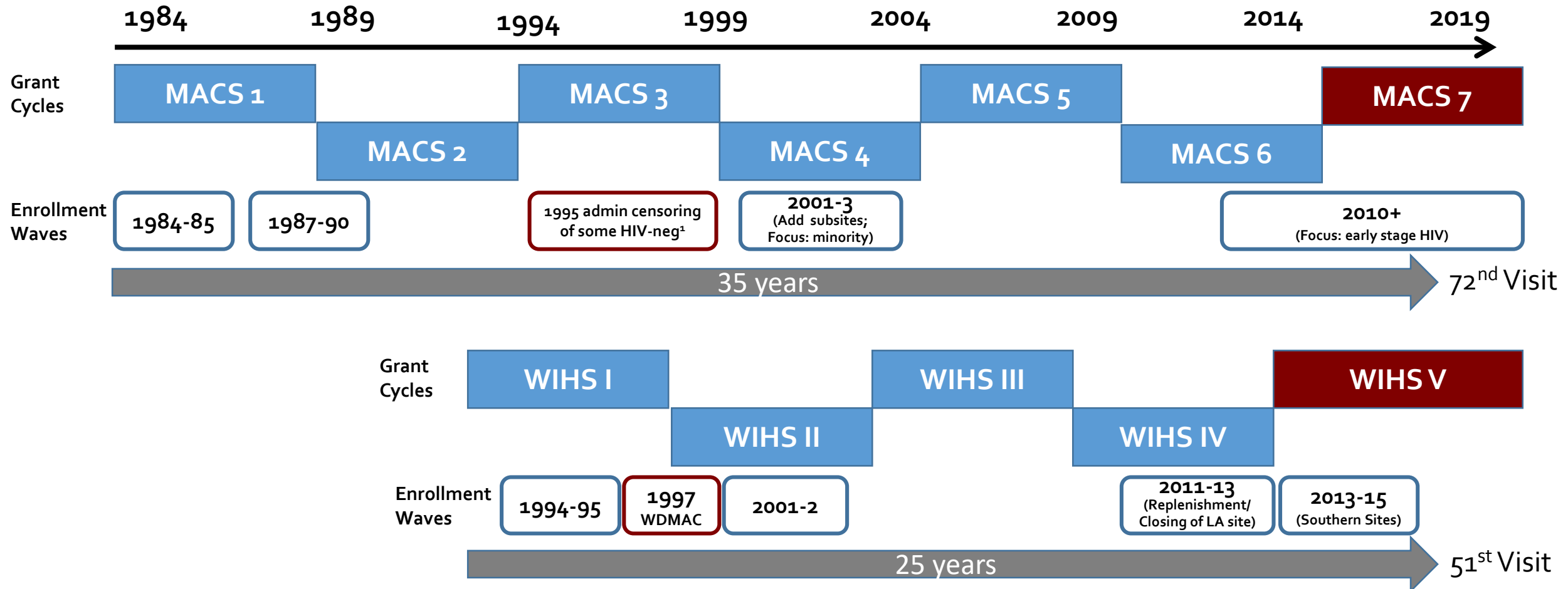

MACS/WIHS Combined Cohort Study (MWCCS) Dossier, 2019

Prepared by:
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email: mwccs@jhu.edu
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Multicenter AIDS Cohort Study (MACS, 1983-2019)

