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Redefining Cardiovascular Risk in the Young: Integrating Longitudinal Evidence, Subclinical Endophenotypes, And the Imperative for Primordial Prevention

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Abstract

Cardiovascular disease (CVD) has been considered an adult condition, but recent longitudinal evidence has shown that its structural bases are laid during fetal development and early childhood. According to the "Decade Link," the vascular health of young adulthood is a biological outcome of the physiological stressors that were encountered a decade ago. The purpose of this review is to summarize the existing data on subclinical indicators of premature vascular aging and assess the effectiveness of existing methods of diagnosis and intervention in the pediatric demographic. Longitudinal cohort studies, such as the KiGGS and i3C, were compared and the role of Deep Learning (DL) and multimodal imaging in identifying arterial remodeling is determined in this review. It was found that adolescent obesity exposes adults to a 3.7-fold higher risk of developing Carotid Intima-Media Thickness (CIMT) and pediatric hypertension doubles the risk of developing a stiffened artery. Moreover, prenatal maternal stress is also highly linked to growth of infant aortic IMT. Whereas the current state of AI-powered diagnostics is capable of establishing subclinical plaques with 90 percent accuracy, conventional behavioral therapies against obesity in adolescents reveal a potentially disastrous failure rate of 98 percent. The long-term vascular memory of childhood stress makes reactive treatments in adolescence largely ineffective and requires a paradigm shift towards primordial prevention, which includes environmental, socioeconomic, and prenatal factors to break the subclinical atherosclerosis pathway before permanent structural damage occurs.

Keywords: Subclinical Atherosclerosis, Carotid Intima-Media Thickness (CIMT), Primordial Prevention

1. INTRODUCTION

Cardiovascular disease (CVD) was regarded over many years as an invisible threat of being the result of aging that usually manifested in the middle or old age. Nonetheless, there is a major shift in longitudinal research that is changing this timeline. According to the 2025 KiGGS study (Buegge, 2025) and the International Childhood Cardiovascular Cohort (i3C) Consortium, the causes of heart disease are not only defined in adulthood but may also start to develop in the wall of blood vessels in childhood. This is a pre-symptomatic stage of vascular remodeling, which involves structural alterations, and is not merely a medical curiosity. It is an important window of opportunity where the destiny of human life is open to change.

1.1. Monitoring Vascular Aging in the Young

It has been discovered that the vascular clock begins to tick far earlier than we previously imagined. Current sonography has ensured that Carotid Intima-Media Thickness (CIMT) and Carotid Stiffness (CS) can be measured with a 98% success rate in the general youth populations giving a clear picture of the internal health of a child. These measurements serve as a red flag; i3C consortium is just one example, high adult cIMT has been proven to be the direct biological extension of obesity, hypertension and dyslipidemia in adolescence. Moreover, the findings of the Bogalusa Heart Study are a constant reminder that this clock does not tick at a similar rate among them all. Black participants and males tend to exhibit greater mean CIMT, which implies that an intricate play of both genetics and systemic stressors starts affecting the heart health at the first stage (Li et al., 2003).

1.2. Measuring the 10 Year Pediatric Risk Correlation

The most unusual finding in contemporary pediatrics is possibly the so-called Decade Link. This notion implies that the health condition of a child today is a strikingly precise foreboding of the health of his vascularity eleven years later, despite the events that occur in the interim (Agbaje, 2024). The motives behind this connection are well known:

The Weight of Adiposity: Adolescent obesity is now the most violent predictor of arterial thickening which raises the risk of high adult cIMT by 3.7-fold (Agbaje, 2024).

The Pressure on the System: Systolic blood pressure (SBP) in a teenager is the only predictor of the future of the arterial stiffness. Hypertension during childhood almost doubles the risk (OR 1.83) of stiffened arteries in the adult life (Yang et al., 2020).

The Lipid Burden: The arteries in effect maintain a kind of ledger book of exposure to cholesterol; the greater the cumulative LDL-C lev (Brown & Goldstein, 1986).

