# Metabolic syndrome and HIV in children

**HOPE Conference**
**January 25, 2022**

**Stephanie Shiau, PhD, MPH**
Assistant Professor
Department of Biostatistics and Epidemiology
Rutgers School of Public Health
stephanie.shiau@rutgers.edu
@stephshiau

RUTGERS
School of Public Health

pHACS
A Study of the National Institutes of Health

PHACS George R. Seage III
Early Career Investigator Award

# Today's Talk

- Definitions of metabolic syndrome (MetS) in adults and children
- Epidemiology of MetS
- MetS in populations living with HIV
- MetS and HIV-associated cognitive impairment in adults
- Our study: MetS and lower neurocognitive performance in youth with perinatally-acquired HIV

# Metabolic syndrome (MetS): a brief history

- 1950: Emerging concepts
  - Obesity as risk factor for diabetes
  - Association between obesity and glucose intolerance/dyslipidemia
- 1988: Gerald Reaven introduced "*Syndrome X*"
  - Framework presented link between insulin resistance and other metabolic abnormalities
- Over the next decade:
  - Descriptions of constellation of inter-related metabolic risk factors that appear to lead to type 2 diabetes and cardiovascular disease
  - Described as "*insulin resistance syndrome", "syndrome X", "dysmetabolic syndrome"*
- 1998: WHO presented criteria for *"metabolic syndrome"*

# MetS has 5 core components

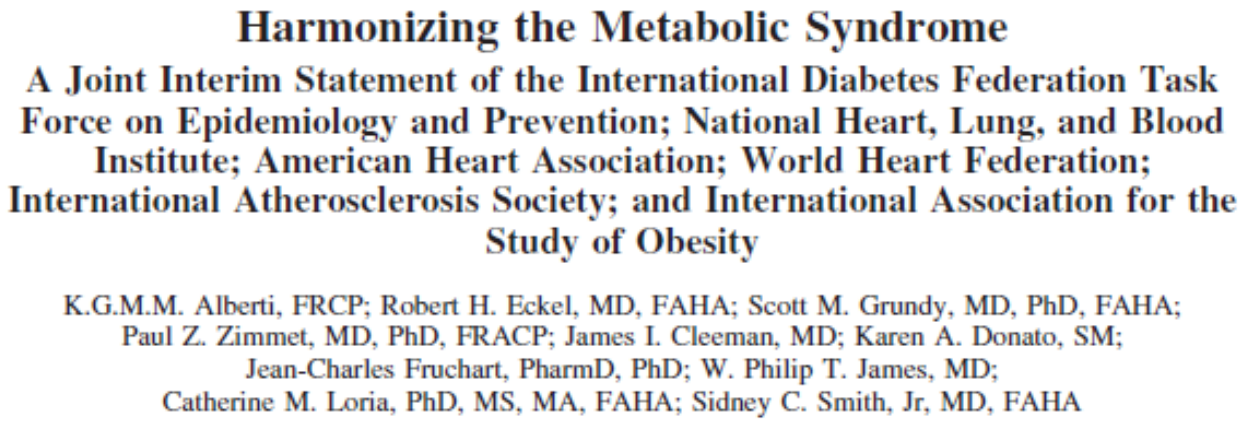
1. Obesity (especially central)
2. Elevated triglycerides
3. Decreased high-density (HDL) cholesterol
4. Hypertension
5. Insulin resistance / Type 2 diabetes

# Changing definitions of MetS in adults

| Definition | WHO (1998) | EGIR (1999) | NCEP/ATP III (2001) | AHA-NHLBI (2005) | IDF (2006) |
|---|---|---|---|---|---|
| **Citation** | Alberti et al. Diabet Med 1998 | Balkau et al. Diabet Med 1999 | NCEP Circulation 2002 | Grundy et al. Circulation 2005 | Alberti et al. Diabet Med 2006 |
| **Mandatory criteria** | Insulin resistance | Insulin resistance (plasma insulin >75$^{th}$ percentile) | None | None | Waist circumference with ethnicity-specific values (or BMI >30) |
| **Additional criteria** | At least two of the following | At least two of the following | At least three of the following | At least three of the following | At least two of the following |
| ***Central obesity*** | Waist/hip ratio: > 0.90 (M), >0.85 (F); or BMI >30 | Waist circumference ≥ 37 in (M), ≥32 in (F) | Waist circumference ≥ 40 in (M), ≥ 35 in (F) | Waist circumference ≥ 40 in (M), ≥ 35 in (F) | Mandatory |
| ***Raised triglycerides*** | TG ≥ 150 mg/dl | TG ≥ 177 mg/dl | TG ≥ 150 mg/dl | TG ≥ 150 mg/dl | TG ≥ 150 mg/dl or treatment |
| ***Reduced HDL cholesterol*** | HDL-C <35 mg/dl (M), <39 mg/dl (F) | HDL-C <39 mg/dl | HDL-C <40 mg/dl (M), <50 mg/dl (F) | HDL-C <40 mg/dl (M), <50 mg/dl (F) | HDL-C <40 mg/dl (M), <50 mg/dl (F) or treatment |
| ***Raised blood pressure*** | ≥140/90 mmHg | ≥140/90 mmHg or antihypertensive medication | ≥130/85 mmHg or antihypertensive medication | ≥130/85 mmHg | Systolic BP >130 or Diastolic BP >85 mmHg or hypertension treatment |
| ***Impaired glucose*** | Mandatory | Mandatory | Fasting plasma glucose ≥110 mg/dl | Fasting plasma glucose ≥100 mg/dl | Fasting plasma glucose ≥100 mg/dl or diagnosed diabetes |

