3rd Annual Cancer Disparities Virtual Symposium: Challenges in Cancer Care for Sexual and Gender Minorities

Saturday, September 18, 2021
Virtual

ANAL CANCER AND NOVEL SCREENING STRATEGIES

Alan G. Nyitray, PhD
Pronouns: he/they
Clinical Cancer Center
Center for AIDS Intervention Research
Medical College of Wisconsin

MEDICAL COLLEGE OF WISCONSIN
CANCER CENTER

FINANCIAL DISCLOSURES

National Institutes of Health

National Institute for Allergy and Infectious Disease

National Cancer Institute

Medical College of Wisconsin

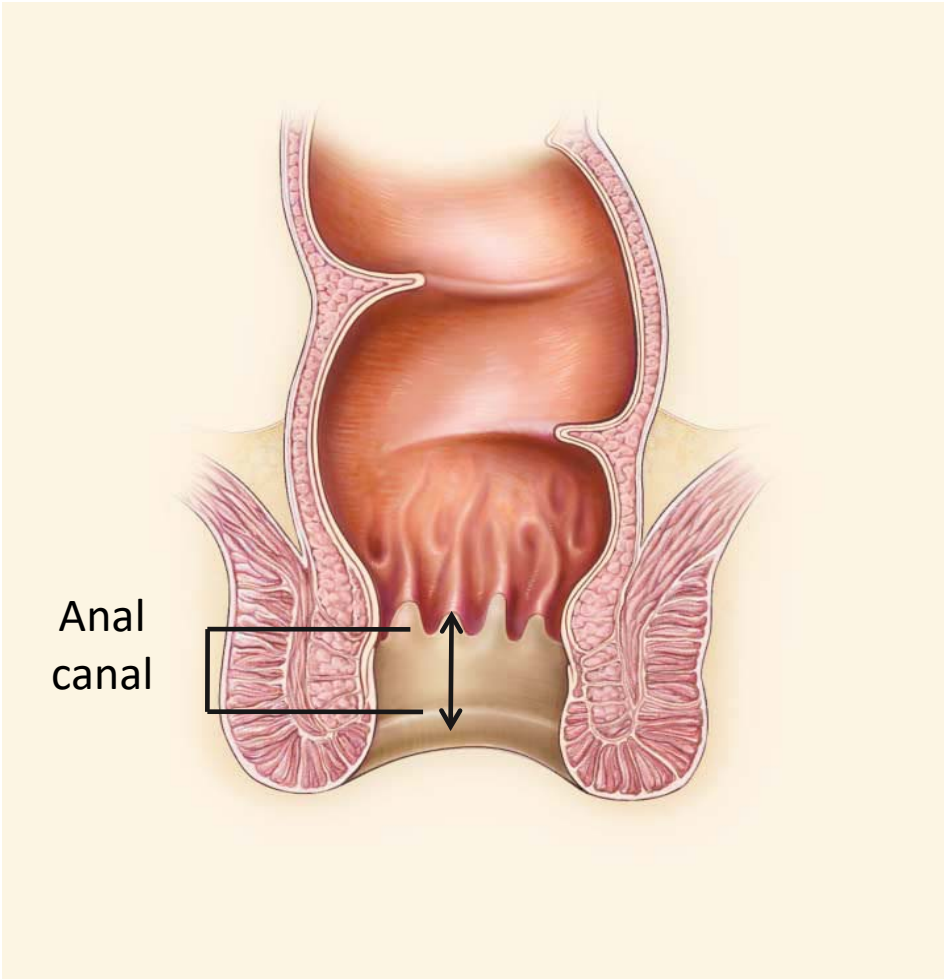
MEDICAL COLLEGE OF WISCONSIN CANCER CENTER

OBJECTIVES

Review HPV and HPV-associated disease

Discuss PAC Study protocols

Review initial PAC Study data

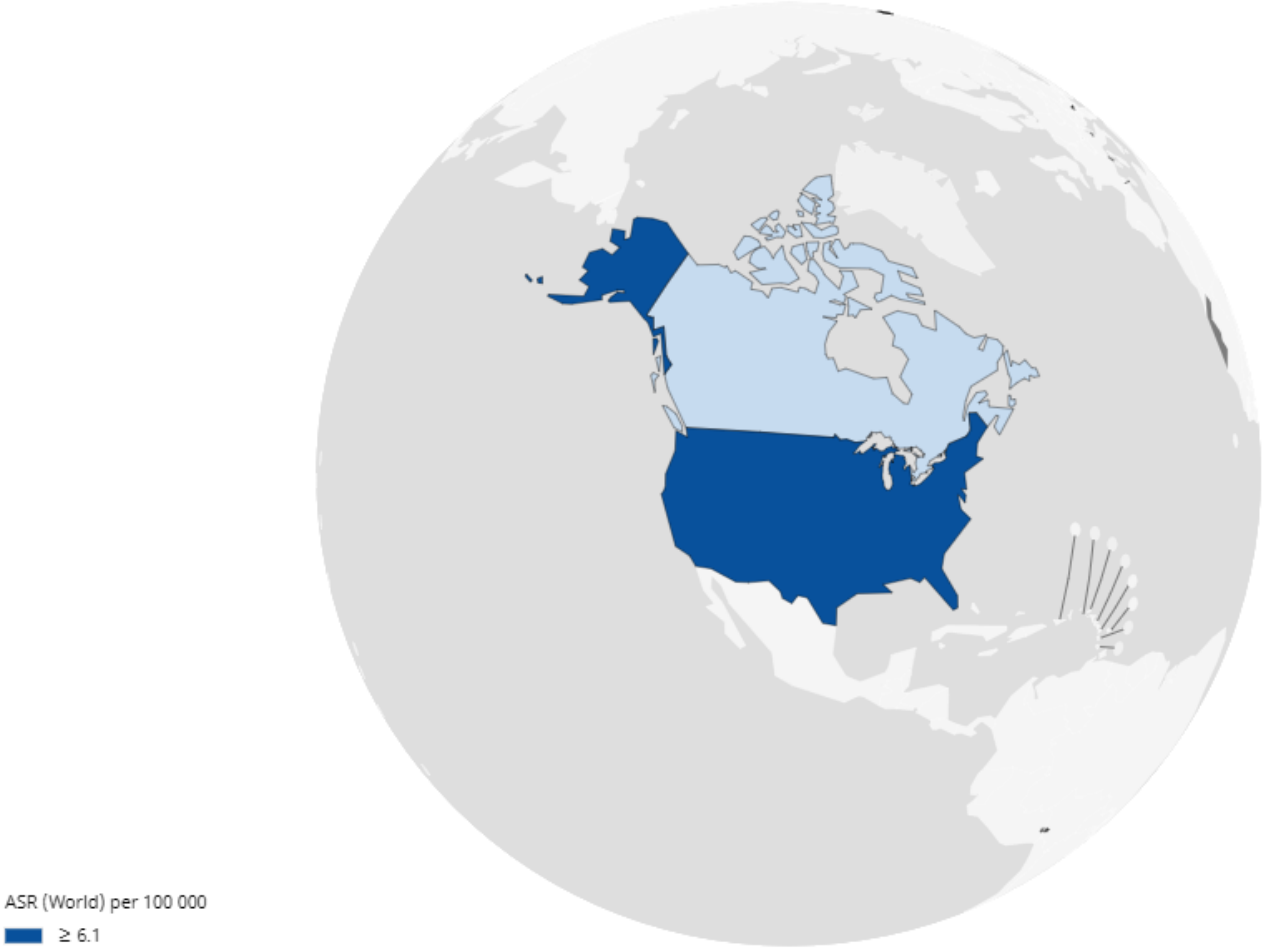


HUMAN PAPILLOMAVIRUSES ARE COMMON

- HPV is common, but transient.
  - E.g., 82% 2-year period prevalence in heterosexual couples
- Low-risk types may cause anogenital condylomas (e.g., 6 & 11).
- More than a dozen cause cancers like cervical cancer, anal cancer, and oral cavity cancer (e.g., 16 & 18).
- Globally, HPV is responsible for about 5% of all cancers.

THE LEGACY OF THE CERVICAL CANCER SCREENING MODEL

Estimated age-standardized incidence rates (World) in 2020, cervix uteri, females, all ages, North America

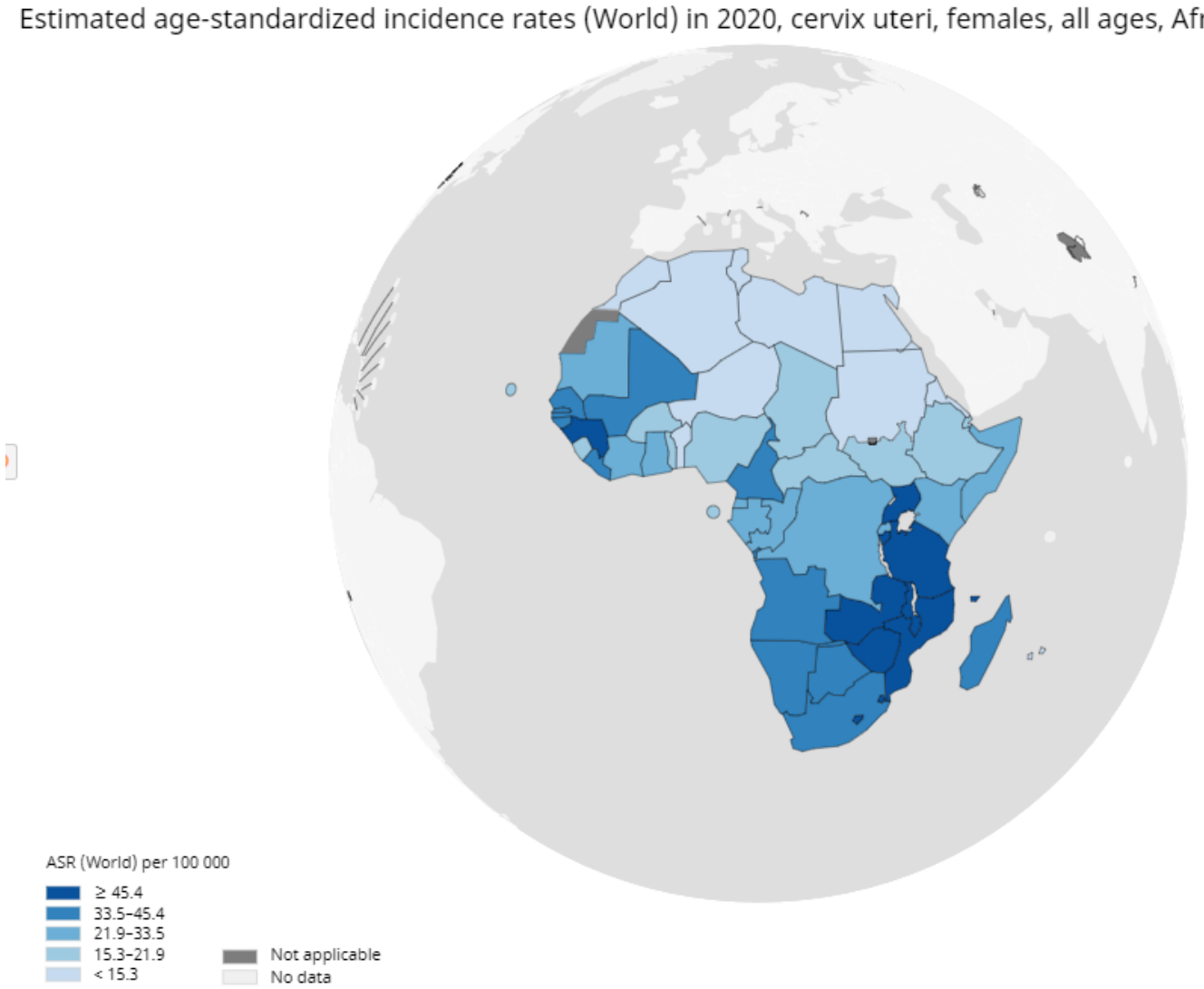


Annual age-adjusted incidence per 100,000 persons

USA	6.2
Canada	5.5

World Health Organization, GLOBOCAN 2020, (http://gco.iarc.fr/today), accessed August 25, 2021

THE LEGACY OF THE CERVICAL CANCER SCREENING MODEL

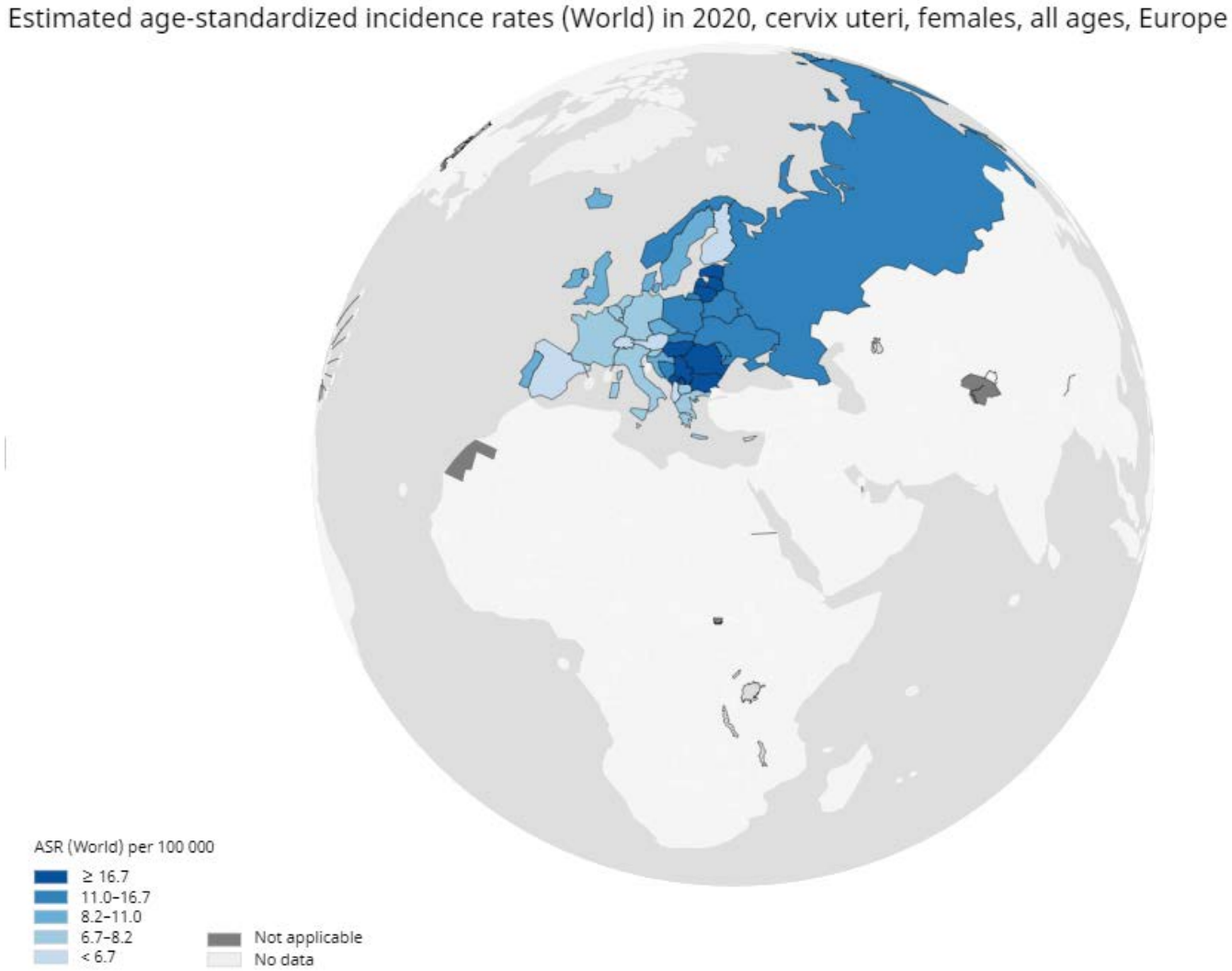


Annual age-adjusted incidence per 100,000 persons

Nigeria	18.4
Kenya	31.3
Tanzania	62.5
Zimbabwe	61.7

World Health Organization, GLOBOCAN 2020, (http://gco.iarc.fr/today), accessed August 25, 2021

