by lowering doses or stopping some medicines to reduce the risk of potentially serious side effects.

Making changes to your medications is a **shared decision** between you and your doctor. You can help with this decision by reviewing your values and preferences using the questions on the next page.

Flip the page for questions that can help you talk about your medications.

Please bring this completed form to your next doctor's appointment.

Diabetes Medications Decision Tool: Your Values and Preferences

Thinking about your values and preferences can help you decide on what to do next.
The following questions can help you talk to your provider about your medication goals.

1. How satisfied are you with your **current diabetes medications**? ***(CIRCLE ONE)***

Not Satisfied				Very Satisfied
1	2	3	4	5

2. How important is it to you to have **blood sugars close to normal**?

Not Important				Very Important
1	2	3	4	5

3. How important is it to you to **avoid major side effects** from your diabetes medications? (examples: low blood sugar leading to falls, confusion)

Not Important				Very Important
1	2	3	4	5

4. How important is it to you for your doctor to **stop or reduce medications** that may no longer be helping?

Not Important				Very Important
1	2	3	4	5

5. How comfortable are you with your doctor **making changes** to your diabetes medications?

Not comfortable				Very comfortable
1	2	3	4	5

Based on your values and preferences, which choice(s) are you leaning toward?

- ☐ I'd like to **discuss stopping/reducing** my diabetes medicines with my doctor
- ☐ I'd like to discuss more with **my family and/or caregivers first**
- ☐ **No change**. Keep my diabetes medicines the same
- ☐ **I'm not sure yet**. I have questions for my doctor

JAMA Internal Medicine | Original Investigation | LESS IS MORE

Diabetes Deprescribing in Older Adults
A Randomized Clinical Trial

Richard W. Grant, MD, MPH; Ilana Peterson, MPH; Jodi M. McCloskey, MPH; Kasia J. Lipska, MD, MHS; Joshua Nugent, PhD; Andrew J. Karter, PhD; Lisa K. Gilliam, MD, PhD

IMPORTANCE Medication-related hypoglycemia is the leading cause of iatrogenic complications among older adults with type 2 diabetes.

OBJECTIVE To compare physician academic detailing (AD) with or without patient previsit activation for insulin and/or sulfonylurea deprescribing in older patients with diabetes.

DESIGN, SETTING, AND PARTICIPANTS This randomized clinical trial was conducted from September 2020 to March 2024 with 6 and 12 months of follow-up in a large integrated health care system in Northern California. Primary care physicians (PCPs) and their patients with type 2 diabetes who were 75 years and older, had hemoglobin A_{1c} of 8.0% or lower, and were treated with insulin and/or sulfonylureas were included.

INTERVENTIONS Participating PCPs attended at least 1 AD session that provided evidence to support diabetes medication reassessment and potential deprescribing strategies in older patients with type 2 diabetes. Prior to their visit with a participating PCP, trial patients were randomly assigned to receive either a previsit activation deprescribing handout (AD plus previsit arm) or an attention control healthy lifestyle handout (AD-only arm).

MAIN OUTCOMES AND MEASURES Primary outcomes (assessed at 6 months) were diabetes medication deprescribing (an aggregate measure) and any patient-reported severe hypoglycemia episodes.