Alberti et al. Diabet Med 1998; Balkau et al. Diabet Med 1999; NCEP Circulation 2002; Grundy et al. Circulation 2005; Albert et al. Diabet Med 2006

# 2009: Harmonization of MetS in adults



Harmonizing the Metabolic Syndrome

A Joint Interim Statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity

K.G.M.M. Alberti, FRCP; Robert H. Eckel, MD, FAHA; Scott M. Grundy, MD, PhD, FAHA; Paul Z. Zimmet, MD, PhD, FRACP; James I. Cleeman, MD; Karen A. Donato, SM; Jean-Charles Fruchart, PharmD, PhD; W. Philip T. James, MD; Catherine M. Loria, PhD, MS, MA, FAHA; Sidney C. Smith, Jr, MD, FAHA

| Definition | Harmonized (2009) |
|---|---|
| **Citation** | Alberti et al. Circulation 2009 |
| **Mandatory criteria** | None |
| **Additional criteria** | At least three of the following |
| ***Central obesity*** | Population and country specific definitions |
| ***Raised triglycerides*** | TG ≥ 150 mg/dl or treatment |
| ***Reduced HDL cholesterol*** | HDL-C <40 mg/dl (M), <50 mg/dl (F) or treatment |
| ***Raised blood pressure*** | Systolic BP >130 and/or Diastolic BP >85 mmHg or hypertension treatment |
| ***Impaired glucose*** | Fasting plasma glucose ≥100 mg/dl or diagnosed diabetes |



Alberti et al. Circulation 2009

# What about defining MetS in children?

- Many different definitions
- No clear consensus
- Focus on individual components clustering of risk factors
- **Many use the adult harmonized criteria (3 of 5)**

| Definition | NHANES (2003) | NHANES (2004) | IDF Ages 10-16 (2007) |
|---|---|---|---|
| **Citation** | Cook et al. Arch Ped Adol Med 2003 | de Ferranti et al. Circulation 2004 | Zimmet et al. Pediatr Diabetes 2007 |
| **Mandatory criteria** | None | None | Waist circumference ≥90th percentile or adult cutoff if lower |
| **Additional criteria** | At least three of the following | At least three of the following | At least two of the following |
| ***Central obesity*** | Waist circumference ≥90th percentile | Waist circumference ≥75th percentile | Mandatory |
| ***Raised triglycerides*** | TG ≥ 110 mg/dl | TG ≥ 100 mg/dl | TG ≥ 150 mg/dl |
| ***Reduced HDL cholesterol*** | HDL-C <40 mg/dl | HDL-C <50 mg/dl | HDL-C <40 mg/dl |
| ***Raised blood pressure*** | BP ≥90th percentile | BP ≥90th percentile | Systolic BP >130 or Diastolic BP >85 mmHg or hypertension treatment |
| ***Impaired glucose*** | Fasting plasma glucose ≥110 mg/dl | Fasting plasma glucose ≥110 mg/dl | Fasting plasma glucose ≥100 mg/dl or diagnosed diabetes |

Magge et al. Pediatrics 2017

# MetS in Children

- Systematic review of all pediatric studies on MetS from 2003 - 2013
- Median prevalence
  - 3.3% (range, 0–19.2%) in the general pediatric population
  - 11.9% (range, 2.8–29.3%) in overweight children
  - 29.2% (range, 10–66%) in obese children.
- Not large differences according to the diagnostic criteria applied: 3.1% with IDF and 4.2% with NCEP-ATP III criteria



Friend et al. Metab Syndro Relat Disord 2013

# Is MetS observed in people living with HIV (PLWH)?

Clinical Infectious Diseases

Metabolic Abnormalities and Cardiovascular Disease Risk Factors in Adults with Human Immunodeficiency Virus Infection and Lipodystrophy

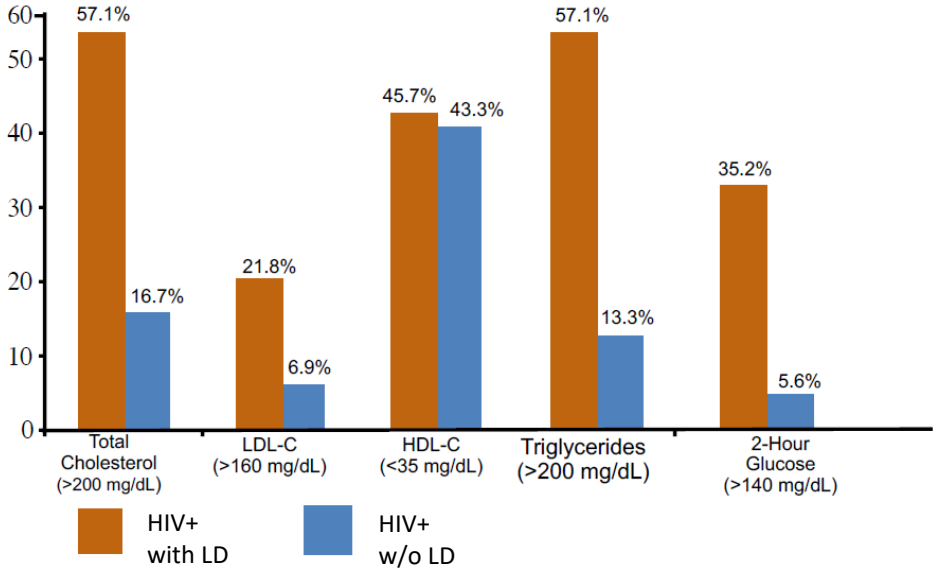
Clinical Infectious Diseases 2001;32:130–9

