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Alysse J. Kowalski Date

Pubertal timing and tempo in urban South Africa – associations with health in adolescence and transitions to adulthood

By

Alysse J. Kowalski

Doctor of Philosophy

Nutrition and Health Sciences

_____	_____
Aryeh D. Stein, PhD, MPH Advisor	O. Yaw Addo, MS, PhD Committee Member
_____	_____
Michael R. Kramer, PhD Committee Member	Reynaldo Martorell, PhD Committee Member
_____	_____
Linda M. Richter, PhD Committee Member	Rachel N. Waford, PhD Committee Member

Accepted:

_____

Lisa A. Tedesco, Ph.D.

Dean of the James T. Laney School of Graduate Studies

_____

Date

Pubertal timing and tempo in urban South Africa – associations with health in adolescence and transitions to adulthood

By

Alysse J. Kowalski

B.S., University of Central Florida, 2007

M.P.H., Emory University, 2014

Advisor: Aryeh D. Stein, PhD, MPH

An abstract of

A dissertation submitted to the Faculty of the

James T. Laney School of Graduate Studies of Emory University in partial fulfillment of the requirements for the degree of

Doctor of Philosophy

in Nutrition and Health Sciences

2020

Abstract

Pubertal timing and tempo in urban South Africa – associations with health in adolescence and transitions to adulthood

By Alysse J. Kowalski

While a universal process, there is substantial interindividual variation in the timing and tempo of puberty. Previous research from high-income countries (HICs) suggests pubertal timing and tempo are associated with adolescent mental health, health risk behavior activity, and pregnancy. As puberty takes place during secondary school, its timing and tempo have also been shown to be associated with schooling performance and completion which have important implications for overall schooling attainment and economic opportunities, though evidence of these associations is limited. Little is known about associations with pubertal timing and tempo in low- and middle-income countries (LMICs) which tend to have higher levels of poverty and environmental stress. The overarching goal of this dissertation was to investigate associations of pubertal timing and tempo with adolescent mental health, risk behavior initiation, and pregnancy and schooling and employment in early adulthood in urban South Africa.

This research used 10+ waves of data from the Birth to Twenty Plus cohort, an observational birth cohort in Soweto-Johannesburg established in 1990. First, using data on adolescent smoking, alcohol, cannabis, illicit drug, and sexual activity initiation, we conducted cluster analyses to identify patterns of health risk behavior initiation. Second, we examined associations of pubertal timing and tempo (genital/breast development class, pubic hair development class, age at menarche) with adolescent emotional and behavioral problems, eating attitudes, and health risk behavior initiation patterns using multinomial and linear regression as appropriate, and examined the consistency of these associations by levels of childhood stress. Third, we used generalized structural equation models to examine associations of pubertal timing and tempo with ordinal measures of schooling attainment and employment status at age 22 y and explored the mediating role of adolescent health risk behavior initiation pattern and adolescent pregnancy.

We identified 3 distinct patterns of adolescent health risk behavior initiation for males and females corresponding to low, moderate, and high-risk, such that individuals following the low-risk pattern initiated behaviors at below average rates compared to the sample population while individuals following the high-risk pattern initiated behaviors at above average rates and tended to do so at a younger age. Pubertal timing and tempo were associated with indicators of adolescent mental health and patterns of risk behavior initiation. In general, individuals who matured earlier and faster relative to their peers had increased internalizing and externalizing problems, poorer eating attitudes (females only), and were more likely to follow the moderate and high-risk health risk behavior initiation patterns, while there was a small protective effect for individuals who matured later and slower. These associations did not differ by level of childhood stress. Individuals with relatively later and slower pubertal timing and tempo had poorer schooling attainment at age 22 y, while females who matured earlier and faster had better employment status. Overall associations were not mediated by patterns of adolescent health risk behavior initiation or pregnancy. We postulate these associations may be explained by differences in socioeconomic status that were not adjusted for by our measure of material asset ownership.

These results illustrate similarities in associations of pubertal timing and tempo with adolescent health measures in urban South Africa with those in HICs, suggesting commonalities across settings. Associations of pubertal timing and tempo with young adult schooling attainment and employment may differ between LMICs and HICs.

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Acknowledgements

This dissertation would not have been possible without the support of several individuals and organizations. I would like to thank the Birth to Twenty Plus participants, caregivers, and research assistants for their over two decades of involvement with the cohort and Linda Richter and Shane Norris for their leadership. The scientific community owes a debt of gratitude to Linda Richter in particular, who saw the value in following a generation to improving the health and wellbeing of South Africans.

I would like to acknowledge the Wellcome Trust (077210/Z/05/Z), DSI-NRF Centre of Excellence hosted by the University of the Witwatersrand, and the South African Medical Research Council all of whom have generously supported the cohort over the years. A special thanks to the staff at the Developmental Pathways for Health Research Unit and Centre of Excellence who hosted me in Johannesburg. Thanks also to members of the COHORTS Collaborative with whom I have had the privilege to work and have learned so much from.

I am appreciative of several sources of financial support including the NIH training grant, the Vanderbilt University, Emory University, Cornell University and Duke University Global Health Consortium and NIH Fogarty International Center, and the Bill & Melinda Gates Foundation.

I am deeply grateful to my mentor and advisor Aryeh Stein who has supported and challenged me over the years. Aryeh is masterful at leading you to water while allowing you to figure things out on your own, and I am a better researcher for this. I am appreciative of my committee members O. Yaw Addo, Michael Kramer, Reynaldo Martorell, Linda Richter, and Rachel Waford, whose diverse areas of expertise have strengthened this work from all angles.

I would like to thank my cohort and extended Nutrition and Health Sciences family for your support, guidance, and enthusiasm. Thanks to Amy Webb Girard for giving me my first opportunity to work in global health and Mo Ali and friends at the Global Diabetes Research Center who encouraged me to apply to PhD programs. Thanks to my family for a lifetime of support. Lastly, thank you Craig for your unwavering support in all that I do.

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Chapter 1: Introduction

While pubertal development is a universal process, there is substantial interindividual variation in its timing, or age of onset, and tempo, or rate of progression such that individuals of the same chronological age will be at different stages of development. These differences in pubertal timing and tempo are associated with myriad health and human capital outcomes for males and females. Generally speaking, earlier pubertal timing and more rapid tempo relative to one's peers is associated with increased internalizing and externalizing problems, eating disorder risk in females, and health risk behavior activity including tobacco, alcohol, cannabis, illicit drug use, early sexual debut, and pregnancy in adolescence (1-16).

As pubertal development takes place during secondary school, pubertal timing and tempo are associated with secondary school performance and completion, associations with long-term implications for overall schooling attainment and economic opportunities. Individuals with earlier pubertal timing have worse schooling performance and are less likely to complete schooling than their on-time peers, while individuals with relatively later pubertal timing have better grades and higher completion rates (2, 3, 17-21). As adults, females with earlier pubertal timing as adolescents have higher schooling attainment, though this has not been associated with employment status or material hardship (17, 22-24).

Associations of pubertal timing and tempo with adolescent health are well characterized in high-income countries, but far less is known about these associations in low- and middle-income countries where 90% of the world's adolescents live (25). The consequences of pubertal development are greatly influenced by the sociocultural environment, which is substantially different in LMICs. LMICs tend to have higher levels of environmental stress due to poverty, lower levels of schooling attainment, and poorer early-life environments relative to HICs and increased stress has been shown to exacerbate associations of pubertal timing with adverse outcomes (26, 27). The lasting influence of pubertal timing and tempo on human capital in adulthood is less understood, in part because few studies have the longitudinal data available to examine these associations. In general, for adolescence and adulthood, far

less is known about males than females, as many studies collect age at menarche for females, which does not have a comparable counterpart for research studies.

This dissertation will contribute unique knowledge about the associations of pubertal timing and tempo with adolescent health and adult schooling attainment and employment status in a middle-income country, using rich longitudinal data. Birth to Twenty Plus (Bt20+) is a birth cohort in Soweto-Johannesburg, South Africa and its approximately 2000 cohort members have grown up in the first decades of democratic South Africa (28). The cohort is well-characterized with detailed life course data, making it an ideal dataset in which to investigate the consequences of pubertal timing and tempo. This proposal builds on previous research from this cohort that characterized pubertal timing and tempo classes to accomplish the following aims:

Research Aim 1

Describe smoking, alcohol, cannabis, illicit drug, and sexual initiation from ages 10 to 18 y, persistence at age 18 y, and patterns of initiation.

> A descriptive analysis of health risk behavior initiation from ages 10 to 18 y and persistence at age 18 y was conducted from repeated measures of smoking, alcohol use, cannabis use, illicit drug use, sexual activity. Adolescent pregnancy was also be considered as a consequential health outcome. Survival analysis was used to estimate risk of health risk behavior initiation by age 18 y. We examined health risk behavior persistence at age 18 y by adolescent stage of initiation. Hierarchical cluster analysis will be used to examine and identify patterns of risk behavior initiation. We examined associations of these initiation patterns with sociodemographic characteristics.

Research Aim 2

Examine associations of pubertal timing and tempo with measures of adolescent mental health and health risk behavior initiation and examine the consistency of associations by level of childhood stress.

We examined associations of pubertal development classes (breast and pubic hair for girls and genital and pubic hair for boys) and age at menarche with adolescent emotional and behavioral problems, eating attitudes, and the health risk behavior initiation patterns developed in Aim 1, using multinomial and linear regression as appropriate. Pubertal development classes were previously created from serial measures of the Tanner sexual maturation scale. We examined the consistency of associations across levels of childhood stress.

Research Aim 3

Examine associations of pubertal timing and tempo with schooling attainment and employment status at age 22 y and explore the mediating role of adolescent health risk behavior initiation and pregnancy.

Using ordinal measures of schooling attainment and employment status, we used sex-specific generalized structural equation models to examine associations of pubertal development classes and age at menarche with schooling attainment and employment status at age 22 y, evaluating potential mediation by adolescent health risk behavior initiation pattern and adolescent pregnancy.

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Chapter 2: Background

Until recently, adolescence has been a relatively neglected stage of the life course by the scientific community (1). In part this is because adolescence is perceived to be the healthiest stage, where individuals have survived the health risks of infancy and childhood and are not yet at risk of chronic disease. However, adolescence remains an important stage in which several mental health conditions emerge and health-related behaviors and habits are formed.

The proportion of the life course spent in adolescence is increasing. The onset of pubertal development is typically considered the start of adolescence, the age of which declined over the twentieth century due to general improvements in nutritional status (2). The end of adolescence is defined by the transition to adulthood, a socially defined endpoint with different meanings in different settings but has been taking place at an older age as individuals stay in education longer and delay marriage and family formation. The World Health Organization defines adolescence as the period from ages 10 to 19 years and ages 20-24 years are often referred to as young adulthood (3, 4).

For the first time, adolescents were included as a key population group in the UN Secretary General's Global Strategy for Women's, Children's, and Adolescents' Health in 2015 (5). It is increasingly recognized that investments in adolescent health pay triple benefits in the future by improving health in adolescence, adulthood, and the next generation. These benefits extend beyond health. Adolescence is a critical stage in human capital formation in which schooling completion and performance have a lasting impact on long-term economic prospects.

Adolescent development

Adolescence is a period of profound physical, cognitive, and social and emotional development. In adolescence, physical development is characterized by major gains in height and weight, changing body proportions, and sexual maturation, the timing and trajectories of which differ by sex (6). Adolescence is also the time when sexual dimorphism becomes externally visible. More specifically, puberty refers to sexual maturation and the development of secondary sex characteristics culminating in

reproductive maturity. These processes are carried out by two independent, though temporally-related, hormonal cascades, gonadarche and adrenarche. We will use the term puberty throughout to refer to the changes from both processes.

Sexual maturation

Gonadarche is the process of sex hormone production initiated by the re-activation of the hypothalamic-pituitary-gonadal (HPG) axis which is active at birth and quiescent throughout childhood until puberty (7). Re-activation of the HPG axis is still not well understood, though it is likely indirectly influenced by upstream signaling pathways such as kisspeptin, leptin, and gonadal steroids (8). Leptin is a peptide hormone produced by adipose tissue, the concentration of which is proportional to energy stores. Leptin targets kisspeptin neurons, which likely stimulates secretion of gonadotrophin releasing hormone (9).

In gonadarche, nocturnal pulsatile release of gonadotrophin releasing hormone from the hypothalamus, stimulates the release of follicle stimulating hormone and lutenizing hormone from the pituitary gland (7). These hormones stimulate production of the sex steroids testosterone, estradiol, and progesterone and maturation of the reproductive organs. By the end of puberty, the uterus will be five times its prepubertal volume (10). The sex steroids bring about the development of testicular enlargement in boys and breast budding, also known as thelarche, in girls. Gonadarche is generally completed in 2 to 4 years (10, 11).

Adrenarche is a temporally related but independent process in which increased androgen production leads to the development of pubic hair (pubarche) and axillary hair. Adrenarche also results in development of the sebaceous gland and emergence of acne as well as development of the apocrine gland resulting in excessive sweating and body odor. Adrenarche is initiated prior to gonadarche, though the two processes overlap. Its evolutionary significance is unclear (10, 11).

Menarche, or the onset of the menstrual cycle in females, is a later stage pubertal event taking place approximately 2 to 2.5 years after breast budding (12). Spermarche, sperm development in the testes, is the counterpart to menarche in boys, though this cannot be reliably recalled or measured (11).

For both males and females there is an initial period of reduced fertility. Initial menarche cycles are often irregular and are not associated with ovulation for the first 12 to 18 months from the start of menarche (10).

Pubertal development proceeds through five stages ranging from 1 (pre-pubescent) to 5 (adult), with stage 2 considered the onset of puberty. Different staging systems have been developed to measure physiological maturity based on secondary sex characteristics. The first of these was developed in the 1960s by Marshall and Tanner (13, 14). The Tanner sexual maturation scales provide a consistent method of monitoring a child's progression through puberty. Separate scales are used for gonadarche and pubarche in males and females.

Pubertal timing and tempo

Puberty can be characterized in terms of its timing, or age of onset, and tempo, or rate of progression. In studies of European girls, the age of breast budding ranges from 8.8 years to 12.8 years with mean 10.8 years (10, 15). Progression through the stages of breast development ranges from 1.5 years in rapid developers to 5 years slow developers. Pubic hair typically emerges 6 months later, though in 30% of girls pubic hair development precedes breast budding (10). Age of menarche ranges from 11 to 15 years and consistently begins after height velocity has begun to decelerate (10). In previous work in the late twentieth century it was found that girls with earlier menarche progressed from stage 2 to menarche more quickly. In contrast, more recent work has shown that girls entering puberty later progress to menarche faster than those entering puberty earlier (16, 17).

In boys, gonadarche begins as early as 10.5 years and as late as 14.5 years and is completed as early as 12.5 years and as late as 16.5 years such that a few boys will not start puberty until others have completed it (10). Adrenarche and gonadarche usually overlap, though adrenarche can precede puberty by 1 to 2 years (8).

Drivers of pubertal timing and tempo

There is substantial interindividual variation in puberty onset. Within the same living conditions there is a 4-5 y variation in pubertal timing (6, 11). Around half of the variation in pubertal timing in thought to be explained by genetics while nutritional status and environmental conditions are also influential (6, 11, 18).

Nutritional status is thought to explain as much as 25% of the variation in pubertal timing (19). Undernutrition is associated with delayed puberty, reduced growth spurt, and later age of menarche. Age of menarche declined in the first half of the twentieth century as a result of general improvements in nutritional status (20). Overnutrition and obesity are associated with earlier pubertal timing and age of menarche takes place nearly half a year younger in obese girls (21). Children born small for gestational age are more likely to have earlier pubertal development and faster progression than children born appropriate for gestational age. They reach peak height velocity at a younger age and have a shorter pubertal growth spurt resulting in shorter adult height (22).

Pubertal timing has also shown to differ by ethnicity. In the US, mean breast development onset is age 8.8, 9.3, 9.7, and 9.7 years for African American, Hispanic, non-Hispanic White, and Asian girls respectively, while mean age of genital development is age 9.14, 10.04, 10.14 years in African American, Hispanic, and non-Hispanic white boys respectively (23, 24). Despite differences in onset, American boys completed puberty around age 15 years regardless of ethnicity, implying differences in tempo (24).

Pubertal onset has been shown to take place at a younger age among children who grew up in environments characterized by chronic stress, parental conflict, harsh parenting, socioeconomic adversity, and father absence (25, 26). There is concern that endocrine disrupting chemicals, which can be synthetic or naturally occurring, interfere with the synthesis or action of normal hormones and cause puberty to start earlier, though this has not been shown definitively in human populations (17). Pubertal timing can also be affected by medical conditions, though these conditions will not be discussed further.

Other physical development

In addition to sexual maturation, both boys and girls experience changes in body size, shape, stature, and composition. The adolescent growth spurt is a period of rapid increases in trunk length while prior to the growth spurt, most height gains come from increasing leg length. In the first three years of the growth spurt, height velocity accelerates such that girls typically grow 6, 8, and 6 cm and boys typically grow 7, 9, and 7 cm, respectively, prior to height velocity decelerating (10). Individuals who reach their peak height velocity earlier in time will reach a higher peak velocity (27).

Girls undergo their growth spurt before boys. For girls the growth spurt takes place between stages 2 and 3 of gonadarche while for boys it takes place between stages 3 and 4. In North American and European individuals, girls reach their peak height velocity between 10 to 14 years while boys reach their peak height velocity between 12 to 16 years (10). During the pubertal growth spurt, there can be as much as a 12 cm difference in height between and early and late maturing boys. Following puberty males are an average of 13 cm taller than girls. This difference is largely attributable to the additional leg growth boys undergo prior to the adolescent growth spurt since boys experience their growth spurt later than girls (10).

Other changes that take place among boys include increased shoulder and chest growth, increased peak muscle velocity and subsequently strength, changes in facial dimensions, appearance of facial hair, and voice deepening. Additional changes that take place in girls include gains in fat mass and widening of the hips and pelvic inlet.

Cognitive and social and emotional development

In contrast to adolescent physical development which has a wide variation in onset, cognitive and social and emotional development are age-dependent processes (28, 29). Cognitive development that takes place over the course of adolescence includes increased capacity for abstract thinking and complex thought in which a problem can be thought about from start to finish. It includes increased capacity for goal setting, a shifting focus from being present-oriented to more future-oriented, and deeper moral thinking and reasoning. The ability to delay gratification and control impulses also develops.

Adolescence is the start of an active phase of social and emotional development that is understood to continue into adulthood and includes the development of self-identity, independence, and emotional regulation. Adolescents process and adapt to the physical changes of puberty. Mood swings and conflict with parents are common in early adolescence and the influence of parents fades and is supplanted by peers. The increasing importance of peer approval can conjure up worry about being normal. Peers continue to be highly influential as young people progress through adolescence as deeper friendships and romantic relationships are formed. Interest in sex also increases steadily during this time. Early adolescence is also a time in which individuals test rules and limits and build their independence (30).

Cognitive and social and emotional development are highly intertwined. In mid-adolescence, there is a gap between the development of the prefrontal cortex, which controls executive functions and the limbic system, the emotional control and reward center of the brain. This gap may explain why behavioral choices are driven by emotion rather than rational decision making (31, 32). By the end of adolescence young people have developed greater ability to control and regulate their emotions. When presented with information, adolescents can make good decisions but have not developed the ability to tune out the environment to the same extent as adults and are more susceptible to exciting and stressful situations, especially in the presence of peers (33, 34).

Associations of pubertal timing and tempo with adolescent outcomes

Pubertal timing and tempo have been shown to be associated with several adolescent health outcomes including mental health, health risk behaviors including substance use and sexual activity, and adolescent pregnancy. Moreover, because adolescence is also an important time for schooling attainment, pubertal timing and tempo have implications for secondary schooling performance and completion which set the stage for long-term schooling attainment and employment prospects. The vast majority of research in this area comes from high-income countries (HICs) and low- and middle-income countries (LMICs) are underrepresented in the literature.

Mental health

The World Health Organization defines mental health as a state of well-being in which an individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and is able to make a contribution to his or her community (35). Many young people report increases in mental health problems in adolescence, though most do not have persistent difficulties (36-38). Mental health problems fall along two dimensions based on how and individual copes and responds to stressors. Internalizing behaviors are behaviors in which distress is expressed inwards and at clinical thresholds can result in diagnoses of include anxiety, somatization, and affective disorders. Externalizing behaviors are behaviors in which distress is expressed in the external world such as acting out, antisocial behavior, hostility, and aggression and at clinical thresholds can result in diagnoses of attention-deficit/hyperactivity disorder, oppositional defiant disorder, and conduct disorder. Findings from meta-analyses consistently show that relative to their on-time peers, both males and females with earlier pubertal timing have increased internalizing and externalizing problems (39, 40). Studies with more specific outcome measures have found early maturation to be associated with increased risk of depression and anxiety (41-54). These associations are not always linear. For boys, evidence suggests both early and late maturing boys are at increased risk of depression (42, 49, 55-57).

Pubertal tempo may also contribute to poorer adolescent mental health, though the evidence is far more limited. In at least one study, individuals with a relatively slower pubertal tempo reported increased depressive symptoms in early adolescence while individuals with relatively faster pubertal tempo reported increased depressive symptoms as they progressed through puberty (54, 57). More rapid pubertal tempo was more strongly associated with increased depressive symptoms in boys than pubertal timing (57).

Early pubertal timing is associated with small but significant increases in externalizing behaviors including disruptive, impulse control, and conduct disorders as defined by the DSM-5 (39). Early pubertal timing has also been associated with related outcomes including delinquent activity and violent behaviors in both girls and boys (39, 43, 47-49, 58-69). In boys, more rapid pubertal tempo has also been associated with increased externalizing problems (48, 70).

Eating disorders emerge in adolescence and are serious mental illnesses with high mortality rates (71). Based on the most recent literature, early pubertal timing is a risk factor for eating disorders for girls but is minimally related to eating disorder risk for boys (72). This association for girls has been found in studies examining both eating disorder symptoms and clinical diagnoses (72).

Substance use

Early maturation is associated with earlier cigarette, alcohol, cannabis, and drug use initiation (73-80). Early maturation is also associated with increased and riskier substance use (73, 81). Whether early maturers continue to have elevated rates of substance use relative to their on-time and late maturing peers across adolescence remains unclear. One study found substance use among early maturers remains elevated throughout adolescence and that on-time and late maturers never "caught up", while another study found that across adolescence, the proportion of substance users increased more for on-time adolescents compared with early developers (78, 80). Lastly, another study reported that while early pubertal timing was associated with substance use initiation, persistence across adolescence differed by sex (79). Among late maturers, the association of pubertal timing with substance use is less consistent. In single studies, late maturation was associated with increased alcohol use among girls and increased smoking among boys but decreased smoking among girls (81, 82).

Sexual debut and pregnancy

A wide body of research links early pubertal timing with earlier sexual initiation and pregnancy in females (83-88). The association of pubertal timing and age at first sexual intercourse is impacted by the social environment including culture-related social factors (86, 89). Age at sexual debut is related to age at first pregnancy (84, 90). The consequences of adolescent pregnancy are significant and include lower levels of schooling achievement, employment, and economic circumstances (91-94). The children of adolescent mothers are more likely to have pregnancies at a young age, resulting in intergenerational consequences (93).

Associations of pubertal timing and tempo with schooling and employment outcomes

Educational careers are cumulative, with secondary school completion and performance particularly important for tertiary schooling and employment prospects. In six studies published in the 1980s and 90s, half reported better schooling performance among early maturing boys, while half found no association (48, 95-97). Dubas et al. found early maturing boys had higher grades in 6th, 7th, and 8th grade, though not by 12th grade suggesting these associations may be restricted to the pubertal period and may resolve by the completion of secondary school (95, 96).

Among girls, findings for associations of pubertal timing with secondary schooling outcomes are mixed. Several studies found earlier pubertal timing was not associated with secondary schooling performance or dropout rate (42, 55, 98-100). In studies that found an association, earlier maturation was associated with poorer academic performance, as measured by grade point average and course failure, whereas later maturation was associated with higher grades (43, 95, 101, 102). These results may be explained by social relationships and interactions. Early maturers are more likely to get in trouble at school and have higher levels of absenteeism and truancy, while late maturers may be less popular and subsequently invest more time in their school work (43, 55, 94, 98).

Far fewer studies have investigated long-term consequences of pubertal timing on schooling attainment and employment and findings have been equivocal. In a Swedish longitudinal cohort followed in the 1980s and 90s, early maturing girls were less likely to complete additional schooling beyond compulsory levels and were more likely to have lower paying, less prestigious jobs (103). In more contemporary studies, early maturing girls were less likely to have a university education while late maturers were more likely to have received their bachelor's degree and spend more time in education when assessed as adults (42, 101, 104). However, maturational timing was not associated with employment status in early adulthood (42, 100).

Few studies have investigated long-term consequences of pubertal timing on schooling attainment and employment, in part because the longitudinal data do not exist. None have done so among males. For

females, studies with follow-up into adulthood have been conducted exclusively in high-income countries and these associations may differ in low- and middle-income settings.

Maturity gap

In high-income countries, early maturation has consistently been shown to be associated with negative health and human capital outcomes in adolescence and adulthood, while findings for late maturation are equivocal. This has not been thoroughly investigated in LMICs where the environmental and cultural milieu differ.

These findings may be explained by the *maturity gap* or *window of vulnerability* in which an individual is physically mature but not cognitively and socioemotionally mature as a result of differences in physical, cognitive, and social and emotional development (11, 29). In contrast to age of puberty onset which varies considerably, cognitive and social and emotional development are age-dependent processes and have less variation in onset and progression. The maturity gap widened following secular declines in the age of puberty in the early part of the twentieth century and is widest for early maturing females who enter puberty earlier relative to their opposite and same-sex peers (2).

This dissertation examines the role of the timing and tempo of pubertal development on mental health and risk behavior initiation in adolescence and human capital formation and employment in young adulthood in urban South Africa. These associations have not been thoroughly investigated in LMICs such as South Africa where the environment is characterized by higher levels of poverty, adversity, and violence and may exacerbate consequences of the maturity gap.

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Chapter 3: Extended Methods

Birth to Twenty Plus cohort

This study used data from the Birth to Twenty Plus (Bt20+) cohort in Soweto-Johannesburg, South Africa. The Bt20+ cohort was founded as the Birth to Ten cohort and was established to study child development and quality of life in urban settings, given increased economic opportunities available in cities. As the cohort was formed during the end of apartheid, it would also offer insights into the impact of social and political change on child health and development. Bt20+ cohort members were born a few months after Nelson Mandela was released from prison and are known as "Mandela's children" as they represent renewed hope and possibility as the first generation who would grow up not directly exposed to apartheid.

The Bt20+ cohort enrolled singleton children who were born during a 6-week period between April and June 1990 and resided in the Soweto-Johannesburg municipal area for a minimum of 6 months after birth (N = 3,273). While the cohort has undergone attrition, most of this attrition took place in early life. As of 2007, when participants were age 17 y, the study team was in contact with >70% of cohort members (1). For the purposes of this dissertation, we filtered the cohort to the 2,568 Black African participants as other population subgroups comprise less than 10% of the population of Soweto-Johannesburg.

Datasets

This dissertation combined multiple Bt20+ datasets in addition to data from the 3rd generation pregnancy and birth surveillance system. These datasets were shared by several individuals in various formats and combined to create analytical datasets. The relevant datasets are summarized in the table below.

Relevant Birth to Twenty Plus datasets

Dataset	Topics included	Source	Format
Y0	Maternal stress and violence experiences	DPHRU Data Team	REDCap CSVs

Y0-2 (Demog)	Maternal age, maternal years of schooling, maternal marital status, household asset ownership	Linda Richter	SPSS dataset
Y5	maternal stress and violence experiences, household asset ownership	DPHRU Data Team	REDCap CSVs
Y7	maternal stress and violence experiences, household asset ownership	DPHRU Data Team	REDCap CSVs
DQ	Fluid intelligence at age 7 y	Linda Richter	SPSS dataset
Growth thematic dataset	HAZ ages 5 and 8 y, BMI at ages 5 and 8 y	Lukhanyo Nyati	CSV
Puberty dataset	Pubertal development trajectories	Elizabeth Lundeen	Stata dataset
Y11	Smoking, alcohol use, drug use, sex, YSR	Linda Richter	SPSS dataset
Y13	Smoking, alcohol use, drug use, sex, EAT	DPHRU Data Team	REDCap CSVs
Y14	Smoking, alcohol use, drug use, sex	DPHRU Data Team	REDCap CSVs
Y14	YSR	Linda Richter	SPSS dataset
Y15	Smoking, alcohol use, drug use, sex	DPHRU Data Team	REDCap CSVs
Y16	Smoking, alcohol use, drug use, sex	DPHRU Data Team	REDCap CSVs
Y17	Smoking, alcohol use, drug use, sex, EAT	DPHRU Data Team	REDCap CSVs
Y18	Smoking, alcohol use, drug use, sex	DPHRU Data Team	REDCap CSVs
Y22	Schooling, employment, pregnancy history	DPHRU Data Team	REDCap CSVs
3G	Bt20 Pregnancy and birth surveillance	Aryeh Stein	Stata dataset

Abbreviations: Y = Year; YSR = Youth Self-Report; EAT = Eating Attitudes Test

Measures of interest

Measures of interest to this dissertation and the study waves they were collected at are summarized in the table below. Datasets were received in various conditions; some had already been cleaned and contained derived variables, while others were raw and had never been analyzed. In the following sections we describe what was measured, how the data were cleaned and processed, what derived variables were created, and any imputation approaches that were used. To do this we have organized the data as coming from 3 periods – pre-puberty, adolescence, and young adulthood.

Measures of interest and study waves collected

	Data collection wave (Bt20+ child's age)													
	0	0-2	5	7	8	9	11	13	14	15	16	17	18	22
Pre-puberty Measures														
Maternal age		X												
Maternal yrs of schooling		X												
Maternal marital status		X												
Household asset ownership		X	X	X										
Stress and violence inventory	X		X	X										
Fluid intelligence				X										
HAZ			X		X									
BMI			X		X									
Adolescent Measures														
Tanner sexual maturity scale						X	X	X	X	X	X	X	X	
Age of menarche						X	X	X	X	X	X	X	X	

Smoking							X	X	X	X	X	X	X	
Alcohol use							X	X					X	
Cannabis use							X	X	X	X				
Drug use							X	X	X	X		X	X	
Sexual activity							X	X	X	X	X	X	X	
Adolescent pregnancy history										X	X	X	X	
Young Adult Measures														
Young adult pregnancy history														X
Schooling attainment														X
Employment history														X

Data collection

All adolescent study visits were conducted at the Developmental Pathways for Health Research Unit at Chris Hani Baragwanath Hospital in Soweto. The caregiver and Bt20+ child were interviewed together through the age 11 y study visit and separately in all subsequent visits.

Data collection used several modalities including interviewer-administered questionnaires, self-complete questionnaires, and direct measurement. Self-complete questionnaires were completed by the Bt20+ child in private and included questions on sensitive topics including smoking, alcohol use, cannabis use, illicit drug use, sexual activity, and pregnancy. The self-complete questionnaire was completed on paper at the age 11, 13, and 14 y study visits and on a computer using a computer-aided self-administered interview system at the age 15, 16, 17, and 18 y study visits. Height-for-age and body mass index were derived from direct measurements. All other measures were collected through interviewer-administered questionnaires conducted in English by interviewers trained in the local vernacular who could translate questions into standardized phrases in local languages as needed.

Pre-puberty measures

In the following pre-puberty, adolescent, and young adult measure sections we describe the measures used from each time period including what they represent, how the data were collected, processed, and cleaned, and any derivations or imputation that were performed. This section describes measures that were used in this dissertation that were collected prior to the start of puberty.

Maternal characteristics at enrollment

Data collected from antenatal visits through age 2 y were previously combined into a single enrollment study wave (referred to as age 0-2 y). These data were thoroughly cleaned, and derived variables were created for the original Lancet series on maternal and child nutrition. The following variables from this dataset were used in the form they were received: maternal age at birth, maternal years of schooling, and maternal marital status.

Household asset ownership

Household asset ownership was used as a proxy measure of socioeconomic position within the cohort at two time points – early life (using data from ages 0-2 y) and childhood (using data from age 7 y supplemented with observations from age 5 y). At each wave (age 0-2 y, 5 y, and 7 y) a series of questions were asked about household ownership of various assets. The assets asked about changed over time. Internal analyses (correspondence Chris Desmond) demonstrated a high correlation ($r > 0.9$) between a simple sum of assets owned and asset scores derived by principle component analysis. Accordingly, we elected to use the simple sum approach. As the number of assets asked about differed at each study visit, we used the number of assets owned and assets inquired about to calculate the percentile of assets owned at each visit. This allowed us to supplement the age 7 y data with data from age 5 y for individuals missing data from the age 7 y visit. We categorized the percentiles of the number of assets owned into tertiles.

Childhood exposure to stress and violence

We created a composite measure of prenatal and childhood stress exposure from maternal report of stress and violence events experienced in the past six months at the age 0-2 y, 5 y, and 7 y study visits as a proxy for the Bt20+ child's exposure to stress. To minimize the degrees of freedom in subsequent modeling, we created a composite variable of the number of visits in which the mother reported experiencing above the sample median number of stress and violence events.

Childhood fluid intelligence

Non-verbal fluid intelligence was assessed using the Raven's Colored Progressive Matrices at age 7 y. Total scores were standardized with mean 99 and standard deviation of 13.8.

Height-for-age Z-score (HAZ)

HAZ was previously calculated using WHO growth standards from height measurements collected by trained research assistants. HAZ measures from ages 5 and 7 y were used in these analyses (2).

Body mass index-for-age Z-score (BMIZ)

BMIZ was previously calculated using WHO growth standards from height and weight measurements collected by trained research assistants. BMIZ measures from ages 5 and 7 y were used in these analyses (2).

Two-way imputation (TWI)

To retain observations with a small amount of nonresponse, we used TWI to impute values for individual items that were part of a scale or thematic set of questions (i.e. particular household assets at a given age). TWI is an imputation approach based on the linear model developed by Bernaards and Sijtsma (3). In TWI item *j* of subject *i* is imputed according to the following formula

$$PM_i + IM_j - OM$$

where PM_i is the person mean or mean of the items that the subject completed. IM_j is the item mean, or mean of item *j* over all subjects, and OM is the overall mean response to an item across all subjects and items.

