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Race disparities in pubertal timing: Implications for cardiovascular disease risk among African American women

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Abstract

Compared to white girls, sexual maturation is accelerated in African American girls as measured by indicators of pubertal development, including age at first menses. Increasing epidemiological evidence suggests that the timing of pubertal development may have strong implications for cardio-metabolic health in adolescence and adulthood. In fact, younger menarcheal age has been related prospectively to poorer cardiovascular risk factor profiles, a worsening of these profiles over time, and an increase in risk for cardiovascular events, including non-fatal incident cardiovascular disease and cardiovascular-specific and all-cause mortality. Yet, because this literature has been limited almost exclusively to white girls/women, whether this same association is present among African American girls/women has not been clarified. In the current narrative review, the well-established vulnerability of African American girls to experience earlier pubertal onset is discussed as are findings from literatures examining the health outcomes of earlier pubertal timing and its antecedents, including early life adversity exposures often experienced disproportionately in African American girls. Gaps in these literatures are highlighted especially with respect to the paucity of research among minority girls/women, and a conceptual framework is posited suggesting disparities in pubertal timing between African American and white girls may partially contribute to well-established disparities in adulthood risk for cardio-metabolic disease between African American and white women. Future research in these areas may point to novel areas for intervention in preventing or lessening the heightened cardio-metabolic risk among African American women, an important public health objective.

Keywords

menarche; puberty; pubertal timing; race; race disparities; cardiovascular disease

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Overview

Compared to white girls, African American girls experience more accelerated sexual maturation as assessed by several indicators of pubertal development, including age at first menses (Chumlea et al., 2003; Freedman et al., 2002; Herman Giddens et al., 1997; Wu, Mendola, & Buck, 2002). A growing epidemiological literature suggests that the timing of pubertal onset may be a key determinant of cardio-metabolic health in adolescence and adulthood. Younger menarcheal age has been related prospectively to poorer cardiovascular risk factor profiles, a worsening of these profiles over time, and an increased risk for cardiovascular events, including non-fatal incident cardiovascular disease and cardiovascular-specific and all-cause mortality (G. Cooper et al., 1999; Frontini, Srinivasan, & Berenson, 2003; Jacobsen, Heuch, & Kvale, 2007; Jacobsen, Oda, Knutsen, & Fraser, 2009; Lakshman et al., 2009; Remsberg et al., 2005). To date, however, this literature has focused almost exclusively on white girls/women, limiting our knowledge of whether links between pubertal timing and cardio-metabolic health are also present among African American girls/women.

Understanding such links among African American girls/women is especially important in addressing a timely research question: Does the tendency to experience earlier pubertal onset put African American girls at disproportionate risk for poorer cardio-metabolic health later in life, potentially explaining (at least in part) well-established disparities in adulthood risk for cardio-metabolic disease between African American and white women? Moreover, evidence suggests that some of the risk factors for earlier pubertal onset, including early life adversity exposures, are experienced disproportionately among African American girls. In this context, better understanding race disparities in pubertal timing, their antecedents (e.g., early life adversity), and their potential differential impacts on health is a critical area for future investigation with important public health and health-equity implications for African American women.

The primary goal of the current review is to provide a narrative examination of the pubertal timing literatures with a specific focus on findings relevant to African American girls/women. The well-established vulnerability of African American girls to experience earlier pubertal onset is discussed as well as findings from literatures examining the antecedents, including early life adversity exposures, and health consequences of earlier pubertal timing. The current review highlights gaps in these literatures especially in relation to the paucity of research among minority girls/women. We posit a conceptual framework that suggests disparities in pubertal timing between African American and white girls may partially contribute to well-established disparities in adulthood risk for cardio-metabolic disease between African American and white women (Figure 1). More specifically, Figure 1 reflects a preliminary model representing one mechanistic pathway (i.e., race [African American vs. white] → early life adversity → pubertal timing → differential cardio-metabolic disease risk) through which race may contribute to differential risk for cardio-metabolic disease between African American and white women.

The secondary goal of the current review is to generate hypotheses for future research studies targeting minority (and especially African-American) girls/women in order to test

and further elaborate on the preliminary model proposed here (Figure 1). This review highlights the importance of drawing on life course models, which specifically consider the timing and time course of relevant risk exposures over the life course (Ben-Shlomo & Kuh, 2002; Lynch & Smith, 2005) as well as the potential social patterning of these risk exposures (Smith, Gunnell, & Ben Shlomo, 2001). Building on these literatures, novel hypotheses may be generated that address, for example, whether risk exposures experienced more commonly among African American vs. white girls may account for earlier pubertal onset (cumulative risk model) and/or whether the risk associated with earlier pubertal onset is exacerbated in certain contexts more common among African American vs. white girls (interactional model). In sum, the current review offers a preliminary conceptual framework for considering these and related research questions to begin to better characterize the role pubertal timing may play in explaining observed increases in cardio-metabolic disease risk among African American girls/women.