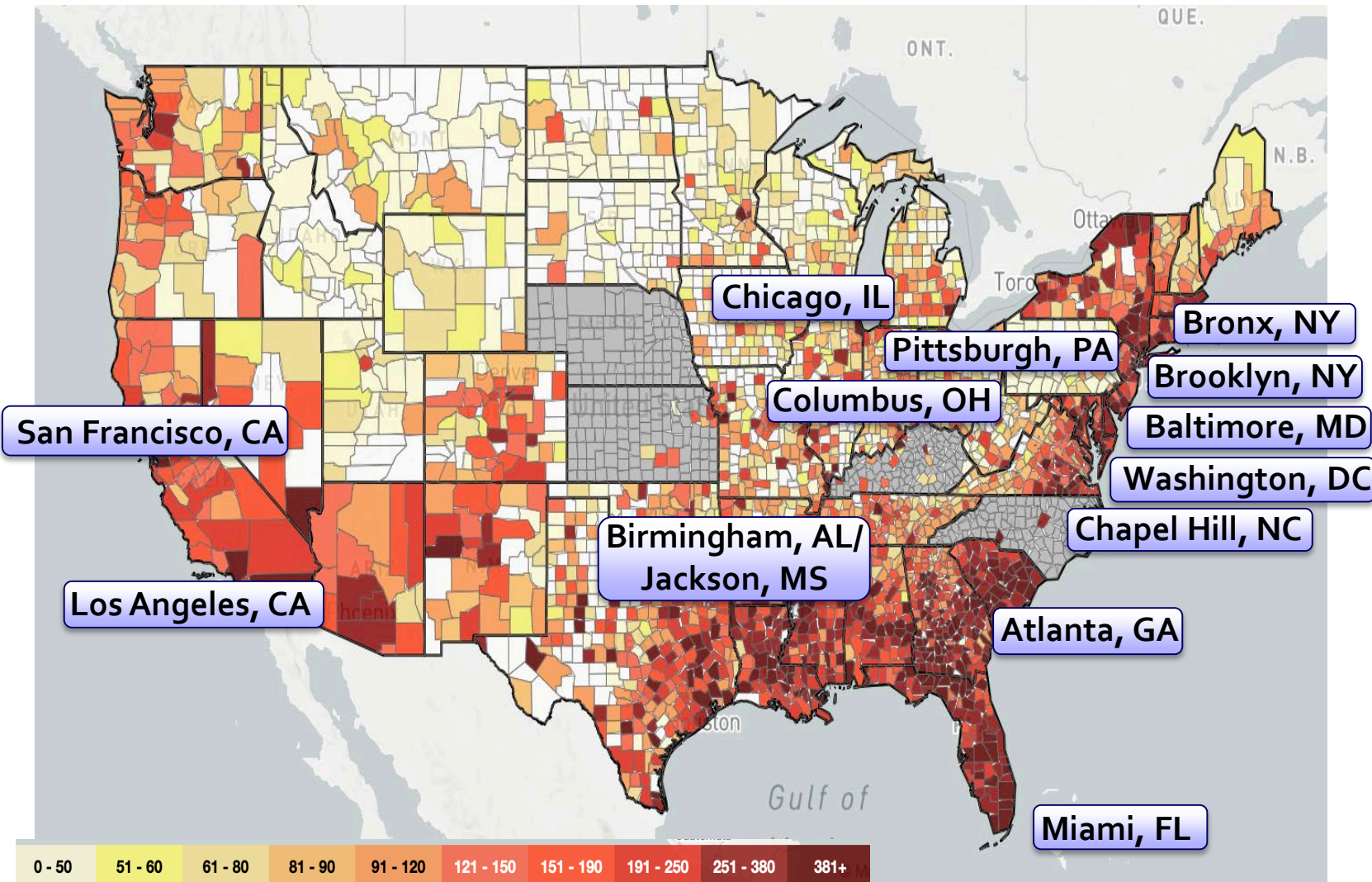
Women's Interagency HIV Study (WIHS, 1993-2019)

Study Timeline



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

MACS/WIHS Combined Cohort Study Sites



- Johns Hopkins serves as the MWCCS Data Analysis and Coordination Center (DACC)
- 57-Member Executive Committee
- >30 Scientific & Operational Working Groups

US Map from *AIDSVu* with shading reflecting 2016 HIV Prevalence per 100K

Types of Data Collected

- ▶ 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 use
- ▶ Lab results
 - Blood Chemistries, Complete Blood Count, Hepatitis, T-Cell flow cytometry, HIV Viral Load, Lipid Panel
- ▶ Physical Examination
- ▶ Outcome verification and adjudication
- ▶ Biorepository of samples
- ▶ Registry matching:
 - National Death Index, Cancer Registry, Renal Disease Registry

Committed* Specimens in Central Repository

	<i>Former MACS Men</i>	<i>Former WIHS Women</i>
Plasma (CPT)	NA	829,523
Plasma (Heparin)	719,074	NA
Plasma (EDTA)	198,945**	12,453**
Serum	953,522	562,441
Cells	345,823	365,955
Cell Pellets	50,580	478,472
Urine (clean void)	89,876	96,903
Urine (supernatant)	NA	95,833
Cervical Vaginal Lavage (CVL)	NA	559,792
Stimulated Saliva	NA	5,372
Stool	7,144	NA
Semen	58,782	NA

* Committed includes all specimens ever sent to Central Repository

** Former MACS/WIHS began repositing EDTA plasma at visit 45/48

MWCCS Visit Timeline: 2020-2026

CCS Visit Structure			2020	2021	2022	2023	2024	2025	2026
	Start of Window	End of Window	J F M A M J J A S O N D	J F M A M J J A S O N D	J F M A M J J A S O N D	J F M A M J J A S O N D	J F M A M J J A S O N D	J F M A M J J A S O N D	J F M A M J
Visit 101									
Core Window	1/1/20	12/31/20							
Completion Window	1/1/20	3/31/21							
Data Freeze, Edits, & Summary Files	4/1/21	6/30/21							
Visit 102									
Core Window	1/1/21	12/31/21							
Completion Window	1/1/21	3/31/22							
Data Freeze, Edits, & Summary Files	4/1/22	6/30/22							
Visit 103									
Core Window	1/1/22	12/31/22							
Completion Window	1/1/22	3/31/23							
Data Freeze, Edits, & Summary Files	4/1/23	6/30/23							
Visit 104									
Core Window	1/1/23	12/31/23							
Completion Window	1/1/23	3/31/24							
Data Freeze, Edits, & Summary Files	4/1/24	6/30/24							
Visit 105									
Core Window	1/1/24	12/31/24							
Completion Window	1/1/24	3/31/25							
Data Freeze, Edits, & Summary Files	4/1/25	6/30/25							
Visit 106									
Core Window	1/1/25	12/31/25							
Completion Window	1/1/25	3/31/26							
Data Freeze, Edits, & Summary Files	4/1/26	6/30/26							

