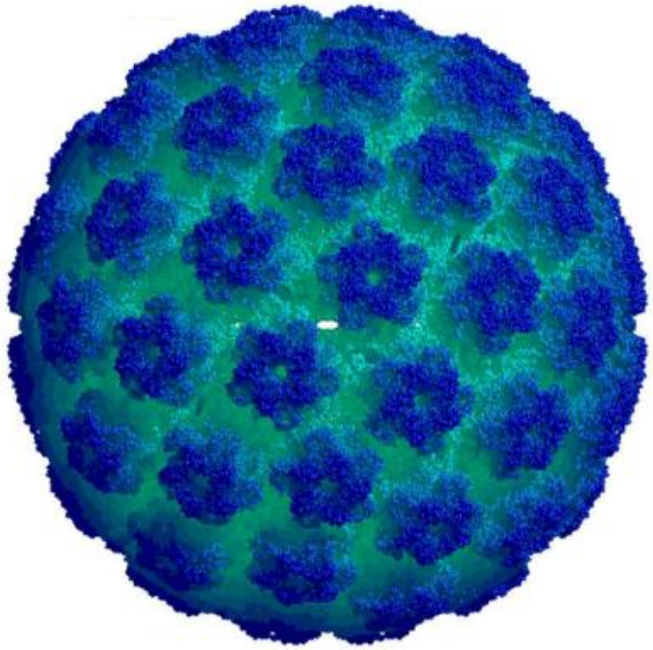
Designing & testing the future of home-based cervical cancer screening: results from a collaborative academic-embedded delivery system pragmatic randomized trial



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Funding: National Cancer Institute - R01CA168598, PI Winer
ClinicalTrials.gov: NCT02005510

Disclosure

None of the coauthors have any conflicts of interest to disclose

HPV and Cervical Cancer

- Human papillomavirus (HPV) is a common sexually transmitted infection.

- Most infections resolve spontaneously – a minority persist and cause pre-cancerous changes to cells of the cervix.

- Almost all cervical cancers are caused by human papillomavirus

Cervical Cancer Screening

- Two screening tests are used for prevention or early detection of cervical cancer:
  - **Pap tests** identify abnormal cells on the cervix
  - **HPV tests** detect the virus that causes these abnormal cells

  - Pap and HPV tests are used individually or in combination (co-testing)

