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Staying Young at Heart: Cardiovascular Disease Prevention in Adolescents and Young Adults

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OPINION STATEMENT

Approaches to the prevention and management of cardiovascular disease (CVD) are often too narrow in scope and initiated too late. While the majority of adolescents are free of CVD, far fewer are free of CVD risk factors, especially lifestyle factors such as poor exercise and dietary habits. Most clinicians are familiar with behavioral and pharmacologic strategies for modifying these and other traditional CVD risk factors such as hypertension, hypercholesterolemia, and diabetes. In this review, we highlight those strategies most applicable to teens and also propose a fundamental reframing that recognizes the importance of early choices and life experiences to achieving cardiovascular health.

Population- and individual-level approaches that support the establishment of positive health behaviors early in life are the foundation of preserving ideal cardiovascular health and promoting positive cardiovascular outcomes. The Positive Youth Development movement supports a frame shift away from seeing young people as merely the sum of their risk factors and instead as developmentally dynamic youth capable of making healthy choices. Informed by the Positive Youth Development framework, our approach to cardiovascular prevention among adolescents is both broad-based and proactive, paying heed as early as possible to social, familial, and developmental factors that underlie health behaviors, and employing evidence- based behavioral, pharmacologic, and surgical treatments when needed.

Keywords

adolescent; young adult; positive youth development; cardiovascular health; primordial prevention; primary prevention

INTRODUCTION

The American Heart Association (AHA) introduced the concept of *ideal cardiovascular health* in 2010 [1•]. The ideal cardiovascular health construct emerged from decades of data showing that adults who reach middle age without traditional CVD risk factors have remarkably low morbidity and mortality from CVD [2–5]. The seven factors that comprise ideal cardiovascular health – maintaining a normal body mass index (BMI), adhering to a healthy diet, staying physically active, abstaining from smoking, and having blood pressure, total cholesterol, and fasting blood glucose levels in the normal range without need for pharmacologic treatment – seem obvious to most people familiar with CVD (Table 1). However, epidemiologic data consistently show that few adults – less than 20% – reach middle age with five or more of the ideal cardiovascular health metrics [6•]. Children and adolescents have better cardiovascular health than adults, but in the US only 50% of teens have five or more cardiovascular health metrics at the ideal levels; prevalence of individual ideal metrics varies from less than 1% to 88% [6•] (Table 2). Even in childhood, having all seven ideal cardiovascular health metrics is extremely rare (less than 1% of the US population), largely due to unhealthy dietary patterns [7]. The overall narrative is one of early and progressive loss of cardiovascular health assets [8], [9•] leading to substantial risk of future CVD outcomes upon reaching young adulthood [10].

Though concerning, these statistics also highlight the potential for tremendous positive gains at a population level if effective preventive efforts are employed. Improving the cardiovascular health of children is a crucial public health priority that will pay dividends well into the future as young people transition into adulthood. Primordial prevention, which refers to the prevention of risk factor development, is well-aligned with the concept of ideal cardiovascular health [11•]. Primary prevention, which refers to the treatment of risk factors in patients who have not yet developed clinical CVD, is also critical. In fact, the AHA recognizes those with risk factors treated to goal as having *intermediate cardiovascular health* [1•]. There is evidence that primordial and primary prevention strategies at both the individual and population level are likely to be cost-saving given the high costs of treating established CVD [12].

Adolescence is a critical time for prevention of CVD. Data from several epidemiologic cohorts confirm that having more ideal cardiovascular health metrics in adolescence [13, 14] and young adulthood [15] is associated with better cardiovascular health later in life. Furthermore, *improvement* in cardiovascular health metrics during the transition from adolescence to adulthood is associated with more favorable intermediate markers of atherosclerosis. In the Young Finns study, each additional ideal cardiovascular health metric gained in adolescence was associated with improved pulse wave velocity in adulthood [8] and in the CARDIA study, each additional metric gained in young adulthood was associated

with lower odds of coronary artery calcification and lower carotid intima media thickness in middle age [16].