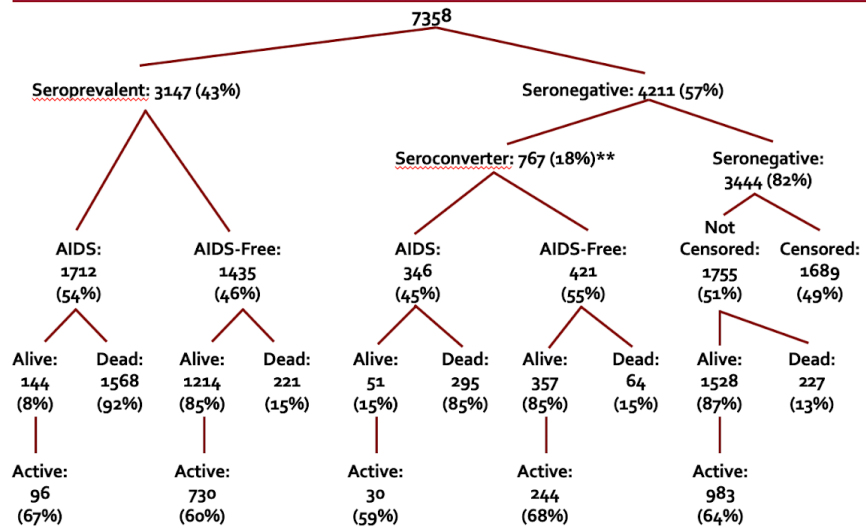
Characteristics of Active Participants*

N=4,106

* MACS and WIHS Participants Who Contributed
Data in the Year Prior to MWCCS

Characteristics of MACS and WIHS (4,106 Active Participants)

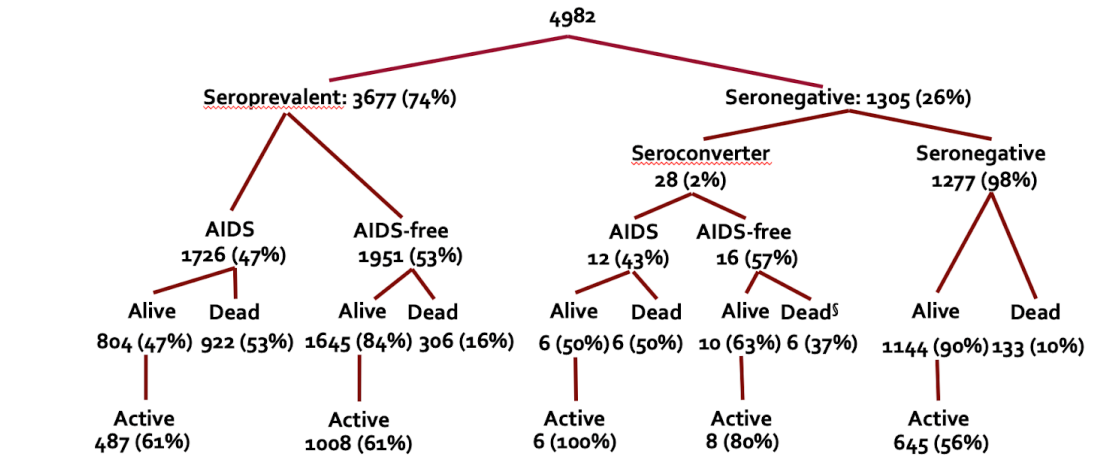
Former MACS Cohort



* HIV & AIDS status as of the end of visit 69 (3/31/19). Deaths through 3/31/19.