1.3. The New Age of Detection

With newer technologies, we keep on in the future as we are able to monitor the young hearts. We are currently moving from the implementation of traditional ultrasound technology into the implementation of multimodal imaging technology (MRI and CT) and Artificial Intelligence based technologies. As an illustration, deep learning models are capable of detecting a carotid plaque with a high accuracy of up to 90 percent, which is very high level of clinical accuracy as compared to the classic clinical models (Guo et al., 2025; Weng et al., 2023). What may be more intriguing is that this risk might be transferred across generations. Recent results of the FinnBrain Birth Cohort show that the pressure story may begin prior to birth, when the level of stress of the pregnant mother directly and significantly influences the thickness of the aorta intima/media (aIMT) of the newly born (Kjeldsen et al., 2020). To preserve the cardiovascular health of their child, they should start acting before their child is born.

2. Genetic, Epigenetic, and Prenatal Foundations of Vascular Risk

Cardiovascular disease (CVD) has been redefining its paradigm to a life-course starting in the womb. Aatsinki et al. (2024) showed that maternal psychological distress in pregnancy is associated with more infant aortic intima-media thickness (Aatsinki et al.,2024).

The picture gets more complicated when it is applied on top of the genetic blueprint of a child. GWAS have identified the existence of genomic loci of silent drivers of future plaque formation like those that regulate interleukin-6 and lipoprotein(a) (Omarov et al., 2024).

3. Hemodynamic Load and the Silent hardening of Youth

3.1. **The Developing Body and Teenage Vascular System**: At puberty, children grow very fast in height and other body dimensions. A 2021 study conducted by Bueschges has indicated that height and age are the primary factors that determine the thickness of a section of the carotid artery known as Carotid Intima-Media Thickness (CIMT).

3.2. **The Significance of Height-Adjusted Diagnostics:** In the case of healthcare workers, the use of height-adjusted centiles is necessary to avoid the misdiagnosis of a normal growth spurt as abnormal thickening (Bueschges, 2025; Urbina et al).

3.3. **Blood Pressure and the Decade Effect:** This age group is more likely to develop elevated BP in the future so the only factor that makes them susceptible to this is their predisposition with regard to their earlier BP levels. Although the level of BP might be normal by the time a child is an adult; being raised with a high level of BP predisposes the adult to have higher levels of arterial stiffness (so-called "Decade Link") and represents an example of the long-term memory of the vascular system (Buechges, 2025; Yang, k; et al; 2025)

4. Adiposity Crisis and Trajectories of Weight.

There is a strong relationship between adolescent obesity and cardiovascular disease in terms of its progression into early atherosclerosis; though, it can only be evaluated through trajectories, not snapshots. As an example, adolescents that are obese have 3.7 times higher risk of developing an increased carotid intima-media thickness (CIMT) than those who were never obese (Turer et al., 2018). Moreover, as important as the degree of obesity is, the rate of new obesity (i.e., the rate of atherosclerosis development in adolescents) is also critical in the progression of atherosclerosis. The adolescent women who transitioned to overweight also had no extra vascular risk factors compared to those who were always heavy; they were at higher risk of vascular risks because of their higher weight gain rate (Terzis et al., 2012).

In this way the shock of the sudden gain in weight would seem especially harmful to the endothelium. Moreover, it is highly difficult to reverse this impact; only 2 per cent of overweight teens who enrolled in a clinical program where they received an intensive diet and physical activity interventions attained and maintained a clinically significant loss of weight (Turer et al., 2018). Moreover, the process of vascular remodeling will be already established in place once an obese adolescent has become clinically obese, hence making it hard to undo. Tracks of the longitudinal obesity examinations indicate that even the so-called metabolically healthy one may just appear healthy in brief durations; therefore, most of these teenagers will eventually turn into hypertensive or dyslipidemic young adults in their 20s (Juonala et al., 2020).

5.The contribution of Low-Grade Systemic Inflammation

Scientific studies identify that inflammation is among the mechanisms that relate fatty tissue and compromised arterial health (Hotamisligil, 2017).