THE LEGACY OF THE CERVICAL CANCER SCREENING MODEL

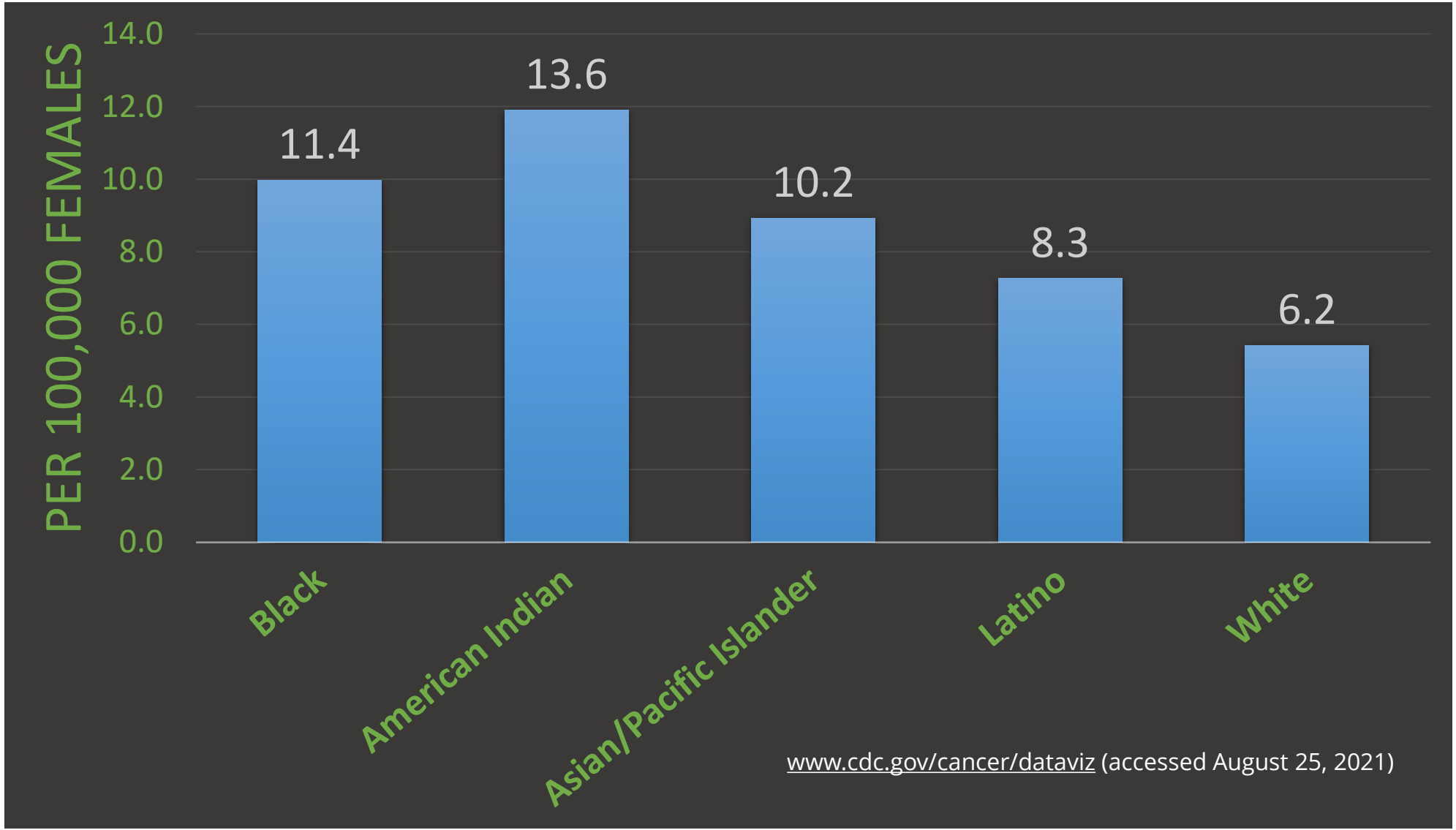


Annual age-adjusted incidence per 100,000 persons

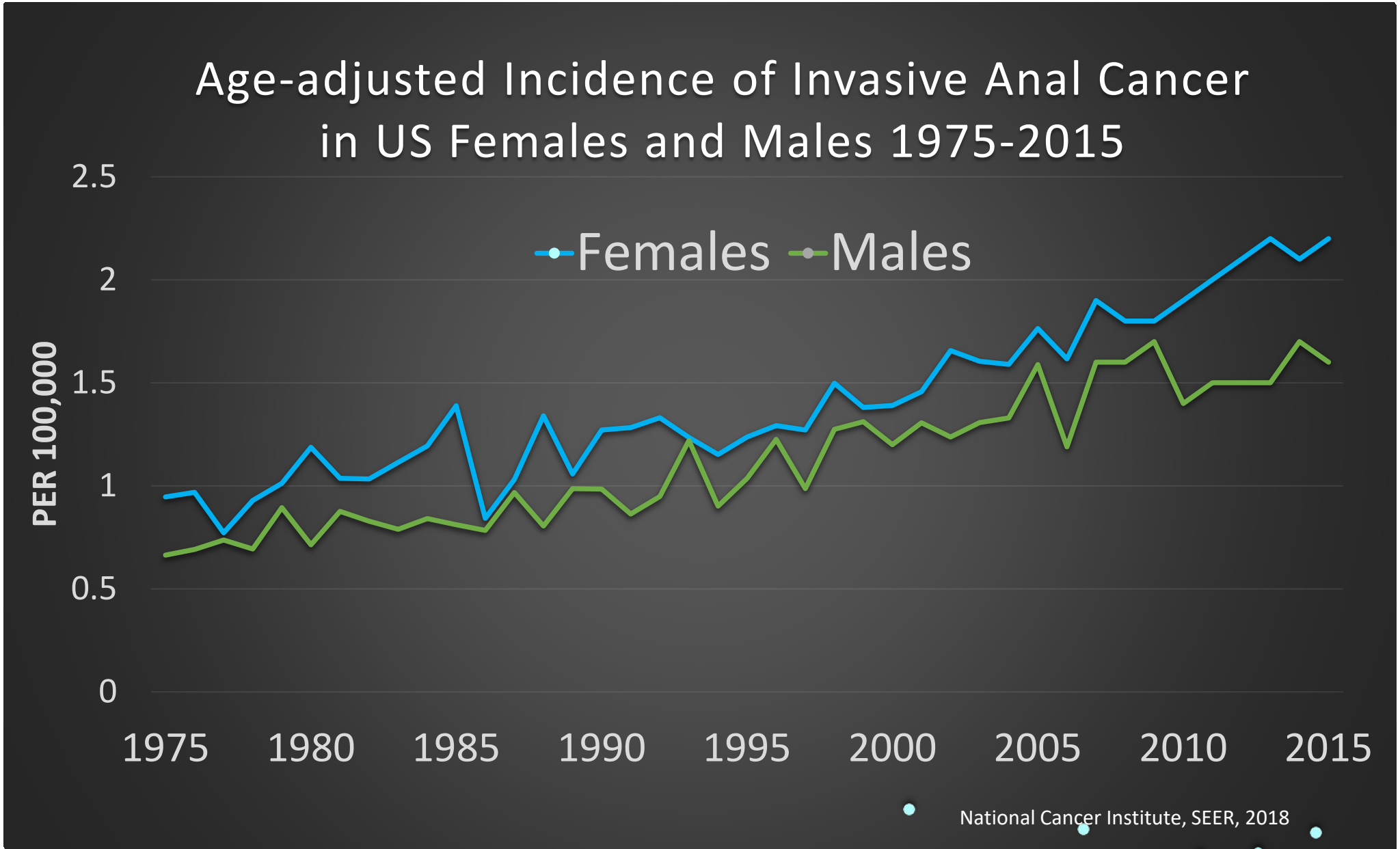
Romania	22.6
Hungary	17.2

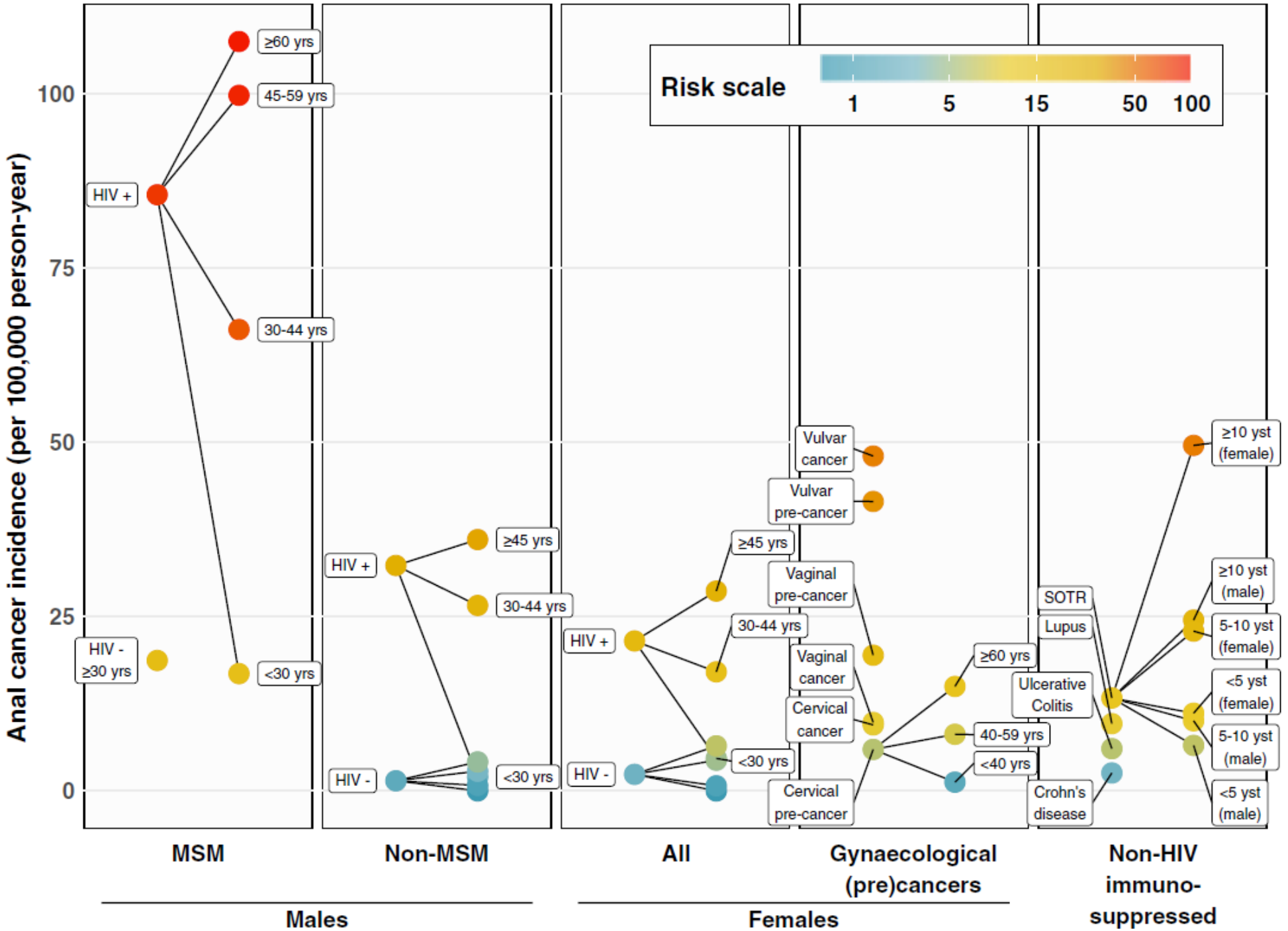
World Health Organization, GLOBOCAN 2020, (http://gco.iarc.fr/today), accessed August 25, 2021

AGE-ADJUSTED CERVICAL CANCER INCIDENCE IN WISCONSIN, 2014-2018



ANAL CANCER INCIDENCE IS INCREASING





Anal cancer risk scale

Clifford et al., IJC 2020, 148(1):38-47

US Preventive Services Task Force recommendations for anal cancer screening do not exist

Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV

Specialists recommend:

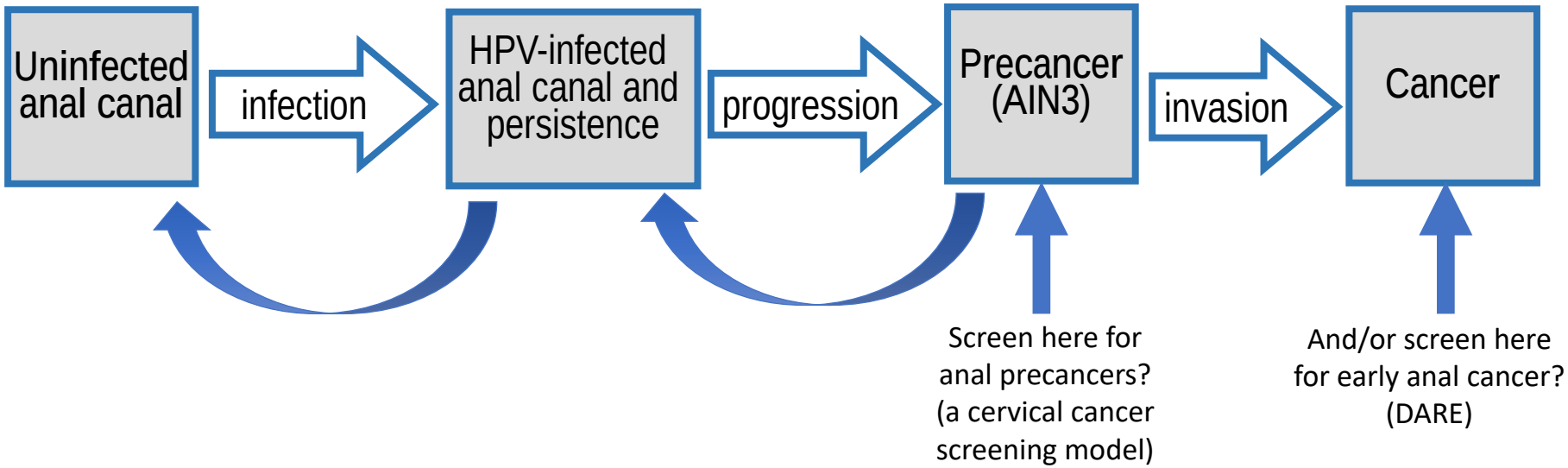
- Digital Anal Rectal Examination-DARE (moderate recommendation)
- Anal Pap or high-resolution anoscopy (optional recommendation)

2021 CDC STI Treatment Guidelines

- DARE should be performed in 1) persons with HIV and 2) MSM without HIV who have a history of receptive anal sex

HRSA, Guidelines for the Prevention and Treatment of Opportunistic Infections in Adults and Adolescents with HIV
https://clinicalinfo.hiv.gov/sites/default/files/guidelines/documents/Adult_OI.pdf
Centers for Disease Control and Prevention, Sexually Transmitted Infections Treatment Guidelines, 2021
https://www.cdc.gov/std/treatment-guidelines/STI-Guidelines-2021.pdf

Natural history of anal HPV infection



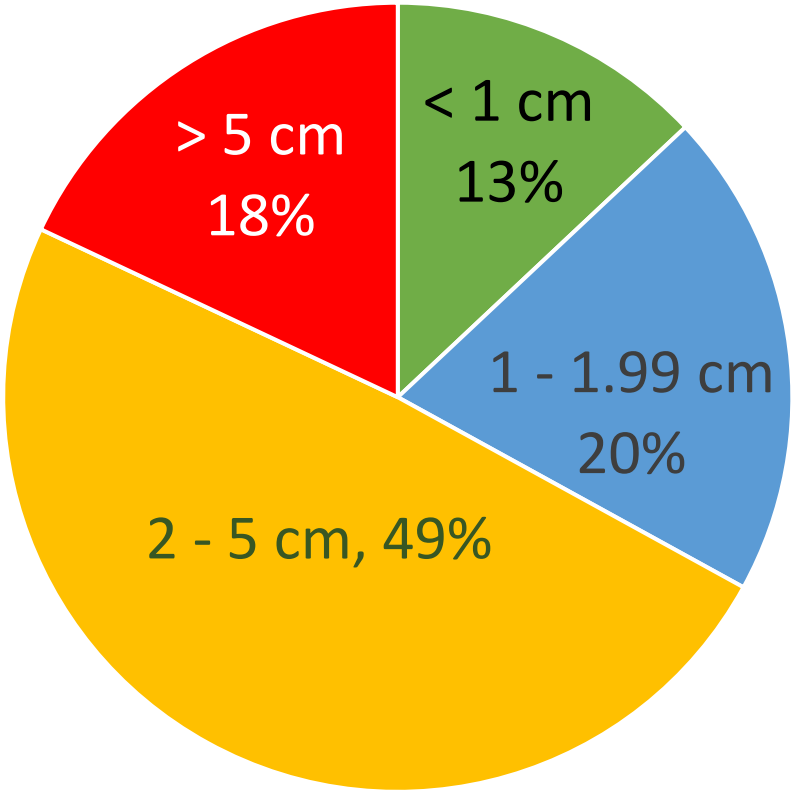
Adapted from Schiffman & Wentzensen, 2010

Problems with the cervical cancer model and DARE for anal precancer or cancer screening

- Cervical Model
  - It's expensive
  - There is no proven treatment for anal precancerous lesions
  - Anal precancerous lesions often regress spontaneously
  - Infrastructure for high-resolution anoscopy is poor
- DARE
  - Likely useful only after invasion

Mean anal canal tumor size at presentation 3.6 cm in diameter

n = 1,622 Texas Cancer Registry, 2000-2010



66 French women and men with early invasive anal cancer (≤1 cm tumors):

5-year disease-specific survival was 100%

Ortholan et al., 2005

15 PLWH with T1N0M0 cancer of the anal verge (below the dentate line):

4-year disease-specific survival was 100%

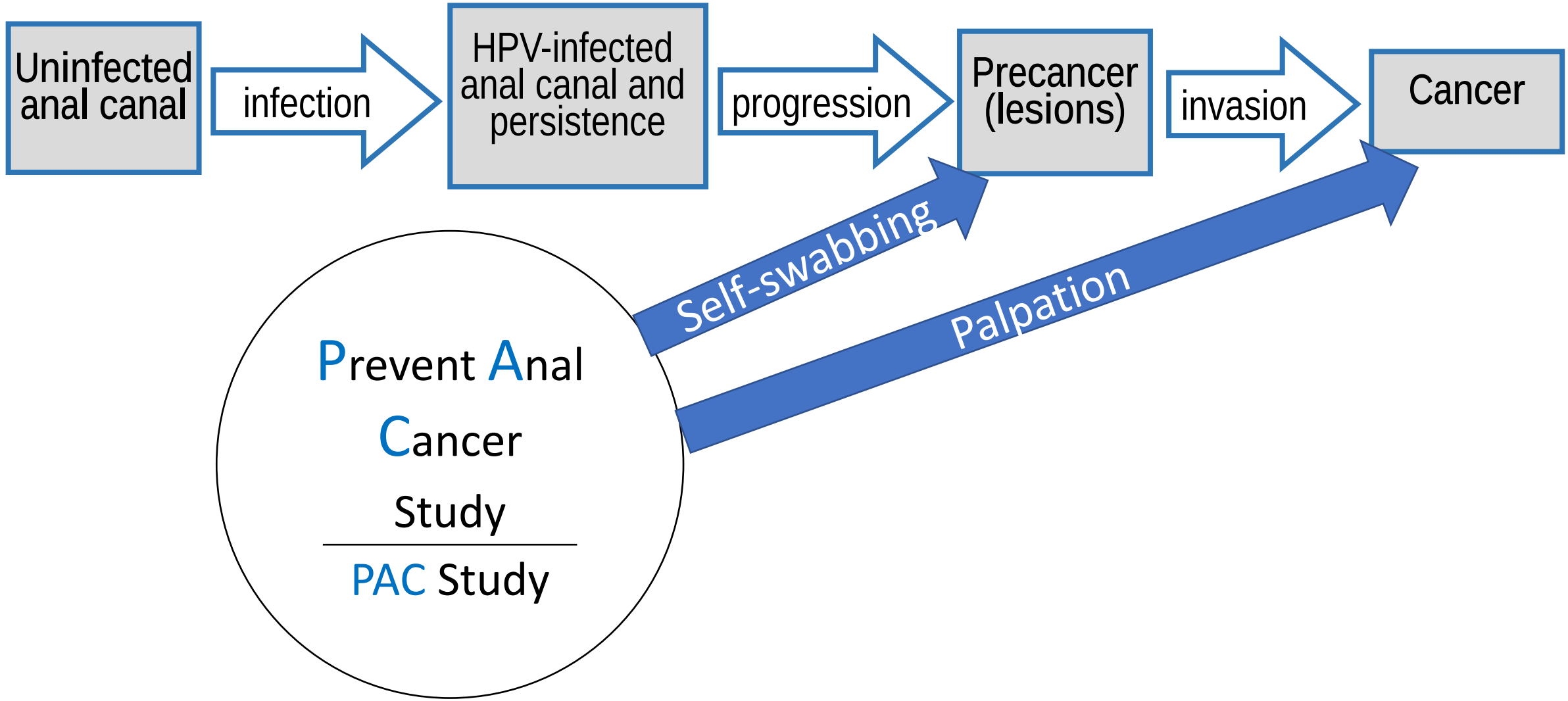
Alfa-Wali et al., 2016

Prevent Anal Cancer Study

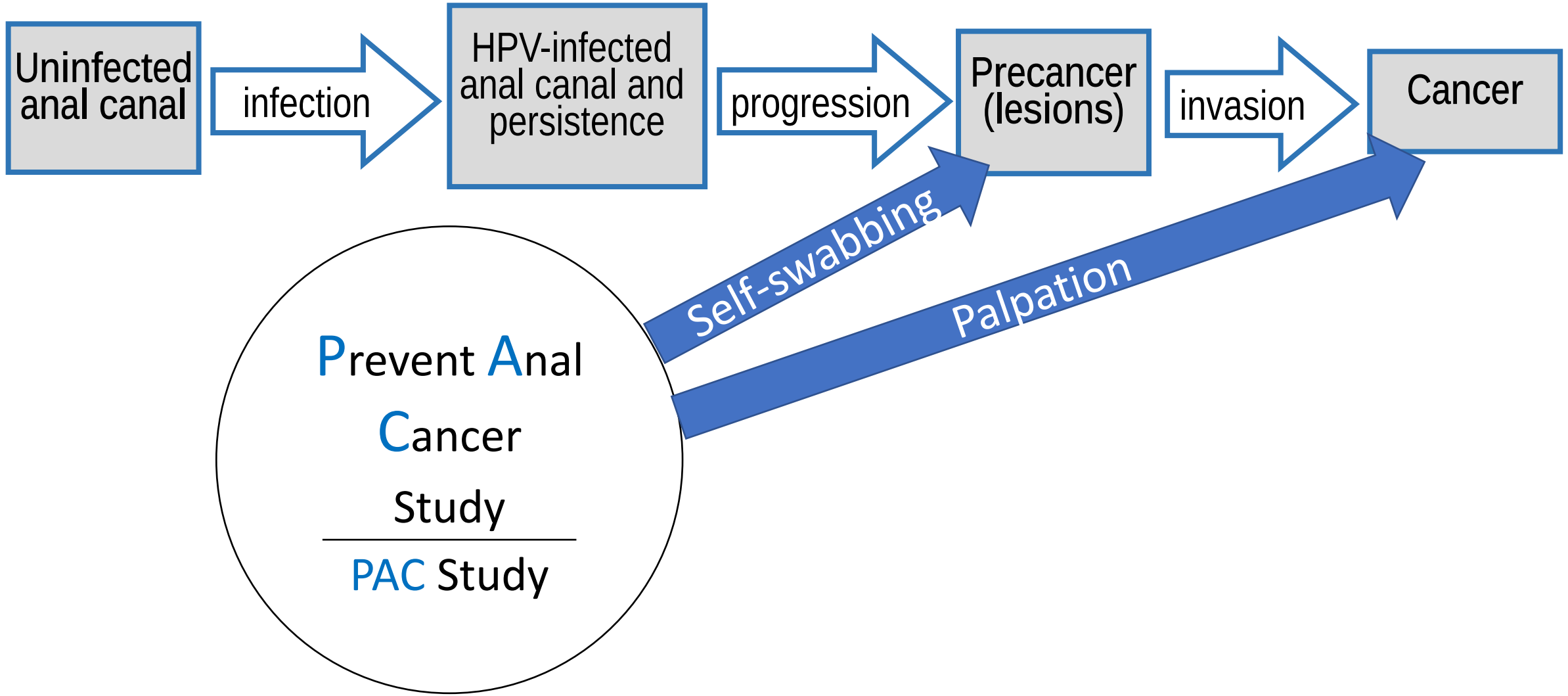
Both PAC studies

- seek to detect cancer earlier when it is more treatable
- address barriers to screening including embarrassment, cost, and lack of health care infrastructure
- target communities at highest risk for anal cancer

PREVENT ANAL CANCER STUDY – TWO APPROACHES



PREVENT ANAL CANCER STUDY – TWO APPROACHES



PAC Self-Swab Study Objectives

1) Determine compliance with annual anal HPV DNA specimen collection and high-resolution anoscopy.

2) Determine factors associated with annual screening compliance.

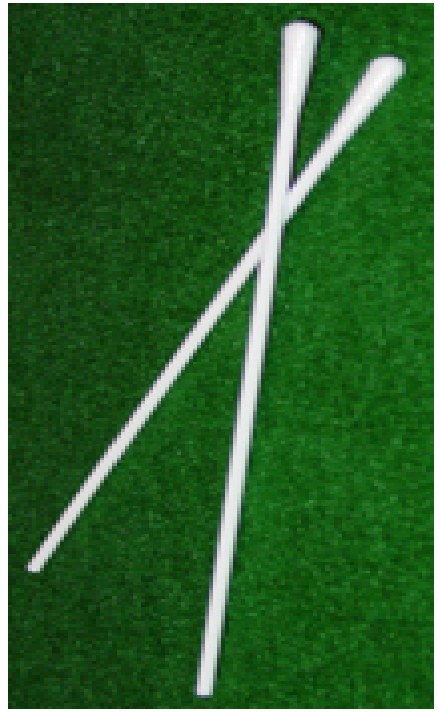
3) Assess the performance of two molecular markers: HPV DNA persistence and host/viral DNA methylation.