** Seroconverters include 123 (of 767) who were HIV+ at entry, but with known date of seroconversion.

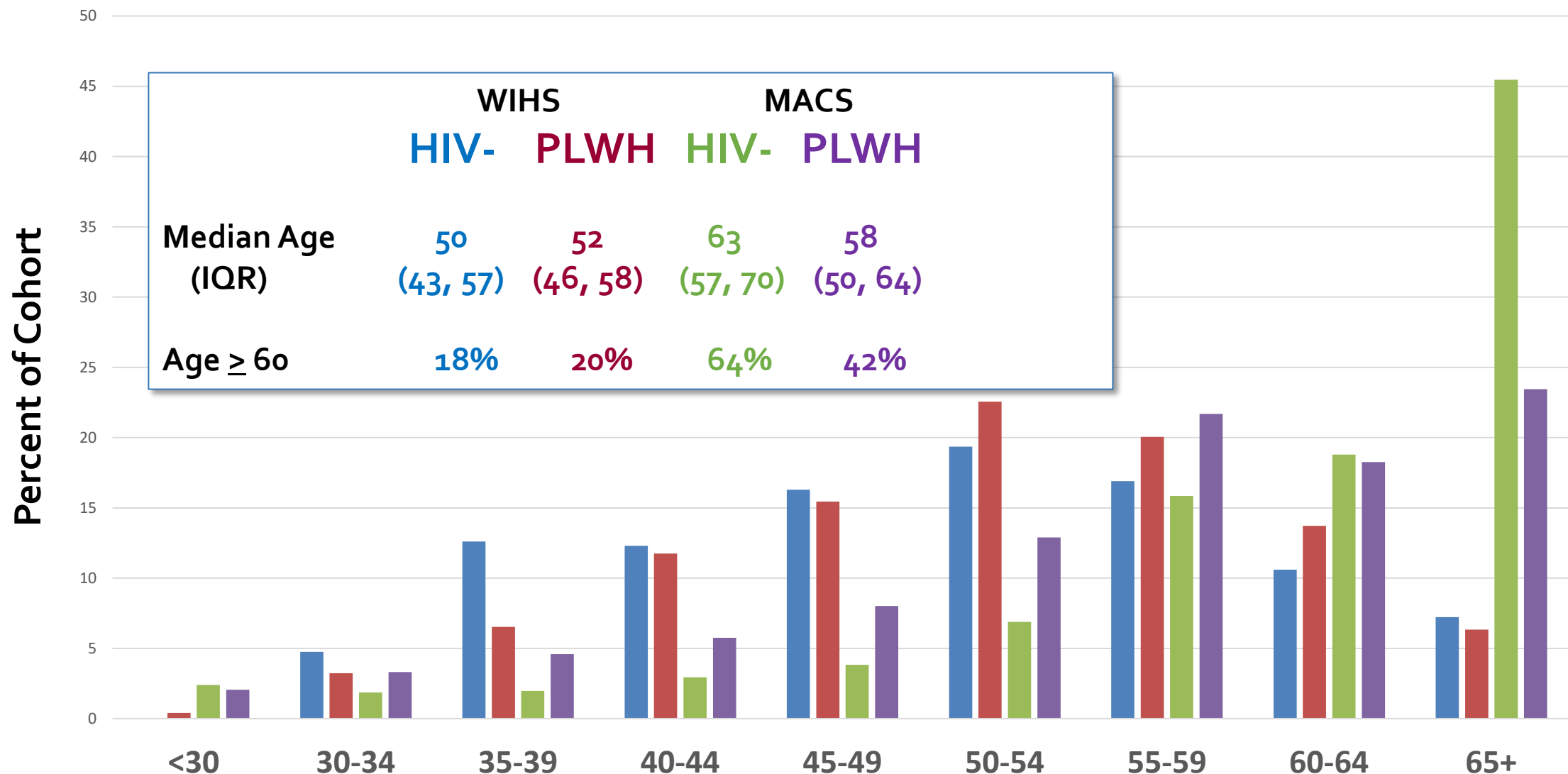
Former WIHS Cohort



* HIV & AIDS status as of the end of visit 49 (3/31/19). Deaths via NDI (through 12/31/14 for site 4; 12/31/16 for sites 2, 3, 83; 12/31/17 for sites 1, 5, 6, 81, 82, 84, 85) and through 3/31/19 via other reports.

§ Three seroconverters found at death.

Age Distribution of Active* Participants



* Active = All participants who contributed data at Visit 48 or 49 for WIHS; 69 or 70 for MACS

Demographics

	Former MACS Men		Former WIHS Women	
	<i>PLWH</i> <i>N=1,024</i>	<i>HIV-</i> <i>N=915</i>	<i>PLWH</i> <i>N=1,516</i>	<i>HIV-</i> <i>N=651</i>
Median Age (IQR)	58 (50, 64)	63 (57, 70)	52 (46, 58)	50 (43, 57)
Race/Ethnicity (%):				
Black/African American	27%	17%	73%	72%
Hispanic/Latino, any race	16%	7%	15%	14%
White	53%	73%	7%	11%
Multiple Races/Other	4%	3%	5%	3%
Median (mean) Follow-up Time, years	16.7 (21.5)	34.0 (27.9)	16.3 (13.3)	16.5 (13.7)