TWI utilizes the person mean and the item mean, taking advantage of more information than either approach would on its own. The person mean accounts for the fact that a subject's responses will be more strongly correlated with one another than with other responses in the sample, while the item mean considers that all items on a scale may not be created equal and would not be expected to receive a similar

response (e.g. items about events that may be rarer or of a different intensity). Imputed values that were out of range were truncated to the nearest plausible value.

We used two-way imputation to assign values to missing items for individuals who completed at least 50% of items on household asset ownership and stress and violence exposure. The household asset ownership completion rate was 64% from Y0-2 and two-way imputation recovered N = 308 observations; 95% at Y5 (recovered N = 9); and 98% at Y7 (recovered N = 4). The maternal report of stress and violence experiences completion rate was 84% at Y0-2 and two-way imputation recovered N = 187 observations; 90% at Y5 (recovered N = 88); and 93% at Y7 (recovered N = 88).

For each variable to which we applied TWI we also created a "companion" variable to serve as a "noise" parameter in future modeling and reduce the artificial precision gained through TWI. For household asset ownership, the age 0-2 y companion variable was based on whether assets had been imputed and the age 7 y companion variable was based on whether the data came from age 7 y or age 5 y. For child stress exposure the companion variable was created from the number of study visits attended (0, 1, 2-3).

Adolescent Measures

Pubertal timing and tempo

Latent class growth analysis was previously applied to serial measures of the Tanner sexual maturation scale (SMS) to group participants into sex-specific pubic hair and genital/breast development trajectories (4-6). The SMS consists of drawings and written descriptions of progressive stages in the development of secondary sexual characteristics—breasts in girls, genitals in boys, and pubic hair in both sexes (7, 8). The stages range from 1 (prepubertal) to 5 (postpubertal) with stage 2 considered to be the onset of puberty. In Bt20+, the SMS was administered annually by a trained healthcare provider in a subset of participants from age 9 y to 11 y and by self-assessment in the entire cohort age 12 y to 16 y following a validation study that reported substantial concordance between the expert and self-assessed ratings (9).

For boys, 3 classes of pubic hair development and 4 classes of genital development were identified. For girls, 3 classes of pubic hair development and 4 classes of breast development were identified. For each trajectory, class 1 has the smallest intercept and slope, reflecting later pubertal timing and slower pubertal tempo relative to the other classes.

Age of menarche

Age of menarche was self-reported from repeated questions about menstruation asked on the self-administered questionnaire at each adolescent visit. Females with an age of menarche >1 SD below the sample mean age of menarche were considered to have early menarche.

Emotional and behavioral adjustment

Youth emotional and behavioral problems were assessed at ages 11 and 14 y using the Achenbach System of Empirically Based Assessment (ASEBA) Youth Self Report (YSR), which is designed for children 11 to 18 years of age (10, 11). Participants were read 112 statements describing behaviors and feelings in English by trained interviewers who could translate the questions into standardized phrases in local languages as needed. Respondents selected the response (never, sometimes, true and very true) that best described them. Participant responses were scored using the six DSM-oriented scales for affective problems, anxiety problems, somatic problems, attention deficit/hyperactivity problems, oppositional defiant problems, and conduct problems. The DSM-oriented scales consist of items that were rated as being “very consistent” with Diagnostic and Statistical Manual of Mental Disorders-4 criteria for diagnostic categories by international experts and were shown to have good internal consistency and (Cronbach’s alphas range from 0.75 to 0.84) and test-retest reliability (Pearson correlation coefficients range from 0.78 to 0.89) in a diverse sample (12). The YSR has been administered previously in South Africa and the DSM scales have shown consistency when applied cross culturally (13-19).

Though participants completed the 1991 version of the YSR, the YSR was updated in 2001 and responses were scored using the 2001 version. We proportionally scored scales to account for 4 DSM

items that were revised and one affective problems item that was inadvertently omitted. Because clinical cutoffs have not yet been validated in the South African context, we report mean scale scores, with higher scores reflecting increased problem behaviors.

The YSR completion rate was >99% for each of the DSM scales at Year 11 and >98% at Y14.

Eating Attitudes

Eating attitudes were assessed using the 26-item Eating Attitudes Test (EAT-26) at ages 13 and 17(20). The EAT-26 consists of 26 items comprising 3 subscales: dieting, bulimia and food preoccupation, and oral control. Previous work determined the EAT-26 had good internal reliability in both early and late adolescence (early adolescence: Cronbach's alpha = 0.71 and late adolescence: Cronbach's alpha = 0.70). The EAT-26 has been previously applied in rural and urban South African settings (21). In Bt20+, minor additional language was added to some items to help clarify the item's intent.

To score the EAT-26, item responses are assigned the following values: always, 3 points; usually, 2 points; often, 1 point; responses of sometimes, rarely, and never are assigned 0 points. Item 25 is reverse scored. The total score is the sum of the item scores and ranges from 0 to 78. Subscale scores are the sum of the subscale items. The dieting scale is the sum of items 1, 6, 7, 10, 11, 12, 14, 16, 17, 22, 23, 24 and 25. The bulimia and food preoccupation scale is the sum of items 3, 4, 9, 18, 21, and 26. The oral control subscale is the sum of items 2, 5, 8, 13, 19, and 20. Participants who score >20 are identified as having unhealthy attitudes towards food, body weight, and eating, and are considered to have a greater risk of developing an eating disorder. However, this cut point has not been validated in South African populations therefore we used continuous scores in subsequent analyses, with higher scores reflecting poorer eating attitudes.

Prior to creating the total and subscale scores, item nonresponse was assessed. Individuals who did not answer any EAT-26 items were excluded from subsequent analyses. The proportion of individuals who did not answer between 1 and 26 items are shown below. Two-way imputation to assign values to missing items for individuals who completed at least 50% of the relevant questions. The EAT completion

rate was 94% at Year 13 and two-way imputation recovered N = 81 observations; 54% at Year 17 and two-way imputation recovered N = 24 observations.

Number of missing EAT-26 items at age 13 y

Num missing items	N	Percent
0	1356	79.7
1	67	3.9
2	10	0.6
4	1	0.1
7	2	0.1
8	1	0.1
26	264	15.5
Total	1701	100

Number of missing EAT-26 items at age 17 y

Num missing items	N	Percent
0	930	54.7
1	23	1.4
2	1	0.1
26	746	43.9
Total	1700	100

Confirmatory factor analyses using diagonally weighted least squares estimation with robust standard errors were conducted at each year to examine the fit of the factor structure. Fit statistics for each year are summarized in the table below. At age 13 y, all EAT-26 items loaded. The root mean square error of approximation (RMSEA) suggested the three factor model had good fit. The comparative fit index (CFI) and Tucker-Lewis index (TLI) suggested the fit was acceptable. At age 17 y, two items did not load, one of which was the reverse scored item. Item 9 also had a negative variance. The RMSEA suggested fit was good while the CFI and TLI suggested the fit was acceptable.

Confirmatory factor analysis fit statistics for age 13 and 17 y EAT-26

	Y13	Y17
Comparative Fit Index	0.880	0.871
Tucker-Lewis Index	0.868	0.858

Root Mean Square Error of Approximation	0.031	0.030
Standardized Root Mean Square Residual	0.089	0.087

A weighted kappa was calculated from quintiles of EAT total scores to determine if it would be appropriate to pool the EAT measures at the different years. A kappa statistic is a measure of agreement, in this case between two repeated measurements of the same instrument. Weighting this measure adjusts for the strength of disagreement. The kappa statistic was low (0.107) suggesting quintile rank-order agreement between the two EAT measures was low and that the measures of eating attitudes at the two time points during adolescence should be considered independently.

Health risk behaviors

Health risk behaviors of interest included smoking, alcohol use, cannabis use, illicit drug use, and sexual activity. A description of each measure including the items used, cleaning efforts, and the creation of derived variables are detailed below.

Smoking

Smoking items consisted of three types of questions, ever initiation, age of initiation, and use in the past 30 days. The smoking questions used from each study visit are listed below.

Adolescent smoking questions

Year	Question asked on survey	Response options
Y11	Have you ever smoked a cigarette?	0, No | 1, Yes
Y11	How old were you the first time you smoked?	Age
Y11	Do you smoke cigarettes now?	0, No | 1, Yes
Y13	Have you ever tried or experimented with cigarette smoking even 1 or 2 puffs?	0, No | 1, Yes
Y13	How old were you when you first tried a cigarette?	Age
Y13	During the past 30 days did you smoke cigarettes?	0, No | 1, Yes
Y14	Have you ever tried or experimented with cigarette smoking even 1 or 2 puffs?	0, No | 1, Yes
Y14	How old were you when you first tried a cigarette?	Age
Y14	During the past month (30 days) did you smoke cigarettes?	0, No | 1, Yes
Y15	Have you ever tried or experimented with cigarette smoking even 1 or 2 puffs?	0, No | 1, Yes
Y15	How old were you when you first tried a cigarette?	Age
Y15	During the past month (30 days) did you smoke cigarettes?	0, No | 1, Yes
Y16	Have you ever tried or experimented with cigarette smoking even 1 or 2 puffs?	0, No | 1, Yes
Y16	How old were you when you first tried a cigarette?	Age
Y16	During the past month (30 days) did you smoke cigarettes?	0, No | 1, Yes

Y17	Have you ever tried or experimented with cigarette smoking even 1 or 2 puffs?	0, No | 1, Yes
Y17	How old were you when you first tried a cigarette?	Age
Y17	During the past month (30 days) did you smoke cigarettes?	0, No | 1, Yes
Y18	Have you ever tried or experimented with cigarette smoking even 1 or 2 puffs?	0, No | 1, Yes
Y18	How old were you when you first tried a cigarette?	Age
Y18	During the past month (30 days) did you smoke cigarettes?	0, No | 1, Yes

Smoking initiation

Smoking initiation was defined as an affirmative response to, "Have you ever tried or experimented with cigarette smoking even 1 or 2 puffs?" Response values other than 0/1 were set to missing. Responses of 'No' were set to 'Yes' if one of the following conditions was met: 1) *self-reported age of initiation* was reported or 2) the respondent reported smoking in the past 30 days. For example, if a participant reported their age of initiation as 15 y but answered 'No' to the *smoking initiation* question, they have been recoded to have 'Yes' for *smoking initiation.*

Self-reported age of smoking initiation

This was the participant's first response to, "How old were you when you first tried a cigarette?" Implausibly high (ages > 2 years above the study visit [e.g. At the age 16 study visit values >18 were set to missing]) and implausibly low (ages < 5y) values were set to missing.

Consistency checks showed responses are largely plausible and reasonable when compared with the study visit year that the respondent reported smoking for the first time. Self-reported age of smoking initiation was consistently ≤ the study visit year where *smoking initiation* was endorsed for the first time. It is important to use the self-reported measure as it is most precise. This is particularly relevant if a participant started smoking at an early age but didn't attend a study visit until late adolescence (e.g. the first positive response to *smoking initiation* may have been at the age 16 visit, but the self-reported age of smoking initiation may have been age 12.).

Smoke in the past 30 days

Smoke 30 days was defined as an affirmative response to, "During the past month (30 days) did you smoke cigarettes?" Response values other than 0/1 were set to missing. Because use in the past 30

days always followed the *smoking initiation* question, responses to the *smoke 30 days* question were set to 'No' if the response to *smoking initiation* was 'No'.

Across year summary measures

Following data cleaning within each individual year, the data were cleaned across years to maximize the amount of information for each participant.

For participants who never reported smoking, a variable for *last known age of not smoking* was created from the participant's exact age at the study visit in which they answered 'No' to *smoking initiation*. Where an exact age was unavailable, *last known age of not smoking* was set to the corresponding study wave. For example, if a participant last reported never smoking at the Y17 study visit but was 18.2 y at the time of the visit, *last known age of not smoking* would have been set to 18. Had an exact age been unavailable, *last known age of not smoking* would have been set to 17.

Where the participant responded 'Yes' to *smoking initiation*, but a *self-reported age of smoking initiation* was not provided, the missing *age of smoking initiation* was set to the participant's exact age at the study visit in which they first responded 'Yes' to *smoking initiation*. If the study visit date was missing and an exact age could not be calculated, the *age of smoking initiation* was set to the corresponding study wave (e.g. in the absence of a *self-reported age of smoking initiation* or exact age, the *age of smoking initiation* was set to 15 if a positive response to *smoking initiation* was first given at the Y15 study visit). Among participants who reported 'Yes' to *smoking initiation*, the source of the information for *age of smoking initiation* is summarized below.

Source of information for age of smoking initiation

Smoking age source	N	Percent
Exact age at visit	63	4.6
Self-reported age	1284	93.9
Study wave	21	1.5
Total	1368	100

The *age of smoking initiation* and *smoking initiation* measures were used to derive a categorical measure of smoking engagement prior to and across adolescence. If a respondent reported smoking, their

age of smoking initiation was used to classify their *stage of smoking initiation* in accordance with the World Health Organization definition (early: 10 to 13 years; mid: 14 to 16 years; late: 17 to 19 years). A respondent's *stage of smoking initiation* was classified as 'childhood' if they reported smoking <10 years. Individuals who responded 'No' to *smoking initiation* at the Y18 study visit were classified as 'never smoke by Y18'. Individuals who were not seen for a Y18 visit but who reported 'No' to *smoking initiation* during at least one visit were classified as 'status unknown at Y18'. For example, if an individual reported 'No' to *smoking initiation* at Y15, but never attended a later visit, they were classified as 'status unknown at Year 18'. A summary of *stage of smoking initiation* is shown below.

Categories of smoking initiation

Stage of smoking initiation	N	Percent
Childhood	68	3.7
Early	488	26.8
Mid	625	34.4
Late	187	10.3
Never by 18y	282	15.5
Status unknown at 18y	168	9.2
Total	1818	100

Alcohol

The alcohol questions used from each study visit are listed below.

Adolescent alcohol use questions

Year	Question asked on survey	Response options
Y11	Have you ever tasted alcohol (for other than religious purposes)?	0, No | 1, Yes
Y11	Have you ever drunk an alcoholic drink? (A drink is defined as one can/bottle of beer, one glass of wine, one tot of liquor, or one mixed drink)	0, No | 1, Yes
Y11	How old, in years, were you the first time you drank alcohol?	Age
Y11	Do you drink alcohol now?	0, No | 1, Yes | 2, Sometimes
Y13	Have you ever tasted alcohol (for other than religious purposes)?	0, No | 1, Yes
Y13	Have you ever drunk an alcoholic drink? (A drink is defined as one can/bottle of beer, one glass of wine, one tot of liquor, or one mixed drink)	0, No | 1, Yes
Y13	How old, in years, were you the first time you drank alcohol?	Age
Y13	Do you drink alcohol now?	0, No | 1, Yes | 2, Sometimes
Y18	Have you ever drunk alcohol for any reason other than religious purposes?	No | Yes
Y18	How old were you when you had alcohol for the first time?	I have never had alcohol Less than 12 years old 12 years old 13 years old 14 years old 15 years old 16 years old 17 years old or older
Y18	In the last month (30 days) have you had alcohol?	No | Yes

Alcohol initiation

Alcohol initiation was defined as an affirmative response to a question about alcohol use. At ages 11 and 13 the question about having an alcoholic drink was part of a skip pattern and was only asked if there was a positive response to, “Have you ever tasted alcohol (for other than religious purposes)?” The question of interest was, "Have you ever drunk an alcoholic drink? (A drink is defined as one can/bottle of beer, one glass of wine, one tot of liquor, or one mixed drink)"

At the age 18 study visit the question was, "Have you ever drunk alcohol for any reason other than religious purposes?" Response values other than 0/1 were set to missing. The age 11 and 13 study visits, missing responses were set to ‘No’ if the respondent reported never having a taste of alcohol. Responses of ‘No’ were set to ‘Yes’ if one of the following conditions was met: 1) a *self-reported age of alcohol initiation* was reported or 2) the respondent reported alcohol use currently (now or in the past 30 days). For example, if a participant reported their age at first alcohol use as 15 but answered ‘No’ to *alcohol initiation*, they have been recoded to have ‘Yes’ for *alcohol initiation*.

Self-reported age at alcohol initiation

This is the participant's first response to an alcohol initiation question. At ages 11 and 13, participants were asked, "How old, in years, were you the first time you drank alcohol?” At the age 18 study visit participants were asked, “How old were you when you had alcohol for the first time?” Questions about alcohol initiation were not asked at the other study waves.

Response options at the Y18 study visit were categorical, though most categories encompassed single years. These categorical responses were set to numeric values. Positive responses to “< 12 years” were assigned values of 11 y. All other responses were assigned numeric values corresponding to the age in the response category. Implausibly high (ages > 2 years above the study visit [e.g. At the age 16 study visit values >18 were set to missing]) and implausibly low (ages < 5y) values were set to missing.

Consistency checks showed responses were largely plausible and reasonable when compared with the study visit year that the respondent reported using alcohol for the first time. *Self-reported age of alcohol initiation* was consistently less than the study visit year where *alcohol initiation* was endorsed for the first time. It is important to use the *self-reported age of alcohol initiation* whenever possible as it is most precise.

Current alcohol use (alcohol use now or in the past 30 days)

Alcohol 30 days was defined as an affirmative response to, a question about recent alcohol use. At the age 11 and 13 study visits the question was, "Do you drink alcohol now?" At the age 18 study visit the question was, "In the last month (30 days) have you had alcohol?" Response values other than 0/1 were set to missing. Because the question about current use always followed the *alcohol initiation* question, responses to the *alcohol 30 days* question were set to 'No' if the response to *alcohol initiation* was 'No'.

Across year summary measures

Following data cleaning within each individual year, the data were cleaned across years to maximize the amount of information for each participant.

For participants who never reported alcohol use, a variable for *last known age of no alcohol use* was created from the participant's exact age at the study visit in which they last answered 'No' to *alcohol initiation*. Where an exact age was unavailable, *last known age of no alcohol use* was set to the corresponding study wave. For example, if a participant last reported never use alcohol at the Y18 study visit but was 19.2 y at the time of the visit, *last known age of no alcohol use* would have been set to 19. Had an exact age been unavailable, *last known age of no alcohol use* would have been set to 17.

Where the participant responded 'Yes' to *alcohol initiation*, but a *self-reported age of alcohol initiation* was not provided, the missing *age of alcohol initiation* was set to the participant's exact age at the study visit in which they first responded 'Yes' to *alcohol initiation*. If the study visit date was missing an exact age could not be calculated the *age of smoking initiation* was set to the corresponding study wave

(e.g. in the absence of a *self-reported age of alcohol initiation* or exact age, the *age of alcohol initiation* was set to 18 if a positive response to *alcohol initiation* was first given at the Y18 study visit). Among participants who reported 'Yes' to *alcohol initiation*, the source of the information for *age of alcohol initiation* is summarized below.

Source of information for age of alcohol use initiation

Alcohol age source	N	Percent
Exact age at visit	31	2.9
Self-reported age	1020	96.3
Study wave	8	0.8
Total	1059	100

The *age of alcohol initiation* and *alcohol initiation* measures were used to derive a categorical measure of alcohol use prior to and across adolescence. If a respondent reported engaging in *alcohol use*, their *age of alcohol initiation* was used to classify their *stage of alcohol initiation* in accordance with the World Health Organization definition (early: 10 to 13 years; mid: 14 to 16 years; late: 17 to 19 years). A respondent's *stage of alcohol initiation* was classified as 'childhood' if they reported initiating alcohol use <10 years.

Individuals who responded 'No' to *alcohol initiation* at the Y18 study visit were classified as 'never alcohol use by Y18'. Individuals who were not seen for a Y18 visit but who reported 'No' to *alcohol initiation* during at least one visit were classified as 'status unknown at Y18'. For example, if an individual reported 'No' to *alcohol initiation* at Y13, but never attended a later visit, they were classified as 'status unknown at Year 18'. A summary of *stage of alcohol initiation* is shown below.

Categories of alcohol use initiation

Stage of alcohol initiation	N	Percent
Childhood	19	1.1
Early	463	26.6
Mid	325	18.7
Late	252	14.5
Never by 18y	409	23.5
Status unknown at 18y	274	15.7
Total	1742	100

Cannabis and Illicit Drug use

The cannabis and illicit drug use questions used from each study visit are listed below.

Adolescent cannabis and illicit drug use questions

Year	Question asked on survey	Response options
Y11	Have you ever used the drug? Marijuana (weed, dagga, grass)	0, No | 1, Yes
Y11	Have you ever used the drug? Cocaine (coke/crack)	0, No | 1, Yes
Y11	Have you ever used the drug? LSD, Mushrooms	0, No | 1, Yes
Y11	Have you ever used the drug? Glue	0, No | 1, Yes
Y11	Have you ever used the drug? Ecstasy	0, No | 1, Yes
Y11	Have you ever used the drug? Mandrax	0, No | 1, Yes
Y13	Have you ever used the drug? Marijuana (weed, dagga, grass)	0, No | 1, Yes
Y13	Have you ever used the drug? Cocaine (coke/crack/rocks)	0, No | 1, Yes
Y13	Have you ever used the drug? LSD, Mushrooms, Acid	0, No | 1, Yes
Y13	Have you ever used the drug? Glue	0, No | 1, Yes
Y13	Have you ever used the drug? Ecstasy	0, No | 1, Yes
Y13	Have you ever used the drug? Mandrax (pinks)	0, No | 1, Yes
Y14	Have you ever used the following drugs? Marijuana (weed, dagga, grass)	No | Yes
Y14	Have you ever used the following drugs? Cocaine (coke/crack/rocks)	No | Yes
Y14	Have you ever used the following drugs? LSD, Mushrooms, Acid	No | Yes
Y14	Have you ever used the following drugs? Sniffing substances such as Glue, Meths, Poppers	No | Yes
Y14	Have you ever used the following drugs? Ecstasy	No | Yes
Y14	Have you ever used the following drugs? Mandrax (pinks)	No | Yes
Y15	Have you ever used the following drugs? Marijuana (weed, dagga, grass)	No | Yes
Y15	Have you ever used the following drugs? Cocaine (coke/crack/rocks)	No | Yes
Y15	Have you ever used the following drugs? LSD, Magic Mushrooms, Acid	No | Yes
Y15	Have you ever used the following drugs? Sniffing Glue, Petrol, Thinners	No | Yes
Y15	Have you ever used the following drugs? Ecstasy	No | Yes
Y15	Have you ever used the following drugs? Mandrax (pinks)	No | Yes
Y17	Have you ever used drugs before?	No | Yes
Y17	Have you ever used the following drugs in the last month (30 days)? Marijuana (weed, dagga, grass)	No | Yes
Y17	Have you ever used the following drugs in the last month (30 days)? Cocaine (coke/crack/rocks)	No | Yes
Y17	Have you ever used the following drugs in the last month (30 days)? LSD, Magic Mushrooms, Acid	No | Yes
Y17	Have you ever used the following drugs in the last month (30 days)? Sniffing Glue, Petrol, Thinners	No | Yes
Y17	Have you ever used the following drugs in the last month (30 days)? Ecstasy	No | Yes
Y17	Have you ever used the following drugs in the last month (30 days)? Mandrax (pinks)	No | Yes
Y18	Have you ever used drugs before?	No | Yes
Y18	Have you ever used the following drugs in the last month (30 days)? Marijuana (weed, dagga, grass, greens)	No | Yes
Y18	Have you ever used the following drugs in the last month (30 days)? Mandrax (buttons)	No | Yes
Y18	Have you ever used the following drugs in the last month (30 days)? Cocaine (crack/rocks)	No | Yes
Y18	Have you ever used the following drugs in the last month (30 days)? LSD (Acid)	No | Yes
Y18	Have you ever used the following drugs in the last month (30 days)? Solvents (Sniffing Glue, Petrol, Thinners)	No | Yes
Y18	Have you ever used the following drugs in the last month (30 days)? Ecstasy	No | Yes

Cannabis initiation

Cannabis initiation was defined as an affirmative response to a *cannabis initiation* question at ages 11, 13, 14, and 15 study visits. At the age 11, 13, 14, and 15 study visits, questions were asked about 'ever use' of specific drugs, including cannabis (e.g. at age 13, "Have you ever used the drug? Marijuana (weed, dagga, grass)"). The age 16 study visit asked about cannabis use in the past 30 days but did not ask about 'ever' cannabis use. The age 17 and 18 study visits used a skip pattern asking about *illicit drug use initiation* and if respondents answered 'Yes' they were asked additional questions about the use of specific drugs in the past 30 days, including cannabis. Because of the different time scales (ever vs. 30 days), only the information from the Y11, 13, 14, and 15 study visits was used. Response values other than 0/1 were set to missing.

Illicit drug use initiation

At the age 11, 13, 14, and 15 study visits, questions were asked about ever using specific drugs (e.g. at age 13, " Have you ever used the following drugs? Cocaine (coke/crack/rocks) "). While the list of drugs enquired about evolved over time, analysis was restricted to drugs for which longitudinal data were available. These included inhalants/glue, ecstasy, Mandrax (Quaaludes), cocaine, and LSD. At the age 17 and 18 study visits, *illicit drug use initiation* was asked about explicitly, "Have you ever used drugs before?" The age 16 study visit contained questions about drug use in the past 30 days but did not contain any questions about 'ever' drug use.

Illicit drug use initiation was defined as an affirmative response to at least one question about ever use of inhalants/glue, ecstasy, Mandrax (Quaaludes), cocaine, or LSD use at ages 11, 13, 14, and 15 or an affirmative response to *illicit drug use initiation* at the age 17 and 18 study visits. Response values other than 0/1 were set to missing.

Calculated age of first cannabis use

Age of cannabis use initiation was not asked on the surveys. Therefore, *calculated age of first cannabis* use was derived from the respondent's exact age the first time they answered 'Yes' to a question

about *cannabis initiation*. Where an exact age was unavailable, *calculated age of first cannabis use* was set to the corresponding study year.

Calculated age of first drug use

Age of drug use initiation was not asked on the surveys. Therefore, *calculated age of first drug use* was derived from the respondent's exact age the first time they answered 'Yes' to a question about *illicit drug use initiation*. Where an exact age was unavailable, *calculated age of first drug use* was set to the corresponding study year.

Across year summary measures

Following data cleaning within each individual year, the data were cleaned across years to maximize the amount of information for each participant.

For participants who never reported cannabis use, a variable for *last known age of no cannabis use* was created from the participant's exact age at the study visit in which they last answered 'No' to *cannabis initiation*. Similarly, for participants who never reported drug use, a variable for *last known age of no drug use* was created from the participant's exact age at the study visit in which they last answered 'No' to *illicit drug use initiation*. For both measures, where an exact age was unavailable the corresponding study wave was used. For example, if a participant last reported never having used drugs at the Y17 study visit but was 18.2 y at the time of the visit, *last known age of no drug use* was set to 18. Had an exact age been unavailable, *last known age of no drug use* would have been set to 17.

Among participants who answered 'Yes' to *cannabis initiation* or *illicit drug use initiation*, the source of the information for *calculated age of cannabis initiation* and *calculated age of drug use* is summarized below.

Source of information for age of cannabis use initiation

Cannabis age source	N	Percent
Exact age at visit	230	61.8
Study wave	142	38.2
Total	372	100

Source of information for age of drug use initiation

Illicit drugs age source	N	Percent
Exact age at visit	344	84.7
Study wave	62	15.3
Total	406	100

The *calculated age of first cannabis use* and *ever cannabis* measures were used to derive a categorical measure of cannabis use across adolescence. If a respondent reported using cannabis, their *calculated age of first cannabis use* was used to classify their *stage of cannabis initiation* in accordance with the World Health Organization definition (early: 10 to 13 years; mid: 14 to 16 years). Individuals who responded 'No' to *cannabis initiation* at the Y15 study visit were classified as 'never cannabis use by Y15'. Individuals who were not seen for a Y15 visit but who reported 'No' to *cannabis initiation* during at least one visit were classified as 'status unknown at Y15'. For example, if an individual reported 'No' to *cannabis initiation* at Y13, but never attended a later visit, they were classified as 'status unknown at Y15'. A summary of *stage of cannabis initiation* is shown below.

Categories of cannabis use initiation

Stage of cannabis initiation	N	Percent
Early	43	2.4
Mid	329	18.6
Never by 15y	1034	58.5
Status unknown at 15y	361	20.4
Total	1767	100

The *calculated age of first illicit drug use* and *illicit drug use initiation* measures were used to derive a categorical measure of illicit drug use across adolescence. If a respondent reported using illicit drugs, their *calculated age of first illicit drug use* was used to classify their *stage of illicit drug use initiation* in accordance with the World Health Organization definition (early: 10 to 13 years; mid: 14 to 16 years; late: 17 to 19 years). Individuals who responded 'No' to *illicit drug use initiation* at the Y18 study visit were classified as 'never illicit drug use by Y18'. Individuals who were not seen for a Y18 visit but who reported 'No' to *illicit drug use initiation* during at least one visit were classified as 'status unknown at Y18'. For example, if an individual reported 'No' to *illicit drug use initiation* at Y17, but

never attended a later visit, they were classified as 'status unknown at Year 18'. A summary of *stage of illicit drug use initiation* is shown below.

Categories of illicit drug use initiation

Stages of illicit drug use initiation	N	Percent
Early	29	1.6
Mid	203	11.3
Late	174	9.7
Never by 18y	1059	58.8
Status unknown at 18y	336	18.7
Total	1801	100

Sexual activity

Sex items consisted of three types of questions, initiation, age of first intercourse, and intercourse in the past 30 days. The sex questions used from each study visit are listed below.

Adolescent sexual activity questions

Year	Question asked on survey	Response options
Y11	Have you ever had sex (made love, gone all the way, penis inserted into vagina or anus)?	0, No | 1, Yes
Y11	How old were you in years when you had sex the first time?	Age
Y13	Have you ever had sex (made love, gone all the way, penis inserted into vagina or anus)?	0, No | 1, Yes
Y13	How old were you in years when you had sex the first time?	Age
Y14	Have you ever had sex (made love, gone all the way, penis inserted into vagina or anus)?	No | Yes
Y14	How old were you in years when you had sex?	Age
Y15	Have you ever had sex (made love, gone all the way, penis inserted into vagina or anus)?	No | Yes
Y15	How old were you in years when you had sex?	Age
Y15	Have you had sex in the last month (made love, gone all the way, penis inserted in vagina or anus)?	No | Yes
Y16	Have you ever had sex (made love/ gone all the way/ penis inserted into vagina or anus)?	No | Yes
Y16	How old were you in years when you had sex?	Age
Y16	Have you had sex in the last month (made love, gone all the way, penis inserted in vagina or anus)?	No | Yes
Y17	Have you ever had sex (made love/ gone all the way/ penis inserted into vagina or anus)?	No | Yes
Y17	How old were you in years when you had sex?	Age
Y17	Have you had sex in the last month (made love, gone all the way, penis inserted in vagina or anus)?	No | Yes
Y18	Have you ever had sex (made love/ gone all the way/ penis inserted into vagina or anus)?	No | Yes
Y18	How old were you in years when you had sex?	Age
Y18	Have you had sex in the last month (made love, gone all the way, penis inserted in vagina or anus)?	No | Yes

Sexual activity initiation

Sexual activity initiation was defined as an affirmative response to, "Have you ever had sex (made love/ gone all the way/ penis inserted into vagina or anus)?" Response values other than 0/1 were set to missing. Responses of 'No' were set to 'Yes' if one of the following conditions was met: 1) *self-reported age of sexual activity* was reported or 2) the respondent reported having sex in the past 30 days. For example, if a participant reported their age at first sex as 15 y but answered 'No' to *ever sex*, their response to *sexual activity initiation* was recoded as 'Yes'.

Self-reported age at sexual initiation

This is the participant's first response to, "How old were you in years when you had sex?" Implausibly high (ages > 2 years above the study visit [e.g. At the age 16 study visit values >18 were set to missing]) and implausibly low (ages < 5y) values were set to missing. Participants with an *age of sexual initiation* less than 12 years of age were excluded from all analyses involving risk behavior outcomes, as this is below the legal age of consent in South Africa. When checked for consistency, the *self-reported age of first sex* was reasonably consistent when compared with the wave at which the participant first said 'Yes' to *ever sex*.

Sex in the past 30 days

Sex 30 days was defined as an affirmative response to, "Have you had sex in the last month (made love, gone all the way, penis inserted in vagina or anus)?" Response values other than 0/1 were set to missing. Because *sex 30 days* always followed *ever sex*, responses to *sex 30 days* were set to 'No' if the response to *ever sex* was 'No'.

Across year summary measures

Following data cleaning within each individual year, the data were cleaned across years to maximize the amount of information for each participant.

For participants who never reported having sex, a variable for *last known age of no sex* was created from the participant's exact age at the study visit in which they answered 'No' to *ever sex*. Where

an exact age was unavailable, *last known age of no sex* was set to the corresponding study wave. For example, if a participant last reported never having had sex at the Y17 study visit but was 18.2 y at the time of the visit, *last known age of no sex* would have been set to 18 y. Had an exact age been unavailable, *last known age of no sex* would have been set to 17 y.

Where the participant responded 'Yes' to *ever sex*, but a *self-reported age at first sex* was not provided, the missing *age of sexual initiation* was set to the participant's exact age at the study visit in which they first responded 'Yes' to *ever sex*. If the study visit date was missing an exact age could not be calculated the *age of sexual initiation* was set to the corresponding study wave (e.g. in the absence of a *self-reported age at first sex* or exact age, the *age of sexual initiation* was set to 15 y if a positive response to *ever smoke* was first given at the Y15 study visit. If the *age of first pregnancy* preceded *age of sexual initiation*, *age of sexual initiation* was set to the *age of first pregnancy*. Among participants who reported 'Yes' to *ever sex*, the source of the information for *age of sexual initiation* is summarized below.

