Integrating Risks for Type 2 Diabetes Across Childhood: A Life Course Perspective
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Type 2 diabetes; Childhood obesity; Life course model; Cumulative risks

Type 2 diabetes (T2DM) emerged among children, due in large measure to a strong physiological link between increased weight states and T2DM. In this article, cumulative risk factors for T2DM across childhood and its underlying mechanisms are reviewed. The points of intervention for T2DM should occur throughout childhood. The use of Halfon and Hochstein’s framework enables practitioners and researchers in the nursing field to better understand a child’s individual risk for T2DM. Only with this long view will prevention and interventions be successful in stemming the tide of the “twin epidemic” threatening children worldwide.

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CURRENT APPROACHES FOR understanding the risk for developing type 2 diabetes (T2DM) in children are focused primarily upon overweight and obesity at the time of diagnosis. This cross-sectional approach has been helpful in providing an understanding of this new phenomenon, but increasingly, it is clear that preventive and treatment strategies need to begin earlier. Models that take a longer view of health development are needed to conceptualize risk profiles differently so that new ways of thinking about prevention, treatment, and research may emerge. This article explores the known risks for T2DM across critical periods of child development (prenatal period, infancy, childhood, and adolescence) and integrates these factors using a life course model of health development.

Background

The prevalence of obesity in children (body mass index [BMI] ≥95th percentile) has nearly tripled over the past three decades in the United States (Ogden, Carroll, & Flegal, 2008; Ogden, Flegal, Carroll, & Johnson, 2002). In 2007, the World Health Organization (WHO) reported that worldwide, nearly 22 million children younger than 5 years were overweight (WHO, 2007). Race and ethnic differences in overweight status are apparent in childhood (Dabelea et al., 2007; Mayer-Davis, 2008). Significantly higher proportions of Hispanic and African American children with ages 5 to 18 years are overweight and obese when compared with similarly aged White children. These overweight and obese children are more likely to be male, are from families with low-income status, and engage in less physical activities (Lutfiyya, Garcia, Dankwa, Young, & Lipsky, 2008). Although both boys and girls with low socioeconomic status (SES) are at a greater risk for being overweight, a recent study indicates that boys are more likely to remain overweight and girls to become overweight during childhood (Sherwood, Wall, Neumark-Sztainer, & Story, 2009). The WHO estimates that more than 75% of overweight children are from low- to middle-income countries, and consistent with U.S. data, adolescent boys are more likely to be overweight than girls in many European countries (WHO, 2007).

T2DM, once known to be a late-adult disease, has emerged among children due in large measure to a strong physiological link between increased weight states and T2DM. Using the National Health and Nutrition Examination Survey data, researchers have found that the rates of T2DM have doubled among U.S. children aged 12 to 19 years over the last 15 years (Ogden et al., 2008). The obesity
epidemic alongside these increasing rates of T2DM in children has been tagged the “twin epidemics” (Smyth & Heron, 2006) and is worrisome as together they portend of a future of worsening health due to the devastating consequences of T2DM. These include chronic renal failure, blindness, coronary artery disease, limb amputation, and central nervous system manifestation (Reagan, 2007). Furthermore, T2DM disproportionately affects youth from racial minority groups when compared with White youth (Lee, 2008). The SEARCH for Diabetes in Youth Study, a national multicenter study, has established rates of T2DM in 15- to 19-year-olds ranging from a low in non-Hispanic Whites of 0.19 per 1,000 to 1.05 per 1,000 in African Americans to a high of 1.74 per 1,000 in Native Americans (Liese et al., 2006).