To aid the reader, here, we describe the organization of the current review: First, we define puberty and the terminology used in the literature to describe aspects of pubertal development, including pubertal timing and tempo. Next, we review parallel findings in two well-established literatures showing race disparities in pubertal timing and cardio-metabolic health. We then review findings in two relevant but incomplete literatures showing earlier pubertal timing may confer risk for poorer cardio-metabolic health and early life adversity may confer risk for earlier pubertal timing. Finally, although speculative, we describe common biological processes that may underlie links between childhood adversity, pubertal timing, and cardio-metabolic health. The organization and review of these literatures, reflecting varying degrees of strength and quality, provide support for the model presented in Figure 1. However, as described above, the relations represented in this model are meant to be hypothesis-generating, requiring future research to clarify the nature of these relations, including whether they are correlational only, possibly causal, or even potentially spurious.

It is also noteworthy that this review considers findings related to girls/women only. To date, studies of pubertal timing in boys are scarce. This is true, in part, because there is no obvious marker of pubertal timing in boys as there is in girls (e.g., menarcheal age), making research in this area more challenging methodologically. Among the limited studies of boys, some findings suggest there may be a relation between earlier pubertal timing and increased cardio-metabolic risk (Hardy, Kuh, Whincup, & Wadsworth, 2006; Hulanicka, Lipowicz, Koziel, & Kowalisko, 2007; Kindblom et al., 2006; Widen et al., 2012) with preliminary data also indicating a potential relation between early life adversity and pubertal timing/tempo (Brown, Cohen, Chen, Smailes, & Johnson, 2004; Negri, Blankson, & Trickett, 2015). However, findings are mixed with respect to the association between obesity and pubertal timing as well as secular trends in the timing of puberty in boys (Tinggaard et al., 2012). This limited and mixed literature precludes consideration of the proposed model (Figure 1) among boys/men at this time.

Pubertal Timing

Puberty reflects a set of biological processes through which sexual maturation and the potential for human reproduction are achieved. In particular, gonadarche describes the

activation of the hypothalamic-pituitary-gonadal axis; an increase in the pulsatile release of gonadotropin-releasing hormone (GnRH) from the hypothalamus signals the release of gonadotropins from the pituitary which, in turn, promotes ovarian follicle maturation and the synthesis of sex steroids that cause the primary physical changes in female puberty, including menarche and ovulation (Ebling, 2005; Plant & Barker-Gibb, 2004). Adrenarche, an independent process typically preceding gonadarche, describes the maturation of the adrenal glands; an increase in androgen production from the adrenal cortex causes pubic hair growth, body odor, and acne (Plant & Barker-Gibb, 2004). In the pubertal timing literature, markers of gonadarche and adrenarche are used to index the timing and the rate of progression (or tempo) through these events, commonly including (but not limited to) age at the onset of breast development (termed “thelarche”), age at the onset of pubic hair growth (termed “pubarche”), and age at the onset of menses (terms “menarche”), with tempo defined as the interval of time in-between these milestones (e.g., in-between pubertal onset and menarche) (Llop-Vinolas et al., 2004; Pantisiotou et al., 2008).

By and large, the majority of studies to date have utilized age at the onset of menses as a marker of female pubertal timing. These studies typically ask adult women to report the age of their first menstrual period retrospectively. Although retrospective, such reports of menarcheal age have been shown to be highly reliable (Bergsten-Brucefors, 1976; Koprowski, Coates, & Bernstein, 2001), with one study showing real-time adolescent reports to correlate .79 with retrospective adulthood reports 33 years later (Must et al., 2002). Fewer studies have included medical provider assessments of Tanner stages (I-V), a well-established system for identifying stages of sexual maturation. In this system, the stages of sexual maturity for breast and pubic hair development are rated separately between stage I (pre-puberty) and stage V (full sexual maturity) based on specified physical characteristics (Marshall & Tanner, 1969). Menarche typically occurs in Tanner stage IV breast development, approximately two to three years after the initiation of breast development (breast budding) (Biro et al., 2006). Notably, support for the use of menarcheal age as a marker of pubertal timing is evidenced by its correlation ($r = .53$) with pubertal onset (defined as the age at which any evidence of breast *or* pubic hair development was observed on a physical exam) (Belsky 2007). Throughout the current review, the terms “age at menarche” or “menarcheal age” are used interchangeably. When another indicator of pubertal timing or tempo is available, this indicator is defined accordingly.