2018 USPSTF Guidelines

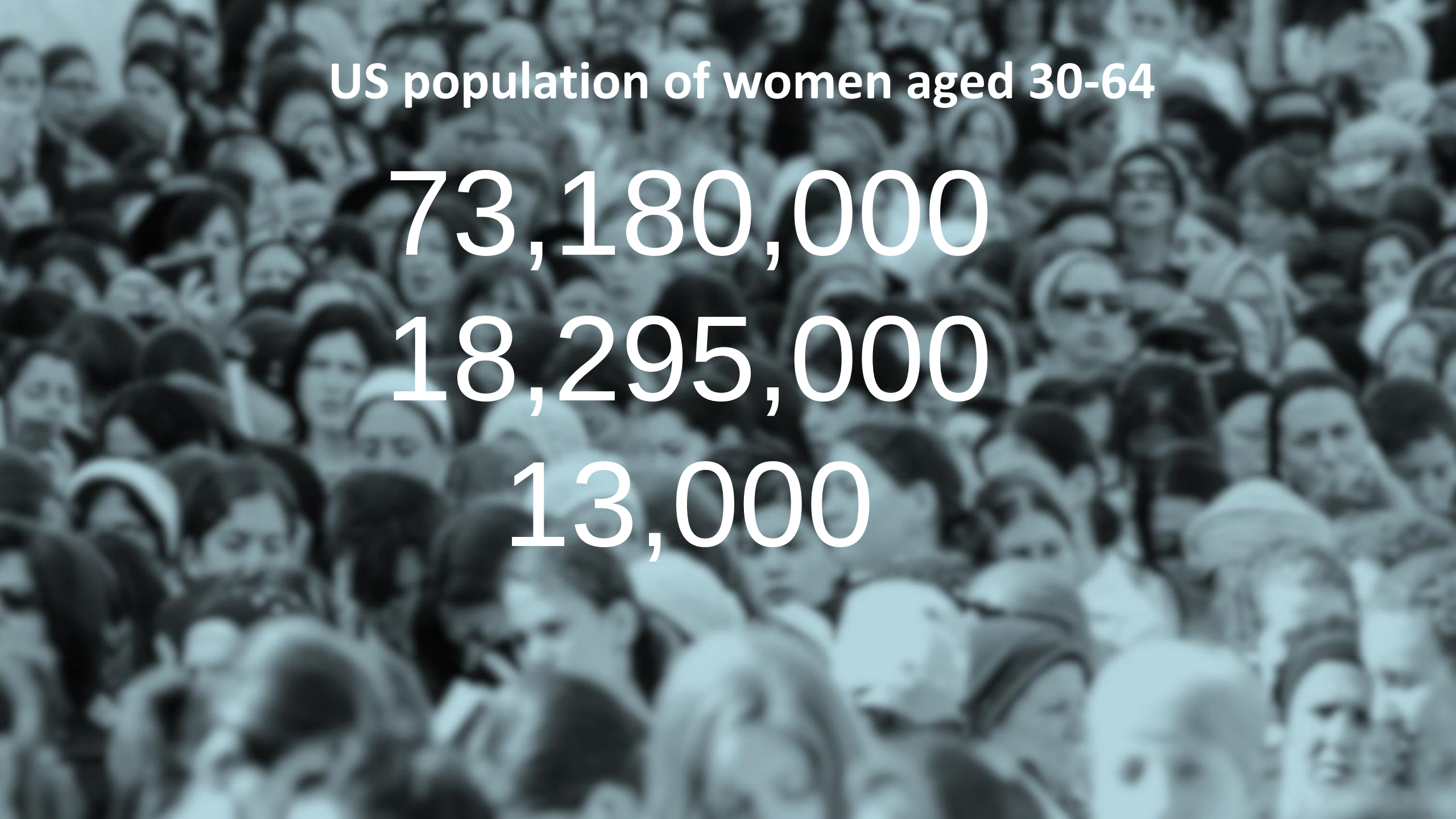
21-29 years: Pap every 3 years

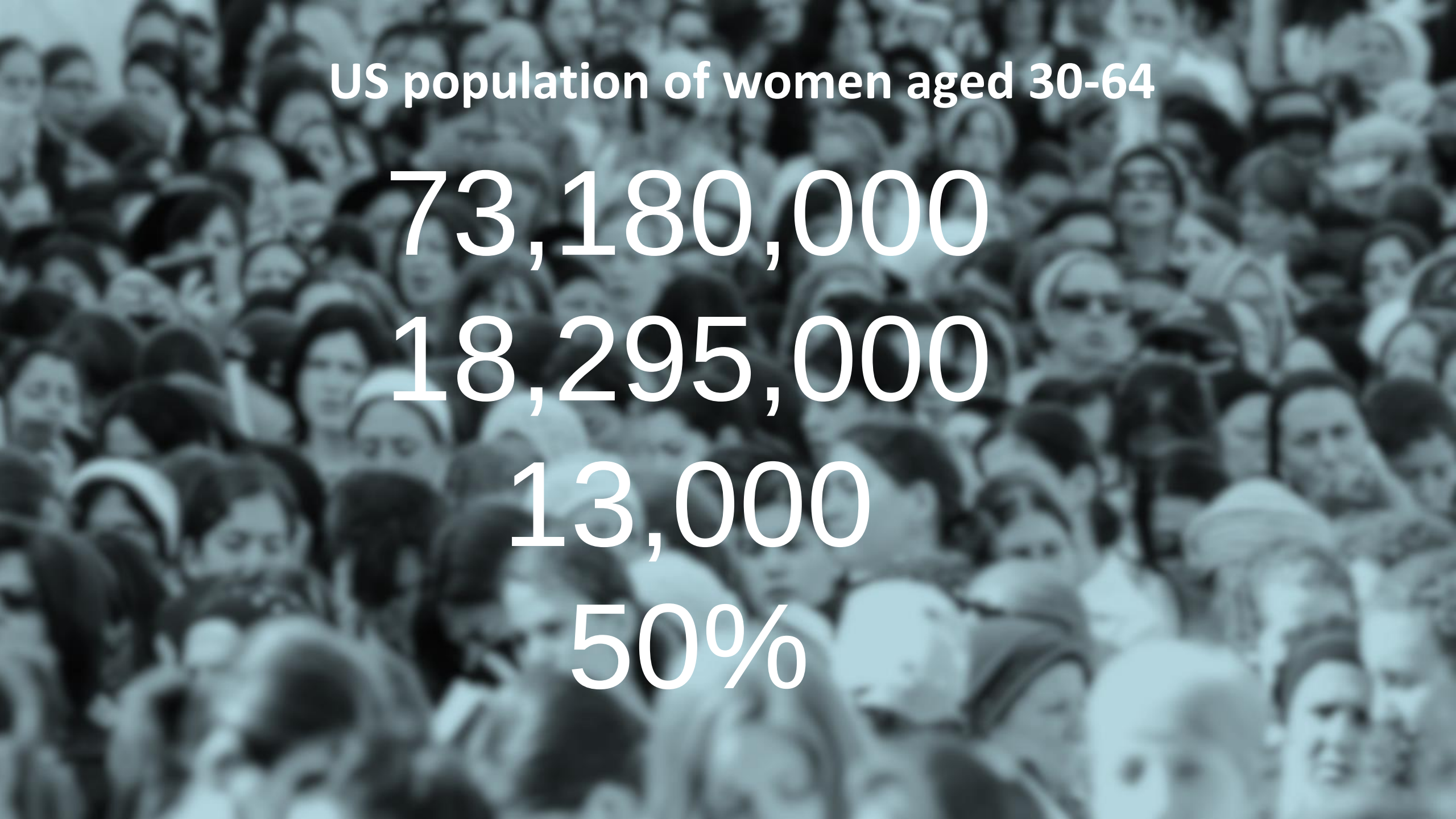
30-65 years: 3 options:

1) Pap every 3 years
2) HPV alone (i.e. “primary HPV”) every 5 years
3) Co-test every 5 years


US population of women aged 30-64
73,180,000


US population of women aged 30-64
73,180,000
18,295,000


US population of women aged 30-64
73,180,000
18,295,000
13,000

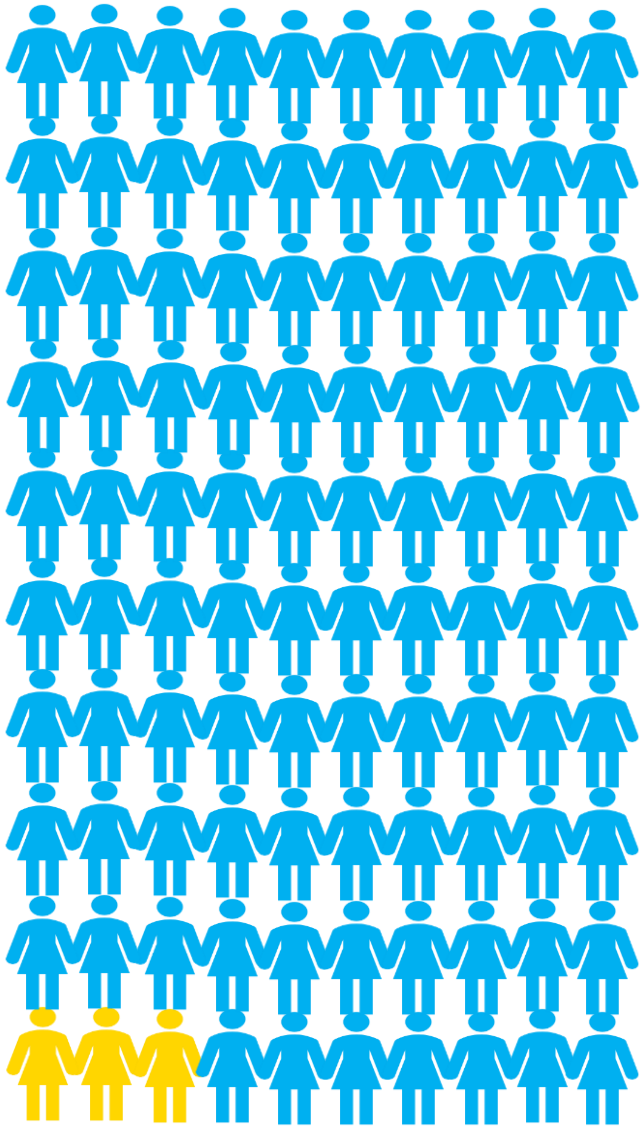

US population of women aged 30-64
73,180,000
18,295,000
13,000
50%


LOVE LIFE
hope


fear
bodyimage
time
childcare
inconvenience
knowledge
transportation
financial
distance
cultural
work

