Brief History and Scientific Highlights of the MACS/WIHS Combined Cohort Study

The Longest Running Observational Study of People Living with HIV(PLWH) and People Vulnerable to HIV
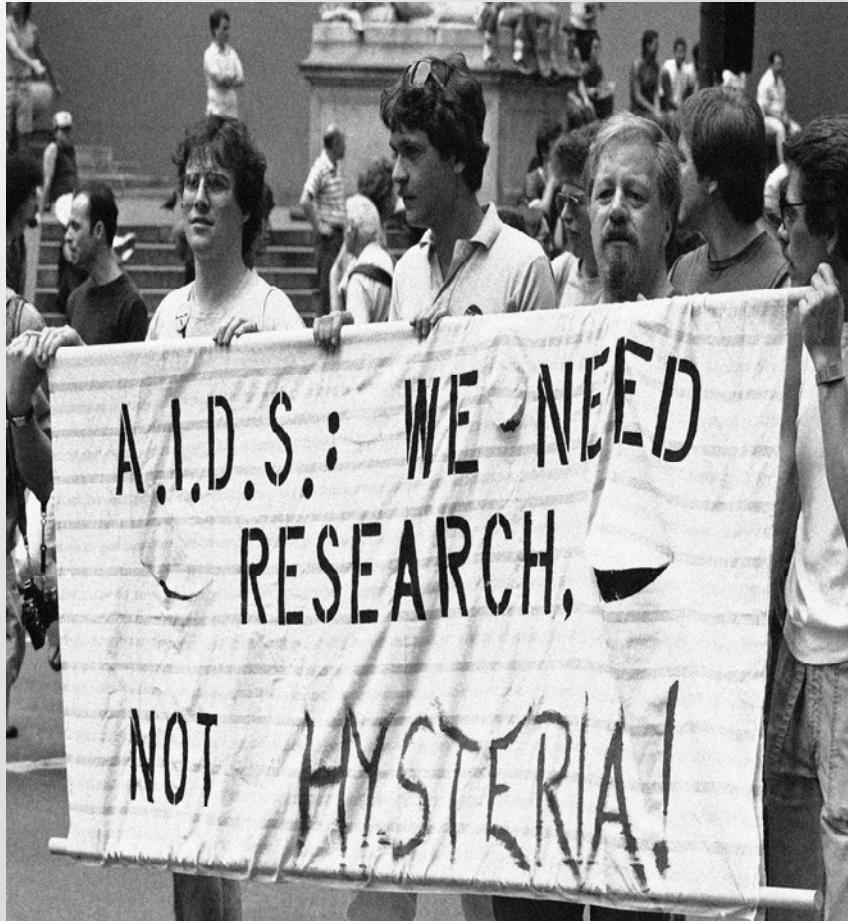
MWCCS Dossier

August 2022

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**In the beginning of the AIDS epidemic,
many people living with HIV were told that they may have only 6 months to live.**

?

Through the advent of therapies, the lives of people with HIV/AIDS changed.

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The trajectory of HIV research is changing as the population with HIV/AIDS is aging.

51%
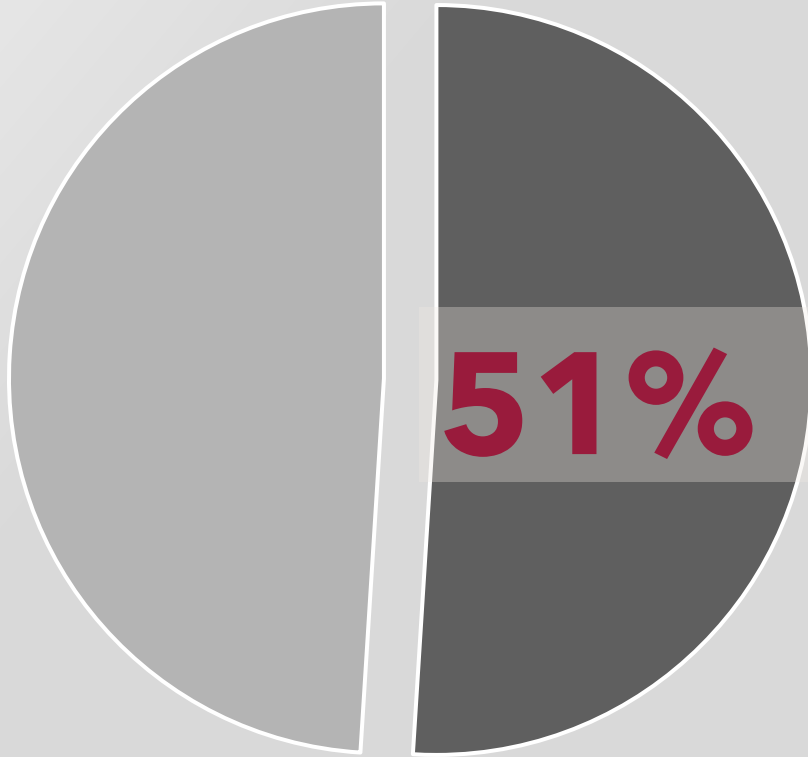
In 2018, half of **people with HIV** in the US are **50 years and above.**
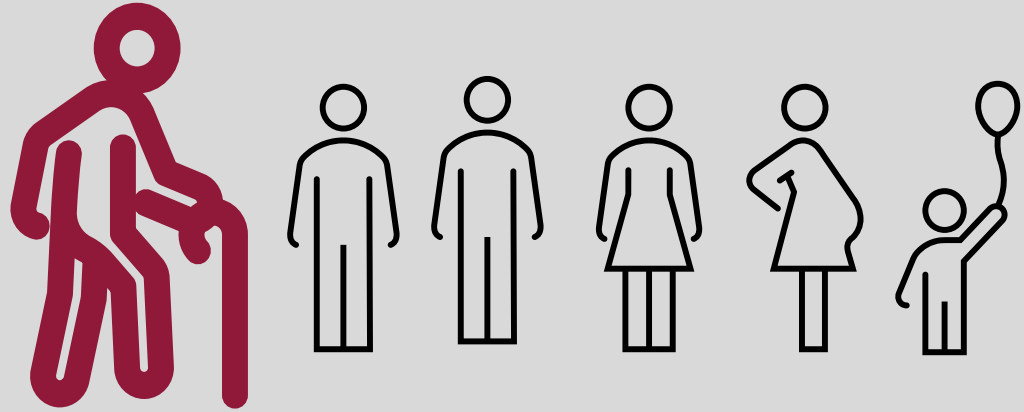
1 in 6 people diagnosed with HIV is aged 50+

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In 2019 two longstanding cohorts, the MACS and WIHS merged into the MWCCS

MACS
MULTICENTER AIDS COHORT STUDY
Established 1983

+

WIHS Women's Interagency HIV Study
Established 1993

=

MWCCS
MACS/WIHS COMBINED COHORT STUDY
Merged 2019

MACS, a cohort study of men with and without HIV, and
WIHS, a cohort study of women with and without HIV
have merged to form **MWCCS,** a combined cohort study with more participants representing a
broader, more diverse population with a *harmonized database*
to study a wider range of HIV/AIDS focus areas and other co-morbidities.