Source of information for age of sex initiation

Sexual activity age source	N	Percent
Age of first pregnancy	69	5.7
Exact age at visit	57	4.7
Self-reported age	1049	87
Study wave	31	2.6
Total	1206	100

The *age of sexual initiation* and *ever sex* measures were used to derive a categorical measure of sexual activity prior to and across adolescence. If a respondent reported having sex, their *age of sexual initiation* was used to classify their *stage of sexual initiation* in accordance with the World Health Organization definition (early: 10 to 13 years; mid: 14 to 16 years; late: 17 to 19 years). Individuals who responded 'No' to *ever sex* at the Y18 study visit were classified as 'never sex by Y18'. Individuals who were not seen for a Y18 visit but who reported 'No' to *ever sex* during at least one visit were classified as 'status unknown at Y18'. For example, if an individual reported 'No' to *ever sex* at Y15, but never attended a later visit, they were classified as 'status unknown at Year 18'. A summary of *stage of sexual initiation* is shown below.

Categories of sexual activity initiation

Stage of sexual activity initiation	N	Percent
Early	104	6
Mid	636	37
Late	466	27.1
Never by 18y	320	18.6
Status unknown at 18y	195	11.3
Total	1721	100

Adolescent Pregnancy

Adolescent pregnancy data came from two sources, responses on the self-complete questionnaire and from a Bt20+ pregnancy and live birth surveillance system (third generation or 3G surveillance system). Pregnancy questions from the self-complete questionnaire are listed below.

Adolescent pregnancy questions

Year	Question asked on survey	Response options
Y15	Have you ever been pregnant?	No | Yes
Y16	Have you ever been pregnant?	No | Yes
Y17	Have you ever been pregnant?	No | Yes
Y18	Have you ever been pregnant?	No | Yes

Adolescent pregnancy

Ever pregnant was defined as an affirmative response to, "Have you ever been pregnant?" which was asked at the age 16, 17, and 18 study visits or an age of first pregnancy captured in the surveillance system. Male responses to this question were set to missing. Response values other than 0/1 were set to missing. Responses of 'No' were set to 'Yes' if an age of pregnancy was recorded in the surveillance system. For example, if a participant had a recorded *age of first pregnancy* of 17 but did not attend the Y17 study visit, their response to *ever pregnant* was set to 'Yes' at Y17. When compared to *self-reported age of first sex* to check for consistency, the majority of women reported their sexual debut occurring prior to reporting a pregnancy.

Across year summary measures

Following data cleaning within each individual year, the data were cleaned across years to maximize the amount of information for each participant.

For participants who never reported having been pregnant, a variable for *last known age of no pregnancy* was created from the participant's exact age at the study visit in which they answered 'No' to *ever pregnant*. Where an exact age was unavailable, *last known age of no pregnancy* was set to the corresponding study wave. For example, if a participant last reported having never been pregnant at the Y17 study visit but was 18.2 y at the time of the visit, *last known age of no pregnancy* would have been set to 18. Had an exact age been unavailable, *last known age of no pregnancy* would have been set to 17.

Age of adolescent pregnancy

Age of adolescent pregnancy was not asked at any of the study visits. *Age at adolescent pregnancy* was derived from the surveillance system, the women's exact age at the study visit at which she reported having been pregnant, or the year of the study visit. Between the age recorded in the surveillance system and the exact age at the study visit, the younger age was retained. If the participant was not in the surveillance system, the exact age from the first study visit in which she reported having ever been pregnant was used. If the exact age was not available, the study wave was used. Among participants recorded as having been pregnant, the source of the information for their age of adolescent pregnancy is summarized below.

Source of information for age of adolescent pregnancy

Adolescent pregnancy age source	N	Percent
3G surveillance age	206	69.4
Exact age at visit	53	17.8
Study wave	38	12.8
Total	297	100

The *age of adolescent pregnancy* and *ever pregnant* measures were used to derive a categorical measure of pregnancy prior to and across adolescence. If a respondent reported having been pregnant, their *age of adolescent pregnancy* was used to classify their *stage of adolescent pregnancy* in accordance with the World Health Organization definition (early: 10 to 13 years; mid: 14 to 16 years; late: 17 to 19 years). Individuals who responded 'No' to *ever pregnant* at the Y18 study visit were classified as 'never pregnant by Y18'. Individuals who were not seen for a Y18 visit but who reported 'No' to *ever pregnant*

during at least one visit were classified as ‘status unknown at Y18’. For example, if an individual reported ‘No’ to *ever pregnant* at Y15, but never attended a later visit, they were classified as ‘status unknown at Year 18’. A summary of *stage of adolescent pregnancy* is shown below.

Categories of age of adolescent pregnancy

Stage of adolescent pregnancy	N	Percent
Early	2	0.2
Mid	71	8.1
Late	224	25.5
Never by 18y	484	55
Status unknown at 18y	99	11.2
Total	880	100

Young Adult Measures

This section describes relevant measures that were used from the young adult data collection wave at age 22 y.

Young adult pregnancy

Young adult pregnancy, defined as pregnancy from age 19 to 22 y, was derived from the adolescent pregnancy variables previously defined and the number of pregnancies self-reported at age 22 y. In this approach we assumed females who reported an adolescent pregnancy were only pregnant once during adolescence. This may have introduced some misclassification if a female had multiple adolescent pregnancies, however this seemed like a reasonable assumption given the median age of adolescent pregnancy was 17.6 y.

Categories of schooling attainment

We used schooling qualification data collected at age 22 y to create ordinal categories of schooling attainment: <matric, matric, and some university schooling. Matric is equivalent to a high school diploma in the South African context and is required for university studies.

Categories of employment

We used current employment status at age 22 y to create ordinal categories of employment (i.e. if an individual was currently unemployed, we did not consider their most recent job). Among employed

individuals, we further used contract type (casual/contract/permanent) to classify individual into ordinal categories of employment: unemployed, currently employed casually or with a short-term contract, or currently employed with a permanent contract.

Extended Analytical Methods

Research Aim 1. Describe smoking, alcohol, cannabis, illicit drug, and sexual initiation from ages 10 to 18 y, persistence at age 18 y, and patterns of initiation.

Relevant Measures

This analysis used data from the age 0-2, 5, 7, 11, 13, 14, 15, 16, 17, and 18 y study waves corresponding to the pre-puberty and adolescent periods. The pre-puberty measures included: maternal age at birth, years of schooling, and marital status, tertiles of household asset ownership at ages 0-2 and 7 y, and categories of childhood stress exposure. The adolescent measures included: smoking, alcohol use, cannabis use, illicit drug use, sexual activity, and adolescent pregnancy among females.

Analytical sample

We excluded cohort members from non-Black African population groups (22% of the cohort) who comprise a small proportion of the population in Soweto-Johannesburg. Of the N = 2568 Black African participants enrolled in the cohort, N = 1822 attended at least one study visit during adolescence and contributed information for at least one risk behavior of interest. We excluded individuals who reported sexual activity prior to age 12 y from the sexual activity and pregnancy analyses as this was before the legal age of consent (N = 82). To maximize sample sizes, we retained participants with data on any of the measures of interest in the analytical dataset; therefore, the sample sizes vary by measure.

Statistical analysis

Risk behavior descriptive analyses

Combining data from individual data waves, we fit Kaplan-Meier curves for each behavior to estimate the probability of "surviving" to age 19 y without initiating a behavior. We considered the first

report of use or activity as an event. If individuals did not report an event, they were censored using their age at the last study visit they attended. In Supplemental Table 2 we summarize the numbers of individuals at risk of initiating a behavior at each year. We used chi-square tests to examine associations between stage of risk behavior initiation and current use or activity at 18 y.

Cluster analysis and risk behavior profiles

We conducted a hierarchical agglomerative cluster analysis among individuals with a known status for each behavior of interest. We used Gower's method to calculate the dissimilarity matrix between individuals based on risk behavior stage of initiation, applied Ward's method to evaluate the similarity between clusters and determine which clusters to combine at each iteration, and calculated a series of fit indices using the NbClust R package (22, 23). For females, a three-cluster solution was indicated by a majority of the fit statistics. Although a two-cluster solution was indicated by the same criterion among males, the addition of a third cluster meaningfully differentiated an additional subgroup of adolescents by subdividing the first cluster into two without crossover from the other cluster (Supplemental Tables 3). We examined associations of sociodemographic characteristics with cluster membership.

Sensitivity analysis

We compared demographic characteristics of individuals included in the analytical sample to those who were excluded to assess potential bias due to attrition prior to adolescence, nonresponse to the risk behavior questions, or reported sexual activity before the age of consent. We compared individuals included in the cluster analysis to individuals with incomplete information to assess selection bias in the cluster analysis. All analyses were sex-specific and conducted using R version 3.5.3 (24). We considered two-sided p-values <0.05 statistically significant.

Research Aim 2. Examine associations of pubertal timing and tempo with measures of adolescent mental health and health risk behavior initiation and examine the consistency of associations by level of childhood stress.

Relevant Measures

This analysis used data from the age 0-2, 5, 7, 11, 13, 14, 15, 16, 17, and 18 y study waves corresponding to the pre-puberty and adolescent periods. The pre-puberty measures included: tertiles of household asset ownership at age 0-2 y, tertiles of household asset ownership at age 7 y, categories of childhood stress exposure, height-for-age z-score at ages 5 and 8 y, and body mass index z-score at ages 5 and 8 y. The adolescent measures included: genital/breast development latent classes, pubic hair development latent classes, age of menarche, patterns of adolescent risk behavior initiation, sociobehavioral adjustment, and eating attitudes.

Analytical sample

We restricted our analytical sample to Black African cohort members for whom we were able to calculate a pubertal development trajectory (N = 1,784). We allowed the sample size to vary for each outcome to use all available data and maximize sample sizes.

Statistical analysis

We examined descriptive characteristics of the sample by sex. We examined the associations of pubertal development trajectories and age of menarche with health risk behavior cluster; affective, anxiety, somatic, attention deficit, oppositional defiant, and conduct problems; and eating attitudes in sex-specific unadjusted and adjusted models, with separate models for each exposure (sex development trajectory, pubic hair development trajectory, and age of menarche among females) with each outcome. For the pubertal development trajectories, we considered the largest class, class 2, as the referent group.

To examine associations with health risk behavior cluster we used multinomial logistic regression which is appropriate when the dependent variable has >2 nominal categories. We considered health risk behavior initiation cluster as a nominal outcome with cluster 1 (low-risk) as the referent group. The

exponentiated beta coefficients can be interpreted as odds ratios of the odds of being classified in health risk behavior 3 compared to health risk behavior 1 and the odds of being classified in health risk behavior 2 compared to health risk behavior cluster 1. To examine associations with affective, anxiety, somatic, attention deficit, oppositional defiant, conduct problems, and eating attitudes we used linear regression with problem score as a continuous outcome. In adjusted models we controlled for household socioeconomic position in early life and childhood and exposure to stress in childhood. Height-for-age z-score and body mass index z-score at ages 5 and 8 y were not consistently associated with the outcomes or exposure and therefore were not adjusted for.

Psychosocial vulnerabilities established prior to puberty have been shown to interact with pubertal timing (25). As such, we assessed heterogeneity of the pubertal timing and tempo estimates across categories of childhood stress by examining interaction p-values. We conducted 42 statistical tests of interaction among males, 2.1 of which would be expected to be significant by chance and 66 statistical tests of interaction among females, 3.3 of which would be expected to be significant by chance, assuming 95% confidence. We observed 3 statistically significant tests of interaction among males and 2 among females. Upon reviewing stratified estimates, the number of significant tests of interaction did not exceed the number expected to occur by chance, therefore we do not present these estimates in the main results.

All analyses were conducted using R version 3.5.3 and we considered two-sided p-values <0.05 statistically significant (24).

Research Aim 3. Examine associations of pubertal timing and tempo with schooling attainment and employment status at age 22 y and explore the mediating role of adolescent health risk behavior initiation and pregnancy.

Relevant Measures

This analysis used data from the age 0-2, 5, 7, 11, 13, 14, 15, 16, 17, 18, and 22 y waves corresponding to the pre-puberty, adolescence, and young adult periods. The pre-puberty measures included: tertiles of household asset ownership at age 0-2 y, tertiles of household asset ownership at age 7

y, categories of childhood stress exposure, and tertiles of non-verbal fluid intelligence score. The adolescent measures included: genital/breast development latent classes, pubic hair development latent classes, age of menarche, early menarche, patterns of adolescent risk behavior initiation, and adolescent pregnancy. The young adult measures included: 19-22 y pregnancy, categories of schooling attainment, and categories of employment.

Analytical sample

We restricted our analysis to N = 1,784 Black African participants for whom we have pubertal development trajectories. To maximize the available data, we allowed the sample size to vary for each dependent variable.

Statistical analysis

Using chi-square tests, we examined covariate and dependent variable characteristics by pubertal development classes and age of menarche.

We examined the associations between the independent pubertal development variables and dependent adolescent and young adult variables using structural equation models. We considered genital/breast development latent classes, pubic hair development, and age of menarche (for girls) as independent variables in separate models. Compared to their peers in other latent classes, individuals in class 1 entered puberty later and progressed through puberty slower, while individuals in the highest class had the earliest pubertal timing and fastest tempo. In models with latent class as the independent variable, we set class 2 as the referent group. We considered adolescent risk behavior initiation, adolescent pregnancy, young adult pregnancy, schooling attainment, and employment as dependent variables. We considered the pre-puberty measures as covariates. For each pre-puberty measure individuals missing values were assigned to a formal ‘missing’ category so individuals with missing covariate data would not be listwise deleted from models.

We used generalized structural equation models to estimate these associations. In specifying the model, we considered the binary (adolescent pregnancy, young adult pregnancy) and ordinal (risk

behavior, schooling, and employment) dependent variables as continuous latent variables using Bernoulli and ordinal probit link functions as appropriate. We used diagonal weighted least squares estimation with 1000 bootstraps and pairwise deletion to fit the model using the 'lavaan' package in R (26). In pairwise deletion we use observations for which both values are observed to compute the appropriate polychoric, polyserial, or Pearson correlations using two variables at a time; this number may vary from pair to pair. We adjusted models for prepubertal characteristics: age 0-2 asset ownership, age 7 asset ownership, child stress exposure, and non-verbal fluid intelligence. All analyses were conducted using R version 3.5.3 with two-sided p-values <0.05 statistically significant (24).

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Chapter 4: Initiation and persistence of health risk behaviors through adolescence in urban South Africa

Manuscript Authors: Alysse J. Kowalski, O. Yaw Addo, Michael R. Kramer, Reynaldo Martorell, Shane A. Norris, Rachel N. Waford, Linda M. Richter*, Aryeh D. Stein*

*Co-senior authors

Abstract

Purpose

To characterize longitudinal patterns of health risk behavior initiation and persistence among urban South African adolescents.

Methods

Birth to Twenty Plus is a longitudinal birth cohort in Soweto-Johannesburg, South Africa. We used reports from Black African participants on smoking, alcohol, cannabis, illicit drugs, and sexual activity and on adolescent pregnancy collected over 7 study visits between ages 11 and 18 y. We fit Kaplan-Meier curves to estimate behavior initiation or adolescent pregnancy, examined current behavior at age 18 y by age of initiation, and performed a clustering analysis to identify patterns of initiation and their sociodemographic predictors.

Results

By age 13 y, cumulative incidence of smoking and alcohol initiation were each >21%, while the cumulative incidence of other behaviors and adolescent pregnancy were <5%. By age 18 y, smoking, alcohol, and sexual activity initiation estimates were each >65%, cannabis (age 15 y) and illicit drug initiation were each >16%; adolescent pregnancy was 31%. At both ages, rates of initiation were higher among males. At age 18 y, current risk behavior activity was lower than lifetime activity and generally unrelated to age of initiation. We identified three clusters reflecting low, moderate, and high-risk patterns of risk behavior initiation. One-third of males and 17% of females were assigned to the high-risk cluster. Sociodemographic factors were not associated with cluster membership.

Conclusions

Among urban dwelling Black South Africans, risk behavior experimentation across adolescence is common and clusters into distinct initiation patterns unrelated to the sociodemographic factors assessed.

Implications and Contribution

The present study demonstrated distinct patterns of risk behavior initiation across adolescence among urban South Africans. Understanding these patterns has implications for the timing of primary and secondary public health interventions and supports integrated prevention efforts that consider multiple behaviors simultaneously.

Introduction

During adolescence, defined by the WHO as ages 10-19 y, the development of the reward and pleasure centers in the brain contributes to risk-taking and sensation-seeking, rendering a degree of experimentation a normative attribute of adolescence (1, 2). Six of the ten leading risk factors of morbidity and mortality among young people ages 15-19 y, and three of the ten among young people age 10 to 14 y, are behavioral, including smoking, alcohol use, drug use, and unsafe sex (3). When established in adolescence, behavioral risk factors have consequences that extend into adulthood. Early tobacco use increases the risk of regular tobacco and cannabis use, use of hard drugs and drug problems, alcohol problems, and early pregnancy (4-7). Earlier age of first alcohol use predicts alcohol abuse and lifetime dependence and other substance use (5, 8-12). Earlier sexual debut increases the number of sexual partners and risk of pregnancy and STIs including HIV (13).

There is a longstanding interest in risk behavior co-occurrence, but far less is known about patterns of risk behavior initiation. This is important because different risk behaviors are initiated at different times; some may act as gateways to other behaviors, and the acceptability of risk behaviors changes over adolescence. To better understand patterns of risk behavior initiation across adolescence requires longitudinal data to consider multiple risk behaviors simultaneously to identify subgroups of individuals with similar patterns of risk behavior engagement (14-16). Previous work has generally examined either multiple behaviors at a single time point or a single behavior at multiple time points. Studies examining multiple behaviors at a single time point cannot account for changes in risk behavior co-occurrence over time (14, 15). Studies examining a single behavior over multiple time points often use latent class growth analysis to provide a detailed understanding of that behavior but do not account for co-occurrence (17-19).

This work has several implications for public health policy makers and practitioners. Improved understanding of patterns of risk behavior initiation would allow for better timing of primary prevention

efforts intended to prevent risk behavior initiation and secondary prevention efforts to mitigate risk behaviors once begun.

Despite being home to 90% of the world's adolescents, there is a paucity of longitudinal data on adolescent health from low and middle-income countries (20). To improve our understanding of health risk behaviors among adolescents in urban South Africa, we describe longitudinal patterns of smoking, alcohol, cannabis, illicit drug, and sexual activity initiation and of adolescent pregnancy; examine current behavior at age 18 y by stage of initiation; and use clustering analysis to characterize patterns of risk behavior initiation.

Methods

Birth to Twenty Plus (Bt20+) cohort

Birth to Twenty Plus (Bt20+) is an observational birth cohort in Soweto-Johannesburg, South Africa. The study enrolled singleton children born between April and June 1990 who resided in the municipal area for a minimum of 6 months after birth (N = 3273). Almost 70% of cohort members were still traceable when they were age 17 y, with the majority of attrition occurring during the preschool years (21).

Ethical approval

Ethical clearance for this study was provided by the University of the Witwatersrand Human Research Ethics Committee for Research on Human Subjects and the Emory University Institutional Review Board.

Data collection

We used data from 7 waves of data collected in adolescence (we refer to these as the age 11, 13, 14, 15, 16, 17, and 18 y study visits) and pregnancy data through age 18 y from ongoing pregnancy and live birth surveillance. Study visits were completed at the Developmental Pathways for Health Research Unit at Chris Hani Baragwanath Hospital in Soweto. Data were collected by interview or using self-

administered questionnaires. Self-administered questionnaires were completed on paper at the Year 11, 13, and 14 study visits, and using an audio computer-aided self-administered interview (CASI) system at ages 15, 16, 17, and 18 y.

Risk behaviors

The risk behaviors of interest include smoking, alcohol use, cannabis use, illicit drug use, and sexual activity. Questions were adapted from the US and South African Youth Risk Behavior Surveys, with additional items developed specifically for the study (22, 23). Questions on smoking and sexual activity were asked at all adolescent study visits; alcohol use at ages 11, 13, and 18 y; cannabis use from age 11 to 15 y; and illicit drug use at ages 11, 13, 14, 15, 17 and 18 y. For each risk behavior, data were captured on three aspects: 1) risk behavior initiation; 2) age of initiation; and 3) use or activity in the past month as of the age 18 y study visit.

Risk behavior initiation

We defined risk behavior initiation as an affirmative response to a Yes/No question about ever engaging in a behavior. We defined *illicit drug use initiation* as an affirmative response to at least one question about ever use of five drugs for which repeated measures were available (inhalants/glue, ecstasy, mandrax (Quaaludes), cocaine, or LSD) at ages 11, 13, 14, and 15 y or an affirmative response to any lifetime drug use at the age 17 and 18 y study visits.

Age of initiation

We defined *age of initiation* using the age of first engagement reported by the Bt20+ participant. If this was unavailable, we used the individual's age at the time of the study visit or, if this could not be calculated from the date of the visit and the date of birth, we assigned the age corresponding to the year of study visit (Supplemental Table 1). Age of initiation was not asked for cannabis and illicit drug use. For these behaviors we assigned the respondent's exact age or the age corresponding to the study year the first time these were reported. For all behaviors we set implausible ages of initiation (ages > 2 years above the study visit OR ages < 5 y) to missing. We categorized individuals as initiating a behavior in childhood

(<11 y), early (11-13 y), mid (14-16 y), or late adolescence (17-18 y), never at age 18 y, and status unknown at age 18 y (2).

Current activity at age 18 y

We defined current activity at 18 y as an affirmative response to a Yes/No question about use or activity in the past 30 days.

Adolescent pregnancy

We defined adolescent pregnancy as an affirmative response to the pregnancy history question, first asked at age 15 y, or having report of pregnancy through age 18 y in the surveillance system. We defined age of adolescent pregnancy using the age captured in the surveillance system, the respondent's exact age at the study visit, or the age corresponding to the study year, in that order.

Sociodemographic characteristics

Maternal age at birth, years of schooling, and marital status were collected at enrollment into the study. We used tertiles of the number of household assets owned as a measure of socioeconomic position in early life (using data from age 0-2 y) and in childhood (using data from age 7 y supplemented with data from age 5 y).

At the age 0-2, 5, and 7 y study visits mothers were asked about stress and violence events experienced in the past six months. We characterized childhood exposure to stress as the number of study waves at which the mother reported more than the sample median number of events.

Data management and preparation

Analytical sample

We excluded cohort members from non-Black African population groups (22% of the cohort) who comprise less than 10% of the population in Soweto-Johannesburg. Of the 2,568 Black African participants enrolled in the cohort, 1,822 attended at least one study visit during adolescence and contributed information for at least one risk behavior of interest. We excluded 82 individuals who

reported sexual activity prior to age 12 y from the sexual activity and pregnancy analyses as this was before the legal age of consent. To maximize sample sizes, we retained participants with data on any of the measures of interest in the analytical dataset; therefore, the sample sizes vary by measure (Supplemental Figure 1, Supplemental Table 2).

Risk behavior descriptive analyses

We fit Kaplan-Meier curves for each behavior to estimate the probability of reaching age 19 y without initiating that behavior. Individuals who did not report an event were censored using their age at the last study visit they attended. We examined current behavior activity at age 18 y and used chi-square tests to examine associations between stage of risk behavior initiation and current activity at 18 y.

Cluster analysis and risk behavior profiles

We conducted a hierarchical agglomerative cluster analysis among 1,126 individuals for whom status was known for all risk behaviors. We used Gower's method to calculate the dissimilarity matrix between individuals based on stage of initiation and applied Ward's method to evaluate the similarity between clusters and determine which clusters to combine at each iteration, and calculated a series of fit indices using the NbClust R package (24, 25). For females, a three-cluster solution was indicated by a majority of the fit statistics. Although a two-cluster solution was indicated by the same criterion among males, the addition of a third cluster meaningfully differentiated an additional subgroup of adolescents by subdividing the first cluster into two, without crossover from the other cluster (Supplemental Tables 3). We examined associations of sociodemographic characteristics with cluster membership.

Sensitivity analysis

We compared demographic characteristics of individuals included in the analytical sample to those who were excluded to assess potential bias due to attrition prior to adolescence, nonresponse to the risk behavior questions, or reported sexual activity before the age of consent. We compared individuals included in the cluster analysis to individuals with incomplete information to assess selection bias in the cluster analysis.

All analyses were sex-specific and conducted using R version 3.5.3 (26). We considered two-sided p-values <0.05 statistically significant.

Results

Sample characteristics

Study participant's mothers were in their mid-twenties and had 9.58 (2.74) years of schooling on average at enrollment, and 66% were single (Table 1). Among Black African participants, those included in the study were born to mothers with an additional year of schooling and who were more likely to be single than those who were excluded. Most excluded individuals were lost to follow-up early in the study and therefore have no information from later study waves.

Cumulative risk behavior initiation by age and stage of adolescence

Kaplan-Meier curves for the probability of "surviving" adolescence without initiating a risk behavior are summarized in Figure 1. By the end of adolescence (age 18 y), estimates of smoking, alcohol, and sexual activity initiation each exceeded 75% and illicit drug use exceeded 30% among males. Patterns were similar among females, but rates of initiation were slightly lower. By age 13 y, estimates of smoking and alcohol initiation were 41.6% and 34.5% among males, respectively and 21.1% and 23.1% among females, respectively. Among both sexes, cannabis use was predominantly initiated in mid-adolescence and drug use initiated in mid- and late adolescence.

Current risk behavior engagement at age 18 y and stage of initiation

Current substance use and sexual activity reported at age 18 y was lower than lifetime use for all behaviors (Table 2). Individuals who first used illicit drugs in late adolescence were twice as likely to report current drug use at age 18 y as compared to individuals who first used illicit drugs earlier in adolescence (64% late vs 33% early among males and 37% late vs 11% early among females) (Table 2). Males who started smoking in late adolescence were less likely to be current smokers at age 18 y than males who started smoking in early adolescence (29% late vs 52% early).

Cluster analysis and risk behavior profiles

We identified a three-cluster solution in which the clusters represent different patterns of risk behavior initiation in adolescence and reflect groups of adolescents with low, moderate, and high-risk patterns based on initiation in a given stage of adolescence within a cluster compared to overall initiation (Figure 2). The high-risk cluster (33% of males and 17% of females) includes individuals who reported risk behavior initiation at rates higher than the group mean. Individuals initiating illicit drug or cannabis use in early or mid-adolescence were almost exclusively classified in the high-risk cluster. Individuals in the moderate risk cluster (33% of males and 60% of females) initiated smoking, alcohol, and sexual activity at rates higher than the group mean in adolescence and did not use cannabis. The remaining individuals were in the low-risk cluster (33% of males and 23% of females) and initiated risk behaviors at rates below the group mean. When these individuals did initiate a behavior, it tended to be in late adolescence. For example, none of the females in the low-risk cluster reported smoking in early or mid-adolescence and 15% reported initiating smoking in late adolescence in comparison to the mean group initiation rates of 20% in early, 37% in mid, and 14% in late adolescence. Females in the moderate and high-risk clusters had similar rates of sexual initiation by age 18 y, though females in the high-risk cluster were more likely to initiate sex in mid-adolescence. Rates of adolescent pregnancy were higher among females in the high-risk cluster compared to females in the low and moderate risk clusters (47% high vs 35% moderate and 19% low). None of the sociodemographic factors examined were associated with cluster membership (Table 3).

Sensitivity analysis

Individuals were required to have a known status at age 18 y for the five behaviors of interest to be included in the cluster analysis. Individuals included in the cluster analysis did not differ from their excluded peers on sociodemographic characteristics including sex, household asset ownership in early life and childhood, and childhood exposure to stress and violence. Percent initiation was comparable between the included and excluded groups in childhood and early adolescence but excluded individuals more

likely to have an unknown status at age 18 y as individuals were lost to follow-up over the course of adolescence (Supplemental Table 4).

Discussion

In this cohort of urban dwelling Black African adolescents, risk behavior experimentation was common and clustered into three distinct profiles that reflect low, moderate, and high-risk patterns of risk behavior initiation across adolescence. Interestingly, household sociodemographic factors did not predict profiles of risk.

Initiation of smoking, alcohol, cannabis, illicit drugs (among males), and sexual activity, and rates of pregnancy by age 18 y were substantially higher in this cohort as compared to those 18 years of age in a 2008 nationally representative cross-sectional survey of South African students (15). The prevalence of smoking initiation was 86% among males and 72% among females in Bt20+ compared to 37% among males and 18% among females in the South African Youth Risk Behaviour Survey (YRBS). In contrast, estimates of alcohol and cannabis initiation at age 18 y were lower in Bt20+ than estimates from 12th graders surveyed in the 2007 United States YRBS (when Bt20 participants were age 17 y), though lifetime smoking and sexual activity were higher (27). Cross-sectional studies are prone to recall bias (28). Additionally, risk patterning may differ by race and urbanicity. While the 2008 South African YRBS age 18 y estimates were not disaggregated by race, at all ages the prevalence of smoking and alcohol use were lower among Black Africans than other South African racial groups (White, Coloured, and Indian), while drug use and sexual activity were higher. Estimates of smoking and alcohol use were 10% and 15% higher, respectively, in the mostly urban Gauteng province, where Bt20+ is located, compared to the national average.

It is unsurprising that among those who ever experimented with substance use, current use at age 18 y was much lower as not all experimentation will become habituated. In Bt20+ more than 60% of individuals who initiated smoking were no longer smoking at age 18 y whereas a greater proportion of

individuals who used alcohol were still using. In the South African YRBS 30% of individuals who initiated smoking were no longer smoking at age 18 y, while 25% to 35% of individuals who initiated alcohol use were still drinking at age 18 y (15). These smaller differences may be attributable to recall bias and differences between an urban and a nationally representative sample.

We identified three distinct subgroups reflecting low, moderate, and high-risk patterns of risk behavior initiation. As clustering analyses are data driven, it is challenging to draw comparisons with other studies. The results of a cluster analysis of university students in the UK identified three clusters based on smoking and alcohol use as well as stress and lifestyle factors (14). Like the moderate and high-risk clusters in this study, one of their clusters was characterized by smoking and binge drinking, though that study did not consider illicit drug use.

In an analysis of a representative sample from the Netherlands, risk behaviors were shown to cluster differently with age. Specifically, smoking, alcohol, and drug use clustered together among adolescents age 12 to 15 y (questions about unsafe sex were not asked of this age group), while at ages 16 to 18 y unsafe sex and alcohol use clustered together, and smoking, drug use, and other delinquent behaviors clustered together (16). Individuals in our high-risk cluster initiated smoking and alcohol use at above average rates in early adolescence and illicit drug use before age 17 y and initiated sexual activity at above average rates in early and mid-adolescence. The Dutch study identified a “healthy” cluster characterized by favorable diet and physical activity behaviors; we did not examine these behaviors in this analysis.

A cluster analysis in the 2008 South African YRBS identified low, intermediate, and high-risk clusters. Individuals in the YRBS high-risk cluster had substance use, sexual behavior, and traffic safety domain scores at least twice the national average (15). In our high-risk cluster, illicit drug use was initiated at greater than twice the national rate and sexual activity initiation was above average.

Finally, the temporal sequencing of risk behavior initiation in our high-risk cluster is consistent with other findings that have shown smoking and alcohol initiation in early adolescence are associated with subsequent cannabis and illicit drug use (6, 10). Bt20+ females in the high-risk cluster were more likely to become pregnant during adolescence, a life-altering event that limits girls' educational and socioeconomic prospects. Associations of socioeconomic status with cluster assignment in other studies have been mixed, with higher socioeconomic status associated with both low risk cluster membership and engagement in increased number of risk behaviors (15, 29, 30). Interestingly, none of the sociodemographic characteristics considered were associated with cluster assignment. Further research is needed to identify predictors of cluster membership.

We used longitudinal data to describe smoking, alcohol, cannabis, illicit drug use, and sexual activity initiation and adolescent pregnancy over the course of adolescence in an urban, middle-income country context underrepresented in the literature. Our study had high response rates and limited attrition during follow up. Due to the longitudinal design, we were able to describe patterns of adolescence risk behaviors initiation prospectively, thus limiting recall bias.

Some limitations should also be considered. The analyses use self-reported data, which may introduce bias, though anonymity was assured during data collection. Furthermore, we used paper-based self-administered questionnaires until age 14 y, after which an audio-CASI was used; both approaches have demonstrated acceptable validity and reliability for sensitive subjects (31-36). Repeated measures of current use were not available consistently, though by using serial measures of lifetime use we were able to examine the age of initiation for five health risk behaviors. Though the data used in this analysis were collected from 2001 to 2009, cross-sectional surveys of youth risk behavior in South Africa from 2002 to 2011 showed little to no change in the prevalence of adolescent risk behaviors (15, 23, 37).

High levels of risk behavior initiation support the use of public health interventions to prevent initiation and long-term persistence. Distinct patterns in initiation inform the type of prevention efforts warranted, when they should be implemented, and which behaviors should be targeted together. By age

13 y, smoking and alcohol use prevalence were already >20% in girls and 35% in boys, therefore primary prevention efforts should be targeted to younger children. By the end of early adolescence, secondary prevention efforts to mitigate risk behavior engagement should be incorporated. As observed in the moderate and high-risk initiation patterns, smoking and alcohol use are often initiated in the same stage of adolescence (early or mid) while cannabis and illicit drug use are more likely to be initiated in mid-adolescence.

These data provide a valuable reference for smoking, alcohol, cannabis, drug use and sexual activity in a well-characterized cohort of Black African adolescents in Soweto-Johannesburg, South Africa to which contemporary studies can be compared. The present study clearly demonstrates high levels of risk behavior experimentation over the course of adolescence that should be addressed by public health interventions to prevent risk behavior initiation and adoption.