Race Differences in Pubertal Timing

Compared to white girls, African American girls experience more accelerated sexual maturation as indicated by observed race differences on several markers of pubertal development, including the initiation of pubic hair and breast development, as well as menarche (Chumlea et al., 2003; Freedman et al., 2002; Herman Giddens et al., 1997; Wu et al., 2002). For example, findings from three large studies, the Bogalusa Heart Study ($n = 2,058$), the Pediatric Research in Office Settings (PROS) Study ($n = 17,066$), and the Third National Health and Nutrition Examination Survey (NHANES III) ($n = 1,623$), show the mean age at menarche was 12.3, 12.2, and 12.1 years for African American girls, respectively, whereas the mean age at menarche for white girls was 12.6, 12.9, and 12.7 years, respectively. In these studies, the significant observed race differences in pubertal

development were largely independent of body size. That is, in the Bogalusa Heart Study and the PROS Study (Freedman et al., 2002; Herman Giddens et al., 1997), race differences in pubertal development persisted after adjustment for height and weight; and, in the NHANES III (Wu et al., 2002), race differences in pubic hair and breast development (but not menarcheal age) persisted after adjustment for both socioeconomic status and body mass index (BMI). In a more recent analysis, models examining race effects on menarcheal age showed that the inclusion of SES indicators reduced the effect estimates of being African American and Hispanic (versus white) by 40% and 50%, respectively, highlighting the importance of SES-related exposures (Deardorff, Abrams, Ekwuru, & Rehkopf, 2014). Notably, race effects of being African American or being Hispanic (versus white) remained significant, however, though limited statistical power in this study precluded formal testing of differences between these race/ethnic groups (Deardorff et al., 2014).

In a recent review, Ramnitz & Lodish (2013) summarized available data from several landmark epidemiological studies (including those referenced above: Bogalusa Heart Study, the PROS Study, and the NHANES III) to examine race differences in pubertal development as well as how these differences have changed over time. A consensus panel examining data between years 1940 to 1994 confirmed a secular trend in the US in which the ages at breast development and menarche declined over time (Euling et al., 2008); due to the underrepresentation of minority girls in older studies, however, fewer data were available to definitively address how this secular trend may differ across race/ethnic groups. Nonetheless, the data available to date are intriguing. For example, in the Bogalusa Heart Study, the median menarcheal age of white girls decreased by 2.0 months over a 20-year study period compared to a 9.5-month decrease for African American girls (Freedman et al., 2002). Similarly, another study documented a smaller decline in median menarcheal age over time for white girls (3.24-month decline) compared to African American girls (5.84-month decline) (Ramnitz & Lodish, 2013). In contrast, with respect to thelarche, age at the onset of breast development was significantly earlier (9.62 versus 9.96 years) for white girls in the more recent Breast Cancer and the Environment Research Program (BCERP, 2004-2008) compared to the older PROS Study (1992-1993), but no historical differences in thelarche were observed for African American girls (Biro et al., 2013). In summary, these findings, at least with respect to menarche, frame the possibility that African American girls, compared to white girls, not only experience pubertal onset at younger ages but may also show sharper decreases in the age of pubertal onset over time.

Race Differences in Cardio-Metabolic Disease Risk

The proposed conceptual model (Figure 1) aims to explain (in part) the well-established race disparities in adulthood risk for cardio-metabolic disease between African American and white women. In this context, we describe the current literature pertaining to these disparities. Specifically, we briefly summarize the literature regarding race differences in cardiovascular risk factors, preclinical atherosclerotic disease, and incident cardiovascular events.

Cardiovascular disease is the leading cause of death in all women as well as in all major race/ethnic subgroups of women in the US (Day, 1996; Rosamond et al., 2007; Y. Zhang,

2010). An abundant literature suggests there are race/ethnic differences in cardiovascular risk factors, markers of preclinical atherosclerotic disease, and incident cardiovascular events, with a general pattern showing increased risk among African American women compared to white women. With respect to cardiovascular risk factors, this pattern has been observed for anthropometric indicators (Matthews et al., 2005; Mensah, Mokdad, Ford, Greenlund, & Croft, 2005; Winkleby, Kraemer, Ahn, & Varady, 1998), lipid profiles (Jha et al., 2003; Matthews et al., 2005), insulin resistance (Giles, Kittner, Hebel, Losonczy, & Sherwin, 1995; Jha et al., 2003; Matthews et al., 2005; Winkleby et al., 1998), blood pressure (Burt et al., 1995; R. S. Cooper, Liao, & Rotimi, 1996; Cornoni-Huntley, Lacroix, & Havlik, 1989; Giles et al., 1995; Jha et al., 2003; Johnson, Heineman, Heiss, Hames, & Tyroler, 1986; Lloyd-Jones et al., 2005; Matthews et al., 2005; Mensah et al., 2005; Nesbitt, 2004; Winkleby et al., 1998), and systemic inflammation (Albert, Glynn, Buring, & Ridker, 2004; Kelley-Hedgpeeth et al., 2008; Khera et al., 2005; Matthews et al., 2005; Nazmi & Victora, 2007). Increased risk among African American women has also been observed for preclinical atherosclerotic disease (Janssen et al., 2012; Lewis et al., 2009; Ohira et al., 2012; Ranjit et al., 2006), including carotid artery IMT and aortic/coronary calcification as well as incident disease (Giles et al., 1995; Gillum, Mussolino, & Madans, 1997; Johnson et al., 1986; Mensah et al., 2005; Roger et al., 2011; Rosamond et al., 2007), including cardiac-related hospitalizations, myocardial infarction, stroke, and cardiac-specific death. With a few exceptions (Karamangla, Merkin, Crimmins, & Seeman, 2010; Scuteri et al., 2008), the vast majority of studies show the effects of race/ethnicity on cardiovascular risk persist independently of statistical control for covariates including SES, although it is widely accepted that variability in SES across race/ethnic groups explains a significant proportion of these effects (e.g. (Matthews et al., 2005)).