Future state

In-Clinic



In-Home

Colposcopy needed

In-clinic testing

Home test negative, screening complete

Pragmatic randomized trial

Compare the effectiveness of two programmatic approaches to increasing cervical cancer screening among women aged 30-64 years who are overdue for cervical cancer screening

Primary

- Early detection and treatment of cervical neoplasia

Secondary

- Cervical cancer screening uptake
- Predictors of screening
- Patient experiences: knowledge, attitudes and barriers towards self-collect and follow-up
- Impact on health system & clinical teams

Over 30 months (February 2014- August 2016) we randomized 20,284 (16,590 individual women)

Main Findings

Benefits

- ✓ Increased screening uptake by 50% compared to usual care
- ✓ Patient-centered: convenient & easy to use
- ✓ No significant difference in CIN2+ detection or treatment

Areas for improvement

- ✓ Improving patient education to address concerns about ability to use kits correctly & distrust in test results
- ✓ Closing systems gaps and improving patient and provider education to increase adherence to diagnostic follow-up after an HPV positive kit result

HEDIS

HEDIS Measures and Technical Resources

Data Submission

Measurement Certification Programs

Reports and Research

HEDIS Users Group (HUG)

Cervical Cancer Screening (CCS)

Assesses women 21–64 years of age who were screened for cervical cancer using either of the following criteria:

- Women age 21–64 who had cervical cytology performed every 3 years.
- Women age 30–64 who had cervical cytology/human papillomavirus (HPV) co-testing performed every 5 years.

Contemporary Clinical Trials 64 (2018) 77–87

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

Rationale and design of the HOME trial: A pragmatic randomized controlled trial of home-based human papillomavirus (HPV) self-sampling for increasing cervical cancer screening uptake and effectiveness in a U.S. healthcare system

Rachel L. Winer[a,b,*], Jasmin A. Tiro[c], Diana L. Miglioretti[b,d], Chris Thayer[e], Tara Beatty[b], John Lin[f], Hongyuan Gao[b], Kilian Kimbel[b], Diana S.M. Buist[b]

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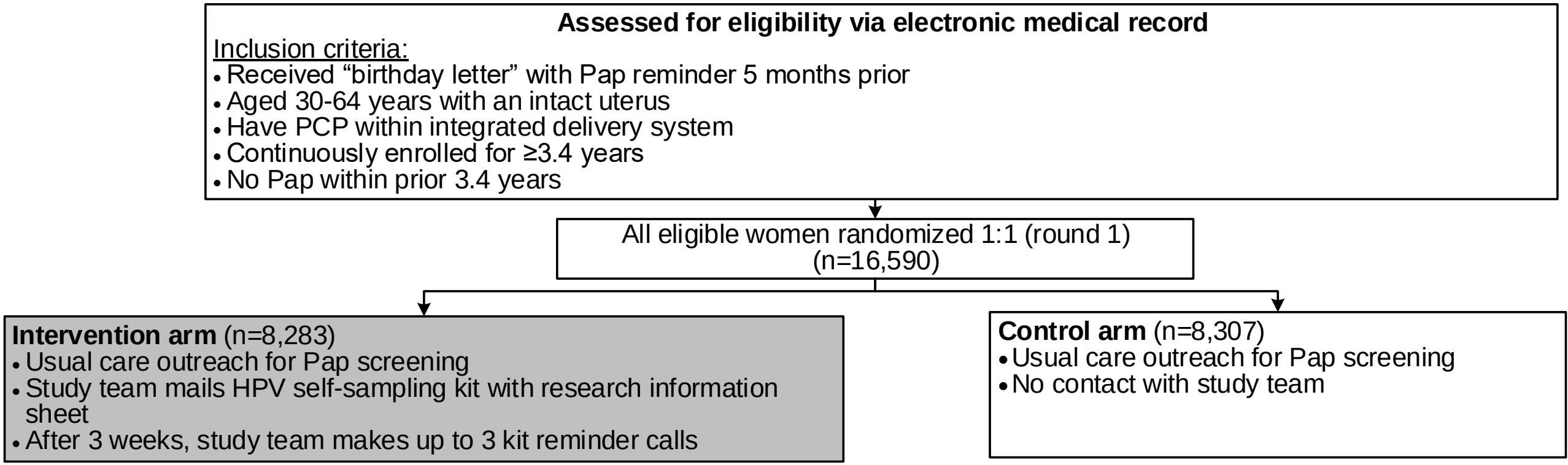
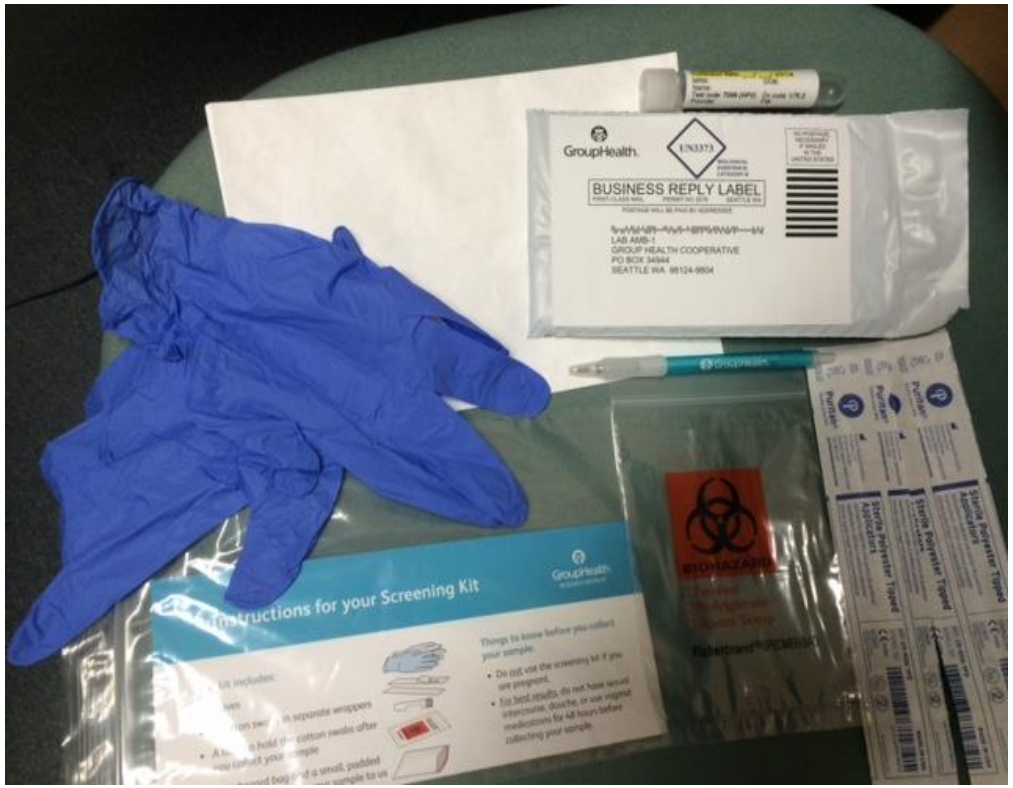
Pragmatic RCT Design