Colleen Hadigan,[1,4] James B. Meigs,[3] Colleen Corcoran,[1] Petra Rietschel,[1] Sarah Piecuch,[1] Nesli Basgoz,[2] Benjamin Davis,[2] Paul Sax,[5] Takara Stanley,[1] Peter W. F. Wilson,[6] Ralph B. D'Agostino,[6] and Steven Grinspoon[1]

[1]Neuroendocrine Unit, [2]Infectious Disease Unit, [3]General Medicine Division, and [4]Combined Program in Pediatric Gastroenterology and Nutrition, Massachusetts General Hospital, and [5]Infectious Disease Unit, Brigham and Women's Hospital, Harvard Medical School, Cambridge; and [6]The Framingham Heart Study, Framingham, Massachusetts

- N=101 HIV, 303 without HIV
- Framingham Offspring Study

**HIV participants with lipodystrophy have increased prevalence of other components of MetS compared to those without lipodystrophy and to those without HIV**




Hadigan et al. Clin Infect Dis 2001

# Epidemiology of MetS in PLWH

- Prevalence of MetS among PLWH is debatable
- Wide range of estimates from 11% to 45%
- Differences in
  - Study design
  - Small sample sizes
  - Demographic characteristics (age, race/ethnicity, sex)
  - MetS definitions used (NHLBI/AHA vs. IDF vs. NCEP-ATPIII)
  - Antiretroviral therapy



Paula et al. AIDS Res Ther 2013; Jerico et al. Diabetes Care 2005

# MetS in children and young adults with HIV


HIV Reports

Metabolic Syndrome in Children and Adolescents Living with HIV

*María Espiau, MD,* Diego Yeste, MD, PhD,† Antoni Noguera-Julian, MD, PhD,‡ María I. González-Tomé, MD, PhD,§ Lola Falcón-Neyra, MD,¶ César Gavilán, MD,‖ María L. Navarro-Gómez, MD, PhD,** María J. Mellado-Peña, MD, PhD,†† Mercedes Gracia-Casanova, MD, PhD,‡‡ María E. Colino-Gil, MD,§§ Maria Méndez, MD,¶¶ Luis M. Ciria Calavia, MD,‖‖ Clàudia Fortuny, MD, PhD,‡ Antonio Carrascosa, MD, PhD,† and Pere Soler-Palacín, MD, PhD,* on Behalf of the CoRISpe-MetS Working Group*

(*Pediatr Infect Dis J* 2016;35:e171–e176)

- N=152, 2-18 years
- MetS
  - IDF: 2%
  - NCEP-ATP III: 6%


RESEARCH ARTICLE

Metabolic risk factors in young adults infected with HIV since childhood compared with the general population

**Elise Arrive[1,2,3]*, Jean-Paul Viard[4,5], Benoît Salanave[6], Catherine Dollfus[7], Sophie Matheron[8,9], Véronique Reliquet[10], Elisa Arezes[1], Laura Nailler[1], Corinne Vigouroux[11,12]*, Josiane Warszawski[1,13,14], on behalf of the ANRS CO19 COVERTE and ENNS study groups[¶]**

PLoS ONE 13(11): e0206745.

- N=268, 18-30 years
- MetS (Harmonized)
  - Men: 13.2% HIV vs. 10.6% non-HIV
  - Women: 10.4% HIV vs. 1.7% non-HIV

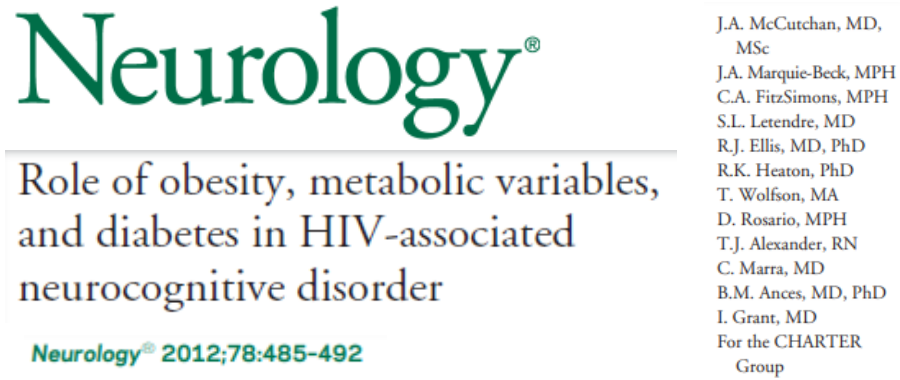
RUTGERS School of Public Health

Espiau et al. Pediatr Infect Dis J 2016; Arrive et al. PLoS ONE 2018

# Consequences of MetS

- Increases risk for:
  - Atherosclerosis leading to myocardial infarctions, stroke, and peripheral vascular disease
  - Fatty liver disease
  - Degenerative joint disease (osteoarthritis)
  - Sleep apnea
  - **Cognitive impairment and depression**
    - Many mechanisms
      - Systemic inflammation and oxidative stress
      - Reduction in regional cerebral glucose metabolism
      - Alterations in transport of insulin; lowering blood brain barrier integrity

# MetS and neurocognition in adults with HIV




- CNS HIV AntiRetroviral Therapy Effects Research (CHARTER)
- N=130, mean age 46 years, 87% male, 57% white
- Central obesity associated with higher prevalence of neurocognitive impairment in PLWH, after accounting for BMI, triglycerides, diabetes, AIDS diagnosis
- Diabetes associated with neurocognitive impairment in older patients.