Pubertal Timing and Health

The proposed conceptual model (Figure 1) depicts a potential pathway between pubertal timing and differential risk for cardio-metabolic health between African American and white women. In this context, we describe the current literature relating pubertal timing to both cardio-metabolic risk factors and cardiovascular-related incident events. Thereafter, we highlight that this literature is primarily limited to white girls/women with two notable exceptions (Feng et al., 2008; Frontini et al., 2003).

Pubertal timing and cardio-metabolic risk factors

Longitudinal investigations have shown that earlier pubertal timing, typically indexed by self-reports of menarcheal age, predicts adulthood obesity and type 2 diabetes (Hardy et al., 2006; He et al., 2010; Laitinen, Power, & Jarvelin, 2001; Lakshman et al., 2008). Younger menarcheal age has also been related prospectively to a host of cardiovascular risk factors in adolescence and adulthood as well as to a worsening of these risk factors over time (Feng et al., 2008; Frontini et al., 2003; Hoyt & Falconi, 2015; Hulanicka et al., 2007; Kivimaki et al., 2008; Lakshman et al., 2009; Pierce, Kuh, & Hardy, 2010; Remsberg et al., 2005; Widén et al., 2012). For example, girls with earlier menarche, defined at the 25th percentile or less (11.9 years), experienced greater increases in insulin, glucose, systolic blood pressure (SBP), and diastolic blood pressure (DBP) over the 13-year study period (ages 8 to 21); these

changes were observed independently of correlated changes in body composition (marked by indicators: fat-free mass and percent body fat) (Remsberg et al., 2005). Similarly, girls with an earlier menarche (<12 years) experienced greater fasting insulin levels in periods of childhood (5-11), adolescence (12-18 years), and adulthood (19-37 years), greater homeostatic model assessment of insulin resistance (HOMA-IR) levels in periods of childhood and adolescence, and greater increases in insulin and HOMA-IR over time; in analyses also including indicators of body composition, earlier menarche was related independently to body fatness and insulin (Frontini et al., 2003). Finally, girls with earlier menarche were at increased odds of experiencing a clustering of cardio-metabolic risk factors in adulthood defined as having 3 or 4 metabolic syndrome components (across components: BMI, fasting insulin, SBP, total cholesterol to HDL ratio) (Frontini et al., 2003).

Pubertal timing and cardiovascular-related incident events

Younger menarcheal age has similarly been related prospectively to cardiovascular-related incident events, including incident cardiovascular disease, incident coronary heart disease, cardiovascular-specific mortality, and all-cause mortality (G. Cooper et al., 1999; Hoyt & Falconi, 2015; Jacobsen et al., 2007; Jacobsen et al., 2009; Lakshman et al., 2009). Associations have been observed in large samples (e.g., 61,319 women) and over long periods of follow-up (e.g., up to 37 years) (Jacobsen et al., 2007). Moreover, associations between younger menarcheal age and cardiovascular-related incident events have been observed even after adjusting for a myriad of covariates, including SES, health behaviors, reproductive factors, and markers of body composition (e.g. BMI, waist circumference) (Lakshman et al., 2009). By and large, findings relating pubertal timing both to cardiovascular risk factors and to cardiovascular events, do not appear to be attributable to variability in body composition (G. Cooper et al., 1999; Feng et al., 2008; Frontini et al., 2003; Hulanicka et al., 2007; Jacobsen et al., 2007; Jacobsen et al., 2009; Lakshman et al., 2009; Remsberg et al., 2005; Widén et al., 2012), although, in a minority of studies, associations between pubertal timing and cardiovascular risk outcomes were attenuated after adjustment for BMI (Kivimaki et al., 2008; Pierce et al., 2010).

Although the extant findings to date generally document a relation between pubertal timing and cardiovascular risk, these studies have focused almost entirely on white girls/women. That is, the studies represented in this literature include ones that have limited their analyses to the examination of white girls/women only (e.g., Adventist Health Study; Fels Longitudinal Study (Jacobsen et al., 2009; Remsberg et al., 2005)); studies that are almost entirely comprised of white girls/women (e.g., Nurses' Health Study (He et al., 2010)); and studies, some birth cohorts, of white women conducted in European countries, including England, Finland, Poland and Norway (Hardy et al., 2006; Hulanicka et al., 2007; Jacobsen et al., 2007; Kivimaki et al., 2008; Pierce et al., 2010; Widen et al., 2012). Two notable exceptions include a study of Chinese women in which the predicted relation between earlier pubertal timing and poorer cardio-metabolic health was also observed (Feng et al., 2008) and the Bogalusa Heart Study, comprised of 65% white and 35% African American women (Frontini et al., 2003). The Bogalusa Heart Study was unique in that it included a subset of African American women sizable enough to be analyzed separately, with findings

suggesting that, in both white and African American women, younger menarcheal age predicted the development of a clustering of adverse levels of metabolic syndrome components in adulthood (Frontini et al., 2003).

