2024 Add Health Users Conference

Add Health Wave VI: Biological & Vital Events Data
Tuesday June 18, 2024
10:15-11:45 AM

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Add Health
The National Longitudinal Study of Adolescent to Adult Health

Biological & Vital Events Data

Biological Data

(1) Aims
(2) Domains
(3) Collection Methods
(4) Update
(5) Quality
(6) Summary
(7) Availability

(1)
Biological Data Aims

Biological Data Aims

- To identify conditions prevalent among U.S. adults and processes underlying their associations with future health and disease

- To collect measures characterizing those processes

- To do so with feasibility of field collection across the U.S., availability of data across waves, and reliability & validity of results in mind

(2)
Biological Data Domains

Biological Data Domains

Domains

Cardiovascular
Anthropometric
Metabolic
Renal
Hepatic
Neurocognitive
Inflammatory/Immune
Infectious
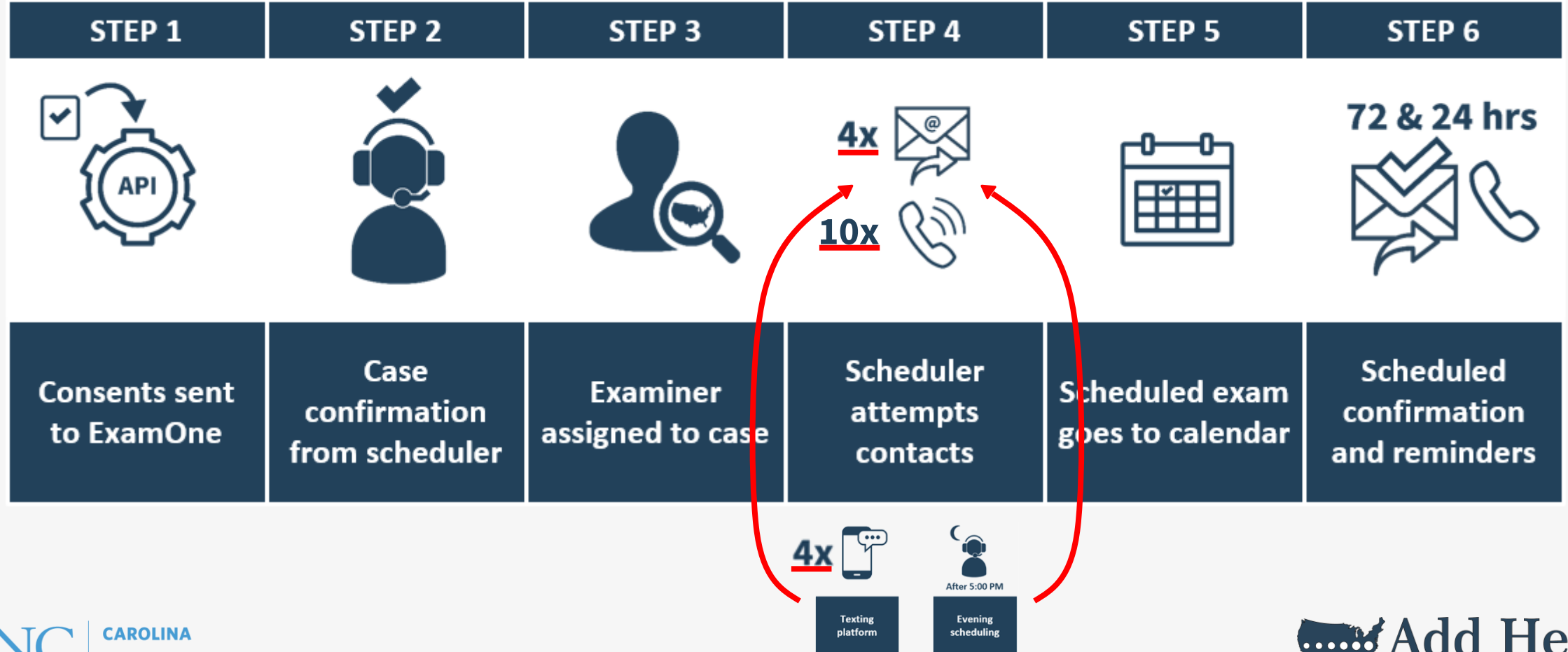Pharmacologic

(3)
Biological Data Collection Methods

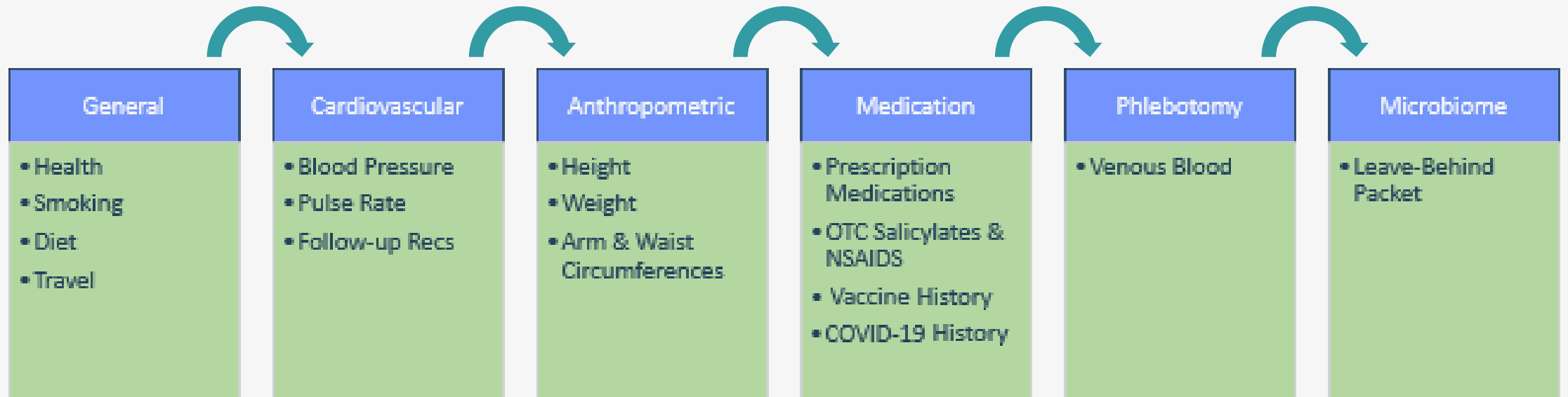# Biological Data Collection Methods

- Consent & Scheduling

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Consents sent to ExamOne	Case confirmation from scheduler	Examiner assigned to case	Scheduler attempts contacts	Scheduled exam goes to calendar	Scheduled confirmation and reminders

Biological Data Collection Methods

- Consent & Scheduling

Hardcopy mailings

STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Consents sent to ExamOne	Case confirmation from scheduler	Examiner assigned to case	Scheduler attempts contacts	Scheduled exam goes to calendar	Scheduled confirmation and reminders

4x

10x

4x

After 5:00 PM

Texting platform

Evening scheduling

72 & 24 hrs

Biological Data Collection Methods

- Home Examination

General	Cardiovascular	Anthropometric	Medication	Phlebotomy	Microbiome
• Health • Smoking • Diet • Travel	• Blood Pressure • Pulse Rate • Follow-up Recs	• Height • Weight • Arm & Waist Circumferences	• Prescription Medications • OTC Salicylates & NSAIDS • Vaccine History • COVID-19 History	• Venous Blood	• Leave-Behind Packet

Biological Data Collection Methods

- General Interview

Biological Data Collection Methods

- ● Cardiovascular Evaluation

- Cardiovascular equipment

AA

- Cardiovascular protocol*
  - trained, certified staff
  - resting, seated respondents
  - arm @ level of heart
  - cuff matched to arm circumference
  - measured SBP, DBP & PR
    - - 3x @ 30 sec intervals
    - - double entered
    - - automatically averaged over last 2
  - provide results, follow-up recs

- Measures
  - Primary
    - systolic blood pressure (SBP)
    - diastolic blood pressure (DBP)
    - pulse rate (PR)
  - Secondary
    - pulse pressure (PP = SBP –DBP)
    - mean arterial pressure (MAP = [SBP + 2 × DBP] ÷ 3)

- Blood Pressure Classification
  - SBP/DBP according to JNC 7 guidelines*

< 120/80 mm Hg	Normal
120-139/80-89 mm Hg	Pre-Hypertension
140-159/90-99 mm Hg	Stage 1 Hypertension
≥ 160/100 mm Hg	Stage 2 Hypertension

  - SBP/DBP according to ACC/AHA guidelines†

< 120/80 mm Hg	Normal
120-129/<80 mm Hg	Elevated
130-139/80-89 mm Hg	Stage 1 Hypertension
≥ 140/90 mm Hg	Stage 2 Hypertension

Biological Data Collection Methods
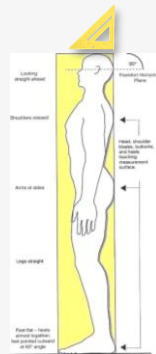
- **Anthropometry**

Anthropometric equipment

CR 2032

Anthropometric protocol
- trained, certified staff
- dressed, unshoed respondents
- standing on uncarpeted floor
- measured
  - height to nearest 0.5 cm
  - weight to nearest 0.1 kg
  - waist to nearest 0.5 cm
    - @ superior border of iliac crest
    - @ end expiration
    - horizontal to floor
- hair/shoe height to nearest 0.5 cm, as needed

Measures
- Primary
  - weight
  - height
  - waist circumference (waist)
  - arm circumference (arm)
- Secondary
  - body mass index (BMI = weight in kg / height in m^2)

Waist & BMI Classification
- Waist according to NHLBI Evidence Report*

≤ 88 (102) cm in ♀ (♂)	Lower Risk
> 88 (102) cm in ♀ (♂)	High Risk

- BMI according to NHLBI Evidence Report*

< 18.5 kg/m^2	Underweight
18.5-24.9 kg/m^2	Normal
25.0-25.9 kg/m^2	Overweight
30.0-34.9 kg/m^2	Obesity, Stage I
35.0-39.9 kg/m^2	Obesity, Stage II
≥ 40.0 kg/m^2	Obesity, Stage III

*Obesity Res 1998;6(S2);51S-210S.

