Associations between newborn telomere length and adiposity in the first decades of life

Farah Qureshi, ScD
Postdoctoral Research Fellow
Harvard T.H. Chan School of Public Health

Contact: fqureshi@mail.harvard.edu | @fqureshi_epi

Early Programming of Health and Disease

- Cardiometabolic conditions have origins that trace back to the prenatal period (Barker 2004)
- Telomere biology is a potential mechanism by which fetal programming of adult disease occurs (Entringer, et al., 2018)
- Newborn telomeres serve as an “initial setting” that influences telomere biology across the lifespan
- They are also believed to be important sentinels for disease, but evidence from prospective studies is lacking

Study Aim

- To examine associations between newborn TL and trajectories in adiposity from birth to adolescence

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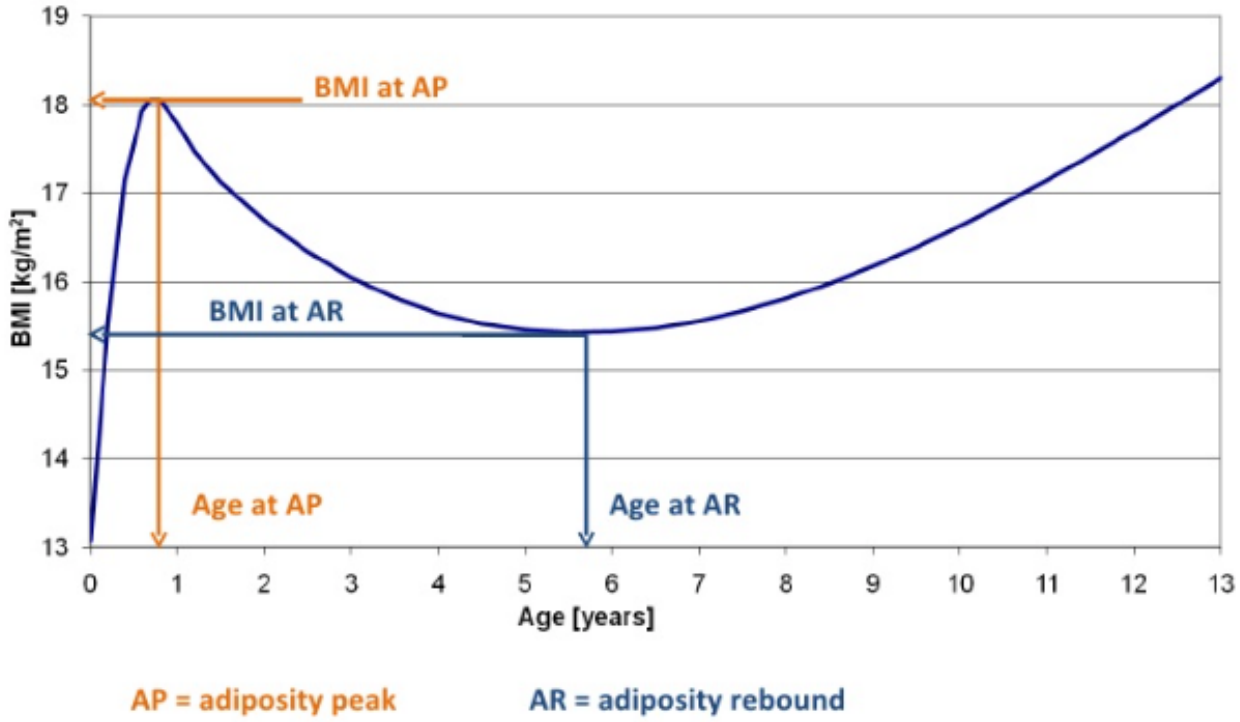
Clinically relevant markers of later life risk