In summary, study findings strongly suggest that the timing of pubertal development has important impacts on cardio-metabolic health that begin in adolescence and extend into adulthood, possibly accounting for significant disease-related morbidity and mortality in later life. This literature points to the processes of pubertal development in playing a possible mechanistic role in promoting risk for cardio-metabolic disease, but is limited by its almost exclusive focus on girls/women of white backgrounds. This is particularly problematic given the notable finding that African American girls, compared to white girls, experience more accelerated pubertal development. As such, it is imperative to gain a better understanding of how the experience of having an earlier pubertal onset may place African American girls at disproportionate risk for poorer cardio-metabolic health.

Early Life Adversity and Pubertal Timing

The proposed conceptual model (Figure 1) depicts a potential pathway between early life adversity and pubertal timing as a mechanism through which race effects on differential risk for cardio-metabolic disease between African American and white women may be (partially) transmitted. In this context, we describe the unique challenges faced by African American girls/women that may put them at disproportionate risk for early life adversity exposures. Next, we describe the current literature relating early life adversity exposures to pubertal timing as well as this literature's major shortcoming that it is primarily limited to white girls/women. Finally, findings are discussed in the context of life course models, including the “weathering” hypothesis (Geronimus, 1992; Geronimus et al., 2010), to provide conceptual framing for future research questions to test and further elaborate on the preliminary proposed model (Figure 1). It is suggested that such models should consider the timing and time course of relevant risk exposures over the life course (Ben-Shlomo & Kuh, 2002; Lynch & Smith, 2005) as well as the potential social patterning of these risk exposures (Smith et al., 2001).

Early life adversity in African American populations

Early life adversity has been defined variably across studies. Here, we use the term “early life adversity” in reference to a range of family-based, socioeconomic, and race-based hardships experienced in the pre-pubertal period. Evidence that African American girls are disproportionately burdened by adversity exposures in early life is suggested by data from the U.S. Census Bureau, estimating that poverty rates are more than twice as high for African American compared to white families (26% versus 12%, respectively) (Macartney, Bishaw, & Fontenot, 2013). In the 100 largest US metropolitan areas, the vast majority (76%) of African American children lived in neighborhoods that were more impoverished than the neighborhoods of the “worst-off” white children (i.e., top 25% of poverty distribution) (Acevedo-Garcia, Osypuk, McArdle, & Williams, 2008). Accounting for these poverty-related findings, at least in part, rates of mother-only family groups were found to be

three times higher for African American versus white families (29% and 10%, respectively) (Vespa, Lewis, & Kreider, 2013).

In a recent review, Williams (Williams, 2012) describes how such difficult circumstances may contribute to observed race disparities in health. Williams (2012) details evidence that (compared to white) African Americans experience 1) increased prevalence rates in 10 of the 15 major causes of death; 2) earlier onset and poorer prognosis of numerous diseases, including CVD (Jolly, Vittinghoff, Chattopadhyay, & Bibbins-Domingo, 2010); and 3) greater impacts of risk exposures even when the exposures are similar to their white counterparts (e.g., smoking) (Berger, Lund, & Brawley, 2007). Experiences, often unique to African Americans, such as institutional racism (e.g., residential segregation) and personal experiences of discrimination may operate 1) by limiting access to resources and opportunities for improved health; 2) by increasing exposures to other health-damaging stressors especially in contexts of concentrated poverty (e.g., unemployment, single parenthood, social disorder, and violence) (Massey, 1995, 2004); and 3) by potentiating risk in so far as high baseline levels of psychosocial stress may intensify the impacts of other risk exposures (e.g., environment pollutants) (Gee & Payne-Sturges, 2004).

Linking early life adversity and pubertal timing

Study findings show that, in addition to established risk factors for earlier pubertal onset, including larger pre-pubertal body size and younger maternal menarcheal age (Ahmed, Ong, & Dunger, 2009; Brooksgunn & Warren, 1988; Lassek & Gaulin, 2007; Sloboda, Hart, Doherty, Pennell, & Hickey, 2007; Towne et al., 2005), family-related adversity exposures have an independent effect on pubertal timing and tempo. In longitudinal studies, girls who experienced greater adversity in early life had an earlier pubertal onset and faster rate of pubertal development; some of these early life adversity experiences included exposures to marital conflict, father absence, negative parenting practices, parent-child relationship difficulties, and greater socioeconomic disadvantage as well as fewer positive parenting and family-based interactions (Belsky, Houts, & Fearon, 2010; Belsky, Steinberg, Houts & Halpern-Felsher, 2010; Belsky et al., 2007; Campbell & Udry, 1995; Deardorff et al., 2011; Ellis & Essex, 2007; Ellis & Garber, 2000; Ellis, McFadyen-Ketchum, Dodge, Pettit, & Bates, 1999; Ellis, Shirtcliff, Boyce, Deardorff, & Essex, 2011; Graber, Brooksgunn, & Warren, 1995; Moffitt Caspi, Belsky, & Silva, 1992; Saxbe & Repetti, 2009; Wiersen, Long, & Forehand, 1993).