The fat tissue may be regarded as an endocrine organ that secretes pro-inflammatory cytokines such as CRP, TNF-alpha (Libby et al., 2018). These consistently elevated levels of markers annoy the inner lining of the arteries in overweight young people. This inflammation causes the arterial walls to become sticky so that the lipids can enter into the sub-endothelial space the, first step in the formation of the plaque (Gimbrone & García-Cardeña, 2016). Systemic inflammation may accelerate the CIMT thickening even

in the presence of normal cholesterol levels (Engelen et al., 2023). The interaction of inflammatory cues with mechanical shear stress of high blood pressure forms an ideal storm of damaging the blood vessel walls. Structural changes occur in the vascular wall which may be extremely challenging to undo in old age

6. The Metabolic stress and Total lipid burden

6.1. The Early Accumulation and Lipid Burden: Blood pressure is the hammer, lipids are the mortar - they block up the works. The cumulative lipid load is much earlier than we believed (Ference et al., 2017).

6.2. **Identification of Metabolic** Red Flags: LDL-C is the most widely used measure, but other measures which can be more specific indicators of insulin resistance in adolescents are the non-HDL part or triglyceride/HDL ratio (Pirillo et al. 2021; Sinaiko et al).

6.3. **The faster aging in adolescents** with chronic disease: In young children with type 1 diabetes, the z-score of their body mass index (BMI) is the best modifiable risk factor that is linked with the early carotid arterial thickening (Buchges, 2025; Jensen, 2021).

7. Socioeconomic and Environmental Stressors

Subclinical atherosclerosis has a different socioeconomic distribution. In 2022, it was found that teenagers in lower-income families are more likely to experience CIMT and stiffness, which commonly relates to allostatic load the accumulation of wear and tear due to the constant stress (Vynckier et al., 2022). The early thickening of the carotid artery is also associated with environmental factors such as air pollution (Ljungman et al., 2019). Combined with poor diets and physical inactivity, these stressors reveal that vascular health is as much a product of the public policy as it is of an individual decision. Addressing these risks would mean going outside the clinic and interacting with the society (Ljungman et al., 2019).

8. Imaging Technological Frontiers: AI and Multimodality Imaging

Some of the new diagnostics have changed the capability of identifying fine changes in blood vessels. Furthermore, multimodal imaging provides a holistic view. Aortic pulse wave velocity has been found by Cardiovascular Magnetic Resonance (CMR) to be a predictive early warning sign in high-risk youth (Büschges, 2025). This allows more sophisticated risk reclassification; a large number of the young people who appear to be low risk on conventional charts have the vascular appearance of high-risk adults (Pahkala et al., 2020). AI and multimodal imaging are the first steps towards the creation of a truly personalized approach to pediatric cardiology (Guo et al., 2025).

9. Early Vascular Aging

The conclusion of the recent long-term information especially the "Decade Link" which was observed in the 2025 KiGGS follow up shows a troubling fact about modern medicine the possibility to prevent cardiovascular disease is far less than it used to be believed (Hoffmann et al., 2025). The existing clinical trends of reacting to the cardiovascular conditions according to the quantified structural variations in the arteries are limited because studies have shown that the alterations might be brought about before one attains adulthood because of the health risk factors that exist at childhood (Büschges, 2025). This way, at the age of 25 years, intervention is normally impossible, since the biological effects of a lifetime exposure to health risks have already been accomplished (Pahkala et al., 2020). This discussion looks at the conflict between the fact that we have more sophisticated diagnostic tools and the fact that we have not made any

progress in the efficacy of our primary prevention strategies.

Table 1: The Progression of Subclinical Vascular Decay in Youth

Stage of Development	Key Risk Exposure	Primary Vascular Marker	Biological Consequence
Prenatal	Maternal Psychological Distress	Increased Aortic IMT (aIMT)	Early "programming" of arterial wall thickness before birth.
Early Childhood	Rapid BMI Trajectory (>4 point jump)	Endothelial Dysfunction	"Shock" to the vessel lining; loss of nitric oxide regulation.
Middle Childhood	Elevated Lipid Burden (Non-HDL)	Sub-endothelial Lipid Migration	The "mortar" begins to accumulate in the vessel wall.
Early Adolescence	Chronic Hypertension (The "Hammer")	Increased Pulse Wave Velocity	Breakdown of elastin fibers; replacement with stiff collagen.
Late Adolescence	Low-Grade Systemic Inflammation	AI-Detected Carotid Plaque	Structural evidence of early-stage heart disease (90% detection).
Young Adulthood	Cumulative "Decade Link"	Advanced CIMT & Stiffness	Irreversible remodeling; high risk for future clinical events.