T2DM is most often diagnosed in children during mid to late adolescence, but the risk factors for T2DM operate across childhood. It is well established that T2DM in children is inextricably linked with childhood obesity, but it is also becoming clear that there is a cluster of risks that begin in early childhood and interact and accumulate over the child’s life to increase the likelihood of T2DM. The stress-response mechanism may be underlying several of these risks, and there is growing interest in the relation between psychological stress and the development of T2DM (Black, 2006). Stress hormones (e.g., cortisol and norepinephrine) are thought to activate the immune and inflammatory response. Insulin resistance is usually present during the inflammatory process and beta-adrenergic stimulation. Increased cytokine activities, such as tumor necrosis factor and interleukin-6, are believed to increase lipolysis in adipocytes, releasing free fatty acids. This ultimately leads to impairment of insulin signaling by blocking insulin receptors in target tissues (Tsotra & Tsigos, 2006).

Insulin has been found to attenuate the stress response. In studies where insulin was administered intranasally, there was a decrease in the levels of stress hormones circulating in the body (Bohringer, Schwabe, Richter, & Schachinger, 2008). This result suggests that insulin may play an important role in the regulation of the hypothalamic-pituitary-adrenal (HPA) axis. Conversely, increased adiposity may alter mood through pro-inflammatory cytokines, which may in turn affect the function of HPA axis (Elenkov, 2008; Reagan, 2007). Underlying these physiological processes is the increasing evidence that the fetal environment may set up the child for heightened stress reactivity and abnormal glucose metabolism (Halfon & Hochstein, 2002).

Thus, the risks for T2DM are complex, are likely to be influenced by the child’s social context, and accumulate as the child ages. It is increasingly clear that an understanding of the risks and etiology for T2DM limited to the conditions at diagnosis is incomplete. To understand which children are at the highest risk for the development of T2DM, a comprehensive life course model that not only accounts for proximal risks but can also account for risks in prior periods is necessary. Halfon and Hochstein propose such a framework that combines physiological regulations and environmental influences to explain individual health trajectories (Halfon, Russ, & Regalado, 2005). According to the life course health development (LCHD) framework, an individual’s health follows a unique trajectory that is determined by the interactions among surrounding contexts, early life experiences, and his or her biological regulatory mechanisms (Halfon et al., 2005). The model is displayed in Figure 1. The arrows pointing up indicate protective factors, which increase or improve the health trajectory across time; the downward-pointing arrows indicate risk factors, which decrease or worsen the health trajectory across time. The curved arrows indicate a cumulative effect in that health in a future state (e.g., adolescence) is

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**Figure 1** Chain of Risks for T2DM for two children (child A and child B). Upward arrows indicate protective health factors, and downward arrows indicate risk factors. Curved arrows indicate cumulative effect of protective/risk factors.
dependent upon sum of the risk and protective factors in the previous states.

The LCHD framework depicts health as “a dynamic, multifactor, and biopsychosocial phenomenon” (Halfon & Hochstein, 2002, p. 434) and is based on several assumptions (Halfon & Hochstein, 2002). First, this model assumes the existence of multiple determinants for any disease entity. Second, health is seen as an adaptive process over the life course. Third, cumulative effects of risk and protective factors determine different health trajectories with the timing and sequence of exposure key to health development. Thus, early life events and exposures are important processes that form the foundation from which later risks exert their influence.

The purpose of this article is to apply Halfon and Hochstein’s LCHD framework to what is known about the risk factors associated with the development of T2DM in children. These risks are linked to the developmental stage in which they occur, and traced out through adolescence, highlighting the critical periods and risk accumulation components of the LCHD framework. Four developmental stages of childhood are used for this analysis: the prenatal period, infancy, childhood, and adolescence. The underlying mechanisms posited to explain these risks are reviewed. A cross-sectional summary of these risks by developmental stage is presented (see Table 1). Figure 1 details the life course model, presenting the factors as a connected chain. These factors accumulate during childhood and either increase or decrease the likelihood that an individual child will develop T2DM by mid adolescence. The life course framework provides a more comprehensive view of the development of T2DM than a simple cross-sectional approach that considers only risks at the time of diagnosis (e.g., obesity at mid adolescence). This life course perspective should prove invaluable for identifying critical periods for prevention, treatment, and research.