Specifically, in the Wisconsin Study of Families, lower parental support and greater marital conflict predicted earlier adrenarche (indexed by higher salivary dehydroepiandrosterone [DHEA] levels, a steroid hormone produced by the adrenal glands), while lower parental support and lower SES predicted earlier breast development (Ellis & Essex, 2007). In the NICHD Study of Early Child Care and Youth Development (SECCYD), harsh/controlling parenting predicted earlier menarche (Belsky, Steinberg, et al., 2010; Belsky et al., 2007), whereas the classification of insecure (vs. secure) infant-mother attachment style at 15 months predicted earlier initiation and completion of puberty as well as earlier menarche (Belsky, Houts, et al., 2010). Earlier initiation of puberty was coded dichotomously as any evidence of breast or pubic hair development and completion of puberty was coded

dichotomously as completed breast or pubic hair development, both using Tanner staging data (Belsky, Houts, et al., 2010). Moreover, a sizable collection of cross-sectional studies show similar associations between early life adversity exposures and earlier/faster pubertal maturation (Bleil et al., 2013; Hoier, 2003; Kim & Smith, 1998; Kim, Smith, & Palermi, 1997; Maestripieri, Roney, DeBias, Durante, & Spaepen, 2004; Manuck, Craig, Flory, Halder, & Ferrell, 2011; Quinlan, 2003; Romans, Martin, Gendall, & Herbison, 2003).

The literature examining the familial antecedents of pubertal timing, however, is almost exclusively limited to white girls. Studies in this literature have typically excluded African Americans or African American participants have represented such a small proportion of the total sample that they could not be analyzed separately (Belsky et al., 2007; Ellis & Essex, 2007; Ellis & Garber, 2000; Ellis et al., 1999; Graber et al., 1995; Saxbe & Repetti, 2009; Wierson et al., 1993). As a result, whether early life adversity experiences confer risk for earlier pubertal onset and faster pubertal development in African American girls remains inconclusive, as do possible race/ethnic differences in the link between early life adversity and pubertal timing/tempo. This gap in the literature is especially problematic as there are particular early life adversity exposures (described above) that African American girls experience disproportionately and, therefore, may put these girls at increased risk for an earlier pubertal onset and, by extension, poorer cardio-metabolic health.

Although this literature emphasizes family relationships in explaining why some girls experience puberty earlier than their same-age peers, it is notable that Belsky et al. (Belsky, Steinberg, & Draper, 1991) have suggested that greater contextual stress in the family, including lower SES, may accelerate sexual maturation as well via the promotion of more problematic family relationships. More broadly, life history theories posit that, in early life, sexual maturation is shaped by the availability of resources in the environment (Chisholm, 1993; Ellis, 2004; Ellis, Figueredo, Brumbach, & Schlomer, 2009), elements of which would be marked by the family's socioeconomic standing. In fact, in previous studies, lower SES in childhood was related to earlier pubertal onset indexed by pubic hair and breast development (measured as a composite of mother and daughter ratings using Tanner staging sketches and mother reports on the Pubertal Development Scale (Petersen, Crockett, Richards, & Boxer, 1988)) (Ellis & Essex, 2007) as well as younger age at menarche (Campbell & Udry, 1995).

Findings are not entirely consistent, however, as null findings have been reported as well (Ellis & Garber, 2000; Ellis et al., 1999; Moffitt et al., 1992). Research is also mixed with respect to whether SES in childhood correlates with the quality of family relationships. For example, Ellis et al. (Ellis et al., 1999) found that lower SES was related to a host of problematic outcomes such as harsher discipline, greater marital conflict, and less mother-daughter affection/positivity, but in other work, SES was unrelated to similar family-related variables (e.g., father absence, marital stress, problematic family relationships) (Ellis & Garber, 2000). The role of family- and SES-related adversity exposures in relation to pubertal timing, thus, is an area in need of further clarification, especially among African American girls in whom poverty-related risk exposures are more prevalent.