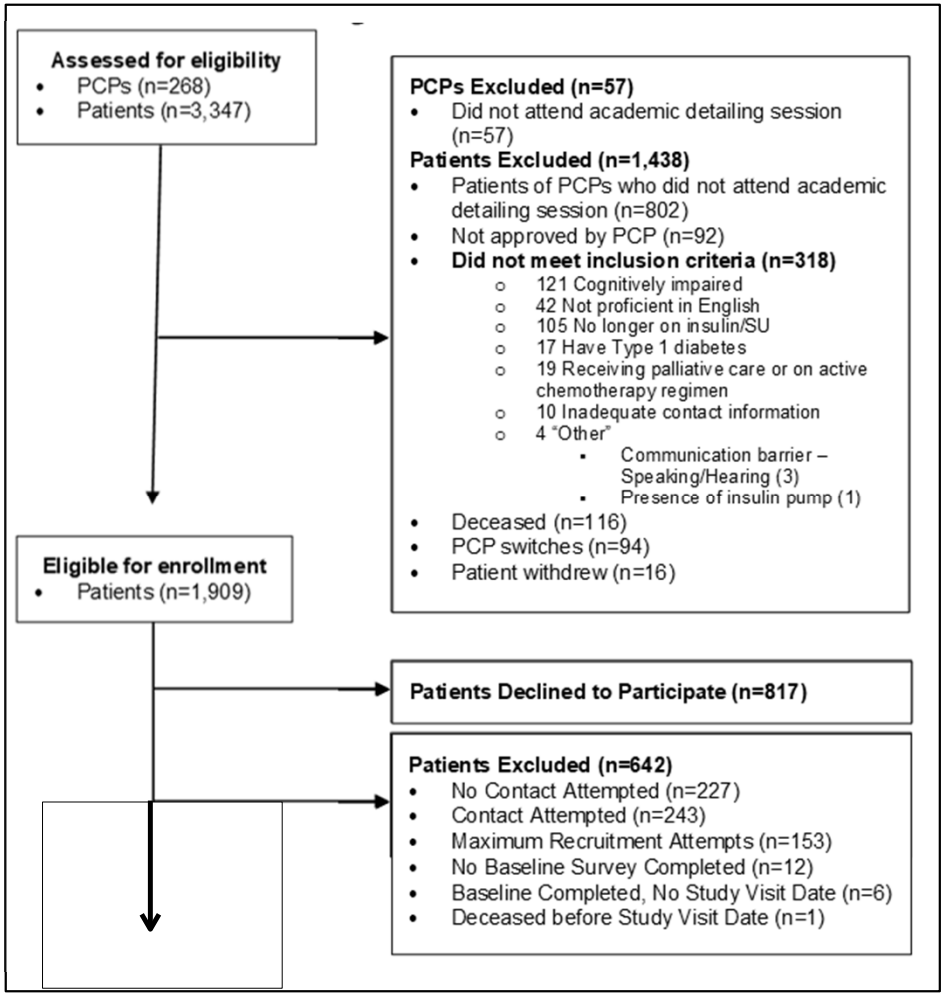
RESULTS A total of 211 PCPs were able to attend at least 1 AD session and treated 450 eligible patients (mean [SD] age, 79.9 [4.0] years; 223 [49.6%] female; mean [SD] concurrent chronic conditions, 6.2 [3.6]; and mean [SD] hemoglobin A_{1c}, 7.5% [1.1%]). At 6 months, there was a statistically significant higher diabetes medication deprescribing rate in the AD plus previsit activation arm compared with the AD-only arm (36 of 232 patients [15.8%] vs 19 of 218 patients [9.0%]; risk difference [RD], 7.5%; 95% CI, 1.5%-13.6%; $P = .01$); this difference persisted at 12 months (50 of 232 patients [22.8%] vs 33 of 218 patients [16.3%]; RD, 7.9%; 95% CI, 0.4%-15.5%; $P = .04$). There was not a statistically significant difference in severe self-reported hypoglycemia at 6 months between the AD plus previsit and AD-only arms (10 of 232 patients [4.7%] vs 13 of 218 patients [6.5%]; RD, −2.3%; 95% CI, −7.1% to 2.5%; $P = .04$).