### Life Course Stages and Risk for T2DM

#### Prenatal Environment and Fetal Programming

The idea that the health of an individual is affected by the intrauterine environment has gained increasing acceptance among researchers in recent years (Gluckman, Hanson, Cooper, & Thornburg, 2008; Swanson, Entringer, Buss, & Wadhwa, 2009). Birth weight has become a key marker for the intrauterine environment and disease in later life, with current epidemiological evidence suggesting that the association of birth weight with T2DM is U-shaped (Boney, Verma, Tucker, & Vohr, 2005; Fernandez-Twinn & Ozanne, 2006; Mayer-Davis, 2008). Children born at either end of the weight continuum are more likely to be at greater risk for T2DM in later life. Low birth weight has been associated with maternal undernutrition, child obesity, and T2DM through the “thrifty phenotype hypothesis” (Hales & Barker, 1992). According to this hypothesis, insulin resistance and obesity as well as T2DM in later life are related to undernutrition in fetal life. Evidence supporting this association originated with a study of men in Hertfordshire, England. This study found an inverse relationship between

### Table 1  Summary of Risk Factors and Potential Mechanisms for Developing T2DM During Childhood

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<th>Risk factors</th>
<th>Prenatal</th>
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<th>Childhood</th>
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Note: Risk factors for T2DM are present throughout childhood. Awareness of these risk factors allows practitioners to identify high-risk children and to provide them with appropriate interventions.
weights both at birth and at 1 year of age and adult mortality rates from coronary heart disease (Barker, 1995).

During mid to late pregnancy, various tissues and organs continue to grow and develop in the fetus. When undernutrition occurs during this critical period of development, the fetus is likely to develop physiological and metabolic adaptations to increase glucose availability to nourish its developing brain. As a consequence, overall fetal growth slows down. To adjust to the low glucose environment during fetal development, the fetus becomes “thrifty” in its use of glucose. A postnatal high caloric environment then is likely to predispose these children to overweight and obesity.

At the other end of the continuum, high birth weight has been associated with later obesity and T2DM. Maternal gestational diabetes and maternal overweight status, with borderline hyperglycemia, are strongly implicated as possible causes (Boney et al., 2005; Mayer-Davis, 2008; Salsberry & Reagan, 2005). Thus, altered nutrition during the fetal period poses a significant risk for the development of T2DM through either an increase in adipose tissue mass, a reduction of pancreatic function, or both (Cottrell & Ozanne, 2008).

Maternal psychosocial stress during pregnancy has also been linked to altered fetal growth and development (Valsamakis, Kanaka-Gantenbein, Malamitsi-Puchner, & Mastorakos, 2006), possibly through pathways facilitated by increases in maternal glucocorticoid levels coupled with dysregulation of materno-placento-fetal barrier. A placental enzyme, 11beta-hydroxysteroid dehydrogenase 2, is known to regulate fetal cortisol concentrations by converting cortisol to inactive cortisone. It is postulated that reduced activity and the expression of this enzyme result in increased fetal exposure to glucocorticoid, causing deleterious effects on fetal development (Bertram & Hanson, 2002; Kajantie, 2008). Both acute and chronic stress in the mother may play a role. Severe and acute life stress during pregnancy, such as an exposure to death or severe illnesses in a close relative, has been associated with a reduced birth weight (Khashan et al., 2008; Precht, Andersen, & Olsen, 2007). Exposure to diffuse and chronic maternal stress, mediated by adverse social environments, such as minority status, lower-middle SES, and lower maternal age, has been associated with elevated maternal serum cortisol levels and slow fetal development (Diego et al., 2006). Further, the increased risk for low birth weight may be mediated through maternal behaviors, including cigarette smoking during pregnancy, more frequent in women who experience increased contextual levels of stress (Lobel et al., 2008). Maternal cigarette smoking during pregnancy, in turn, has been shown to result in an increased risk of later childhood obesity (Salsberry & Reagan, 2005) in a dose-dependent fashion (Sharma, Cogswell, & Li, 2008).