We are now in a technologic irony state. It has been demonstrated that adolescent obesity is associated with the creation of heart diseases and the use of an artificial intelligence (AI) measure/diagnosis can lead to labeling/identification of adolescents who are at risk of developing heart disease, due to their overweight status (Guo et al., 2025). Meanwhile, our first weapon of therapeutic effect, behavioral lifestyle change, is a remnant of a time that did not consider the biological set points of the contemporary teenager.

The inquiry is whether to declare these teenagers as AI diagnosed high-risk of heart attack in the future and whether we will have any reasonable or effective treatment to them considering the 98% failure rate of behavior-based weight loss diet (Turer et al., 2018). This diagnostic-therapeutic lag implies that we have been way ahead of our ability to perceive the disaster coming when compared with our capacity to direct the patient out of it. The consideration here should be that even though technology has improved our sight, the root biological and social causes of obesity and hypertension have not been entirely resolved yet. We are effectively viewing a slow-motion car crash with the finest camera resolution available, but we are still trying to get to the brake pedal (Vynckier et al., 2022).

9. Vascular Memory: The Perpetual Account of Childhood Stress.

The most significant lesson of the past decade of study is, perhaps, the notion of the so-called vascular memory. Childhood high blood pressure (hypertension) has been found to be the most accurate predictor of stiff blood vessels (arterial stiffness) in adulthood regardless of whether the person will eventually successfully control his blood pressure in adulthood (Bueges, 2025; Yang et al., 2020). The implication of this finding is that the walls of large blood vessels of adolescents can be viewed as a biological record of physiological stress occurring in the early years of life.

This is a mechanistically structured degradation story. The arterial system is so plastic during high-growth stages of a child. Delicate elastin fibers when exposed to high hemodynamic loads or the so-called lipid load will be overstretched and eventually substituted by rigid and non-elastic collagen fibres (Koskinen et al., 2017). It is not just a temporary inflammatory condition, but a structural remodeling condition that is permanent. Even more dramatic effects of allostatic load have been observed in adolescents of low-socioeconomic conditions, with further weathering due to long-term systemic stressors causing a much faster aging of the heart and arteries (Vynckier et al., 2022). It implies that even the healthy decisions that an adult makes during his/her 30s might not be sufficient to completely repair the structural scars of a harsh childhood. We are learning that the body does not really forget a high-pressure environment, although the clinical numbers may improve later in life.

9.1 The Bio-Psycho-Social Interplay of Arterial Health

To really comprehend the why of the early vascular deterioration, we have to go out of that microscope and view the environment that the adolescent lives in. The physiological effects of individual behaviors are not the only factors affecting subclinical atherosclerosis; the social determinants of health have a great impact on individual physiological reactions. According to the study of Vynckier, et al. (2022), it is evident that there is a socioeconomic gradient of arterial health, with adolescents with low-income backgrounds having more advanced CIMTs than adolescents with higher-income backgrounds with or without dietary or exercise practices.

This implies that the physical manifestation of the struggle is the physical appearance of stress on the vessel wall. The sympathetic nervous systems of children will always be produced in excess of normal levels when they are exposed to a state of chronic hyper-vigilance (as a result of neighborhood violence, housing insecurities, or exposure to environmental toxins including fine particles matter, etc) (Dong et al., 2023).. Therefore, pediatric atherosclerosis has to be considered not only as a metabolic disorder, but as a biological document of a children social reality. Our clinical interventions cannot end at the office door, then, but must be extended into policies regulating housing, air quality, and access to food (Büschges, 2025).

9.2 The Metabolic Hijacking and the Inflammatory Perfect Storm.

The relationship between obesity and cardiovascular disease is low grade, systemic inflammation. Excess fat is more than a storage of energy, but also contributes to inflammation by releasing different pro-inflammatory cytokines. To illustrate, a state of inflammation, with the continuous release of cytokines such as C-reactive protein (CRP) and Interleukin-6, will be induced in the case of obese adolescents and will lead to the adhesion and migration of lipids into the blood vessel walls (Wu et al 2023).