MWCCS has (as of 5/17/22):
- **>3500 Active Participant**
- **>3000 Publications**
- **Increased focus on Aging and Co-morbidities**

MACS/WIHS Timelines

1984 1989 1994 1999 2004 2009 2014 2019

Enrollment Waves

| 1984-85 | 1987-90 | | 1995 admin censoring of some HIV-[1] | 2001-3 (Add subsites; Focus: minority) | | 2010+ (Focus: early stage HIV) |

MACS was ongoing for 35 years

Enrollment Waves
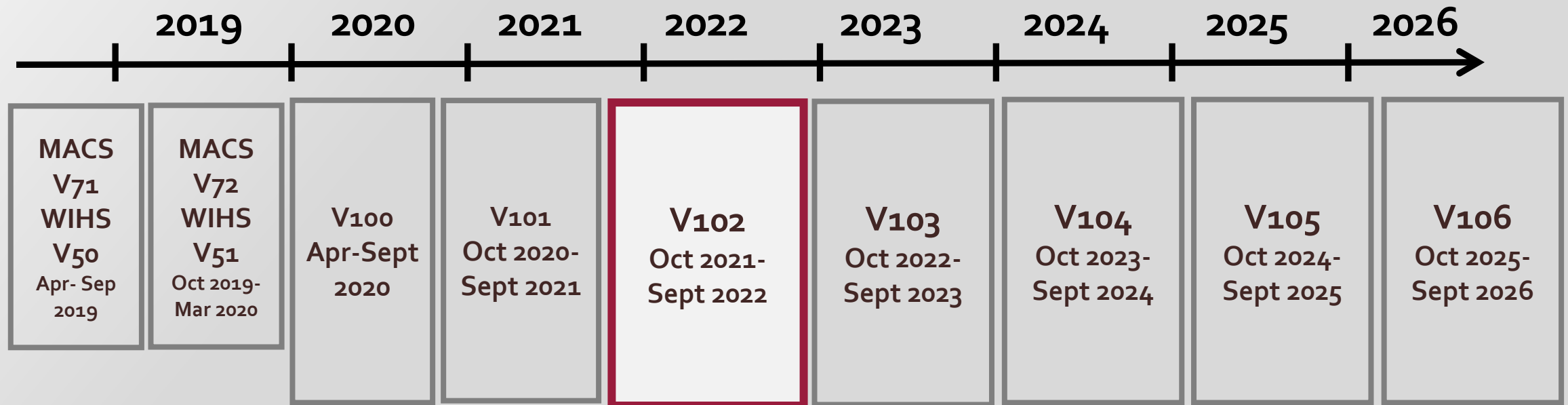
| 1994-95 | 1997 WDMAC | 2001-2 | | 2011-13 (Replenishment/ Closing of LA site) | 2013-15 (Southern Sites) |

WIHS was ongoing for 25 years

[1] In April 1995, 2255 HIV-negative men were administratively censored from further follow-up, per an NIH decision.

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MW CCS Timeline

| Year | 2019 | 2020 | 2021 | 2022 | 2023 | 2024 | 2025 | 2026 |

MACS V71 WIHS V50
Apr- Sep 2019

MACS V72 WIHS V51
Oct 2019- Mar 2020

V100
Apr-Sept 2020

V101
Oct 2020- Sept 2021

V102
Oct 2021- Sept 2022

V103
Oct 2022- Sept 2023

V104
Oct 2023- Sept 2024

V105
Oct 2024- Sept 2025

V106
Oct 2025- Sept 2026

Historic data (1984-2020) now in a harmonized database

During 2020-2022,
- Covid-19 pandemic: phone only data collection (Mar-Sept '20)
- 1st CCS visit (V101): in-person & virtual (Oct '20-Sept '21)
- Enrollment of new participants (V101-103)
- Annual Specimen collection
- 2 visits per year (core visit, shorter visit)