Animal studies provide important evidence that is often not possible to obtain in human studies. Animal studies designed to examine the effects of maternal stress on fetal development and later adult disease development are completed in one of two ways: an administration of exogenous corticosteroid mimicking the physiological stress response or an administration of “restraint stress” to pregnant animals. For example, an exposure of a pregnant dam to dexamethasone in late gestation is associated with a lower birth weight in both male and female offspring, and the development of metabolic syndrome in male offspring (O’Regan, Kenyon, Seckl, & Holmes, 2004). Stress through physical restraint on a pregnant dam is associated with reduced body weight in both male and female offspring, reduced adrenal and pancreas size, and decreased serum glucose and cortisol levels at birth in rats (Lesage et al., 2004). In addition, adult offspring of a stressed dam shows higher levels of leptin and glucose with significantly higher food intake after animals undergo a period of fasting (Lesage et al., 2004). These animal studies are important because they provide evidence to support the observational findings in humans that increased prenatal exposure to stress can induce intrauterine growth retardation and insulin resistance, both factors associated with development of T2DM.

Other animal studies reveal that alterations in gene expression or gene products in signaling pathways may contribute to the association between intrauterine environment and birth size. Maternal nutrient deficiency may mediate epigenetic modulation during fetal development and ultimately alter gene expression of the fetus (Devaskar & Thamotharan, 2007). Within animal models, several epigenetic changes have been found among offsprings that experiences intrauterine stress (Lillycrop, Phillips, Jackson, Hanson, & Burdge, 2005; Park, Stoffers, Nicholls, & Simmons, 2008; Sinclair et al., 2007). Further research is needed to test these relationships.

Thus, the risks for T2DM begin within the intrauterine environment when maternal undernutrition and higher stress levels may influence or program the fetus to be more likely to develop obesity and T2DM. This is the beginning point for the health trajectory illustrated in Figure 1, which unfolds during childhood. Whether these programming effects are reversible is currently unknown and under intense investigation. Animal studies have shown inconsistent results (Cottrell & Ozanne, 2008; de Boo & Harding, 2006), and the child’s growth patterns immediately following birth are of particular interest. The children who are thin at birth but have a period of rapid weight gain during childhood are at the greatest risk for developing T2DM. Children who have restricted growths during the fetal period have reduced muscle mass that cannot utilize an abundant supply of glucose. Subsequently, becoming overweight with existing insulin resistance may result in T2DM as early as mid childhood (Cottrell & Ozanne, 2008; de Boo & Harding, 2006; Valsamakis et al., 2006).

Infancy

Feeding practices during infancy and subsequent child health outcomes, especially child obesity, have received significant attention over the last decade. Although exact mechanisms of how early feeding practices may affect future
weight states are unknown, breast-feeding is believed to be protective against developing future obesity (Armstrong & Reilly, 2002; Taveras et al., 2004; Weyermann, Brenner, & Rothenbacher, 2007). Evidence from epidemiological studies indicates that breast-feeding moderately decreases the risk for developing obesity after controlling for gender, birth weight, and low income (Armstrong & Reilly, 2002). Growth is likely to follow a different pattern in an infant exclusively breast-fed for more than 9 months from that of a bottle-fed infant or that of an infant switched to bottle-feeding after 6 months (van Dijk & Innis, 2009). Although breast-feeding duration is associated with maternal age, marital status, education, and smoking during pregnancy (Li et al., 2008), various mechanisms to explain a breast-feeding effect have been suggested. Two major mechanisms are of importance: biological paths related to leptin and behavioral paths related to the establishment of healthy eating patterns.

It has been speculated that the hormone leptin in breast milk may be associated with a decreased risk for future obesity. In a rodent model, a permanent reversal of an intrauterine programming effect among the offspring of a food-restricted dam was achieved by leptin administration in early infancy (Vickers et al., 2005). Human studies, however, examining the relationship between breast milk, leptin level, and risk of obesity are inconclusive (Miralles, Sanchez, Palou, & Pico, 2006; Weyermann et al., 2007). However, breast-feeding has been associated with lower blood glucose and serum insulin levels in infancy, as well as a reduced risk of T2DM in later life (Owen, Martin, Whincup, Smith, & Cook, 2006). Whether this protection is mediated by a decreased obesity risk or is an independent result remains an open question.