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Biological Data Collection Methods

- Phlebotomy

- Phlebotomy Equipment

- Phlebotomy Protocol
  - trained, certified phlebotomists
  - fasting (ideally) respondents
  - draw blood
  - centrifuge
  - package
  - ship
  - assay @ LCBR
  - return results

Tube Order (Volume)
- 1 – Tiger Top SST (8.5 ml)
- 2 – EDTA (10 ml)
- 3 – EDTA (3 ml)
- 4 – Tiger Top SST (5 ml)
- 5 – PAXGene (2.5 ml)

Biological Data Collection Methods

- Biomarker Assays

	Category	Assay	Specimen	Volume	Testing Schedule	Location	Equipment	Assay description
Metabolic Domain	Glucose Homeostasis	Glucose (Serum)	serum	500 µl*	daily	UVMMC	Ortho Vitros 5600	Vitros GLU slides
		HbA1C	whole blood	1000 µl	twice/week	UVMMC	Sebia Capillarys 3	Sebia Capillary Electrophoresis
	Lipids	Total Cholesterol	serum	500 µl*	daily	UVMMC	Ortho Vitros 5600	Vitros CHOL slides
		HDL Cholesterol	serum		daily	UVMMC	Ortho Vitros 5600	Vitros dHDL slides
		Triglycerides	serum		daily	UVMMC	Ortho Vitros 5600	Vitros TRIG slides
		LDL Cholesterol	serum		daily	UVMMC	Ortho Vitros 5600	Calculated. If Trig>400, then direct LDL slides
	Renal Function	Creatinine	serum	500 µl*	daily	UVMMC	Ortho Vitros 5600	Vitros CREA slides
	Hepatic Injury	AST	serum	500 µl*	daily	UVMMC	Ortho Vitros 5600	Vitros AST slides
		ALT	serum		daily	UVMMC	Ortho Vitros 5600	Vitros ALT slides
Infectious Domain	Neurocognition	NF-L	EDTA plasma	200 µl	3 batches (2023, 2024, 2025)	LCBR lab	Quanterix HD-X	Simoa Human Neurology 4-Plex "A"
		Tau	EDTA plasma		3 batches (2023, 2024, 2025)	LCBR lab	Quanterix HD-X	Simoa Human Neurology 4-Plex "A"
		GFAP	EDTA plasma		3 batches (2023, 2024, 2025)	LCBR lab	Quanterix HD-X	Simoa Human Neurology 4-Plex "A"
		UCH-L1	EDTA plasma		3 batches (2023, 2024, 2025)	LCBR lab	Quanterix HD-X	Simoa Human Neurology 4-Plex "A"
		HSV	Serum	120 µl**	twice/year	LCBR lab	Biotek ELx8081IU	Gold Standard Diagnostics HSV 1&2 IgG EIA
	Inflammation & Immune Function	hsCRP	serum	120 µl**	twice/year	LCBR lab	Siemens BNII	Siemens CRP immunonephelometric assay
		IL-10	serum		twice/year	LCBR lab	MSD Quick-Plex 120	Mesoscale Discovery Pro-Inflammatory Panel
		IL-1B	serum		twice/year	LCBR lab	MSD Quick-Plex 120	Mesoscale Discovery Pro-Inflammatory Panel
		IL-6	serum		twice/year	LCBR lab	MSD Quick-Plex 120	Mesoscale Discovery Pro-Inflammatory Panel
		IL-8	serum		twice/year	LCBR lab	MSD Quick-Plex 120	Mesoscale Discovery Pro-Inflammatory Panel
		TNF-α	serum		twice/year	LCBR lab	MSD Quick-Plex 120	Mesoscale Discovery Pro-Inflammatory Panel
		CMV	serum		twice/year	LCBR lab	Biotek ELx808IU	Gold Standard Diagnostics CMV igG EIA
	COVID-19	SARS CoV-2 Spike IgG	Serum	20 µl	3 batches (2023, 2024, 2025)	LCBR lab	MSD Quick-Plex 120	Mesoscale V-Plex SARS-CoV-2 Panel 2 IgG Kit
		SARS CoV-2 Nucleocapsid IgG	Serum		3 batches (2023, 2024, 2025)	LCBR lab	MSD Quick-Plex 120	Mesoscale V-Plex SARS-CoV-2 Panel 2 IgG Kit
		Total SARS CoV-2 RBD IgG	Serum		3 batches (2023, 2024, 2025)	LCBR lab	MSD Quick-Plex 120	Mesoscale V-Plex SARS-CoV-2 Panel 2 IgG Kit

* All Ortho Vitros assays are run from a single 500 µl sample of serum

** All assays run twice/year will be run from a single pooled sample of 120 µl of serum

NEW!

NEW!

Biological Data Collection Methods

- Biomarker Classification

- Metabolic, glucose homeostasis*
  - glucose
  - glycosylated hemoglobin (HbA1c)
  - according to ADA guidelines†
    - fasting glucose (mg/dl)
      - ≤ 99 normal
      - 100-125 impaired
      - ≥ 126 diabetes
    - non-fasting glucose (mg/dl)
      - ≥ 200 diabetes
    - HbA1c (%)
      - 5.7-6.4 increased risk for diabetes
      - ≥ 6.5 diabetes

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Biological Data Collection Methods

- Biomarker Classification

- Metabolic, lipids
  - Primary*
    - total cholesterol (TC)
    - high density lipoprotein cholesterol (HDL-C)
    - triglycerides (TG)
  - Secondary*
    - low density lipoprotein cholesterol (LDL-C = TC - HDL-C - TG ÷ 5)†
    - TC:HDL-C ratio (= TC / HDL-C)
    - non-HDL-C (= TC - HDL-C)

  - According to NCEP ATP III guidelines‡§

TC (mg/dl)	< 200	desirable
	200-239	borderline high
	≥ 240	high
HDL-C (mg/dl)	< 40	low
	≥ 60	high
LDL-C (mg/dl)	< 100	optimal
	100-129	near optimal
	130-159	borderline high
	160-189	high
	≥ 190	very high
TG‡ (mg/dl)	< 150	normal
	150-199	borderline high
	200-499	high
	≥ 500	very high

  - According to AHA/ACC guidelines‡∥

LDL-C (mg/dl)	160-189	moderate
	≥ 190	severe hypercholesterolemia
TG (mg/dl)	175-499	moderate
	≥500	severe hypertriglyceridemia

*Fasting or non-fasting. †Estimated using the Friedewald equation when TG < 400 mg/dl. Directly assayed when TG ≥ 400 mg/dl. Clin Chem 1972;18(6):499.
‡Fasting. §Circulation 2002;106(25):3143. ∥JACC 2018. pii:S0735-1097(18)39034-X.

Biological Data Collection Methods

- **Biomarker Classification**
  - Renal
    - Primary
      - creatinine
    - Secondary
      - estimated glomerular filtration rate (eGFR)*

        eGFR $= 142 \times \min(Scr/\kappa, 1)^\alpha \times \max(Scr/\kappa, 1)^{-1.2} \times 0.9938^{Age}$ [$\times 1.012$ (if ♀)],

        where:

        Scr $=$ serum creatinine

        κ $= 0.7$ (♀) or 0.9 (♂)

        α $= -0.241$ (♀) or -0.302 (♂)
    - According to KDIGO guidelines†

≥ 90 ml/min/1.73 m^2	Normal or high (G1)
60-89	Mildly decreased (G2)
45-59	Mildly to moderately decreased (G3a)
30-44	Moderately to severely decreased (G3b)
15-29	Severely decreased (G4)
<15	Kidney failure (G5)

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Biological Data Collection Methods

- Biomarker Classification

- Hepatic
  - Primary
    - Aspartate Aminotransferase (AST)
    - Alanine Aminotransferase (ALT)
  - Secondary
    - AST/ALT ratio = AST ÷ ALT
  - AST/ALT ≥ 2.0 *suggests* alcohol-related liver disease*

Biological Data Collection Methods

- **Biomarker Classification**

- Neurocognitive
  - Primary
    - Neurofilament light (NfL)
    - Tau
    - Glial fibrillary acidic protein (GFAP)
    - Ubiquitin C-terminal hydrolase L1 (UCH-L1) **NEW!**
  - ↑s correlated with
    - brain / spinal cord injury
    - neurodegenerative disease

} polypeptides or proteins in brain & spinal cord neurons or glia cells

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Biological Data Collection Methods

- ● Biomarker Classification

- Inflammatory / Immune
  - High sensitivity C-reactive protein (hsCRP)
  - According to CDC / AHA guidelines*

< 1 mg/L	low
1-3 mg/L	average
> 3 mg/L	high
> 10 mg/L	must trigger searches for factors capable of confounding hsCRP-based risk estimates

  - Cytokines
    - interleukins (IL-1B, 6, 8 & 10)
    - tumor necrosis factor-alpha (TNF-α)

    } proteins secreted by immune cells

  - According to known functions†
    - pro-inflammatory: IL-1β, 6, & 8; TNF-α
    - anti-inflammatory: IL-6 & 10

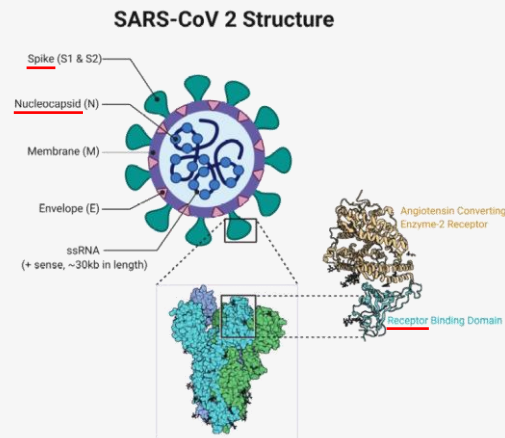# Biological Data Collection Methods

- Biomarker Classification

- Infectious
  - Herpes simplex virus (HSV) IgG
  - According to kit guidelines
    < 16.0 U/ml (negative)   16.0-19.9 U/ml (equivocal)   ≥ 20.0 U/ml (positive)

  - Cytomegalovirus (CMV) IgG
  - According to kit guidelines
    < 8.0 EU/ml (negative)   8.0-9.9 EU/ml (equivocal)   ≥ 10.0 EU/ml (positive)

  - Severe acute respiratory syndrome-related coronavirus 2 (SARS CoV-2) IgG
  - According to kit & CDC guidelines*
    > 1,960 AU/ml (spike+)   > 5,000 AU/ml (nucleocapsid+)   > 538 AU/ml (receptor+)

NEW!

NEW!

SARS-CoV 2 Structure

Spike (S1 & S2)
Nucleocapsid (N)
Membrane (M)
Envelope (E)
ssRNA (+ sense, ~30kb in length)
Angiotensin Converting Enzyme-2 Receptor
Receptor Binding Domain

Vaccination	S	N	Interpretation
Yes	+	+	Vaccinated & previous infection
Yes	+	-	Vaccinated & no previous infection
No	+	+	Unvaccinated & previous infection
No	-	-	Unvaccinated & no previous infection
?	+	+	? vaccinated & previous infection
?	+	-	Vaccinated & no previous infection
?	-	-	Unvaccinated & no previous infection

S = spike, N = nucleocapsid, and R = receptor IgG.

