Two Randomized Controlled Trials of Nudges to Encourage Referrals to Centralized Pharmacy Services for Evidence-Based Statin Initiation in High-Risk Patients:
The SUPER LIPID Program

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ASCVD RISK REDUCTION INITIATIVE

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Disclosures

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Gaps in evidence-based statin prescriptions

- In patients with or at high risk for ASCVD, statins reduce major adverse cardiovascular events by 33-50%

- > 50% of U.S. adults with an indication are not prescribed statins at guideline-recommended intensity

- In hypothetical patient scenarios, the vast majority of clinicians indicate they would prescribe statins to patients for whom they're indicated

- Physicians have limited time to cover acute and preventive needs in office visits, and do not have time allocated to population health management

- Pharmacists can be used to increase statin prescriptions to appropriate patients as part of a population health management strategy, but it is uncertain how to optimize referrals of appropriate patients

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Objectives

- To test two strategies for integration of centralized pharmacy services for lipid management into clinician workflow:
    - Interruptive, pop-up EHR notification strategy (visit-based)
    - Asynchronous strategy (non-visit-based)

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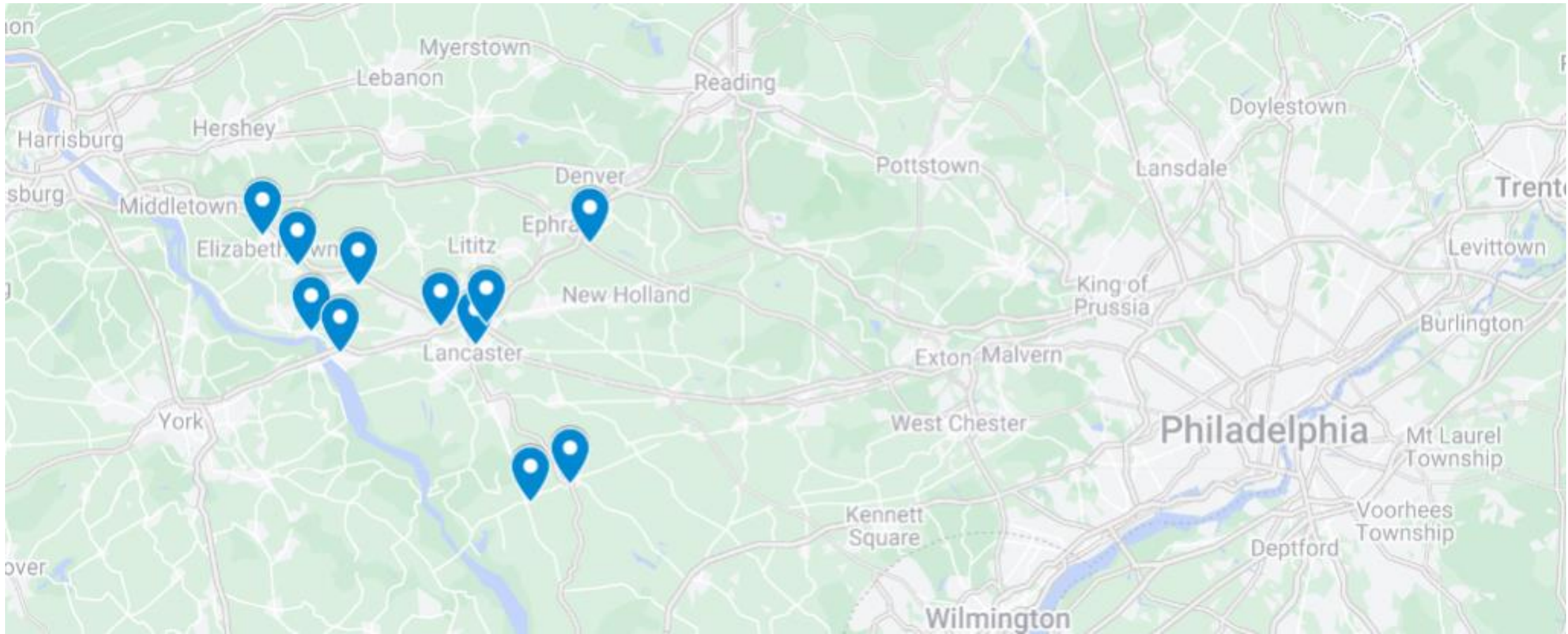
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Methods

- Two parallel clinical trials:
  - Stepped wedge trial of visit-based interruptive pop-up EHR notification with recommendation to refer patients to centralized pharmacy for consideration of statin initiation versus usual care
  - Cluster randomized trial of non-visit-based, automatically-placed orders for referral to centralized pharmacy for consideration of statin initiation versus usual care

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Patient population

- Eligible patients identified via EHR algorithms

- Patients assigned a primary care provider at participating clinics who were not prescribed a high- or moderate-intensity statin, despite an indication:
  - ASCVD risk > 10% by pooled cohort equation
  - Diabetes mellitus
  - LDL-C > 190 mg/dl
  - Familial hyperlipidemia
  - Established ASCVD

- Exclusion criteria:
  - Documented allergy or intolerance to statins
  - GFR < 30 ml/min or on hemodialysis
  - Prescribed PCSK9 inhibitor
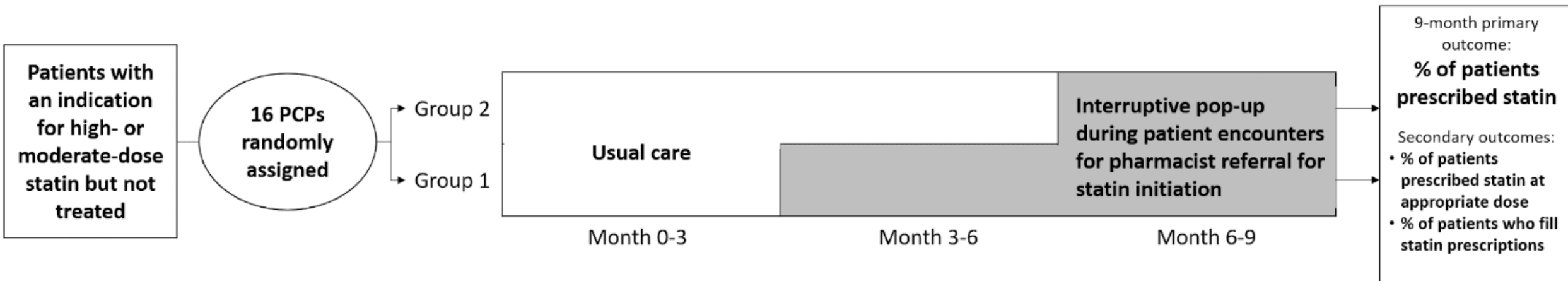 - Pregnant or breast-feeding
  - Hospice

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Trial sites

Methods – pharmacist protocol

- Upon receiving a referral, pharmacists reviewed the chart and confirmed that the patient was appropriate for treatment with statin
    - Patients with contraindications to statin initiation and those who had declined statins when offered by a clinician within the past 2 years were not contacted
- Pharmacists then called the patients, discussed initiation of statins, and (if the patient agreed) prescribed a statin and ordered follow-up labs as indicated

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Methods – stepped wedge RCT of visit-based intervention

Methods – stepped wedge RCT of visit-based intervention
Statistical analyses and power calculation