McCutchan et al. Neurology 2012

# MetS and neurocognition in adults with HIV


(J Acquir Immune Defic Syndr 2019;81:95–101)

Metabolic Syndrome and Neurocognitive Deficits in HIV Infection

*Beverly Yu, BS,[a] Elizabeth Pasipanodya, PhD,[b] Jessica L. Montoya, PhD,[b] Raeanne C. Moore, PhD,[b,c] Sara Gianella, MD,[d,e] Allen McCutchan, MD,[e] Ron Ellis, MD,[b,f] Robert K. Heaton, PhD,[b] Dilip V. Jeste, MD,[b] David J. Moore, PhD,[b] and María J. Marquine, PhD[b]*

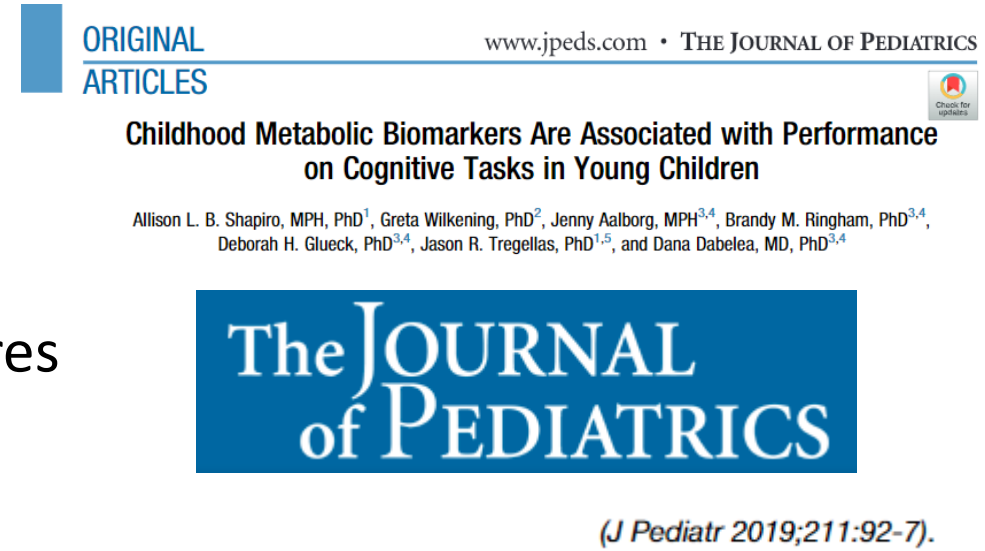
- Multi-dimensional Successful Aging cohort study at UCSD
- 109 PLHIV and 92 controls, mean age 50.8 years, ~70% male, ~60% white
- Analyzed MetS as a cluster
- MetS had an independent effect on global neurocognitive deficits among PLHIV, but not among controls
- Among PLHIV, MetS was most strongly associated with the neurocognitive domains of learning, fine motor skills, and executive function.



Yu et al. J Acquir Immue Def Syndr 2019

# MetS and neurocognition in children

- Healthy Start study
- 4-6 years, 60% NHW, 20% NHB, 18% Hispanic, 2% Other
- Metabolic biomarkers:
  - Glucose, insulin, HOMA-IR, BMI-for-age Z-scores
- Cognitive function by NIH Toolbox
  - Cognitive flexibility (Dimensional Card Sort)
  - Attention/inhibitory control (Flanker)
  - Receptive language (Picture Vocabulary Test)


ORIGINAL ARTICLES

www.jpeds.com • THE JOURNAL OF PEDIATRICS

Childhood Metabolic Biomarkers Are Associated with Performance on Cognitive Tasks in Young Children

Allison L. B. Shapiro, MPH, PhD[1], Greta Wilkening, PhD[2], Jenny Aalborg, MPH[3,4], Brandy M. Ringham, PhD[3,4], Deborah H. Glueck, PhD[3,4], Jason R. Tregellas, PhD[1,5], and Dana Dabelea, MD, PhD[3,4]

The JOURNAL of PEDIATRICS

(J Pediatr 2019;211:92-7).