*https://www.cdc.gov/coronavirus/2019-ncov/hcp/testing/antibody-tests-guidelines.html
Figure: https://www.ncbi.nlm.nih.gov/books/NBK554776/

Biological Data Collection Methods

- Therapeutic Classification

- Medications
  - prescriptions according to Multum Lexicon Plus®
  - example therapeutic classes
    - antihypertensives
    - antihyperlipidemics
    - antidiabetics
    - anti-inflammatories
    - narcotics
    - antidepressants
    - antipsychotics
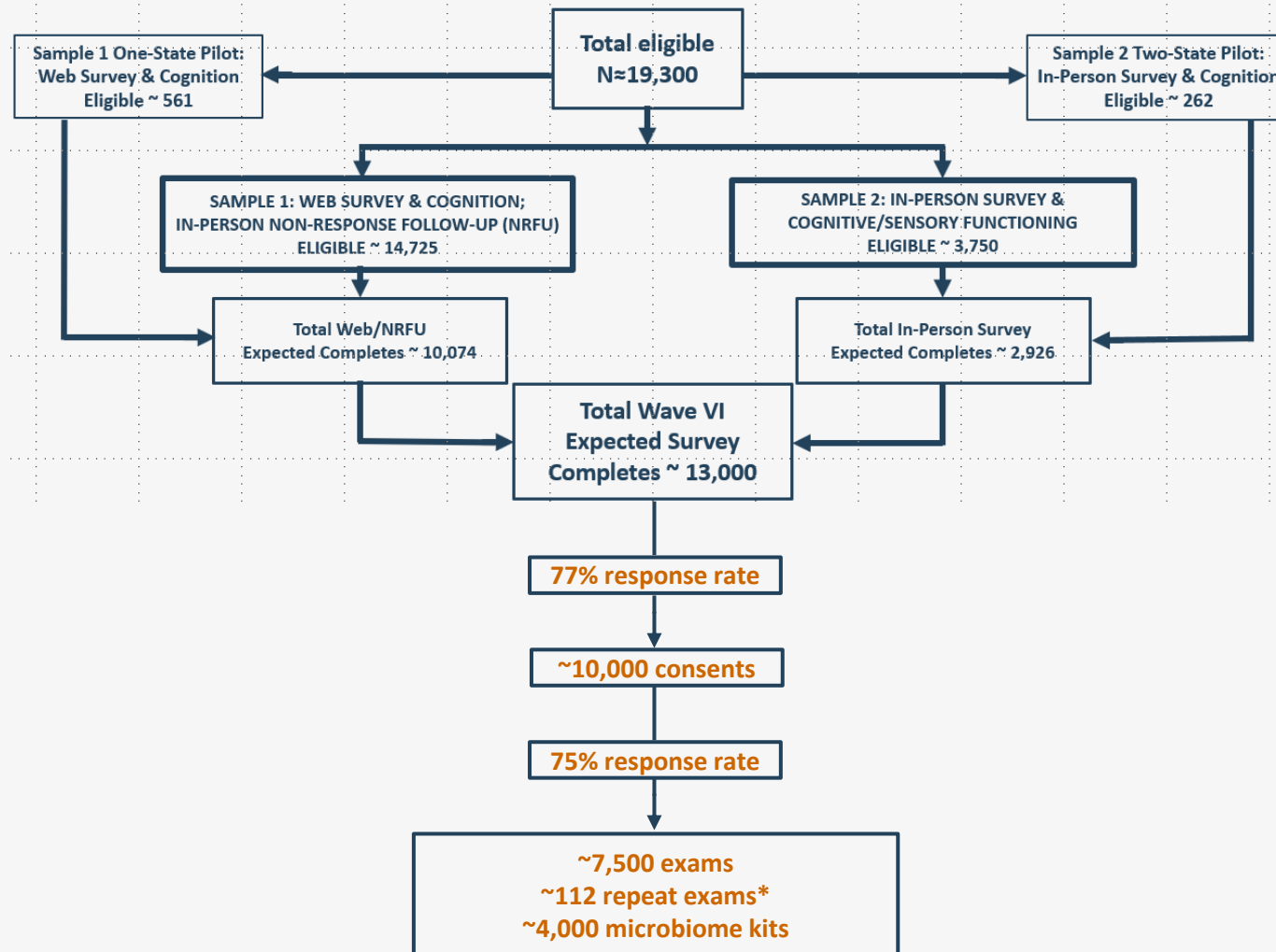   - anxiolytics
    - anticonvulsants

(4)
Biological Data Update

Biological Data Update

- Goals (Survey)

- Goals (Exam)

Total eligible
N≈19,300

Sample 1 One-State Pilot:
Web Survey & Cognition
Eligible ~ 561

Sample 2 Two-State Pilot:
In-Person Survey & Cognition
Eligible ~ 262

SAMPLE 1: WEB SURVEY & COGNITION;
IN-PERSON NON-RESPONSE FOLLOW-UP (NRFU)
ELIGIBLE ~ 14,725

SAMPLE 2: IN-PERSON SURVEY &
COGNITIVE/SENSORY FUNCTIONING
ELIGIBLE ~ 3,750

Total Web/NRFU
Expected Completes ~ 10,074

Total In-Person Survey
Expected Completes ~ 2,926

Total Wave VI
Expected Survey
Completes ~ 13,000

77% response rate

~10,000 consents

75% response rate

~7,500 exams
~112 repeat exams*
~4,000 microbiome kits

*To estimate intra-individual variation

Biological Data Update

- Through 06/07/24

Home Examination Consent*

Consent	n	%
Yes	6,618	(71)
No, not right now	2,712	(29)
Missing	56	(1)
Total	9,386	(100)

*Among survey completes

Specimen Storage Consent*

Consent	n	%
Yes	6,564	(99)
No	52	(1)
Missing	2	(0)
Total	6,618	(100)

*Among survey completes / exam consents

Interest in Recruitment*

Interest	n	%
Yes	1,534	(57)
No	1,175	(43)
Missing	3	(0)
Total	2,712	(100)

*Among survey completes / exam non-consents

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Biological Data Update

- Through 05/31/24

Add Health Wave VI Milestones Report
Last Updated: 05/31/2024

Biological Data Update

- Goals (Survey)

- Goals (Exam)

Total eligible
N≈19,300

Sample 1 One-State Pilot:
Web Survey & Cognition
Eligible ~ 561

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Eligible ~ 262

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COGNITIVE/SENSORY FUNCTIONING
ELIGIBLE ~ 3,750

Total Web/NRFU
Expected Completes ~ 10,074

Total In-Person Survey
Expected Completes ~ 2,926

Total Wave VI
Expected Survey
Completes ~ 13,000

Through 06/14/24
9,623 (74% of goal)

77% response rate   **71% (+ 17% in ongoing recruitment)**

~ 10,000 consents   **6,828 (68% of goal)**

75% response rate   **57%**

~7,500 exams   **4,393 (59% of goal)**
~112 repeat exams*   **104 (93% of goal)**
~4,000 microbiome kits   **1,074 (27% of goal)**

*To estimate intra-individual variation

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Biological Data Update

- Demographics, Overall Through 06/06/24 n = 4,321 (respondents)

CHARACTERISTICS, OVERALL*		N	%
FEMALE		2600	60%
RACE/ETHNICITY:	NON-HISPANIC WHITE	2763	64%
	NON-HISPANIC BLACK	793	18%
	HISPANIC	450	10%
	ASIAN	127	3%
	PACIFIC ISLANDER	32	1%
	AMERICAN INDIAN	28	1%
	MIDDLE EASTERN/NORTH AFRICAN	4	0%
	OTHER/BIRACIAL/MULTIRACIAL	120	3%
RESPONDENT GROUP:	SAMPLE #1 PILOT	143	3%
	SAMPLE #2 PILOT	93	2%
	SAMPLE #1	3694	85%
	SAMPLE #2	376	9%
	NRFU	15	0%

*Unweighted

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Biological Data Update

- Demographics, IIV† Study Through 06/06/24 n = 104 (respondents)

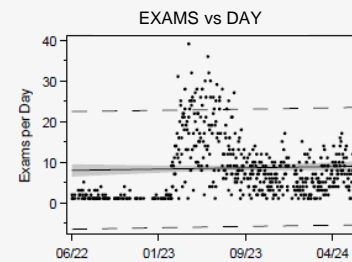| CHARACTERISTICS, IIV STUDY*	N	%
FEMALE	43	41%
RACE/ETHNICITY: NON-HISPANIC WHITE	29	28%
NON-HISPANIC BLACK	34	33%
HISPANIC	26	25%
OTHER	15	14%

Biological Data Update

- Health Through 06/06/24 n = 4,429 (exams)*

HEALTH CHARACTERISTICS*	N	%
OVERALL HEALTH IS GOOD OR BETTER	3619	82%
ON A SPECIAL DIET	887	20%
SMOKE TOBACCO PRODUCTS	933	21%
COVID VACCINATION	3395	77%

*Unweighted. Includes IIV & redraw exams.

Biological Data Update

- Visits Through 06/06/24

  n = 4,429

  (exams)*

EXAM DAY OF WEEK

EXAM START HOUR

CONSENT-EXAM vs DAY

EXAMS vs DAY

EXAM START TIME vs DAY

EXAM DURATION vs DAY

FASTING HOURS vs DAY
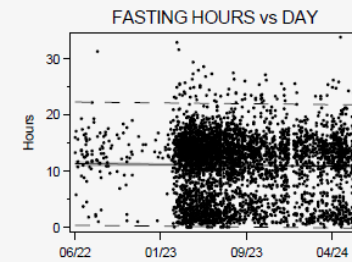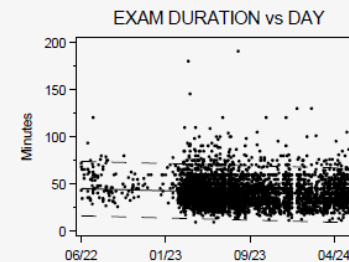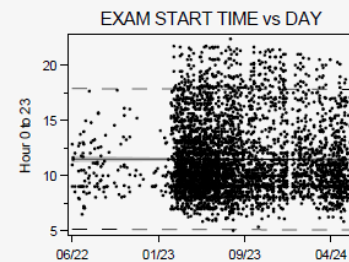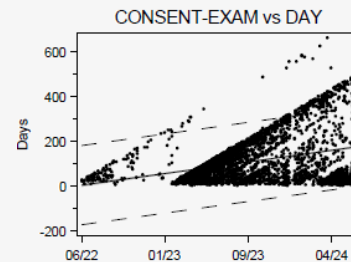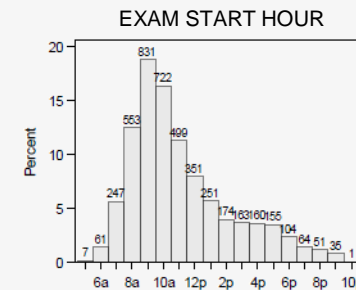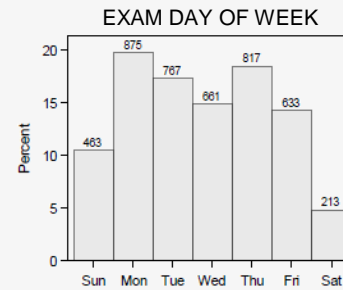
VARIABLE	MEAN	SD	P25	P50	P75
Consent-Exam Interval (d)	104.8	96.3	37.0	72.0	137.0
Exams / Day (n)	8.6	7.3	3.0	7.0	12.0
Start Time (hr)	11.5	3.3	9.1	10.5	13.0
Duration (min)	40.8	14.7	30.0	38.0	48.0
Fasting (hr)	10.9	5.6	6.3	12.4	14.7

Biological Data Update

- Cardiovascular Measures Through 06/06/24 n = 4,429 (exams)*
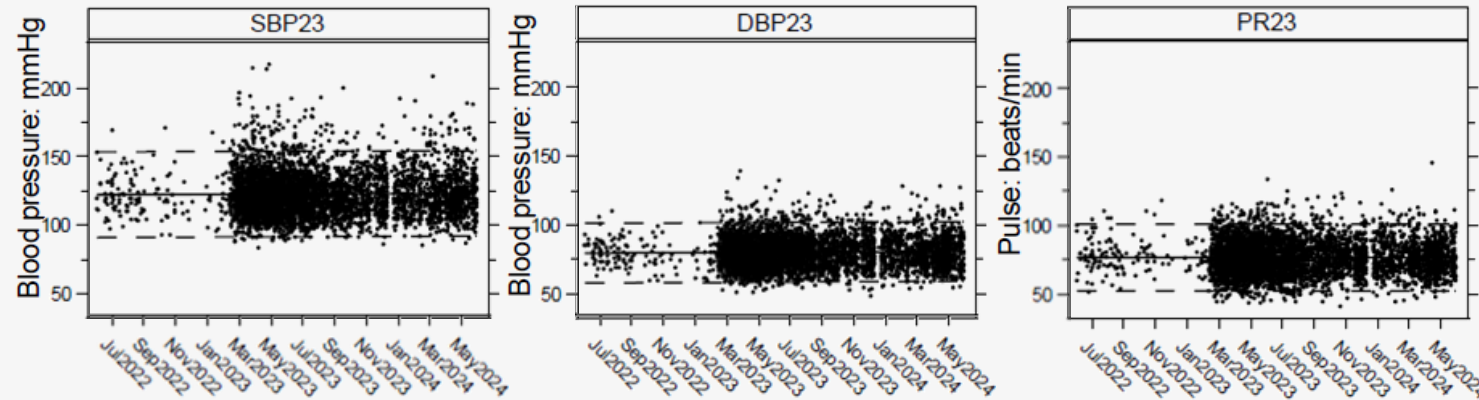
VARIABLE	MEAN	SD	P25	P50	P75	P90	P95	
SBP23 (mm Hg)†	123	16	112	121	132	143	151	— 120-129 (Elevated)
DBP23 (mm Hg)†	80	11	73	80	87	94	99	— 80-89 (Stage 1)
PR23 (bpm)†	76	12	68	76	84	93	98	— ≤ 60 (Bradycardia) ≥ 100 (Tachycardia)

†Average of last two readings

*Unweighted. Includes IIV & redraw exams.