Early life adversity and adulthood health

A growing number of studies document links between early life adversity exposures and risk for poorer cardio-metabolic health in adulthood. Reviews of this literature show early life adversity exposures are related to CVD-specific outcomes (CHD, stroke, angina, and atherosclerosis) (Galobardes, Smith, & Lynch, 2006) as well as all-cause and disease-specific mortality (Galobardes, Lynch, & Smith, 2004, 2008). Early life adversity exposures have also been linked to intermediate health outcomes, including adulthood risk for obesity and central adiposity, conventional cardiovascular risk factors, and incident metabolic syndrome and Type 2 diabetes (Alastalo et al., 2013; Danese et al., 2009; Janicki-Deverts, Cohen, Matthews, & Jacobs, 2012; Lehman, Taylor, Kiefe, & Seeman, 2005, 2009; Midei & Matthews, 2011; Midei, Matthews, Chang, & Bromberger, 2013; Rich-Edwards et al., 2010; Riley, Wright, Jun, Hibert, & Rich-Edwards, 2010). Interestingly, effect sizes are sometimes largest in samples of women (Wegman & Stetler, 2009) and in some studies associations were present in women only (Galobardes et al., 2006). To date, the pathways potentially explaining observed links between early life adversity and adulthood health have not been elucidated. In the current review, we focus on pubertal timing (known to be influenced by pre-pubertal adversity exposures) as a mediated pathway (Figure 1) through which race effects on differential risk for cardio-metabolic disease in adult women may be (partially) transmitted. However, the current model is not meant to exclude consideration of other mediated pathways or possible direct links between early life adversity exposures and adulthood health.

Utilizing life course models in understanding adulthood health

Seeking to explain variability in the emergence of poor health and disease in adulthood, life course epidemiology, as detailed in Lynch & Smith (Lynch & Smith, 2005), considers the timing and time course of relevant risk exposures over the life course—inclusive of a range of socio-environmental factors (Ben-Shlomo & Kuh, 2002). In this framework, life course models have focused on critical and sensitive periods (e.g., in utero, puberty) during which times the occurrence of risk exposures are hypothesized to be particularly salient if not determinative (Barker, 1992; Bleil et al., 2015; Jasik & Lustig, 2008) as well as on the accumulation of risk exposures, accounting for the number of risk exposures, their duration, sequence (“chains of risk”), and potential clustering (Goosby, Cheadle, & McDade, 2016; Kuh, Ben-Shlomo, Lynch, Hallqvist, & Power, 2003; Lynch & Smith, 2005). But no matter the specific conceptual emphasis of a given life course model, it is widely accepted across these models that such risk exposures do not occur at random but rather are socially patterned (Smith et al., 2001). As such, these models may help to explain profound social and racial inequalities in health both at the individual and population levels.

The “weathering” hypothesis in particular proposes that stress exposures, many experienced disproportionately (and some uniquely—i.e., racial discrimination) in marginalized groups, may accumulate over time, resulting in excessive wear and tear on the body and subsequent increased risk for poor health and disease (Geronimus, 1992; Geronimus et al., 2010). In fact, a growing body of evidence documents associations between experiences of racial discrimination and deleterious health outcomes among African Americans (Goosby & Heidbrink, 2013; Goosby, Malone, Richardson, Cheadle, & Williams, 2015). Future research

would be well served to leverage these life course models in considering how the experiences of African American girls in early life may independently, in sequence, and/or in interaction with other social and biological risk factors promote race disparities in pubertal onset and subsequent cardio-metabolic disease. As an example, leveraging of the “weathering” hypothesis may raise alternate interpretations of the proposed model (Figure 1) by suggesting that pubertal development is not a mechanism per se but rather that accelerated biological aging may simply shift concomitant trajectories of pubertal and cardio-metabolic disease development downwardly. This is highlighted as an example only regarding how existing life course models may be applied in the context of the current review.

In summary, study findings are strongly suggestive that, even independently of well-established risk factors for earlier pubertal onset (i.e., pre-pubertal BMI), early life adversity exposures may promote trajectories of earlier/faster pubertal maturation. This literature is important in pointing to modifiable, family-based risk factors that appear to set the stage for pubertal development and possible future risk for cardio-metabolic disease. It is limited, however, by its almost exclusive focus on white girls. This is true despite a robust literature suggesting African American girls are disproportionately burdened by early life adversity exposures especially with respect to poverty-related hardships which may be promoted and/or exacerbated by experiences of institutional racism and discrimination (Massey, 2004; Williams, 2012). In this context, it is imperative to more fully understand how the early life adversity experiences, including a range of family- and SES-related stressors that African American girls face, may contribute to their risk for earlier pubertal onset and subsequent cardio-metabolic disease. In addition, consideration of these relations would be best addressed in the context of life course models which provide a framework for examining the timing and time course of risk exposures as well as their social patterning, both in explaining variations in the emergence of disease generally (Ben-Shlomo & Kuh, 2002; Lynch & Smith, 2005; Smith et al., 2001) as well as in explaining race disparities in the emergence of disease (Geronimus, 1992; Geronimus et al., 2010).