MWCCS Sites in US HIV Epidemic Prevalent Areas*
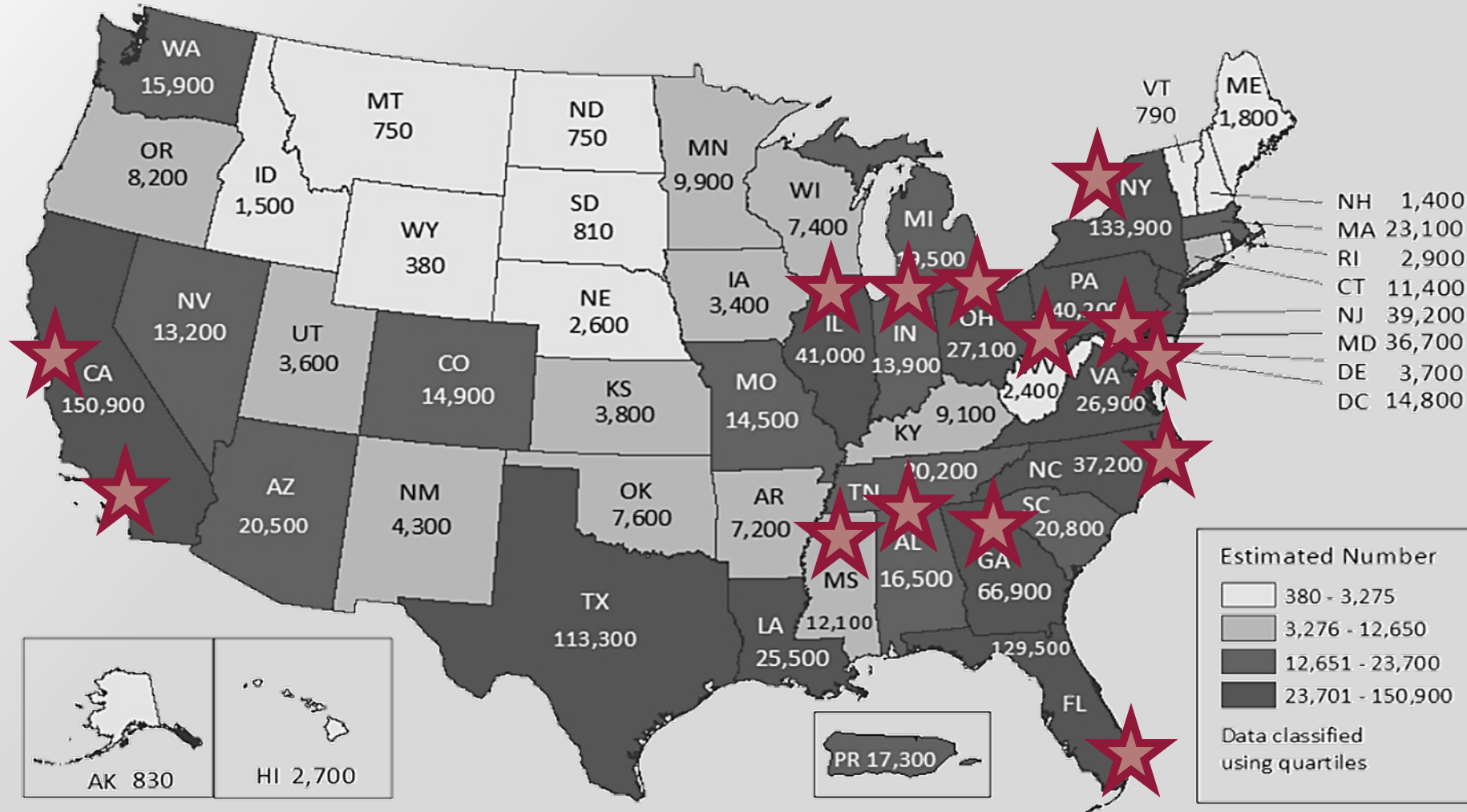
Study sites spread across the Northeast, South, Midwest, and West Coast.

For more information regarding study sites and contact persons, please visit https://statepi.jhsph.edu/mwccs/study-locations/

WA 15,900
OR 8,200
MT 750
ND 750
MN 9,900
VT 790
ME 1,800
ID 1,500
SD 810
WI 7,400
MI 9,500
NY 133,900
NH 1,400
MA 23,100
RI 2,900
CT 11,400
NJ 39,200
MD 36,700
DE 3,700
DC 14,800
WY 380
IA 3,400
PA 40,200
NV 13,200
UT 3,600
CO 14,900
NE 2,600
IL 41,000
IN 13,900
OH 27,100
WV 2,400
VA 26,900
CA 150,900
KS 3,800
MO 14,500
KY 9,100
NC 37,200
AZ 20,500
NM 4,300
OK 7,600
AR 7,200
TN 20,200
SC 20,800
MS 12,100
AL 16,500
GA 66,900
TX 113,300
LA 25,500
FL 129,500
AK 830
HI 2,700
PR 17,300

Estimated Number
380 - 3,275
3,276 - 12,650
12,651 - 23,700
23,701 - 150,900
Data classified using quartiles

*Estimated HIV Prevalence among Persons Aged ≥13 years, by Area of Residence 2019

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Enrollment (as of 5/17/22)

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Participants

Site (Subsite)	# Enrolled:
Atlanta, GA	281
Baltimore, MD	349
Birmingham, AL / Jackson, MS	266
Bronx, NY	386
Brooklyn, NY	280
Chapel Hill, NC	200
Chicago (Cook County), IL	278
Chicago (Northwestern), IL	285
Los Angeles, CA	462
Miami, FL	184
Pittsburgh, PA	299
San Francisco, CA	297
Washington DC	248
TOTAL:	**3,815**

Participant Characteristics, By HIV Status, Gender and Age (5/17/22)

Characteristics		Carryover Participants [N=3,210] N (%)	New Enrollees [N=609] N (%)
HIV Status	PLWH	1,988 (61.8)	355 (57.1)
	HIV-	1,231 (38.2)	267 (42.9)
Gender*	CIS Male	1,424 (44.2)	351 (56.3)
	CIS Female	1,790 (55.6)	247 (39.7)
	Trans Man	2 (0.1)	1 (0.2)
	Trans Woman	3 (0.1)	13 (2.1)
	Gender Fluid	-	6 (1.0)
	Identity not listed	-	5 (0.8)
Age in years: Median (IQR)	PLWH	57 (50-63)	49 (38.5-56)
	HIV-	61 (51-68)	52 (43-58)