Adiposity Trends in the First Decade of Life



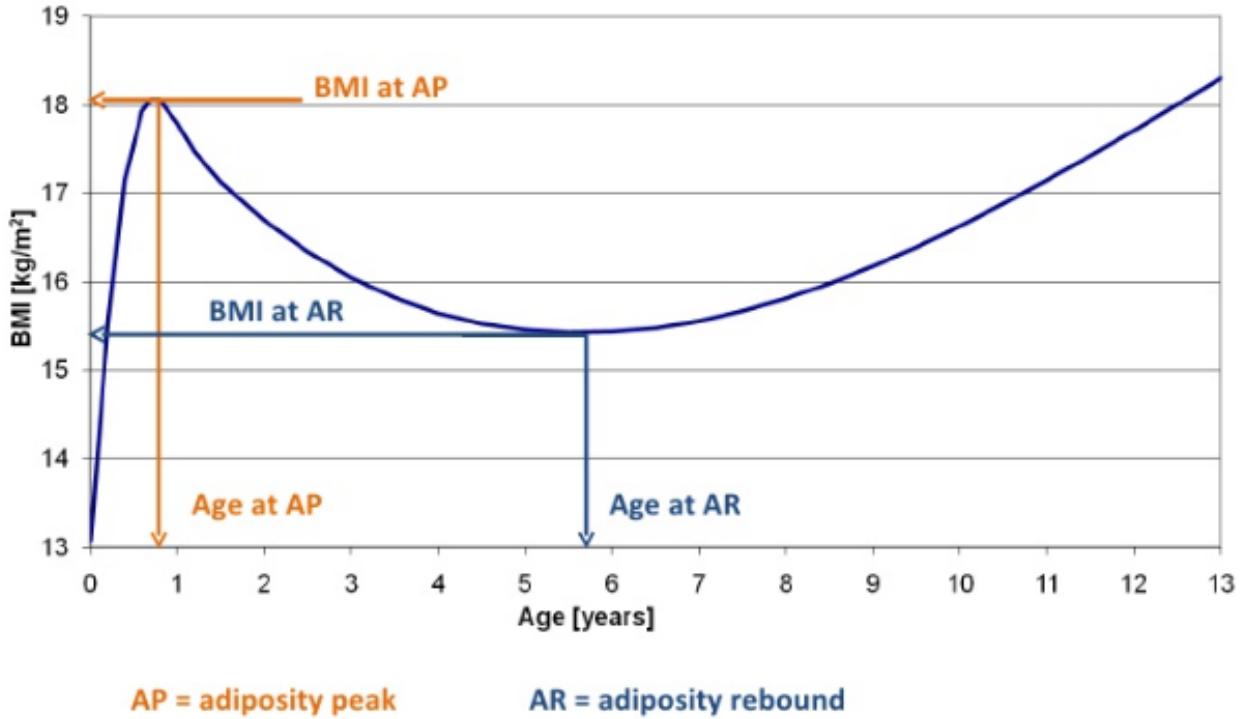
Source: Sovio, et al., 2010

BMI Growth Patterns

Peak and Rebound

Later peak
Larger peak magnitude

Poorer health



Earlier rebound
Larger rebound magnitude

Poorer health

Source: Sovio, et al., 2010

Hypotheses

- To examine associations between newborn TL and trajectories in adiposity from birth to adolescence
- Shorter telomeres will be associated with:
  1. Higher levels of adiposity over time
  2. A later age of BMI peak
  3. An earlier age of BMI rebound

Project Viva

PROJECT Viva
A Study of Health for the Next Generation

- On-going birth cohort based in eastern Massachusetts
- N=2,128 singleton liveborn children recruited prenatally in 1999-2002
- Followed from fetal life to late adolescence
- Predominantly white, socioeconomically advantaged
- Telomere length obtained from cord blood of 444 children at birth
- **Analytic sample:** N=375 children with valid telomere length data and available BMI growth data

Relative Telomere Length (RTL)

- Telomere/single copy gene (albumin) ratio
- Measures obtained in triplicate via qPCR
- Analyses accounted for correlations between measurements obtained from the same sample plate
- T/S ratio analyzed two ways:
  - Continuous standardized measure (per 1-SD shorter)
  - Binary measure of “shorter TL” defined as T/S ratio ≤1.0