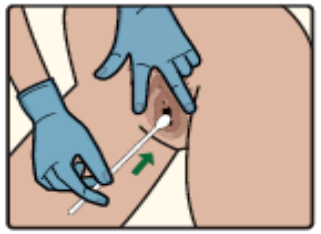
Your kit includes:

- Gloves
- 2 cotton swabs in separate wrappers
- A tube to hold the cotton swabs after you collect your sample
- A biohazard bag and a small, padded envelope for mailing your sample to us

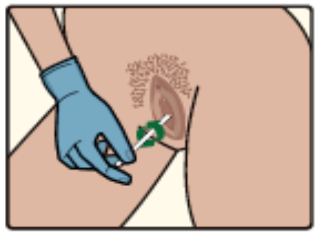
Things to know before you collect your sample:

- Do <u>not</u> use the screening kit if you are pregnant.
- <u>For best results</u>, do not have sexual intercourse, douche, or use vaginal medications for 48 hours before collecting your sample.

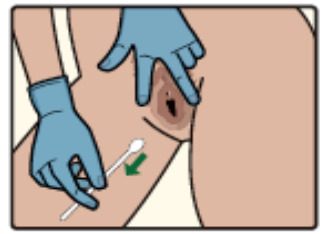
1 Wash and dry your hands, then put on the gloves. Next, open the tube and take the first cotton swab out of the wrapper.



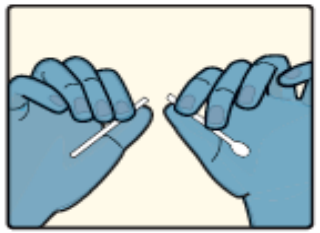
2 Spread apart the skin outside your vagina. With the other hand, gently push the cotton swab into your vagina as far as it will go without hurting—like you would with a tampon.



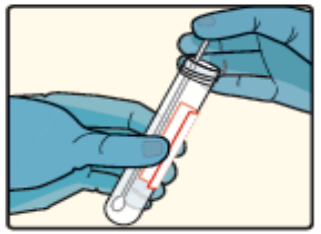
3 Rotate the cotton swab inside your vagina three full turns, keeping it as far inside as you can.



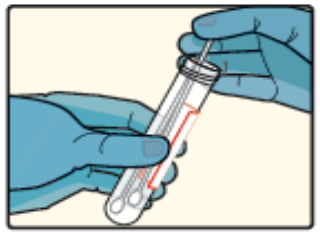
4 Take the cotton swab out of your vagina while spreading apart the outside skin.



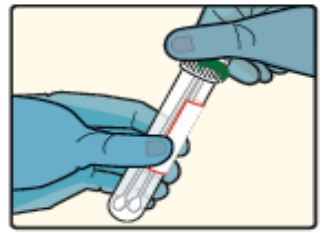
5 Hold the cotton swab at the middle with your fingers and **<u>break it in half.</u>** Try not to touch the cotton tip.



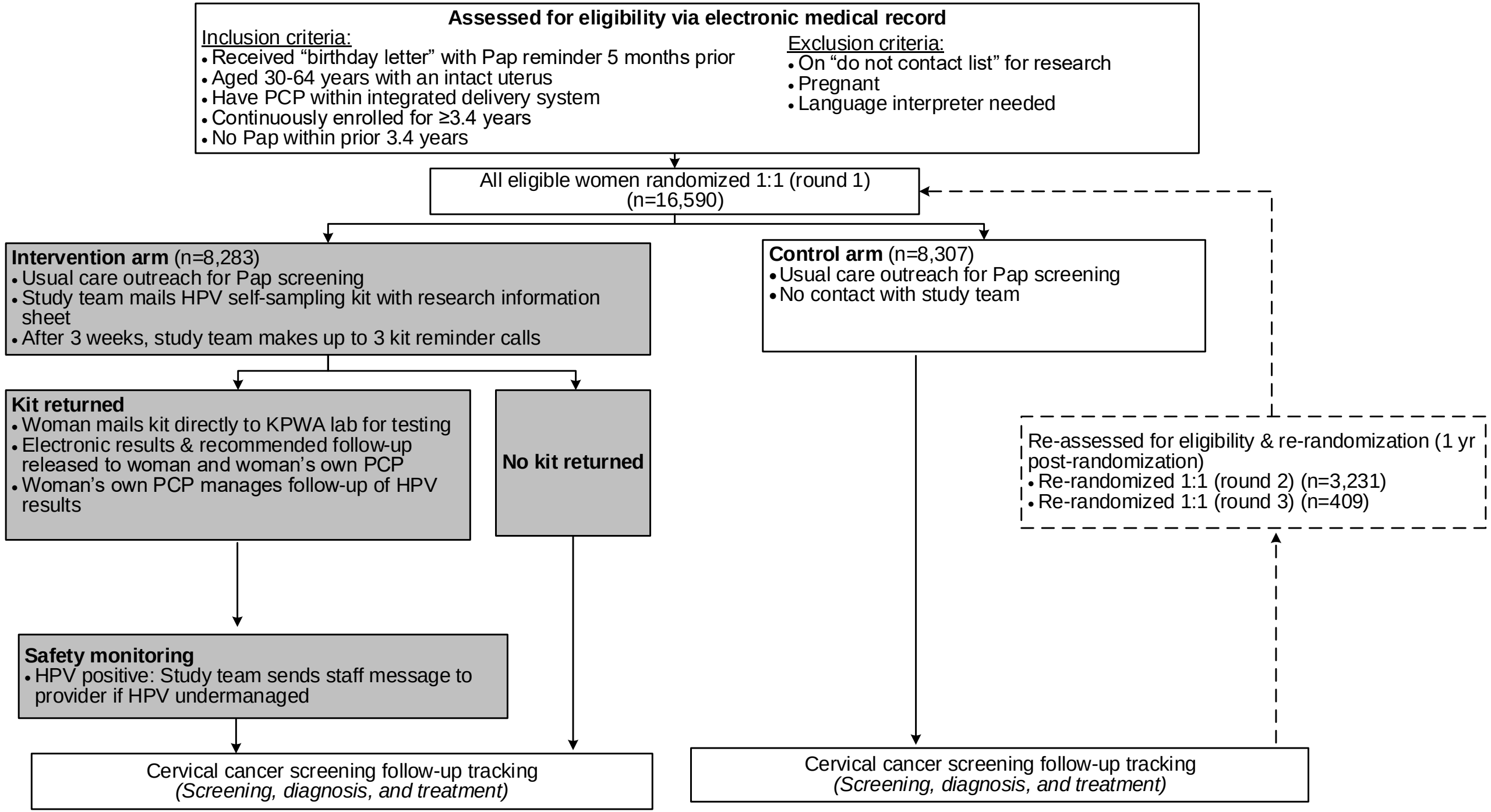
6 Put the cotton swab into the tube, then set the tube within easy reach. Throw away the broken end.