Shapiro et al. J Pediatr 2019

**A: Glucose and cognitive flexibility**

**B-D: Glucose, insulin, and HOMA-IR and inhibitory control**

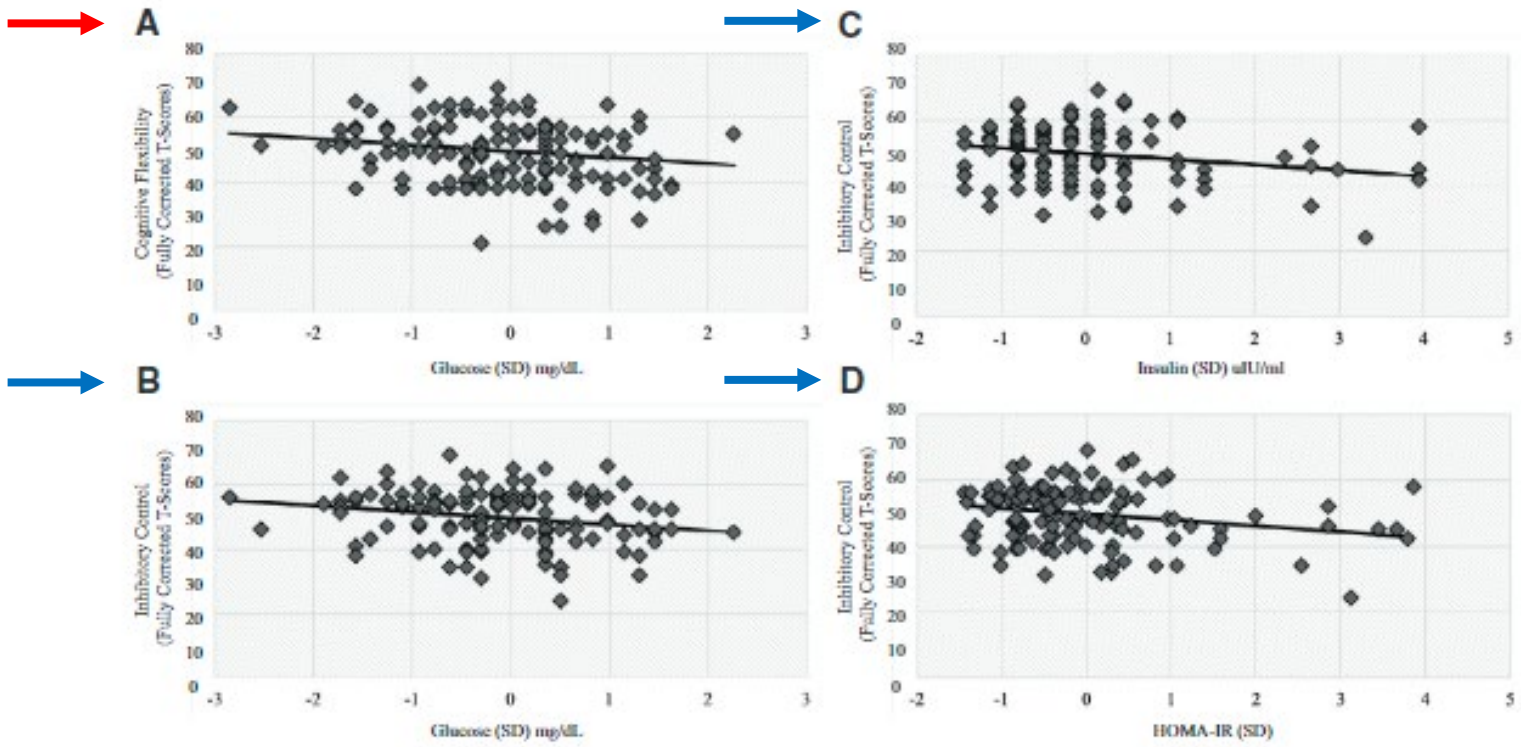



**Figure.** Observed NIH Toolbox scores for cognitive flexibility and inhibitory control by SD of **A** and **B,** fasting blood glucose, **C,** insulin, and **D,** HOMA-IR values overlaid by the fitted regression line.

RUTGERS School of Public Health

Shapiro et al. J Pediatr 2019

# Metabolic syndrome and neurocognitive function in youth with perinatally-acquired HIV and youth who are HIV-exposed uninfected

**Authors: Stephanie Shiau[1], Wendy Yu[2], Denise Jacobson[2], Sharon Nichols[3], Mitchell Geffner[4], Janet Chen[5], Sahera Dirajlal-Fargo[6], Elizabeth J. McFarland[7], Karen Surowiec[8], Jennifer Jao[9], for the Pediatric HIV/AIDS Cohort Study (PHACS)**

[1]Department of Biostatistics and Epidemiology, Rutgers School of Public Health, Piscataway, NJ, USA; [2]Center for Biostatistics in AIDS Research, Harvard T.H. Chan School of Public Health, Boston, MA, USA;
[3]Department of Neurosciences, University of California, San Diego, La Jolla, CA, USA; [4]The Saban Research Institute, Children's Hospital Los Angeles, Los Angeles, CA, USA;
[5]Department of Pediatrics, Drexel University College of Medicine, Philadelphia, PA, USA; [6]University Hospitals Cleveland Medical Center and Rainbow Babies and Children's Hospital, Case Western Reserve University, Cleveland, OH, USA;
[7]Department of Pediatrics, University of Colorado School of Medicine, Aurora, CO, USA; [8]Department of Pediatrics, New Jersey Medical School, Newark, NJ, USA;
[9]Department of Pediatrics, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

pHACS Pediatric HIV/AIDS Cohort Study — A Study of the National Institutes of Health

amp Adolescent Master Protocol

NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development

RUTGERS School of Public Health

# Background (1)

- The increased effectiveness of combination ART has led to declines in morbidity and mortality in adults living with HIV; however, neurocognitive complications of HIV remain prevalent.
- Neurodevelopmental deficits are also reported in youth with HIV, even among those initiating ART early in life.
- In addition, metabolic complications of HIV infection and ART, including dyslipidemia, fat redistribution, and insulin resistance have been documented.

# Background (2)

- The MetS concept was developed to identify individuals at increased risk for diabetes and cardiovascular disease.
  - Components: (1) abdominal obesity, (2) elevated triglycerides, (3) low high-density lipoprotein (HDL) cholesterol, (4) elevated blood pressure, and (5) impaired fasting glucose.
- MetS is commonly present in adults living with HIV.
- In the general adult population, cardiovascular risk factors, including specific components of MetS, have been linked to lower cognitive performance and brain abnormalities.

# Background (3)

- Studies in adults living with HIV on ART have reported associations between cardiovascular risk factors and cognitive impairment.
- **It is unclear whether these observed associations extend to youth living with perinatally-acquired HIV (YPHIV) or who are HIV-exposed uninfected (YPHEU).**
- YPHIV have lifelong exposure to HIV and ART which may drive persistent inflammation and immune activation, and these processes, in turn, may underlie metabolic and cognitive problems.

# Objectives

- To examine the association of individual MetS components with neurocognitive outcomes at baseline in YPHIV and YPHEU.
- To examine the association between individual MetS components at baseline and change in neurocognitive outcomes over time in YPHIV.