NCI 7 R01 CA215403 02

PAC Self-Swab Study Randomization

400 MSM and transpersons who have sex with men randomized 1:1

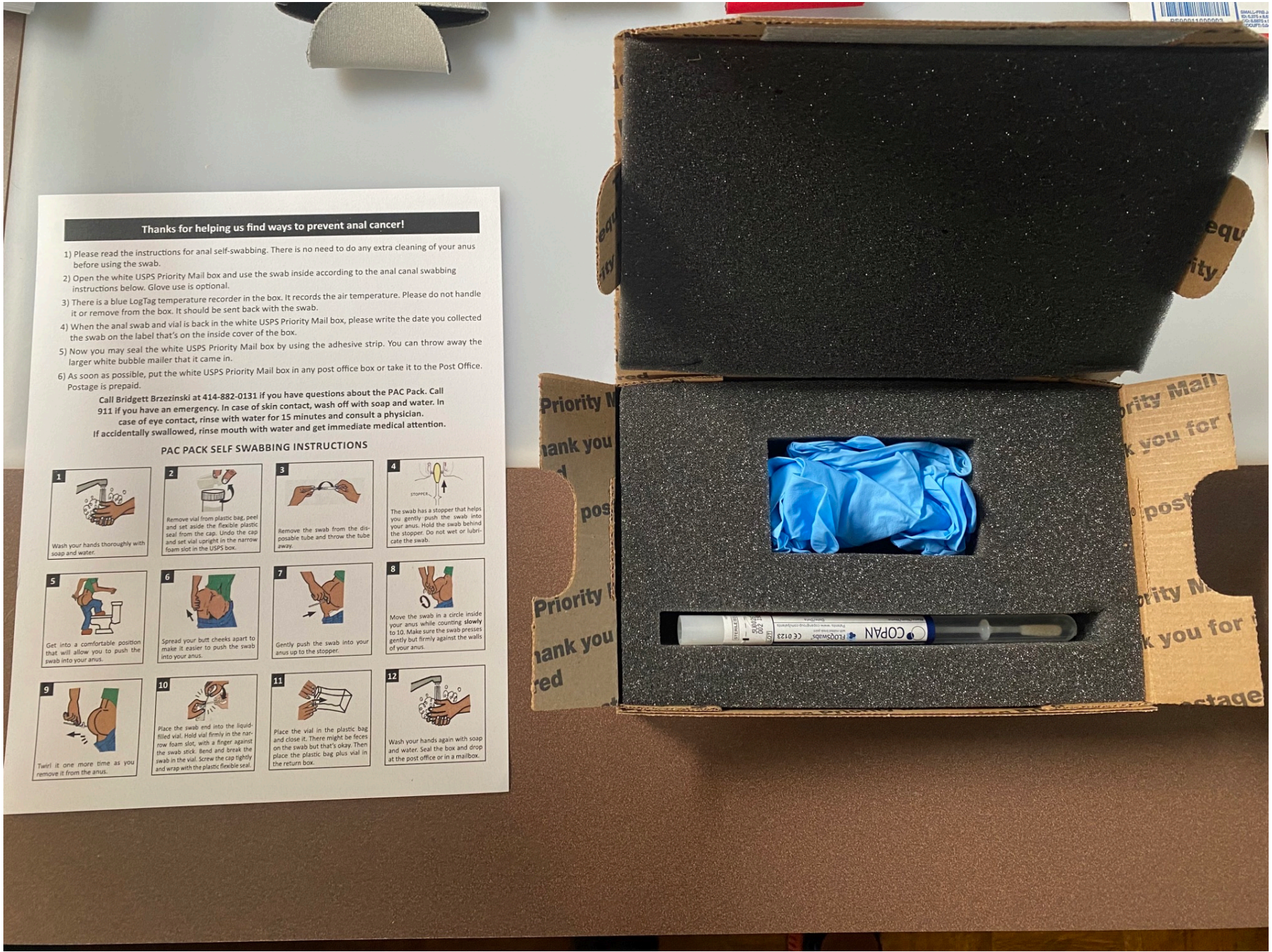
- 200 in self-swabbing arm at home (PAC Pack)
- 200 in clinician-swabbing arm at a clinic
  - Persons can choose from one of five clinics in the city



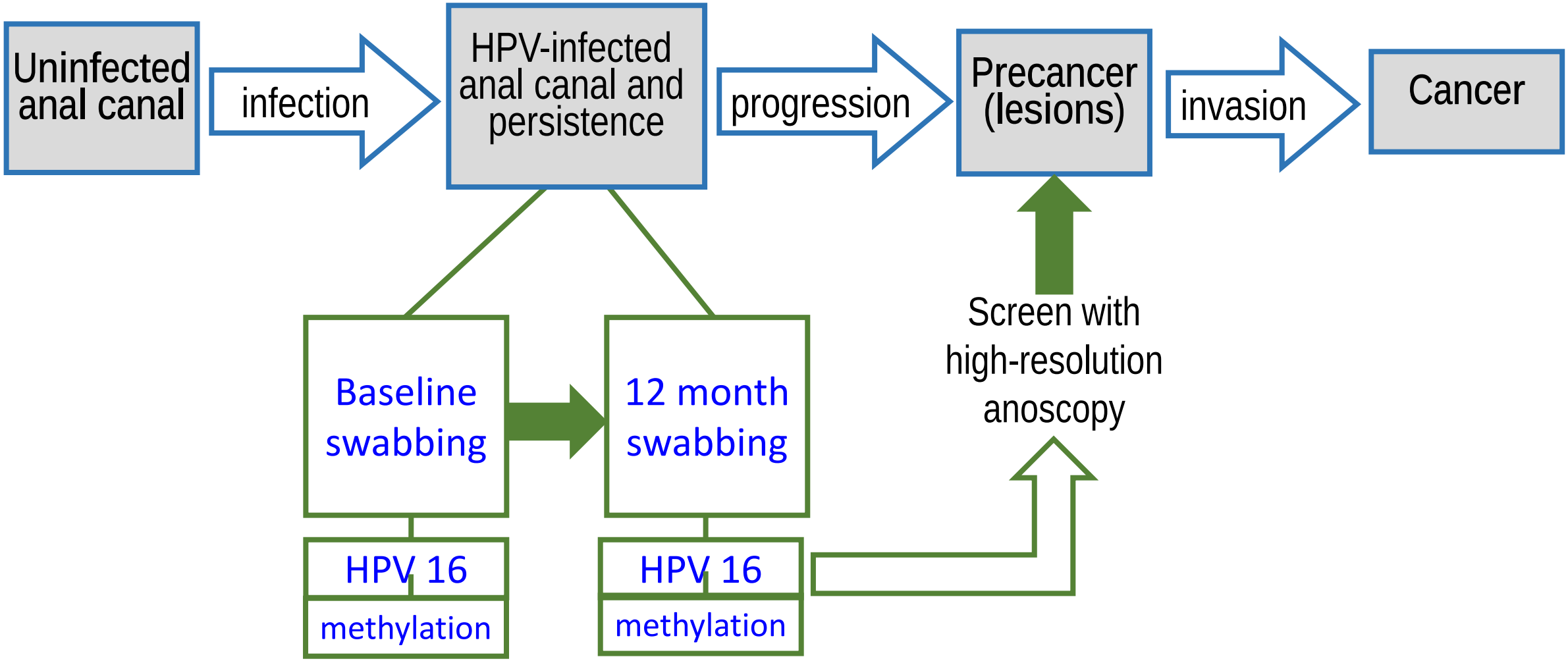
- ≥ 25 years of age
- Milwaukee MSA residence
- Not on anti-coagulants, e.g., Plavix
- No diagnosis or hemophilia, cirrhosis with bleeding varices, or thrombocytopenia
- Remain in Milwaukee for at least 1 year

NCI 7 R01 CA215403 02

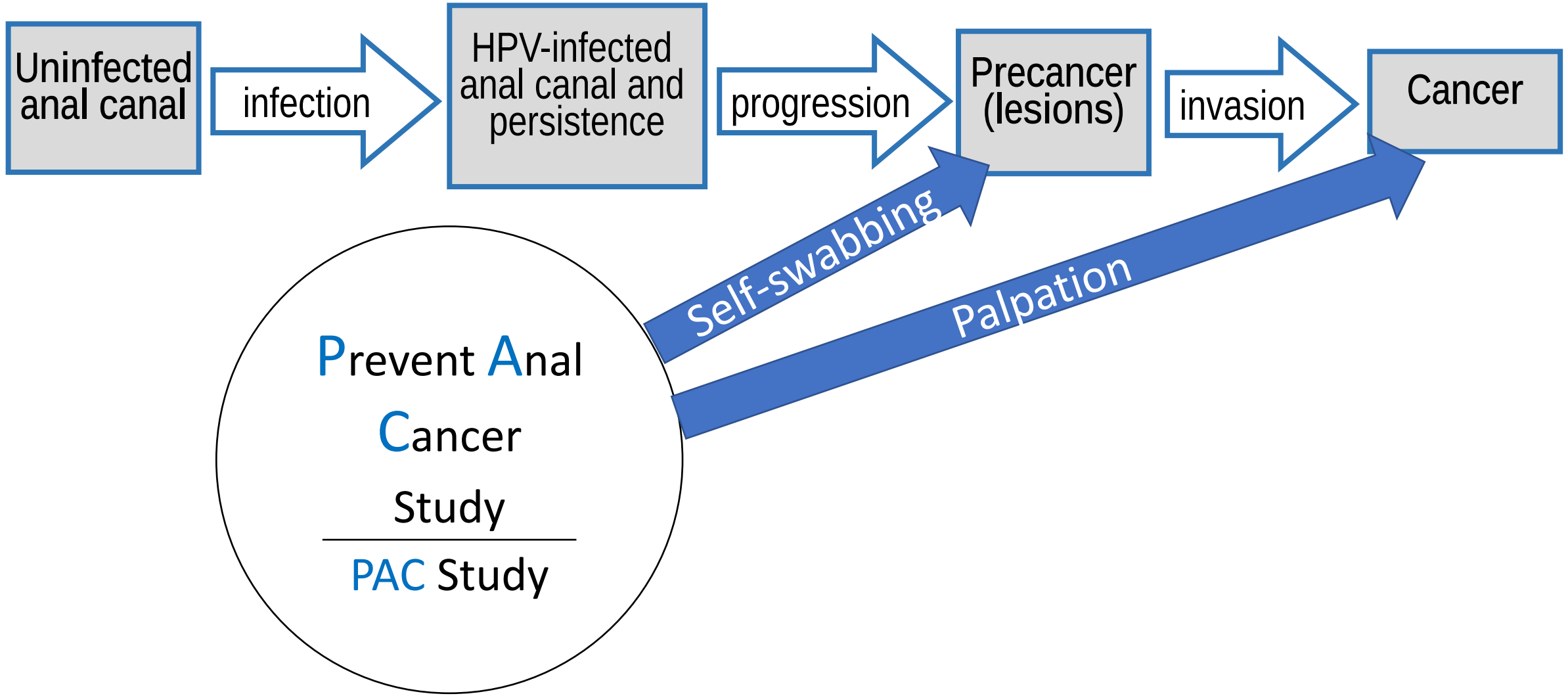
PAC Pack


Thanks for helping us find ways to prevent anal cancer!
1) Please read the instructions for anal self-swabbing. There is no need to do any extra cleaning of your anus before using the swab.
2) Open the white USPS Priority Mail box and use the swab inside according to the anal canal swabbing instructions below. Glove use is optional.
3) There is a blue LogTag temperature recorder in the box. It records the air temperature. Please do not handle it or remove from the box. It should be sent back with the swab.
4) When the anal swab and vial is back in the white USPS Priority Mail box, please write the date you collected the swab on the label that's on the inside cover of the box.
5) Now you may seal the white USPS Priority Mail box by using the adhesive strip. You can throw away the larger white bubble mailer that it came in.
6) As soon as possible, put the white USPS Priority Mail box in any post office box or take it to the Post Office. Postage is prepaid.
Call Bridgett Brzezinski at 414-882-0131 if you have questions about the PAC Pack. Call 911 if you have an emergency. In case of skin contact, wash off with soap and water. In case of eye contact, rinse with water for 15 minutes and consult a physician. If accidentally swallowed, rinse mouth with water and get immediate medical attention.
PAC PACK SELF SWABBING INSTRUCTIONS
1
Wash your hands thoroughly with soap and water.
2
Remove vial from plastic bag, peel and set aside the flexible plastic seal from the cap. Undo the cap and set vial upright in the narrow foam slot in the USPS box.
3
Remove the swab from the disposable tube and throw the tube away.
4
STOPPER
The swab has a stopper that helps you gently push the swab into your anus. Hold the swab behind the stopper. Do not wet or lubricate the swab.
5
Get into a comfortable position that will allow you to push the swab into your anus.
6
Spread your butt cheeks apart to make it easier to push the swab into your anus.
7
Gently push the swab into your anus up to the stopper.
8
Move the swab in a circle inside your anus while counting slowly to 10. Make sure the swab presses gently but firmly against the walls of your anus.
9
Twirl it one more time as you remove it from the anus.
10
Place the swab end into the liquid-filled vial. Hold vial firmly in the narrow foam slot, with a finger against the swab stick. Bend and break the swab in the vial. Screw the cap tightly and wrap with the plastic flexible seal.
11
Place the vial in the plastic bag and close it. There might be feces on the swab but that's okay. Then place the plastic bag plus vial in the return box.
12
Wash your hands again with soap and water. Seal the box and drop at the post office or in a mailbox.
COPAN
FLOQSwabs
Priority
you for

PERSISTENCE BIOMARKER
PAC SELF-SWAB STUDY



PREVENT ANAL CANCER STUDY – TWO APPROACHES

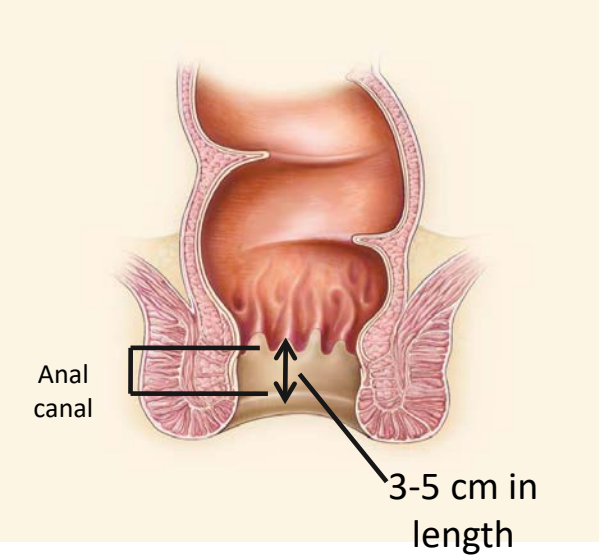


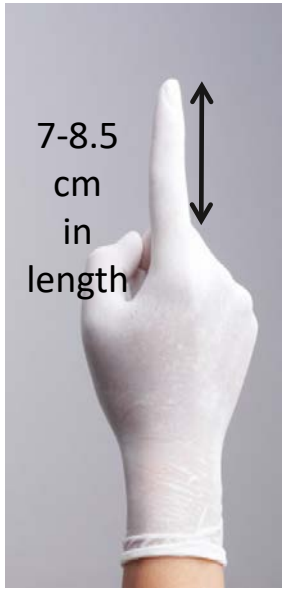
PAC PALPATION STUDY ASSESSES THE ABILITY OF PERSONS TO RECOGNIZE AN ANAL ABNORMALITY

Since most anal cancers have a tumor that can be felt with a finger…

Can MSM and transpersons palpate an anal abnormality ?