The acquisition of healthy feeding behaviors during infancy and early childhood may be key to the prevention of or delaying of the development of T2DM. Breast-feeding may be important in achieving these behaviors because studies suggest that breast-feeding may help the infant develop healthier lifelong eating patterns, including a self-regulation pattern that reduces the likelihood of overeating. Moreover, breast-feeding, has been suggested to result in less restrictive feeding style in mothers (Taveras et al., 2004). Mothers who breast-fed at least 6 months were less likely to be disturbed with the child’s food intake at age 1 year. However, it is unclear whether this is due to maternal behavioral characteristics that increase the decision to breast-feed a longer period or something inherent in the breast-feeding process. Maternal demographic factors such as race, low educational level, and low household income are associated with restrictive feeding style (Taveras et al., 2004). The breast-feeding and feeding behavior paths that are laid down in infancy may lead to differential health outcomes seen in children by racial and SES categories (Mayer-Davis et al., 2008; Woo, Dolan, Morrow, Geraghty, & Goodman, 2008). Improvement in social support system may be necessary to increase the duration of breast-feeding among mothers with low income (Li et al., 2008).

Thus, an infant’s future risk for T2DM is influenced by the maternal decision on breast-feeding and its duration. During infancy, eating preferences and behaviors are established and influence the growth, development, and health path taken through this developmental phase. Infancy builds upon the set of risks and protective factors laid down in utero. Upward arrows in Figure 1 illustrate protective factors increasing the child’s health capital, whereas downward arrows show health risks result in its loss.

Childhood

Children do not live alone. Their health behaviors and physical health are directly influenced by how their immediate caregivers perceive and practice eating rituals. Increased parental BMI is a strong indicator for childhood obesity (Danielzik, Czerwinski-Mast, Langnase, Diba, & Muller, 2004; Davison, Francis, & Birch, 2005; Gibson et al., 2007; Zeller et al., 2007). Children of single mothers who have high BMIs and low income are likely to become obese because of decreased accessibility to less energy dense and nutritional food (Gibson et al., 2007). Girls from obesogenic family environments and those from nonobesogenic families have very different weight trajectories (Davison et al., 2005). That is, the girls from families practicing high-energy dietary intake and low physical activities are more likely to have consistently higher BMIs than those from nonobesogenic families. In addition, negative mealt ime family interactions and conflicted family environments are significantly associated with overweight among children ages 6 to 18 years old (Zeller et al., 2007). Regular family mealt ime as opposed to disorganized meal patterns has a positive effect on child’s food preference and feeding patterns, resulting in reduced risk of becoming overweight (Zeller et al., 2007).

Shortened sleep duration is linked to altered hormonal regulations of food intake, energy balance, and weight maintenance (Lumeng et al., 2007). Chronic sleep disturbances may shift the hormonal control toward weight gain, and altered regulation of leptin and ghrelin may be responsible for the weight gain (Lumeng et al., 2007). Average sleep duration less than 12 hours per day before 2 years of age may be associated with child’s overweight status at age 3 years (Taveras et al., 2008). When combined with hours of television viewing more than 2 hours per day, the risk of overweight at 3 years of age will be significantly higher than shortened sleep hours alone. A similar finding is reported among preadolescent children (Lumeng et al., 2007) with more apparent effects among boys than girls (Ievers-Landis, Storfer-Isser, Rosen, Johnson, & Redline, 2008). However, the difference in gender may be attributed to other confounding factors and hormonal effects (Ievers-Landis et al., 2008). Unhealthy family routines can set up an individual’s health behavior, which is manifested as undesirable food preference, eating habits, shortened sleep
duration, and physical inactivity. This, in turn, negatively affects one’s biology through hormonal disturbances toward development of T2DM.