Chronic Disease Indicators

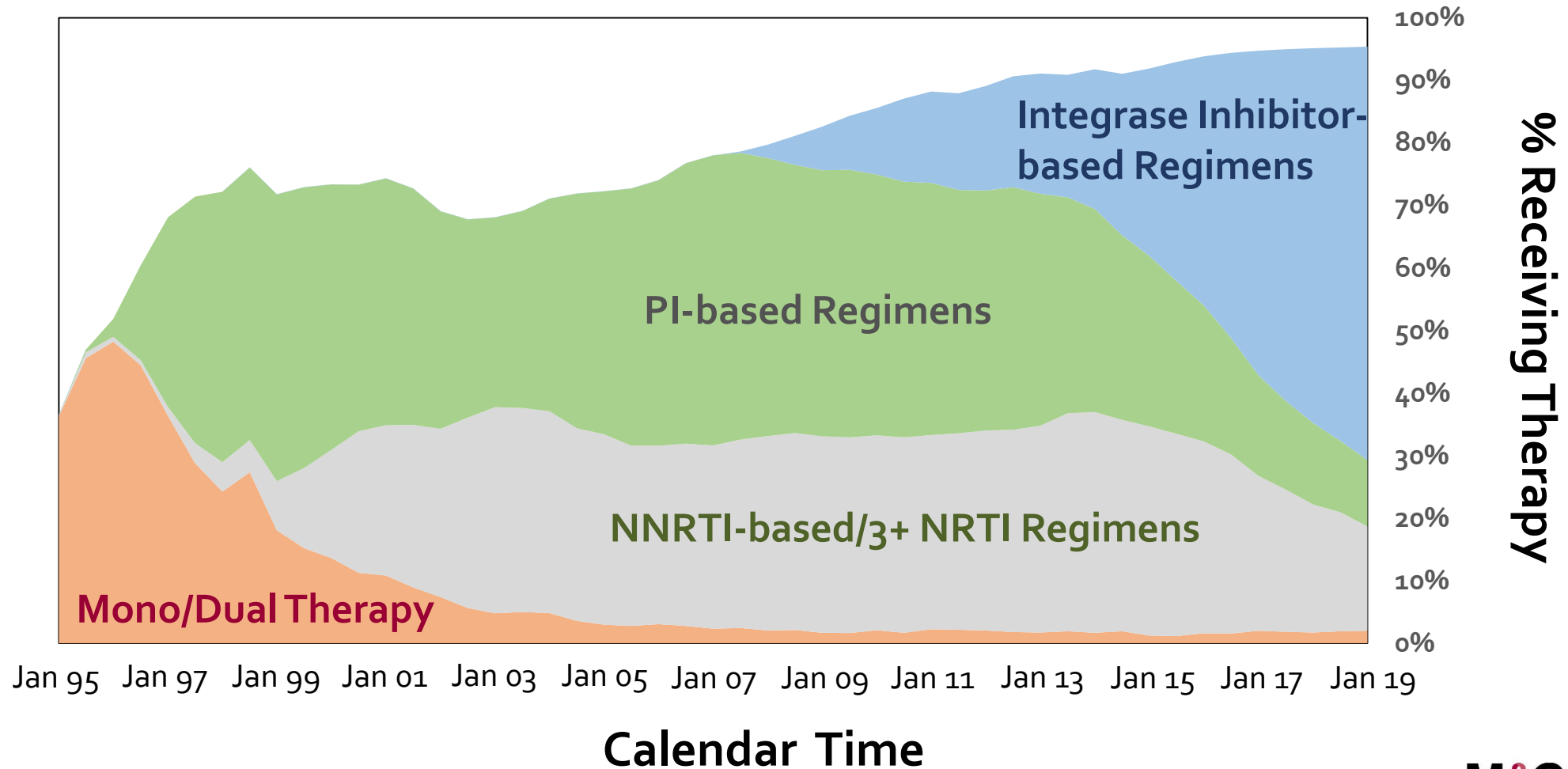
	Former MACS Men		Former WIHS Women	
	<i>PLWH</i> <i>N=1,024</i>	<i>HIV-</i> <i>N=915</i>	<i>PLWH</i> <i>N=1,516</i>	<i>HIV-</i> <i>N=651</i>
Smoking (%)				
Current	22%	14%	34%	43%
Former	47%	53%	32%	30%
BMI Median (IQR)	26 (24, 30)	27 (24, 30)	31 (26, 37)	32 (27, 38)
% BMI >30 [>40]	23% [2%]	26% [3%]	54% [18%]	58% [18%]
Hypertension (SBP \geq 140, DBP \geq 90, meds)	50%	55%	53%	53%
Diabetes (HbA _{1c} \geq 6.5%, FG \geq 126, meds)	16%	13%	25%	25%
Dyslipidemia (LDL $>$ 130, HDL $<$ 40)	34%	28%	36%	32%
Chronic Kidney Disease CKD-Epi eGFR <60 [<30]	14% [1%]	8% [0.1%]	15% [2%]	7% [2%]
% with Confirmed Cancers (%ADE)	11% (4%)	8%	6% (1%)	4%
ECHO Completed (%)	64%	60%	72%	71%
PFT Completed (%)	64%	57%	73%	69%