400 Chicago and 400 Houston participants





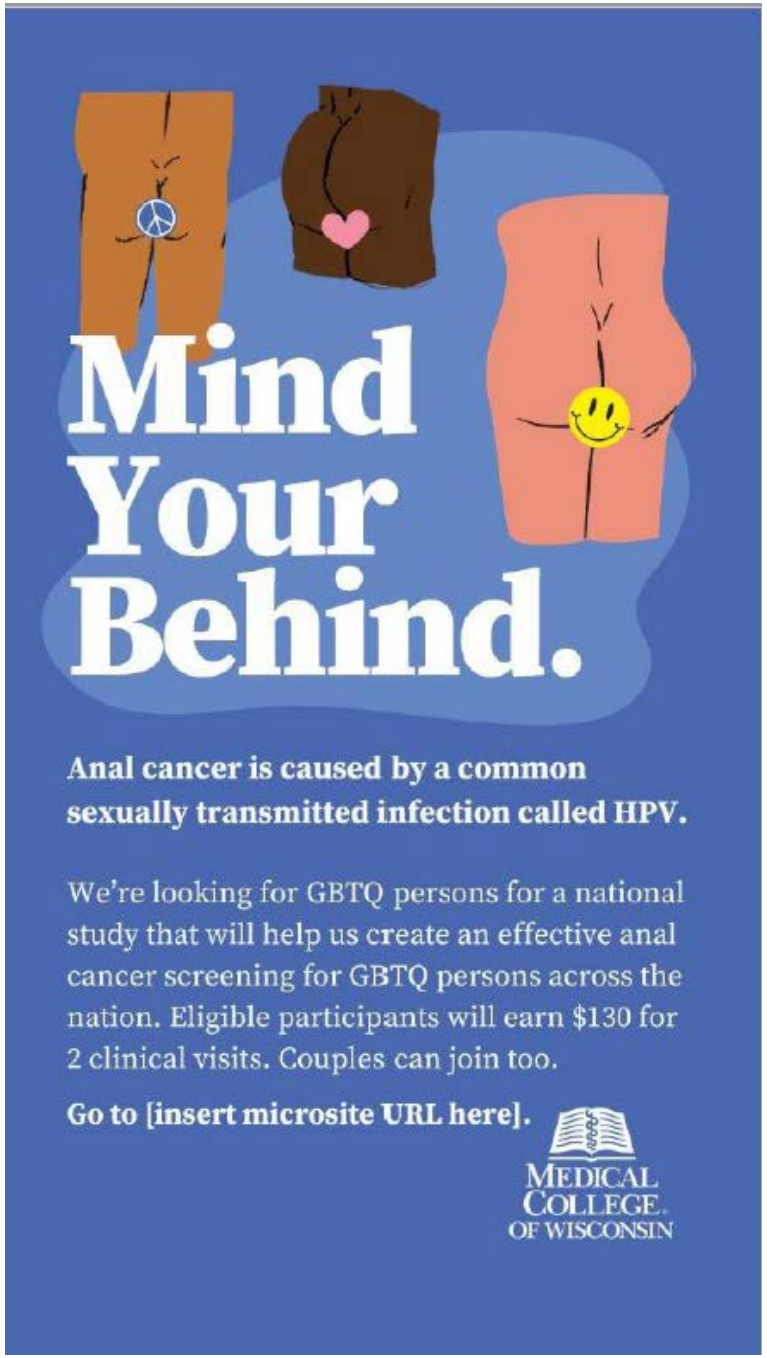
NCI 1 R01 CA232892 01

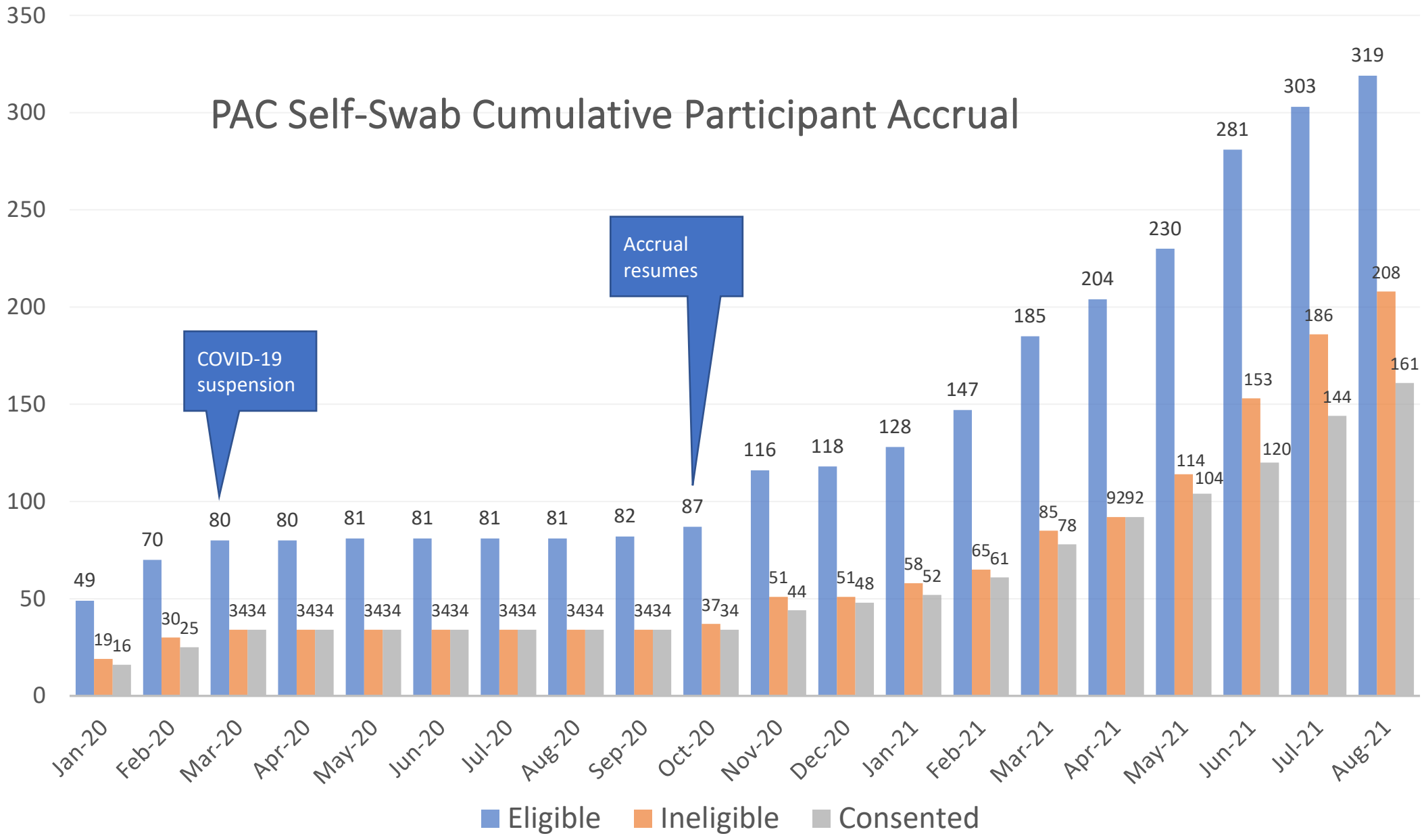
PAC Palpation Study Objectives

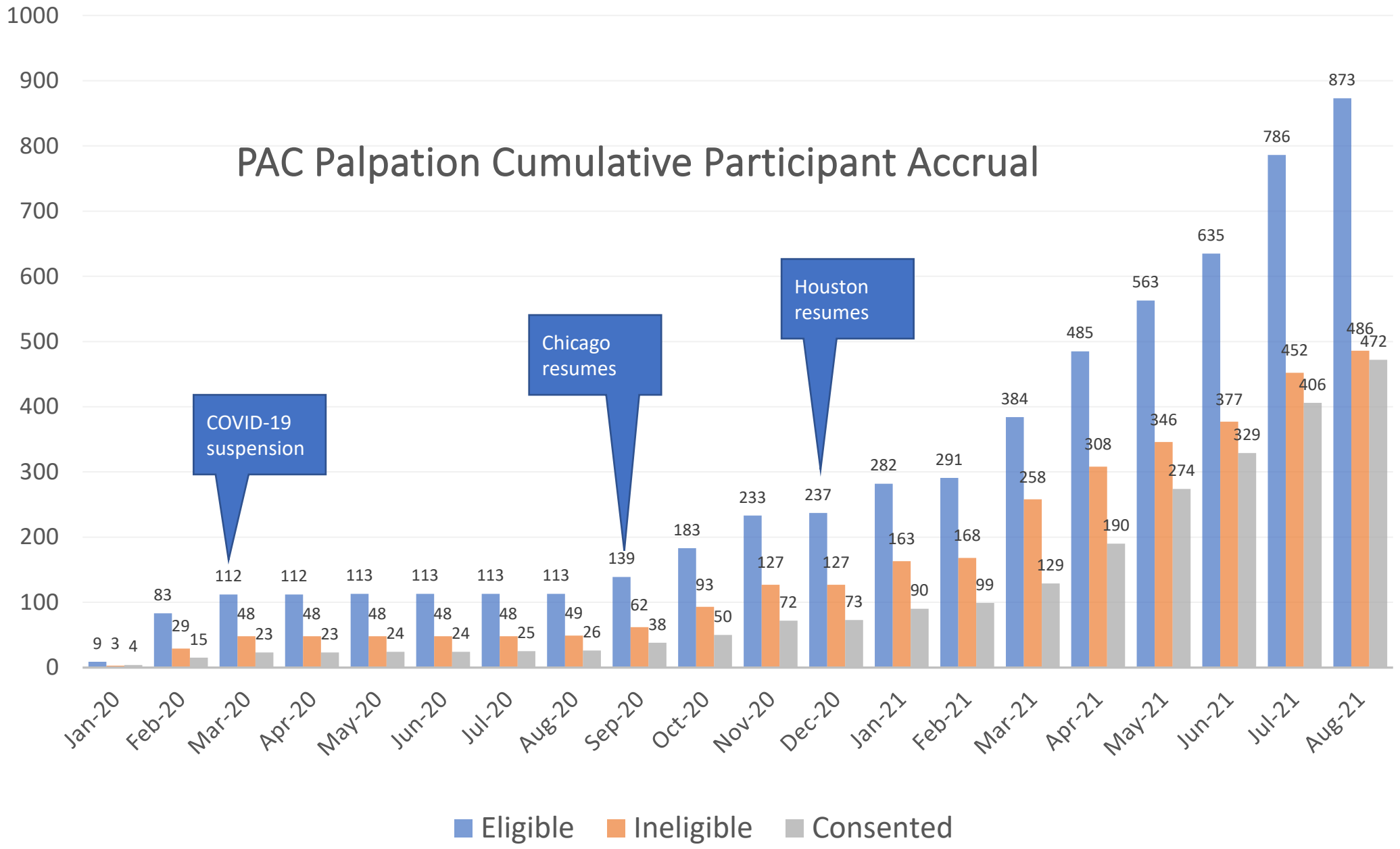
1) Estimate the anal self-exam and anal companion exam sensitivity and specificity.

2) Determine factors associated with concordance between self/companion-exams and clinician's exam.

3) Estimate the impact of the exams on quality of life and evaluate cost-effectiveness.




PAC Self-Swab Cumulative Participant Accrual
COVID-19 suspension
Accrual resumes
350
300
250
200
150
100
50
0
Jan-20
Feb-20
Mar-20
Apr-20
May-20
Jun-20
Jul-20
Aug-20
Sep-20
Oct-20
Nov-20
Dec-20
Jan-21
Feb-21
Mar-21
Apr-21
May-21
Jun-21
Jul-21
Aug-21
49
19
16
70
30
25
80
34
34
80
34
34
81
34
34
81
34
34
81
34
34
81
34
34
82
34
34
87
37
34
116
51
44
118
51
48
128
58
52
147
65
61
185
85
78
204
92
92
230
114
104
281
153
120
303
186
144
319
208
161
Eligible
Ineligible
Consented


PAC Palpation Cumulative Participant Accrual
COVID-19 suspension
Chicago resumes
Houston resumes
1000
900
800
700
600
500
400
300
200
100
0
Jan-20
Feb-20
Mar-20
Apr-20
May-20
Jun-20
Jul-20
Aug-20
Sep-20
Oct-20
Nov-20
Dec-20
Jan-21
Feb-21
Mar-21
Apr-21
May-21
Jun-21
Jul-21
Aug-21
9 3 4
83 29 15
112 48 23
112 48 23
113 48 24
113 48 24
113 48 25
113 49 26
139 62 38
183 93 50
233 127 72
237 127 73
282 163 90
291 168 99
384 258 129
485 308 190
563 346 274
635 377 329
786 452 406
873 486 472
Eligible
Ineligible
Consented