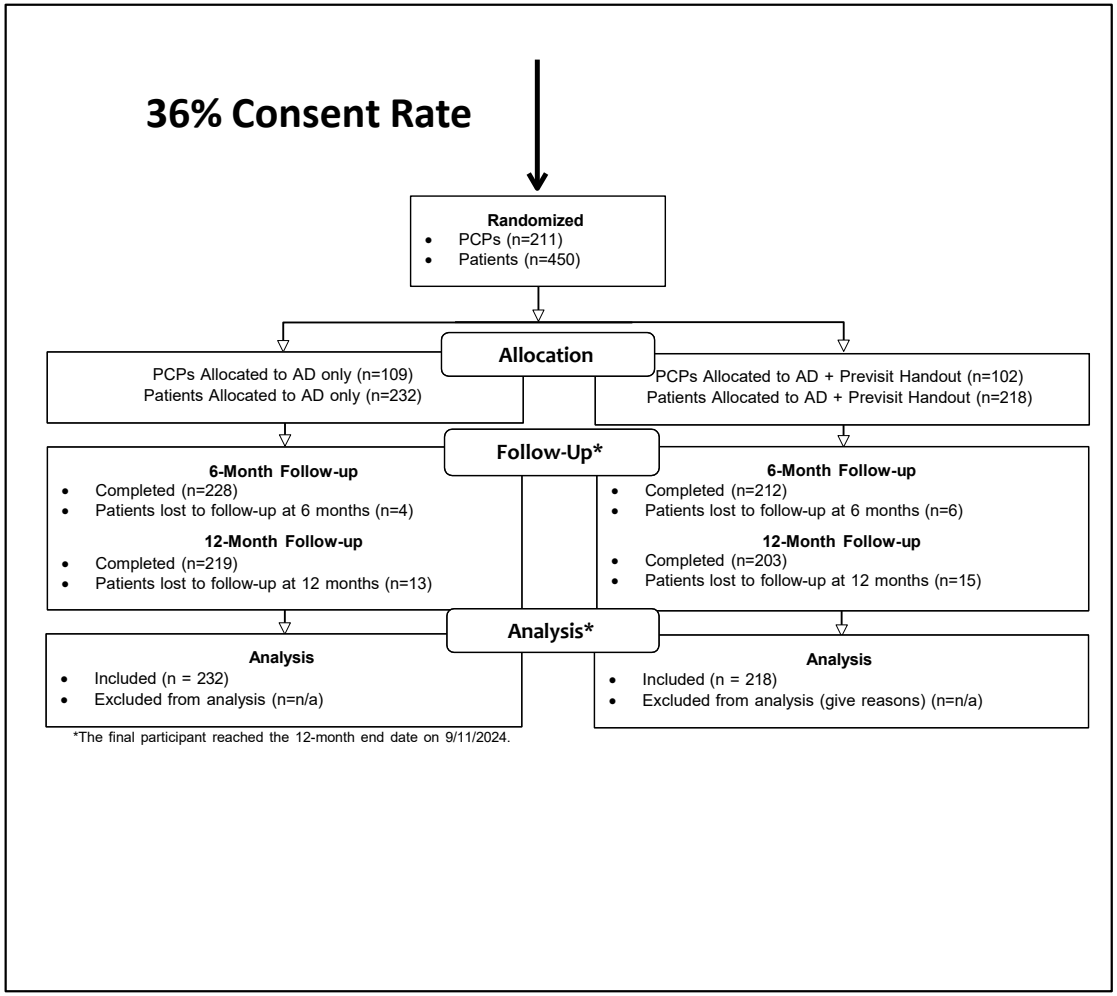
CONCLUSIONS AND RELEVANCE In this randomized clinical trial, AD with previsit activation was a simple and effective strategy for increasing diabetes medication deprescribing in older patients with type 2 diabetes.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT04585191

CONSORT
TRANSPARENT REPORTING of TRIALS

Physician and Patient CONSORT Flow Diagram





Comparative Effectiveness RCT Results

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

	Academic Detailing Pre-Visit Handout (n = 232)	**Academic Detailing alone (n = 218)**	**Risk Difference (95% CI)**	**P-value**
6-month follow-up				
Diabetes medication deprescribing, %	**15.8%**	**9.0%**	**7.5% (0.6%,14.4%)**	**0.02**
ED hypoglycemia-related admissions	0	4 (1.9%)	-1.9% (-3.8%, -0.2%)	0.037
12-month follow-up				
Diabetes medication deprescribing, %	22.8%	16.3%	7.9% (-0.7%,16.5%)	0.06
ED hypoglycemia-related admissions	4 (1.8%)	8 (3.9%)	-2.1% (-5.3%, 1.1%)	0.32

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

- No differences between arms in:
  - Self-reported severe hypoglycemia events
    - 10 events (4.7%) vs. 13 events (6.5%)
  - Problem Areas in Diabetes scores
  - Perceived Efficacy in Patient-Physician Interactions scores

- Patients receiving the previsit activation handout more likely to have diabetes discussion documented in the progress note
  - 59.9% vs 48.6%; adjusted RD, 11.3% (2.1%-20.4%); *P* = 0.02

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

No negative clinical consequences identified:

- Hyperglycemia-related Emergency department/hospital admissions were much less common than hypoglycemia-related admissions
  - Did not differ by study arm (<1% each arm)
- Similarly, there were no differences in glycemic control (HbA1c >8%) between study arms at 6 or 12 months.
  - 25.7% vs. 26.8% at 12 months
- Of the 49 patients who were deprescribed at 6 months, only 7 (14.3%) were no longer deprescribed at 12 months
  - 4 patients in AD plus handout arm vs. 3 patients in AD-only arm

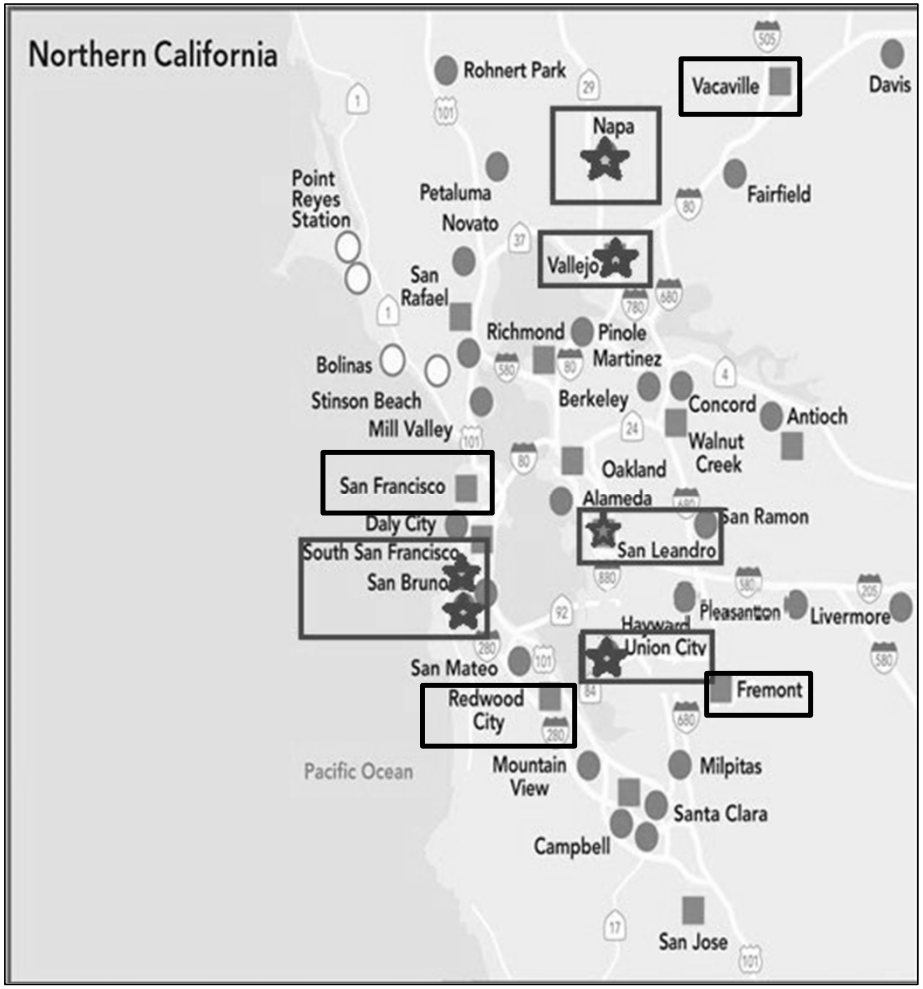
Usual Care Temporal Cohort Results

Question: How did RETRO-DM deprescribing rates (i.e., among PCPs exposed to AD) compare to “usual care” rates over 1 year?

Cohort Analysis Study Design

- Studied ***all*** eligible patients of ***all*** PCPs who attended Academic Detailing sessions in the first study year
  - Included **781** RETRO-DM eligible patients
  - No selection bias by patient RCT consent

- Two contemporaneous comparisons cohorts:
  - 35 PCPs in RETRO-DM primary care practices who were unable to attend AD sessions and their **265** study-eligible patients
  - 260 PCPs in neighboring KPNC medical facilities not involved in RETRO-DM and their **1331** study-eligible patients