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Tables and Figures

Table 1. Demographic characteristics of Black African Birth to Twenty Plus participants by inclusion status[a]

	Included (n = 1822)	Excluded (n = 746)	p-value[b]
Sex - Males	880 (48%)	369 (49%)	0.62
- Females	942 (52%)	377 (51%)	
Maternal age at birth	25.81 (6.26)	25.95 (5.87)	0.59
Maternal years of schooling	9.58 (2.74)	8.53 (3.59)	< 0.01
Marital status - Single	1206 (66%)	425 (57%)	< 0.01
- Partnered	608 (34%)	320 (43%)	
Asset tertile in early life - 1	624 (34%)	287 (38%)	< 0.01
- 2	362 (20%)	87 (12%)	
- 3	512 (28%)	76 (10%)	
- Missing	324 (18%)	296 (40%)	
Asset tertile at age 7 y - 1	664 (36%)	78 (10%)	< 0.01
- 2	398 (22%)	33 (4%)	
- 3	466 (26%)	45 (6%)	
- Missing	294 (16%)	590 (79%)	
Child stress in early life - Below median	498 (27%)	210 (28%)	0.02
- Above median	401 (22%)	129 (17%)	
- Missing	923 (51%)	407 (55%)	
Child stress at age 5 y - Below median	750 (41%)	79 (11%)	< 0.01
- Above median	441 (24%)	28 (4%)	
- Missing	631 (35%)	639 (86%)	
Child stress at age 7 y - Below median	921 (51%)	87 (12%)	< 0.01
- Above median	542 (30%)	35 (5%)	
- Missing	359 (20%)	624 (84%)	

[a] Presented as N (%) or mean ± SD.
[b] Chi-square or t-test p-values.

Table 2. Risk behavior activity at age 18 y by stage of initiation

			Stage of initiation among current activity[a]				
Measure	N initiate behavior	N current behavior	Childhood	Early	Mid	Late	p-value[b]
Males							
Smoking	719	278	18 (44%)	130 (52%)	115 (53%)	15 (29%)	0.01
Alcohol use	537	300	2 (33%)	132 (59%)	109 (72%)	57 (56%)	0.02
Illicit drug use	273	89	NA	4 (33%)	22 (22%)	62 (64%)	< 0.01
Sexual activity	577	222	NA	40 (52%)	135 (54%)	47 (41%)	0.05
Females							
Smoking	649	140	8 (50%)	37 (25%)	71 (27%)	24 (23%)	0.15
Alcohol use	521	210	2 (18%)	62 (38%)	85 (49%)	61 (42%)	0.05
Illicit drug use	133	30	NA	1 (11%)	7 (16%)	21 (37%)	0.04
Sexual activity	629	293	NA	3 (50%)	136 (61%)	154 (52%)	0.10

[a] Displayed as N (%) of individuals who initiated a behavior in a given stage that reported current behavior activity at age 18 y.

[b] Chi-square p-values testing differences in stage of initiation among current users.

Table 3. Bivariate associations of selected sociodemographic characteristics with patterns of risk behavior initiation[a]

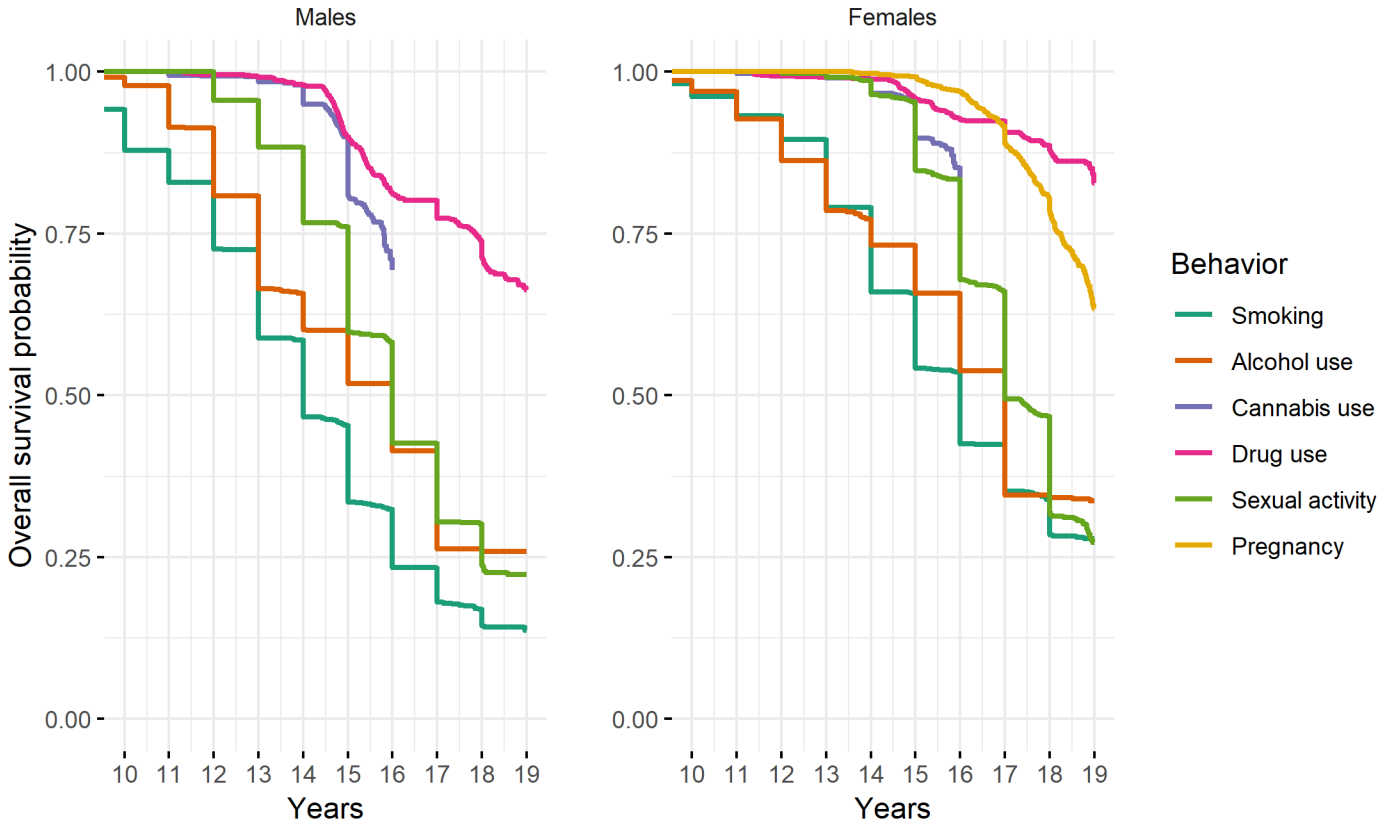
	Males				Females			
	Low risk (n = 169)	Moderate risk (n = 159)	High risk (n = 172)	p-value[b]	Low risk (n = 131)	Moderate risk (n = 342)	High risk (n = 98)	p-value[b]
Maternal years of schooling	9.58 (2.6)	9.87 (2.6)	9.61 (2.4)	0.53	9.7 (2.5)	9.64 (3.0)	9.8 (2.4)	0.89
Maternal age at birth	26.08 (6.4)	25.43 (6.3)	26.17 (6.7)	0.54	26.13 (6.2)	25.85 (6.4)	26.15 (6.5)	0.87
Marital status - Single/Separated/Divorced	110 (65%)	105 (66%)	100 (58%)	0.26	83 (63%)	234 (69%)	62 (63%)	0.37
- Partnered	59 (35%)	54 (34%)	72 (42%)		48 (37%)	105 (31%)	36 (37%)	
Asset tertile in early life - 1	58 (41%)	53 (42%)	64 (46%)	0.76	49 (43%)	115 (41%)	25 (32%)	0.06
- 2	28 (20%)	30 (24%)	27 (19%)		37 (33%)	78 (28%)	19 (24%)	
- 3	55 (39%)	42 (34%)	48 (35%)		27 (24%)	90 (32%)	35 (44%)	
Early life assets imputed - 0	145 (86%)	145 (91%)	146 (85%)	0.18	107 (82%)	290 (85%)	83 (85%)	0.70
- 1	24 (14%)	14 (9%)	26 (15%)		24 (18%)	52 (15%)	15 (15%)	
Asset tertile at age 7 y - 1	67 (47%)	55 (42%)	56 (39%)	0.58	50 (44%)	115 (38%)	34 (42%)	0.06
- 2	34 (24%)	36 (28%)	46 (32%)		33 (29%)	84 (28%)	12 (15%)	
- 3	41 (29%)	39 (30%)	41 (29%)		30 (27%)	102 (34%)	34 (42%)	
Age 7 asset source - assets from Y7	140 (99%)	129 (99%)	140 (98%)	0.66	108 (96%)	284 (94%)	75 (94%)	0.84
- assets from Y5	2 (1%)	1 (1%)	3 (2%)		5 (4%)	17 (6%)	5 (6%)	
Child stress - Above median stressful events never	73 (46%)	67 (46%)	66 (42%)	0.43	43 (36%)	140 (43%)	41 (46%)	0.54
- Above median stressful events 1X	50 (31%)	57 (39%)	56 (36%)		48 (40%)	120 (37%)	33 (37%)	

- Above median stressful events 2 or 3X	36 (23%)	23 (16%)	35 (22%)		29 (24%)	67 (20%)	15 (17%)	
Number of stress measures - Attended 1 study visit	26 (16%)	36 (24%)	23 (15%)	0.19	19 (16%)	60 (18%)	19 (21%)	0.88
- Attended 2 study visits	73 (46%)	57 (39%)	75 (48%)		59 (49%)	158 (48%)	43 (48%)	
- Attended 3 study visits	60 (38%)	54 (37%)	59 (38%)		42 (35%)	109 (33%)	27 (30%)	

[a] Presented as N (%) or mean ± SD.

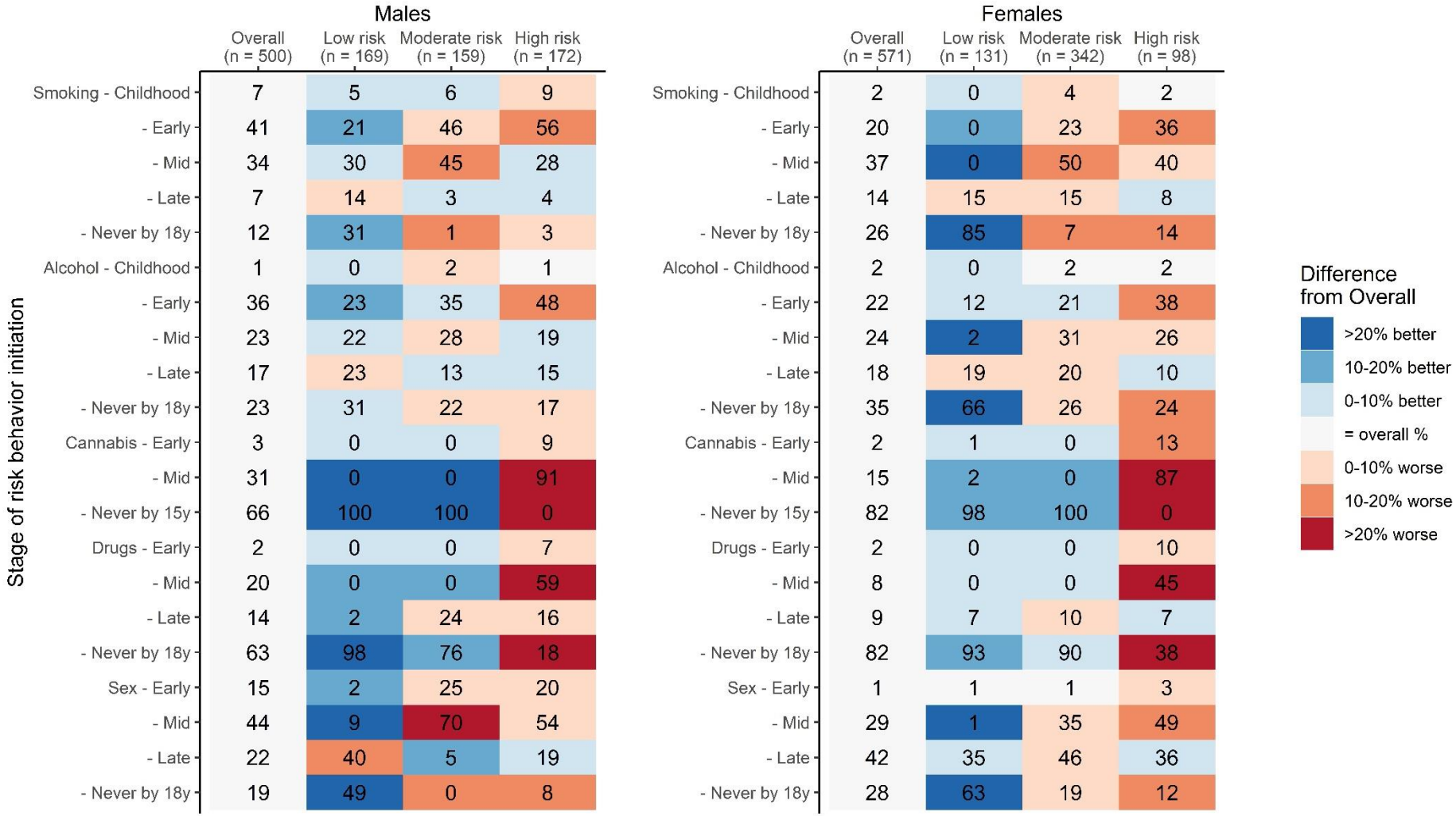
[b] Chi-square p-values testing differences across patterns of risk behavior initiation.

Figure 1. Cumulative survival probability of smoking, alcohol use, marijuana use, illicit drug use, and sexual activity initiation and pregnancy through age 18 y[a]



[a] As age of first smoke, alcohol use, and sexual activity were primarily determined from self-reported integer age, these curves follow a stepwise decline in contrast to the more gradual declines in the marijuana use, illicit drug use, and pregnancy curves, which were primarily determined from the participant's exact calendar age at the study visit.

Figure 2. Patterns of percent risk behavior initiation by stage of childhood and adolescence[a]



[a] Cell color reflects the degree to which percent initiation in a given cluster differs from the overall study population – blue cells reflect below average initiation while red cells reflect above average percent initiation, with deeper shades reflecting greater absolute differences. "Never" initiation was reverse color-coded such that cluster percentages higher than the overall percentage reflect "better" health.

Supplemental Tables and Figures

Supplemental Table 1. Source of age of risk behavior initiation[a]

Age of initiation source	Smk % (n = 1368)	Alc % (n = 1059)	Mar % (n = 372)	Drug % (n = 406)	Sex % (n = 1206)
Reported by participant	93.9	96.3	NA	NA	87
Age at study visit	4.6	2.9	61.8	84.7	4.7
Year of study visit	1.5	0.8	38.2	15.3	2.6
Age of first pregnancy	NA	NA	NA	NA	5.7

[a] Smk = smoking; Alc = alcohol use; Mar = marijuana use; and Sex = sexual activity.

Supplemental Table 2. Number of individuals at risk of initiating each behavior at each year[a]

	Males					Females					
Age	Smk N risk	Alc N risk	Mar N risk	Drug N risk	Sex N risk	Smk N risk	Alc N risk	Mar N risk	Drug N risk	Sex N risk	Preg N risk
<11	771	813	768	867	796	904	881	879	934	923	877
11	722	746	754	857	790	868	826	864	919	915	877
12	627	648	745	848	751	826	752	845	909	906	877
13	499	430	660	822	685	720	580	770	894	888	875
14	378	374	539	745	578	593	535	644	862	850	870
15	263	323	36	657	434	480	481	52	813	734	850
16	172	258	NA	641	302	365	393	NA	806	570	792
17	100	163	NA	485	168	251	253	NA	669	338	611
18	28	67	NA	164	38	84	105	NA	246	70	195

[a] Smk = smoking; Alc = alcohol use; Mar = marijuana use; Sex = sexual activity; and Preg = pregnancy.

Supplemental Table 3. Comparison of health risk behavior cluster classification when fitting 2- versus 3-cluster solution among males

	Cluster 1 (n = 328)	Cluster 2 (n = 172)
- Cluster 1	169 (52%)	0 (0%)
- Cluster 2	159 (48%)	0 (0%)
- Cluster 3	0 (0%)	172 (100%)

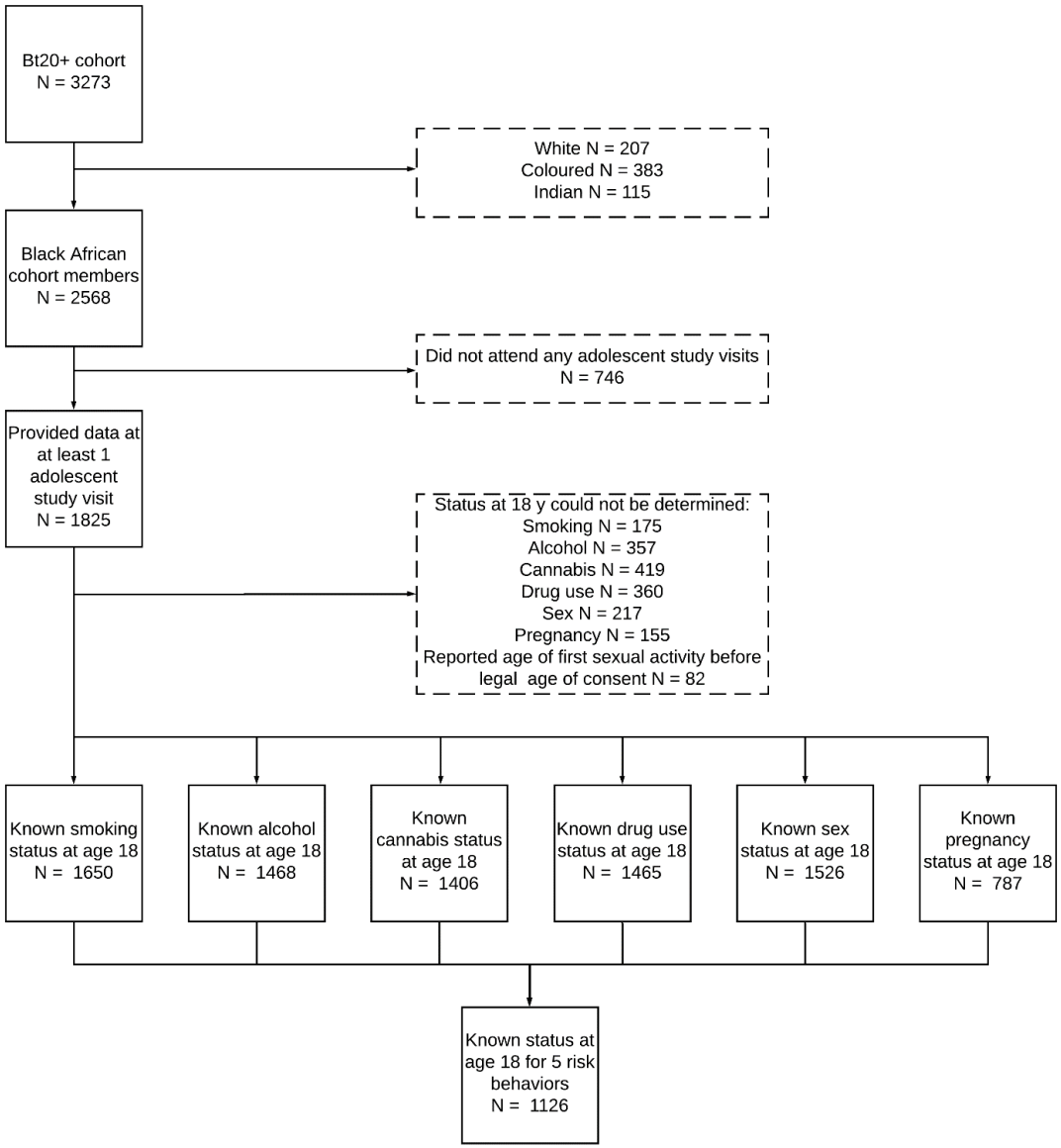
Supplemental Table 4. Descriptive characteristics of individuals included in the cluster analysis and individuals without known smoking, alcohol use, marijuana use, illicit drug use, and sexual activity status at age 18 y who were excluded from the cluster analysis[a]

	Included (n = 1071)	Excluded (n = 751)	p-value[b]
Sex - Males	500 (47%)	380 (51%)	0.11
- Females	571 (53%)	371 (49%)	
Asset tertile in early life - 1	364 (34%)	260 (35%)	0.89
- 2	219 (20%)	143 (19%)	
- 3	297 (28%)	215 (29%)	
- Missing	191 (18%)	133 (18%)	
Asset tertile at age 7 y - 1	377 (35%)	287 (38%)	0.14
- 2	245 (23%)	153 (20%)	
- 3	287 (27%)	179 (24%)	
- Missing	162 (15%)	132 (18%)	
Child stress - Above median stressful events never	430 (40%)	275 (37%)	0.43
- Above median stressful events 1X	364 (34%)	269 (36%)	
- Above median stressful events 2 or 3X	205 (19%)	140 (19%)	
- (Missing)	72 (7%)	67 (9%)	
Stage of smoking initiation - Childhood	48 (4%)	20 (3%)	< 0.01
- Early	320 (30%)	168 (22%)	
- Mid	380 (35%)	245 (33%)	
- Late	115 (11%)	72 (10%)	
- Never by 18y	208 (19%)	74 (10%)	
- Status unknown at 18y	0 (0%)	168 (22%)	
- Missing	0 (0%)	4 (1%)	
Stage of alcohol initiation - Childhood	13 (1%)	6 (1%)	< 0.01
- Early	302 (28%)	161 (21%)	

- Mid	250 (23%)	75 (10%)	
- Late	188 (18%)	64 (9%)	
- Never by 18y	318 (30%)	91 (12%)	
- Status unknown at 18y	0 (0%)	274 (36%)	
- Missing	0 (0%)	80 (11%)	
Stage of marijuana initiation - Early	30 (3%)	13 (2%)	< 0.01
- Mid	243 (23%)	86 (11%)	
- Never by 18y	798 (75%)	236 (31%)	
- Status unknown at 18y	0 (0%)	361 (48%)	
- Missing	0 (0%)	55 (7%)	
Stage of illicit drug use - Early	22 (2%)	7 (1%)	< 0.01
- Mid	145 (14%)	58 (8%)	
- Late	121 (11%)	53 (7%)	
- Never by 18y	783 (73%)	276 (37%)	
- Status unknown at 18y	0 (0%)	336 (45%)	
- Missing	0 (0%)	21 (3%)	
Stage of sexual activity initiation - Early	82 (8%)	22 (3%)	< 0.01
- Mid	388 (36%)	248 (33%)	
- Late	347 (32%)	119 (16%)	
- Never by 18y	254 (24%)	66 (9%)	
- Status unknown at 18y	0 (0%)	195 (26%)	
- Missing	0 (0%)	101 (13%)	

[a] Presented as N (%).
[b] Chi-square p-values.

Supplemental Figure 1. Analytical sample flow diagram



Chapter 5: Associations of pubertal timing and tempo with adolescent mental health and health risk behavior initiation: longitudinal findings from the Birth to Twenty Plus cohort

Manuscript Authors: Alysse J. Kowalski, O. Yaw Addo, Michael R. Kramer, Reynaldo Martorell, Shane A. Norris, Rachel N. Waford, Linda M. Richter*, Aryeh D. Stein*

*Co-senior authors

Abstract

Purpose

Early and rapid pubertal development is associated with poor adjustment and increased risk behavior engagement in adolescence in high-income countries. Little is known about these associations in low- and middle-income countries where the context differs.

Methods

We used longitudinal data from 1,784 urban Black South Africans. Using latent classes of pubertal timing and tempo (previously derived from Tanner sexual maturation staging measures) and age of menarche, we examined associations with measures of emotional and behavioral problems, eating attitudes, and patterns of health risk behavior initiation in adolescence and examined if these associations were modified by childhood stress.

Results

Relative to peers, individuals with earlier pubertal timing and faster pubertal tempo (earlier/faster) reported increased health risk behavior initiation (e.g. AOR [95% CI] high vs. low-risk pattern for genital development = 5.7 [1.7, 19.06]; AOR for breast development = 3.45 [1.13, 10.49]) and externalizing problems (e.g. β [95% CI] oppositional defiant problems for genital development = 1.16 [0.43, 1.89]; β attention deficit problems for female pubic hair development = 1.11 [0.31, 1.92]). Earlier/faster maturing females also reported increased affective problems (β = 1.03 [0.02, 2.05]) and eating attitudes (β = 4.58 [1.92, 7.24]) for pubic hair development. There were no statistical interactions between childhood stress and pubertal timing and tempo.

Conclusion

In urban South Africa, early/rapid maturation was associated with poorer adolescent health while later/slower maturation was protective.

Implications and Contribution

Early maturing urban Black South African adolescents are at higher risk of initiating health risk behaviors and elevated externalizing problems in adolescence while late maturers are at slightly lower risk. Targeted efforts to promote mental health and reduce substance access may support early maturers during adolescence.

Introduction

Puberty signifies the onset of adolescence, a stage of profound biological, cognitive, emotional, and social development. Initiated by reactivation of the hypothalamic-pituitary axis, gonadarche results in the production of sex steroids, leading to the first visible signs of puberty, testicular enlargement and breast development (1). In girls, menarche takes place approximately 2.5 years after breast development (1). In a temporally related but independent process, adrenarche increases androgen production leading to pubic hair development, axillary hair, and acne. Other changes that take place in puberty include increases in height and major alterations in body composition and regional fat distribution.

Puberty can be described in terms of age of onset, or *timing* and rate of progression, or *tempo*, which are influenced by genetic, environmental, and nutritional factors. Within similar living conditions both timing and tempo vary substantially (2). As a result, adolescents of the same calendar age will be at different stages of puberty. Puberty changes adolescents' interactions with the social environment such that adolescents may be treated in accordance with their physical appearance rather than their age-dependent cognitive and emotional development (1). This and other biopsychosocial processes influence emotional and behavioral adjustment and may interact with psychosocial vulnerabilities established prior to adolescence (3).

Extensive research links early maturation with increased internalizing and externalizing problems, including substance use and risky sexual behavior in both sexes (4-6). Previous work has also suggested associations between late maturation and adolescent maladjustment, though this was not supported by findings from a recent meta-analysis (6, 7). Less is known about the association of adjustment and pubertal tempo. In a study of New York City public school students, pubertal tempo was more strongly associated with depressive symptoms than pubertal timing among boys but not girls (8). In a nationwide study in the US, faster pubertal tempo was associated with increased internalizing and externalizing problems in girls though only intermittently related to these outcomes in boys (9).

Furthermore, emotional and behavioral development are shaped by socio-cultural context. In the 1932 Oakland Growth Study, early maturing boys were rated more popular, relaxed, and attractive while late maturation was socially disadvantageous (10). In contrast, in findings from the 1989 Iowa Youth and Families Project, early maturation no longer conferring an advantage for early maturing males and was associated with increased externalizing and internalizing problems (11). These studies highlight the relevance of time and place in the social interpretation of puberty.

Associations between maturation and maladjustment have been shown cross-culturally, however these findings are almost exclusively from high-income countries. Given the important role socio-cultural contexts plays in responding to increasing physical maturity it is prudent to examine these associations in low-and middle-income countries. The current study examined associations of pubertal timing and tempo with adolescent emotional and behavioral problems, eating attitudes, and health risk behavior initiation in urban South Africa. Understanding these associations has implications for interventions to promote healthy emotional and behavioral adjustment.

Methods

Birth to Twenty Plus (Bt20+) cohort

We used data from the Birth to Twenty Plus (Bt20+) cohort in South Africa. Bt20+ is an observational birth cohort that enrolled singleton children born between April and June 1990 who resided in the Soweto-Johannesburg municipal area for a minimum of 6 months after birth (N = 3273). The cohort has been relatively stable since preschool, with 70% of members traceable at the age 17 y study visit (12).

Ethical approval

This study was approved by the University of the Witwatersrand Human Research Ethics Committee for Research on Human Subjects and the Emory University Institutional Review Board.

Data collection

Adolescent study visits (coinciding with cohort member ages 11, 13, 14, 15, 16, 17, and 18 y) were conducted by trained research assistants. Data were collected using interviewer-administered questionnaires (emotional and behavioral problems, eating attitudes, sexual maturation), self-administered questionnaires (risk behaviors), and direct measurement (height and weight).

Exposures

Sex-specific latent classes of genital/breast development and pubic hair development were previously identified from repeated self-rated measures of the Tanner sexual maturation scale; the self-rated approach was validated for the study population (13, 14). Three latent classes of pubic hair development and 4 latent classes of genital/breast development were identified for boys and girls. Individuals in class 1 started puberty later and progressed through puberty slower than their peers in other classes and individuals in the highest class had the earliest pubertal timing and fastest tempo.

Menarche status and subsequent age of menarche were asked at each adolescent study visit as part of the self-administered questionnaire. There was no comparable measure for males.

Outcomes

For both sexes, three patterns of health risk behavior initiation (low, moderate, and high) were previously identified from timing of smoking, alcohol, marijuana, illicit drug, and sexual activity initiation through age 18 y (15).

The Achenbach System of Empirically Based Assessment Youth Self Report (YSR) was administered at ages 11 and 14 y to assess emotional and behavioral problems which can impair mental health (16). Questions were administered in English by trained interviewers who could translate the questions into standardized phrases in local languages as needed. Participant responses were scored using six DSM-oriented scales for affective problems, anxiety problems, somatic problems, attention deficit/hyperactivity problems, oppositional defiant problems, and conduct problems. The selected items were rated as being “very consistent” with Diagnostic and Statistical Manual of Mental Disorders-4

criteria for diagnostic categories by international experts and shown to have good internal consistency and test-retest reliability in a diverse sample (17). The YSR has been administered previously in South Africa and the DSM scales have shown consistency when applied cross-culturally (18, 19). Because clinical cutoffs have not yet been validated in the South African context, we report mean scores for each scale, with higher scores reflecting increased problem behaviors.

Eating disorders are mental disorders characterized by abnormal eating habits that significantly impair physical health and/or psychosocial functioning (20). The Eating Attitudes Test (EAT) is widely used to screen for eating disorder risk and has three subscales (dieting, bulimia and food preoccupation, and oral control) which measure symptoms and concerns typical of eating disorders (21). The 26-item EAT (EAT-26) was administered at ages 13 and 17 y. The EAT-26 had good internal reliability in early and late adolescence and has been previously applied in urban South Africa (22). We report mean scores because thresholds have not been validated in South African populations. Higher scores reflect poorer eating attitudes.

Covariates

Household asset ownership was used as a measure of socioeconomic position at two time points – age 0-2 y and age 7 y (supplemented with observations from age 5 y). We calculated tertiles from the number of assets owned. We used maternal reports of stress and violence events experienced in the past six months at the age 0-2, 5, and 7 y study visits as measures of childhood stress exposure. We characterized childhood stress as the number of visits in which the mother reported experiencing above the sample median number events. Height-for-age z-scores (HAZ) and body mass index for age z-scores (BMIZ) at ages 5 and 8 y were used as measures of child growth (23).

Analytical sample

Black Africans are the largest population group in Soweto-Johannesburg and comprise 78% of the Bt20+ cohort. We restricted our analytical sample to 1,784 Black African cohort members for whom

we have a pubertal development trajectory and allowed the sample size to vary for each outcome to maximize the available data (Supplemental Figure 1).

Two-way imputation

For the YSR, EAT, asset ownership, and childhood stress measures, we used two-way imputation (TWI) to assign values to missing items for individuals who completed at least 50% of the relevant questions. TWI is a deterministic imputation approach that utilizes the person mean and the sample item mean to assign a response value to a missing item (24). The EAT completion rate was 54% at age 17 y and imputation recovered N = 24 observations. The household asset ownership completion rate was 64% from Y0-2 and imputation recovered N = 308 observations. Completion rates for other measures were ≥90%.

Statistical analysis

We examined associations of pubertal development classes and age of menarche with risk behavior initiation pattern; six internalizing and externalizing problem scales; and eating attitudes in sex-specific models. To examine associations with risk behavior initiation pattern we used multinomial logistic regression with the low-risk pattern as the outcome referent group. The exponentiated coefficients can be interpreted as the relative odds of being classified in a particular risk behavior initiation pattern compared to the low-risk pattern. We used linear regression to examine associations with internalizing problems, externalizing problems, and eating attitudes. In all regression models, class 2 pubertal development was the referent group. We controlled for household socioeconomic position in early life and childhood and childhood stress. We did not adjust for childhood HAZ or BMIZ following bivariate analysis.

We assessed heterogeneity of the pubertal timing and tempo estimates across categories of childhood stress by examining interaction p-values. Upon reviewing stratified estimates, the number of significant tests of interaction did not exceed the number expected to occur by chance, therefore we do not present these estimates in the main results.

All analyses were conducted using R version 3.5.3 with two-sided p-values <0.05 statistically significant (25).

Results

Most individuals were in genital/breast development classes 2 and 3 and class 2 for pubic hair development; mean age of menarche was age 12.7 y (Table 1.) On average, individuals were slightly short and heavy for their age at age 5 y. At age 8 y, on average, individuals were closer to normal weight and were still slightly short for their age. Twenty-one percent of individuals were exposed to above median stress at 2-3 childhood study visits.

A third of males and 17% of females were classified in the high-risk risk behavior initiation pattern (Table 2). Among individuals who reported initiating a behavior, mean ages of smoking, alcohol, and sexual activity initiation were lower among males than females, with mean age of sexual activity initiation over a year earlier among males (age 15.3 y) compared to females (age 16.6 y).

In general, scores on internalizing scales decreased from 11 y to 14 y, while scores on externalizing scales increased. Except for conduct problems, mean scores on the DSM adjustment scales were slightly higher for females than males at both ages. Eating attitude scores were similar between sexes at ages 13 y (10.0 males, 9.9 females) and 17 y (10.0 males, 11.1 females).

Adjusted associations of pubertal development with health risk behavior pattern, emotional and behavioral problems, and eating attitudes among males

Relative to genital development class 2, earlier and more rapid development reflected in classes 3 and 4 was associated with increasing odds of following the moderate or high-risk health risk behavior pattern compared to low-risk health risk behavior pattern (class 3: moderate AOR = 1.86 [1.03, 3.34]; high AOR =2.42 [1.37, 4.28]; class 4: moderate AOR = 5.61 [1.65, 19.07]; high AOR = 5.7 [1.7, 19.06]) (Table 3). Later and slower pubic hair development (class 1), relative to class 2, was associated with decreased odds of following the moderate and high-risk health risk behavior pattern compared to low-risk pattern (class 1: moderate AOR = 0.34 [0.18, 0.64]; high AOR = 0.62 [0.35, 1.09]).