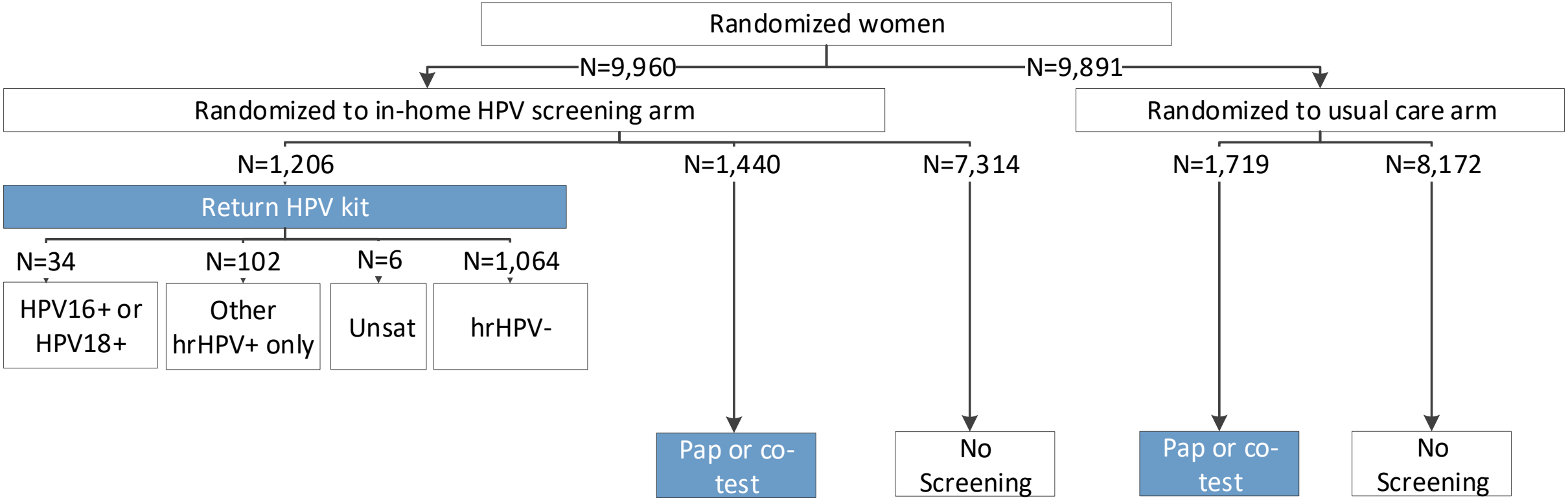


7 **Take the second swab out of the wrapper, then <u>repeat steps 2-6.</u>** When you're done, both swabs will be in the tube.