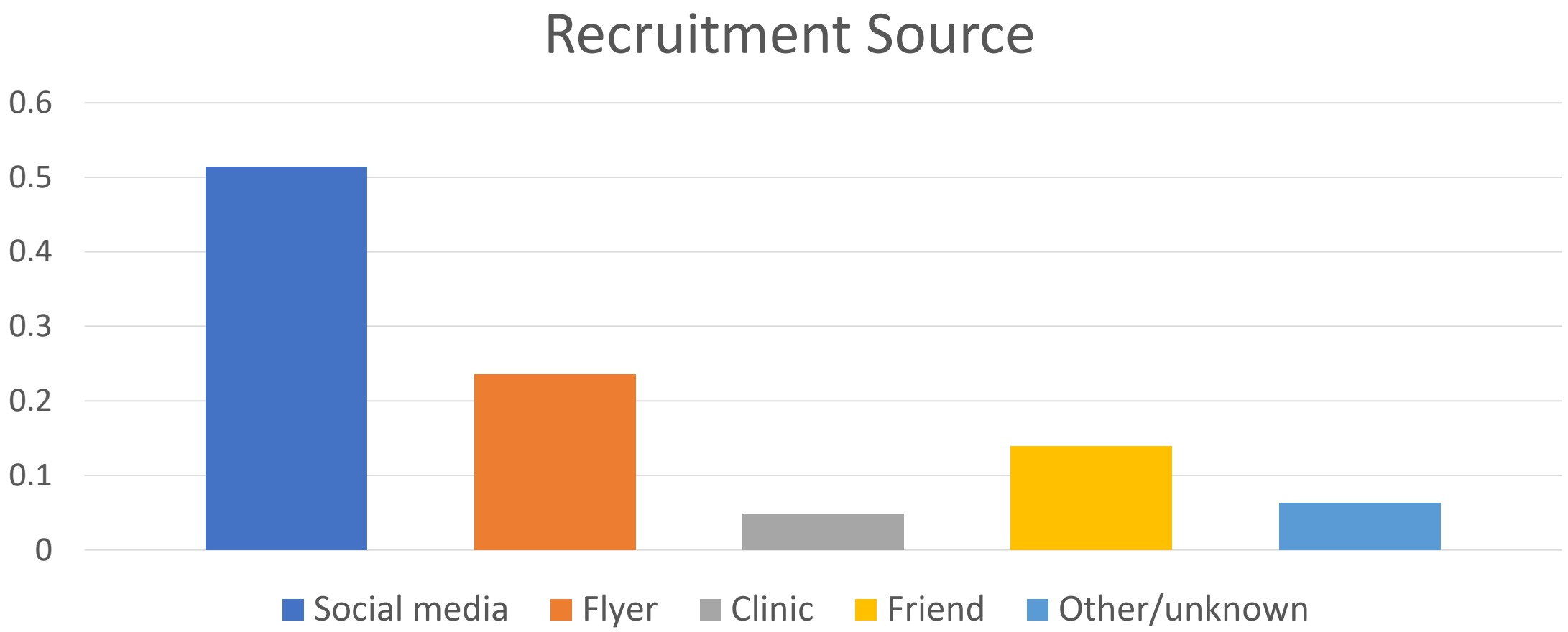
PAC Study enrollment
January 3, 2020 – August 17, 2021

	total	PAC Self-Swab MKE	PAC Palp CHI + HTX
Assessed for eligibility	2039	622	1417
Eligible	1333	479	854
Consented & enrolled	526	151	375
Randomized	426	144	282

PAC Study enrollment
January 3, 2020 – August 17, 2021

	total	PAC Self-Swab MKE	PAC Palp CHI + HTX
Assessed for eligibility	2039	622	1417
Eligible	1333	479	854
Consented & enrolled	526	151	375
Randomized	426	**144**	282

PAC Self-Swab Study (n=144)



PAC Self-Swab Study

Age, years	
Median (range)	*46 yrs (25-71 yrs)*
	n (%)
25-34	46 (31.9)
35-44	23 (16.0)
45-54	29 (20.1)
55-64	38 (26.4)
≥65	8 (5.6)

PAC Self-Swab Study

Gender identity	n (%)
Man	136 (94.4)
Trans woman	4 (2.8)
Non-binary	3 (2.1)
Another	1 (0.7)

PAC Self-Swab Study

Sexual orientation	n (%)
Gay	121 (84.6)
Bisexual	16 (11.2)
Queer	5 (3.5)
Heterosexual	1 (0.7)

PAC Self-Swab Study

Race and ethnicity	n (%)
Race	
White	103 (72.0)
Black/African American	32 (22.4)
Asian American	0
Another	8 (5.6)
Hispanic/Latinx ethnicity	
Yes	16 (11.2)
No	127 (88.8)

PAC Self-Swab Study

HIV	n	(%)
Positive	35	(24.3)
Negative	109	(75.7)

PAC Self-Swab Study

Medical condition*	n (%)
Yes	34 (23.8)
No	109 (76.2)

* Here is a list of medical conditions that may make it harder to use the swab. Has a doctor ever said that you have any of the following?(check all that apply)

Arthritis, carpal tunnel syndrome, obesity, diabetes, fibromyalgia, chronic lower back pain, stroke, cerebral palsy, motor neuron diseases, movement disorders, multiple sclerosis, spina bifida, spinal cord injury, visual impairment, deafness

PAC Self-Swab Study - Randomization

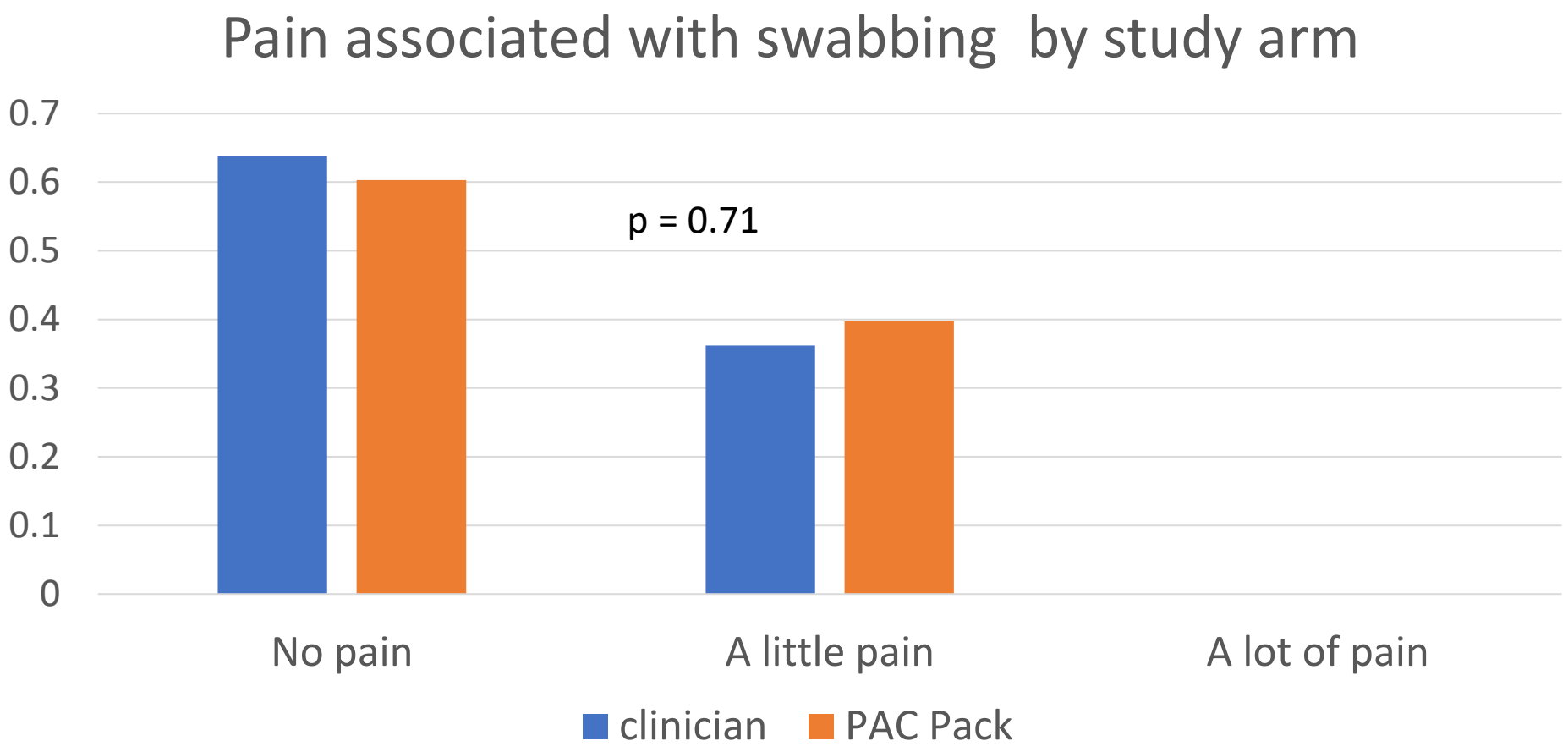
or

n = 73

n = 71

Currently, there are no differences by study arm regarding age, race, ethnicity, or HIV status.

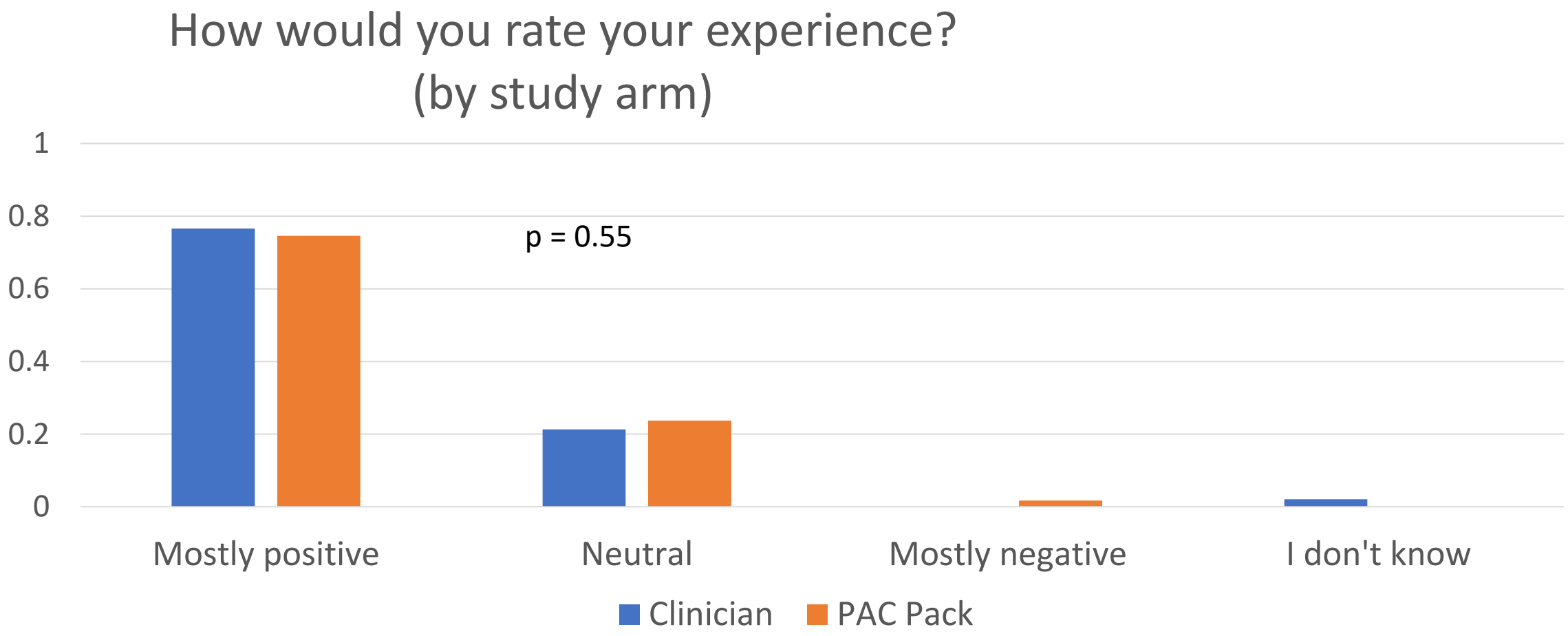
PAC Self-Swab Study (n=144)



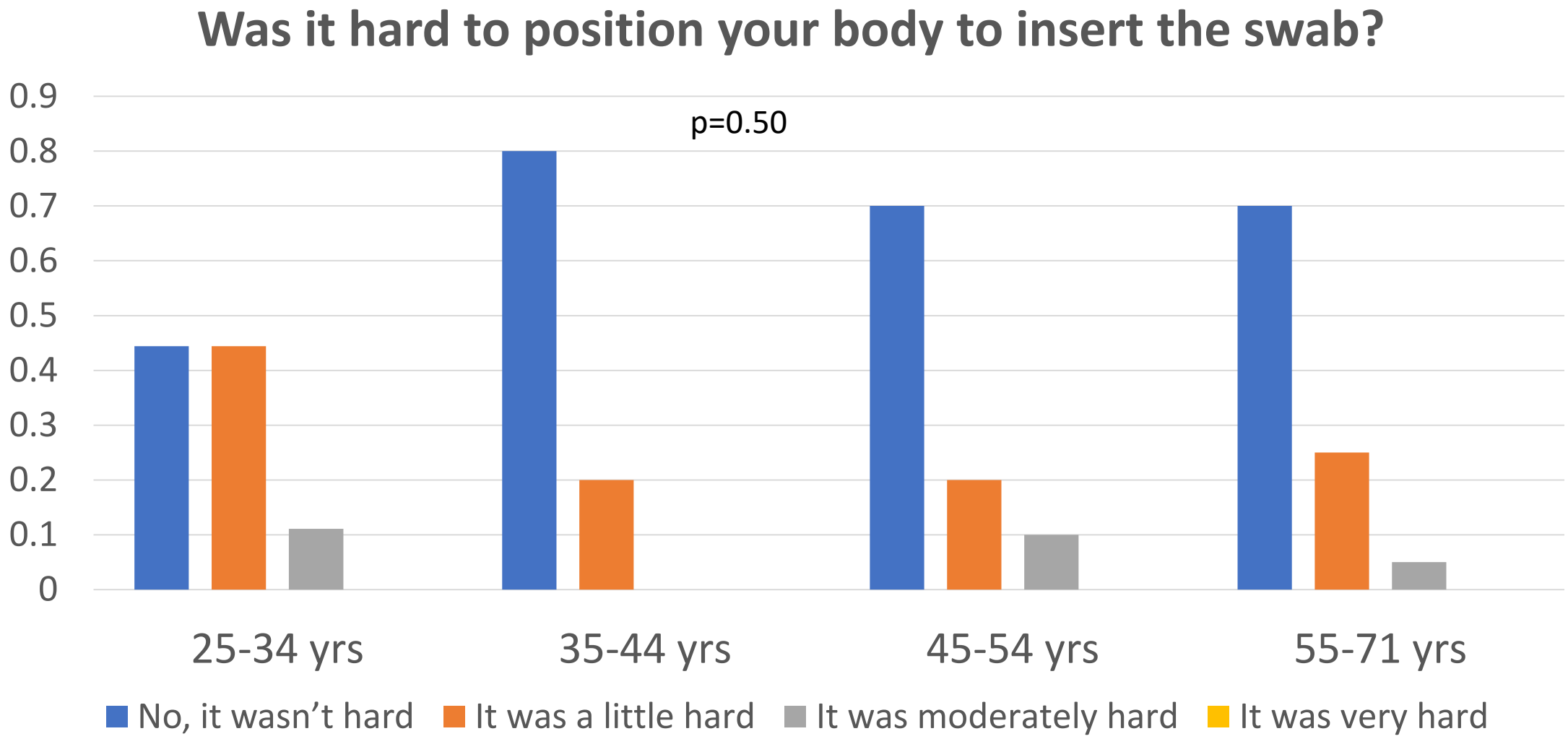
PAC Self-Swab Study (n=144)