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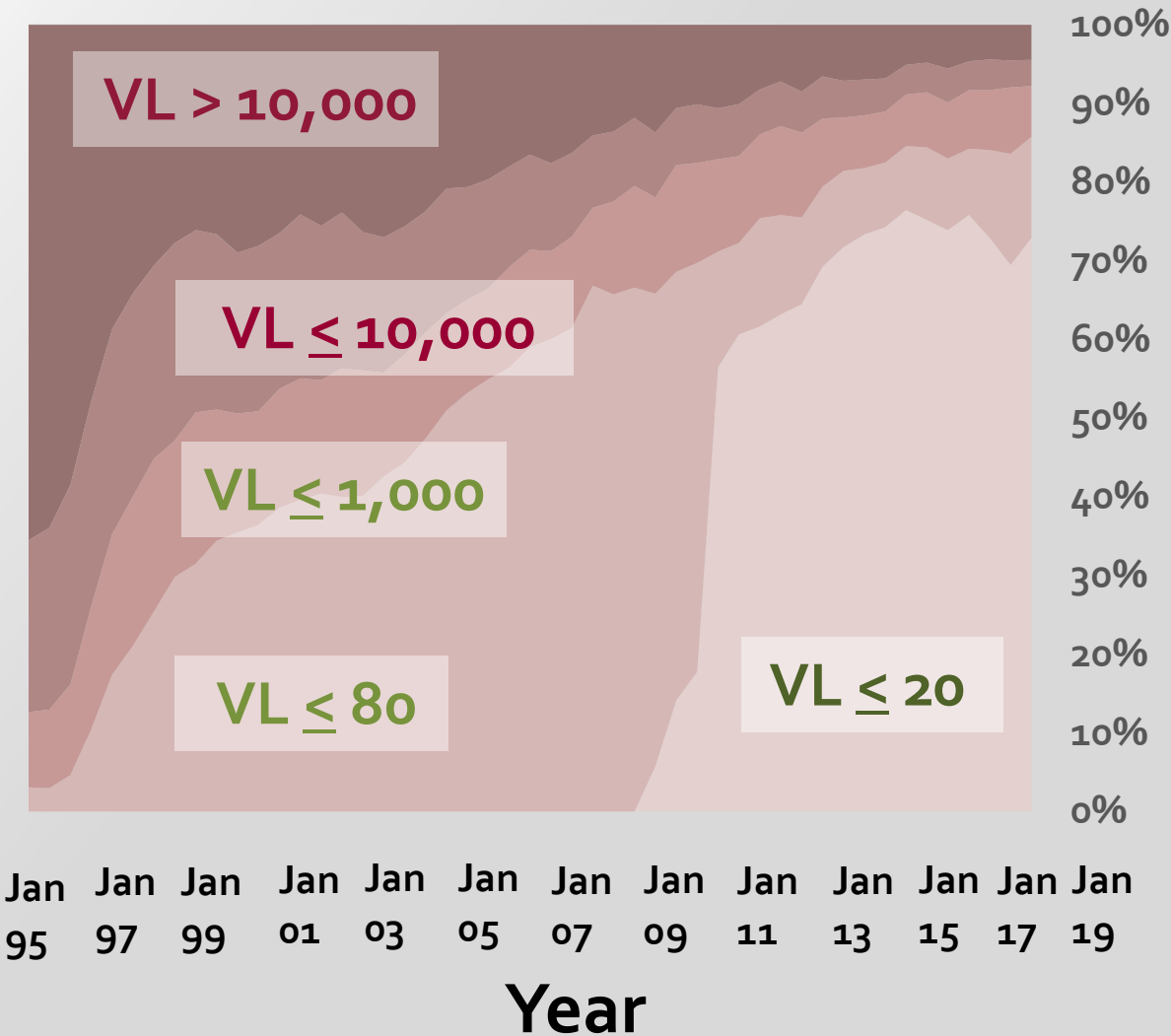Age Distribution of Active Participants (5/17/22)
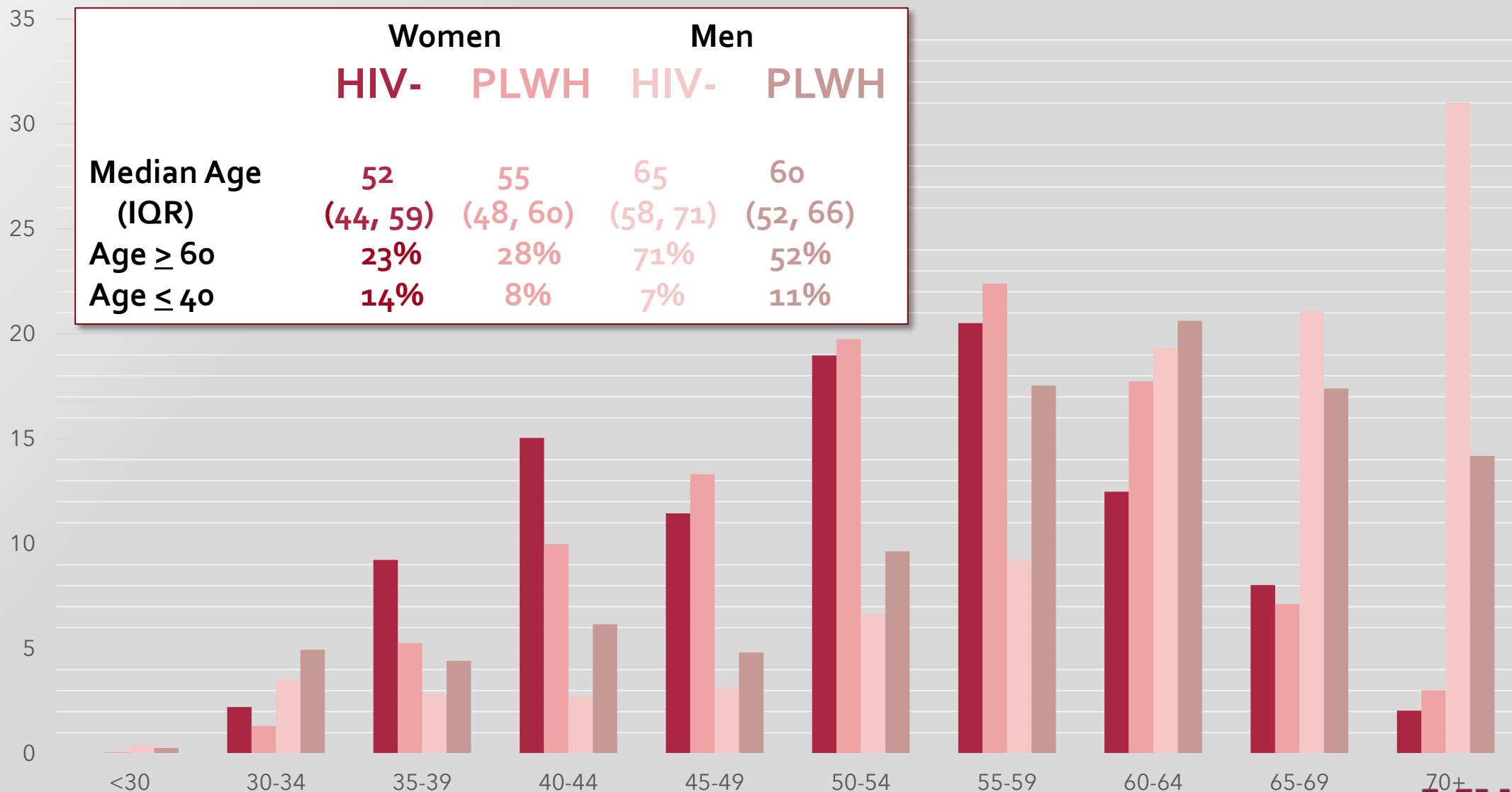
Participant Characteristics, By Ethnicity and Race (5/17/22)

| Carryover + New	Female: Hispanic/Latinx	Male: Hispanic/Latinx	Female: Not Hispanic/ Latinx	Male: Not Hispanic / Latinx	TOTAL (%)
Black/ African American	54	17	1,489	523	2,083 (54)
White	75	128	184	959	1,346 (35)
American Indian / Alaskan Native	5	10	9	3	27 (1)
Multiracial	19	18	55	22	114 (3)
Other	122	74	35	22	253 (7)
TOTAL (%)	275 (7)	247 (6)	1,772 (46)	1,529 (40)	3,823