- Analyses conducted under the intention-to-treat principle, including all patients for whom the interruptive pop-up notification appeared or would have appeared at the time of their visit

- Generalized estimating equations to compare intervention and usual care arms, with terms to account for clustering by PCP

- Assuming each PCP sees an average of 60 eligible patients per 3-month block (total n = 2880), ICC of 0.05, and baseline prescription rate of 30% in the usual care arm ▢ 80% power to detect an OR 1.6, corresponding to a 10.7% absolute increase in statin prescriptions

Results – stepped wedge RCT of visit-based intervention
Baseline characteristics

|	Group 1 BPA started month 3 (n = 970)	Group 2 BPA started month 6 (n = 672)	p value
Age	68.9 ± 10.1	67.8 ± 9.2	0.08
Female sex	35.9%	55.4%	< 0.001
Black race	1.0%	1.0%	0.69
Hispanic	0.8%	0.9%	0.83
ASCVD risk by PCE	19.7 ± 10.8%	18.4 ± 10.1%	0.04
Baseline LDL	101 ± 33	111 ± 34	< 0.001
Hypertension	74.8%	70.8%	0.07
Current smoker	12.9%	12.6%	0.39

Results – stepped wedge RCT of visit-based intervention
Response to notification

- PCPs saw the notification ~ 11.5 times per month

- Overall notification fired 3579 times in 913 patients over 6 months

- An order was entered in response to the notification 165 times (4.6% of all BPA firings, 18% of all patients)
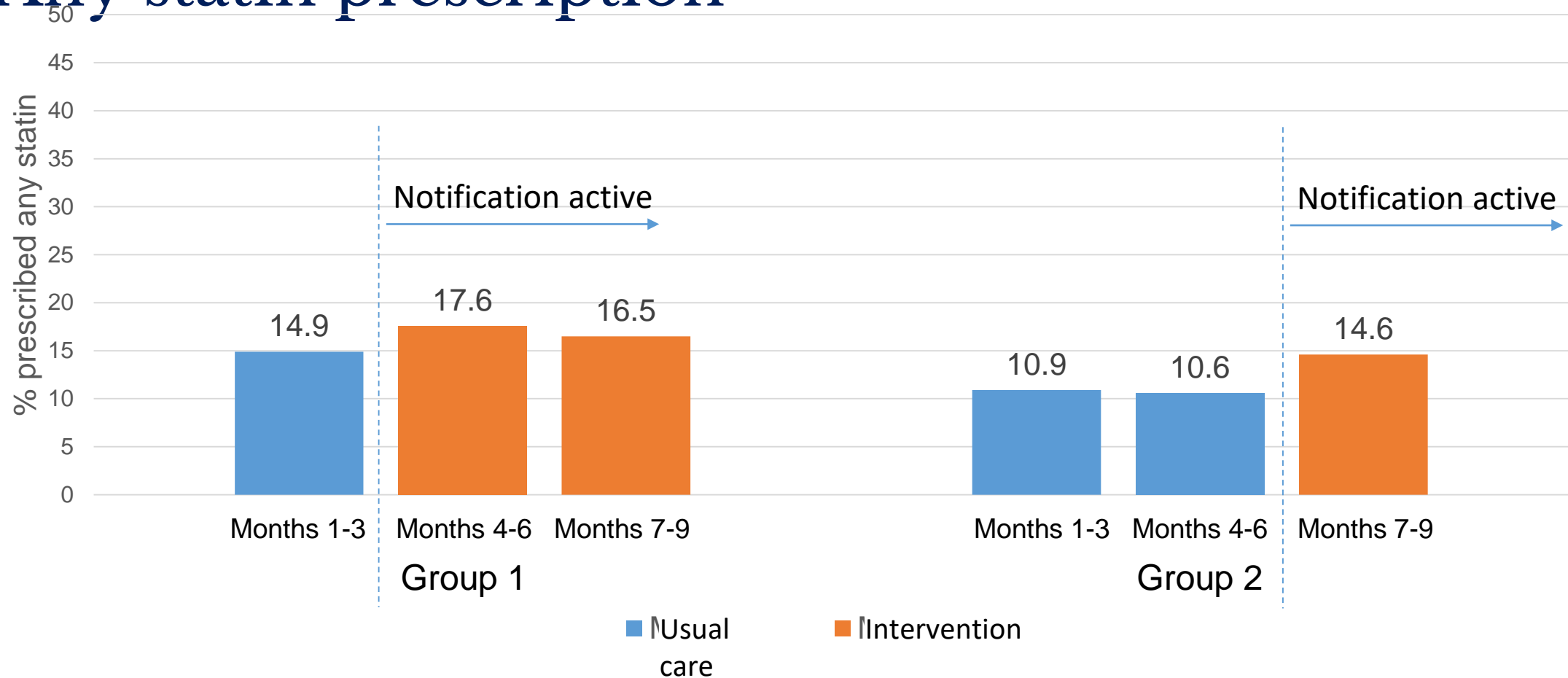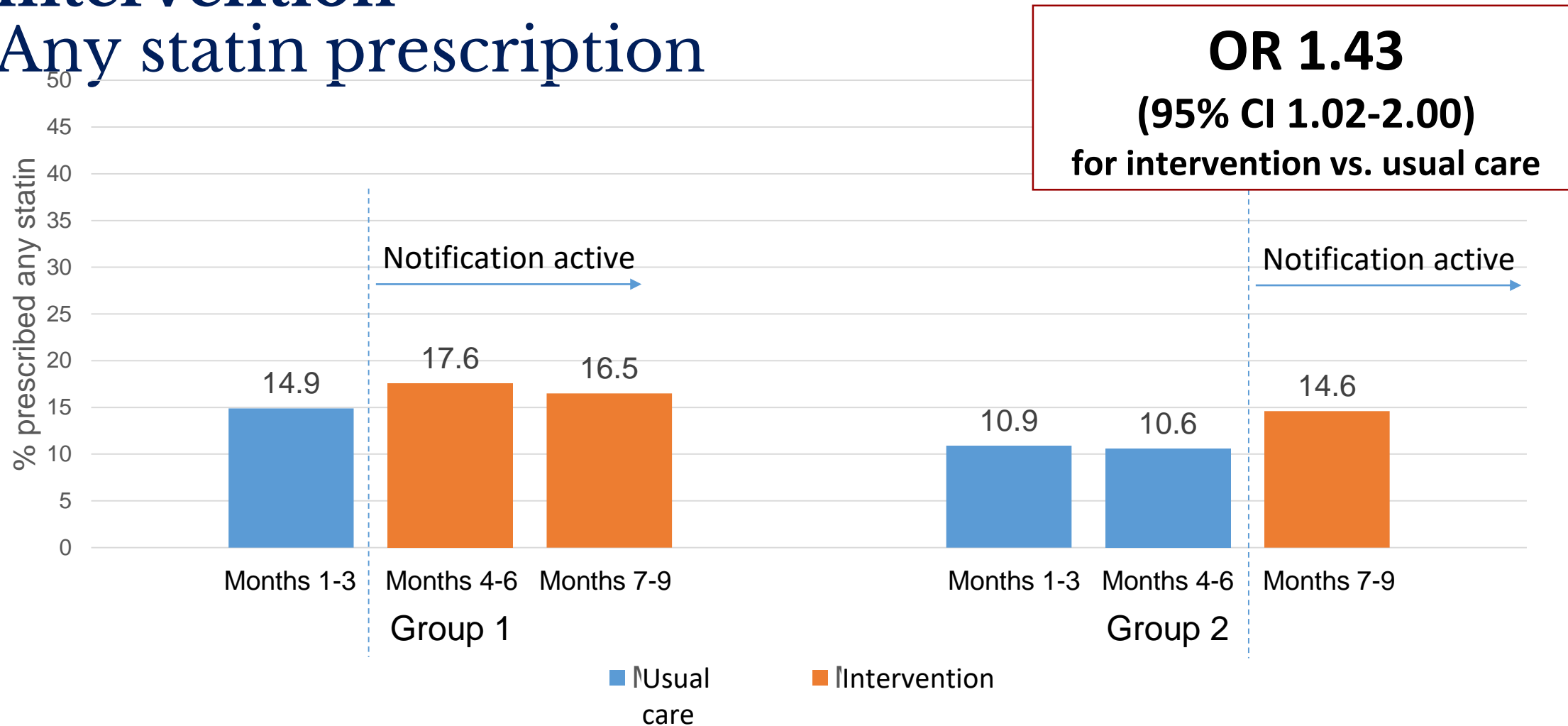
Results – stepped wedge RCT of visit-based intervention
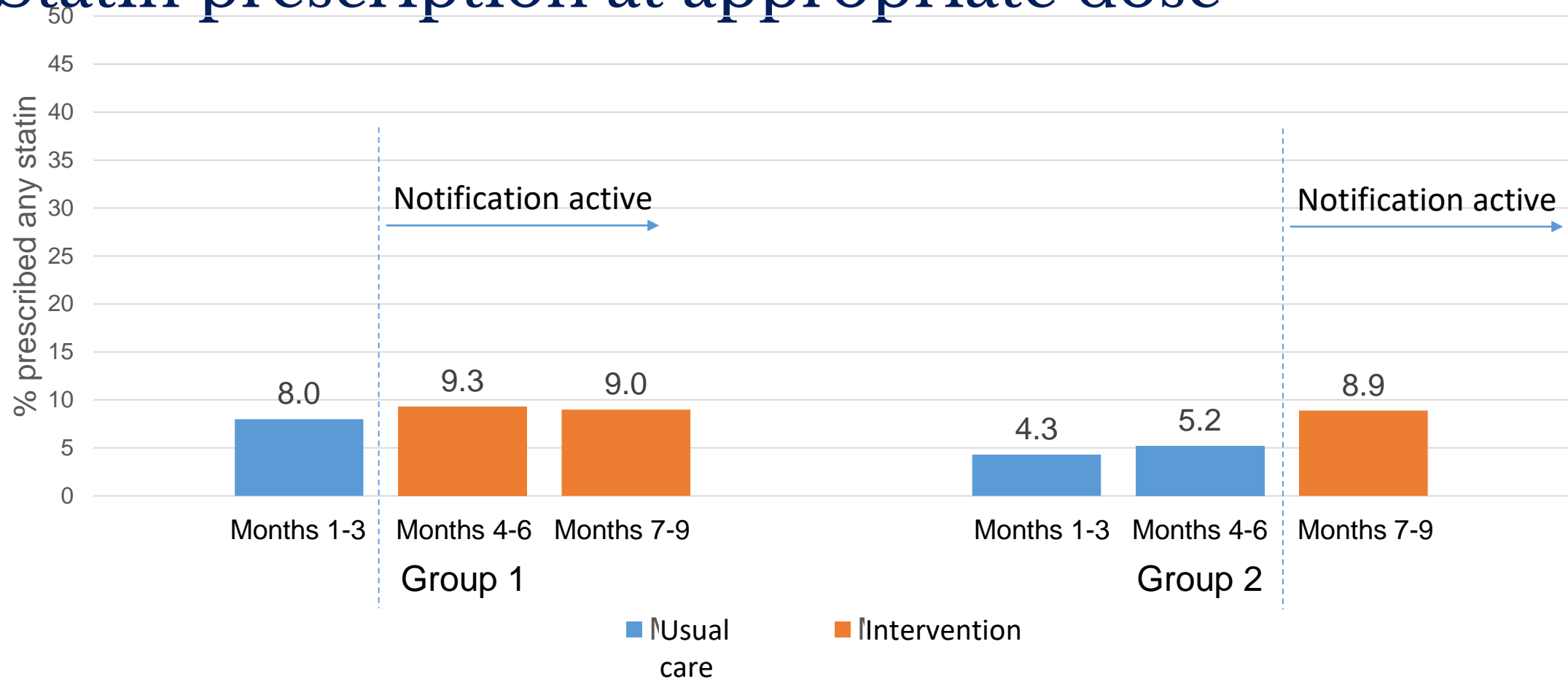## Any statin prescription