Earlier and more rapid genital development was associated with increased externalizing problems at age 14 y: relative to class 2, genital development class 3 was associated with increased attention deficit (class 3 β = 0.66 [0.02, 1.3]), oppositional defiant (class 3 β = 0.64 [0.23, 1.06]), and conduct problems (class 3 β = 0.95 [0.24, 1.66]) though class 4 was only associated with oppositional defiant problems (class 4 β = 1.16 [0.43, 1.89]). Later and slower pubic hair development was associated with decreased externalizing problems at ages 11 y and 14 y; relative to class 2, pubic hair development class 1 was associated with decreased oppositional defiant problems at 11 (β = -0.38 [-0.72, -0.04]) and 14 y (β = -0.62 [-1.04, -0.19]) and decreased conduct problems at 14 y (β = -1.07 [-1.78, -0.35]). With respect to internalizing problems, earlier and faster pubic hair development (class 3) relative to class 2, was associated with decreased affective problems score at age 14 y (β = -1.26 [-2.1, -0.41]).

Associations between pubic hair development and eating attitudes were U-shaped. Both earlier/more rapid and later/slower pubic hair development (classes 3 and 1), relative to class 2 were associated with increases in unhealthy eating attitudes in late adolescence (class 1 β = 2.1 [0.45, 3.74]; class 3 β = 2.14 [-0.02, 4.29]).

Adjusted associations of pubertal development with health risk behavior pattern, emotional and behavioral problems, and eating attitudes among females

Relative to class 2, earlier and more rapid breast development classes 3 and 4 were associated with increasing odds of following the moderate (class 3 AOR = 1.8 [0.97, 3.34]; class 4 AOR = 1.99 [0.89, 4.44]) or high-risk (class 3: 3.44 [1.38, 8.58]; class 4: 3.45 [1.13, 10.49]) patterns compared to the low-risk pattern (Table 4). Similarly, later and slower pubic hair development reflected in class 1 relative to class 2, was associated with decreasing odds of following the moderate (class 1 AOR = 0.58 [0.35, 0.95]) or high-risk (class 1 AOR = 0.54 [0.27, 1.1]) patterns compared to the low-risk pattern as was later age of menarche (moderate risk AOR = 0.82 [0.66, 1.0]; high AOR = 0.53 [0.39, 0.71]).

Earlier and faster pubertal development was associated with increased internalizing and externalizing problems in mid-adolescence. Earlier and faster pubic hair development (class 3) relative to

class 2 was associated with increased affective problems score (β = 1.03 [0.02, 2.05]) and increased age of menarche was associated with a small decrease at age 14y (β = -0.29 [-0.58, 0]). Earlier and faster pubic hair development (class 3) relative to class 2 was associated with increased attention deficit score (β = 1.11 [0.31, 1.92]) and increased age of menarche was associated with a small decrease in attention deficit (β = -0.47 [-0.7, -0.24]) and oppositional defiant (β = -0.19 [-0.35, -0.03]) scores.

Relative to pubic hair development class 2, earlier and more rapid development was associated with a sizeable increase in unhealthy eating attitudes in late adolescence (β = 4.58 [1.92, 7.24]).

For both sexes, though additional pubertal development and health risk behavior, emotional and behavioral problems, or eating attitude associations were statistically significant, when viewed in context with the other findings, they were not part of a discernable pattern of associations. Unadjusted model results can be found in Supplemental Tables S1 and S2. We found 3 statistically significant interactions between childhood stress exposure and associations of pubertal development and adolescent adjustment among males and 2 significant interactions among females, within the expected number of type I errors (Supplemental Table 3).

Discussion

Multiple indicators of pubertal timing and tempo were associated with emotional and behavioral problems, eating attitudes, and initiation of health risk behaviors in a cohort of urban Black South African adolescents. Adolescents who matured relatively earlier and faster than their peers reported more externalizing problems and were more likely to follow the high-risk health risk behavior initiation pattern, while there were some protective associations among adolescents who matured later and slower. Additionally, early maturing girls reported increased affective problems in mid-adolescence and poorer eating attitudes in late adolescence.

Relative to peers, individuals with earlier pubertal timing and faster pubertal tempo were more likely to follow the moderate and high-risk health risk behavior initiation patterns, with some evidence of a dose response. The moderate and high-risk patterns reflect above average smoking, alcohol use, and

sexual activity initiation compared to the overall levels and, in the high-risk pattern, above average marijuana and illicit drug use. These findings are consistent with meta-analysis and systematic review findings that have shown small, positive associations in both sexes between early pubertal timing and both substance use and earlier age of intercourse, a worrying connection given earlier substance use is more likely to result in misuse and dependency and earlier sexual activity increases the risk of STIs, including HIV, and adolescent pregnancy (4, 6, 26-30). The converse was also true; later and slower maturers were more likely to follow the low-risk pattern, consistent with previous longitudinal studies which also did not observe an increase in substance use among late maturers, though such consequences may not manifest until adulthood (5, 7, 31).

Earlier and faster maturation was associated with increased externalizing problems in mid-adolescence in both sexes while later maturation was associated with fewer externalizing problems. Two contemporary meta-analyses also found small positive associations between early maturation and externalizing behaviors for both sexes and other systematic reviews have shown associations of early menarche with norm violations, delinquent behaviors, and criminal activity (6, 30, 32). The consequences of earlier and faster maturation may be more severe for females than males, as females have higher adjustment scores in response to the physical changes of puberty and the additional contribution of early puberty may tip the scales, as evidenced by studies showing an increased risk of substance use and disruptive behavior disorders in late adolescence (33, 34). In this study, later maturation was associated with fewer externalizing problems in mid-adolescence. This is consistent with the majority of prior research among females, though some studies report elevated externalizing symptoms among late maturers (7).

In our study, earlier and faster maturation was associated with increased affective problems among females in mid-adolescence, consistent with other findings. Early pubertal timing was shown to have a small positive effect on internalizing symptoms in meta-analyses and accelerated pubertal tempo has been associated with increased depressive symptoms in females (6, 8, 9, 29, 30, 34). In our study, Bt20+ males who matured earlier and faster reported fewer affective problems than their peers. This is

inconsistent with a recent meta-analysis which found a small positive effect of early pubertal timing on internalizing symptoms, though more rapid pubertal tempo has been shown to be associated with increased depressive symptoms (8).

We did not observe associations between pubertal timing and tempo and internalizing problems at age 11 y, though our latent classes reflect the overall pubertal trajectory and many individuals had not entered puberty at the time of assessment (13). Earlier and faster maturing females reported increased unhealthy eating attitudes, consistent with studies that have shown early pubertal timing was associated with increased disordered eating symptoms and rates of eating disorders (35).

The consistency of our findings with the contemporary body of evidence generated overwhelmingly in high-income countries suggests commonalities in adolescent development across settings. The maturational disparity hypothesis postulates that males and females who mature earlier than their peers are at increased risk of psychological distress due to the mismatch between their physical and cognitive and emotional development and has received the most empirical support compared to alternative hypotheses (36). Indeed, our findings were most consistent with this hypothesis. While we did not find evidence of statistical interactions between childhood stress and associations of pubertal timing and tempo, maternal exposure to stress and violence may not be an adequate proxy for the child's experience.

Strengths of this study include the use of multiple pubertal development indicators and adolescent outcomes to provide a comprehensive picture of consequences of offset maturation in an LMIC and for males, both of which are underrepresented in the literature. We used high-quality pubertal development indicators collected annually during adolescence, reducing the likelihood of recall bias. Additionally, the Tanner SMS and self-rating approach was validated for use in this population.

Limitations include the age of the data which were collected between 2001-2009. Although the biology of puberty has not changed, the advent of social media has radically changed adolescent communication and peer interactions. Furthermore, adolescent mental health problems, self-harm, and suicide have all increased in the twenty-first century, particularly for young women (37, 38). Due to small

sample sizes select latent class estimates are imprecise, particularly associations with health risk-behavior initiation patterns. While we have not adjusted for multiple comparisons, we interpreted the results holistically, focusing on patterns of association. Our results are not generalizable to other population subgroups beyond Black South Africans, and previous research has suggested these associations differ within a population (39).

There will always be a subset of individuals who enter puberty earlier and mature faster than their peers and may benefit from interventions at the individual, family, or peer levels (40). Individual-focused interventions to strengthen coping strategies and problem-solving prior to adolescence may allow the early maturer to better navigate puberty. Family-level interventions delivered prior to puberty may support parent-child relationship quality during puberty. Peer interventions may focus on forming and maintaining healthy peer networks.

We found consistent evidence that internalizing and externalizing problems and health risk behavior initiation were higher among early maturing boys and girls and some evidence later and slower maturation was protective. These findings are some of the first from an LMIC. Future work should confirm these findings and examine the pathways by which these associations arise.

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Tables and Figures

Table 1. Demographic characteristics of Birth to Twenty Plus analytical sample[a]

Measure	Males N	Males (n = 861)	Females N	Females (n = 923)
Asset tertile in early life - 1	700	299 (43%)	764	308 (40%)
- 2		155 (22%)		203 (27%)
- 3		246 (35%)		254 (33%)
Early life assets imputed - 0	857	750 (88%)	917	785 (86%)
- 1		107 (12%)		133 (14%)
Asset tertile at age 7 y - 1	708	307 (43%)	786	337 (43%)
- 2		192 (27%)		200 (25%)
- 3		209 (30%)		250 (32%)
Age 7 asset source - assets from Y7	708	689 (97%)	786	747 (95%)
- assets from Y5		19 (3%)		40 (5%)
Child stress - Above median stressful events never	785	341 (43%)	856	340 (40%)
- Above median stressful events 1X		283 (36%)		337 (39%)
- Above median stressful events 2 or 3X		161 (21%)		180 (21%)
Number of stress measures - Attended 1 study visit	785	148 (19%)	856	149 (17%)
- Attended 2 study visits		351 (45%)		420 (49%)
- Attended 3 study visits		286 (36%)		288 (34%)
BMIZ 5 y[b]	585	0.33 (0.96)	651	0.21 (0.91)
HAZ 5 y[b]	585	-0.68 (0.92)	651	-0.64 (0.91)
BMIZ 8 y[b]	486	-0.04 (0.9)	493	-0.03 (0.96)
HAZ 8 y[b]	488	-0.62 (1)	493	-0.69 (0.94)
Age of menarche	--	--	906	12.7 (1.22)
Genital/breast development class[c]				

- 1 (later/slower)	861	55 (6%)	923	212 (23%)
- 2		316 (37%)		229 (25%)
- 3		429 (50%)		351 (38%)
- 4 (earlier/faster)		61 (7%)		131 (14%)
Pubic hair development class[c]				
- 1 (later/slower)	861	253 (29%)	923	310 (34%)
- 2		504 (59%)		499 (54%)
- 3 (earlier/faster)		104 (12%)		114 (12%)

[a] Presented as N (%) or mean ± SD.

[b] Based on WHO Child Growth Standards

[c] Latent classes derived from repeated measures of the Tanner sexual maturation scale. Individuals in class 1 started puberty later and progressed through puberty slower than their peers in other classes and individuals in the highest class had the earliest pubertal timing and fastest tempo (Lundeen EA, Norris SA, Martorell R, et al. Early Life Growth Predicts Pubertal Development in South African Adolescents. The Journal of nutrition 2016;146:622-629.).

Table 2. Descriptive characteristics of adolescent emotional and behavior adjustment, eating attitudes, and risk behavior initiation[a]

Measure	Males N	Males (n = 861)	Females N	Females (n = 923)
Health risk behavior pattern[b] - Low risk	498	169 (34%)	569	130 (23%)
- Moderate risk		157 (32%)		341 (60%)
- High risk		172 (35%)		98 (17%)
Age of first smoke	711	13.3 (2.5)	643	14.5 (2.3)
Age of first alcohol use	534	14.0 (2.3)	516	14.4 (2.4)
Age of first marijuana use	245	14.8 (0.9)	126	14.6 (1.1)
Age of first illicit drug use	272	16.2 (1.7)	133	16.3 (1.9)
Age of first sexual activity	571	15.3 (1.7)	621	16.6 (1.4)
Age of adolescent pregnancy	--	--	293	17.6 (1.3)
Affective problems (range 0-26)	565	3.3 (2.4)	624	3.5 (2.8)
Anxiety problems (range 0-12)	565	3.7 (1.8)	616	3.9 (1.8)
Somatic problems (range 0-14)	572	2.9 (2.2)	629	3.9 (2.3)
Attention deficit problems (range 0-14)	573	2.6 (2.5)	630	3.5 (2.7)
Oppositional defiant problems (range 0-10)	572	1.3 (1.5)	630	1.6 (1.6)
Conduct problems (range 0-30)	570	2.5 (2.6)	630	2.2 (2.2)
Affective problems (range 0-26)	565	3.2 (2.7)	624	4.2 (3.5)
Anxiety problems (range 0-12)	565	3.2 (1.8)	616	3.3 (1.9)
Somatic problems (range 0-14)	572	0.6 (1.6)	629	0.9 (2.1)
Attention deficit problems (range 0-14)	573	3.3 (2.9)	630	4.1 (2.8)
Oppositional defiant problems (range 0-10)	572	1.8 (1.9)	630	2.4 (2)
Conduct problems (range 0-30)	570	3.1 (3.1)	630	2.6 (2.6)
Total eating attitudes (range 0-78)	463	10 (7.1)	487	9.9 (7.7)
Dieting (range 0-39)	463	5.1 (4.1)	487	5 (4.4)

Bulimia and food preoccupation (range 0-18)	463	1.7 (2.5)	487	1.4 (2.3)
Oral control (range 0-21)	463	3.2 (2.9)	487	3.5 (3.5)
Total eating attitudes (range 0-78)	463	10 (6.7)	487	11.1 (8.7)
Dieting (range 0-39)	463	5.2 (4.4)	487	5.9 (5.5)
Bulimia and food preoccupation (range 0-18)	463	1.5 (2.2)	487	1.6 (2.6)
Oral control (range 0-21)	463	3.3 (2.9)	487	3.6 (3.6)

[a] Presented as N (%) or mean ± SD.

[b] Risk behavior patterns derived from a cluster analysis of adolescent smoking, alcohol, cannabis, illicit drug, and sexual activity initiation (Kowalski AJ, Addo OY, Kramer MR, et al. Initiation and persistence of health risk behaviors through adolescence in urban South Africa. Under review.).

Table 3. Adjusted associations of male genital and pubic hair development classes with adolescent emotional and behavioral adjustment, eating attitudes, and patterns of risk behavior initiation[a]

	Gen class 1 (Later and slower)	Gen class 2	Gen class 3	Gen class 4 (Earlier and faster)	PH class 1 (Later and slower)	PH class 2	PH class 3 (Earlier and faster)
Pattern of risk behavior initiation	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)	OR (95% CI)	Ref	OR (95% CI)
Low-risk	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Moderate risk	0.85 (0.23, 3.15)	Ref	**1.86 (1.03, 3.34)**	**5.61 (1.65, 19.07)**	**0.34 (0.18, 0.64)**	Ref	1.66 (0.68, 4.09)
High-risk	1.01 (0.3, 3.46)	Ref	**2.42 (1.37, 4.28)**	**5.7 (1.7, 19.06)**	0.62 (0.35, 1.09)	Ref	2.17 (0.92, 5.14)
Sociobehavioral adjustment	β (95% CI)	Ref	β (95% CI)	β (95% CI)	β (95% CI)	Ref	β (95% CI)
Age 11 y							
Aff	0.16 (-0.91, 1.22)	Ref	-0.07 (-0.58, 0.44)	0.37 (-0.54, 1.28)	-0.09 (-0.62, 0.44)	Ref	0.09 (-0.64, 0.81)
Anx	**1.25 (0.42, 2.08)**	Ref	0.28 (-0.12, 0.68)	-0.26 (-0.97, 0.45)	-0.35 (-0.77, 0.06)	Ref	-0.4 (-0.97, 0.17)
Som	-0.86 (-1.84, 0.11)	Ref	0.18 (-0.29, 0.64)	0.11 (-0.73, 0.94)	**-0.56 (-1.04, -0.08)**	Ref	0.46 (-0.2, 1.12)
Attn Def	0.15 (-1, 1.3)	Ref	0.25 (-0.31, 0.8)	0.44 (-0.55, 1.42)	-0.53 (-1.09, 0.04)	Ref	0.48 (-0.3, 1.26)
Opp Def	-0.33 (-1.01, 0.36)	Ref	0.11 (-0.22, 0.44)	0.44 (-0.14, 1.03)	**-0.38 (-0.72, -0.04)**	Ref	0.22 (-0.25, 0.68)
Conduct	-0.18 (-1.33, 0.98)	Ref	-0.02 (-0.57, 0.52)	0.85 (-0.12, 1.82)	-0.24 (-0.8, 0.33)	Ref	**0.86 (0.09, 1.63)**
Age 14 y							
Aff	0.88 (-0.34, 2.11)	Ref	**0.8 (0.17, 1.42)**	-0.22 (-1.32, 0.88)	-0.48 (-1.11, 0.15)	Ref	**-1.26 (-2.1, -0.41)**
Anx	-0.13 (-0.98, 0.73)	Ref	-0.08 (-0.5, 0.35)	-0.13 (-0.89, 0.63)	-0.19 (-0.61, 0.24)	Ref	-0.13 (-0.71, 0.45)
Som	0.47 (-0.29, 1.24)	Ref	0.25 (-0.14, 0.63)	0.09 (-0.59, 0.77)	-0.05 (-0.44, 0.34)	Ref	0.01 (-0.52, 0.54)
Attn Def	1.27 (-0.01, 2.55)	Ref	**0.66 (0.02, 1.3)**	0.52 (-0.61, 1.66)	-0.45 (-1.1, 0.21)	Ref	-0.75 (-1.64, 0.13)
Opp Def	-0.3 (-1.14, 0.54)	Ref	**0.64 (0.23, 1.06)**	**1.16 (0.43, 1.89)**	**-0.62 (-1.04, -0.19)**	Ref	0.42 (-0.15, 0.99)
Conduct	0.15 (-1.26, 1.56)	Ref	**0.95 (0.24, 1.66)**	-0.04 (-1.29, 1.2)	**-1.07 (-1.78, -0.35)**	Ref	-0.67 (-1.64, 0.3)
Eating attitudes	β (95% CI)	Ref	β (95% CI)	β (95% CI)	β (95% CI)	Ref	β (95% CI)
Age 13 y							
Total	-0.72 (-3.75, 2.32)	Ref	-0.61 (-2.06, 0.84)	-0.78 (-3.28, 1.73)	-0.42 (-1.92, 1.07)	Ref	-0.33 (-2.32, 1.65)
Dieting	0.04 (-1.68, 1.75)	Ref	-0.34 (-1.16, 0.48)	-0.24 (-1.66, 1.18)	-0.15 (-0.99, 0.7)	Ref	0.4 (-0.72, 1.52)
Bulimia	0.09 (-0.97, 1.16)	Ref	0.24 (-0.27, 0.74)	0.15 (-0.73, 1.03)	-0.11 (-0.63, 0.42)	Ref	-0.13 (-0.82, 0.57)
Oral control	-0.84 (-2.04, 0.35)	Ref	-0.51 (-1.08, 0.06)	-0.69 (-1.68, 0.3)	-0.17 (-0.76, 0.42)	Ref	-0.6 (-1.39, 0.18)
Age 17 y							
Total	-0.11 (-3.09, 2.87)	Ref	-1.57 (-3.17, 0.04)	1.18 (-1.6, 3.95)	**2.1 (0.45, 3.74)**	Ref	2.14 (-0.02, 4.29)
Dieting	-0.01 (-1.97, 1.94)	Ref	-1 (-2.06, 0.05)	1.02 (-0.8, 2.84)	**1.21 (0.12, 2.29)**	Ref	1.07 (-0.35, 2.49)
Bulimia	-0.22 (-1.2, 0.76)	Ref	-0.23 (-0.76, 0.3)	0.42 (-0.5, 1.33)	0.26 (-0.28, 0.8)	Ref	0.62 (-0.09, 1.33)
Oral control	0.13 (-1.12, 1.37)	Ref	-0.34 (-1.01, 0.33)	-0.26 (-1.42, 0.9)	0.63 (-0.06, 1.31)	Ref	0.44 (-0.46, 1.34)

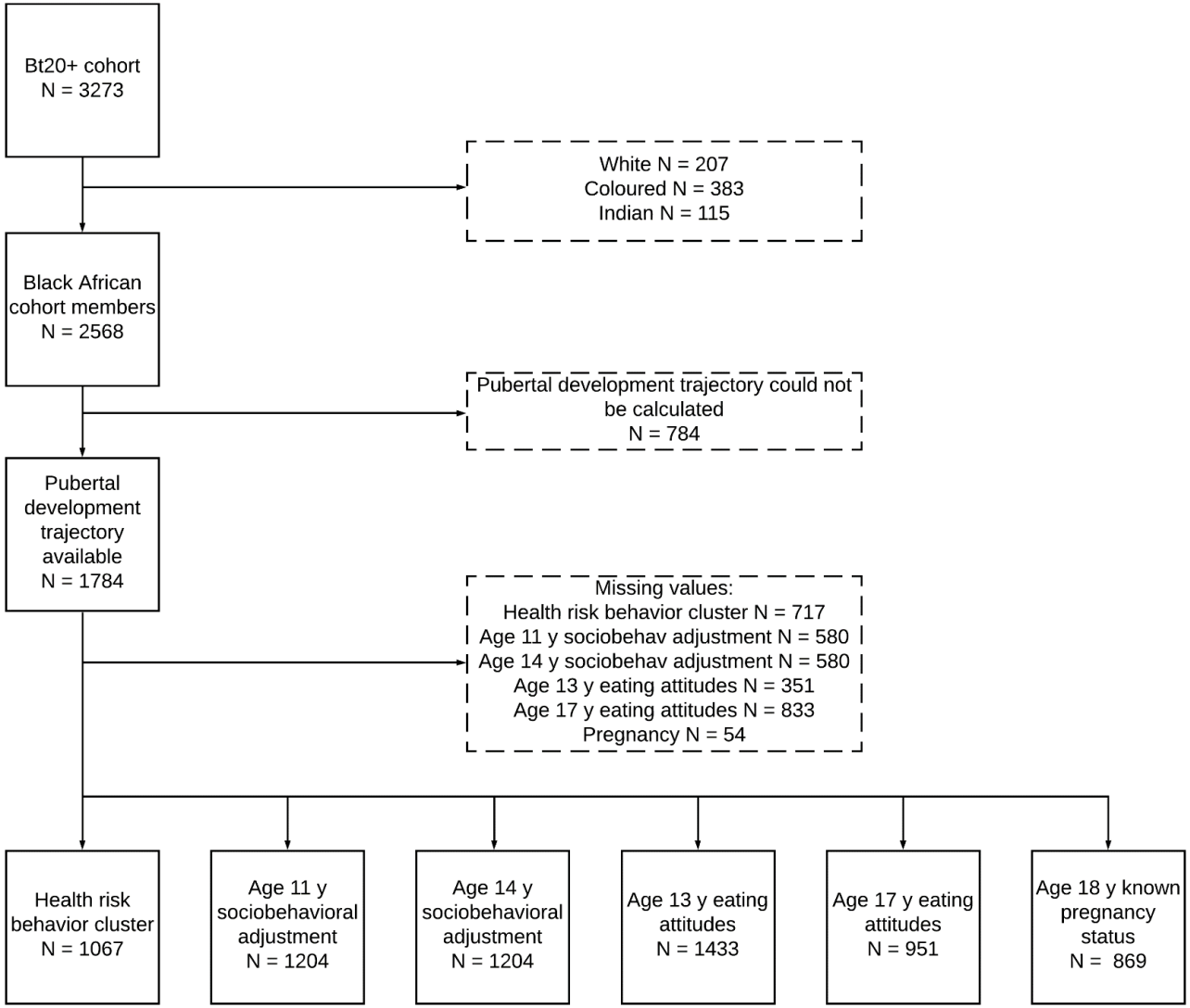
[a] Pattern of risk behavior initiation estimates are adjusted odds ratios from multinomial logistic regression. All other estimates are beta coefficients from linear regression. Models adjusted for household asset ownership at age 0-2 y, household asset ownership at age 7 y, childhood stress exposure, and companion variables for each measure. Abbreviations: Gen class, genital development class; PH class, pubic hair development class; Aff, affective problems; Anx, anxiety problems; Som, somatic problems; Attn Def, attention deficit problems; Opp Def, oppositional defiant problems; Conduct, conduct problems.

Table 4. Adjusted associations of female breast and pubic hair development classes and age of menarche with adolescent emotional and behavioral adjustment, eating attitudes, and patterns of risk behavior initiation[a]

	Br class 1 (Later and slower)	Br class 2	Br class 3	Br class 4 (Earlier and faster)	PH class 1 (Later and slower)	PH class 2	PH class 3 (Earlier and faster)	Age of menarche
Pattern of risk behavior initiation	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)
Low-risk	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Moderate risk	0.88 (0.46, 1.66)	Ref	1.8 (0.97, 3.34)	1.99 (0.89, 4.44)	**0.58 (0.35, 0.95)**	Ref	1.49 (0.62, 3.63)	**0.82 (0.66, 1)**
High-risk	1.25 (0.45, 3.45)	Ref	**3.44 (1.38, 8.58)**	**3.45 (1.13, 10.49)**	0.54 (0.27, 1.1)	Ref	2.12 (0.74, 6.04)	**0.53 (0.39, 0.71)**
Sociobehavioral adjustment	β (95% CI)	Ref	β (95% CI)	β (95% CI)	β (95% CI)	Ref	β (95% CI)	β (95% CI)
Age 11 y								
Aff	-0.36 (-1.12, 0.4)	Ref	-0.65 (-1.31, 0.01)	-0.6 (-1.43, 0.22)	0.41 (-0.15, 0.97)	Ref	0.13 (-0.64, 0.89)	-0.11 (-0.32, 0.1)
Anx	0.2 (-0.29, 0.7)	Ref	-0.05 (-0.48, 0.38)	0.12 (-0.42, 0.66)	0.06 (-0.3, 0.43)	Ref	0.01 (-0.49, 0.51)	-0.02 (-0.16, 0.11)
Som	-0.25 (-0.91, 0.4)	Ref	0.05 (-0.52, 0.62)	0.11 (-0.6, 0.83)	-0.14 (-0.62, 0.34)	Ref	-0.39 (-1.05, 0.27)	-0.12 (-0.3, 0.06)
Attn Def	-0.57 (-1.33, 0.19)	Ref	0.02 (-0.64, 0.68)	0 (-0.83, 0.83)	0.24 (-0.31, 0.8)	Ref	0.46 (-0.31, 1.22)	-0.19 (-0.4, 0.02)
Opp Def	0.06 (-0.35, 0.47)	Ref	0.18 (-0.18, 0.53)	-0.04 (-0.49, 0.41)	-0.12 (-0.42, 0.18)	Ref	0.39 (-0.02, 0.8)	-0.1 (-0.22, 0.01)
Conduct	-0.26 (-0.88, 0.35)	Ref	-0.09 (-0.63, 0.44)	-0.14 (-0.81, 0.53)	0.18 (-0.27, 0.63)	Ref	0.16 (-0.45, 0.77)	-0.16 (-0.33, 0.01)
Age 14 y								
Aff	0.11 (-0.88, 1.1)	Ref	0.32 (-0.55, 1.19)	0.72 (-0.39, 1.84)	0.21 (-0.53, 0.95)	Ref	**1.03 (0.02, 2.05)**	**-0.29 (-0.58, 0)**
Anx	-0.27 (-0.82, 0.28)	Ref	-0.01 (-0.5, 0.47)	0.04 (-0.58, 0.66)	**-0.44 (-0.85, -0.03)**	Ref	0.31 (-0.26, 0.87)	-0.12 (-0.28, 0.04)
Som	-0.11 (-0.69, 0.48)	Ref	-0.03 (-0.54, 0.49)	0.39 (-0.27, 1.05)	-0.23 (-0.67, 0.21)	Ref	-0.29 (-0.89, 0.32)	-0.13 (-0.3, 0.04)
Attn Def	-0.67 (-1.45, 0.1)	Ref	0.35 (-0.33, 1.03)	0.37 (-0.51, 1.24)	0.09 (-0.5, 0.67)	Ref	**1.11 (0.31, 1.92)**	**-0.47 (-0.7, -0.24)**
Opp Def	-0.47 (-1.02, 0.07)	Ref	-0.05 (-0.53, 0.42)	-0.23 (-0.84, 0.38)	-0.22 (-0.63, 0.19)	Ref	0.21 (-0.35, 0.77)	**-0.19 (-0.35, -0.03)**
Conduct	-0.21 (-0.94, 0.52)	Ref	0.48 (-0.16, 1.12)	0.69 (-0.13, 1.51)	-0.4 (-0.94, 0.15)	Ref	0.32 (-0.44, 1.07)	-0.16 (-0.38, 0.05)
Eating attitudes	β (95% CI)	Ref	β (95% CI)	β (95% CI)	β (95% CI)	Ref	β (95% CI)	β (95% CI)
Age 13 y								
Total	1.85 (-0.04, 3.74)	Ref	0.36 (-1.33, 2.05)	1.93 (-0.18, 4.04)	1.37 (-0.03, 2.78)	Ref	1.56 (-0.4, 3.53)	0.18 (-0.38, 0.74)
Dieting	0.58 (-0.48, 1.63)	Ref	0.71 (-0.23, 1.66)	**2.12 (0.94, 3.3)**	0.14 (-0.65, 0.93)	Ref	**1.37 (0.27, 2.48)**	-0.11 (-0.43, 0.2)
Bulimia	0.39 (-0.16, 0.95)	Ref	-0.31 (-0.81, 0.18)	**-0.67 (-1.29, -0.04)**	**0.63 (0.22, 1.05)**	Ref	0.05 (-0.54, 0.63)	0.1 (-0.06, 0.27)
Oral control	**0.88 (0.04, 1.72)**	Ref	-0.03 (-0.78, 0.72)	0.48 (-0.46, 1.41)	0.6 (-0.02, 1.23)	Ref	0.15 (-0.73, 1.02)	0.19 (-0.06, 0.44)
Age 17 y								
Total	-0.91 (-3.45, 1.63)	Ref	0.2 (-2.18, 2.58)	0.28 (-2.6, 3.16)	1.7 (-0.23, 3.64)	Ref	**4.58 (1.92, 7.24)**	-0.32 (-1.11, 0.47)
Dieting	-0.63 (-2.19, 0.93)	Ref	-0.07 (-1.53, 1.39)	0.73 (-1.04, 2.5)	1.04 (-0.16, 2.24)	Ref	**2.51 (0.87, 4.15)**	-0.14 (-0.63, 0.34)
Bulimia	-0.33 (-1.08, 0.43)	Ref	-0.24 (-0.95, 0.47)	-0.82 (-1.68, 0.04)	0.27 (-0.32, 0.86)	Ref	0.79 (-0.01, 1.6)	0.05 (-0.19, 0.28)
Oral control	0.04 (-1.01, 1.1)	Ref	0.51 (-0.47, 1.5)	0.37 (-0.82, 1.56)	0.39 (-0.42, 1.2)	Ref	**1.27 (0.17, 2.38)**	-0.23 (-0.55, 0.1)

[a] Pattern of risk behavior initiation estimates are adjusted odds ratios from multinomial logistic regression. All other estimates are beta coefficients from linear regression. Models adjusted for household asset ownership at age 0-2 y, household asset ownership at age 7 y, childhood stress exposure, and companion variables for each measure. [b]Pattern of risk behavior initiation estimates are adjusted odds ratios from multinomial logistic regression. All other estimates are beta coefficients from linear regression. Abbreviations: Br class, breast development class; PH class, pubic hair development class; Aff, affective problems; Anx, anxiety problems; Som, somatic problems; Attn Def, attention deficit problems; Opp Def, oppositional defiant problems; Conduct, conduct problems.