Ethnicity: Unknown ethnicity excluded due to small numbers (N=8)
Race: Native Hawaiian/Pacific Islander (N=5) and Asian (N=18) included with Other

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Changes in Viral Load Profiles Among PLWH / Changes in CD4 Count Profiles Among PLWH
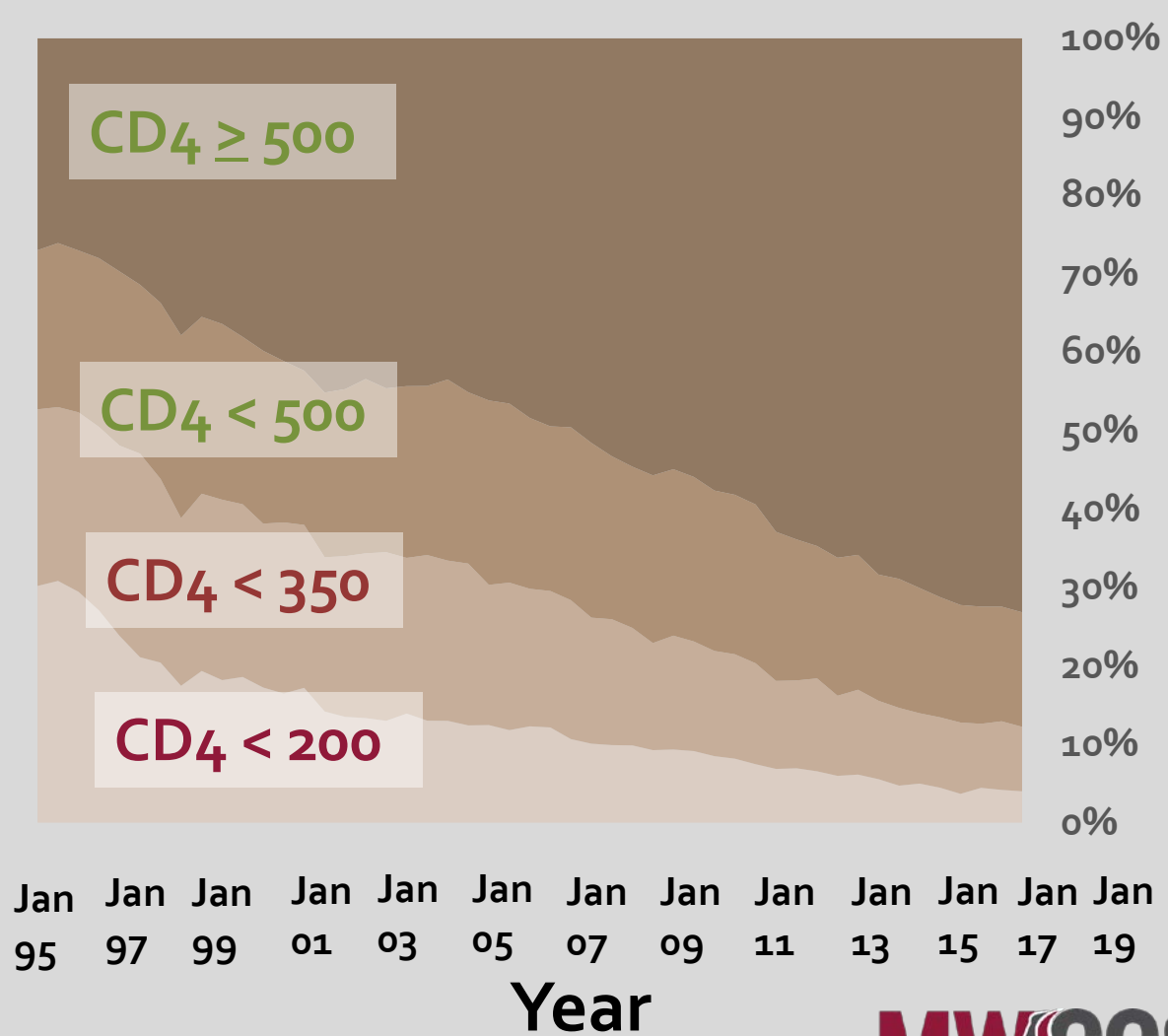
TaqMan v2.0 HIV-1, sensitive to 20 copies HIV RNA/mL, implemented in 2009

MWCCS — MACS/WIHS COMBINED COHORT STUDY

CD4, Viral Load, and ART use among PLWH (5/17/22)

Characteristic	N (%)		
	Women [N=1291]	**Men [N=747]**	**Total [N=2038]**
Current CD4	N=1178	N=423	N=1601
<200	64 (5)	8 (2)	72 (5)
200-349	100 (8)	35 (8)	135 (8)
350-499	140 (12)	87 (21)	227 (14)
≥ 500	874 (74)	293 (69)	1167 (73)
Current HIV RNA	N=1015	N=366	N=1381
Undetectable (no signal)[1]	557 (55)	208 (57)	765 (55)
"Undetectable" (< 20 cp/mL)[2]	154 (15)	80 (22)	234 (17)
Detectable ($\geq$ 20 cp/mL)	304 (30)	78 (21)	382 (28)
Current ART use	N=1289	N=681	N=1970
Reported ART at V101 interview	1245 (97)	661 (97)	1906 (97)

[1] 4 women had lower limit of 30 cp/mL (no signal)

[2] 4 women had lower limit of 30 cp/mL ("Undetectable")

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MWCCS studies many areas, including, but not limited to...

Cardiovascular and Pulmonary disease	Sleep Quality	Neuro-cognitive ability	Frailty and Physical disability

Cancer	HIV Pathogenesis	Metabolic, liver, and kidney dysfunction	Psychosocial and Behavioral conditions	Health disparities

For more information on our study aims:
https://statepi.jhsph.edu/mwccs/science/

For information on our scientific working groups:
https://statepi.jhsph.edu/mwccs/working-groups/

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Chronic Health Indicators (5/17/22)