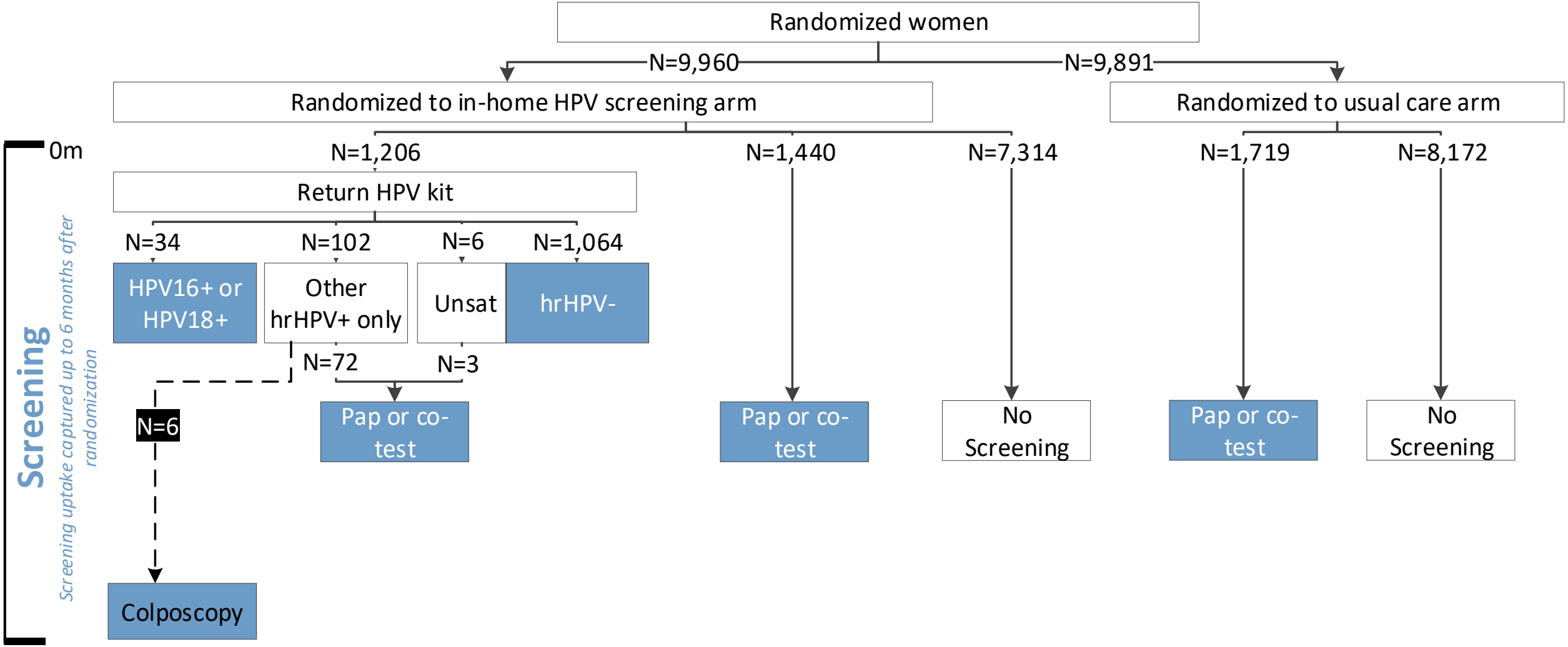


8 Close the tube, throw away the gloves, and wash your hands.


Assessed for eligibility via electronic medical record
Inclusion criteria:
• Received "birthday letter" with Pap reminder 5 months prior
• Aged 30-64 years with an intact uterus
• Have PCP within integrated delivery system
• Continuously enrolled for ≥3.4 years
• No Pap within prior 3.4 years
Exclusion criteria:
• On "do not contact list" for research
• Pregnant
• Language interpreter needed
All eligible women randomized 1:1 (round 1) (n=16,590)
Intervention arm (n=8,283)
• Usual care outreach for Pap screening
• Study team mails HPV self-sampling kit with research information sheet
• After 3 weeks, study team makes up to 3 kit reminder calls
Control arm (n=8,307)
• Usual care outreach for Pap screening
• No contact with study team
Kit returned
• Woman mails kit directly to KPWA lab for testing
• Electronic results & recommended follow-up released to woman and woman's own PCP
• Woman's own PCP manages follow-up of HPV results
No kit returned
Re-assessed for eligibility & re-randomization (1 yr post-randomization)
• Re-randomized 1:1 (round 2) (n=3,231)
• Re-randomized 1:1 (round 3) (n=409)
Safety monitoring
• HPV positive: Study team sends staff message to provider if HPV undermanaged
Cervical cancer screening follow-up tracking (Screening, diagnosis, and treatment)
Cervical cancer screening follow-up tracking (Screening, diagnosis, and treatment)

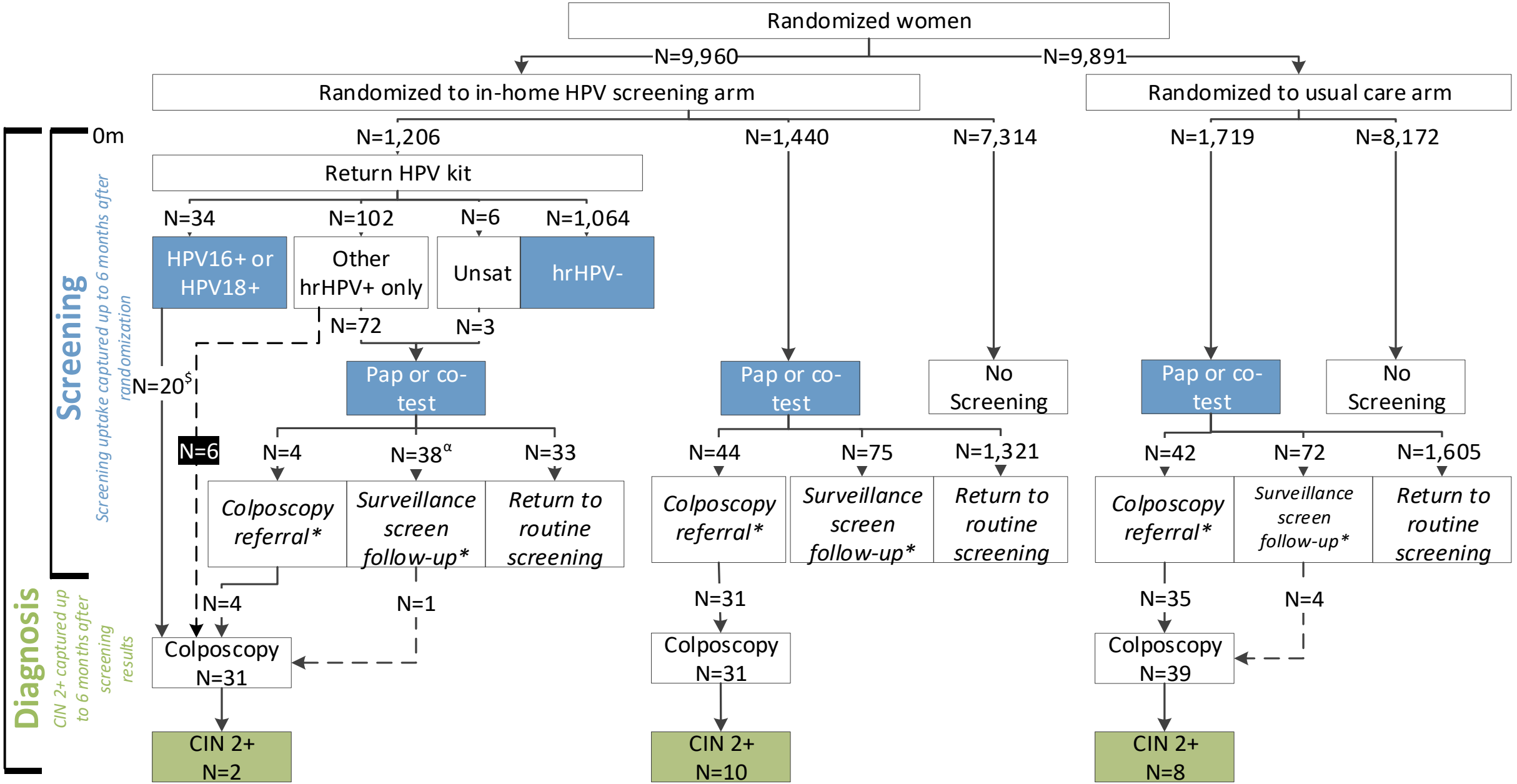


	Mailed HPV Kit	Usual Care	RR (95% CI)
Screening initiation	2646 (26.6%)	1917 (17.4%)	1.53 (1.45-1.61)