Figure 1. Birth to Twenty Plus analytical sample



Supplemental Tables

Supplemental Table 1. Unadjusted associations of sex development classes with health risk behavior clusters, Y11 and Y14 Youth Self Report, and Y13 and Y17 Eating Attitudes[a]

	Gen class 1 (Later and slower)	Gen class 2	Gen class 3	Gen class 4 (Earlier and faster)	PH class 1 (Later and slower)	PH class 2	PH class 3 (Earlier and faster)
Pattern of risk behavior initiation	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)	OR (95% CI)	Ref	OR (95% CI)
Low-risk	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Moderate risk	1.17 (0.45, 3.01)	Ref	1.5 (0.94, 2.4)	**3.56 (1.3, 9.77)**	**0.57 (0.35, 0.93)**	Ref	**2.25 (1.02, 4.99)**
High-risk	1.17 (0.44, 3.11)	Ref	**2.16 (1.35, 3.45)**	**4.01 (1.46, 11.05)**	0.73 (0.45, 1.16)	Ref	**2.52 (1.15, 5.51)**
Sociobehavioral adjustment	β (95% CI)	Ref	β (95% CI)	β (95% CI)	β (95% CI)	Ref	β (95% CI)
Age 11 y							
Aff	0.24 (-0.63, 1.11)	Ref	-0.08 (-0.51, 0.35)	0.27 (-0.56, 1.1)	-0.01 (-0.46, 0.44)	Ref	-0.06 (-0.71, 0.59)
Anx	0.6 (-0.05, 1.25)	Ref	0.27 (-0.06, 0.59)	-0.31 (-0.92, 0.3)	-0.25 (-0.59, 0.08)	Ref	-0.27 (-0.75, 0.21)
Som	-0.68 (-1.49, 0.12)	Ref	0.26 (-0.14, 0.65)	0.15 (-0.61, 0.9)	-0.4 (-0.81, 0.01)	Ref	0.38 (-0.21, 0.98)
Attn Def	0.04 (-0.88, 0.96)	Ref	0.38 (-0.07, 0.84)	0.41 (-0.46, 1.28)	-0.44 (-0.91, 0.03)	Ref	**0.73 (0.06, 1.41)**
Opp Def	-0.21 (-0.76, 0.34)	Ref	0.22 (-0.06, 0.49)	0.45 (-0.08, 0.97)	**-0.31 (-0.6, -0.03)**	Ref	0.37 (-0.04, 0.78)
Conduct	-0.33 (-1.3, 0.64)	Ref	-0.08 (-0.56, 0.39)	0.48 (-0.42, 1.38)	0.05 (-0.44, 0.54)	Ref	**0.72 (0.02, 1.42)**
Age 14 y							
Aff	**1.15 (0.19, 2.12)**	Ref	**0.75 (0.26, 1.24)**	-0.12 (-1.05, 0.81)	-0.41 (-0.92, 0.09)	Ref	**-0.97 (-1.67, -0.26)**
Anx	0.08 (-0.59, 0.76)	Ref	-0.13 (-0.46, 0.2)	-0.29 (-0.93, 0.35)	-0.08 (-0.42, 0.27)	Ref	-0.13 (-0.61, 0.36)
Som	0.35 (-0.22, 0.91)	Ref	0.07 (-0.21, 0.36)	0.06 (-0.48, 0.6)	-0.12 (-0.41, 0.17)	Ref	0.02 (-0.39, 0.43)
Attn Def	**1.05 (0.01, 2.09)**	Ref	0.52 (-0.01, 1.04)	0.51 (-0.49, 1.5)	-0.38 (-0.92, 0.16)	Ref	-0.52 (-1.28, 0.23)
Opp Def	-0.41 (-1.08, 0.25)	Ref	0.29 (-0.04, 0.62)	**1.11 (0.48, 1.74)**	-0.47 (-0.81, -0.13)	Ref	**0.56 (0.09, 1.04)**
Conduct	0.03 (-1.09, 1.15)	Ref	0.33 (-0.23, 0.9)	0.38 (-0.69, 1.45)	-0.4 (-0.98, 0.18)	Ref	-0.29 (-1.1, 0.52)
Eating attitudes	β (95% CI)	Ref	β (95% CI)	β (95% CI)	β (95% CI)	Ref	β (95% CI)
Age 13 y							
Total	-0.29 (-2.72, 2.13)	Ref	-0.61 (-1.77, 0.54)	-0.71 (-2.83, 1.41)	-0.18 (-1.39, 1.02)	Ref	0.03 (-1.63, 1.7)
Dieting	-0.27 (-1.67, 1.14)	Ref	-0.21 (-0.88, 0.46)	-0.27 (-1.5, 0.96)	-0.15 (-0.85, 0.55)	Ref	0.46 (-0.5, 1.42)
Bulimia	0.43 (-0.43, 1.3)	Ref	0.24 (-0.17, 0.66)	0.27 (-0.49, 1.03)	-0.2 (-0.63, 0.23)	Ref	-0.01 (-0.6, 0.59)
Oral control	-0.46 (-1.45, 0.54)	Ref	**-0.64 (-1.12, -0.17)**	-0.71 (-1.58, 0.16)	0.17 (-0.32, 0.66)	Ref	-0.42 (-1.1, 0.26)
Age 17 y							
Total	0.85 (-1.59, 3.3)	Ref	**-1.43 (-2.75, -0.1)**	0.43 (-2.05, 2.91)	**2.34 (0.98, 3.71)**	Ref	1.82 (-0.12, 3.77)
Dieting	0.42 (-1.18, 2.01)	Ref	-0.85 (-1.71, 0.01)	0.83 (-0.79, 2.45)	**1.27 (0.38, 2.16)**	Ref	1.14 (-0.13, 2.41)
Bulimia	-0.28 (-1.09, 0.53)	Ref	-0.36 (-0.8, 0.08)	0.03 (-0.79, 0.85)	0.38 (-0.08, 0.83)	Ref	0.42 (-0.22, 1.07)

Oral control	0.72 (-0.33, 1.77)	Ref	-0.22 (-0.78, 0.35)	-0.43 (-1.49, 0.63)	**0.7 (0.12, 1.29)**	Ref	0.26 (-0.58, 1.1)

[a] Pattern of risk behavior initiation estimates are adjusted odds ratios from multinomial logistic regression. All other estimates are beta coefficients from linear regression. Abbreviations: Gen class, genital development class; PH class, pubic hair development class; Aff, affective problems; Anx, anxiety problems; Som, somatic problems; Attn Def, attention deficit problems; Opp Def, oppositional defiant problems; Conduct, conduct problems.

Supplemental Table 2. Unadjusted associations of female breast and pubic hair development classes and age of menarche with adolescent emotional and behavioral adjustment, eating attitudes, and patterns of risk behavior initiation[a]

	Br class 1 (Later and slower)	Br class 2	Br class 3	Br class 4 (Earlier and faster)	PH class 1 (Later and slower)	PH class 2	PH class 3 (Earlier and faster)	Age of menarche
Pattern of risk behavior initiation	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)	OR (95% CI)	Ref	OR (95% CI)	OR (95% CI)
Low-risk	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Moderate risk	0.66 (0.38, 1.15)	Ref	1.4 (0.82, 2.39)	1.48 (0.72, 3.04)	**0.53 (0.34, 0.82)**	Ref	1.31 (0.62, 2.76)	0.85 (0.72, 1.01)
High-risk	0.93 (0.42, 2.09)	Ref	**2.21 (1.06, 4.61)**	**2.8 (1.12, 6.97)**	0.6 (0.34, 1.08)	Ref	1.9 (0.8, 4.54)	**0.62 (0.5, 0.79)**
Sociobehavioral adjustment	β (95% CI)	Ref	β (95% CI)	β (95% CI)	β (95% CI)	Ref	β (95% CI)	β (95% CI)
Age 11 y								
Aff	-0.22 (-0.86, 0.42)	Ref	**-0.63 (-1.19, -0.07)**	-0.31 (-1.03, 0.4)	0.25 (-0.23, 0.73)	Ref	0.06 (-0.6, 0.72)	-0.11 (-0.28, 0.06)
Anx	0.11 (-0.3, 0.52)	Ref	-0.01 (-0.36, 0.35)	0.35 (-0.11, 0.81)	0.04 (-0.27, 0.34)	Ref	0.2 (-0.23, 0.62)	-0.04 (-0.15, 0.07)
Som	-0.2 (-0.74, 0.33)	Ref	0.04 (-0.42, 0.5)	0.24 (-0.35, 0.84)	-0.21 (-0.61, 0.19)	Ref	-0.17 (-0.72, 0.38)	**-0.15 (-0.3, -0.01)**
Attn Def	-0.49 (-1.12, 0.14)	Ref	0.15 (-0.4, 0.7)	0.31 (-0.4, 1.02)	0.1 (-0.38, 0.57)	Ref	0.61 (-0.05, 1.27)	-0.18 (-0.35, -0.01)
Opp Def	-0.05 (-0.41, 0.31)	Ref	0.05 (-0.27, 0.36)	0.08 (-0.32, 0.49)	-0.14 (-0.41, 0.13)	Ref	0.34 (-0.03, 0.71)	-0.16 (-0.25, -0.06)
Conduct	0.1 (-0.41, 0.62)	Ref	-0.14 (-0.59, 0.31)	0.06 (-0.52, 0.64)	0.38 (-0.01, 0.77)	Ref	0.29 (-0.24, 0.82)	-0.05 (-0.19, 0.09)
Age 14 y								
Aff	0.03 (-0.78, 0.84)	Ref	0.22 (-0.49, 0.93)	**0.98 (0.07, 1.9)**	-0.12 (-0.73, 0.49)	Ref	**1.04 (0.19, 1.89)**	**-0.39 (-0.62, -0.16)**
Anx	-0.11 (-0.56, 0.34)	Ref	-0.05 (-0.45, 0.35)	0.22 (-0.28, 0.73)	**-0.38 (-0.72, -0.05)**	Ref	0.22 (-0.25, 0.69)	**-0.17 (-0.3, -0.05)**
Som	-0.16 (-0.64, 0.31)	Ref	-0.09 (-0.51, 0.33)	0.28 (-0.25, 0.82)	-0.18 (-0.54, 0.18)	Ref	-0.24 (-0.74, 0.26)	-0.08 (-0.21, 0.05)
Attn Def	-0.34 (-0.98, 0.3)	Ref	0.48 (-0.09, 1.04)	0.66 (-0.06, 1.39)	-0.15 (-0.63, 0.33)	Ref	**1.29 (0.62, 1.96)**	-0.44 (-0.62, -0.27)
Opp Def	-0.43 (-0.88, 0.03)	Ref	0.03 (-0.37, 0.43)	0.12 (-0.4, 0.64)	**-0.42 (-0.77, -0.08)**	Ref	0.38 (-0.1, 0.86)	**-0.33 (-0.46, -0.2)**
Conduct	0 (-0.6, 0.59)	Ref	0.48 (-0.05, 1)	**0.78 (0.1, 1.45)**	-0.41 (-0.86, 0.04)	Ref	0.35 (-0.28, 0.98)	**-0.18 (-0.35, -0.02)**
Eating attitudes	β (95% CI)	Ref	β (95% CI)	β (95% CI)	β (95% CI)	Ref	β (95% CI)	β (95% CI)
Age 13 y								
Total	0.96 (-0.64, 2.56)	Ref	0.21 (-1.21, 1.64)	1.29 (-0.51, 3.09)	0.9 (-0.31, 2.11)	Ref	0.67 (-1.02, 2.36)	-0.07 (-0.52, 0.38)
Dieting	0.23 (-0.67, 1.13)	Ref	**0.84 (0.03, 1.64)**	**1.86 (0.85, 2.87)**	0.05 (-0.64, 0.73)	Ref	**0.97 (0.01, 1.93)**	-0.25 (-0.51, 0.01)
Bulimia	0.26 (-0.21, 0.74)	Ref	-0.18 (-0.6, 0.25)	-0.43 (-0.96, 0.11)	**0.39 (0.03, 0.75)**	Ref	-0.07 (-0.57, 0.43)	0.02 (-0.12, 0.15)
Oral control	0.47 (-0.26, 1.19)	Ref	-0.45 (-1.09, 0.2)	-0.15 (-0.96, 0.67)	0.46 (-0.09, 1.01)	Ref	-0.23 (-0.99, 0.54)	0.16 (-0.04, 0.37)
Age 17 y								
Total	-0.35 (-2.61, 1.9)	Ref	-0.01 (-2.08, 2.06)	0.88 (-1.64, 3.4)	0.86 (-0.87, 2.59)	Ref	2.31 (-0.03, 4.65)	-0.33 (-1, 0.33)
Dieting	-0.04 (-1.44, 1.37)	Ref	-0.01 (-1.31, 1.28)	1.08 (-0.49, 2.65)	0.05 (-0.64, 0.73)	Ref	**0.97 (0.01, 1.93)**	-0.13 (-0.54, 0.29)

Bulimia	-0.28 (-0.94, 0.38)	Ref	-0.24 (-0.85, 0.37)	-0.64 (-1.38, 0.1)	**0.39 (0.03, 0.75)**	Ref	-0.07 (-0.57, 0.43)	0.01 (-0.19, 0.21)
Oral control	-0.03 (-0.95, 0.89)	Ref	0.25 (-0.6, 1.09)	0.43 (-0.6, 1.46)	0.46 (-0.09, 1.01)	Ref	-0.23 (-0.99, 0.54)	-0.22 (-0.49, 0.06)

[a] Pattern of risk behavior initiation estimates are adjusted odds ratios from multinomial logistic regression. All other estimates are beta coefficients from linear regression. Abbreviations: Br class, breast development class; PH class, pubic hair development class; Aff, affective problems; Anx, anxiety problems; Som, somatic problems; Attn Def, attention deficit problems; Opp Def, oppositional defiant problems; Conduct, conduct problems.

Supplemental Table 3. Associations of genital/breast development and pubic hair development classes with adolescent emotional and behavioral adjustment modified by childhood stress[a]

	Gen/Br class 1 β (95% CI)	Gen/Br class 2 β (95% CI)	Gen/Br class 3 β (95% CI)	Gen/Br class 4 β (95% CI)	PH class 1 β (95% CI)	PH class 2 β (95% CI)	PH class 3 β (95% CI)
Males							
Som 11 y 0X	--	--	--	--	-0.57 (-1.19, 0.05)	Ref	0.54 (-0.32, 1.4)
Som 11 y 1X	--	--	--	--	-1.17 (-1.94, -0.41)	Ref	-1.33 (-2.52, -0.13)
Som 11 y 2-3X	--	--	--	--	0.36 (-0.46, 1.18)	Ref	1.75 (0.64, 2.87)
Attn Def 14 y 0X	0.81 (-0.71, 2.33)	Ref	0.8 (-0.01, 1.6)	2.25 (0.6, 3.9)	--	--	--
Attn Def 14 y 1X	0.77 (-0.85, 2.4)	Ref	-0.32 (-1.23, 0.59)	-0.37 (-1.95, 1.21)	--	--	--
Attn Def 14 y 2-3X	2.74 (-0.14, 5.62)	Ref	1.9 (0.63, 3.17)	-0.24 (-2.38, 1.9)	--	--	--
Conduct 14 y 0X	--	--	--	--	-0.96 (-1.87, -0.05)	Ref	0.21 (-1.05, 1.47)
Conduct 14 y 1X	--	--	--	--	0.56 (-0.51, 1.64)	Ref	-0.93 (-2.45, 0.58)
Conduct 14 y 2-3X	--	--	--	--	-1.9 (-3.27, -0.53)	Ref	-0.75 (-2.49, 0.98)
Females							
Attn Def 11 y 0X	--	--	--	--	-0.05 (-0.84, 0.74)	Ref	1.63 (0.48, 2.77)
Attn Def 11 y 1X	--	--	--	--	0 (-0.75, 0.75)	Ref	-0.9 (-1.99, 0.18)
Attn Def 11 y 2-3X	--	--	--	--	0.83 (-0.25, 1.91)	Ref	1.03 (-0.3, 2.37)
Som 14 y 0X	0.15 (-0.62, 0.92)	Ref	0.29 (-0.37, 0.96)	1.34 (0.51, 2.18)	--	--	--
Som 14 y 1X	-0.72 (-1.49, 0.06)	Ref	-0.51 (-1.2, 0.18)	-0.75 (-1.6, 0.09)	--	--	--
Som 14 y 2-3X	0.6 (-0.5, 1.7)	Ref	0.1 (-0.86, 1.06)	0.27 (-1.19, 1.73)	--	--	--

[a] Estimates are β (95% CI) from linear regressions. Abbreviations: Gen/Br class, genital/breast development class; PH class, pubic hair development class; Som, somatic problems; Attn Def, attention deficit problems; Conduct, conduct problems.

Chapter 6: Associations of pubertal timing and tempo with schooling attainment and employment in adulthood in urban South Africa

Manuscript Authors: Alysse J. Kowalski, O. Yaw Addo, Michael R. Kramer, Reynaldo Martorell, Rachel N. Waford, Linda M. Richter*, Aryeh D. Stein*

*Co-senior authors

Abstract

Objective

Education is a key component of human capital formation. Few studies have examined the lasting influence of pubertal timing and tempo on schooling attainment and employment in adulthood and none have examined mediation by adolescent risk behavior or pregnancy.

Methods

Using data from 1,784 participants from the Birth to Twenty Plus cohort in Soweto-Johannesburg, South Africa, we used structural equation models to examine associations of pubertal timing and tempo with schooling attainment and employment at age 22 y and examined the mediating role of adolescent risk behavior initiation and pregnancy. We used latent classes of genital/breast development and pubic hair development previously derived from repeated measures of the Tanner sexual maturation scale and age at menarche for females.

Results

At age 22 y, high school equivalency completion (matric) was 57% for males and 72% for females, though unemployment was similar at 53% and 51%, respectively. Relative to peers, individuals who entered puberty later and progressed through puberty slower had lower schooling attainment at age 22 y. Females who matured earlier and faster had better employment status at age 22 y. We did not find evidence of mediation by adolescent risk behaviors or pregnancy in overall associations.

Conclusion

Adolescents who mature later and slower than their peers have lower schooling attainment as adults, while earlier and faster maturing females had better employment status in urban South Africa. These associations may be explained by unmeasured confounding resulting from intangible advantages of increased socioeconomic status.

Introduction

Human capital is the accumulated knowledge, skills, and health that enable individuals to realize their potential as productive citizens and is important for economic growth and building inclusive societies (1). Education and training build knowledge and skills while physical and mental health allow individuals to partake in education and training and put these knowledge and skills into practice. Factors that prevent individuals from reaching their full potential result in unrealized human capital.

Puberty is a profound physiological transformation culminating in reproductive maturity and the development of secondary sex characteristics and occurs with other physical development including the adolescent growth spurt and changes in body composition. Despite being a universal process, there is wide variation in the age of onset, or timing of puberty and its pace, or tempo. This variability is such that a small number of youths will finish puberty before others have started.

Though the physical disruption of puberty is short-lived, its consequences may be long lasting. Educational careers are cumulative, with secondary school performance an important determinant of future schooling and employment opportunities. Few studies have examined long-term consequences of pubertal timing on schooling attainment and employment, in part because they lack the longitudinal data needed to do so. Early maturing girls have been found to complete less schooling than their on-time maturing peers (2-6) and late maturers were more likely to have received their bachelor's degree (7) and spend more time in education when assessed as adults (8). However, maturational timing was not associated with employment status in early adulthood (7, 9).

Variation in pubertal timing and tempo has repercussions for health risk behavior initiation. Boys and girls with earlier puberty onset experiment with more health risk behaviors in adolescence (10, 11). It is well established that health risk behavior activity (i.e. smoking, alcohol use, and cannabis use) in adolescence is associated with lower schooling attainment, unemployment, and lower socioeconomic status in adulthood (12-15). Adolescent parenthood is associated with lower schooling attainment and socioeconomic status in adulthood (16-18).

Limited research has investigated the persistence of pubertal timing and tempo associations beyond adolescence and we were unable to identify any studies with such data for males. Few studies have been able to collect the longitudinal data needed to answer such questions and the lack of an indicator comparable to menarche has likely contributed to the dearth of research among males. The studies that do exist have been conducted exclusively in high-income countries and these associations may differ in low- and middle-income settings. Moreover, the potential mediating role of adolescent health risk behavior activity and pregnancy have not been investigated.

In this study we will address some of these gaps by examining the association of pubertal timing and tempo with schooling attainment and employment in early adulthood in urban South Africa. Furthermore, we will explore the mediating roles of adolescent health risk behavior and pregnancy in these associations.

Methods

Study population

We used data from the Birth to Twenty Plus (Bt20+) birth cohort in Soweto-Johannesburg, South Africa. Bt20+ participants were born between April to June 1990 and resided in the area for a minimum of 6 months after birth (N = 3,267). The cohort has been followed over time and has been stable since childhood. Seventy percent of participants were traceable at age 17 y (19).

Data collection

Study visits were conducted at the Development Pathways for Health Research Unit at Chris Hani Baragwanath academic hospital by trained research assistants. We used data from the age 0-2, 5, 7, 11, 13, 14, 15, 16, 17, 18, and 22 y waves, which correspond to the child's age at the start of data collection (Supplemental Table 1). Data were collected by interview or self-administered questionnaires. Self-administered questionnaires were completed on paper at the age 11, 13, and 14 study visits, and using an audio computer-aided self-administered interview system at later visits. Adolescent pregnancy data was supplemented with data from an ongoing pregnancy and live birth surveillance system.

Independent variables

Previously, latent class growth analysis was used to identify sex-specific latent classes of genital/breast and pubic hair timing and tempo from repeated self-rated measures of the Tanner sexual maturation scale (SMS), the self-rated approach was validated for the population (20-22). Three classes of pubic hair development and 4 classes of genital/breast development were identified for boys and girls. Compared to their peers in other classes, individuals in class 1 entered puberty later and progressed through puberty slower, while individuals in the highest class had the earliest pubertal timing and fastest tempo. Age of menarche was ascertained from a menarche status question on the self-complete questionnaire included at each adolescent study visit. Early menarche was defined as an age of menarche > 1 SD below the mean age of menarche.

Dependent variables

For both sexes, timing of smoking, alcohol, cannabis, illicit drug, and sexual activity initiation through age 18 y were previously used in a cluster analysis to identify three distinct patterns of health risk behavior initiation (low-, moderate, and high-risk) (REF). Individuals in the high-risk pattern tended to try more risk behaviors than the overall sample and did so at a younger age. In contrast, individuals in the low-risk pattern tended to try fewer behaviors than the overall sample and did so at an older age.

We defined adolescent pregnancy as an affirmative response to the pregnancy history question on the questionnaire (first asked at age 15 y) or having report of pregnancy through age 18 y in the surveillance system. We used the adolescent pregnancy measure and number of pregnancies reported at age 22 y to identify young adult pregnancies between ages 19 and 22 y.

We used schooling qualification data collected at age 22 y to create ordinal categories of schooling attainment: <matric, matric, and at least some university schooling. A matric is the South African equivalent of a high school diploma and is required for university studies. Similarly, we used age 22 y employment history data to create ordinal categories of employment: unemployed, currently employed casually or with a short-term contract, or currently employed with a permanent contract.

Covariates

We used tertiles of the number of household assets owned as a measure of socioeconomic position at age 0-2 y and age 7 y (supplemented with observations from age 5 y). We characterized childhood exposure to stress as the number of study waves (0, 1, 2-3) at which the mother reported experiencing more than the sample median number of stress and violence events from an inventory. The stress and violent events inventory was administered at ages 0-2, 5, and 7 y. Non-verbal fluid intelligence was assessed at age 7 y using the Ravens Colored Progressive Matrices. Scores were standardized and categorized into tertiles.

We used two-way imputation (TWI) to assign values to missing household asset and stress and violence event items for individuals who completed at least 50% of the relevant questions. TWI is a deterministic imputation approach that uses the person mean and sample mean for an item to assign a value to a missing item (23) TWI recovered N = 308 observations for household asset ownership at age 0-2 y where the completion rate was 64%. Completion rates for other imputed measures were ≥90%. Following TWI, we additionally created an informative missing category for each covariate.

Analytical sample

Black Africans are the dominant population subgroup in Soweto-Johannesburg and comprises 78% of Bt20+ participants. We restricted our analysis to N = 1,784 Black African participants for whom we have pubertal development classes. We allowed the sample size to vary for each dependent variable to maximize the available data (Supplemental Figure 1).

Statistical analysis

Using chi-square tests, we examined covariate and dependent variable characteristics by pubertal development classes and early menarche.

We conceptualized the associations between the pubertal development, adolescent, and young adult measures (Figure 1, Figure 2). In specifying the model, we considered the binary (adolescent pregnancy, young adult pregnancy) and ordinal (risk behavior, schooling, and employment) dependent

variables as continuous latent variables using Bernoulli and ordinal probit link functions as appropriate. When a pubertal development class was considered the independent variable, we set class 2 as the referent group. We fit generalized structural equation models (gSEM) using diagonal weighted least squares maximum likelihood estimation with 1000 bootstraps and pairwise deletion. We adjusted models for prepubertal characteristics: age 0-2 asset ownership, age 7 asset ownership, child stress exposure, and non-verbal fluid intelligence.

All analyses were conducted using R version 3.5.3 with two-sided p-values <0.05 statistically significant (24). gSEM were fit using the '*lavaan*' package (25).

Results

Selected characteristics of the analytical sample are shown in Table 1. Seven percent of males and 14% of females were in the earliest and fastest genital/breast development classes while 6% of males and 23% of females were in the late and slow genital/breast development class. For pubic hair development, 12% each of males and females were in the early and fast development class while 29% of males and 34% of females were in the late and slow class. Mean age of menarche was 12.7 years and 17% of girls experienced early menarche. In males, mean age of genital development onset ranged from 11.6 y in the earlier and fastest class to 14.4 in the later and slower class and mean age of pubic hair onset ranged from 11.9 y to 13.3 y, respectively (Table 2, Table 3). In females, mean age of breast development onset ranged from 12 y in the earlier and faster class to 13.4 y in the later and slower class and mean age of pubic hair onset ranged from 10.8 y in the earliest and fastest class to 13.0 y in the later and slower class. Thirty-five percent of males and 17% of females were assigned to the high-risk risk behavior initiation pattern (Table 1). One-third of females were pregnant <19 y and one-third were pregnant between ages 19 and 22 y. As of 22 y, 42% of males and 50% of females had earned their matric, though among both sexes >50% were unemployed.

Pubertal timing and tempo differed by household asset ownership (Table 2, Table 3). Males and females from households in a higher asset tertile were more likely to be in earlier and faster pubertal

development classes and experience early menarche (females). Females with fluid intelligence scores in the lowest tertile were more likely to be in the late and slow breast and pubic hair development classes compared to girls in the other tertiles. Associations of prepubertal measures with adolescent and early adult measures are shown in Supplemental Table 2 and Supplemental Table 3.

SEM results, males

Compared to the referent class, earlier and faster genital (classes 3 and 4) and pubic hair (class 3) development were positively associated with risk behavior initiation pattern among males, with a larger effect for earliest and fastest genital development (class 3 β [95% CI] = 0.36 [0.1, 0.62]; class 4 β = 0.58 [0.1, 0.95]). There was no association with later and slower maturation (Table 4).

Later and slower pubic hair development (class 1) was associated with lower schooling attainment at 22 y in total and direct effects compared to the referent group (class 2). There was a negative indirect association of earlier and faster genital (classes 3 and 4) and pubic hair development (class 3) with schooling attainment at 22 y among males compared to the referent group, with a dose response for genital development (class 3 β = -0.08 [-0.17, -0.02]; class 4 β = -0.12 [-0.25, -0.02]). These indirect associations were canceled out by positive direct associations, such that total associations with schooling at 22 y were null. The timing and tempo of genital and pubic hair development were not associated with employment at 22 y. Unadjusted associations can be found in Supplemental Table 4.

SEM results, females

Compared to the referent class, earlier and faster breast development was positively associated with risk behavior initiation pattern (class 4 β = 0.31 [0.01, 0.69]) while increasing age of menarche was negatively associated (β = -0.16 [-0.25, -0.08]) (Table 5).

Pubertal timing and tempo are associated with adolescent pregnancy via an indirect path through adolescent risk behavior initiation pattern which includes sexual debut. Relative to the normative class, earlier and faster breast development (class 4) was positively associated with adolescent pregnancy (β = 0.09 [0.01, 0.2]) and increasing age of menarche was negatively associated with adolescent pregnancy (β

= -0.04 [-0.07, -0.01]) in unadjusted models. These associations were no longer significant following adjustment. Pubertal timing and tempo were not associated with young adult pregnancy.

Later and slower pubic hair development (class 1) relative to class 2 and older age of menarche were associated with lower schooling attainment at 22 y, with total effects driven by direct effects. Earlier and faster breast development was positively associated with schooling attainment through direct associations in unadjusted models, though these were no longer significant following adjustment (Supplemental Table 5).

Early and rapid breast development (class 4) relative to the normative group was positively associated with employment at 22 y; 84% of this association was through a direct association while 16% was through an indirect association through schooling attainment. Compared to class 2, there was a negative indirect effect of later and slower pubic hair development (class 1) with employment at 22 y; the direct effect was also negative though the total effect was not statistically significant.

In unadjusted models, class 3 breast development (relative to class 2) was associated with employment at 22 y through an indirect path (Supplemental Table 5). Conversely, later and slower pubic hair development (class 1 relative to class 2) and older age of menarche were negatively associated with employment at 22 y, also through indirect associations. Total associations for these indirect effects were null and the indirect associations were not significant in adjusted models.

Discussion

Using longitudinal data from the Bt20+ cohort in Soweto-Johannesburg, South Africa, we examined the associations of pubertal timing and tempo with schooling attainment and employment in early adulthood. We further explored the mediating roles of adolescent risk behavior initiation and pregnancy in females in these associations. We found individuals with later puberty onset and slower pubertal tempo relative to their peers have lower schooling attainment as young adults. Girls who matured earlier and faster than their peers had better employment outcomes, while pubertal timing and tempo were

not associated with employment for males. These overall associations were not significantly mediated by risk behavior initiation or adolescent pregnancy.

In both males and females, individuals with later pubertal timing and slower pubertal tempo had lower schooling attainment as young adults. This contrasts with findings from high-income countries which have either been null or in the opposite direction. In studies of European and Swedish women, women who were older at menarche relative to peers were more likely to have earned a bachelor's degree or spent more total years in schooling when assessed in adulthood, respectively (6, 8). These associations are hypothesized to arise from social mechanisms in which early maturers shift their engagement to older peer circles, contributing to increased risk behavior engagement and lower schooling attainment. We were not able to identify any studies with long-term follow-up on schooling attainment for males.

These differences between LMICs and HICs highlight the role of context and the importance of examining exposure-outcome associations in different settings. Other associations have been shown to differ in different contexts. For example, child growth is positively associated with schooling attainment in HICs and LMICs, though the magnitude differs substantially. A one standard deviation increase in childhood height-for-age (HAZ) was associated with an additional half year of schooling in Philippines but only an additional month in the UK and less than a month in Finland (26). These differences fall along a socioeconomic gradient in which the HAZ-schooling attainment association is stronger in LMICs and weaker in HICs. HAZ can be a marker of deficient environments in which gains in HAZ reflect improvements in the environment and in turn, increased schooling attainment (27). As there are far fewer environmental deficiencies in HICs, HAZ largely reflects variation in height in the population and does not reflect systemic deficiencies as evidenced by the weaker associations of HAZ with schooling attainment in HICs.

Malnutrition, as measured by lower HAZ, is associated with delays in puberty onset (28). By extension, age of puberty onset can also be viewed as a marker of environmental deficiency in childhood. Therefore, the pubertal timing-schooling association we examined in Bt20+ can be thought of as an association of environmental circumstances with schooling attainment such that poorer environmental

circumstances, reflected as later pubertal timing and slower tempo, are associated with lower schooling attainment. Though this contrasts with findings from HICs where late maturers tend to have higher schooling attainment, the contribution of deficient environments in LMICs may overwhelm social pathways that play out in some HIC settings.

Were environmental deficiencies driving the observed puberty-schooling association, this should have been attenuated following adjustment for SES. However, our SES measure was limited to physical asset ownership and did not account for other intangible aspects of deficient environments which remain uncontrolled for in our models and may explain our findings.

At age 22 y, 53% of males and 51% of females were unemployed, comparable with International Labor Organization statistics for this age group (29). Bt20+ females who matured earlier and faster relative to their peers had better employment as young adults. For females we identified two studies examining the associations of pubertal timing or tempo with employment outcomes. In the Christchurch Health and Development Study age of menarche was not found to be associated with unemployment lasting 3 months or measures of poverty or material hardship (9). In the Great Smoky Mountains Study, earlier age at menarche was associated with lower occupational status, though this was not significant (30). As described above, associations may differ in different contexts. Our observed association for females may reflect unmeasured confounding by socioeconomic status such that females from higher socioeconomic strata may have an advantage in the labor market.

No such association was observed for males, which may reflect gender differences in the labor market. In the South African economy, there are more manual labor jobs in which physical strength is advantageous. These positions are low-skilled and would not be expected to be associated with schooling. Additionally, in contrast to females, if the types of positions available to males are disproportionately casual or contract based, our employment measure would not detect a socioeconomic advantage within this category. We were unable to identify any studies examining the associations of pubertal timing or tempo with employment outcomes in males.

We hypothesized any association of pubertal timing and tempo with schooling attainment and employment would be mediated through adolescent risk behavior or adolescent parenthood, which are associated with lower schooling attainment, unemployment, and lower socioeconomic status in adulthood (12-18). However, we found no evidence that total associations of pubertal timing and tempo with schooling or employment were mediated through adolescent risk behavior initiation or pregnancy. In males, though there was a significant indirect association of pubertal timing and tempo with schooling attainment, this was canceled out by the positive direct association such that the overall association was null. Associations of pubertal timing and tempo with adolescent and young adult pregnancy were null. Early pregnancy has previously been shown to be higher among early maturers (31, 32). However, 34% of Bt20+ females reported a pregnancy prior to age 19 y, which may have obscured any association with pubertal timing and tempo. Indeed, age of adolescent pregnancy was over seven months younger among early maturers.

This study makes several contributions to the literature. To the best of our knowledge, it is the first to examine the lasting influence of pubertal timing and tempo into adulthood in the context of a middle-income country, as well as the first to examine these associations for males. We do so with multiple high-quality indicators of pubertal timing and tempo. The rich longitudinal data and temporal sequencing of events substantially reduced the potential for reverse causality, and we were able to adjust for fluid intelligence prior to puberty onset.

This study is not without limitations. Our employment measure is crude and assumes positions with permanent contracts are superior to those with short-term contracts which may not adequately differentiate job quality. We were unable to use recent advancements in causal mediation frameworks in our analysis as current statistical software cannot support structural equation models with multiple non-continuous mediators. While we can examine qualitative directional associations between measures, coefficients for different associations in our model cannot be compared quantitatively, precluding us from commenting on the magnitude of associations. As we previously described, there may be unmeasured confounding from deficiencies in the postnatal and childhood environment. Lastly, given dynamics in the

labor market, the changing economy, rural and urban differences, and structural disadvantages in the South African education system and labor markets for Black Africans, these findings have limited generalizability. However, they will be useful in understanding how associations between maturation, schooling qualifications, and employment opportunities change over time in transitioning economies.

The public health implications of these findings are two pronged. First, efforts to reduce deficiencies in the environment should continue in order to eliminate disparities in human capital potential along socioeconomic gradients. Second, late maturers would benefit from increased support in secondary school, either through school-based or parenting support interventions.

Among urban Black South Africans, individuals with relatively late puberty onset and slower progression had lower schooling attainment as young adults while early maturing females had better employment status. Though literature on long-term consequences of pubertal timing and tempo on schooling attainment and employment are limited, our findings from the Birth to Twenty Plus cohort differ from those in HICs and may be explained by the outsized role of deficient environments, which override other pathways observed in HICs and potential mediation by risk behaviors and adolescent pregnancy. Further research is needed to examine these associations in transitioning economies to reduce gaps in human capital.