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- Anthropometrics Through 09/15/23 n = 4,429 (exams)*
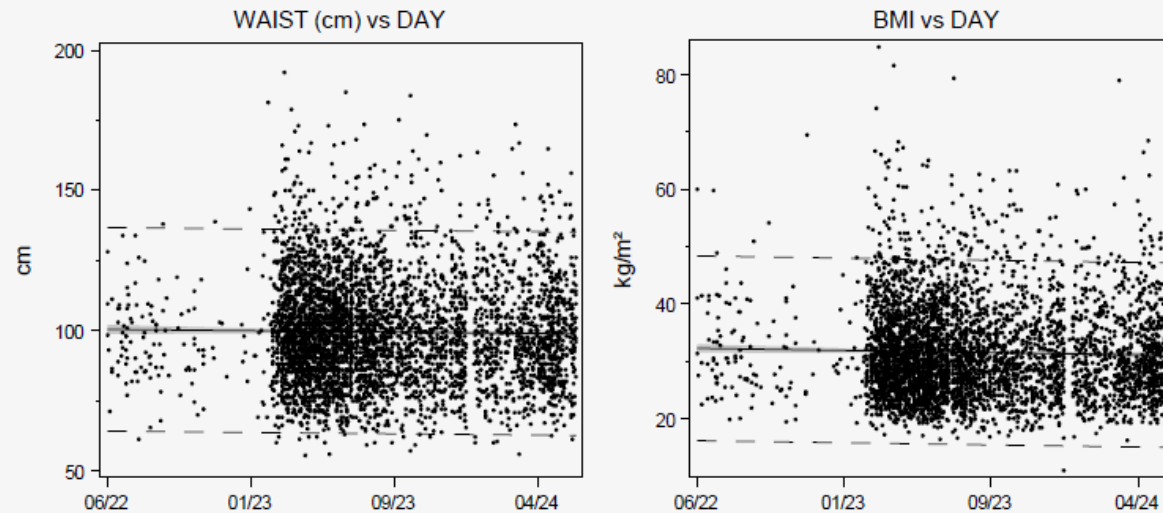
VARIABLE	MEAN	SD	P25	P50	P75	P90	P95	
Waist (cm)	99.5	18.5	86.5	97.0	110.0	124.0	132.5	> 88♀ or 102♂ (High Risk)
BMI (kg/m²)	31.6	8.2	25.8	29.9	35.8	42.4	47.2	> 25 (Overweight or Obese)

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Biological Data Update

- Metabolic Measures Through 05/23/24 n = 4,027 (exams)*
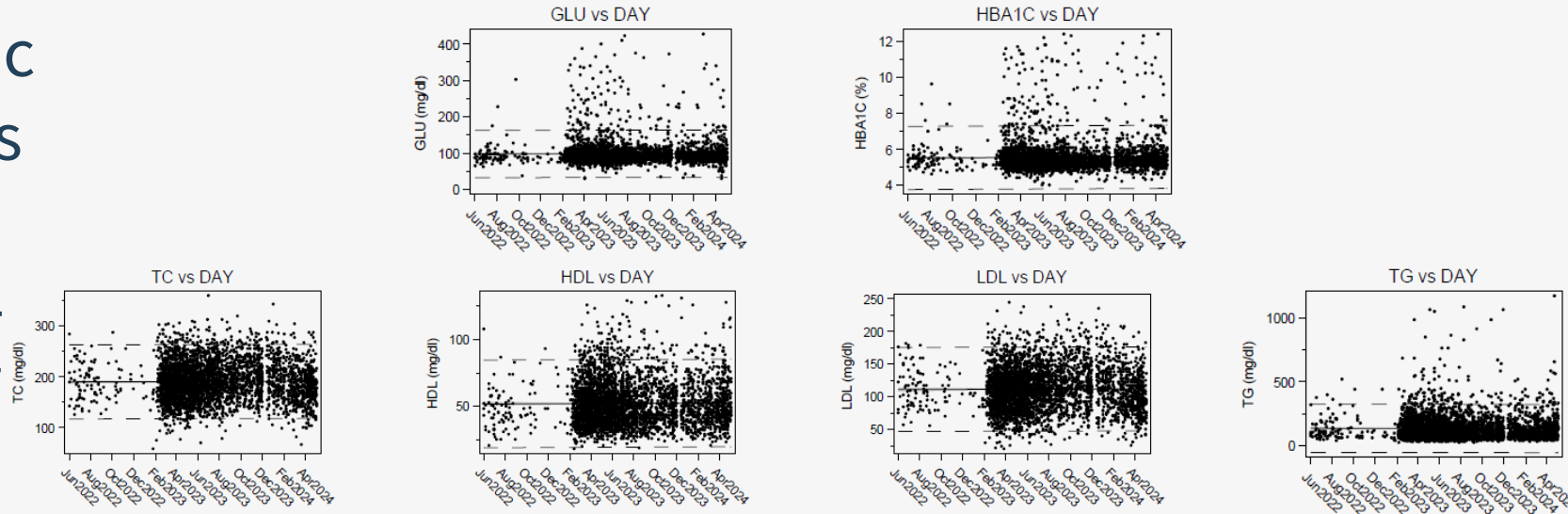
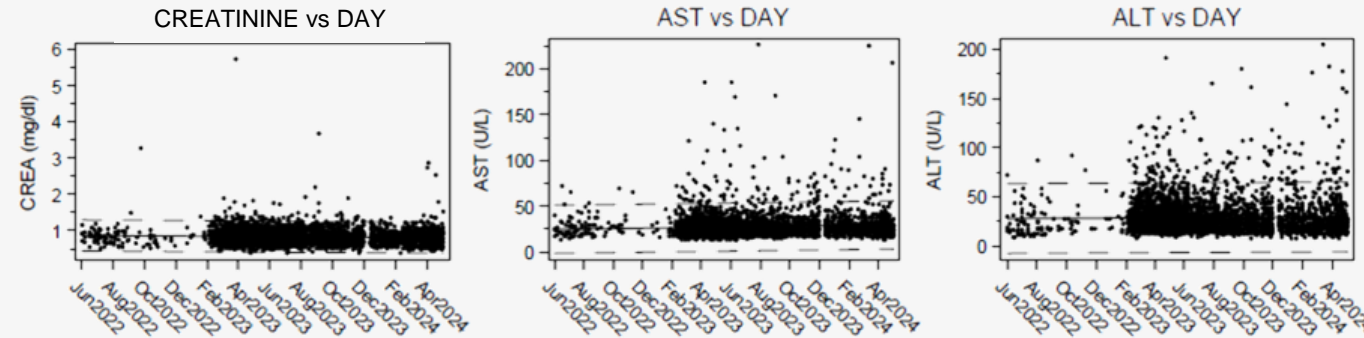| ASSAY	MEAN	SD	P25	P50	P75	P90	P95	
Glucose (mg/dL)	99	35	85	92	101	116	141	— ≥ 100 (Impaired Fasting Glucose)[†]
HbA1C (%)	5.6	1.0	5.1	5.4	5.6	6.1	6.9	— ≥ 5.7 (↑ Risk Diabetes)
TC (mg/dL)	190	37	165	188	213	240	254	
HDL-C (mg/dL)	52	17	40	49	61	75	85	
LDL-C (mg/dL)	112	33	88	110	132	155	169	— ≥ 160 (Hypercholesterolemia)[†]
TG (mg/dL)	135	109	75	109	160	233	298	— ≥ 175 (Hypertriglyceridemia)[†]

*Unweighted. Includes IIV & redraw exams. †Fasting.

Biological Data Update

- Renal & Hepatic Measures Through 05/23/24 n = 4,027 (exams)*

CREATININE vs DAY   AST vs DAY   ALT vs DAY

ASSAY	MEAN	SD	P5	P10	P25	P50	P75	P90	P95	P99	
Creatinine (mg/dL)	0.8	0.4	0.6	0.6	0.7	0.8	0.9	1.1	1.2	1.4	
eGFR (mL/min/1.73 m²)	100	15	73	79	90	103	111	115	117	121	— < 90 (Decreased)
AST (U/L)	28	16	17	18	21	24	30	38	46	82	
ALT (U/L)	29	20	13	15	18	24	33	48	61	108	
AST/ALT	1.1	0.3	0.6	0.7	0.8	1.0	1.3	1.5	1.6	2.1	— ≥ 2.0 (Suggests ALD)