Antiretroviral Medication Exposure*

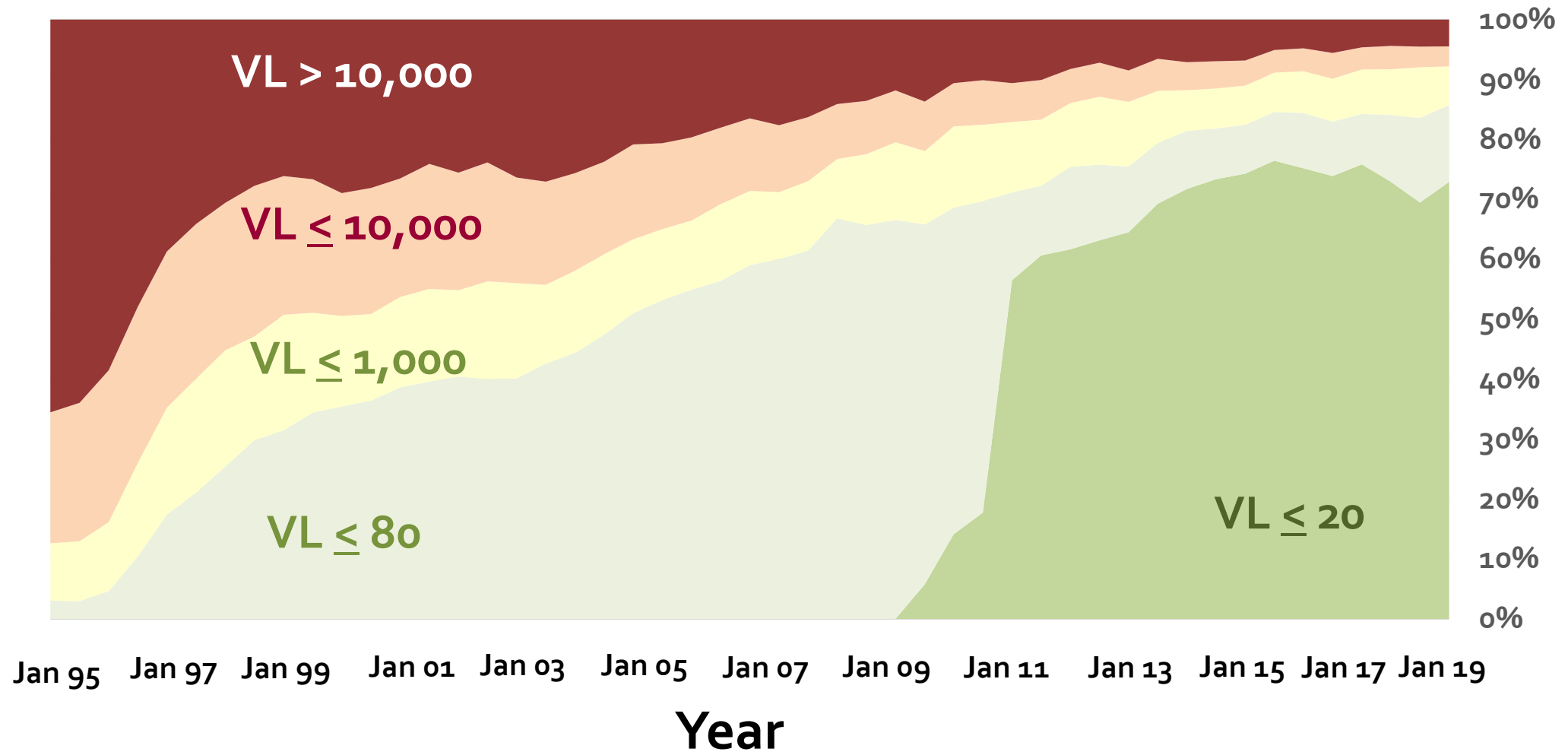
	Former MACS Men	Former WIHS Women
	<i>PLWH N=1024</i>	<i>PLWH N=1,516</i>
% currently on any Therapy	94%	94%
% with previous exposure to d4T, ddI, ddC	48%	29%
% with previous exposure to Monotherapy	29%	21%
% Ever with Low CD4:		
<500 cells/mm ³	88%	90%
<200 cells/mm ³	32%	44%

* At most recent visit

Antiretroviral Therapy Use Among MACS and WIHS PLWH (active participants only)