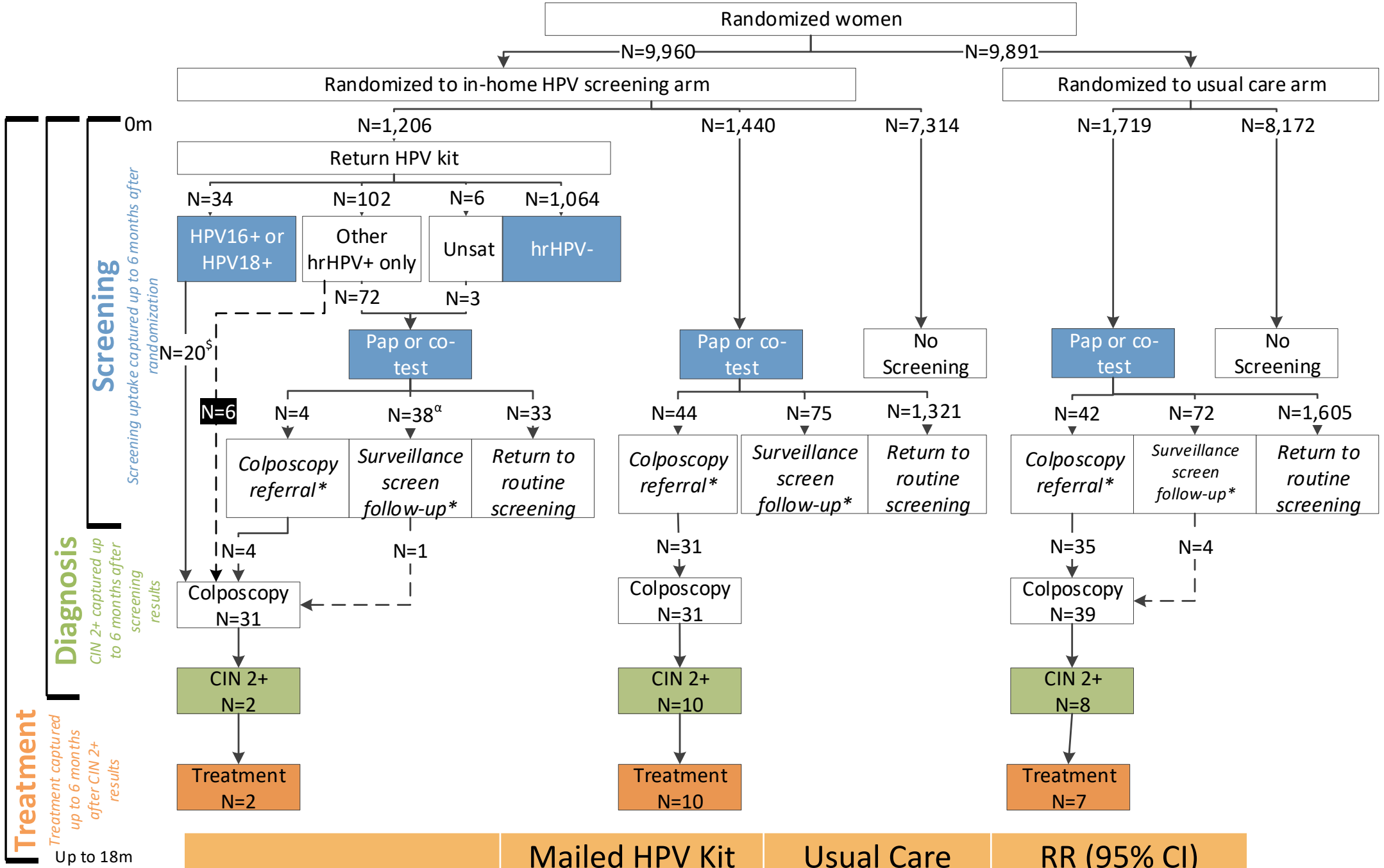


	Mailed HPV Kit	Usual Care	RR (95% CI)
Screening completed	2618 (26.3%)	1917 (17.4%)	1.51 (1.43-1.60)