In this review, we will examine the most recent advances in evidence-based primordial and primary prevention of CVD in adolescents transitioning to young adulthood. We will also explore Positive Youth Development (PYD), a foundational concept in adolescent health promotion that highlights the importance of psychosocial assets and resources in understanding how life-long preservation of ideal cardiovascular health can actually occur. Beyond prevention of risk factors, true primordial prevention must address the full spectrum of influences that support or erode ideal cardiovascular health throughout the life course.

TREATMENT

Positive Youth Development – Reframing Treatment as Prevention

Establishment and maintenance of healthy behaviors (*primordial prevention*), including adherence to a healthy dietary pattern, being physically active, and abstaining from tobacco use, are the mainstays of CVD prevention in teens. As such, there has been great interest in understanding the developmental processes and influences that can support the establishment of healthful behaviors from early in life. PYD is a conceptual framework highlighted in *Healthy People (2020)* that offers important insights in this regard. PYD focuses on each youth's development of personal assets and resources rather than mitigation of vulnerabilities and problems [17]. Typically applied in community-based contexts, PYD programs seek to provide opportunities that will capitalize on a youth's strengths and unique contributions, usually combining skill-building, supportive youth-adult relationships, and opportunities to exert influence and serve in leadership capacities. The assets that derive from PYD help youth avoid risk behaviors and promote thriving across multiple domains [18], [19].

Insofar as poor cardiovascular health behaviors are risk behaviors, proactive strength and asset development through PYD approaches may create a foundation for primordial cardiovascular prevention (Figure 1). A growing literature highlights important linkages between PYD and psychosocial well-being during adolescence and cardiovascular health in adulthood. Early life socioeconomic adversity negatively affects young adult cardio-metabolic risk in part through negative effects on psychosocial development related to self-esteem, positive affect, and educational attainment [20•]. Childhood attention regulation, cognitive ability, and positive home environments are significantly associated with favorable cardiovascular risk levels in adulthood [21]. Favorable socioeconomic status and self-regulatory behavior, a key mediating construct in PYD, are strong predictors of the full ideal cardiovascular health construct in adulthood [22•].

Population-level and community-based interventions in schools, workplaces, and broader communities will be critical in realizing the potential of PYD interventions in primordial CVD prevention. Recent small-scale interventions have begun to apply PYD strategies in promoting cardiovascular health awareness and action among adolescents in school settings although linkages to specific health behavior outcomes have not yet been characterized [23]. Clinicians primarily involved in direct patient care can contribute meaningfully to these

broader efforts by elucidating key issues at the patient and family level and proactively supporting community- based and advocacy efforts to address upstream influences on health decisions and behaviors among youth.

In the clinic setting, providers can use a PYD-consistent framework when counseling patients and families regarding lifestyle choices and medication adherence. Strength-based approaches [24], [25••] invoke PYD concepts and operationalize them into clinical contexts, engaging young people around health behavior decisions by ensuring that each teen's assets and resources are elucidated and incorporated into clinical problem solving and decision-making. Among strength-based approaches, Motivational Interviewing [26••], [27] continues to garner significant attention as a foundation for effective person-centered clinical counseling to optimize health behaviors [28], [29], [30].