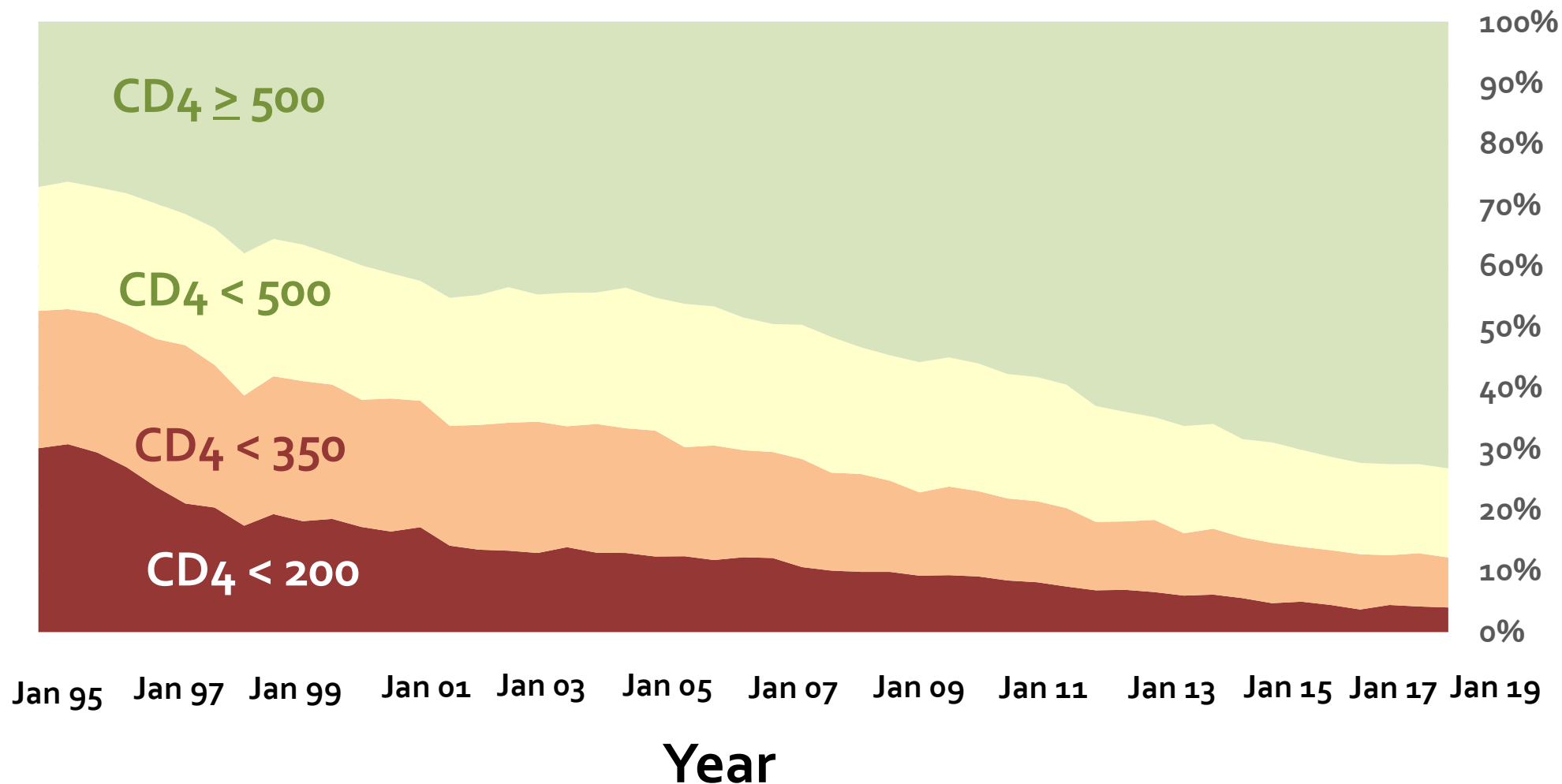


Viral Load Among PLWH (active participants only)



TaqMan v2.0 HIV-1, sensitive to 20 copies HIV RNA/mL, implemented in 2009

CD4 Cell Counts Among PLWH (active participants only)



Select Outcomes

Confirmed Incident Cancers in MACS and WIHS through 3/31/2019

- Sources of cancer confirmation in both cohorts
 - Medical record abstraction, cancer registry match, autopsy, biopsy, death certificate match
- Excluded cancer records
 - Cancers documented solely by self-report/next of kin
 - Benign tumors
 - Most *in situ* tumors (except breast and melanoma)
 - Basal cell and squamous cell skin cancers (not recorded in cancer registries)
 - Prevalent cancers diagnosed before/at/shortly following enrollment
- Cancer Classification
 - Data from completed forms were reviewed to determine (if possible) the topology and morphology for each diagnosed cancer which was then classified according to Surveillance, Epidemiology, and End Results (SEER) Program “site-recode” definition for ICD-O-3/WHO 2008.
(https://seer.cancer.gov/siterecode/icdo3_dwhocheme/index.html)