The physical environment of a community may also influence choices of health behaviors (Gordon-Larsen, Nelson, Page, & Popkin, 2006). Low SES neighborhoods are likely to have greater access to fast-food restaurants (Hemphill, Raine, Spence, & Smoyer-Tomic, 2008; Li, Harmer, Cardinal, Bosworth, & Johnson-Shelton, 2009) and lower accessibility to healthy food (Baker, Schootman, Barnidge, & Kelly, 2006; Franco, Diez Roux, Glass, Caballero, & Brancati, 2008). Physical activities of children and adolescents are promoted with an increased sense of safety. This may be exemplified by increased neighborhood greenness (Bell, Wilson, & Liu, 2008) and neighborhood walkability in terms of intersection design (Spence, Cutumisu, Edwards, & Evans, 2008). Shorter distance between intersections seems to promote caregivers to take young children for walks. Although younger children from low-income communities may be no less active, there are fewer physical activity facilities available (Voss, Hosking, Metcalf, Jeffery, & Wilkin, 2008), with physical activity level and BMI likely to be impacted by the access to these physical activity facilities (Gordon-Larsen et al., 2006).

In childhood, the health trajectory is influenced by the context surrounding the child—exercise, food preferences, food availability, sleeping patterns, and time use all influence the unfolding of the child’s health, most visibly measured by the weight status of the child. These contexts unfold upon a child whose biological and behavioral foundations were laid down in utero and during the infancy period. The curved arrows in Figure 1 illustrate these cumulating relationships.

Adolescence

Adolescents experience dramatic body composition changes during puberty. This occurs in a gender-specific fashion. Girls tend to increase fat and lean mass gradually and in equal ratio, whereas boys have a dramatic increase in lean body mass (Brufani et al., 2009; Moran et al., 2008). Total body fat percentage decreases in normal-weight boys during this period (Moran et al., 2008). Similarly, overweight and obese boys reduce their total fat percentage but with central adiposity (Brufani et al., 2009), increasing their risk for decreased insulin sensitivity (Maffeis et al., 2008; Taksali et al., 2008).

Pubertal insulin resistance may play an important role in the onset of T2DM among overweight adolescents. Studies have examined the changes in biochemical markers during puberty, with a common finding related to pancreatic beta-cell function and a surge in insulin resistance during puberty; however, the latter is usually transient and recovers by the end of puberty (Brufani et al., 2009). Worsened insulin resistance despite increased lean mass in boys is somewhat puzzling. Attempts to explain this surge of insulin resistance by pubertal hormonal changes have produced inconclusive results (Goran & Gower, 2001). Further study is indicated to explain the relationship between body composition changes and pubertal insulin resistance.

Weight gain during the pubertal period may have detrimental effects as the risk of developing T2DM increases if beta-cell function does not recover during puberty. Because overweight children do experience earlier puberty and a longer period of maturation with various hormonal changes, they have an added risk for developing T2DM (Goran & Gower, 2001; Goran, Shaibi, Weigensberg, Davis, & Cruz, 2006; Weiss et al., 2005; Xekouki et al., 2007). Comparison of biochemical markers in different Tanner stages is often used to find predictors for T2DM in adolescents. For example, changes in insulin sensitivity are apparent among children in different Tanner stages. A significant decrease in insulin sensitivity has been found among children who progressed to Tanner Stages III and IV from Stage I (Goran & Gower, 2001). A rise in acute insulin reaction, which may not be fully compensated for by a fall of insulin sensitivity, suggests that a decrease in insulin sensitivity is related to either compensation in beta-cell function or inadequate beta-cell response (Goran & Gower, 2001). Similarly, a decrease in insulin sensitivity and beta-cell function is especially apparent with weight gain during progression through Tanner Stages IV and V (Goran et al., 2006).