How much bleeding after the swabbing? n (%)			
	Total	Clinician	PAC Pack
No bleeding	99 (94.3)	43 (91.5)	56 (96.6)
A little	1 (1.0)	0	1 (1.7)
A lot of bleeding	0	0	0
I don't know	5 (4.8)	4 (8.5)	1 (1.7)
		p=0.18	

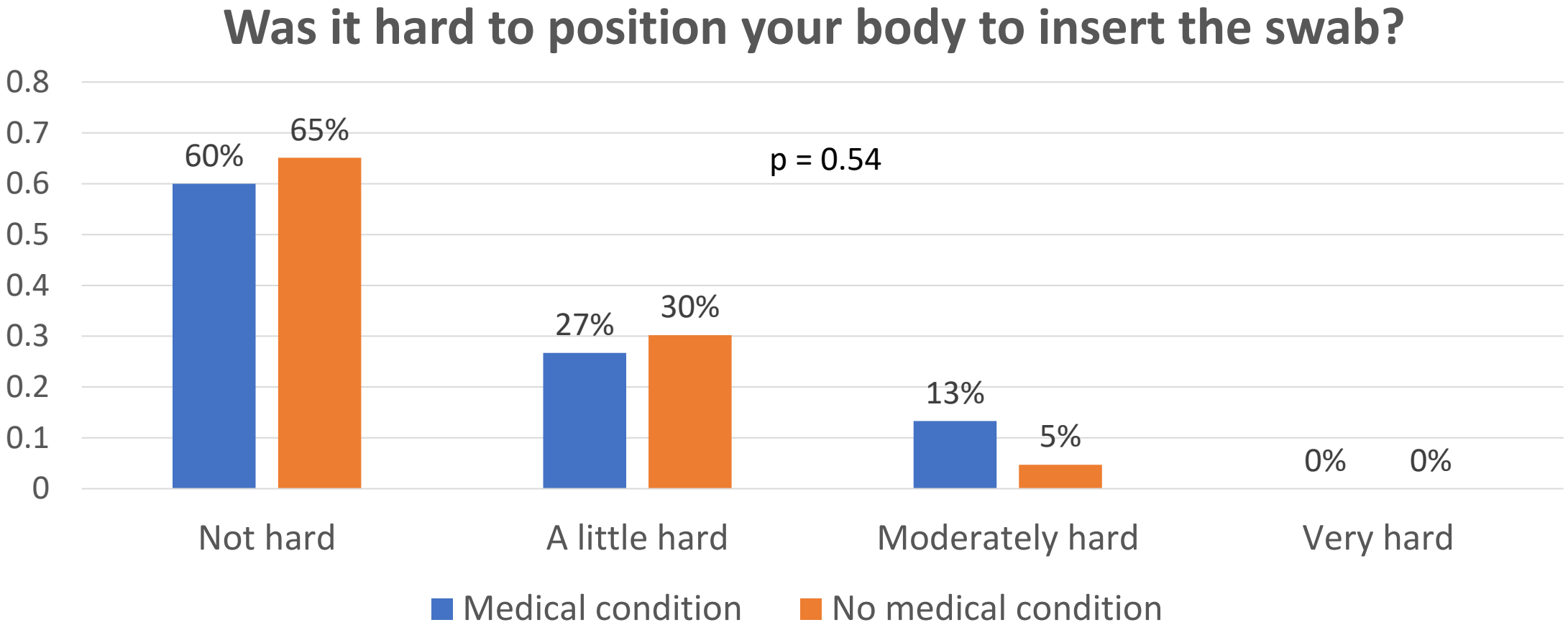
PAC Self-Swab Study (n=144)



PAC Self-Swab Study – Use of the PAC Pack by age (n=73)



PAC Self-Swab Study – Use of the PAC Pack by medical condition* (n=73)



*Arthritis, carpal tunnel syndrome, obesity, diabetes, fibromyalgia, chronic lower back pain, stroke, cerebral palsy, motor neuron diseases, movement disorders, multiple sclerosis, spina bifida, spinal cord injury, visual impairment, deafness

PAC Self-Swab Study – High-resolution anoscopy (n=15)

Highest grade lesion identified by biopsy, n (%)	
Histologically normal	7 (46.7)
Histologically abnormal	8 (53.3)
LSIL	0
HSIL/AIN2	5 (33.3)
HSIL/AIN3	3 (20.0)

LSIL - Low-grade squamous intraepithelial lesions
HSIL - High-grade squamous intraepithelial lesions
AIN - Anal intraepithelial neoplasia

CrossPAC Data

Milwaukee + Chicago + Houston

Where possible, survey and clinical data collection were standardized across all three cities to support investigations with larger sample sizes.

CrossPAC Data

Survey data

- Anal cancer
  - Knowledge
  - Worry
  - HPV vaccination
  - Screening motivation and intentions
  - Self-screening
  - Cost-effectiveness
- Anal pathology history
- DARE, Pap cytology, high-resolution anoscopy history
- Medical conditions, HIV and cancer
- Social support
- Sexual behavior
- Sexual satisfaction
- ATOD use
- COVID-19 experiences

Clinical data

- Anal pathology
- DARE practice

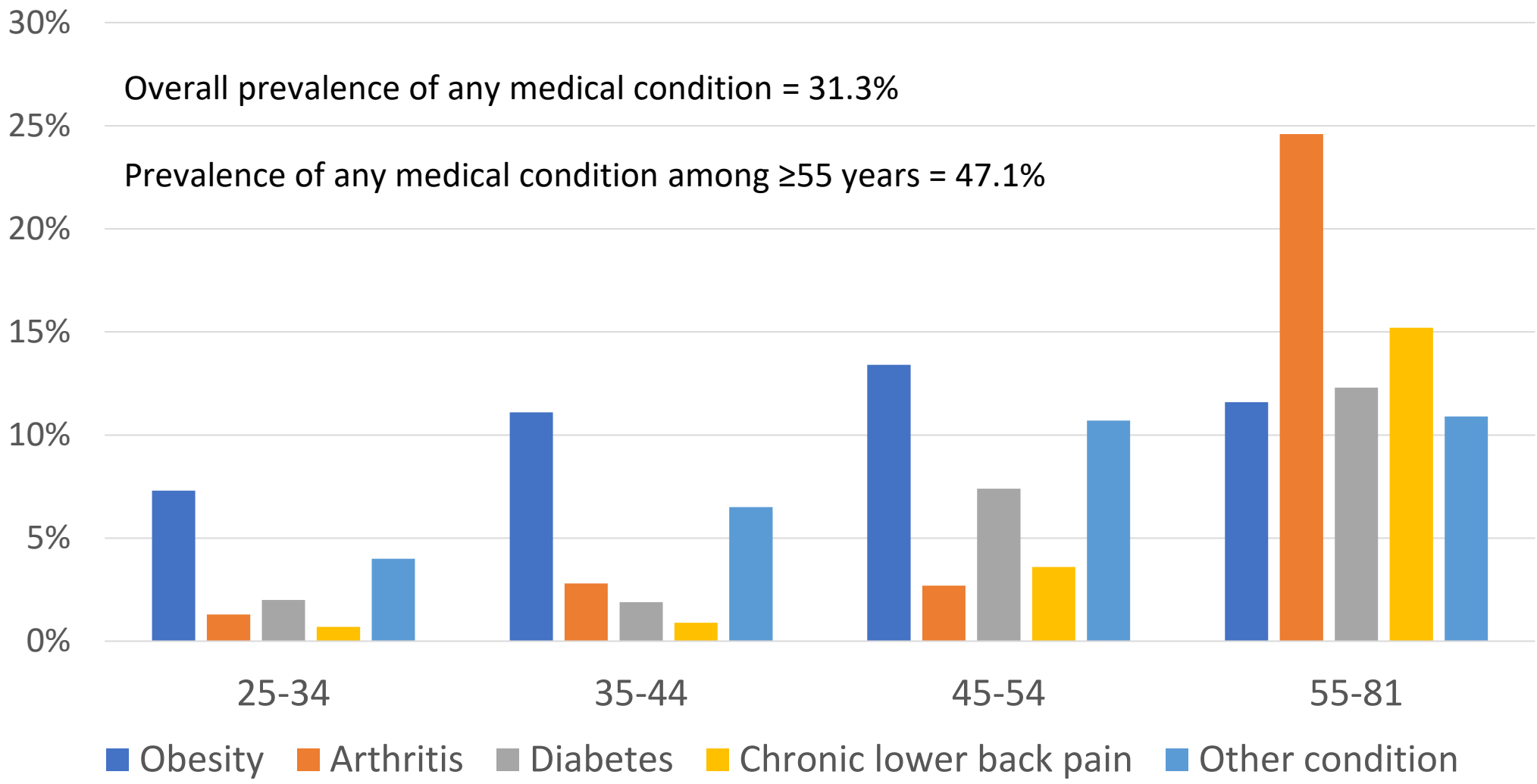
PAC Study enrollment
January 3, 2020 – August 17, 2021

	total	PAC Self-Swab MKE	PAC Palp CHI + HTX
Assessed for eligibility	2039	622	1417
Eligible	1333	479	854
Consented & enrolled	526	151	375
Randomized	426	144	282

PAC Study enrollment
January 3, 2020 – August 17, 2021

	total	PAC Self-Swab MKE	PAC Palp CHI + HTX
Assessed for eligibility	2039	622	1417
Eligible	1333	479	854
Consented & enrolled	**526**	151	375
Randomized	426	144	282

CrossPAC Data, Medical conditions (>5%) by age, (n=526)



CrossPAC Data, Cancer by age, n (%)

	Total n=526	25-34 yrs	35-44 yrs	45-54 yrs	55-81 yrs
Any cancer	28 (5.3)	1 (0.6)	2 (1.8)	1 (0.9)	24 (17.0)
Skin	23 (4.4)	1 (0.6)	2 (1.8)	0	20 (14.2)
Prostate	6 (1.2)	0	0	1 (0.9)	5 (3.6)
Oral	1 (0.2)	0	0	0	1 (0.7)
Colorectal	1 (0.2)	0	0	0	1 (0.7)

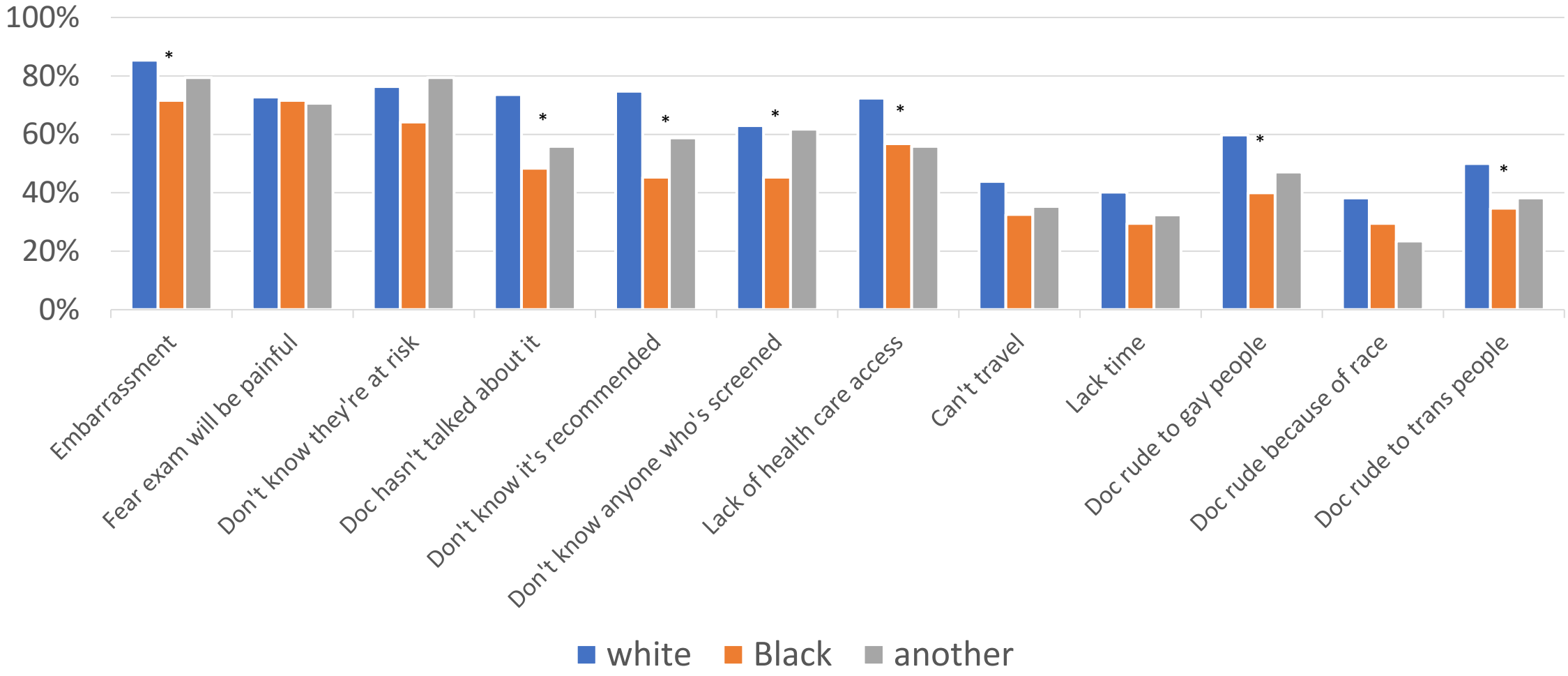
Bold indicates an association between cancer and age, $p<0.05$.