	PLWH [N = 1957]		HIV- [N = 1243]		Total
	Women [N= 1283][1]	Men [N =674][1]	Women [N = 580][1]	Men [N = 663][1]	[N = 3200]
BMI: Median (IQR)[2] % BMI >30 % BMI >40	32.2 (26.8, 38.5) 60% 22%	26.6 (24.4, 30.6) 29% 6%	32.9 (28.1, 39.6) 66% 24%]	27.5 (24.6, 31.4) 32% 6%	30.3 (25.8, 36.5) 52% 18%
Hypertension[3]: N(%)	882 (69)	415 (62)	375 (65)	389 (59)	2061 (64)
Systolic BP [mm Hg] (IQR)[4]	126 (114, 140)	128 (117, 137)	127 (114, 142)	128 (117, 139)	127 (115, 140)
Diastolic BP [mm Hg] (IQR)[4]	75 (68, 83)	79 (72, 87)	75 (69, 83)	77 (70, 84)	76 (69, 84)
Diabetes[5]: N(%)	344 (26)	153 (23)	134 (23)	136 (21)	757 (24)
High Cholesterol[6]: N(%)	741 (59)	420 (67)	296 (52)	379 (63)	1836 (60)
Osteopenia/porosis, Low Bone Mineral Density: N(%)	23 (2)	11 (2)	12 (2)	7 (1)	53 (2)

[1] Sex at birth used for gender classification as it is needed to calculate CVD risk, eGFR and other gender-based variables in chronic health dataset

[2] BMI % calculated among subset without missing data. Total for BMI = 2500: PLWH women = 1183 , PLWH men =414, HIV- female = 520 and HIV- male = 383

[3] Hypertension: SBP ≥ 130, DBP ≥ 80, use of medication with or without self-report diagnosis

[4] Total for BP = 2359: PLWH women = 1201, PLWH men = 355 , HIV- female = 526 and HIV- male = 277

[5] Diabetes: ever self- reported medication, confirmation of a) fasting glucose ≥ 126 or HbA1c ≥ 6.5 % or self reported diabetes. Once participant meets DM definition, then DIABETES becomes yes thereafter; only defined for women who are not pregnant at visit

[6] High cholesterol: Total cholesterol ≥ 200 mg/dl, fasting LDL ≥ 130 mg/dl, HDL < 40 mg/dl, fasting triglycerides ≥ 150 mg/dl, med use with self-report or diagnosis in past. High cholesterol % calculated among subset without missing data. Total for high cholesterol = 3048: PLWH female = 1250, PLWH male = 420, HIV- female =567 and HIV- male = 605

Chronic Health Indicators (5/17/22)

	N (%)				
	PLWH [N = 2038]		**HIV- [N = 1320]**		**Total [N =3358]**
	Women [N = 1298]	Men [N = 740]	Women [N = 589]	Men [N = 731]	
Hepatitis C	60 (5)	42 (6)	31 (5)	14 (2)	147 (4)
Cancer history [1]	156 (16)	155 (26)	46 (12)	168 (30)	525 (20)
Broken bones, ever [2]	339 (35)	248 (47)	163 (44)	275 (52)	1025 (43)
Fracture in past year [3]	26 (2)	15 (2)	17 (3)	24 (4)	82 (3)
ACC/AHA CVD Risk Score (IQR)[4]	0.05 (0.02, 0.11)	0.11 (0.06, 0.19)	0.05 (0.01, 0.12)	0.13 (0.07, 0.24)	0.07 (0.02, 0.14)
Race-free Estimated Glomerular Rate (eGFR): median [mL/min/1.73 m2] (IQR)[3]	79.4 (64.7, 94.7)	80.1 (66.4, 93.9)	88.2 (73.1, 101.6)	88.6 (76.2, 98.2)	83 (67.9, 97.1)
eGFR classification:[3]					
≥90 (normal or high)	370 (29)	135 (20)	240 (41)	179 (27)	924 (29)
60- 89 (mildly decreased)	598 (49)	222 (32)	221 (38)	178 (27)	1219 (38)
45-59 (mildly to moderately decreased)	153 (12)	51 (8)	39 (7)	19 (3)	262 (8)
30-44 (moderately to severely decreased)	43 (3)	11 (2)	15 (3)	6 (1)	75 (2)
<30 (severely decreased to kidney failure)	119 (9)	255 (38)	65 (11)	280 (42)	720 (22)

[1] Cancer hx % calculated among subset without missing data. Total = 2506: PLWH female = 971, PLWH male = 595, HIV- female = 372 and HIV- male = 568

[2] Broken bones ever % calculated among subset w/o missing data. Total = 2382: PLWH female = 966, PLWH male = 519, HIV- female = 372 and HIV- male = 525

[3] Fractured bones in past year and eGFR classification %s calculated among subset without missing data. Total =3200: PLWH women = 1283, PLWH men = 674, HIV-women = 580, HIV- men = 663

[4] ACC/AHA CVD Risk Score or Pooled Cohort Equation. Total for CVD Risk score = 1940: PLWH female = 1009, PLWH male = 281, HIV- female = 423 and HIV- male = 227

Cardiovascular and Pulmonary Characteristics (5/17/22)[1]

	N (%)				
	PLWH [N=1958]		**HIV- [N=1252]**		**Total**
	Women	Men	Women	Men	[N=3210]
Hospitalized angina[2]	28 (2)	16 (2)	15 (3)	20 (3)	79 (2)
Heart attack / Myocardial infarction (MI)	49 (4)	33 (5)	25 (4)	25 (4)	132 (4)
Hospitalized heart failure (HF)[2]	22 (2)	6 (<1)	14 (2)	8 (1)	50 (2)
Stroke	35 (3)	24 (4)	16 (3)	9 (1)	84 (3)
Transient Ischemic Attack (TIA)[3]	49 (4)	23 (3)	18 (3)	17 (3)	107 (3)
Atrial fibrillation	3 (<1)	20 (3)	0 (0)	38 (6)	61 (2)
Atrial flutter	0 (0)	12 (2)	1 (<1)	16 (2)	29 (<1)
Any heart/blood vessel procedure	45 (4)	61 (9)	22 (4)	74 (11)	202 (6)
Hospitalized Chronic Obstructive Pulmonary Disease (COPD), Emphysema, Chronic bronchitis[4]	51 (4)	9 (1)	26 (5)	10 (1)	96 (3)
Hospitalized pneumonia	42 (3)	84 (12)	21 (4)	41 (6)	188 (6)
Hospitalized asthma	83 (6)	15 (2)	54 (9)	25 (4)	177 (6)

[1] Self-reported history from BLHH and FPHH (ever). Added FPHH when able; due to use by carryover participants at baseline
[2] Angina and heart failure do not have hospitalized (since last visit) in the FPHH
[3] TIA went down overall by two
[4] COPD in past two reports used 'EVER' COPD vs. Hospitalized COPD, which is why numbers have changed

COVID-19 Metrics (5/17/22)