Biological Mechanisms Linking Childhood Adversity, Pubertal Timing, and Cardio-metabolic Health

The study findings described in this review raise the possibility that variations in pubertal development have consequential and lasting impacts on adulthood health. However, *why* the biological underpinnings of puberty, when experienced earlier versus later and/or at differing rates, promote cardio-metabolic disease in adulthood remains unknown. Although speculative, it is possible that the critical organizational processes that occur during puberty may be disrupted under circumstances of higher pre-pubertal risk—including greater early life adversity—inalterably affecting the course of sexual maturation and associated hormonal and metabolic factors relevant to the development of adulthood cardio-metabolic diseases. Specific mechanisms relevant to the role of pubertal development in cardio-metabolic health include obesity, insulin resistance, and inflammation-related processes. Evidence supporting a role for these processes as potential biological mechanisms in

explaining links between early life adversity, pubertal timing, and cardio-metabolic health is described below.

First, with respect to the role of insulin resistance, study findings show markers of early life adversity are related prospectively to obesity, insulin resistance, glycemic control (in non-diabetic persons), incident metabolic syndrome, as well as type 2 diabetes (Midei & Matthews, 2011; Midei et al., 2013; Rich-Edwards et al., 2010; Widom, Czaja, Bentley, & Johnson, 2012). In addition, earlier pubertal timing has been shown to predict post-pubertal weight gain and greater increases in insulin resistance over time, even independently of pre-pubertal body mass (Frontini et al., 2003; Remsberg et al., 2005). Finally, evidence shows obesity, central adiposity, and insulin resistance predict type 2 diabetes and CVD morbidity and mortality (Carey et al., 1997; Janssen, Katzmarzyk, & Ross, 2002; Lapidus et al., 1984; Ogden, Yanovski, Carroll, & Flegal, 2007).

Second, with respect to the role of inflammation, study findings show markers of early life adversity are related prospectively to higher levels of inflammation in adolescence and adulthood (Danese et al., 2009; Danese, Pariante, Caspi, Taylor, & Poulton, 2007; G. Miller & Chen, 2007; G. E. Miller & Chen, 2010; Slopen, Kubzansky, McLaughlin, & Koenen, 2013; Slopen et al., 2010). In addition, younger menarcheal age as well as smaller gains in height over time (an indirect marker of faster pubertal tempo) has been related to higher C-reactive protein (CRP) levels (Clancy, Klein, et al., 2013; McDade, Reyes-Garcia, Tanner, Huanca, & Leonard, 2008; S. M. M. Zhang et al., 2007). More generally, common reproductive functions such as ovulation involve inflammatory processes (Clancy, Baerwald, & Pierson, 2013; Critchley, Kelly, Brenner, & Baird, 2001; Espey, 1980).

Finally, evidence suggests inflammation may be a causal factor in promoting hypertension, insulin resistance, and atherosclerosis, leading to longer-term disease outcomes such as diabetes and CVD (Black, 2003; Hotamisligil, 2006; Libby & Theroux, 2005; Pradhan, Manson, Rifai, Buring, & Ridker, 2001; Pradhan & Ridker, 2002; Ridker, Hennekens, Buring, & Rifai, 2000; Ridker, Rifai, Stampfer, & Hennekens, 2000). Taken together, these findings suggest future studies should consider how variations in the biology of pubertal timing may overlap with metabolic and inflammatory processes possibly explaining links to cardio-metabolic health. Such studies of shared biological underpinnings should be examined in the context of life course models in which correlated trajectories of risk are considered over time.

Summary and Conclusions

In summary, African American (compared to white) girls experience more accelerated sexual maturation as marked by indicators of earlier pubertal timing. A growing epidemiological literature suggests that earlier pubertal timing may be a key risk factor for poorer cardio-metabolic health in adolescence and adulthood. To date, however, studies have focused almost exclusively on white girls/women, limiting our knowledge of whether associations between pubertal timing and cardio-metabolic health are also present among African American girls/women. This omission is striking given the well-established

observation that African American (compared to white) women are at considerable increased risk for cardio-metabolic disease.

In this context, the current review posed the question: Does the tendency to experience an earlier pubertal onset put African American girls at disproportionate risk for poorer cardio-metabolic health, potentially explaining (at least in part) well-established disparities in adulthood risk for cardio-metabolic disease between African American and white women? Moreover, evidence suggests that some of the risk factors for earlier pubertal onset, including early life adversity exposures, are experienced disproportionately among African American girls. In Figure 1, a conceptual framework is presented representing one mechanistic pathway (i.e., race [African American vs. white] → early life adversity → pubertal timing → differential cardio-metabolic disease risk) through which race effects on differential risk for cardio-metabolic disease between African American and white women may be (partially) transmitted. We suggest that future investigations be conducted that draw on life course models to examine the timing, time course, and social patterning of risk factors among African American girls/women that may help elucidate the role of pubertal maturation in explaining long-standing race disparities in cardio-metabolic health. Studies, some existing already (e.g., The National Longitudinal Study of Adolescent to Adult Health), that have some, if not all, of the necessary data should begin to test and elaborate on the proposed conceptual model (Figure 1). Ultimately, these efforts may point to novel areas for intervention in preventing or lessening cardio-metabolic risk in African American girls/women, an important public health objective.

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Figure 1. Conceptual model representing a mediated pathway through which race effects on differential risk for cardio-metabolic disease between African American and white women may be transmitted.