Results – stepped wedge RCT of visit-based intervention
Any statin prescription

OR 1.43
(95% CI 1.02-2.00)
for intervention vs. usual care

% prescribed any statin

Group 1
- Months 1-3: 14.9
- Months 4-6: 17.6 (Notification active)
- Months 7-9: 16.5

Group 2
- Months 1-3: 10.9
- Months 4-6: 10.6
- Months 7-9: 14.6 (Notification active)

Usual care   Intervention

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Results – stepped wedge RCT of visit-based intervention
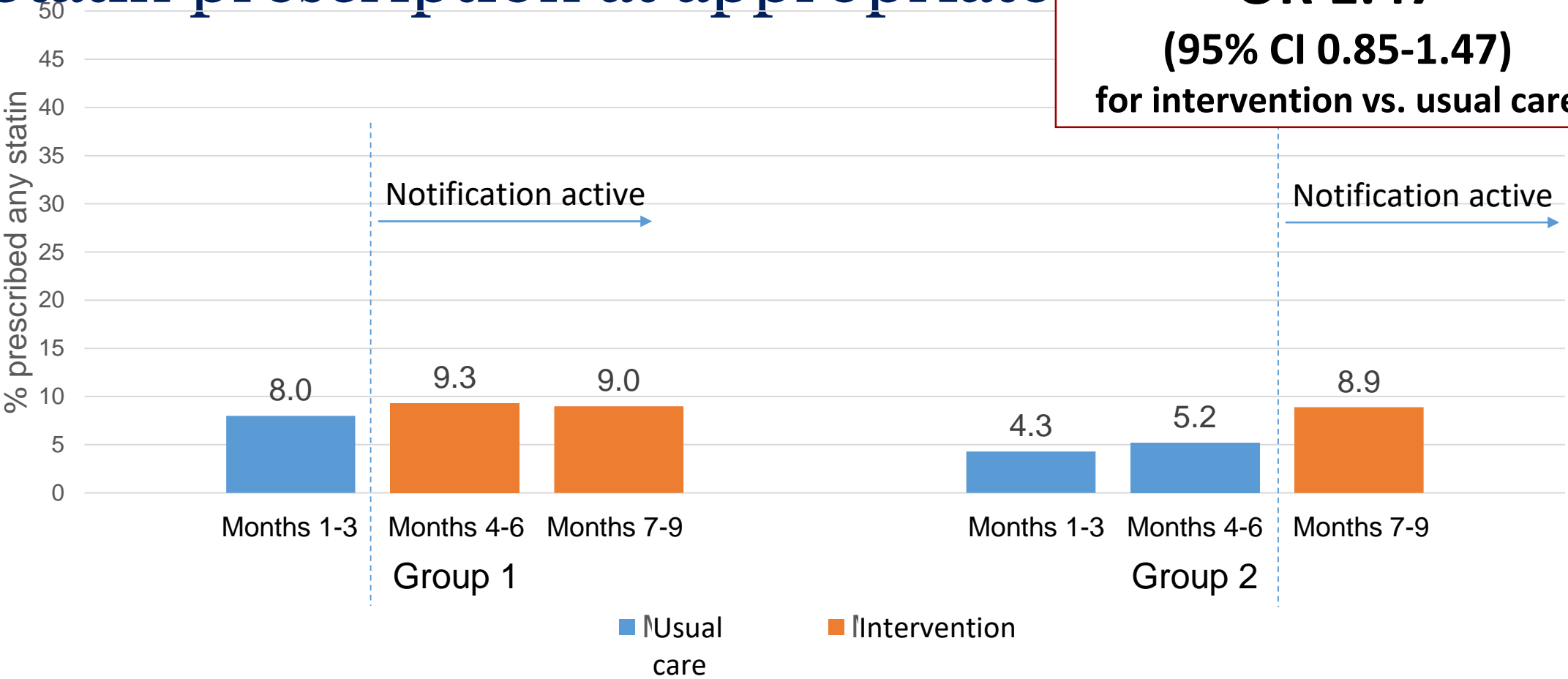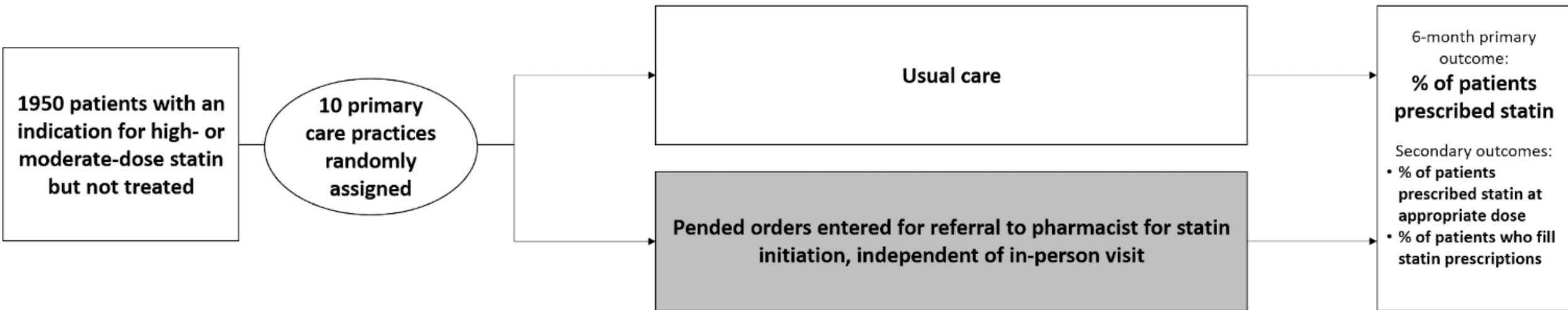## Statin prescription at appropriate dose

Results – stepped wedge RCT of visit-based intervention
Statin prescription at appropriate

OR 1.47
(95% CI 0.85-1.47)
for intervention vs. usual care

Methods – cluster RCT of non-visit-based intervention

1950 patients with an indication for high- or moderate-dose statin but not treated

10 primary care practices randomly assigned

Usual care

Pended orders entered for referral to pharmacist for statin initiation, independent of in-person visit

6-month primary outcome:
% of patients prescribed statin

Secondary outcomes:
- % of patients prescribed statin at appropriate dose
- % of patients who fill statin prescriptions

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Methods – cluster RCT of non-visit-based intervention
Statistical analyses and power calculation

- Analyses conducted under the intention-to-treat principle: eligible patients were identified prior to the start of the intervention period, and were analyzed in the group to which they were assigned (even if they became ineligible prior to being contacted by pharmacy)

- Generalized estimating equations to compare intervention and usual care arms, with terms to account for clustering by practice

- 10 practices with ~ 195 patients per practice (n = 1950), ICC of 0.05, and baseline prescription rate of 30% in the usual care arm ⮕ 80% power to detect a 12.1% absolute increase in statin prescriptions

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Results – cluster RCT of non-visit-based intervention
Baseline characteristics

	Intervention (n = 975)	Usual care (n = 975)	p value
Age	63.3 ± 10.3	64.6 ± 9.7	< 0.001
Female sex	45.6%	41.8%	0.09
Black race	5.6%	5.2%	0.006
Hispanic	6.2%	7.9%	0.26
ASCVD risk by PCE	17.4 ± 9.2%	16.7 ± 8.4%	0.23
Baseline LDL	118 ± 33	115 ± 43	0.005
Hypertension	63.4%	57.0%	0.004
Current smoker	24.1%	15.0%	< 0.001

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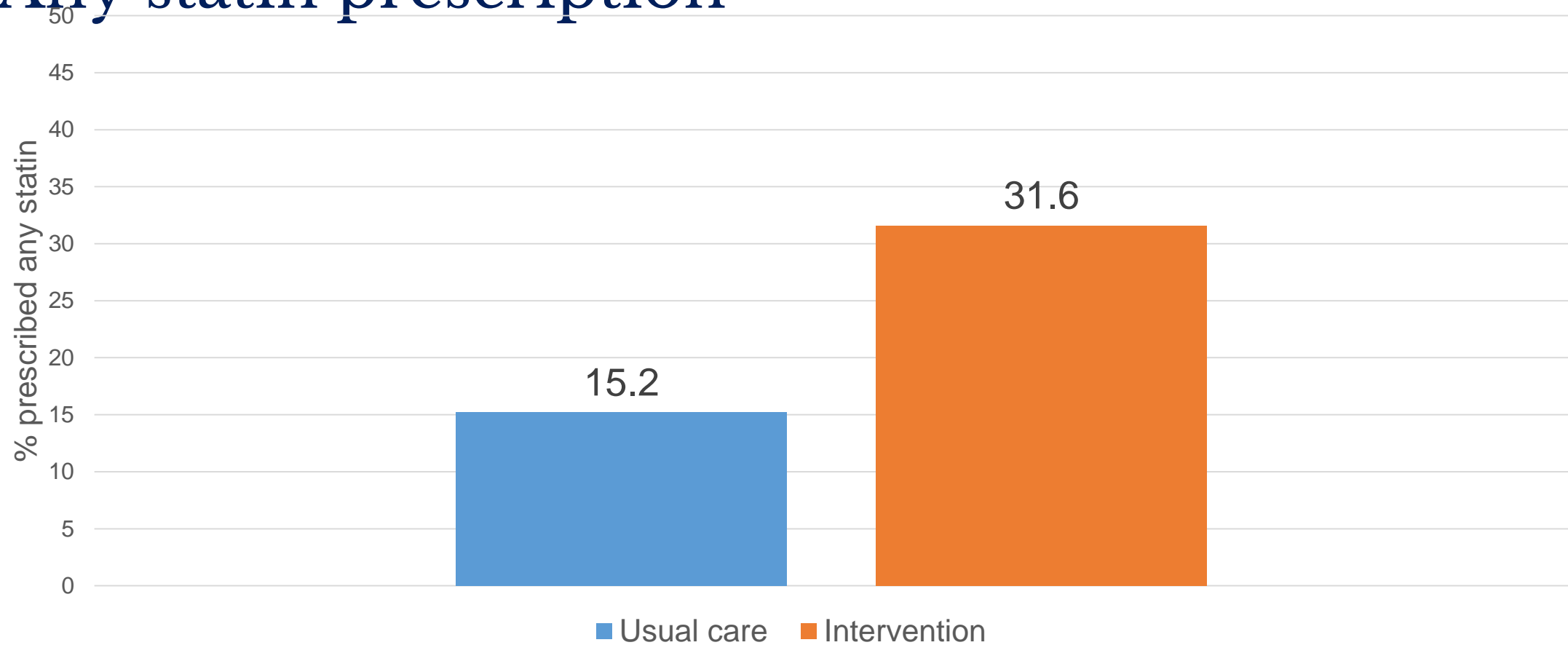
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Results – cluster RCT of non-visit-based intervention
Response to orders placed for cosign