Adiposity

- BMI measurements collected in Viva exams at 6 mo, 3y, 7y, 13y, and from medical records from well-child visits from birth to age 18
- Repeated assessments were used to quantify the **age and magnitude of BMI peak and BMI rebound** (Aris, et al., 2018; Aris, et al., 2019)
- Subsample of 199 children had direct measures of **total and abdominal fat mass** obtained at 7y and 13y via whole-body DXA scan
  - Considered individually and as a change score (standardized)

Source: Sovio, et al., 2010

Covariates Considered for Inclusion

- Race/ethnicity
- Parental education (college or higher)
- Yearly household income (≥$70,000)
- Gestational age at birth
- Birthweight for sex and gestational age z-scores
- Mother's age
- Father's age
- Mother's BMI
- Father's BMI
- Pregnancy characteristics
  - Parity
  - Smoking status
  - Diabetes-related condition
  - Hypertension –related condition

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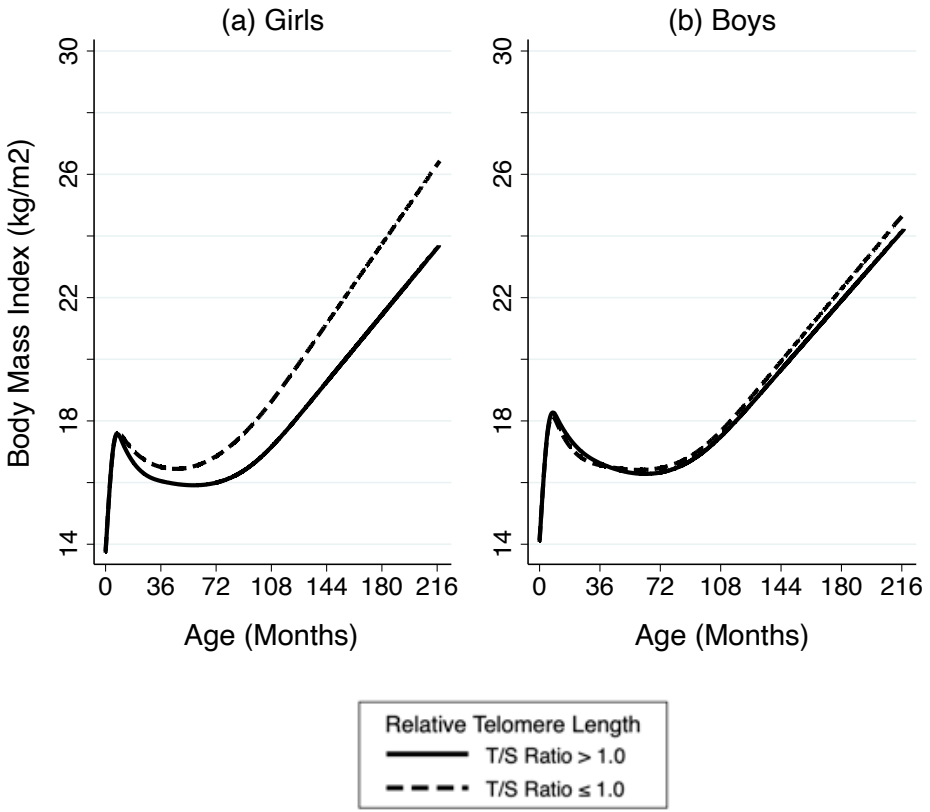
No substantive associations observed with RTL so all analyses were unadjusted

Statistical Analyses

- Plotted BMI growth patterns by RTL using mixed effects models with natural cubic spline functions
- Generalized estimating equations (GEE) with a gaussian distribution evaluated links between RTL and BMI growth
- Sensitivity analyses also used GEE to examine directly assessed adiposity measures
- All analyses were stratified by sex and interactions were tested