CrossPAC Data, Reasons to screen for anal cancer by age, n (%)

Suggested by	Total n=526	25-34 yrs	35-44 yrs	45-54 yrs	55-81 yrs
A doctor	401 (76.4)	124 (77.5)	80 (72.1)	94 (83.2)	103 (73.1)
A community health worker	211 (40.2)	74 (46.3)	47 (42.3)	43 (38.1)	47 (33.3)
A partner	167 (31.8)	68 (42.5)	35 (31.5)	38 (33.6)	26 (18.4)

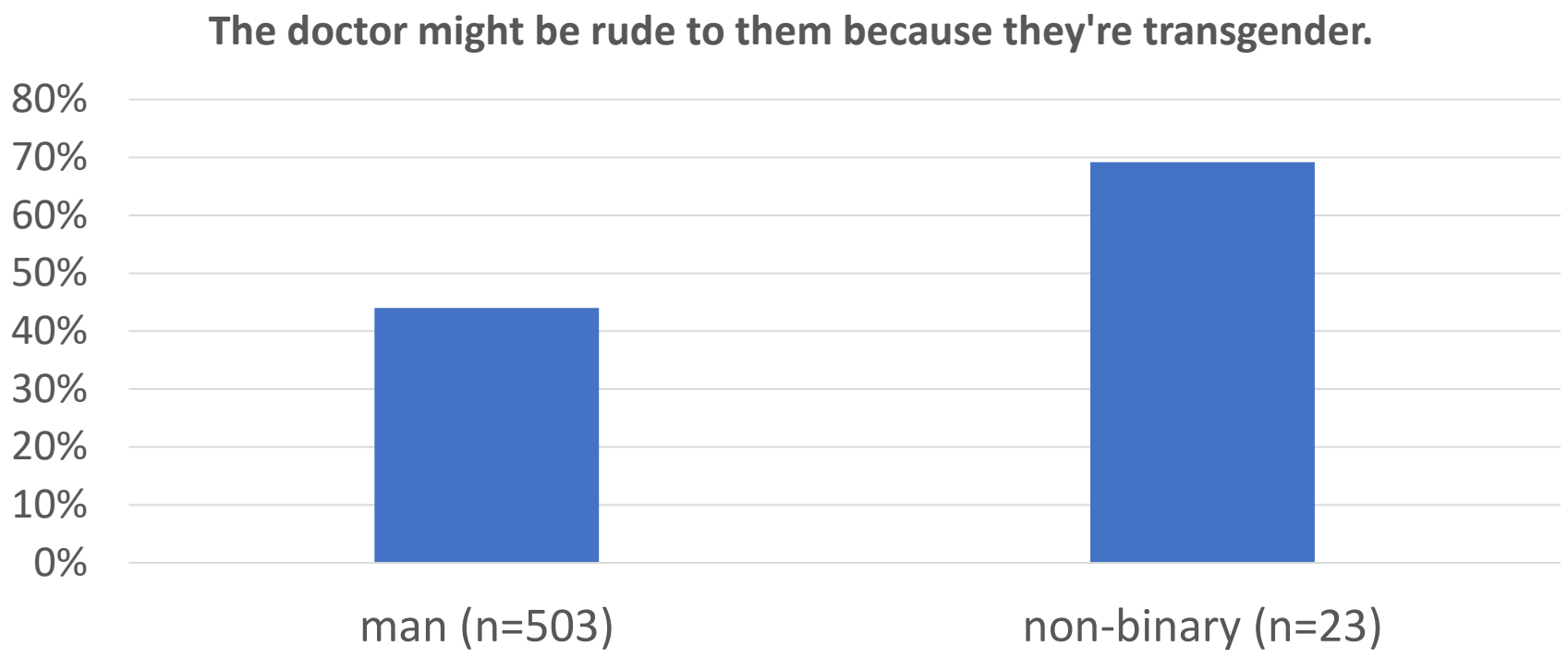
Bold indicates statistical significance by chi square using a 0.05 alpha standard.

CrossPAC Data, Reasons why some won't screen for anal cancer by race (n=526)



Asterisk indicates statistical significance by chi square using a 0.05 alpha standard.

CrossPAC Data, Reasons why some won’t screen for anal cancer by gender identity



p value < 0.05

CrossPAC Data, Clinical visits

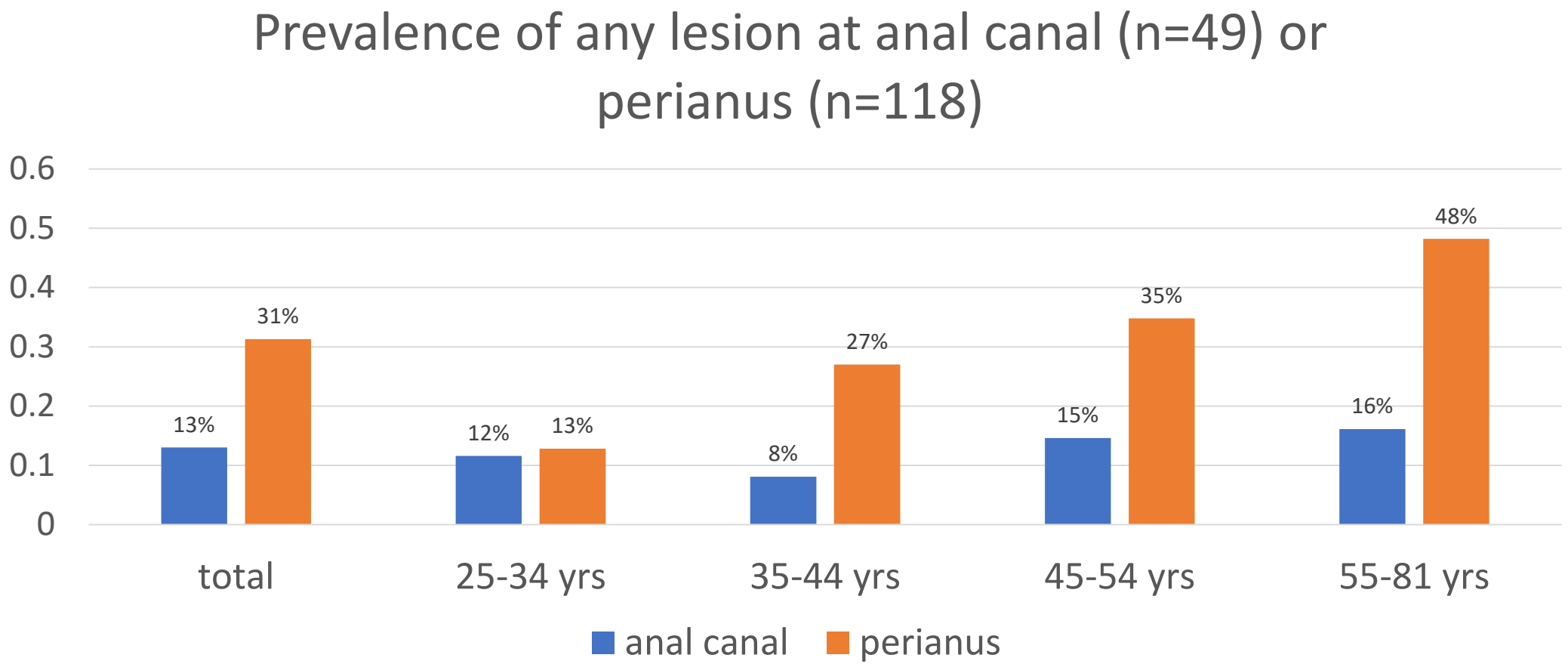
- Digital Anal Rectal Examinations are part of each clinical visit in both PAC Studies (n=377)

CrossPAC Data, Clinically observed lesions, n (%)

	total n=377	Referred for follow-up
Anal canal	49 (13.0)	16 (32.7)
Perianal region	118 (31.3)	14 (11.9)

Lesion includes any abnormality: enlarged hemorrhoids, skin tag, scar, condyloma, suspicious mass, etc.

CrossPAC Data, Clinically observed lesions by age, (n=377)

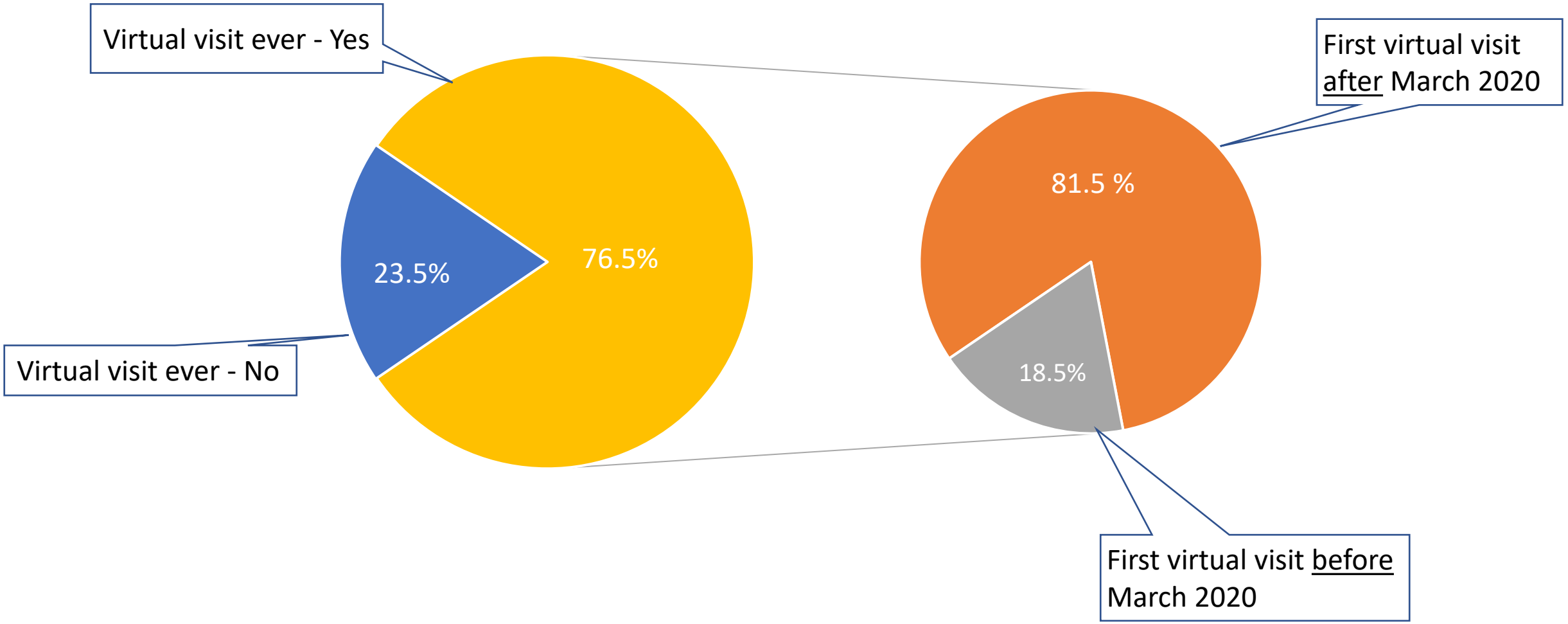


CrossPAC Data, Clinically observed lesions

Lesion size	median (range)
Anal canal	0.2 cm (0.1 cm-1.5 cm)
Perianus	0.3 cm (0.1 cm-3.0 cm)

DARE can detect very small lesions.

CrossPAC Data, Virtual health care (n=468*)



* Question added after start of COVID-19 pandemic.

March 2020. Stay-at-home. Studies suspended. *How might the pandemic affect our studies and anal cancer screening?*

COVID-19, HIV, and Sexuality Study

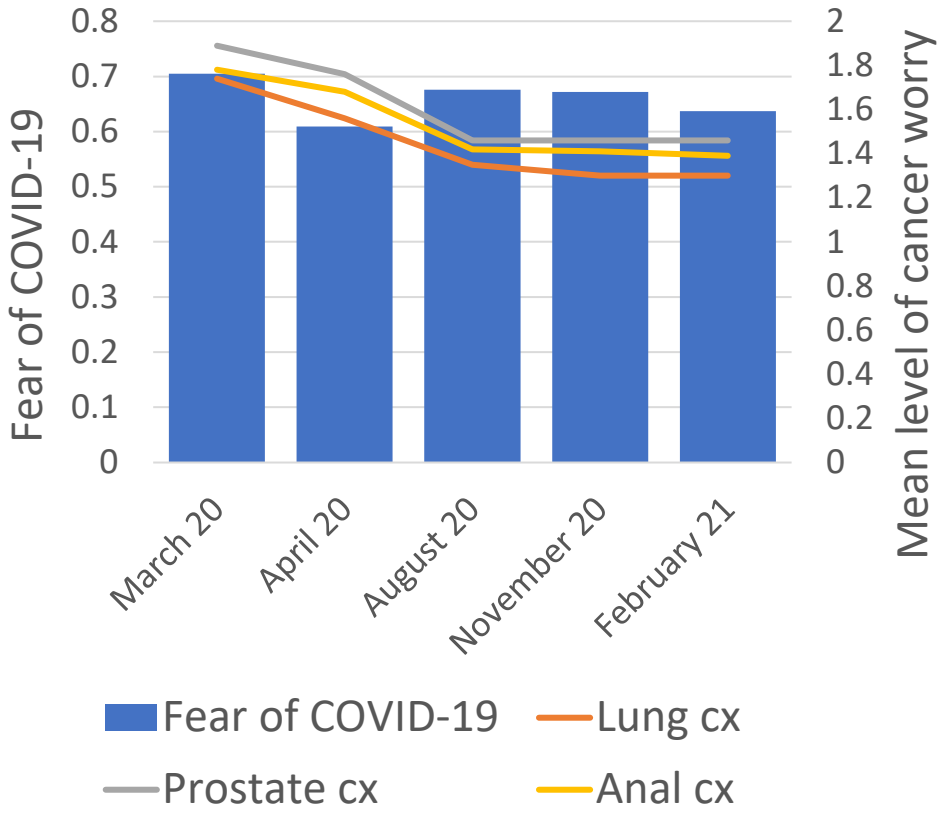
-Cohort design

-5 online surveys over 10 months

-Inclusion: residence in Milwaukee, Chicago, Houston, Minneapolis, or Detroit MSAs

n=437 at enrollment

Hypothesis: fear of COVID-19 would be inversely associated with worry about cancer.



TAKE AWAY

- Anal cancer is rare overall, but common among MSM, especially MSM with HIV
- There are no uniform guidelines for anal cancer screening
- Medical conditions are very common in this population and should be assessed in self-screening for anal cancer

Acknowledgements

Thanks to….

-The participants enrolled in the study

-The PAC Study Team in …

Milwaukee

- Christopher Ajala
- Bridgett Brzezinski
- Esmeralda Lezama-Ruiz
- Maritza Pallo
- Sarah Lundeen
- Dr. Timothy Ridolfi
- Holton Street Clinic
- Inclusion Health Clinic
- Sixteenth Street Community Health Centers
- Vivent Health
- Anal Dysplasia Program

Chicago

- Dr. Anu Hazra
- DeJuan Washington
- Rey Flores
- Jared Kerman
- Ellen Almirol
- Dr. John Schneider
- Andrew Richardson

Houston

- Lou Weaver
- Derek Smith
- Dr. Gordon Crofoot and the Crofoot Clinic staff
- Dr. Maria E. Fernandez
- Dr. Elizabeth Chiao
- Dr. Vanessa Schick
- Dr. Michael Swartz
- Dr. Ashish Deshmukh
- Dr. Michael Wilkerson
- Dr. Lu-Yu Hwang