Diet and Lifestyle

In the Clinic

- Individual counseling to improve diet and physical activity can decrease risks of obesity, hypertension, and dyslipidemia [31], [32]. A key example of the importance of clinical counseling is the STRIP study in which repeated individualized dietary counseling starting in infancy until 20 years of age led to less intake of saturated fat, lower LDL levels, better CV health scores [9•] and a lower risk of metabolic syndrome [33].
- Clinical counseling should always attend to family dynamics and the home environment as key roots of health behaviors. The approach to clinical counseling should be developmentally appropriate, incorporating both direct counseling of teens as well as family- specific advice. Finally, any conversation around health behaviors should incorporate a longitudinal perspective as to how such behaviors will evolve and translate as young people move out of the home and into the work force or to higher education settings [34••].
- Counseling to promote lifestyle change is the mainstay of management of adolescent hypertension, consistent with the 2004 National High Blood Pressure Education Program Working Group (NHBPEP) [35] and the 2011 NHLBI guidelines [36••]. Regular physical activity, decreased sedentary activities, and dietary changes including salt restriction and increased intake of fresh produce, lean meats, and whole grains should be encouraged. For obesity-related hypertension, weight reduction strategies that combine dietary and physical activity components appear to be more effective for improving hypertension than either alone [37•].
- Counseling to promote lifestyle change is also the foundation of management of adolescent dyslipidemias. Dietary changes centered on lowering saturated fat intake can reduce LDL-C and total cholesterol levels [36••]. The NHLBI guidelines specifically advise limiting total fat intake to 30% of total calories, saturated fat to 7–10%, and total cholesterol to 300 mg/day. While mono- and polyunsaturated fats have beneficial CV effects [36] and plant stanols and

sterols may help reduce LDL-C levels [38], the utility of omega-3 fatty acids for high TG levels remains unclear [39], [40].

- Non-pharmacologic treatment of Type II diabetes centers on weight reduction in order to improve glycemic control [41••], [42].
- Clinical counseling and guidance of patients to smoking cessation resources remain essential in controlling tobacco usage among teens [43••], [44].

In the Community

- Both school-based [45] and out-of-school [46] programs can directly engage teens in health behavior change. Health care providers can actively support efforts to improve and scale such community-based initiatives.
- Neighborhood features such as food outlets and physical activity resources are associated with CVH [47•] and broad population-level dietary changes can be brought about through regulatory changes [48•]. Providers are uniquely positioned to engage in advocacy to effect broader-based changes to social and structural determinants of health behaviors among teens.
- Technological supports are useful in altering health behaviors [49], [50], [51] and providers who are privy to both the technology usage patterns and CV health behaviors of teens can inform the development of such supports.

Pharmacologic Treatment

Primary prevention of CVD through the pharmacologic treatment of established risk factors will be necessary for some teens. The NHLBI 2011 Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents (referred to hereafter as the 2011 NHLBI Pediatric Guidelines) [36••] provide evidence-based guidelines for treatment of adolescents with hypertension, hyperlipidemia, obesity, and diabetes. Pharmacologic treatment considerations for each of these conditions, as well as for tobacco dependence, are reviewed below.

Hypertension

- Blood pressure should be checked at least annually for adolescents ages 12 to 17 years and at every visit for young adults ages 18 to 21 years. National data suggest approximately 80% of teens are meeting this measure [52], but that many young adults are unaware of their hypertension [53]. Hypertension in adolescents is defined as a blood pressure greater than the 95th for age/sex/height (see tables at [36••]) and as 140/90 for young adults if confirmed on two separate occasions. Pharmacologic treatment is recommended if a) left ventricular hypertrophy is present on echocardiogram (expected of approximately 30% of teens with hypertension [54]), b) blood pressure does not normalize after 3–6 months of lifestyle changes, or c) blood pressure is 99th + 5mm Hg for those ages 12 to 17 years or 160/100 for young adults. Unfortunately, rigorous evidence guiding the choice of antihypertensives in

patients under age 18 is generally poor [55••], and the data below represent small trials and author personal experience.

- Calcium-channel blockers are an excellent choice for teens without diabetes or chronic kidney disease due to their low side effect profile and lack of need for laboratory monitoring. A starting dose of amlodipine 2.5 mg daily, titrated up to 5–10 mg daily, has been shown to be effective and safe for long term use in adolescents [56].
- For teens with diabetes or chronic kidney disease, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) should be used. Enalapril (starting dose 2.5mg daily, titrated to a maximum dose of 40mg daily), lisinopril (starting dose 5mg daily, titrated to a maximum dose of 40mg daily), losartan (starting dose 25mg daily, titrated to a maximum dose of 100mg daily) and valsartan (starting dose 40mg daily, titrated to a maximum dose of 160mg daily) all have excellent data for use in adolescents [56]. Routine measurement of electrolytes and kidney function is required. Pregnancy is contraindicated while using ACE inhibitors or ARBs and thus a reliable form of contraception must also be prescribed for sexually active females. The use of either the levonorgestrel releasing intrauterine device or the etonorgestrel implant is recommended given they do not lead to increases in blood pressure and do not rely on the teen remembering to take them [57].