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Tables and Figures

Table 1. Sample characteristics

Measure	Males N	Males (n = 861)	Females N	Females (n = 923)
Asset tertile in early life - 1	700	299 (35%)	765	308 (33%)
- 2		155 (18%)		203 (22%)
- 3		246 (29%)		254 (28%)
- (Missing)		161 (19%)		158 (17%)
Asset tertile at age 7 y - 1	708	307 (36%)	787	337 (37%)
- 2		192 (22%)		200 (22%)
- 3		209 (24%)		250 (27%)
- (Missing)		153 (18%)		136 (15%)
Child stress - Above median stressful events never	785	341 (40%)	857	340 (37%)
- Above median stressful events 1X		283 (33%)		337 (37%)
- Above median stressful events 2 or 3X		161 (19%)		180 (20%)
- (Missing)		76 (9%)		66 (7%)
Non-verbal fluid intelligence	361	99.4 (14.8)	379	98.5 (12.8)
Tertiles of non-verbal fluid intelligence score - 1	361	127 (15%)	379	124 (13%)
- 2		108 (13%)		146 (16%)
- 3		126 (15%)		109 (12%)
- (Missing)		500 (58%)		544 (59%)
Genital/breast development class - 1	861	55 (6%)	923	212 (23%)
- 2		316 (37%)		229 (25%)
- 3		429 (50%)		351 (38%)
- 4		61 (7%)		131 (14%)
Pubic hair development class - 1	861	253 (29%)	923	310 (34%)
- 2		504 (59%)		499 (54%)
- 3		104 (12%)		114 (12%)
Age of menarche	--	--	906	12.7 (1.2)

Early menarche - 0	--	--	906	754 (83%)
- 1		--		152 (17%)
Risk behavior cluster - Cluster 1	498	169 (34%)	569	130 (23%)
- Cluster 2		157 (32%)		341 (60%)
- Cluster 3		172 (35%)		98 (17%)
Adolescent pregnancy - 0	--	--	869	576 (66%)
- 1		--		293 (34%)
Age of adolescent pregnancy	--	--	293	17.6 (1.3)
19-22 y pregnancy - 0	--	--	695	469 (67%)
- 1		--		226 (33%)
Schooling attainment 22 y - < Matric	689	295 (43%)	741	209 (28%)
- Matric, no university schooling		289 (42%)		368 (50%)
- Matric, some university schooling		105 (15%)		164 (22%)
Contract-based employment 22 y - Unemployed	563	297 (53%)	619	316 (51%)
- Employed, contract or casual		153 (27%)		164 (26%)
- Employed, permanent contract		113 (20%)		139 (22%)

Table 2. Early life characteristics by measures of pubertal development among males

	Gen class 1 (n = 55) *Later and slower*	Gen class 2 (n = 316)	Gen class 3 (n = 429)	Gen class 4 (n = 61) *Earlier and faster*	Genital dev p	PH class 1 (n = 253) *Later and slower*	PH class 2 (n = 504)	PH class 3 (n = 104) *Earlier and faster*	Pubic hair dev p
Age of puberty onset	14.4 (1.3)	13.0 (1.2)	12.2 (1.4)	11.6 (0.9)	< 0.01	13.3 (1.3)	12.2 (1.2)	11.9 (1.0)	< 0.01
Asset tertile in early life - 1	21 (38%)	122 (39%)	138 (32%)	18 (30%)	0.04	98 (39%)	165 (33%)	36 (35%)	0.15
- 2	11 (20%)	54 (17%)	72 (17%)	18 (30%)		43 (17%)	93 (18%)	19 (18%)	
- 3	9 (16%)	80 (25%)	138 (32%)	19 (31%)		64 (25%)	144 (29%)	38 (37%)	
- NA	14 (25%)	60 (19%)	81 (19%)	6 (10%)		48 (19%)	102 (20%)	11 (11%)	
Asset tertile at age 7 y - 1	27 (49%)	124 (39%)	137 (32%)	19 (31%)	0.02	107 (42%)	167 (33%)	33 (32%)	0.02
- 2	15 (27%)	70 (22%)	91 (21%)	16 (26%)		62 (25%)	106 (21%)	24 (23%)	
- 3	11 (20%)	64 (20%)	116 (27%)	18 (30%)		49 (19%)	128 (25%)	32 (31%)	
- NA	2 (4%)	58 (18%)	85 (20%)	8 (13%)		35 (14%)	103 (20%)	15 (14%)	
Child stress - 1	25 (45%)	120 (38%)	176 (41%)	20 (33%)	0.19	99 (39%)	199 (39%)	43 (41%)	0.52
- 2	20 (36%)	97 (31%)	141 (33%)	25 (41%)		85 (34%)	163 (32%)	35 (34%)	
- 3	9 (16%)	67 (21%)	71 (17%)	14 (23%)		49 (19%)	90 (18%)	22 (21%)	
- NA	1 (2%)	32 (10%)	41 (10%)	2 (3%)		20 (8%)	52 (10%)	4 (4%)	
Childhood developmental quotient - 1	10 (18%)	53 (17%)	54 (13%)	10 (16%)	0.65	45 (18%)	71 (14%)	11 (11%)	0.33
- 2	7 (13%)	42 (13%)	55 (13%)	4 (7%)		30 (12%)	65 (13%)	13 (12%)	
- 3	6 (11%)	43 (14%)	65 (15%)	12 (20%)		35 (14%)	69 (14%)	22 (21%)	
- NA	32 (58%)	178 (56%)	255 (59%)	35 (57%)		143 (57%)	299 (59%)	58 (56%)	

Abbreviations: Gen class, genital development class; PH class, pubic hair development class

Table 3. Early life characteristics by measures of pubertal development among females

	Br class 1 (n = 212) *Later and slower*	Br class 2 (n = 229)	Br class 3 (n = 351)	Br class 4 (n = 131) *Earlier and faster*	Breast dev p	PH class 1 (n = 310) *Later and slower*	PH class 2 (n = 499)	PH class 3 (n = 114) *Earlier and faster*	Pubic hair dev p	Not early men (n = 754)	Early men (n = 152)	Early men p
Age of puberty onset	13.4 (1.2)	13.1 (1.0)	12.2 (1.1)	12.0 (1.2)	< 0.01	13.0 (1.4)	12.1 (1.1)	10.8 (1.1)	< 0.01	12.6 (1.3)	11.5 (1.3)	< 0.01
Asset tertile in early life - 1	76 (36%)	85 (37%)	105 (30%)	42 (32%)	0.13	112 (36%)	159 (32%)	37 (32%)	0.03	272 (36%)	33 (22%)	< 0.01
- 2	52 (25%)	53 (23%)	71 (20%)	27 (21%)		76 (25%)	111 (22%)	16 (14%)		161 (21%)	36 (24%)	
- 3	50 (24%)	49 (21%)	111 (32%)	44 (34%)		77 (25%)	133 (27%)	44 (39%)		195 (26%)	55 (36%)	
- NA	34 (16%)	42 (18%)	64 (18%)	18 (14%)		45 (15%)	96 (19%)	17 (15%)		126 (17%)	28 (18%)	
Asset tertile at age 7 y - 1	95 (45%)	90 (39%)	115 (33%)	37 (28%)	< 0.01	128 (41%)	175 (35%)	34 (30%)	0.35	296 (39%)	36 (24%)	< 0.01
- 2	47 (22%)	48 (21%)	74 (21%)	31 (24%)		66 (21%)	109 (22%)	25 (22%)		165 (22%)	35 (23%)	
- 3	35 (17%)	56 (24%)	114 (32%)	45 (34%)		73 (24%)	140 (28%)	37 (32%)		187 (25%)	58 (38%)	
- NA	35 (17%)	35 (15%)	48 (14%)	18 (14%)		43 (14%)	75 (15%)	18 (16%)		106 (14%)	23 (15%)	
Child stress - 1	65 (31%)	80 (35%)	142 (40%)	53 (40%)	0.15	123 (40%)	170 (34%)	47 (41%)	0.09	272 (36%)	63 (41%)	0.23
- 2	84 (40%)	91 (40%)	109 (31%)	53 (40%)		108 (35%)	195 (39%)	34 (30%)		287 (38%)	45 (30%)	
- 3	47 (22%)	41 (18%)	73 (21%)	19 (15%)		65 (21%)	90 (18%)	25 (22%)		146 (19%)	31 (20%)	
- NA	16 (8%)	17 (7%)	27 (8%)	6 (5%)		14 (5%)	44 (9%)	8 (7%)		49 (6%)	13 (9%)	
Childhood developmental quotient - 1	33 (16%)	40 (17%)	39 (11%)	12 (9%)	0.03	61 (20%)	55 (11%)	8 (7%)	< 0.01	102 (14%)	21 (14%)	1.00
- 2	40 (19%)	42 (18%)	46 (13%)	18 (14%)		49 (16%)	82 (16%)	15 (13%)		121 (16%)	24 (16%)	
- 3	16 (8%)	28 (12%)	46 (13%)	19 (15%)		27 (9%)	71 (14%)	11 (10%)		90 (12%)	19 (12%)	
- NA	123 (58%)	119 (52%)	220 (63%)	82 (63%)		173 (56%)	291 (58%)	80 (70%)		441 (58%)	88 (58%)	
19-22 y pregnancy - 0	100 (62%)	116 (69%)	175 (67%)	78 (74%)	0.28	153 (66%)	250 (67%)	66 (73%)	0.43	387 (67%)	82 (71%)	0.41
- 1	60 (38%)	52 (31%)	86 (33%)	28 (26%)		79 (34%)	123 (33%)	24 (27%)		192 (33%)	33 (29%)	

Abbreviations: Br class, breast development class; PH class, pubic hair development class; Early men, early menarche (age >1 SD below mean).

Table 4. Adjusted structural equation models for associations of pubertal timing and tempo with adolescent risk behavior initiation patterns, schooling attainment at 22 y, and employment at 22 y among males[a]

	Direct effect β (95% CI)	Indirect effect β (95% CI)	Total effect β (95% CI)
Genital development (N = 767)[b]			
Risk behavior pattern ~ class 1	0.05 (-0.31, 0.66)	--	0.05 (-0.31, 0.66)
School 22 y ~ class 1	-0.08 (-0.47, 0.34)	-0.01 (-0.16, 0.07)	-0.09 (-0.5, 0.32)
Employ 22 y ~ class 1	-0.14 (-0.77, 0.3)	0 (-0.03, 0.03)	-0.14 (-0.77, 0.31)
Risk behavior pattern ~ class 3	**0.36 (0.1, 0.62)**	--	**0.36 (0.1, 0.62)**
School 22 y ~ class 3	0.09 (-0.08, 0.35)	**-0.08 (-0.17, -0.02)**	0.01 (-0.15, 0.27)
Employ 22 y ~ class 3	-0.15 (-0.37, 0.12)	0 (-0.02, 0.01)	-0.15 (-0.37, 0.12)
Risk behavior pattern ~ class 4	**0.58 (0.1, 0.95)**	--	**0.58 (0.1, 0.95)**
School 22 y ~ class 4	0.12 (-0.23, 0.54)	**-0.12 (-0.25, -0.02)**	0 (-0.34, 0.41)
Employ 22 y ~ class 4	0.02 (-0.29, 0.48)	0 (-0.03, 0.03)	0.02 (-0.29, 0.48)
Pubic hair development (N = 767)[c]			
Risk behavior pattern ~ class 1	-0.17 (-0.41, 0.09)	--	-0.17 (-0.41, 0.09)
School 22 y ~ class 1	**-0.21 (-0.48, -0.04)**	0.03 (-0.02, 0.1)	**-0.17 (-0.44, -0.01)**
Employ 22 y ~ class 1	0.07 (-0.22, 0.27)	0 (-0.03, 0.04)	0.07 (-0.21, 0.27)
Risk behavior pattern ~ class 3	**0.35 (0.04, 0.71)**	--	**0.35 (0.04, 0.71)**
School 22 y ~ class 3	0.14 (-0.13, 0.46)	**-0.07 (-0.19, -0.01)**	0.07 (-0.22, 0.38)
Employ 22 y ~ class 3	0.04 (-0.31, 0.37)	0 (-0.03, 0.02)	0.04 (-0.32, 0.37)

[a] Models are adjusted for household asset ownership at ages 0-2 y and 7 y, child stress exposure, and non-verbal fluid intelligence at age 7 y.
[b] Referent group = class 2.
[c] Referent group = class 2.

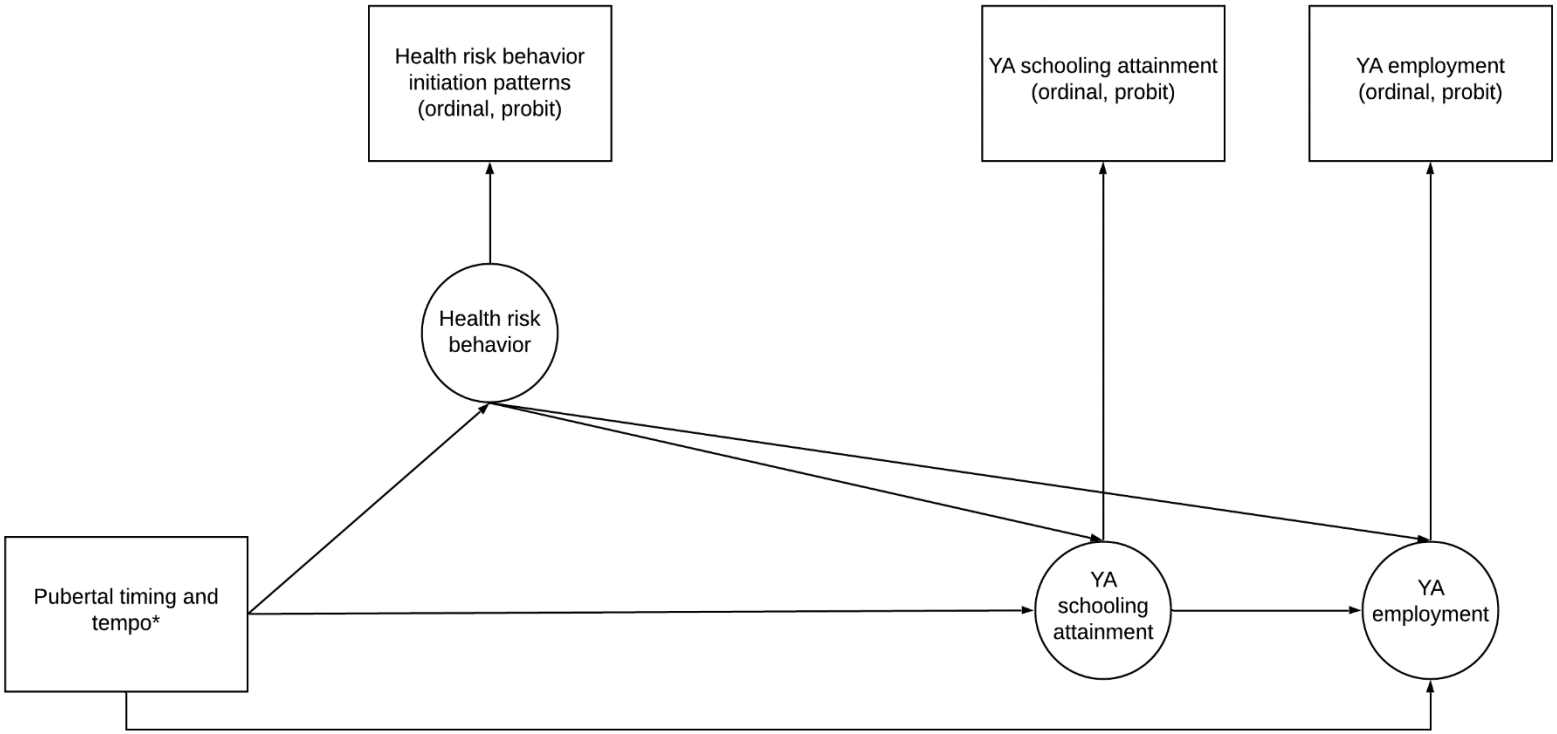
Table 5. Adjusted structural equation models for associations of pubertal timing and tempo with adolescent risk behavior initiation patterns, adolescent pregnancy, pregnancy from 19 to 22 y, schooling attainment at 22 y, and employment at 22 y among females[a]

	Direct effect β (95% CI)	Indirect effect β (95% CI)	Total effect β (95% CI)
Breast development (N = 877)[b]			
Risk behavior pattern ~ class 1	-0.06 (-0.42, 0.24)	--	-0.06 (-0.42, 0.24)
Adolescent pregnancy ~ class 1	--	-0.02 (-0.16, 0.07)	-0.02 (-0.16, 0.07)
Young adult pregnancy ~ class 1	--	0 (-0.01, 0.04)	0 (-0.01, 0.04)
School 22 y ~ class 1	-0.07 (-0.33, 0.2)	0.01 (-0.07, 0.06)	-0.06 (-0.32, 0.18)
Employ 22 y ~ class 1	0.16 (-0.1, 0.57)	-0.02 (-0.12, 0.05)	0.14 (-0.1, 0.51)
Risk behavior pattern ~ class 3	0.18 (-0.12, 0.48)	--	0.18 (-0.12, 0.48)
Adolescent pregnancy ~ class 3	--	0.05 (-0.12, 0.14)	0.05 (-0.12, 0.14)
Young adult pregnancy ~ class 3	--	0 (-0.03, 0.02)	0 (-0.03, 0.02)
School 22 y ~ class 3	0.14 (-0.06, 0.44)	-0.02 (-0.1, 0.03)	0.12 (-0.07, 0.39)
Employ 22 y ~ class 3	0.16 (-0.15, 0.43)	0.05 (-0.01, 0.16)	0.2 (-0.05, 0.48)
Risk behavior pattern ~ class 4	**0.31 (0.01, 0.69)**	--	**0.31 (0.01, 0.69)**
Adolescent pregnancy ~ class 4	--	0.09 (-0.12, 0.23)	0.09 (-0.12, 0.23)
Young adult pregnancy ~ class 4	--	-0.01 (-0.06, 0.02)	-0.01 (-0.06, 0.02)
School 22 y ~ class 4	0.25 (-0.09, 0.57)	-0.03 (-0.12, 0.09)	0.22 (-0.08, 0.5)
Employ 22 y ~ class 4	**0.41 (0.02, 0.79)**	0.08 (-0.01, 0.25)	**0.49 (0.17, 0.88)**
Pubic hair development (N = 877)[c]			
Risk behavior pattern ~ class 1	-0.17 (-0.45, 0.08)	--	-0.17 (-0.45, 0.08)
Adolescent pregnancy ~ class 1	--	-0.05 (-0.12, 0.08)	-0.05 (-0.12, 0.08)
Young pregnancy ~ class 1	--	0 (-0.01, 0.02)	0 (-0.01, 0.02)
School 22 y ~ class 1	**-0.32 (-0.55, -0.16)**	0.02 (-0.01, 0.08)	**-0.31 (-0.53, -0.13)**
Employ 22 y ~ class 1	-0.16 (-0.31, 0.18)	**-0.09 (-0.2, -0.03)**	-0.25 (-0.4, 0.05)
Risk behavior pattern ~ class 3	0.14 (-0.2, 0.5)	--	0.14 (-0.2, 0.5)
Adolescent pregnancy ~ class 3	--	0.04 (-0.1, 0.14)	0.04 (-0.1, 0.14)
Young adult pregnancy ~ class 3	--	0 (-0.03, 0.01)	0 (-0.03, 0.01)

School 22 y ~ class 3	-0.08 (-0.35, 0.23)	-0.01 (-0.07, 0.04)	-0.09 (-0.35, 0.21)
Employ 22 y ~ class 3	0.15 (-0.14, 0.47)	-0.01 (-0.09, 0.09)	0.14 (-0.12, 0.47)
Age of Menarche (N = 874)			
Risk behavior pattern ~ menarche	**-0.16 (-0.25, -0.08)**	--	**-0.16 (-0.25, -0.08)**
Adolescent pregnancy ~ menarche	--	-0.05 (-0.1, 0.07)	-0.05 (-0.1, 0.07)
Young adult pregnancy ~ menarche	--	0.03 (-0.01, 0.11)	0.03 (-0.01, 0.11)
School 22 y ~ menarche	**-0.13 (-11.7, 0)**	0.04 (-0.07, 11.6)	**-0.09 (-0.16, -0.02)**
Employ 22 y ~ menarche	-0.04 (-0.13, 66.17)	-0.03 (-66.23, 0.05)	-0.07 (-0.14, 0.04)

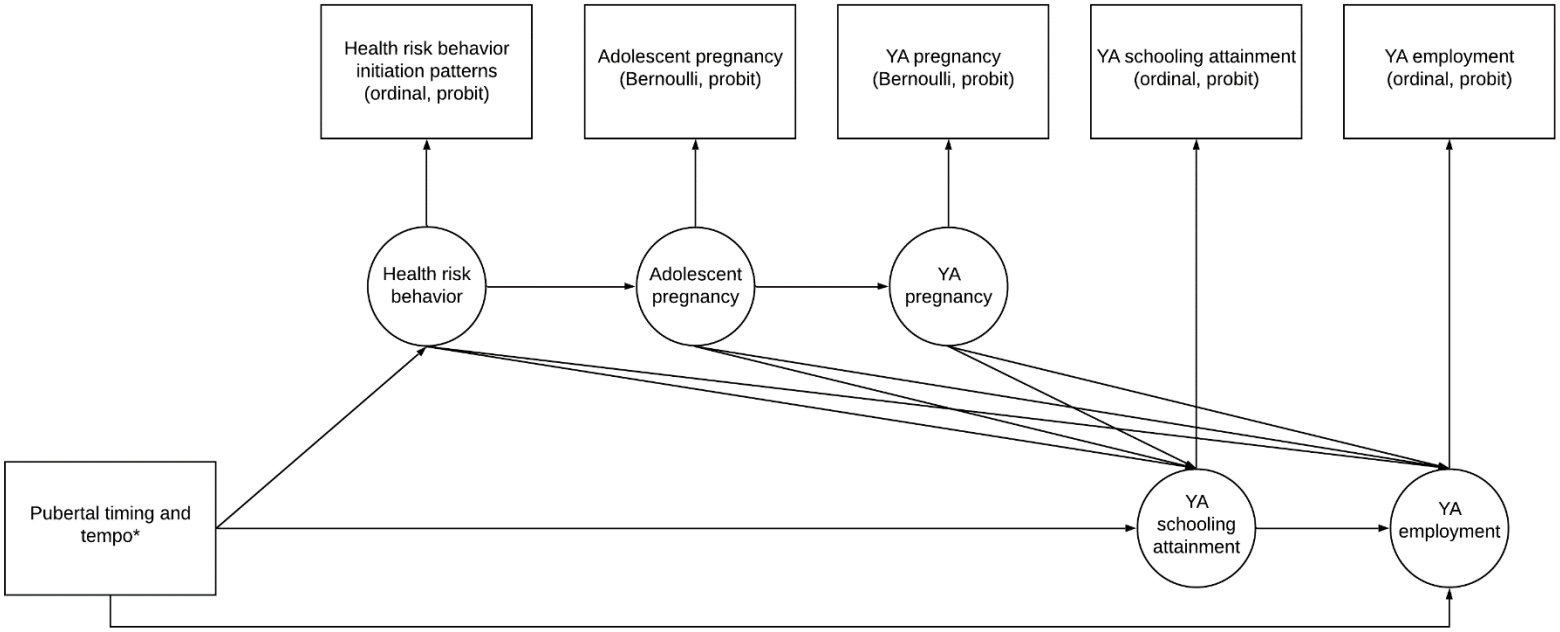
[a] Models are adjusted for household asset ownership at ages 0-2 y and 7 y, child stress exposure, and non-verbal fluid intelligence at age 7 y.
[b] Referent group = class 2.
[c] Referent group = class 2.

Figure 1. Simplified structural equation model, males



*Two indicators of pubertal timing and tempo were used in separate models, classes of genital development and classes of pubic hair development.
YA = young adult.

Figure 2. Simplified structural equation model, females



*Three indicators of pubertal timing and tempo were used in separate models, latent classes of breast development, latent classes of pubic hair development, and age at menarche. YA = young adult.

Supplemental Tables and Figures

Supplemental Table 1. Selected measures and wave of data collection

	Participant age at start of data collection wave											
Measure	0-2	5	7	9	11	13	14	15	16	17	18	22
Tanner sexual maturity scale				X	X	X	X	X	X	X	X	
Age of menarche				X	X	X	X	X	X	X	X	
Smoking					X	X	X	X	X	X	X	
Alcohol use					X	X					X	
Cannabis use					X	X	X	X				
Drug use					X	X	X	X		X	X	
Sexual activity					X	X	X	X	X	X	X	
Pregnancy history								X	X	X	X	X
Schooling attainment												X
Employment history												X
Household asset ownership	X	X	X									
Stress and violence inventory	X	X	X									
Non-verbal fluid intelligence			X									

Supplemental Table 2. Early life characteristics by adolescent and adult response variables among males

	Health risk behavior pattern				Schooling				Employment			
	Low (n = 169)	Moderate (n = 157)	High (n = 172)	p	< Matric (n = 295)	Matric, no university schooling (n = 289)	Matric, some university schooling (n = 105)	p	Unemployed (n = 297)	Employed, contract or casual (n = 153)	Employed, permanent contract (n = 113)	p
Asset tertile in early life - 1	58 (34%)	53 (34%)	64 (37%)	0.85	125 (42%)	92 (32%)	30 (29%)	0.07	115 (39%)	56 (37%)	31 (27%)	0.34
- 2	28 (17%)	29 (18%)	27 (16%)		48 (16%)	57 (20%)	19 (18%)		49 (16%)	31 (20%)	27 (24%)	
- 3	55 (33%)	42 (27%)	48 (28%)		72 (24%)	84 (29%)	38 (36%)		77 (26%)	42 (27%)	35 (31%)	
- NA	28 (17%)	33 (21%)	33 (19%)		50 (17%)	56 (19%)	18 (17%)		56 (19%)	24 (16%)	20 (18%)	
Asset tertile at age 7 y - 1	67 (40%)	55 (35%)	56 (33%)	0.78	125 (42%)	95 (33%)	35 (33%)	< 0.01	111 (37%)	58 (38%)	34 (30%)	0.54
- 2	34 (20%)	35 (22%)	46 (27%)		79 (27%)	62 (21%)	20 (19%)		68 (23%)	35 (23%)	29 (26%)	
- 3	41 (24%)	38 (24%)	41 (24%)		55 (19%)	80 (28%)	30 (29%)		65 (22%)	41 (27%)	29 (26%)	
- NA	27 (16%)	29 (18%)	29 (17%)		36 (12%)	52 (18%)	20 (19%)		53 (18%)	19 (12%)	21 (19%)	
Child stress - 1	73 (43%)	67 (43%)	66 (38%)	0.53	114 (39%)	120 (42%)	39 (37%)	0.19	109 (37%)	62 (41%)	43 (38%)	0.68
- 2	50 (30%)	56 (36%)	56 (33%)		99 (34%)	83 (29%)	44 (42%)		102 (34%)	51 (33%)	37 (33%)	
- 3	36 (21%)	22 (14%)	35 (20%)		62 (21%)	62 (21%)	13 (12%)		55 (19%)	32 (21%)	22 (19%)	
- NA	10 (6%)	12 (8%)	15 (9%)		20 (7%)	24 (8%)	9 (9%)		31 (10%)	8 (5%)	11 (10%)	
Tertiles of non-verbal fluid intelligence score - 1	38 (22%)	19 (12%)	21 (12%)	0.09	66 (22%)	48 (17%)	13 (12%)	0.01	58 (20%)	28 (18%)	18 (16%)	0.24
- 2	22 (13%)	22 (14%)	23 (13%)		45 (15%)	43 (15%)	20 (19%)		34 (11%)	29 (19%)	23 (20%)	
- 3	24 (14%)	20 (13%)	31 (18%)		37 (13%)	64 (22%)	25 (24%)		55 (19%)	23 (15%)	21 (19%)	
- NA	85 (50%)	96 (61%)	97 (56%)		147 (50%)	134 (46%)	47 (45%)		150 (51%)	73 (48%)	51 (45%)	

Supplemental Table 3. Early life characteristics by adolescent and adult response variables among females

	Health risk behavior				Adolescent pregnancy			Schooling				Employment			
	Low (n = 130)	Moderate (n = 341)	High (n = 98)	p	No (n = 576)	Yes (n = 293)	p	< Matric (n = 209)	Matric, no university schooling (n = 368)	Matric, some university schooling (n = 164)	p	Unemployed (n = 316)	Employed, contract or casual (n = 164)	Employed, permanent contract (n = 139)	p
Asset tertile in early life - 1	48 (37%)	115 (34%)	25 (26%)	0.11	170 (30%)	119 (41%)	< 0.01	94 (45%)	128 (35%)	37 (23%)	< 0.01	116 (37%)	50 (30%)	43 (31%)	0.25
- 2	37 (28%)	78 (23%)	19 (19%)		128 (22%)	63 (22%)		41 (20%)	87 (24%)	40 (24%)		73 (23%)	38 (23%)	25 (18%)	
- 3	27 (21%)	89 (26%)	35 (36%)		171 (30%)	72 (25%)		38 (18%)	98 (27%)	63 (38%)		77 (24%)	50 (30%)	50 (36%)	
- NA	18 (14%)	59 (17%)	19 (19%)		107 (19%)	39 (13%)		36 (17%)	55 (15%)	24 (15%)		50 (16%)	26 (16%)	21 (15%)	
Asset tertile at age 7 y - 1	49 (38%)	114 (33%)	34 (35%)	0.08	184 (32%)	132 (45%)	< 0.01	106 (51%)	145 (39%)	30 (18%)	< 0.01	119 (38%)	58 (35%)	52 (37%)	0.81
- 2	33 (25%)	84 (25%)	12 (12%)		132 (23%)	66 (23%)		44 (21%)	84 (23%)	39 (24%)		69 (22%)	44 (27%)	30 (22%)	
- 3	30 (23%)	102 (30%)	34 (35%)		173 (30%)	61 (21%)		34 (16%)	93 (25%)	68 (41%)		83 (26%)	44 (27%)	41 (29%)	
- NA	18 (14%)	41 (12%)	18 (18%)		87 (15%)	34 (12%)		25 (12%)	46 (12%)	27 (16%)		45 (14%)	18 (11%)	16 (12%)	
Child stress - 1	42 (32%)	139 (41%)	41 (42%)	0.25	225 (39%)	99 (34%)	0.10	71 (34%)	134 (36%)	67 (41%)	0.27	105 (33%)	67 (41%)	60 (43%)	0.42
- 2	48 (37%)	120 (35%)	33 (34%)		201 (35%)	116 (40%)		81 (39%)	138 (38%)	59 (36%)		120 (38%)	54 (33%)	47 (34%)	
- 3	29 (22%)	67 (20%)	15 (15%)		106 (18%)	64 (22%)		48 (23%)	75 (20%)	24 (15%)		69 (22%)	35 (21%)	24 (17%)	
- NA	11 (8%)	15 (4%)	9 (9%)		44 (8%)	14 (5%)		9 (4%)	21 (6%)	14 (9%)		22 (7%)	8 (5%)	8 (6%)	
Tertiles of non-verbal fluid intelligence score - 1	21 (16%)	50 (15%)	9 (9%)	0.25	86 (15%)	37 (13%)	0.19	36 (17%)	70 (19%)	18 (11%)	< 0.01	47 (15%)	29 (18%)	21 (15%)	0.26
- 2	23 (18%)	52 (15%)	17 (17%)		90 (16%)	55 (19%)		46 (22%)	74 (20%)	26 (16%)		59 (19%)	37 (23%)	24 (17%)	
- 3	18 (14%)	49 (14%)	7 (7%)		78 (14%)	28 (10%)		16 (8%)	58 (16%)	35 (21%)		42 (13%)	27 (16%)	29 (21%)	
- NA	68 (52%)	190 (56%)	65 (66%)		322 (56%)	173 (59%)		111 (53%)	166 (45%)	85 (52%)		168 (53%)	71 (43%)	65 (47%)	
19-22 y pregnancy - 0	87 (76%)	182 (66%)	62 (75%)	0.07	312 (67%)	157 (69%)	0.65	114 (60%)	222 (65%)	130 (82%)	< 0.01	193 (66%)	109 (71%)	91 (69%)	0.45
- 1	27 (24%)	95 (34%)	21 (25%)		155 (33%)	71 (31%)		77 (40%)	118 (35%)	28 (18%)		101 (34%)	44 (29%)	40 (31%)	

Supplemental Table 4. Unadjusted structural equation models for associations of pubertal timing and tempo with adolescent risk behavior initiation patterns, schooling attainment at 22 y, and employment at 22 y