# Study Population

- Adolescent Master Protocol (AMP) of the Pediatric HIV/AIDS Cohort Study (PHACS) network
  - 451 YPHIV and 227 YPHEU from 2007-2009
  - 15 clinical sites in the US and PR
- **Included in analysis:** youth with a neurocognitive assessment at age≥10 years ("baseline") and all five MetS components measured between 1 year before and 3 months after that baseline assessment
- Participants with a second neurocognitive examination approximately 3 years after baseline ("year 3") were included in longitudinal analyses.

# Outcomes: Neurocognitive Function

- Neurocognitive function
  - Baseline
  - Change in neurocognitive function between baseline and year 3 exam
  - Measured using Wechsler Intelligence Scale for Children (WISC-IV; 10-16 years) or Wechsler Adult Intelligence Scale (WAIS-IV; ≥16 years).
- Indices
  - Full-scale IQ score
  - Domain scores
    - verbal comprehension
    - perceptual reasoning
    - working memory
    - processing speed

# Exposures: Metabolic Syndrome

- Individual components of MetS (abdominal obesity, elevated triglycerides, low HDL cholesterol, high blood pressure, and impaired fasting glucose) at baseline.
- Based on IDF criteria
- For this analysis, we used two definitions for MetS—the first meeting ≥3 and the second ≥2 of the five individual components

# Covariates

- Information on potential covariates was obtained from clinical charts, questionnaires, or physical examinations (Tanner stage).
- For both YPHIV and YPHEU groups, the following covariates were considered as potential confounders: sex, age, self-reported race/ethnicity, primary language, income, and Tanner stage.
- For YPHIV, we also considered age at ART initiation, nadir CD4, peak HIV RNA level, and antiretroviral (ARV) use.

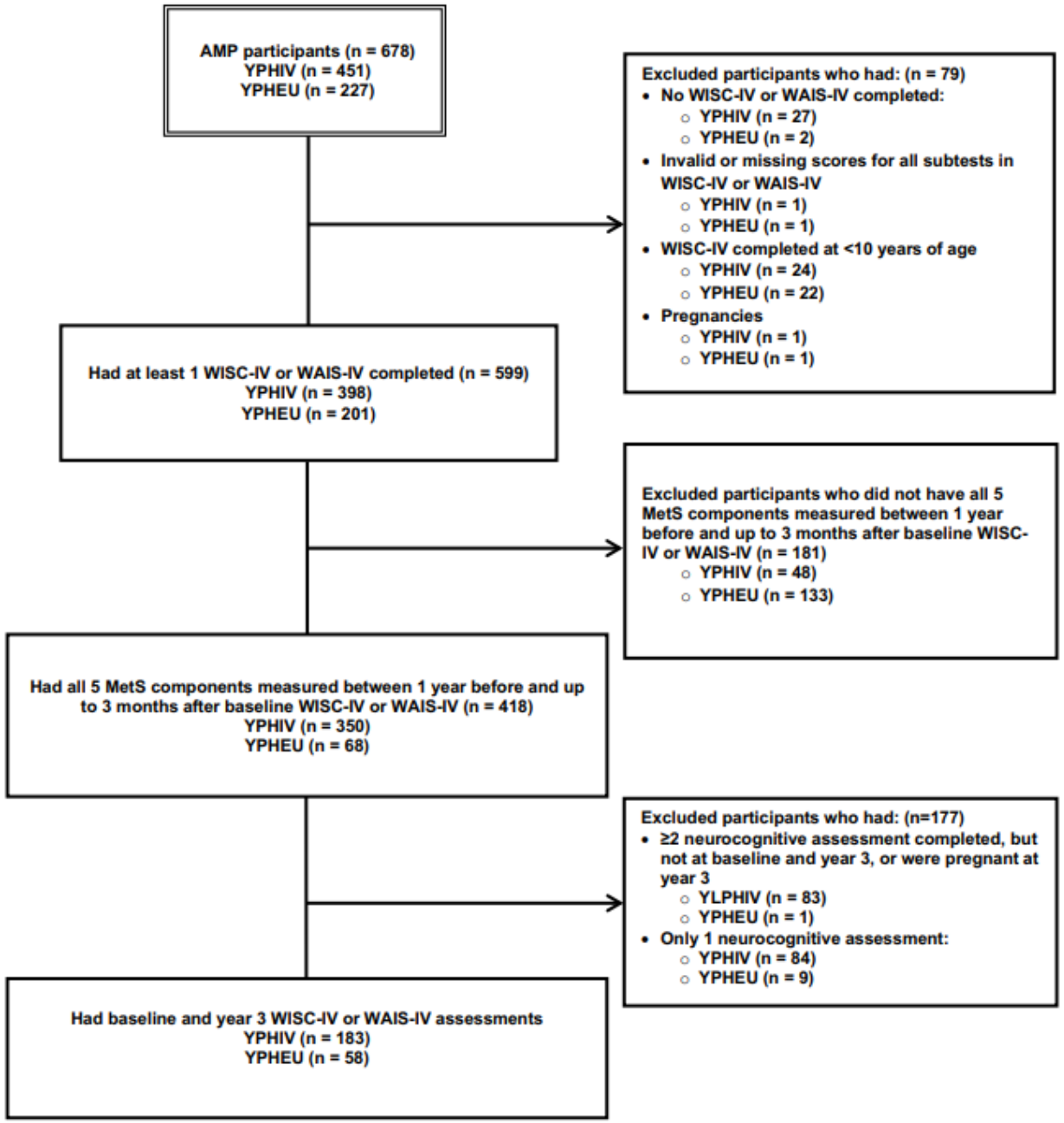
# Statistical Analysis (1)

- Baseline sociodemographic and clinical characteristics, as well as the distribution of exposure and outcome measures, were compared between YPHIV and YPHEU using t-, Wilcoxon, and Chi-square tests as appropriate.
- **Baseline**
  - Within YPHIV and YPHEU separately, we assessed the association between each binary MetS component and each neurocognitive index at baseline by fitting linear regression models using generalized estimating equations with robust variance, unadjusted and adjusted for potential confounders.
  - Given limited power, no formal test for effect modification by HIV status was conducted.