Biological Data Update

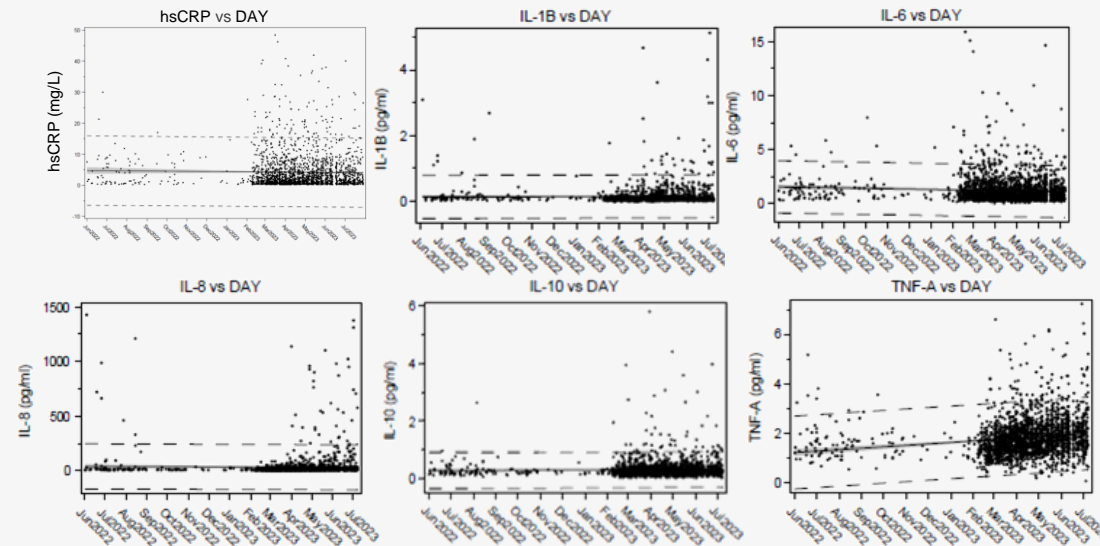- Neurocognitive Measures Through 08/16/23 n = 2,498 (exams)*
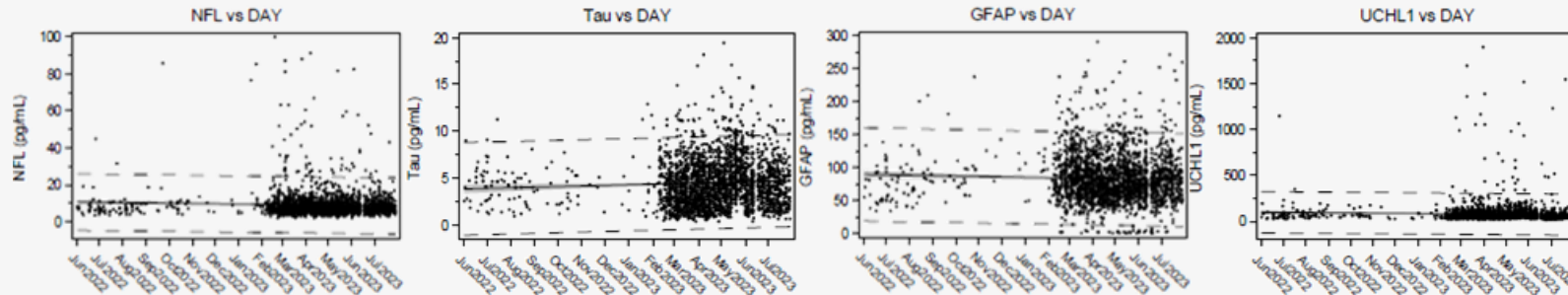
ASSAY	MEAN	SD	P25	P50	P75	P90	P95
NfL *(pg/mL)*	10	19	6	7	10	13	18
Tau *(pg/mL)*	5	3	3	4	6	8	9
GFAP *(pg/mL)*	86	77	60	78	99	128	150
UCH-L1 *(pg/mL)*	105	669	44	56	80	120	165

Biological Data Update

- Inflammatory /Immune Measures Through 08/16/23 n = 2,498 (exams)*

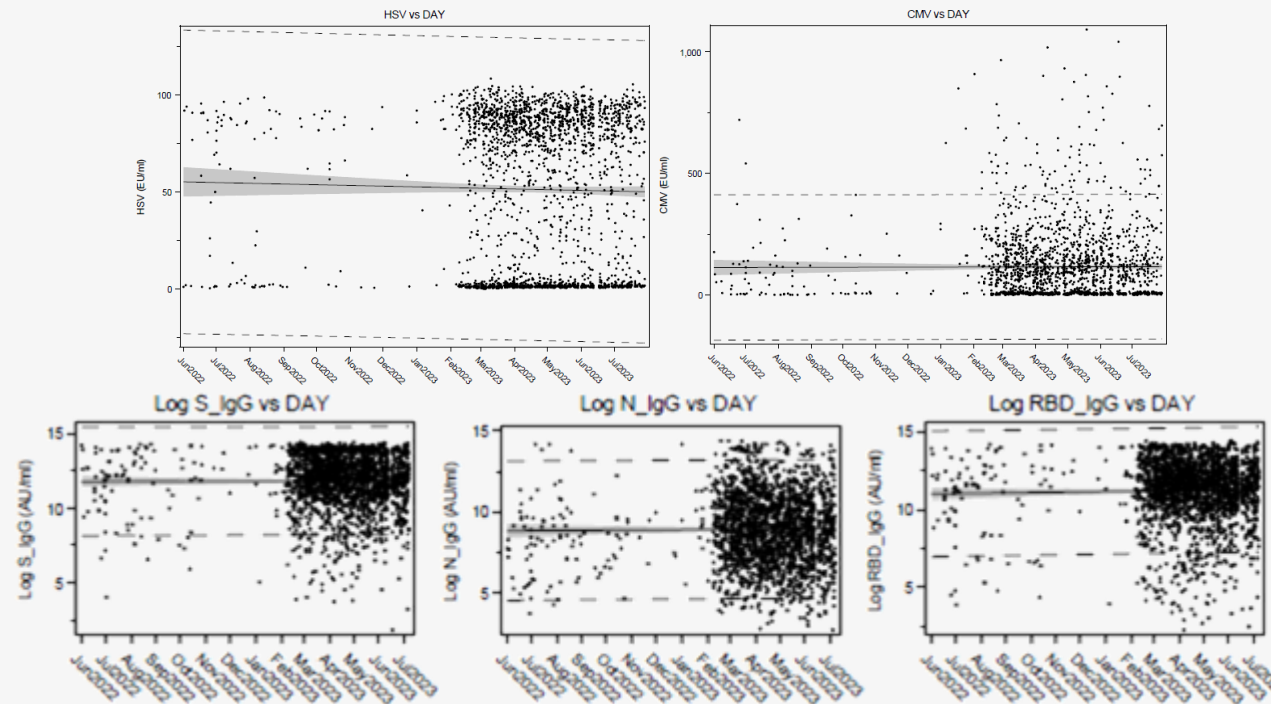| ASSAY	MEAN	SD	P25	P50	P75	P90	P95
hsCRP (ug/ml)	4.3	6.4	0.8	2.1	5.2	10.1	15.1
IL-1B (pg/ml)	0.18	0.89	0.04	0.07	0.12	0.29	0.48
IL-6 (pg/ml)	1.38	4.23	0.55	0.88	1.43	2.31	3.33
IL-8 (pg/ml)	39.0	150.9	9.9	13.5	19.1	34.1	88.3
IL-10 (pg/ml)	0.34	0.93	0.17	0.23	0.33	0.49	0.72
TNF-α (pg/ml)	1.84	0.99	1.33	1.71	2.15	2.65	3.16

— < 3 (High)

*Unweighted. Includes IIV & redraw exams. Cytokines through 07/26/23 (n=2,288).

Biological Data Update

- Infectious Measures Through 08/16/23 n = 2,498 (exams)*

ASSAY	MEAN	SD	P1	P5	P10	P25	P50	P75	
HSV IgG (EU/mL)	51.3	39.8	0.5	0.8	1.0	1.9	70.2	88.1	— ≥ 20.0 (+)
CMV IgG (EU/mL)	117.9	159.4	1.0	2.5	3.8	7.6	70.3	163.9	— ≥ 10.0 (+)
S* IgG (log AU/ml)	11.8	1.8	5.6	8.2	9.3	11.0	12.1	13.1	— ≥ 7.6 (+)
N* IgG (log AU/ml)	8.9	2.2	3.9	5.3	6.1	7.4	9.0	10.5	— ≥ 8.5 (+)
R* IgG (log AU/ml)	11.2	2.1	4.1	6.8	8.5	10.4	11.6	12.6	— ≥ 6.4 (+)

*SARS-CoV2 spike (S), nucleocapsid (N) & receptor binding domain (R).
AU = absorbance units. EU = equivalent units.

Biological Data Update

- Medications Through 06/04/24

  n = 4,429

  (exams)*

PRESCRIPTION MEDICATIONS*	N	%
NONE	1743	39%
1 - 2	1327	30%
3 OR MORE	1321	30%

(5)
Biological Data Quality

Biological Data Quality

- Data Quality Controls
  - train staff uniformly
  - follow standardized protocol
  - use standard, tested equipment
  - automate processes
  - monitor missing data
  - monitor measurement error
    trend / cyclicity
    digit preference
    inaccuracy
    unreliability
  - find & fix threats to data quality
  - recognize & reward efforts to that end

Biological Data Quality

- Monitor Reliability Through 05/23/24

CARDIOVACULAR & ANTHROPOMETRIC MEASURES*

MEASURE	N	ICC	(95% CI)
SBP23	104	0.74	(0.66,0.83)
DBP23	104	0.73	(0.64,0.82)
PR23	104	0.67	(0.56,0.78)
Arm	104	0.90	(0.86,0.94)
Height	104	0.95	(0.94,0.97)
Weight	104	0.99	(0.98,0.99)
Waist	104	0.96	(0.95,0.98)
BMI	104	0.97	(0.96,0.98)

METABOLIC, HEPATIC & RENAL MEASURES*

ASSAY	N	ICC	(95% CI)
GLU	96	0.84	(0.78,0.90)
HBA1C	96	0.99	(0.98,0.99)
TC	96	0.91	(0.87,0.94)
HDL	96	0.87	(0.82,0.92)
LDL	96	0.89	(0.85,0.94)
TG	96	0.70	(0.60,0.81)
AST	96	0.75	(0.65,0.84)
ALT	96	0.84	(0.77,0.90)
CREA	96	0.93	(0.90,0.96)

*Unweighted

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Add Health
The National Longitudinal Study of Adolescent to Adult Health

Biological Data Quality

- Monitor Reliability Through 08/16/23 & 07/26/23

NEUROCOGNITIVE MEASURES*

ASSAY	N	ICC	(95% CI)
NfL	28	0.96	(0.93,0.99)
Tau	28	0.85	(0.74,0.96)
GFAP	28	0.64	(0.42,0.87)
UCHL1	28	0.91	(0.84,0.98)

INFLAMMATORY / IMMUNE MEASURES*

ASSAY	N	ICC	(95% CI)
hsCRP	28	0.74	(0.57,0.92)
IL-1B	27	0.69	(0.45,0.92)
IL-6	27	0.63	(0.38,0.87)
IL-8	27	0.81	(0.67,0.94)
IL-10	27	0.82	(0.68,0.95)
TNF-A	27	0.92	(0.85,0.98)

INFECTIOUS MEASURES*

ASSAY	N	ICC	(95% CI)
HSV IgG (EU/ml)	28	1.00	(0.99,1.00)
CMV IgG (EU/ml)	28	0.96	(0.93,0.99)
S IgG (AU/ml)	24	1.00	(0.99,1.00)
N IgG (AU/ml)	24	1.00	(0.99,1.00)
R IgG (AU/ml)	24	0.99	(0.99,1.00)

*SARS-CoV2 spike (S), nucleocapsid (N) & receptor binding domain (R). AU = absorbance units. EU = equivalent units.