	N (%)		
Metric	**PLWH [N=2501]**	**HIV- [N=1619]**	**Total [N=4120]**
Ever Tested for COVID-19	1590 (64)	1016 (63)	2606 (63)
Ever Infected with COVID-19	195 (8)	118 (7)	313 (8)
COVID-19 Hospitalizations			
With Diagnosis	10 (<1)	4 (<1)	14 (<1)
Suspected	74 (3)	37 (2)	111 (3)
Not Hospitalized	2196 (88)	1410 (87)	3606 (88)
Unknown	221 (9)	168 (10)	390 (9)
Metric	**PLWH [N=1436]**	**HIV- [N=870]**	**Total [N=2307]**
COVID Vaccination Status			
Fully Vaccinated	1080 (75)	647 (74)	1728 (75)
Partially Vaccinated	62 (4)	29 (3)	91 (4)
Unvaccinated	274 (19)	181 (21)	455 (20)
Unknown	20 (1)	13 (1)	33 (1)

Data and Specimen Collection

We collect data on:

Demographics

HIV medication and adherence

Frailty, aging

Neuropsychology

Attitude and beliefs

Healthcare utilization

Quality of life, depression

Behaviors (substance use and sexual behavior)

Medical conditions and medication

Chronic conditions and co-infection

Lab results performed on:

Blood Chemistries, Complete Blood Count, Hepatitis, T-Cell flow cytometry, HIV Viral Load, Lipid Panel

Physical Examination performed

Outcome verification and adjudication

Biorepository of samples

Registry matching:

National Death Index, Cancer Registry, Renal Disease Registry

For more information on data collection forms: https://statepi.jhsph.edu/mwccs/data-collection-forms/
Or info on data/specimen collection procedures: https://statepi.jhsph.edu/mwccs/manual-of-operations/

Specimens in Central Repository (05/01/20)

Specimen	Date Range Collected		Current Participants		
	MACS	**WIHS**	**PLWH**	**HIV (-)**	**TOTAL**
Plasma	1984-2019	1994-2019	78,244	48,176	107,922
Plasma (EDTA)	2006-2019	2014-2019	40,841	17,169	58,010
Serum	1984-2019	1994-2019	72,345	48,176	120,521
Peripheral Blood	1994-2019	1994-2019	76,704	29,234	105,938
Cell Pellets	1994-2019	1994-2019	38,637	15,337	53,974
Urine (clean void)	1984-2019	1994-2019	44,060	16,864	60,924
Urine (supernatant)	NC	1994-2019	15,253	6,293	21,546
Cervicovaginal Lavage (CVL)	NC	1994-2019	38,043	16,021	54,064
Oral sample	1984-1993	1995-2004	1,558	607	2,165
B cell lines	N/A	NC	509	195	704
Stool	1984-1985	NC	2798	1,148	3,946
Semen	1984-1993	N/A	1,437	372	1,809

Table was summarized from Table 6 of : https://pubmed.ncbi.nlm.nih.gov/33675224/
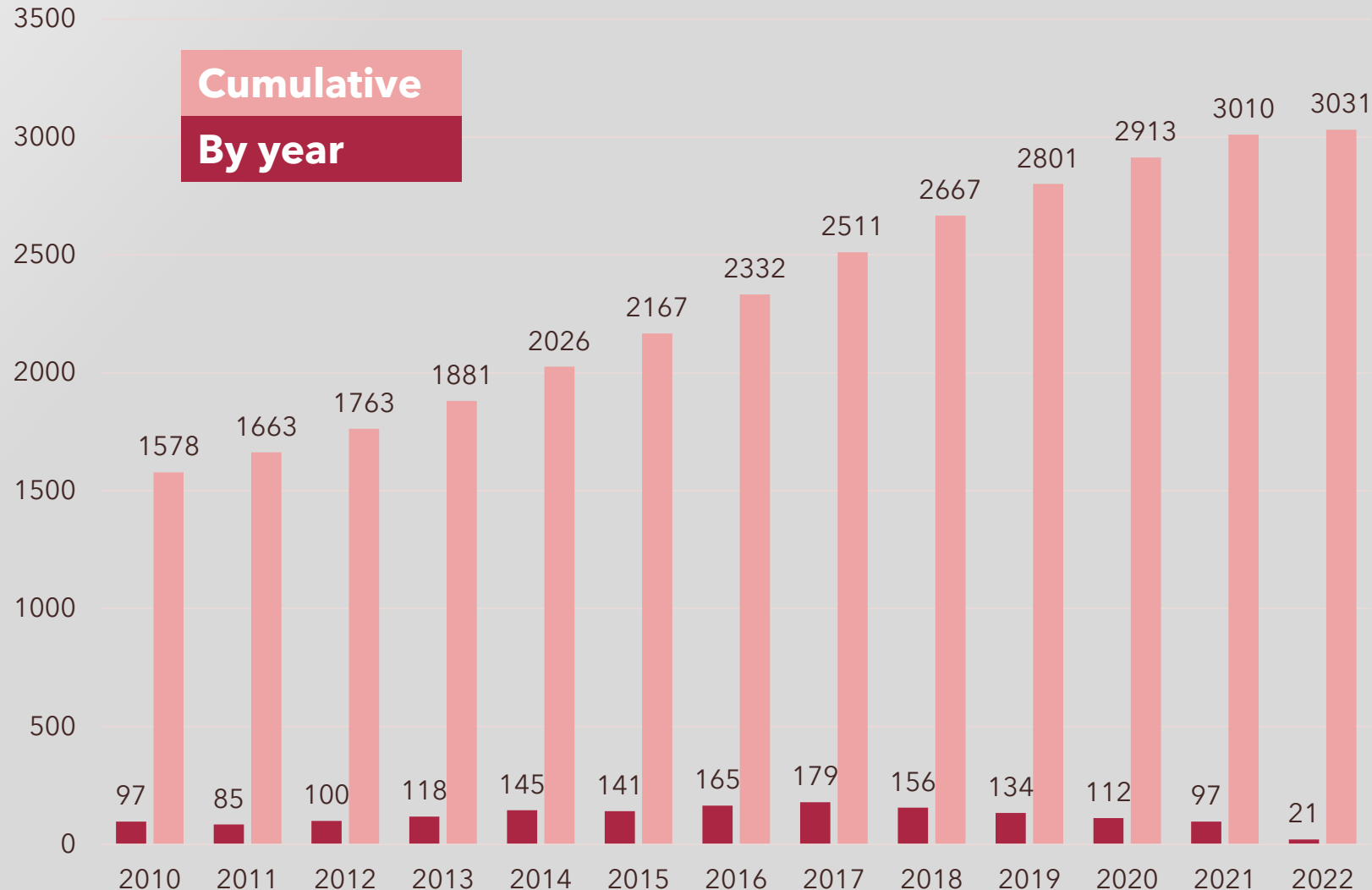
Characteristics of the MACS/WIHS Combined Cohort Study: Opportunities for Research on Aging With HIV in the Longest US Observational Study of HIV (D'Souza, et al, 2021)