- 719 orders cosigned (73.7%) and referral to centralized pharmacy initiated

Pie chart legend:
- Target dose statin started — 28%
- Patient declined statin — 19%
- Patient not reached — 18%
- Patient considering statin — 12%
- Statin contraindicated — 6%
- Patient previously declined statin — 10%
- Other — 8%

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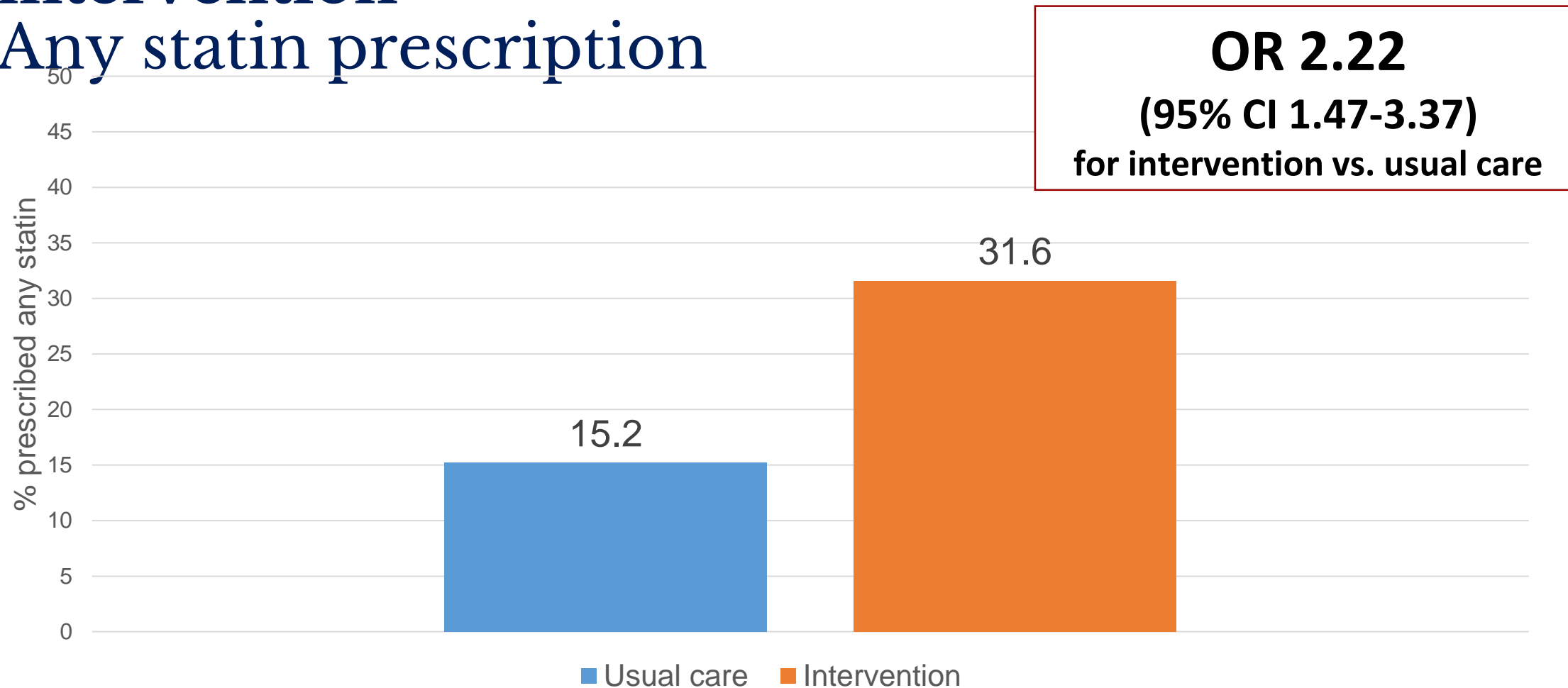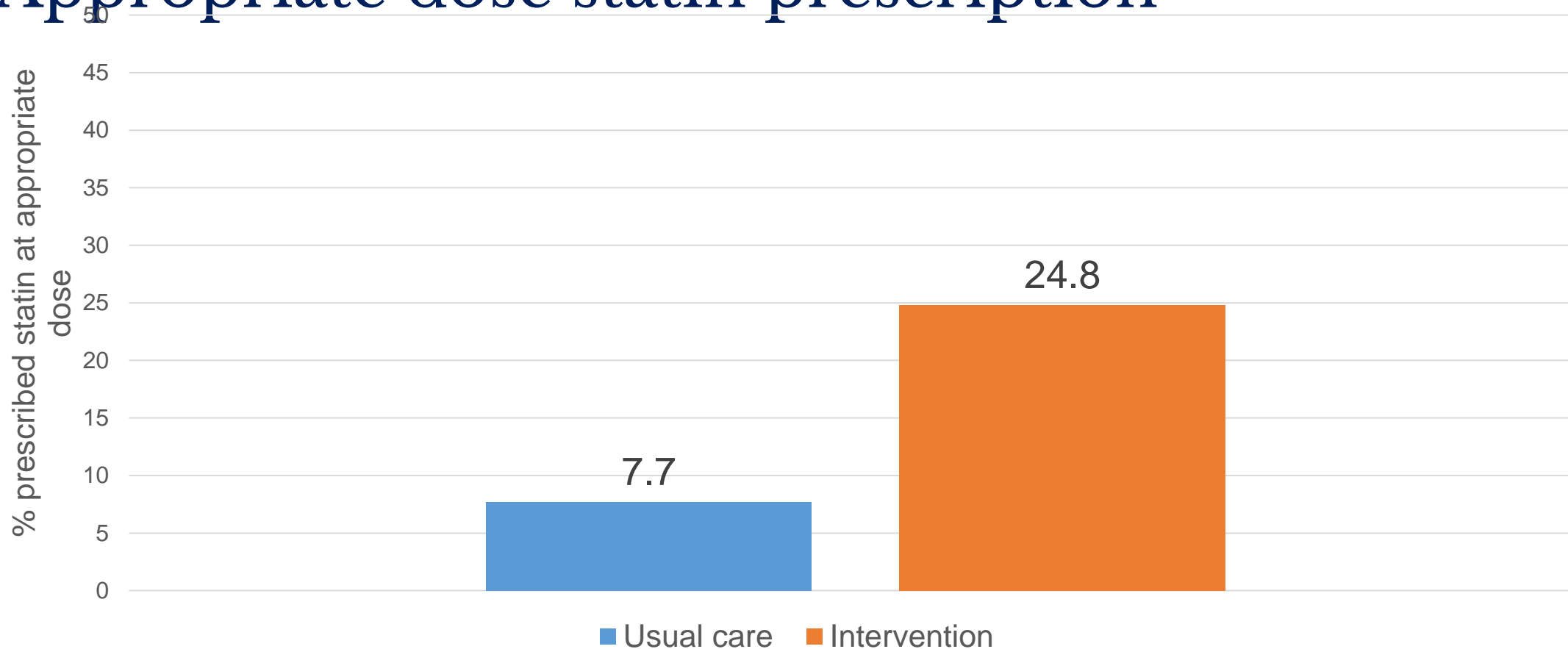
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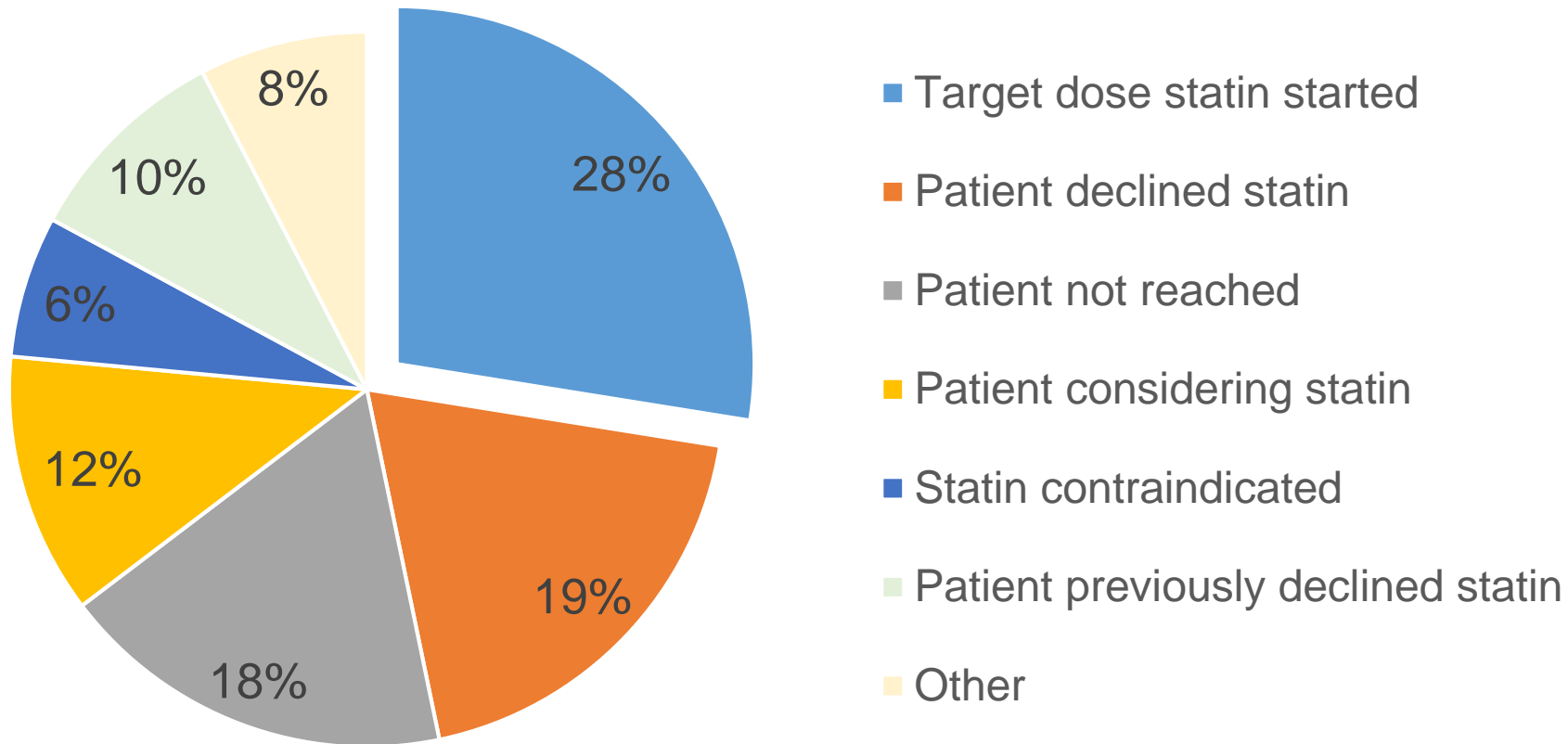
Results – cluster RCT of non-visit-based intervention
Any statin prescription