Cholesterol

- Cholesterol screening is recommended for all young people ages 17–21 years and for younger teens with risk factors for CVD (family history of early CVD or personal history of diabetes, hypertension, obesity, or tobacco smoking) [36••]. Treatment recommendations for elevated low density lipoprotein cholesterol (LDL-C) in this age group differ between the 2011 NHLBI Pediatric Guidelines and the 2013 American College of Cardiology and American Heart Association (ACC-AHA) Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults [58]. Both guidelines recommend adolescents with an LDL-C >190mg/dL be offered HMG-CoA reductase inhibitor (statin) therapy. Adolescents with an LDL-C between 130–190 mg/dL may be candidates for statin therapy based on the 2011 NHLBI Pediatric Guidelines; a patient centered discussion on the risks and benefits of long-term statin therapy is recommended [58].
- Atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, and simvastatin are all approved for use in adolescent boys and postmenarchal girls. Atorvastatin and rosuvastatin have the strongest evidence base in children [59•]. The 2011 NHLBI Pediatric Guidelines recommend a starting dose of atorvastatin 20mg daily, although patients with an LDL-C of 190mg/dL will often need 40mg of atorvastatin to achieve the 50% reduction in LDL-C suggested by the 2013 ACC-AHA Adult Guidelines. The Pediatric Guidelines recommend routine monitoring of the fasting lipid profile and liver function tests every 3–4 months in the first year and every six months thereafter; adult

guidelines recommend a repeat fasting lipid panel only to assess for the anticipated therapeutic response and do not recommend monitoring live function or muscle enzymes. As with the ACE inhibitors and ARBs, pregnancy is contraindicated with statin use, although recent data suggest no fetal harm during first trimester exposure [60]. The levonorgestrel intrauterine device and the etonorgestrel implant are excellent choices for sexually active females on statin therapy given they do not cause significant worsening of lipid levels.

Diabetes

- Diabetes prevalence is increasing in teens, largely due to a rising prevalence of Type II diabetes. Estimates from the 1999–2010 National Health and Nutrition Examination Survey found an overall diabetes prevalence of 0.84% in adolescents ages 12–19 years. Type II diabetes accounted for 43% of the cases, with one-third of the Type II diabetes cases undiagnosed or unknown to the individual [61].
- Teens who are overweight or obese and have two additional risk factors for diabetes (family history of Type II diabetes in a first or second degree relative, race/ethnicity at higher risk for diabetes, or signs of insulin resistance) should be screened for Type II diabetes [36••], although the cost-effectiveness of this screening strategy is debated [62••]. The American Diabetes Association recommends fasting plasma glucose for screening in this age group [63]. The performance of glycated hemoglobin (HbA1C) as a screening test in youth is debated [64–66], but may have more practical utility in teens reluctant to return for fasting labs. Islet cell autoantibodies should be sent in all pre-pubertal patients and considered in post-pubertal patients because insulin treatment is usually required for these patients [62••].
- Both teens with Type II diabetes and teens with Type I diabetes are at increased risk for CVD and need aggressive glucose control as well as prevention, identification, and treatment of other CVD risk factors. Data confirm that having a greater number of the ideal cardiovascular health metrics, even in adolescents with Type I diabetes, is associated with improved subclinical markers of atherosclerosis [67].
- Patients with Type II diabetes who are asymptomatic and have a HbA1C <9% should be offered metformin monotherapy as the first-line treatment [62••]. The usual starting dose is 500mg once daily, increased by 500mg weekly to a maintenance dose of 2000mg daily as tolerated. This can be given either as a divided dose twice a day or once daily dosing with an extended release preparation. Metformin monotherapy has been shown to lead to sustainable glycemic control in approximately half of teens with Type II diabetes [68].
- Patients with Type II diabetes who are symptomatic or who have a HbA1c ≥9% should be started on metformin and a basal insulin preparation, such as insulin glargine, at 0.25–0.5 units/kg [62••]. Once the glycemic control improves to a HbA1c <6.5%, insulin can be down-titrated and ultimately