UNC CAROLINA POPULATION CENTER

Add Health
The National Longitudinal Study of Adolescent to Adult Health

Biological Data Quality

- Find & Fix Threats Through 06/06/24 n = 4,429 (exams)*

EXAM CONDITION	N	%	Most Recent
→ EXAM ON FRIDAY or SATURDAY	846	19%	2024.06.01
EXAM ON SUNDAY	463	10%	2024.06.02
EXAM START TIME: 1:00 PM or later (Mon–Thurs)	905	20%	2024.06.06
FASTING < 8 HR	1180	27%	2024.06.06
→ FASTING < 9 HR	1276	29%	2024.06.06
USED WRONG VERSION OF TABLET SOFTWARE	0	0%	
EXAM TRANSCRIBED FROM PAPER (self-reported)	32	1%	2024.05.28
EXAM NOT UPLOADED SAME DAY	277	6%	2024.06.04
DID NOT USE MICROLIFE BP UNIT	9	0%	2024.06.03
DID NOT USE HEALTH-O-METER SCALE	9	0%	2024.04.30
EQUIPMENT ERRORS: BP MONITOR	47	1%	2024.04.28
EQUIPMENT ERRORS: SCALE	10	0%	2023.09.26
BP CUFF DID NOT FIT (arm > 52 cm)	9	0%	2024.03.14
DID NOT USE PREFERRED UNITS: ARM (cm)	5	0%	2024.04.30
HEIGHT (cm)	6	0%	2024.04.30
WEIGHT (kg)	6	0%	2024.04.30
WAIST (cm)	6	0%	2024.04.30
at least 1 above	15	0%	2024.04.30
TERMINATED B/C OF HIGH BP	25	1%	2024.05.31
→ ANY MEDS FROM MEMORY	1076	24%	2024.06.04
REFUSED PHLEBOTOMY	218	5%	2024.06.04
FAILED PHLEBOTOMY	77	2%	2024.06.06
→ COLLECT-CENTRIFUGE > 2 HR	25	1%	2024.05.19
REFUSED MICROBIOME PACKET	47	1%	2024.04.29

Biological Data Quality

- Find & Fix Threats Through 06/06/24
  n = 4,094
  (exams)*

KIT CONDITION	N	%	Most Recent
Normal	3442	84%	2024.06.06
Only 1 ice pack in cooler	33	1%	2024.05.31
Sample leaked in biohazard bag, all contents discarded	14	0%	2024.05.30
Package not picked up on same day as home exam; examiner error	12	0%	2024.02.12
B6ID on Manifest does not match tubes	0	0%	*
Package received > 24 hours from home exam; FedEx error	25	1%	2024.05.02
➡ Kit age >48 hours, samples discarded	212	5%	2024.06.05
Room temperature	196	5%	2024.06.06
Kit Manifests error	160	4%	2024.06.04

TUBE CONDITION	5 SERUM #1		5 SERUM #2		5 KEDTA		3 KEDTA		4 Packed Cells		10 PAXgene	
	N	%	N	%	N	%	N	%	N	%	N	%
Normal (sample >0 ml)	3755	92%	3684	90%	3682	90%	3839	94%	3835	94%	3830	94%
Empty tube (0 ml)	15	0%	62	2%	43	1%	43	1%	45	1%	54	1%
➡ Hemolyzed	111	3%	141	3%	152	4%	0	0%	0	0%	0	0%
Clotted	1	0%	0	0%	0	0%	0	0%	1	0%	0	0%
Whole blood centrifuged	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Tube broken	2	0%	2	0%	6	0%	0	0%	0	0%	1	0%
Incorrect Sample Type	0	0%	0	0%	6	0%	0	0%	5	0%	0	0%
Frozen	1	0%	1	0%	1	0%	3	0%	3	0%	1	0%
➡ Room Temperature	209	5%	204	5%	204	5%	209	5%	205	5%	208	5%
Incorrect or Missing B6ID on tube	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Tube missing; no tube in kit	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Total:	4094	100%	4094	100%	4094	100%	4094	100%	4094	100%	4094	100%

*Unweighted. Includes IIV & redraw exams.

Biological Data Quality

- Recognize & Reward Efforts

Respondent Rating of Examiners

Examiners (y-axis)
Rating Score: 3 4 5 6 7 8 9 10
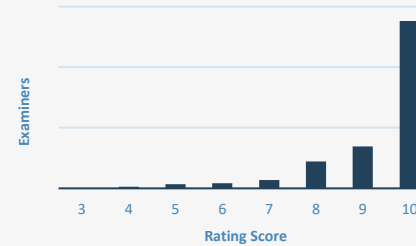
Weekly Exam Feedback

Field Supervisor	Health Professional	Visits		Centrifuge Incidents		Equipment Incidents		Metrics Incidents		Paper Form Incidents		Respondent ID Incidents		Upload Delay Incidents		Incidents	
		This Week	Total	This Week	Total	This Week	Total	This Week	Total	This Week	Total	This Week	Total	This Week	Total	This Week	Total

Weekly Lab Feedback

Field Supervisor	Health Professional	Visits	Total	Blood Hemolyzed		Not Shipped Same Day		Insufficient Volume		Blood Warm		Missing Tubes		Total	
				Week	Total	Week	Total	Week	Total	Week	Total	Week	Total	Week	Total

Gold Star Program

Reward Eligibility

Biological Data Summary

- Summary
  - In the field ~ 2 years
  - Exam consent, specimen storage consent & recruitment interest high (71%; 99%; 57%)
  - 4,429 respondent exams (62% female; 64% non-Hispanic white)
  - 104 IIV exams   (41% female; 28% non-Hispanic white)
  - On average, started ~11:30 AM, followed ~11 hr fast, lasted ~41 min
  - Risk factors, common diseases & medication use prevalent
  - Quality assurance / control systems @ work
  - Preliminary data quality encouraging (ICC range: 0.63-1.00)

(6)

Biological Data Availability

Biological Data Availability

- Wave VI (pending)
- Waves I-IV (now)
  - Restricted or Public Use Data & Documentation
    UNC CPC link: https://data.cpc.unc.edu/
  - Public Use Data & Documentation
    UM ICPSR link: https://www.icpsr.umich.edu/

Biological Data Availability

- Ancillary Studies
  - Link: https://addhealth.cpc.unc.edu/data/ancillary-studies/
  - Questions: addhealth_ancillary@unc.edu
  - Definition: An independently supported study that either
    - 1) requires identifiers to link 2° data sources, <u>or</u>
    - 2) uses archived biospecimens, <u>or</u>
    - 3) collects new survey or biological data
  - Application Process:
    - 1) submit a concept proposal
    - 2) address feedback based on its review
    - 3) submit a full proposal
    - 4) collaboratively develop a budget

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Add Health
The National Longitudinal Study of Adolescent to Adult Health

Biological Data Availability

- <u>Schematic</u>

STAGES

| Preliminary Review | Application Submission | Application Review & Approval | Data Cleaning | Data Dissemination |

STEPS

Preliminary Review	Application Submission	Application Review & Approval	Data Cleaning	Data Dissemination
1. Review Ancillary Studies website. 2. Review Research Guidelines for Ancillary Studies pdf. 3. Submit Concept Proposal for review.	1. Address feedback from the preliminary review. 2. Submit the Add Health Ancillary Study Proposal Form. 3. Work with the Ancillary Studies Coordinator to develop a cost estimate.	1. Research Committee reviews proposal. 2. Receive approval letter. 3. Submit the signed Data and Material Use Agreement. 4. Apply for a Restricted-use data contract. 5. Provide IRB approval. 6. Submit processing fee.	1. Receive Preliminary Data. 2. Create documentation. 3. Deductive Disclosure review. 4. Review codebooks created by Add Health. 5. Set a release date.	1. Destroy Preliminary Data. 2. Request the final released file using CPC Data Portal. 3. Prepare publications, Manuscripts, and presentations using the final released file.

MODE

| Researchers provide a brief (1-page) Concept Proposal | Researchers complete Ancillary Study Proposal Form | Go to CPC Data Portal to apply for Restricted-use data contract | Communication via email with the Ancillary Studies Coordinator | To request the final released file go to CPC Data Portal |

TIMELINE

| Eight months in advance of grant application deadline | Six months in advance of grant application deadline | 12 - 16 weeks | 6 -12 months | 4 - 6 weeks |

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Add Health — The National Longitudinal Study of Adolescent to Adult Health

Biological Data Availability

- Ancillary Studies
  - Review Criteria
  - Scientific Merit[*]
  - Consistency with scientific
    - 1) objectives of Add Health
    - 2) priorities of funders, esp.
      - NIA Division of Behavioral and Social Research
      - NICHD Population Dynamics Branch
  - Ability to leverage unique Add Health characteristics
  - Minimal overlap with its study portfolio
  - Acceptable participant burden
  - Parsimonious biospecimen use
  - Minimal burden to staff & biospecimen reserves

*Significance, approach, innovation, investigators & environment

Vital Events Data

(1)
Vital Events Data Aims

Vital Events Data Aims

- To establish a scalable infrastructure for surveillance of chronic disease events, initially by ascertaining decedents

- To anticipate the epidemiologic transition to rapid increases in chronic disease morbidity and mortality with age

(2)
Vital Events Data Collection Methods

Vital Events Data Collection Methods
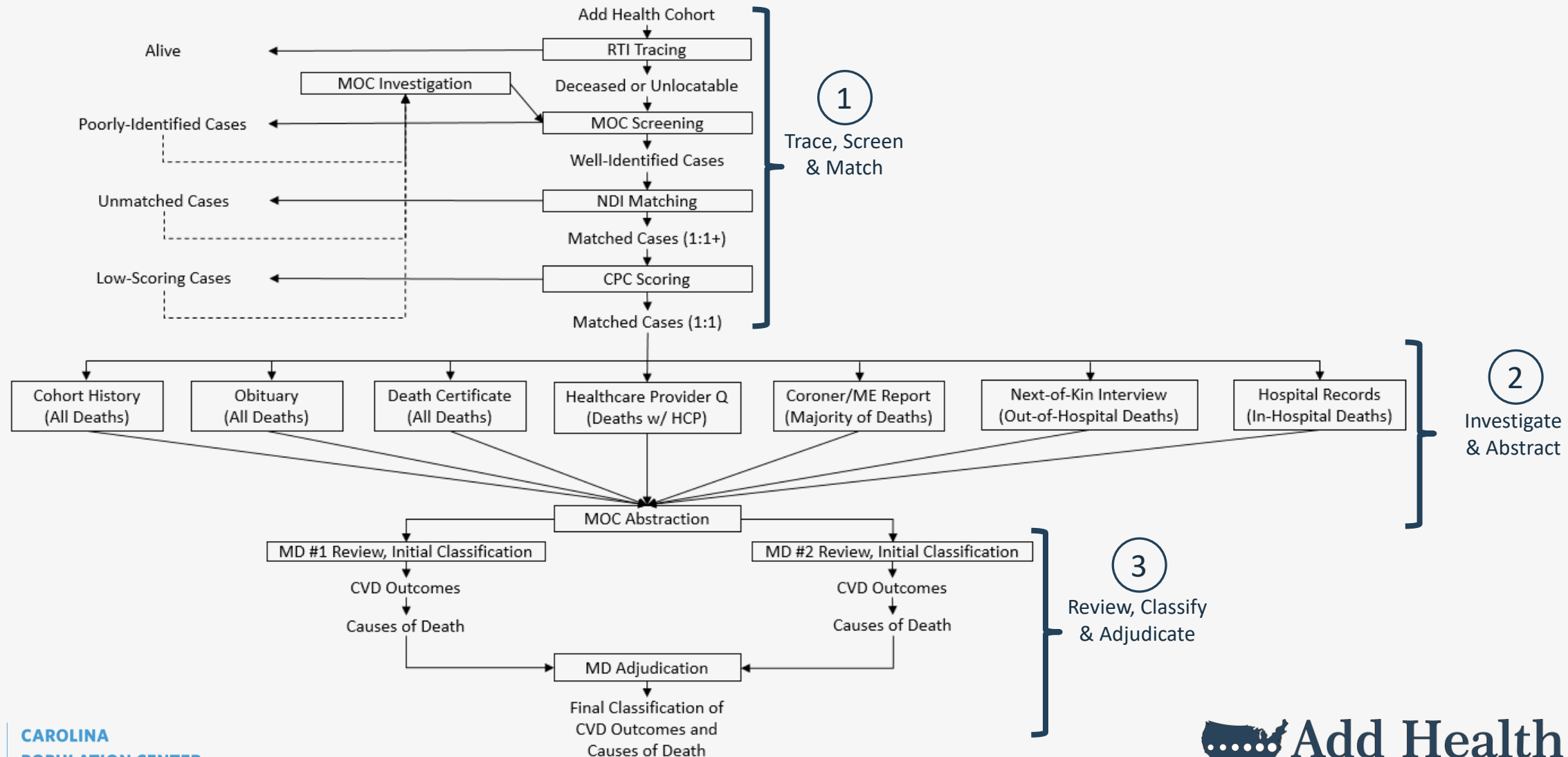
Vital Events Data Update