Confirmed Incident Cancers by Cohort and HIV Status

Cancer	SEER Code(s)	Former MACS		Former WIHS	
		PLWH	HIV-	PLWH	HIV-
All		1041	210	318	62
Oral Cavity	20020-20090	11	10	11	0
Colon	21041-21049	8	8	9	4
Rectum	21051-21052	8	9	7	0
Anus	21060	36	5	14	0
Liver	21071	13	5	13	5
Pancreas	21100	5	6	9	1
Other Digestive Systems	21010-21030,21072,21080-21110,21130	6	6	10	4
Lung and Bronchus	22030	25	15	52	16
Other Respiratory	22010-22020	2	5	7	1
Bones/ Joints	23000	1	1	0	0
Soft Tissues	24000	0	3	4	0
Melanoma	25010	20	25	4	0
Other non-epithelial skin ca	25020	1	1	0	0
Breast	26000	0	0	48	16

(Continued on next slide)

Confirmed Incident Cancers (continued)

<i>Cancer</i>	<i>SEER Code(s)</i>	Former MACS		Former WIHS	
		<i>PLWH</i>	<i>HIV-</i>	<i>PLWH</i>	<i>HIV-</i>
Cervix	27010	-	-	9	0
Uterus	27020-27030	-	-	10	3
Ovary	27040	-	-	2	0
Vagina	27050	-	-	3	0
Vulva	27060	-	-	6	0
Prostate	28010	43	56	-	-
Testis	28020	8	2	-	-
Penis	28030	1	0	-	-
Bladder/Ureter	29010,29030	5	10	1	0
Kidney and renal pelvis	29020	6	3	4	1
Brain/CNS	31010, 31040	2	2	4	3
Thyroid/Pituitary	32010, 32020	6	3	4	2
Hodgkin's Disease	33011-33012	14	4	5	1
NHL	33041-33042	231	14	52	1
Multiple Myeloma	34000	6	4	5	0
Leukemia	35010-35043	4	4	4	2
Mesothelioma	36010	0	0	1	0
Kaposi's Sarcoma	36020	565	2	10	0
Miscellaneous/Unknown	37000	14	7	10	2

Hepatitis Status at Baseline and Last Test

	Former MACS Men		Former WIHS Women	
	<i>PLWH</i>	<i>HIV-</i>	<i>PLWH</i>	<i>HIV-</i>
<i>Baseline:</i>	<i>N=3,270</i>	<i>N=4,088</i>	<i>N=3,677</i>	<i>N=1,305</i>
Anti-HCV+	11%	5%	30%	19%
HCV RNA+	8%	3%	24%	14%
HBsAg+	8%	4%	3%	<1%
<i>Last Test Result (may be baseline result):</i>	<i>N=3,873</i>	<i>N=3,485</i>	<i>N=3,702</i>	<i>N=1,280</i>
Anti-HCV+	13%	6%	32%	20%
HCV RNA+	9%	4%	20%	12%
HbsAg+	7%	3%	No follow-up	No follow-up

NHLBI Substudy Timeline 2016-2019

NHLBI Supplement	Visit 65/44 (Apr 1, 2016- Sept 30, 2016)	Visit 66/45 (Oct 1, 2016- Mar 31, 2017)	Visit 67/46 (Apr 1, 2017- Sept 30, 2017)	Visit 68/47 (Oct 1, 2017- Mar 31, 2018)	Visit 69/48 (Apr 1, 2018- Sept 30, 2018)	Visit 70/49 (Oct 1, 2018- Mar 31, 2019)	Visit 71/50 (April 1, 2019- Sept 30, 2019)	Data Cleaned and Available as of 10/1/19
Resting and Ambulatory (ZIO Patch) ECG	Planning	MACS Data Collection		WIHS Data Collection (resting ECG only)				MACS & WIHS
Pulmonary Function Testing		Planning	MACS Data Collection		WIHS Data Collection → through 12/19			MACS (WIHS ready 3/20)
ECHO			Planning	MACS Data Collection				MACS (WIHS ready 3/20)
					WIHS Data Collection → through 12/19			
Sleep Study				Planning	MACS Data Collection			In progress (MACS ready 1/20)

Enrollment In NHLBI Substudies

Data collected in these substudies in large number of participants, now available in >2000 participants for several measures!

	MACS	WIHS	Total
ECG			
Resting ECG	1633 (82%)	2011 (90%)	3644
Ambulatory (ZIO Patch) ECG	1281 (64%)	NA	1281
Pulmonary Function Testing			
Pre-bronchodilation	1214 (60%)	1536 (70%)	2750
Post-bronchodilation	1178 (58%)	1432 (66%)	2610
Completed DLCO	1134 (56%)	632 (74%)*	1766
ECHO	1195 (60%)	1476 (77%)	2671
Sleep Study – Nox data	851 (44%)	NA	851

* Denominator limited to WIHS sites offering DLCO