withdrawn if metformin monotherapy and lifestyle changes keep the HbA1c below 6.5%

- Patients with either Type II diabetes with acidosis or Type I diabetes should be started on insulin alone, with both basal and short-acting preparations. Once the acidosis resolves and glycemic control improves, patients with Type II diabetes who do not have islet cell autoantibodies are candidates for withdrawal of insulin and initiation of metformin monotherapy as above.
- Use of thiazolidinediones in addition to metformin has been shown to improve glycemic control in teens with Type II diabetes [68] although these medications are not currently FDA approved for use in the US in this age group. Newer agents used in adults with Type II diabetes, including glucagon-like peptide-1 analogs, are still considered experimental in this age group [69].

Obesity

- Pharmacologic treatment of obesity is largely off-label in teens, with the exception of orlistat which is approved for patients ages 12 and older and the sympathomimetic drugs (such as phentermine) which are approved for patients ages 16 and older. Weight loss in obese teens is less with orlistat (mean decrease in body mass index of 0.83 kg/m²) compared to the sympathomimetics (mean decrease in body mass index of 2.20 kg/m² with sibutramine, now off the market due an increase in cardiovascular events in adults) [70]. However, orlistat is recommended as first line given less than 1% of the drug is systemically absorbed and its side effects are limited to the gastrointestinal issues of bloating and diarrhea and malabsorption of fat-soluble vitamins. There is also a concern for abuse of the sympathomimetics with teens.
- Metformin has been shown to reduce body mass index on average by 1.38 kg/m² in trials of obese adolescents without diabetes [71] and can be considered for adolescents with signs of insulin resistance or risk factors for diabetes.

Tobacco Dependence

- Pharmacologic assistance for smoking cessation with nicotine replacement therapy (NRT), bupropion, or varenicline should be offered to patients 18 and over who desire to quit smoking and should be given in combination with behavioral support [72].
- Concerns exist about the toxicity of nicotine on the developing adolescent brain based on animal models [73]. However, given that long-term exposure to nicotine through tobacco addiction is clearly harmful, NRT may be beneficial to some adolescents with nicotine dependence. NRT is available for patients under age 18 with a prescription (in contrast to adults, where it is available over the counter). Dosage should be based on the number of cigarettes smoked per day; with most adolescent smokers started at the 7mg/patch or 14mg/patch

dose, unless they are very heavy smokers. Nicotine gum or lozenges can also be prescribed for adolescents; the 2mg strength for each is recommended for this age group. Nicotine nasal spray is not well tolerated by teens and therefore not recommended [74].

- Data on the efficacy of NRT in patients younger than 18 is mixed, with some studies showing abstinence rates of up to 20% with NRT [75]. However abstinence rates with NRT are not clearly superior to counseling alone in trials with adolescents, and data on long-term abstinence after NRT in teens is discouraging [76]. This may reflect challenges with adherence and/or motivations for smoking beyond nicotine dependence in this age group.
- There are very few trials of bupropion or varenicline with adolescents [77] [76••] and due to concerns about mood dysregulation with their use, off-label use in teens is discouraged.