Usual Care Comparison Cohort #1

35 PCPs unable to attend RETRO-DM AD sessions:

- Napa
- Vallejo
- South San Francisco
- San Bruno
- San Leandro
- Union City

Usual Care Comparison Cohort #2

260 PCPs from neighboring practices

- Vacaville
- San Francisco
- Redwood City
- Fremont

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

	PCPs who attended AD sessions (n = 125)	PCPs in CE-RCT practices unable to attend AD (n = 35)	PCPs from neighboring facilities not in CE-RCT (n = 260)	p-value
Age, years (SD)	45.1 (7.9)	47.0 (8.0)	45.1 (8.3)	0.44
Women, %	72.8	45.7	64.6	0.01
Years in Practice (SD)	18.4 (8.8)	17.5 (8.9)	19.6 (9.0)	0.32
Panel Size (SD)	2549 (832)	2584 (989)	2463 (996)	0.76

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

	Academic Detailing	Usual Care	Effect Estimate aOR (95% CI)	P-value
Usual Care within CE-RCT practices (PCPs unable to attend, n= 35)	19.1%	12.4%	1.83 (1.11, 3.01)	0.018
Usual Care, neighboring KPNC practices during same time period (n = 260)	19.1%	15.2%	1.34 (1.015 - 1.76)	0.039

Effect Estimates are adjusted Odds Ratios (aORs) and 95% Confidence Intervals (CIs); aORs, CIs, and p-values are derived from multilevel logistic regression models adjusted for baseline patient differences and with random intercept for PCP

RETRO-DM Conclusions

- Academic detailing is associated with higher deprescribing rates
- Activating the patient prior to the visit increases deprescribing
- Most patients (**75%-82%**) were not deprescribed
  - Age 75+ years; T2D on insulin or SU; A1c < 8%

Pragmatic considerations:

- *Intervention:* Get on practice calendar, make AD relevant
- *Consent:* PCPs provide assent (no direct data collection)
- *Outcomes:* Extensive code development (including NLP) to define prescription states; structured chart abstraction

A second safety strategy is more effective hypoglycemia prevention

Goal of SAGE study for participants receiving intervention:

Help empower you to:

- Know when you are going low
- Record and reflect on low sugar events
- Learn how to prevent future hypoglycemia

SAGE

Safer Aging with Diabetes Monitoring

Safer Aging (SAGE) with Diabetes Monitoring

Question: Can monitoring coupled with education reduce serious hypoglycemic events in older adults treated with insulin?

Patient Eligibility: age 75+ years; T2D on insulin

Design: Pragmatic randomized clinical trial

Intervention = Hands on training on how to apply and use a continuous glucose monitor followed by 2 group sessions with diabetes pharmacists to trouble shoot and problem solve hypoglycemia events

ClinicalTrials.Gov NCT06296485

SAGE
Safer Aging with Diabetes Monitoring

Safer Aging (SAGE) with Diabetes Monitoring

Primary Outcome: Hypoglycemia at 6- and 12-months

Definition: Self-reported (symptomatic and/or requiring help from others) and/or hypoglycemia-related utilization (emergency department, hospital or outpatient new events)

Additional Outcomes:

- Patient Self-report (confidence managing hypoglycemia, diabetes-related stress)
- Technology Proficiency survey

SAGE
Safer Aging with Diabetes Monitoring

SAGE: Pragmatic Issues for RCT Implementation

- Intervention Design:
  - Engaging older patients in technology use (CGM, apps, Teams)
- RCT Complexity:
  - Initially a 3-arm study
    - Usual care vs. 3 group sessions vs. 3 group sessions + 1:1 pharmacist
  - Scheduling group session cohorts
  - Virtual and recorded options
- "Contamination"
  - Usual care use of CGM

SAGE
Safer Aging with Diabetes Monitoring

SAGE: Pragmatic Issues for RCT Implementation

- Intervention Design:
  - Engaging older patients in technology use (CGM, apps, Teams)
- RCT Complexity:
  - Initially a 3-arm study
    - Usual care vs. 3 group sessions vs. 3 group sessions ~~*+ 1:1 pharmacist*~~
  - Scheduling group session cohorts
  - Virtual and recorded options
- "Contamination"
  - Usual care use of CGM

SAGE
Safer Aging with Diabetes Monitoring

Safer Aging (SAGE) with Diabetes Monitoring

SAGE
Safer Aging with Diabetes Monitoring

Intervention

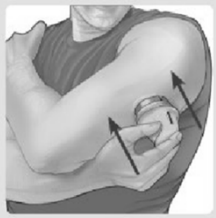
3 Group sessions:

- Session 1 = Technology teaching (in-person)
  - Explain CGM & apply CGM
  - Download and connect to monitoring app
  - Review Teams meeting process (for virtual sessions 2 & 3)

Continuous Glucose Monitor

Know when you're going low

- See current reading
- Hear alarm when below 70 mg



Place Sensor Applicator over site and push down firmly to apply Sensor.