# Statistical Analysis (2)

- **Longitudinal**
  - We assessed the association between each baseline categorical MetS component and the change in each neurocognitive index over time by fitting linear regression models using GEE with robust variance, specifying the distribution as normal and the identity link, unadjusted and adjusted for confounders.
- Statistical analyses were performed using SAS® 9.4 (SAS Institute, Cary, NC).

# Study Population




RUTGERS
School of Public Health

# Participant characteristics

| Characteristic | | YPHIV (N=350) | YPHEU (N=68) | P-value |
|---|---|---|---|---|
| Age years | Median (Q1, Q3) | 12.8 (11.5, 14.5) | 11.6 (10.7, 13.4) | <0.001 |
| Sex | M | 160 (46%) | 32 (47%) | 0.84 |
| | F | 190 (54%) | 36 (53%) | |
| Race/ethnicity | Not non-Hispanic Black | 126 (36%) | 33 (49%) | 0.054 |
| | Non-Hispanic Black | 223 (64%) | 35 (51%) | |
| Annual income | ≤$20,000 | 151 (46%) | 44 (68%) | 0.001 |
| | >$20,000 | 180 (54%) | 21 (32%) | |
| Primary language reported in WISC-IV or WAIS-IV | English | 304 (87%) | 50 (74%) | 0.002 |
| | Spanish | 27 (8%) | 15 (22%) | |
| | Bilingual/Other | 19 (5%) | 3 (4%) | |
| One of primary caregivers is biological mother | Yes | 127 (37%) | 46 (68%) | <0.001 |
| | No | 219 (63%) | 22 (32%) | |



No differences in the distribution of sex, Tanner stage, caregiver education, and physical activity