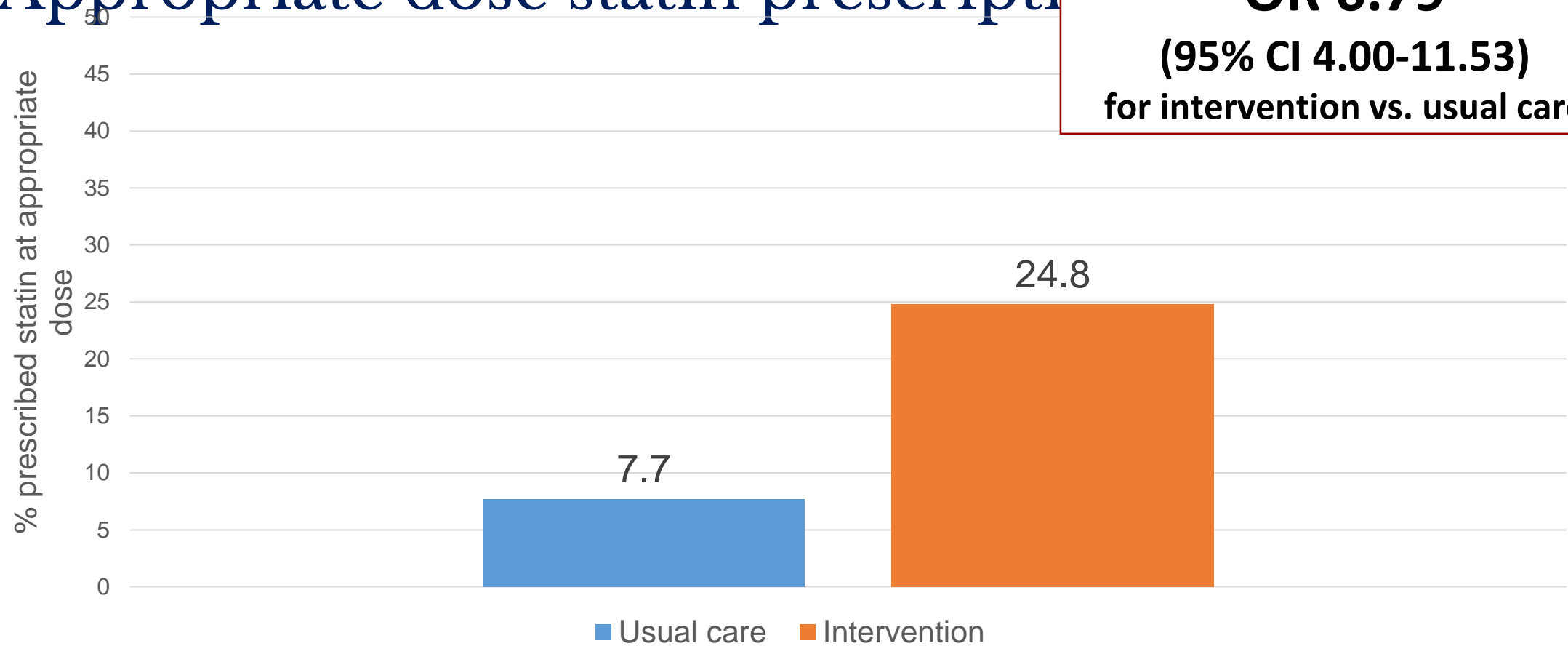# Results – cluster RCT of non-visit-based intervention
Any statin prescription