– – – ► Non-guideline recommended management

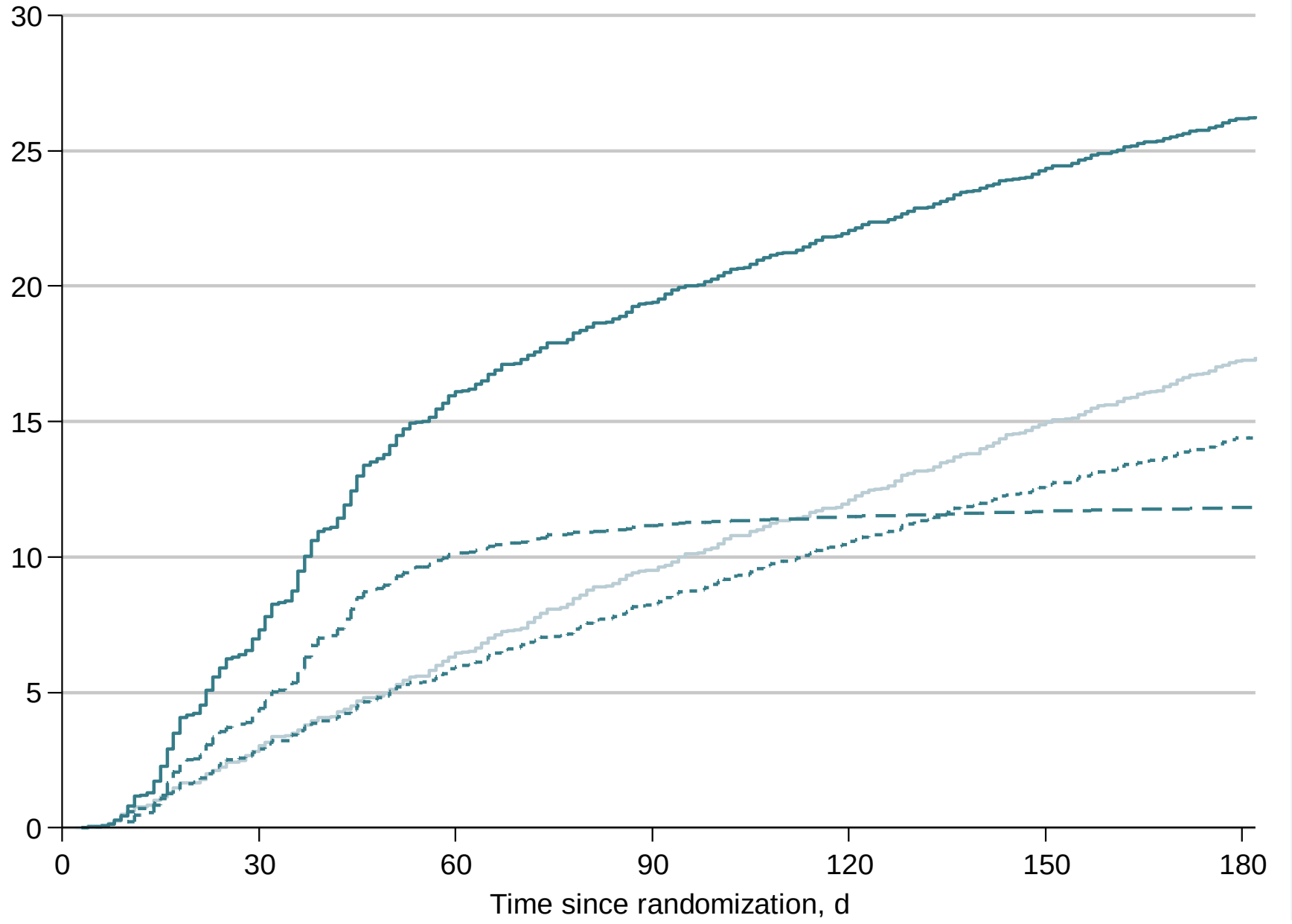


	Mailed HPV Kit	Usual Care	RR (95% CI)
CIN2+	12 (0.1%)	8 (0.1%)	1.49 (0.61-3.64)



	Mailed HPV Kit	Usual Care	RR (95% CI)
Treatment Received	12 (0.1%)	7 (0.1%)	1.70 (0.67-4.32)

Time to screening uptake



No. at risk							
Control	9891	9612	9267	8952	8708	8418	8185
Intervention	9960	9265	8370	8032	7775	7545	7351
Intervention Group, Kit	9960	9542	8954	8850	8817	8797	8783
Intervention Group, Pap	9960	9683	9376	9142	8918	8708	8528

Main Findings

Benefits

- ✓ Increased screening uptake by 50% compared to usual care
- ✓ Patient-centered: convenient & easy to use
- ✓ No significant difference in CIN2+ detection or treatment

Areas for improvement

- ✓ Improving patient education to address concerns about ability to use kits correctly & distrust in test results
- ✓ Closing systems gaps and improving patient and provider education to increase adherence to diagnostic follow-up after an HPV positive kit result

Semi-structured interviews

Goal: Describe women's attitudes, emotional responses, and informational needs after receiving a positive kit result and completing recommended follow-up.

Focused on 3 domains:

1) Reaction to mailed HPV kit
2) Reaction to positive test results
3) Understanding about different screening and follow-up strategies (Pap vs. HPV tests)

JOURNAL OF WOMEN'S HEALTH
Volume 00, Number 00, 2018

DOI: 10.1089/jwh.2018.7070

Understanding Patients' Perspectives and Information Needs Following a Positive Home Human Papillomavirus Self-Sampling Kit Result

Jasmin A. Tiro, PhD,[1] Andrea C. Betts, MPH,[1,2] Kilian Kimbel, BA,[3] Diana S.M. Buist, PhD,[3] Constance Mao, MD,[4] Hongyuan Gao, MS,[3] Lisa Shulman, MSW,[3] Colin Malone, MPH,[5] Tara Beatty, MA,[3] John Lin, BA,[6] Chris Thayer, MD,[7] Diana L. Miglioretti, PhD,[3,8] and Rachel L. Winer, PhD[3,5]

- 46 women interviewed (out of 75 invited) with HPV+ kit result
  - 38 completed all recommended follow-up
  - 8 did not complete all recommended follow-up

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Likes

- Test convenience
- Private setting

Opportunities

- Improving access to information on interpreting HPV test results and next steps (will be true for primary HPV testing too)
- Education on HPV and role in cervical cancer
- Understanding discordant results

Malone et al Under review

Survey of women's experiences with unsolicited mailed kits

Goal:

- Identify HPV/cervical cancer knowledge, perceived risk, and Pap attitudes associated with returning a HPV self-screening kit
- Characterize HPV kit-user experiences, barriers, and future screening intentions and preferences

Compared 116 kit returners (272 invited) & 119 non-returners (1083 invited)

Likes

- Easy to follow instructions
- Swab easy to insert
- Easy to use kit correctly
- Convenient to mail back kit
- Felt in control of health after using kit

Opportunities

- 8% reported pain
- 12% felt physically uncomfortable when using the kit
- 6% using it was embarrassing
- 9% was not sure got a good sample from vagina
- 6% wasn’t sure if they could trust the screening kit

Main Findings

Benefits

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Areas for improvement

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Contemporary Clinical Trials Communications 15 (2019) 100413

Contents lists available at ScienceDirect

Contemporary Clinical Trials Communications

journal homepage: www.elsevier.com/locate/conctc

Improving the promise of embedded pragmatic trials: Surmountable barriers encountered in an evaluation of home-based HPV self-sampling to increase cervical cancer screening in overdue women

D.S.M. Buist[a,*], J.A. Tiro[b], C. Thayer[c], T. Beatty[a], D.L. Miglioretti[a,d], J. Lin[e], R.L. Winer[e]

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What it took to get this off the ground

- A lot of meetings!
  - ~1.5 years of discussion and negotiation with: Lab; Primary care & OB/GYN; Prevention and Outreach teams
- Negotiating on target population
- Alignment with evolving guidelines
- Multiple clinical champions and clinical co-investigator
- Extensive back and forth with IRB for approval

Additional challenges & methodological opportunities

- Blinding research team
- Trial fidelity vs. rapid evaluation and correction during the course of the study
- Reviewing records to ensure providers have done correct follow-up for a test they did not order and are not (necessarily) familiar with – while avoiding potential performance bias
- Ensuring successful integration with the clinical delivery system and appropriate measurement of system impact
- Critical monitoring of system changes

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Thank you & questions

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