- Tracing, Screening & Matching

Deaths
Through
12/31/22
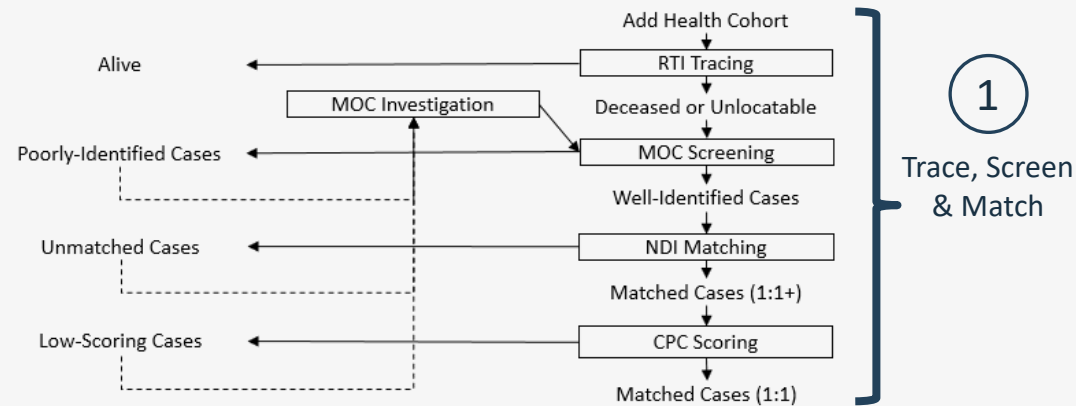
694 Decedents Matched 1:1

Source: NDI, 1994- 2022

Vital Events Data Update

- Tracing, Screening & Matching

Geographic Distribution of Deaths Through 12/31/22

Decedents
- ≥ 40
- 11-39
- 1-10
- 0
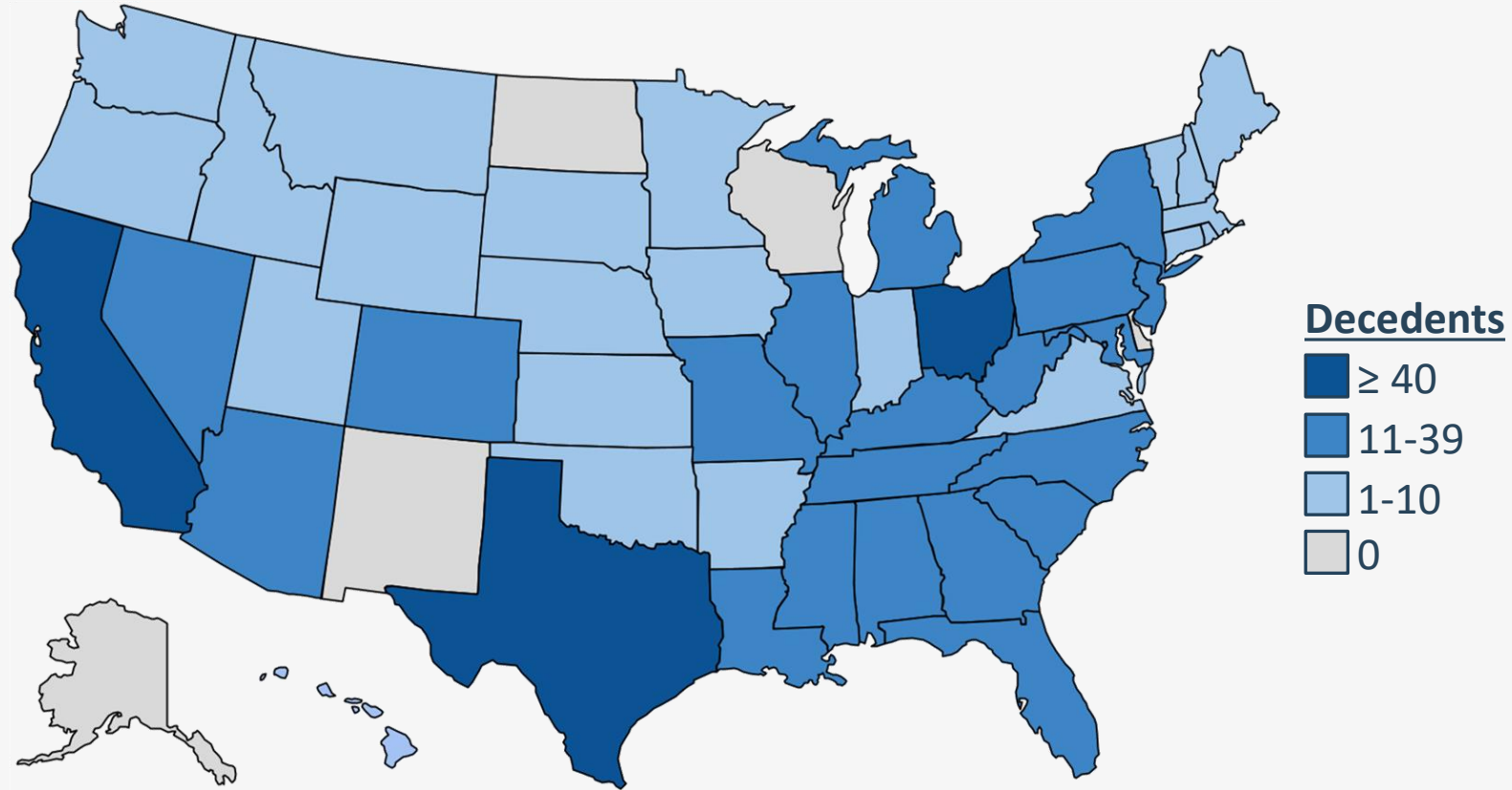
Source: NDI, 1994- 2022

Vital Events Data Update

- Tracing, Screening & Matching

Temporal Distribution of Deaths Through 12/31/22
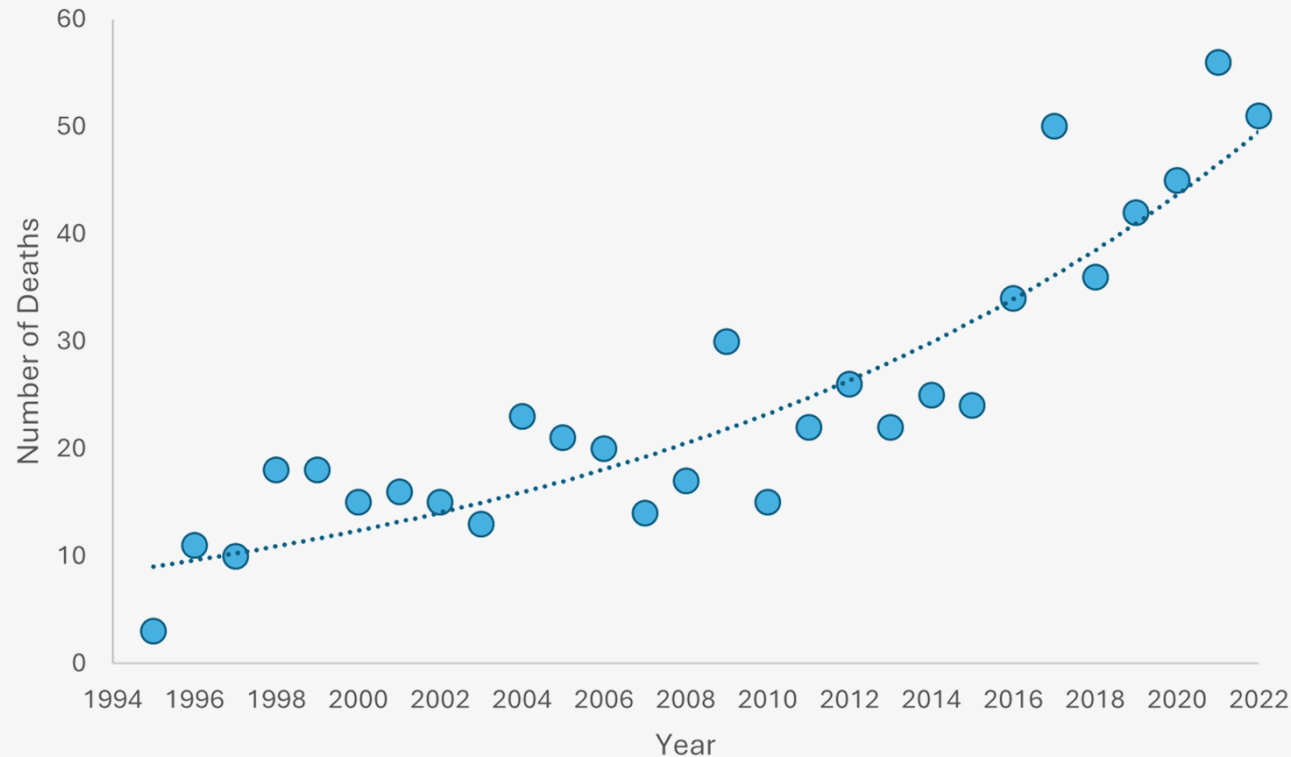
Vital Events Data Update

- Tracing, Screening & Matching

Demographic Distribution of Deaths Through 12/31/22

Characteristic		Mean (Range) or %
Age, years		33.2 (14-48)
Female		38%
Race/ethnicity	EA	53%
	AA	25%
	HL	12%
	A/PI	5%
	AI/AN	3%
	O/M	2%

AA = African American. AI/AN = American Indian/Alaskan Native.
A/PI = Asian/Pacific Islander. EA = European American.
HL = Hispanic/Latino. O/M = Other/Multiple.

Vital Events Data Update

- Investigation & Abstraction

Through 06/11/24

Matched Cases (1:1)

| Cohort History (All Deaths) | Obituary (All Deaths) | Death Certificate (All Deaths) | Healthcare Provider Q (Deaths w/ HCP) | Coroner/ME Report (Majority of Deaths) | Next-of-Kin Interview (Out-of-Hospital Deaths) | Hospital Records (In-Hospital Deaths) |

MOC Abstraction

② Investigate & Abstract
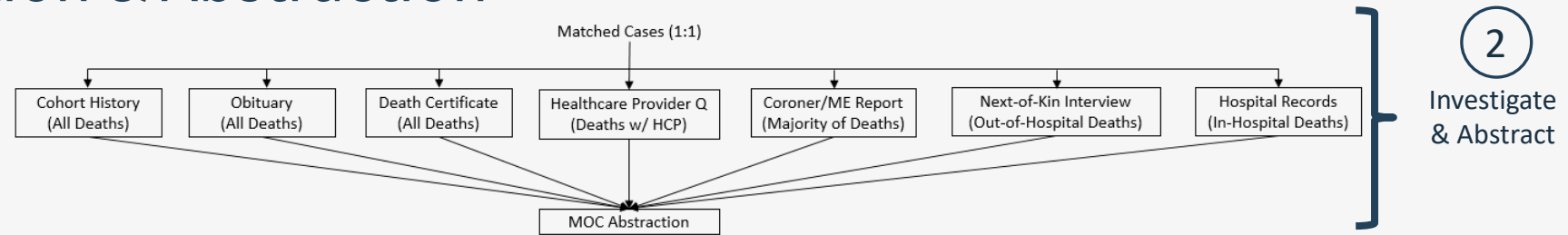
Executed Add Health-State* Agreements to Provide Death Certificates
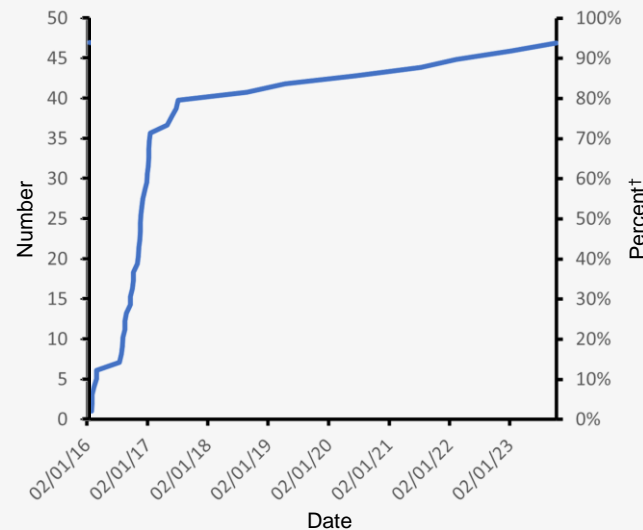
Date

*Includes U.S. states, U.S. Army, U.S. Marines & Mexico.
†Denominator = states with an Add Health decedent.