OR 2.22
(95% CI 1.47-3.37)
for intervention vs. usual care

% prescribed any statin

15.2 — Usual care
31.6 — Intervention

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Results – cluster RCT of non-visit-based intervention
Appropriate dose statin prescription

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Results – cluster RCT of non-visit-based intervention
Appropriate dose statin prescripti[on]

OR 6.79
(95% CI 4.00-11.53)
for intervention vs. usual care

% prescribed statin at appropriate dose

7.7

24.8

■ Usual care   ■ Intervention

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Limitations

- Visit-based trial did not reach enrollment goal

- Randomization at the level of practice and physician ⬚ imbalance between groups

- No direct comparison between BPA and pended order strategies

- No data collected on statin adherence or effects on longer-term cardiovascular event rates

Conclusions

- In two simultaneous pragmatic trials:
  - An asynchronous strategy of orders to centralized pharmacy placed for cosign increased prescriptions of any statin by 16 percentage points versus usual care, and of appropriate dose statin by 17 percentage points
  - An interruptive EHR notification strategy had a smaller effect on statin prescriptions and no effect on appropriate dose statin prescription
- A centralized asynchronous model could be an effective adjunct to visit-based clinical interactions in increasing statin prescribing for high-risk patients

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Thanks to the team!

PennMedicine downtown

- Kayla Clark, MPH
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- Kevin Volpp, MD, PhD

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- Wendell Kellum, MD
- Dwight Eichelberger, MD
- John Wood, MD
- Zachary Bricker, MSN, RN
- Andrea Dooley-Wood, PharmD
- Greta Kemmer, PharmD
- Jennifer Smith, PharmD

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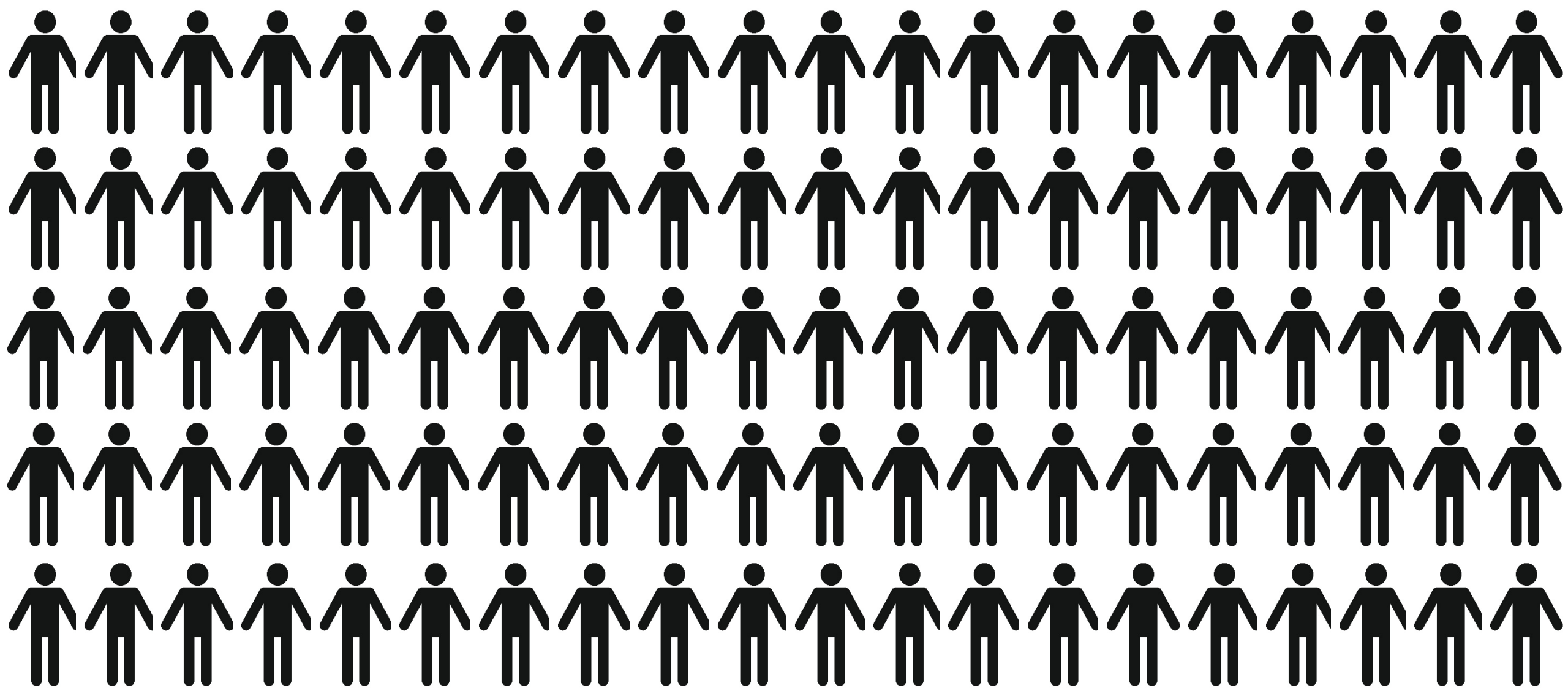Institute for Translational Medicine and Therapeutics