This inflammation is the reason why certain adolescents with the normal level of LDL-C may possess abnormal CIMT. In case these teenagers are chronically inflamed by their sleep deprivation, their physical inactivity and/or diets with high fructoses, their lipid load does not necessarily need to be large to lead to pathological alterations in blood vessels. The combination of both mechanical (blood pressure) and

inflammatory (inflammation) stresses to the child heart, will eventually result in becoming prematurely old within out due to the aging of the heart (Pearson et al 2021). Moreover, some of the metabolic activities during puberty will contribute to insulin resistance and form cyclic effects in which teenagers develop problems in their most unstable stage in terms of the vascular health.

9.3 The Geographic and Structural Bias

Although both the KiGGS Research and the Young Finns study provide new knowledge of high quality, there are also certain limitations, that have to be taken into consideration in all existing literature. Most of the good literature we possess is data that was only collected on high-income groups (primarily in Europe) that produces a geographic bias in the possibility of extrapolating reference centile values of populations in the ethnic groups that are in the Global South. Thus, it is probable that a strong genetic and environmental dissimilarity will exist between these two groups of population (Büschges, 2025; Dong et al., 2023).

Moreover, the use of the Common Carotid Artery (CCA) as a surrogate in regard to systemic atherosclerosis has its opponents. Although the CCA is readily available to sonography, it is not necessarily a good indicator of the early alterations in the coronary or femoral arteries. This single-vessel myopia needs to be tackled by addressing the move to multimodality imaging, including Cardiovascular Magnetic Resonance (CMR) to assess the aorta (Hrabak Paar et al., 2024). There is also the issue of the survivor bias of longitudinal studies, with the most vulnerable population, consisting of people of unstable or highly stressed backgrounds, being the most likely to lose their 20-year follow-ups, and as a result, we will underestimate how severe this crisis is in the general population.

9.4 The Clinical Imperative: Shifting to Primordial Prevention

It is the analysis of this information that leads us to one inevitable conclusion, namely that the medical community is already ten years too late. The Decade Link is testimony that the harm that is measurable at age 25 was put into the body at age 15. When we prevent heart disease at an adolescent stage only after the teen has become overweight or hypertensive, we are in fact, doing damage control.

True primordial prevention is the notion that one should start tackling problems long before any remodeling has been initiated. It would mean that we need to redirect our attention to the prenatal stage of child development, as well as the first one-thousand days in the life of a child (Aatsinki et al., 2024). We must come to terms with the fact that biological setpoints of vascular health are determined in the nursery and not the high school gym (Mustonen et al., 2018). To alter the path of premature atherosclerosis, we must cease to think of it as a disease of adults that has its onset in childhood and regard it as a disease of children that will manifest itself someday in adults.

The challenge of 2026 and beyond is to not only watch the clock run out and use our advanced AI and imaging, but also to fundamentally change how we protect the next generation of hearts.

Conclusion

The production of the Decade Link and longitudinal cohort data requires a radical re-assessment of pediatric cardiovascular risk. Atherosclerosis can no longer be considered a latent adult disease, but an active and quantifiable process, which is initiated by fetal programming and enhanced by metabolic stress during adolescence. Although the advent of Deep Learning and multimodality imaging has provided us with unexampled diagnostic accuracy, detecting a 90% probability of carotid plaque in an asymptomatic young adult is an empty win when our interventional outcomes are not improving.

The evidence is that, the structural damage of the vessel wall has already been etched by the time clinical

obesity or hypertension is diagnosed during late adolescence. Our specialty is moving towards the focus of clinical practice with teenagers and into the nurseries and prenatal period, where we will discover the future of the field in primordial prevention. We need to integrate AI-enhanced screening with systemic health reform to reverse the inflammation-inducing social and environmental factors to be successful in reversing the premature trajectory of the decay. By acting these days before the irreversible subclinical changes can take place, we shall be in a position to be able to reset the vascular clock of the next generation.

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