Safer Aging (SAGE) with Diabetes Monitoring

<u>Sessions 2 & 3</u> = Experience-based group teaching with clinical pharmacist (virtual)

Review & Discuss Hypoglycemia Journal

Hypoglycemia Journal

SAGE
Safer Aging with Diabetes Monitoring

<u>Reflection Questions</u>:

In the past 2 weeks…

1) Did you have any low readings that surprised you?

2) Did information from your CGM readings lead you to make any changes to your medications, diet, or physical activity level? Please describe any changes made.

3) What questions do you have for the study pharmacist?

<u>SAMPLE JOURNAL ENTRY</u>

Please make notes when you experience low blood sugar symptoms and/or your sugars go below 70 mg/dL. Check any boxes that apply.

Day & Date	**Time**	**<u>If you checked your glucose reading, what was it?</u>**	
Monday, 12/11/23	☐Morning ☐Afternoon ☒Night	**What did you feel?** ***Notes:*** Shaky, tired, confused ☐ Did not feel symptoms	**Why did it happen?** ***Notes:*** Took insulin later than usual and did not eat my usual dinner ☐ Not sure/ don't remember
What changes can you make to prevent this from happening again? Stay on same schedule with medications and meals. Set alarms to remind me when it is time for insulin. Eat at regular times.			

Safer Aging (SAGE) with Diabetes Monitoring – *In Progress*

	Cumulative	Target	% of Target
Number Enrolled	196	360	54.4%

Consent Rate: 196 out of 1227 (16.0%)

Not Eligible Reasons:

- **Cognitive Impairment:** 86 out of 655 (13.3%)
- **CGM:** 114 out of 655 (17.4%)
- **Failed Hypo Screen:** 134 out of 655 (20.5%)

SAGE
Safer Aging with Diabetes Monitoring

SAGE Conclusions

A Qualitative Study of Older Adult Perspectives on Continuous Glucose Monitoring for Type 2 Diabetes
Tanenbaum ML *et al. JGIM* **40**, 2624–2633 (2025).

- Intervention development:
  - Perceived CGM barriers included challenges with wearability and reliability, burdens to others, distrust of technology, sensory and learning challenges, insufficient clinician support or engagement, and access and payer hurdles.
  - Non-users were able to formulate many usability questions, providing a snapshot of informational needs for this age group.
- Enrollment and group sessions experiences: New clinical insights

Pragmatic considerations:

- *Intervention: Technology* -> First session had to be in person
- *Design:* Simplify to 2-arm study
- *Contamination:* 17% exclusion, “once randomized always analyzed”, follow weekly rates for trend

Thank You!

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

Comparison of eligible PCPs who attended vs did not attend Academic Detailing sessions

	Attended (n = 211 PCPs)	**Unable to Attend (n = 57 PCPs)**	**p-value**
Age, years (SD)	44.8 (8.2)	45.7 (8.1)	0.5
Women, %	67.8%	54.4%	0.06
Years in Practice (SD)	17.8 (9.2)	16.9 (9.4)	0.53
Panel Size (SD)	2456 (920)	2257 (966)	0.16

Reducing Treatment Risk in Older Adults with Diabetes Mellitus (RETRO-DM)

6- and 12-month loss to follow-up, overall and by study arm

	Overall	AD + Handout	AD Only	p-value
6-month loss to follow up	**2.2%**	1.7%	2.8%	0.46
Death, n	6	2	4	
Loss of membership, n	1	0	1	
Worsened Health, n	2	1	1	
Withdrawal of consent, n	1	1	0	
12-month loss to follow up	**6.2%**	5.6%	6.9%	0.92
Death, n	17	7	10	
Loss of membership, n	1	0	1	
Worsened Health, n	6	3	3	
Withdrawal of consent, n	4	3	1	