Vital Events Data Update

- Investigation & Abstraction
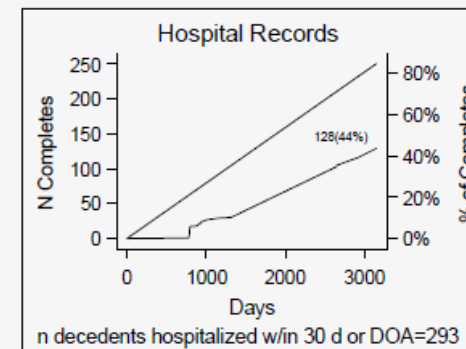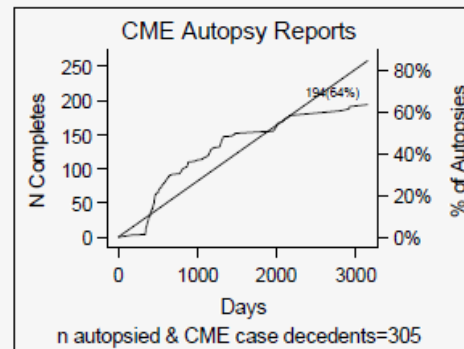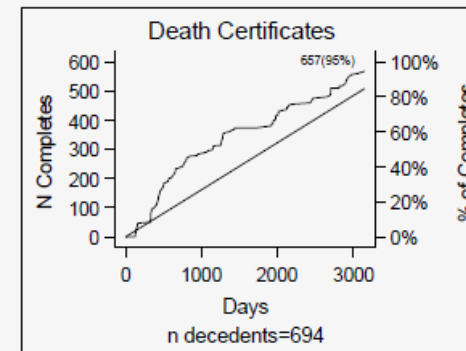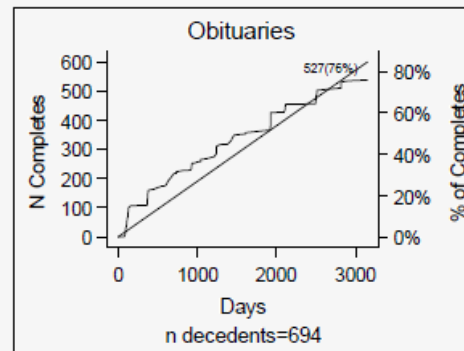
  Through
  06/11/24

Vital Events Data Update

- Investigation & Abstraction

Manner & Underlying Cause of Death Through 12/31/22

Manner of Death*	%
Accidental	39.0
Natural	38.9
Suicide	12.0
Homicide	8.4
Undetermined	1.7

*From death certificate

Underlying Cause of Death†	%
Motor Vehicle Accident	16.1
Cardiovascular Disease	15.1
Accidental Drug Intoxication	13.9
Suicide	11.1
Cancer	9.4
Homicide	7.2
Other Natural Cause	7.0
Infectious Disease	3.7
Other Accident	3.3
Unknown/Undetermined	3.3
Respiratory Disease	2.5
Digestive Disease	2.3
COVID-19	2.2

†From ICD Codes (NDI)

Vital Events Data Update

- Review, Classification & Adjudication

Through 06/11/24
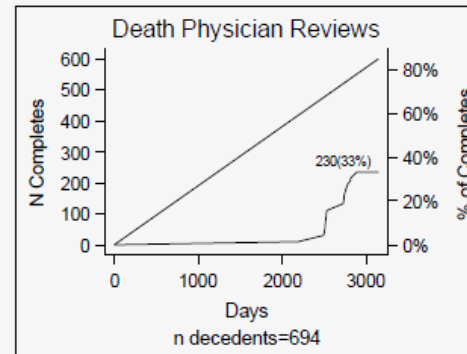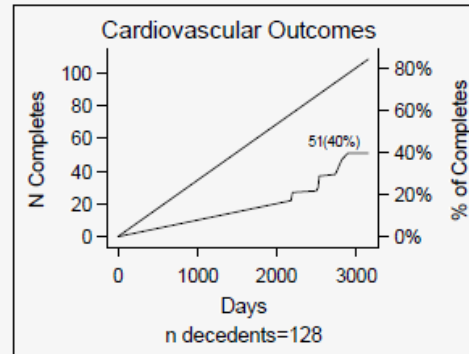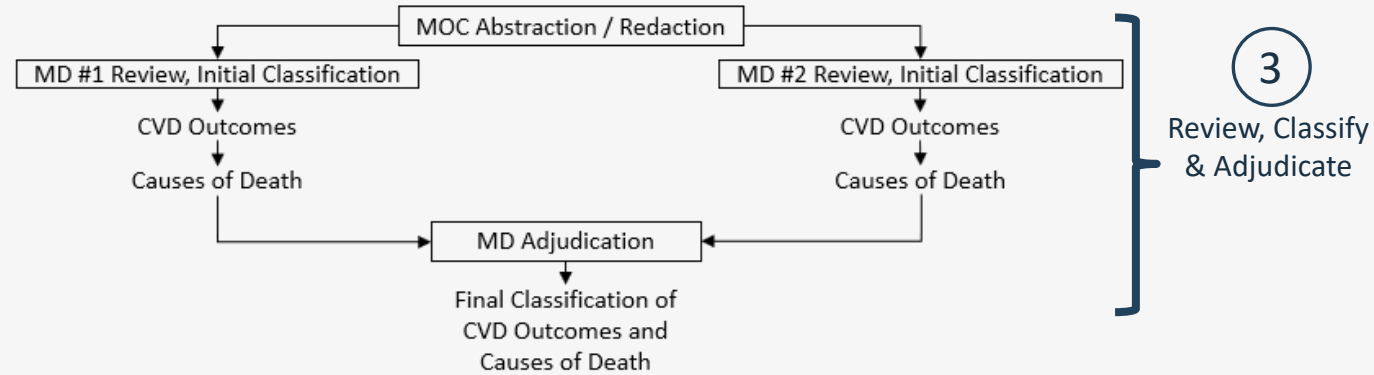
(4)
Vital Events Data Quality

Vital Events Data Quality

- ## Quality Control
  Through
  06/11/24

Mean (95% CI) Item-Specific, Between-Abstractor % Agreement & PABAK, by Abstraction Form
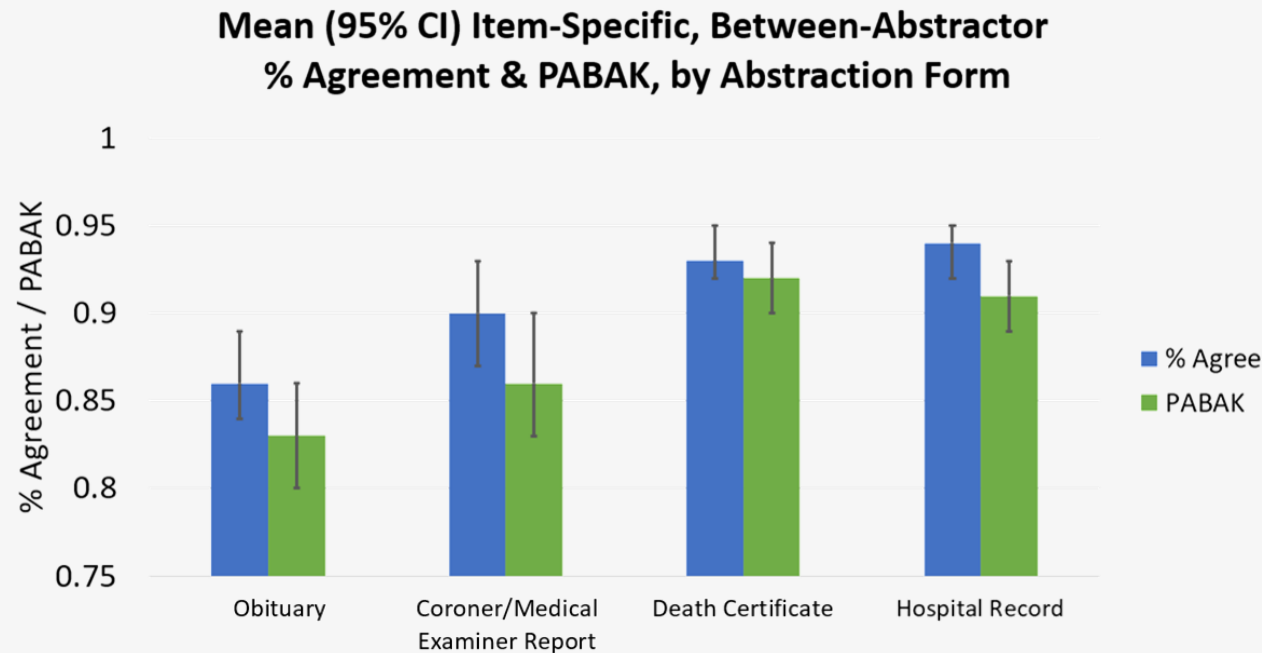
Among a random sample of 28 decedents and an oversample of 28 hospitalized decedents enriched 3:1 for cardiovascular disease. PABAK = prevalence- and bias-adjusted kappa coefficient. 95% CI = 95% confidence interval. Mean, biomarker-specific intra-class correlation coefficient (95% CI) = 0.96 (0.95-0.98).

(5)

Vital Events Data Summary

Vital Events Data Summary

- Summary
  - In the field > 8 years
  - Decedents 1994-2022 = 694
  - Cumulative mortality = 3.3%
  - Natural causes account for > 2/5
  - Quality assurance / control systems @ work
  - Physician review, classification & adjudication ongoing
  - Preliminary data quality encouraging (PABAK range: 0.83-0.92)

(6)

Vital Events Data Availability

Vital Events Data Availability

- 1994-2021 (now)
  - Restricted Use Data & Documentation
    - (1) vital status & underlying cause of death
    - (2) ordered causes of death
    - (3) all causes of death w/ entity-axis codes
    - (4) all causes of death w/ record-axis codes
  - UNC CPC link: https://data.cpc.unc.edu/
    https://doi.org/10.17615/8s1b-qd86

- 2022 Updates of 1-4 (pending), include
  - **NEW!** (5) opioid-related cause of death classification
  - (6) death certificate data w/ occupational codes

Acknowledgements