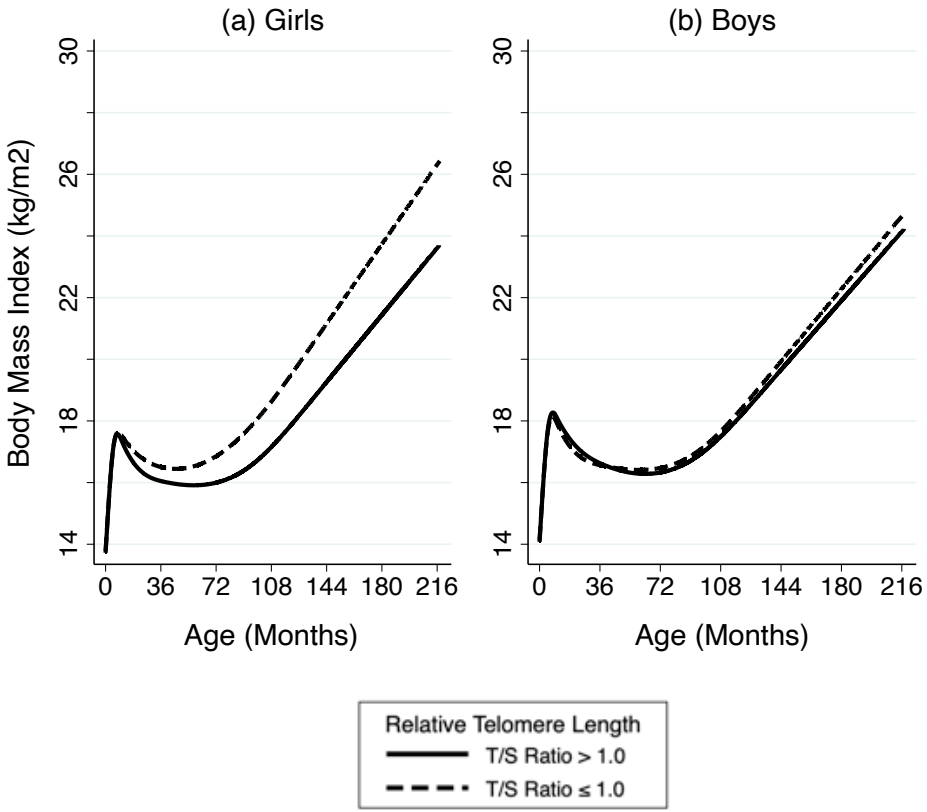
BMI Peak (BMIP)

- Continuous RTL not related to any BMIP measure for boys or girls
- No associations between shorter RTL and magnitude of BMIP
- Shorter RTL associated with **later age of BMIP for girls only** ($p<0.05$)
  - **β_{girls}=0.99 (0.16, 1.82)**
  - β_{boys}=0.04 (-0.36, 0.44)



BMI Rebound (BMIR)

- Continuous RTL not related to any BMIR measure for boys or girls
- No associations between shorter RTL and magnitude of BMIR
- Shorter RTL associated with **earlier of BMIR for both boys and girls:**
  - 4.2 months for girls
  - 7.3 months for boys
- No evidence of sex interaction



Shorter RTL Related to More Fat Mass in Girls

Table: Unadjusted associations between RTL ≤ 1.0 and directly assessed fat mass measurements, stratified by sex (N=199).*

	Age 7		Age 13	
	β (95% CI)	*p*	β (95% CI)	*p*
Total Fat Mass, kg/m^2				
Boys	0.08 (-0.41, 0.58)	0.74	0.05 (-0.95, 1.04)	0.93
Girls	0.83 (0.09, 1.56)	0.027	**1.90 (0.59, 3.20)**	**0.004**
Abdominal Fat Mass, kg/m^2				
Boys	0.06 (-0.16, 0.29)	0.59	-0.05 (-0.51, 0.41)	0.82
Girls	0.38 (0.04, 0.73)	0.029	**0.92 (0.24, 1.60)**	**0.008**

* Red indicates gender interaction $p<0.05$

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No substantial associations with changes in fat mass

Summary of Key Findings

- No associations between continuous RTL and BMI growth milestones
- Shorter RTL (T/S ratio ≤1.0) were associated with later BMI peak and earlier rebound
- Associations generally stronger for girls (BMI peak)
- Shorter RTL also associated with greater fat mass for girls only
- Shorter RTL not related to change in fat mass, but a small association between continuous RTL and increases in fat mass was noted in girls

Thank You!

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- Research staff

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