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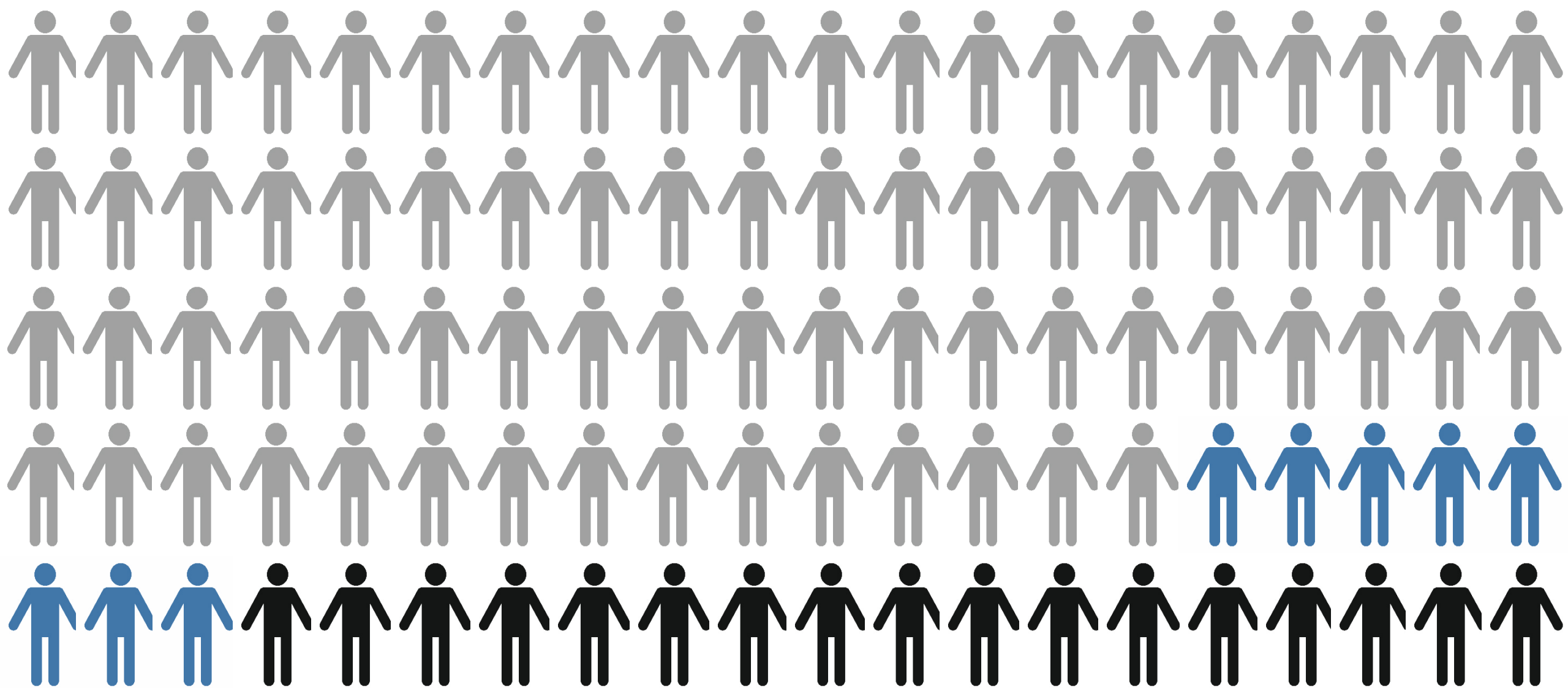
Extra slides

Implications

- What are the clinical implications of a 17 percentage point increase in prescriptions of statins in high-risk patients?
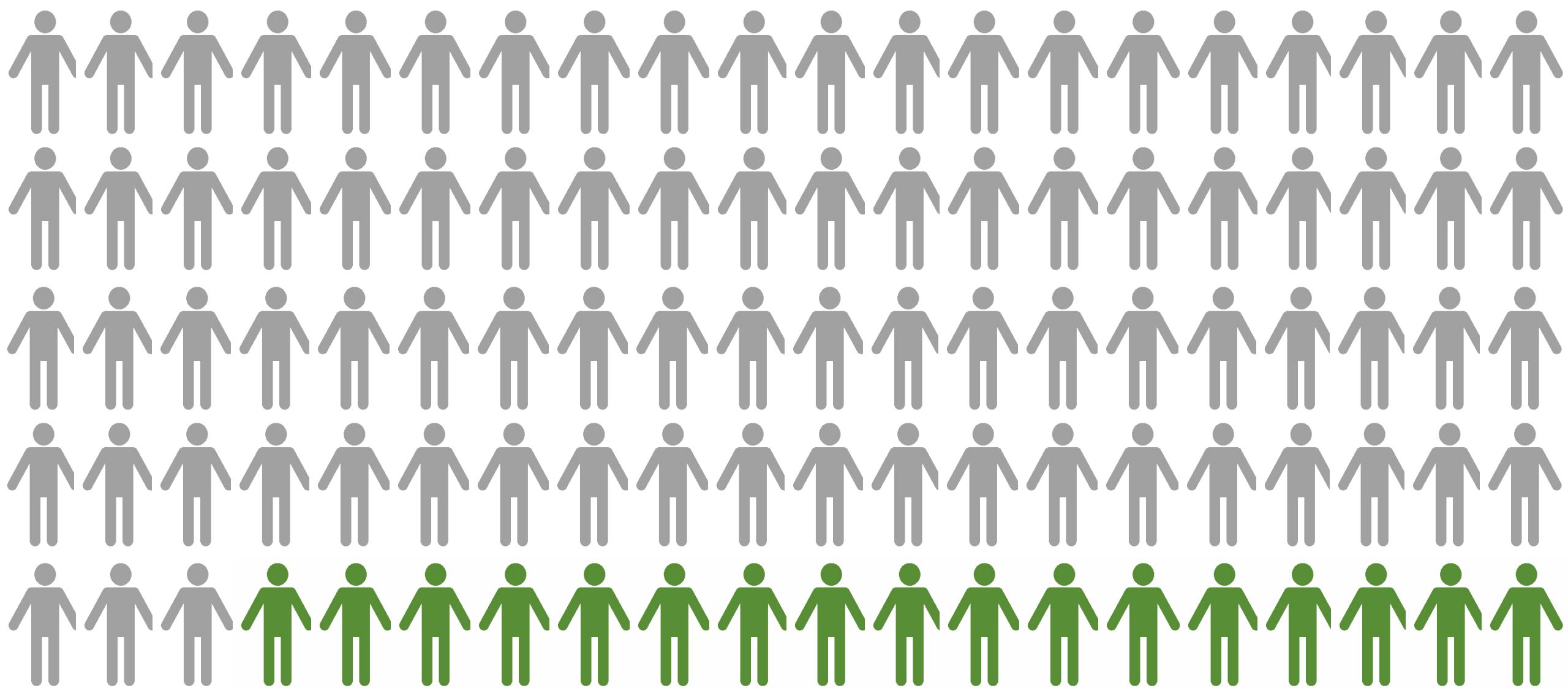
100 patients with an indication for a statin, not prescribed a statin...

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75 not prescribed a statin

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8 prescribed a statin in the course of usual care

17 prescribed a statin by involving centralized pharmacy
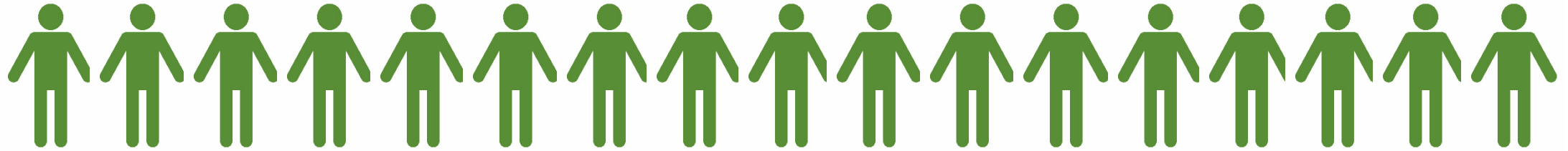
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ASCVD risk = 17% risk of CV death, MI, stroke over 10 years

Relative risk reduction from statins = 33%

ASCVD risk of this group, after statin initiation = ~ 11%

Absolute risk reduction = ~ 6%

Number needed to treat = ~ 17

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ASCVD risk = 17% risk of CV death, MI, stroke over 10 years

Relative risk reduction from statins = 33%

ASCVD risk of this group, after statin initiation = ~ 11%

Absolute risk reduction = ~ 6%

Number needed to treat = ~ 17

1 cardiovascular event saved per 100 orders placed

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