- Data protocols for the MACS and WIHS were similar but not identical, this study described how these two cohorts were merged to have a unified protocol.
- This study was able to:
  - Harmonized definition for co-morbidities
  - Harmonized database and specimen collection of the two cohorts
  - Present key characteristics of participants in the two cohorts
    - Key demographics, race/ethnicity, gender
    - Co-morbidity profiles of participants
    - Health Behavioral and Mental Status Characteristics
- This will bring forth a new era in HIV/AIDS research as we learn more about the effect of HIV seropositivity, aging and other co-morbidities
- Please look at their findings in: https://pubmed.ncbi.nlm.nih.gov/33675224/

Optimal lung cancer screening criteria among persons living with HIV (Sellers, et al, 2022)
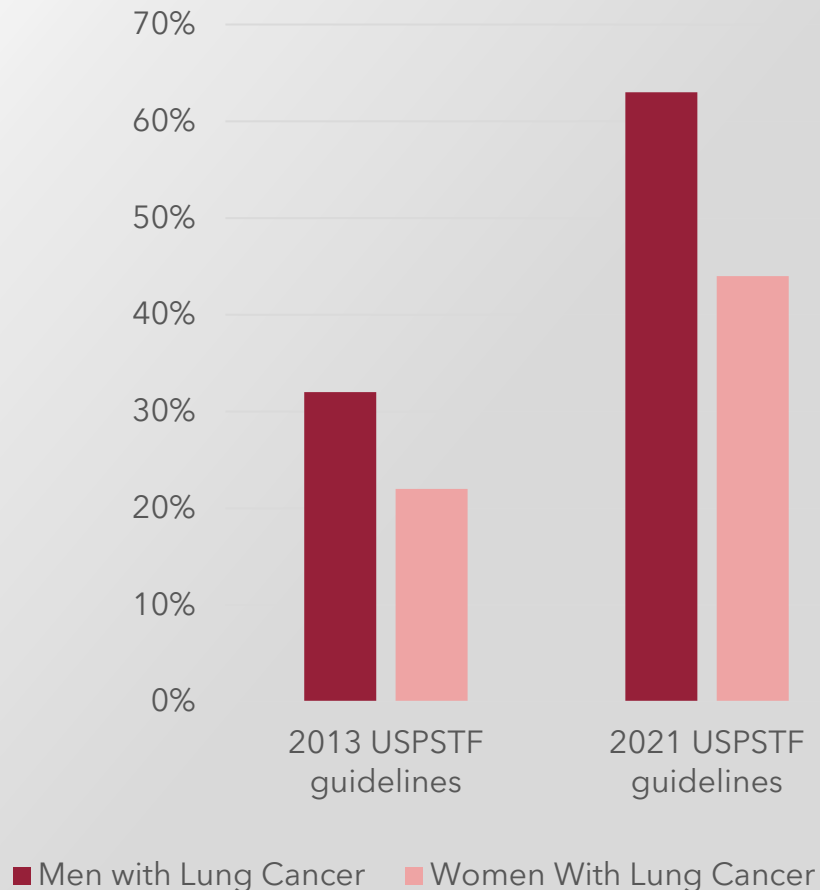
- PLWH are at a higher risk for lung cancer but were not well-represented in the National Lung Screening Trial which was the basis for 2013 USPSTF lung cancer screening guidelines

- Retrospective analysis was done using MWCCS data

- 52 women and 19 men with lung cancer; 1950 women and 1599 men without lung cancer

- 11 women (22%) and 6 men (32%) met the 2013 guidelines

- 22 women (44%) and 12 men (63%) met the 2021 guidelines

  - More PLWH with lung cancer are eligible for screening based on the 2021 USPSTF guidelines

  - Increased sensitivity of 2021 guidelines is attributed to decreased age and tobacco exposure thresholds in women

The online pre-print can be found at:
https://pubmed.ncbi.nlm.nih.gov/35125470/

Examples of Recent Articles (2021)

Article Title	Journal	Authors	Topic Area
Prevalence of COVID-19-Related Social Disruptions and Effects on Psychosocial Health in a Mixed-Serostatus Cohort of Men and Women.	Journal of Acquired Immune Deficiency Syndromes	M. Friedman et al.	Psychosocial and Behavior Covid-19
The IDOze Study: The Link between Sleep Disruption and Tryptophan-Kynurenine Pathway Activation in Women with HIV	Journal of Infectious Diseases	A. Rogando et al.	Sleep
HIV serostatus and incident coronary artery stenosis in men with a baseline zero coronary artery calcium	AIDS	S. Sarkar et al.	Cardiovascular
Risk of smoking-related cancers among women and men living with and without HIV.	AIDS	N. Hessol et al.	Cancer

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Examples of Recent Articles (2022)

Article Title	Journal	Authors	Topic Area
SARS-CoV-2 Infection Among People Living With HIV Compared With People Without HIV: Survey Results From the MACS-WIHS Combined Cohort Study	Journal of Acquired Immune Deficiency Syndromes	G. D'Souza et al.	HIV Pathogenesis Covid-19
Distinct Lipidomic Signatures in People Living With HIV: Combined Analysis of ACTG 5260s and MACS/WIHS	The Journal of Clinical Endocrinology and Metabolism	J. Jao et al.	Metabolic Dysfunction
Optimal Lung Cancer Screening Criteria among persons living with HIV	Journal of Acquired Immune Deficiency Syndromes	S. Sellers et al.	Pulmonary Cancer
Polypharmacy is Associated with Falls in Women With and Without HIV	Journal of Acquired Immune Deficiency Syndromes	C. Psomas et al.	Aging/Frailty

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Interested in working with us?

Please visit
https://statepi.jhsph.edu/mwccs/work-with-us/
for a comprehensive guide of the process

Administered by NHLBI and co-funded by 13 institutes:

NIAID, NICHD, NHGRI, NIA, NIDCR, NINDS, NIMH, NIDA, NINR, NCI, NIAAA, NIDCD and NIDDK