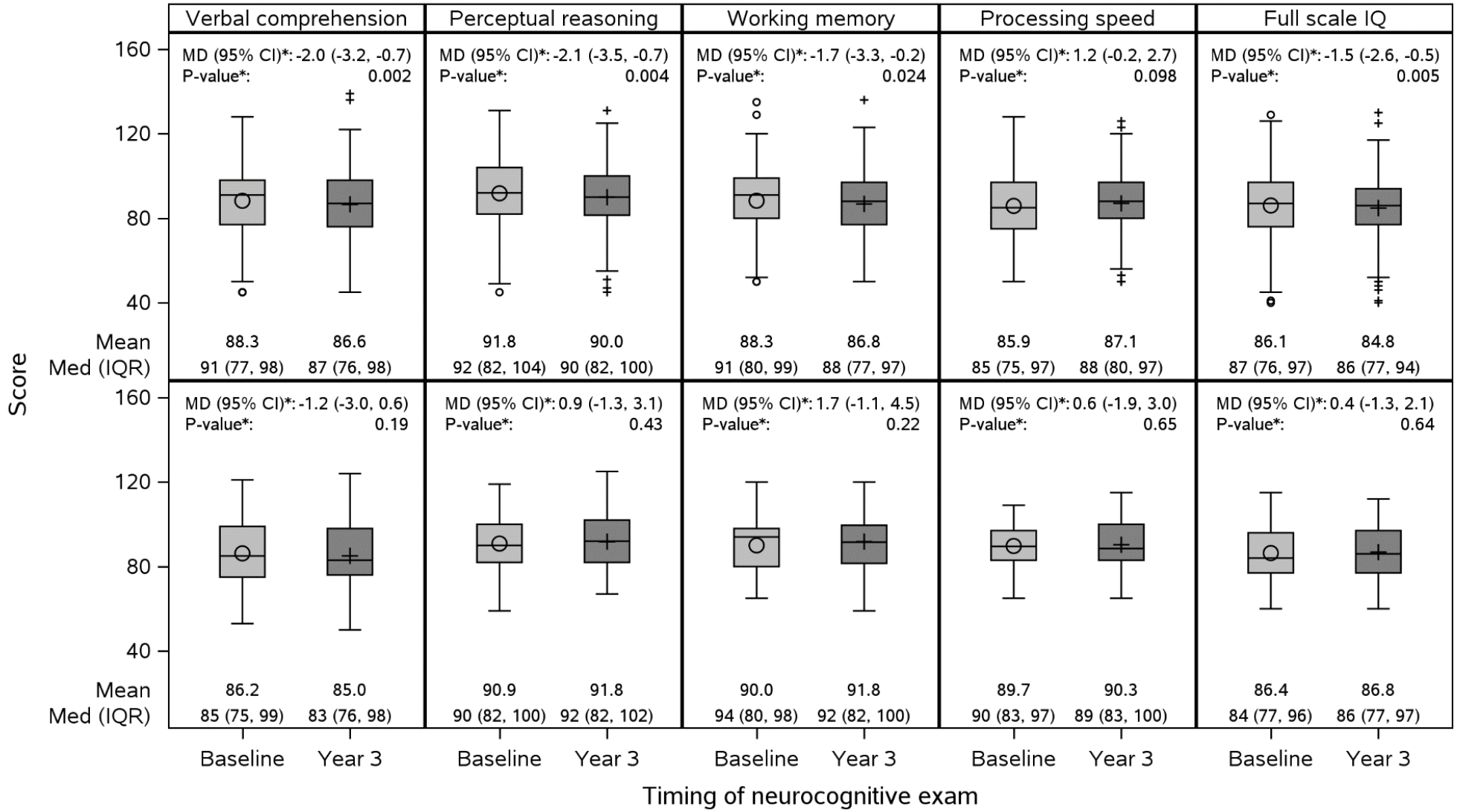
# Prevalence of MetS components

| MetS components, N (%) | YPHIV (N=350) | YPHEU (N=68) | P-value |
|---|---|---|---|
| Abdominal obesity | 60 (17%) | 23 (34%) | 0.002 |
| Elevated triglycerides | 76 (22%) | 5 (7%) | 0.006 |
| Low HDL cholesterol | 74 (21%) | 9 (13%) | 0.13 |
| Elevated blood pressure | 21 (6%) | 2 (3%) | 0.31 |
| Impaired fasting glucose | 9 (3%) | 5 (7%) | 0.045 |
| Fulfilled criteria for ≥2 MetS components | 52 (15%) | 12 (18%) | 0.56 |
| Fulfilled criteria for≥3 MetS components | 12 (3%) | 5 (7%) | 0.13 |

# Baseline analysis of neurocognitive indices

- YPHIV:
  - No associations between baseline MetS components and baseline neurocognitive indices were observed in unadjusted or adjusted models
- YPHEU:
  - Elevated TG was associated with lower mean Verbal Comprehension (−10.0; 95% CI:−17.7,−2.2), Perceptual Reasoning (−7.9; 95%CI:−13.2,−2.5), and FSIQ (−7.5; 95%CI:−14.6,−0.5) scores.
  - IFG was associated with a lower mean Verbal Comprehension score (−12.7; 95%CI:−24.7,−0.7) in models adjusted for age, sex, race/ethnicity, primary language, household income, and Tanner stage.

# Longitudinal analysis of neurocognitive indices




RUTGERS
School of Public Health

# Longitudinal analysis of neurocognitive indices

- Elevated BP at baseline was associated with a greater decrease in mean Perceptual Reasoning scores over time (−4.3; 95%CI:−8.8, 0.3) in adjusted analyses
- Meeting criteria for ≥2 MetS components was associated with a greater decrease in mean Processing Speed scores over time (−5.1; 95%CI:−9.4,−0.8) in adjusted analyses.

# Discussion (1)

- First study to examine the association between components of MetS and neurocognitive outcomes in YPHIV and YPHEU
- 3% of YPHIV and 7% of YPHEU met criteria for ≥3 MetS components and 15% of YPHIV and 18% of YPHEU met criteria for ≥2 MetS components
  - A systematic review of 85 studies found a median MetS prevalence (≥3 MetS components) of 3.3% (range 0–19.2%) in the general pediatric population
  - No consensus definition for pediatric MetS

# Discussion (2)

- Among YPHIV who met criteria for ≥2 MetS components, the most common components were reduced HDL (65%) and elevated TG (63%).
- The profile of abnormal lipids without abdominal obesity observed among the YPHIV in our study falls in line with reports of a “thin and hypercholesterolemic” pattern in other studies of YPHIV.

# Discussion (3)

- Among YPHIV, we found that elevated BP was associated with a decrease in Perceptual Reasoning scores over time.
  - Hypertension could mediate the effects of HIV and ART on cognition and has been linked to cognitive function in the general population.
- Among YPHIV, we also found that meeting criteria for≥2 MetS components was associated with lower Processing Speed scores over time.

# Discussion (4)

- In cross-sectional analyses, YPHEU with elevated TG had lower Verbal Comprehension, Perceptual Reasoning, and FSIQ scores, and those with IFG had a lower mean Verbal Comprehension score.
- These associations have been reported in HIV-unexposed and uninfected adults.

# Limitations

- Our study was limited by the lack of a comparison group of HIV-unexposed and uninfected youth.
- Eligible YPHEU for this analysis was also a small group (n=68) and may be subject to selection bias
- No consensus guidelines or validated diagnostic criteria for MetS in youth.

# Conclusions

- In conclusion, in our study, 15% of YPHIV and 18% of YPHEU met criteria for≥2 of the individual MetS components.
- Components of MetS in YPHIV (elevated BP) and YPHEU (elevated TG and IFG) were associated with lower neurocognitive performance index scores in childhood and adolescence.
- Future studies to elucidate how modifying metabolic risk factors early in life may improve short- and long-term neurocognitive outcomes in this population are warranted.

# Acknowledgements

**Co-Authors:** Wendy Yu, Denise Jacobson, Sharon Nichols, Mitchell Geffner, Janet Chen, Sahera Dirajlal-Fargo, Elizabeth J. McFarland, Karen Surowiec, Jennifer Jao

**PHACS George R. Seage III Early Career Investigator Award**

**PHACS is funded by:**

NIH National Institutes of Health

Under cooperative agreements HD052102 (Harvard T.H. Chan School of Public Health), HD052104 (Tulane University School of Medicine), and P01HD103133 (Harvard T.H. Chan School of Public Health for the Pediatric HIV/AIDS Cohort Study (PHACS) 2020).

pHACS A Study of the National Institutes of Health

**We thank the study participants, clinical sites, PHACS Community Advisory Boards, Frontier Science, and Westat.**

R21HD104558, K01DA053157

R25MH108389 - Sustained Training in Aging and HIV Research (STAHR)