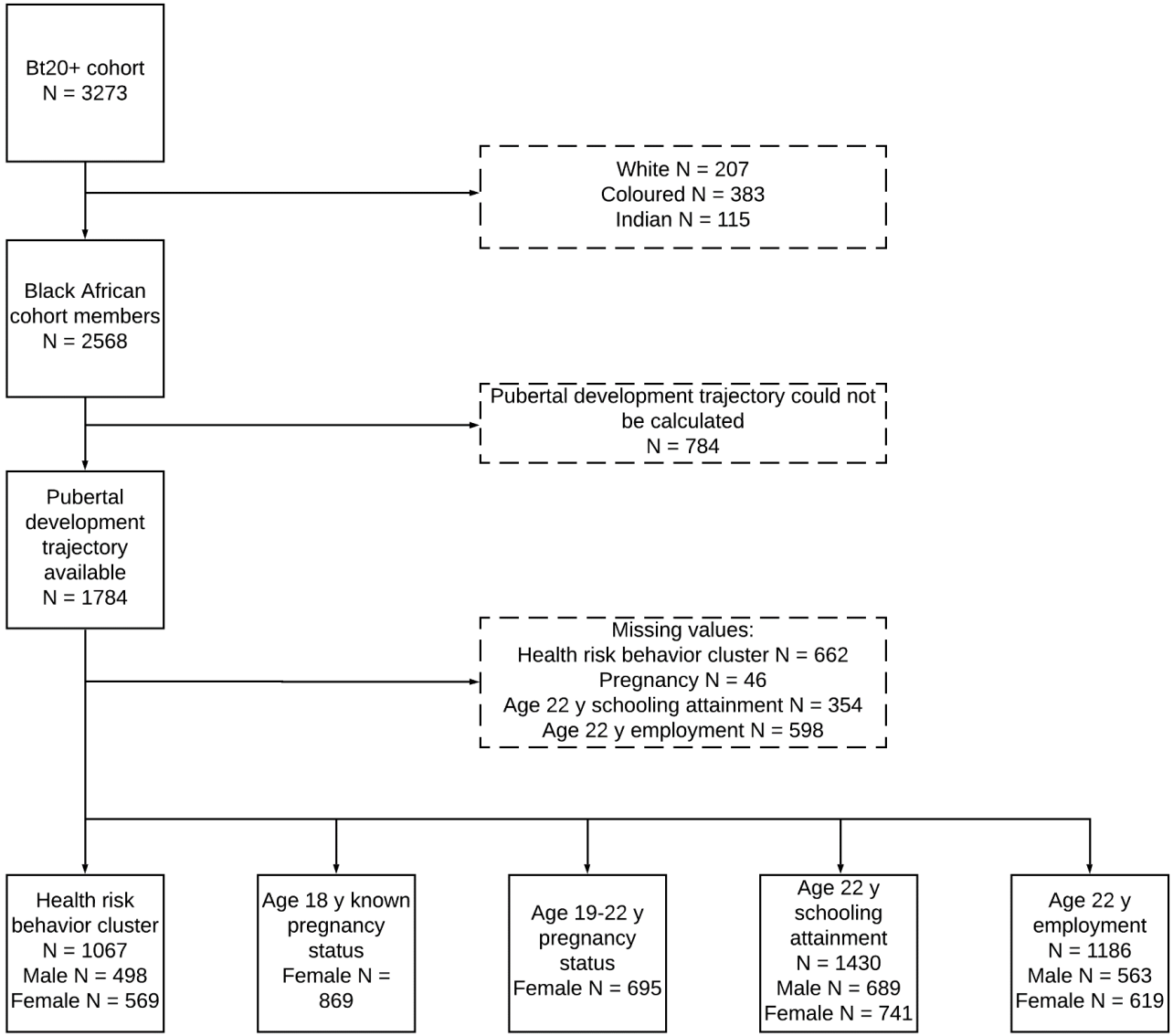
	Direct effects β (95% CI)	Indirect effects β (95% CI)	Total effects β (95% CI)
Genital development trajectory (N = 767)			
riskbehav ~ sex1	0.08 (-0.3, 0.65)	--	0.08 (-0.3, 0.65)
school ~ sex1	-0.15 (-0.56, 0.23)	-0.01 (-0.16, 0.06)	-0.16 (-0.62, 0.2)
employ ~ sex1	-0.15 (-0.73, 0.25)	0 (-0.04, 0.03)	-0.15 (-0.73, 0.25)
riskbehav ~ sex3	**0.36 (0.13, 0.59)**	--	**0.36 (0.13, 0.59)**
school ~ sex3	0.12 (-0.04, 0.37)	**-0.07 (-0.16, -0.02)**	0.05 (-0.11, 0.29)
employ ~ sex3	-0.15 (-0.37, 0.12)	0 (-0.01, 0.02)	-0.15 (-0.36, 0.13)
riskbehav ~ sex4	**0.56 (0.12, 0.86)**	--	**0.56 (0.12, 0.86)**
school ~ sex4	0.16 (-0.28, 0.52)	**-0.11 (-0.23, -0.02)**	0.05 (-0.35, 0.41)
employ ~ sex4	0.01 (-0.32, 0.44)	0 (-0.02, 0.03)	0.01 (-0.31, 0.43)
Pubic hair development trajectory (N = 767)			
riskbehav ~ ph1	-0.16 (-0.39, 0.1)	--	-0.16 (-0.39, 0.1)
school ~ ph1	**-0.25 (-0.53, -0.1)**	0.03 (-0.02, 0.09)	**-0.22 (-0.49, -0.06)**
employ ~ ph1	0.01 (-0.25, 0.24)	0 (-0.04, 0.03)	0.01 (-0.25, 0.23)
riskbehav ~ ph3	**0.35 (0, 0.67)**	--	**0.35 (0, 0.67)**
school ~ ph3	0.16 (-0.15, 0.43)	-0.07 (-0.17, 0)	0.09 (-0.21, 0.35)
employ ~ ph3	-0.01 (-0.3, 0.33)	0 (-0.02, 0.02)	-0.01 (-0.29, 0.33)

Supplemental Table 5. Unadjusted structural equation models for associations of pubertal timing and tempo with adolescent risk behavior initiation patterns, adolescent pregnancy, pregnancy from 19 to 22 y, schooling attainment at 22 y, and employment at 22 y among females

	Direct effects β (95% CI)	Indirect effects β (95% CI)	Total effects β (95% CI)
Breast development trajectory (N = 877)			
riskbehav ~ sex1	-0.06 (-0.37, 0.21)	--	-0.06 (-0.37, 0.21)
adolescent pregnancy ~ sex1	--	-0.02 (-0.11, 0.06)	-0.02 (-0.11, 0.06)
young adult pregnancy ~ sex1	--	0 (-0.01, 0.01)	0 (-0.01, 0.01)
school ~ sex1	-0.11 (-0.36, 0.12)	0 (-0.02, 0.04)	-0.1 (-0.35, 0.12)
employ ~ sex1	0.13 (-0.12, 0.47)	-0.03 (-0.1, 0.03)	0.1 (-0.17, 0.44)
riskbehav ~ sex3	0.2 (-0.06, 0.45)	--	0.2 (-0.06, 0.45)
adolescent pregnancy ~ sex3	--	0.06 (-0.02, 0.13)	0.06 (-0.02, 0.13)
young adult pregnancy ~ sex3	--	0 (-0.01, 0)	0 (-0.01, 0)
school ~ sex3	**0.19 (0.03, 0.46)**	-0.01 (-0.05, 0.01)	**0.18 (0.01, 0.44)**
employ ~ sex3	0.12 (-0.14, 0.37)	**0.06 (0.01, 0.15)**	0.18 (-0.07, 0.44)
riskbehav ~ sex4	**0.32 (0.03, 0.64)**	--	**0.32 (0.03, 0.64)**
adolescent pregnancy ~ sex4	--	**0.09 (0.01, 0.2)**	**0.09 (0.01, 0.2)**
young adult pregnancy ~ sex4	--	0 (-0.02, 0.01)	0 (-0.02, 0.01)
school ~ sex4	**0.34 (0.08, 0.61)**	-0.02 (-0.09, 0.01)	**0.31 (0.05, 0.57)**
employ ~ sex4	**0.37 (0.04, 0.7)**	**0.1 (0.02, 0.21)**	**0.47 (0.16, 0.8)**

Pubic hair development trajectory (N = 877)			
riskbehav ~ ph1	-0.17 (-0.39, 0.02)	--	-0.17 (-0.39, 0.02)
adolescent pregnancy ~ ph1	--	-0.05 (-0.11, 0.01)	-0.05 (-0.11, 0.01)
young pregnancy ~ ph1	--	0 (0, 0.01)	0 (0, 0.01)
school ~ ph1	**-0.38 (-0.57, -0.22)**	0.01 (-0.01, 0.05)	**-0.37 (-0.56, -0.2)**
employ ~ ph1	-0.15 (-0.3, 0.12)	**-0.1 (-0.18, -0.05)**	-0.26 (-0.41, 0.01)
riskbehav ~ ph3	0.17 (-0.13, 0.48)	--	0.17 (-0.13, 0.48)
adolescent pregnancy ~ ph3	--	0.05 (-0.04, 0.14)	0.05 (-0.04, 0.14)
young adult pregnancy ~ ph3	--	0 (-0.01, 0)	0 (-0.01, 0)
school ~ ph3	-0.06 (-0.32, 0.24)	-0.01 (-0.05, 0.01)	-0.07 (-0.33, 0.23)
employ ~ ph3	0.13 (-0.14, 0.42)	-0.01 (-0.08, 0.08)	0.13 (-0.15, 0.43)
Menarche (N = 874)			
riskbehav ~ menarche	**-0.14 (-0.24, -0.06)**	--	-0.14 (-0.24, -0.06)
adolescent pregnancy ~ menarche	--	**-0.04 (-0.07, -0.01)**	-0.04 (-0.07, -0.01)
young adult pregnancy ~ menarche	--	0 (0, 0.01)	0 (0, 0.01)
school ~ menarche	**-0.16 (-0.23, -0.08)**	0.01 (0, 0.04)	**-0.14 (-0.21, -0.07)**
employ ~ menarche	-0.03 (-0.09, 0.08)	**-0.05 (-0.08, -0.02)**	-0.08 (-0.14, 0.02)

Supplemental Figure 1. Analytical sample



Chapter 7: Discussion

In this dissertation we investigated associations of pubertal timing and tempo with health outcomes in adolescence and human capital outcomes in young adulthood. In adolescence, we examined myriad mental health and risk behavior measures to paint a comprehensive picture of associations of pubertal timing and tempo on health. In young adulthood, we investigated whether pubertal timing and tempo have a lasting impact and affect outcomes beyond health including schooling attainment and employment.

Relative to their on-time maturing peers, individuals with earlier pubertal onset, or timing, are at greater risk of experiencing detrimental health outcomes in adolescence including mental health outcomes such as internalizing and externalizing problems, eating attitudes, and clinical diagnoses of depression and eating disorders and risk behaviors such as tobacco, alcohol, cannabis, and illicit drug use and earlier sexual debut and risky sexual activity (1-16). Among late maturers, associations with adverse adolescent health outcomes have been inconsistent though a thorough meta-analysis published in 2017 did not find an association between relatively later pubertal timing and internalizing and externalizing problems, including substance use and risky sexual activity (17-22).

Far fewer studies have examined the pace of progression through puberty, or tempo. Studies that have, have found inconsistent and at times conflicting associations of pubertal tempo with mental health symptoms. For example, faster pubertal temp was associated with increased depressive symptoms in one study and decreased depressive symptoms in another (21, 23). Studies examining associations of pubertal timing and tempo with the same outcome have also yielded mixed results (21). This may be in part because the relationship between pubertal timing and tempo is unclear. In some studies, individuals with earlier pubertal timing have a slower tempo and individuals with later pubertal timing have a faster tempo. In others, there is a direct relationship between pubertal timing and tempo such that individuals with earlier timing have a faster tempo (24, 25).

Summary of findings

Research Aim 1. Describe smoking, alcohol, cannabis, illicit drug, and sexual initiation from ages 10 to 18 y, persistence at age 18 y, and patterns of initiation.

In our first aim, we characterized adolescent smoking, alcohol use, cannabis use, illicit drug use, sexual activity, and adolescent pregnancy among Black participants in the Bt20+ cohort. While adolescence is a period of experimentation, over 75% of males had experimented with smoking and alcohol use and had sex and around 30% had experimented with cannabis (through age 15 y) and illicit drugs through age 18 y. Overall experimentation rates were slightly lower among females and started later. Reports of current risk behavior activity at age 18 y were much lower suggesting not all experimentation results in habituation.

As risk behaviors are known to cluster together (26). We conducted sex-specific hierarchical cluster analyses which identified 3 distinct patterns for each sex which correspond to low, moderate, and high-risk patterns of risk behavior initiation. Individuals following the low risk pattern reported below average risk behavior initiation; those following the moderate risk pattern reported above average smoking and alcohol initiation; and those following the high-risk pattern reported above average risk behavior initiation including cannabis and illicit drug use. Pattern membership was not predicted by the sociodemographic characteristics examined, though increasing risk pattern was associated with increased likelihood of adolescent pregnancy.

Compared to cross-sectional nationally representative estimates from the 2008 South African Youth Risk Behaviour Survey (YRBS), rates of smoking, alcohol, cannabis, illicit drugs (among males), and sexual activity initiation, and rates of adolescent pregnancy through age 18 y were each substantially higher in the Bt20+ cohort (27). These differences may be attributable to study designs (longitudinal vs. cross-sectional), risk patterning by race, and differences in urbanicity.

Research Aim 2. Examine associations of pubertal timing and tempo with measures of adolescent mental health and health risk behavior initiation and examine the consistency of associations by level of childhood stress.

In our second aim, we examined associations of pubertal timing and tempo with measures of adolescent mental health (internalizing problems, externalizing problems, and eating attitudes) and patterns of risk behavior initiation. There is a direct relationship between pubertal timing and pubertal tempo in the Bt20+ cohort such that earlier pubertal onset was associated with more rapid pubertal development and later onset was associated with slower pubertal development (28).

For emotional and behavioral problems, we found that earlier and more rapid pubertal timing and tempo were associated with small but consistent increases in internalizing and externalizing problems at age 14 y. Pubertal timing and tempo were not associated with internalizing and externalizing problems at age 11 y. Given the large number of statistical tests conducted and that we were likely underpowered to detect small effect sizes, we based our conclusions on the consistency of the directionality and magnitude of estimates across the three internalizing scales and three externalizing scales at a given age rather than statistical significance. Age 17 y eating attitudes were poorer for early maturing females. For males, we observed a U-shaped association in which both earlier and faster and later and slower maturing males had poorer eating attitudes. Age 13 y eating attitudes were not associated with pubertal timing and tempo. We found that individuals who matured earlier and faster than their peers were at increased risk of following the moderate and high-risk health risk behavior initiation patterns over the low risk pattern, while individuals who matured later and slower than their peers were at slightly reduced risk of following the moderate and high-risk patterns compared to the low risk pattern.

Our results from the Bt20+ cohort were consistent across multiple indicators of pubertal timing and tempo and the observed associations were largely consistent with those reported in high-income settings (2, 3, 29-35). There is consensus that early maturers are at increased risk of detrimental health

outcomes because the maturity gap, in which individuals are physically mature before they are cognitively and socioemotionally mature (36, 37).

Research Aim 3. Examine associations of pubertal timing and tempo with schooling attainment and employment status at age 22 y and explore the mediating role of adolescent health risk behavior initiation and pregnancy.

In our third aim, we examined associations of pubertal timing and tempo with schooling attainment and employment in young adulthood. We found that for both sexes, later and slower pubertal development was associated with lower schooling attainment at age 22 y and that earlier and faster pubertal development was associated with better employment among females, though not males. These associations resulted from direct associations and were not mediated by risk behavior activity or adolescent pregnancy. Though the literature on non-health-related outcomes is scant, our findings were in contrast to the few studies examining long-term associations of pubertal timing on schooling which have consistently found females with later age at menarche have higher schooling attainment (18, 33, 38, 39). One explanation for these unexpected results is that our measure of socioeconomic status was based on material asset ownership and may not have captured immaterial dimensions of socioeconomic status which may have conferred advantages for early maturers and resulted in unmeasured confounding in our models.

Strengths and Limitations

Strengths

Data used in this dissertation come from a longitudinal birth cohort from South Africa, a middle-income country underrepresented in the literature. Given the influence of context on pubertal timing, risk behavior initiation, and human capital formation, these data begin to fill a critical gap in the literature.

Bt20+ has multiple high-quality measures of pubertal timing and tempo. While many studies use age of menarche and do not have a comparable measure for males, Bt20+ has latent classes of pubic hair development and genital or breast development for both sexes in addition to age at menarche for females.

These measures were derived from repeated measures of the Tanner sexual maturation scales. While pubertal staging typically requires clinical assessment by a medical professional, a local validation study concluded South African youth could reliably rate their stage of development (40). Subsequently the Tanner sexual maturation scales were administered at each adolescent study visit. This undoubtedly increased the feasibility of such assessment in a population study by reducing invasiveness to the participant and saving time and costs by not needing to compensate clinicians.

Though gonadarche and pubarche are independent, temporally related processes, their repeated measures reflect general progress through pubertal development. Menarche is a later stage event in pubertal development, but consistently tracked with the latent classes in our findings.

This dissertation used data collected over the span of 22 years, including 7 data waves from adolescence. This breadth of data allowed us to examine several adolescent health outcomes including emotional and behavioral problems and eating attitudes related to 7 mental health conditions, and risk behaviors including smoking, alcohol use, cannabis use, illicit drug use, and sexual activity. We were also able to go beyond health to examine human capital and employment outcomes during the transition to adulthood.

Longitudinal data collection improves data quality and strengthens the analysis. Though it can introduce inconsistencies, repeated measures reduce the likelihood of recall bias as events are reported closer to when they took place. The prospective nature of data collection allows us to take advantage of the temporality of events to reduce the risk of reverse causality and make stronger inferences. We were also able to adjust for many key confounders. For example, in our analyses with schooling attainment, we were able to adjust for a measure of childhood fluid intelligence as it is a known predictor of schooling attainment (41).

Limitations

As this body of work was a series of secondary analyses, the cohort was not conceptualized and powered to detect the longitudinal associations or heterogeneity of effects we investigated. Despite this,

the use of multiple indicators of pubertal timing and tempo allowed us to examine associations more holistically.

Attrition and subsequent missing data are common in birth cohorts. We made several decisions regarding missing data while processing and analyzing the data that may have introduced bias. In processing the data, we used deterministic imputation approaches, which have been to work well relative to likelihood based approaches (42).

Individuals for whom pubertal development trajectories could be calculated did not differ from the sample at-large. When processing the adolescent risk behavior data, we considered the adolescent data as a set and backfilled or carried data forward, as appropriate, and created a "status unknown at age 18 y" category for individuals who were lost to follow-up by age 18 y but had never reported engaging in a behavior.

In the initial hierarchical cluster analysis of risk behavior initiation, we included a category of "status unknown at age 18 y" in each risk behavior measure. However, in the initial clustering, individuals with an unknown status at age 18 y emerged as their own cluster. We subsequently restricted the cluster analysis to individuals with a known initiation status for each of the 5 risk behaviors of interest. This may have introduced bias if individuals who were lost to follow up with an unknown status were systematically different from individuals with a known status, though in a sensitivity analysis of individuals included in the cluster analysis compared to their excluded peers there was no difference in sociodemographic characteristics between the two groups and percent risk behavior initiation was comparable between the included and excluded groups in childhood and early adolescence prior to loss to follow-up.

Attrition and small sample sizes were also a concern in the generalized structural equation models which used data from enrollment through age 22 y. For covariates, we created an informative missing category so as not to drop individuals who were missing covariate data but had exposure and outcome data. This implied that individuals in the informative missing category were like one another and distinct

from the observed value categories. When included in models, these covariates adjusted for a mixture of that characteristic and attributes of the informative missing category and did not fully adjust for confounding by the characteristic of interest.

Bt20+ is an urban cohort and findings from these analyses are not generalizable to rural South African communities. Adolescent risk behavior activity is higher in urban areas, eating disorders are thought to be an imported phenomenon stemming from globalization that would start in urban areas, and there are strong differences in urban and rural school systems and labor markets (43). Schooling and employment findings also may not hold outside of South Africa. Though there has been systematic oppression of one population subgroup over another in other countries, the legacy of the structural disadvantages codified under apartheid is still present in disparities in the education system today.

Aspects of the general environment may have changed since the Bt20+ participants went through adolescence in the 2000s. For example, more individuals may have entered puberty at a younger age as a result of increased childhood obesity rates (44, 45). Adolescent cognitive and social and emotional development take cues from and interact with the environment, but peer interactions have been have been radically transformed by smartphones and social media in the last decade (46, 47). Schooling requirements have also changed, and schooling is now compulsory from age seven years (grade 1) to age 15 years (grade 9). The labor market in a developing economy is exceptionally dynamic and the types of jobs available, and subsequent schooling qualifications required for these jobs, change over time.

Life History Theory

Life history theory is an evolutionary developmental theoretical framework that attempts to explain the timing of sexual maturation and reproductive events in terms of strategies for distributing metabolic resources between the competing demands of growth and reproduction (48-51). The two fundamental tradeoffs in life history theory are 1) the tradeoff between current and future reproduction and 2) the trade-off between number and fitness of offspring (48). These trade-offs are illustrated by variations in pubertal timing and time to first reproductive event and are inevitable as metabolic resources

used for one purpose cannot be used for another. Much of the life history theory research has been conducted in females using age of menarche as an indicator of pubertal timing. These tradeoffs are more relevant to females and there is no comparable indicator for males.

Natural selection favors earlier reproductive development. Earlier reproduction is associated with lower probability of mortality prior to reproduction, results in a longer reproductive life span, and increases total reproductive output of lineages through shorter generation times (48). Competing selection pressures favor later reproductive development. Longer periods of growth result in larger adult body size, which generally translates into lower adult mortality rates, and greater energy stores to devote to reproduction (49, 52).

It is well accepted that pubertal timing, sexual debut, and reproductive events are associated as they are chronologically linked. In life history theory pubertal timing is conceptualized as an indicator of reproductive strategy. The costs and benefits of the timing of reproductive development are expected to be adaptive in response to ecological conditions. Central questions in life history theory are when individuals should reach sexual maturity and what development experiences and environmental cues bias individuals towards relatively early versus late development. Two classes of mid-level theories, energetics theory and psychosocial theories have been proposed to answer these questions (48, 53-55). Both agree that pubertal timing is responsive to the environment, but they differ in the nature, extent, and direction of environmental influences and the subsequent effects of pubertal timing on reproductive variables.

In life history theory pubertal timing is conceptualized as an indicator of reproductive strategy and adapts in response to ecological conditions. Certain ecological conditions bias individuals towards early maturation while others bias individuals towards late development. Mid-level theories have been proposed to explain the nature, extent, and direction of different environmental influences on pubertal timing and subsequent reproductive variables, we focus on aspects related to pubertal timing as these are most relevant to this dissertation. Two classes of mid-level theories, energetics and psychosocial theories relate variation in reproductive development to individual differences in experiences of stress, particularly

childhood exposures (48, 53-55). Stressors fall into two groups, psychosocial stressors and physical, or energetic, stressors. Energetic stressors include nutritional deprivation, intensive physical exercise, and poverty. Psychosocial stressors include trauma (i.e. war), parental mental health, parental absence, residence in a stepfamily, marital discord, harsh parental discipline, absence of familial warmth, and stressful life events.

Energetics theory explains pubertal timing in terms of chronic resource availability and hypothesizes that children who experience chronically poor nutritional environments will grow slowly, experience late pubertal development, and achieve relatively small adult size, whereas children who experience chronically rich nutritional environments will experience the opposite (53). There is strong evidence to support this hypothesis (56-63). Children who experience chronically poor nutritional environments, assessed directly in studies of diet and indirectly in studies of socioeconomic status, undergo pubertal development at a relatively later age.

Psychosocial theories posit that humans are sensitive to features of their childhood environments and these features bias children towards different reproductive strategies. In high stress environments, pubertal timing and sexual debut will be accelerated, while childhood environments characterized by low stress would function in the opposite manner (48, 54, 55). There is consistent evidence that pubertal timing, sexual maturity, and reproduction are accelerated following childhood environments characterized by high levels of psychosocial stress (48).

Life history theory applied to the Birth to Twenty Plus cohort

The Bt20+ cohort was established in a pivotal period in South Africa's history as it transitioned to democracy. The dissolution of apartheid started following Nelson Mandela's release from prison in 1990 and formally ended in 1994 following the first open, non-racial elections, four years after the cohort was established. Violence persisted following the end of apartheid with the poor carrying the largest burden of crime and violence. In addition to the political transformation, family and community life were

reconfigured by urbanization, modernity, weakening of traditional gender roles, the AIDS epidemic, racial inequality, poverty, and Black political empowerment (64).

Apartheid's legacy is visible in society in the economic inequality, inadequate housing, failing schools, poor nutrition and health, and violence in Black communities. The first nationally representative household income and living standards survey in 1993 indicated half of all Black South Africans lived in poverty. In 1998 these households were surveyed a second time and it was estimated that 60% of South Africa's poor were trapped in chronic structural poverty lacking the assets and entitlements to move out of poverty over time (64).

To apply life history theory to the Bt20+ cohort, we first need to describe pubertal timing within the cohort. Mean age of genital development among Bt20+ males was 12.7 y. Among females, mean age of breast development onset was 12.3 y and mean age at menarche was 12.7 y. In a cohort in the rural Mpumalanga province in South Africa, puberty onset was later with the mean age at menarche at 14.5 y (65). Pubertal development took place later in Bt20+ compared to the UK in the 1990s where the mean ages of genital and breast development onset were 11.1 y and 11.0 y, respectively (37).

Secular trends demonstrated a decline in age at menarche in the first half of the twentieth century accepted to be the result of improved nutrition (37, 66, 67). It is possible these improvements were not experienced fully in South Africa and would be experienced in urban communities before rural ones. Indeed, the authors of the Mpumalanga study suggested the urban nutritional environment was more energy dense than rural settings (65). While some of the over one-year difference in pubertal timing between Bt20+ and the UK may be explained by genetic differences between the study populations, other factors likely contributed.

In life history theory, pubertal timing reflects a reproductive strategy that places an individual along a fast-slow continuum (68). Individuals shifted towards the fast-continuum perceive a high risk of mortality or that the resources in their environment are threatened. Individuals shifted towards the slow-

continuum do not perceive threats to their reproductive success and favor continued growth and delayed reproduction. Mid-level energetics and psychosocial theories differ in their conceptualization of how the reproductive strategy is determined and the role of physical and psychosocial stressors.

Energetics theory states pubertal timing will be delayed following childhood conditions characterized by nutritional deprivation (53). Pubertal timing in Bt20+ was later than puberty onset in the UK, though earlier than in rural South Africa. There is some evidence of childhood nutritional deprivation in Soweto-Johannesburg. Height-for-age z-score (HAZ) is an indicator of nutritional status and would be negative in the presence of malnutrition. In Bt20+, mean HAZ was -0.68 (SD 0.92) at age 5 y and -0.62 (0.92) at age 8 y among males and 0.64 (0.91) at age 5 y and -0.69 (0.94) at age 8 y among females. Males were slightly short for their age throughout childhood while females were slightly tall for their age at age 5 y but short for their age at age 8 y. The extent of nutritional deprivation required to shift pubertal timing is unknown. While these HAZ values do not reflect extreme malnutrition, it is possible that they may have been enough to signal an energetically constrained environment and delay sexual maturation.

According to psychosocial theories, childhood circumstances characterized by high psychosocial stress would be expected to accelerate pubertal timing (48, 54, 55). As described, early life and childhood for Bt20+ participants were characterized by high levels of stress and violence. Families were further strained by the loss or absence of fathers; >60% of Bt20+ participants were born to single mothers. Though Soweto-Johannesburg was characterized by high psychosocial stress in the 1990s, it is challenging to evaluate if pubertal development was accelerated for children growing up in that time without a comparison group. Were conditions worse in urban environment compared to rural, this could explain the earlier age of puberty onset in Bt20+ compared to the cohort in rural Mpumalanga but this would not be the case if conditions were similar nationwide and puberty onset was still later than in the UK.

Reactivity of the stress response system is thought to be heightened by both highly stressful and highly protective features of the environment. In an extension of stress reactivity theory applied to one of

the psychosocial theories, psychosocial acceleration theory, Boyce and Ellis hypothesize that there is a U-shaped relationship between early exposures and stress reactivity profiles such that high stress-reactivity phenotypes emerge in response to both highly stressful and highly protected early social environments (69). Conditions in Soweto-Johannesburg in early life and childhood may have been extreme enough to delay maturation and may explain why pubertal timing was later in Bt20+ relative to the UK.

In summary, we found some evidence to support energetics theory in Bt20+ as pubertal timing was earlier in Bt20+ than rural South Africa but delayed relative to the UK and there was evidence of some malnutrition in Bt20+. The dissolution of apartheid was a period of high psychosocial stress, but it is unclear if this was experienced nationally or if there were differences between urban and rural communities which could explain why pubertal timing was lower in Bt20+ compared to the rural cohort. Alternatively, psychosocial stress may have been so extreme as to delay pubertal timing, explaining why pubertal timing was delayed relative to the UK cohort. How life history theories play out when conditions of both nutritional deprivation and psychosocial stress are present in the environment is not well understood, and further research is needed to disentangle how these interact to influence pubertal timing generally and within the Bt20+ cohort.

Future directions

Implications for public health

High rates of risk behavior experimentation identified in Aim 1 suggest the need for ongoing risk behavior surveillance among South African youth. The South African Youth Risk Behavior Survey (YRBS) was administered in 2002, 2008, and 2011, but we were unable to locate more recent results (27, 70, 71). Ongoing surveillance is essential for monitoring population trends, evaluating the effectiveness of intervention efforts, and emerging health concerns (i.e. vaping). Though expensive, surveilling adolescent behavior has the potential to inform public health action yielding benefits not only in adolescence, but also in adulthood and future generations.

If considered in conjunction with subsequent findings, the detailed incidence data may inform timing of interventions. For example, smoking and alcohol prevention efforts would need to take place prior to adolescence as there was a large increase in smoking and alcohol initiation in early adolescence and sex education should take place in early adolescence as the largest increase in sexual debut was in mid-adolescence.

As the analyses conducted in Aims 2 and 3 were some of the first to examine these associations in the South African context, we caution against making public health decisions based solely on these results, though these findings should be considered in concert with others in the future.

The findings from Aim 2 suggest early maturers are at greatest risk of experiencing adverse health outcomes. Graber, Nichols, and Brooks-Gunn described potential interventions to support early maturers at each level of the socioecological framework (72). At the individual-level, interventions promoting positive self-image and strengthening coping strategies may allow the early maturer to better navigate puberty. Family-level interventions delivered prior to puberty may support parent-child relationship quality during puberty. Peer interventions may focus on forming and maintaining healthy peer networks. At the organizational level, there is an emphasis on providing adolescent friendly health services in which adolescents feel respected and comfortable talking about their health needs. Policy-level interventions could include reducing marketing to adolescents and curbing substance access through enforcing or adopting policies.

To the best of our knowledge, there have not been interventions designed that specifically target early maturers. Given pubertal development is externally visible, it is challenging to envision public health interventions that would target individuals based on their physical appearance, except for perhaps within the health system. However, other programs aimed at supporting adolescent mental health and healthy socioemotional development generally, including those described above, may have additional benefits for early maturers.

Implications for research

While applying these findings for public health decision making may be premature, they do have implications for future research. Identifying characteristics that predict risk behavior initiation patterns may present opportunities to target individuals at high risk of following the high-risk pattern in adolescence through interventions. If predictors were found to be causal, they may also begin to elucidate the mechanisms by which high-risk risk behavior initiation unfolds. While the sociodemographic factors we examined in Aim 1 did not predict risk behavior pattern membership, our Aim 2 findings suggest pubertal timing and tempo do. Other candidate predictors to consider include child emotional and behavioral problems as well as the schooling stage (i.e. primary or secondary) at the time of puberty onset (73, 74).

Our findings from Aim 2 were generally consistent with results from HICs, which align with the maturity gap (2, 3, 22, 29-32, 34-37). As the adolescent growth spurt takes place during the pubertal transition, incorporating age at peak height velocity would provide an additional indicator of pubertal development to assess consistency across associations. These findings are analogous to "main effects" of pubertal timing and tempo with patterns of risk behavior initiation and emotional and behavioral problems and should be replicated in future research. Future research should also investigate potential mediators and moderators of these associations including stress, peers, parental relationship quality, and school stage in adolescence (75-77). For example, adolescents experiencing both offset pubertal timing and poor parental relationships may be at high-risk of substance misuse (75). Similarly, the pathways by which pubertal timing and tempo are associated with adolescent risk behavior initiation or mental health in the South African context are unknown. These are complex biopsychosocial interactions in which the social environment takes cues from an individual's maturity status, which alters the way in which it interacts with the individual. For example, early maturers are more likely to associate with deviant peers, which may act as a gateway to substance use either through increased access, peer pressure, or a combination of the two (76, 78-80).

Due to the substantial time spent in school, the school setting in which young people undergo pubertal development may affect their experience. Individuals who mature earlier and faster may do so while still in primary school when they are the oldest pupils in the school whereas late maturers may not undergo puberty until they are in secondary school and some of the youngest learners in the school. The transition to from primary to secondary school in South Africa is a big transition for young people (81). Primary schools are smaller and tend to be closer to home while secondary schools have a larger catchment area and generally require learners to travel a greater distance from home. Late maturers who are physically smaller and immature may experience additional stress if they are picked on or excluded at above average rates.

We postulated our Aim 3 findings may be explained by unmeasured confounding due to intangible aspects of socioeconomic status. Alternative explanations for the observed findings should continue to be explored. For example, a social mechanism in which individuals who mature early receive preferential treatment in the classroom as has been observed with taller individuals and should be explored (82). Additional future steps may include redefining socioeconomic status as a more holistic latent construct or extending analyses further into adulthood as age 22 y is still a transitional age in which schooling may still be in progress and early employment may not reflect an individual's career trajectory. While we did not quantify the relationships between pubertal timing and tempo, risk behavior initiation, adolescent and young adult pregnancy, schooling, and employment, this will be important to do going forward as public health and educational decisionmakers need to make informed decisions on where to invest limited resources.

Furthermore, it would be worthwhile to take a step backwards and investigate associations of psychosocial antecedents with pubertal timing and tempo and their interplay with previously identified biological antecedents in the cohort. In the cohort, increased childhood BMIZ and HAZ were associated with earlier and faster pubertal timing and tempo (28). As described in life history theory, when experienced in childhood several psychosocial stressors are antecedents of pubertal timing (83-95).

Conclusions

Bt20+ participants were in a unique period in South Africa's history and grew up in a dynamic urban environment. This dissertation examines associations of pubertal timing and tempo with health outcomes in adolescence and schooling and employment outcomes in young adulthood among individuals growing up in urban South Africa.

We examined these associations in a middle-income country underrepresented in the literature. Closing this research gap is important given nearly 90% of the world's adolescents live in LMICs (96). In contrast to HICs, LMICs are generally characterized by greater adversity and it was possible associations would look different or be of different magnitude. The directionality of associations of pubertal timing and tempo with mental health and risk behavior initiation in adolescence were consistent with those from HICs. This suggests at least some commonalities in the adolescent experience across contexts and supports developmental explanations in which early maturers are at greatest risk of adverse health outcomes because they are physically mature before they are cognitively and socioemotionally mature (2, 3, 22, 29-32, 34-37). Future research should continue to look at contextual differences as well as explore pathways through which observed associations take place. In time this will amass a body of evidence that can be leveraged to support healthy development in adolescence and the transition to adulthood in urban South Africa.

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