Furthermore, psychological stress or depressed mood may lead to maladaptive behavior especially when individuals are not equipped with the appropriate coping resources: social support, optimism, mastery, and self-esteem (Taylor & Stanton, 2007). Increased preference for energy-dense food under stressful situations is demonstrated in animal models (Teegarden & Bale, 2008). In humans, stress-sensitive individuals may be especially prone to binge eating behaviors under stressful situations. Adolescent boys and children from low SES minority groups may be more likely to eat unhealthy food and use eating as a coping mechanism (Jenkins, Rew, & Stenglanz, 2005). Adolescents who are overweight are more likely than normal-weight counterparts to use eating as a coping strategy (Martyn-Nemeth, Penckofer, Gulanick, Velsor-Friedrich, & Bryant, 2009). Conversely, being overweight is associated with psychological stress, depressed mood, and maladaptive behavior (Bender, Fuhlbrigge, Walders, & Zhang, 2007; Doyle, le Grange, Goldschmidt, & Willfrey, 2007; Gray & Leyland, 2008). In addition, overweight adolescents who experience frequent teasing by peers and family members are more likely to practice unhealthy eating (Libbey, Story, Neumark-Sztainer, & Bouterle, 2008). Although these associations may be especially prevalent among younger adolescents (Swallen, Reither, Haas, & Meier, 2005), stress level and coping strategies may very well influence weight status. Combined with the trend in earlier onset of puberty among girls over the past 30 years, correlated with the amount of body fat (Kaplowitz, 2008), there may be a relation among increased obesity, early puberty, maladaptive coping behaviors, and development of T2DM.
Finally, during adolescence, significant biological changes occur in the child, which may be influenced by the child’s weight status, the individual’s contextual stress, their response to this stress, and the child’s psychological states during this highly volatile time. It is clear from the above review that the presentation of health during adolescence has a long tail that began in utero. Figure 1 again details how this health trajectory builds across childhood.

Summary and Conclusions

As detailed within each stage, Figure 1 illustrates how Halfon and Hochstein’s framework can be used to better understand a child’s individual risk for T2DM. The arrows pointing up indicate protective factors, which increase or improve the health trajectory across time; the downward-pointing arrows indicate risk factors, which decrease or worsen the health trajectory across time. The curved arrows indicate a cumulative effect in that health in a future state (e.g., adolescence) is dependent upon sum of the risk and protective factors in the previous states. For example, as drawn in Figure 1, the health trajectory of child A is below that of child B throughout childhood. From the above review of literature, assume the following scenario. Child A experiences greater health risks in each of development periods, for example, maternal obesity and gestational diabetes during fetal life, followed by bottle-feeding, a childhood with little activity, increased screen time, and a diet high in energy-dense foods. By age 11 years or so, the child is overweight. By age 15 years, this child is experiencing glucose intolerance and is diagnosed with T2DM. The health of child B is always greater than child A, and this child’s health capital increases at a greater rate than child A, resulting in a child at the end of adolescence with greater health capital, and the difference between the two has widened considerably. Child B’s scenario may be the following: intrauterine life without exposure to maternal increased stressors and/or increased glucose, breast-fed for 15 months, physical activities throughout childhood, enters adolescence at a healthy weight, and at the end of adolescence is poised to enter adulthood with strong health reserves.

So the key question is always how do we successfully improve the health of child A (and child B)? The strength of this model is that the points of intervention occur throughout childhood. It is not isolated to intervening at mid childhood when the child is diagnosed as overweight. On this understanding of risk factors, prevention begins during prenatal life and continues during each developmental stage. Likewise, researchers interested in understanding the development of T2DM should keep in mind the “programming” for T2DM that likely occurs during earlier life. Only with this long view will prevention and interventions be successful in stemming the tide of the “twin epidemic” threatening children worldwide.

References

Baker, E. A., Schootman, M., Barnidge, E., & Kelly, C. (2006). The role of race and poverty in access to foods that enable individuals to adhere to dietary guidelines. Preventing Chronic Disease, 3, A76.


retardation in rats is associated with progressive epigenetic silencing of Pdx1. *Journal of Clinical Investigation*, 118, 2316–2324.