Surgical Treatment

- Bariatric surgery is approved for adolescents with a BMI ≥ 35 kg/m² with serious comorbidities (Type II diabetes, moderate to severe sleep apnea, pseudotumor cerebri, or severe non-alcoholic steatohepatitis) or a BMI ≥ 40 kg/m² with less serious comorbidities (hypertension, hyperlipidemia, insulin resistance, or mild sleep apnea) [78].
- A systematic review of published studies reporting the outcomes of 637 adolescents who underwent bariatric surgery between the years of 1981–2011 found a mean post-operative BMI difference at one year of -13.5 kg/m² [79]. Similar to studies in adults, Roux-en-Y gastric bypass had the greatest weight loss outcomes and adjustable gastric banding had the least. Data on resolution of co-morbidities was poorly documented, but most studies reporting these outcomes found complete resolution of CVD risk factors including hypertension, dyslipidemia, Type II diabetes, and sleep apnea at one year.
- The Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) study is the largest prospective cohort study of adolescents undergoing weight loss surgery at five academic referral centers. Teen-LABS investigators reported complication rates of adolescent bariatric surgery of 8–15% within the first 30 days, including 5% requiring early reoperation for major surgical complications; no deaths were reported [80].
- Longer-term successes and complications of bariatric surgery in teens beyond one year are unknown. Significant concerns exist regarding the effects of bariatric surgery on adolescent physical and emotional development [81], including risks for vitamin deficiencies, bone loss, and psychiatric conditions such as eating disorders. While some investigators have projected that adolescent bariatric surgery will become cost-effective three years after the operation due to decreased obesity-related comorbidities [82], the likelihood of weight regain and need for reoperation over such a long period of follow-up is substantial.

CONCLUSIONS

Preservation of ideal cardiovascular health and prevention of cardiovascular disease among adolescents and young adults must begin early and extend across the full scope of young people's lived experiences from the clinic, into their neighborhoods, in their schools, and into their homes. While cardiovascular prevention among older adults is typically limited to primary or secondary prevention of cardiovascular outcomes, in adolescence and young adulthood true primordial prevention is possible. Current data suggest that the vast majority of adolescents have already ceded much of their positive cardiovascular health assets well before adulthood, demanding redoubled efforts to preserve cardiovascular health early on. Positive Youth Development concepts are helpful in shifting the focus of cardiovascular care away from simply addressing risk factors among some to conceiving of what positive cardiovascular development might actually look like for all. CVD prevention must incorporate a deep understanding of the importance of youth developmental trajectories and social determinants of health, along with application of evidence-based behavioral and pharmacological tools when risk factors emerge and primary prevention is needed. Such a coordinated and comprehensive approach will help shift the narrative away from early and progressive loss of cardiovascular health to prolonged preservation of cardiovascular health assets well into adulthood.

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- denotes reference of importance
- denotes reference of outstanding importance
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Figure 1. Conceptual pathway from Positive Youth Development and Strength-based Clinical Care to Cardiovascular Health Promotion and Disease Prevention.

Table 1

Definitions of Poor, Intermediate, and Ideal Cardiovascular Health Metrics for Adolescents ages 12–19 years according to the American Heart Association 2020 Strategic Goals [1••]

	Poor	Intermediate	Ideal
Current Smoking	Tried during the prior 30 d	--	Never tried; never smoked whole cigarette
Body Mass Index[*]	>95 th percentile	85 th –95 th percentile	<85 th percentile
Physical Activity	None	>0 and <60 min of moderate or vigorous every day	60 min of moderate or vigorous every day
Healthy diet pattern, number of components[†]	0–1	2–3	4–5
Total cholesterol, mg/dL	200	170–199	<170
Blood pressure[‡]	>95 th percentile	90 th –95 th percentile or SBP 120 mm Hg or DBP 80 mm Hg	<90 th percentile
Fasting plasma glucose, mg/dL	126	100–125	<100

^{*} Calculated as (Weight in Kilograms / (Height in Meters x Height in Meters)) and classified according to 2000 Centers for Disease Control and Prevention Body Mass Index-for-age growth charts

[†] Defined based on expert consensus to approximate a healthy dietary pattern consistent with a Dietary Approaches to Stop Hypertension [DASH]–type eating pattern: 4.5 cups/d of fruits and vegetables, 2 servings/wk of fish, 3 servings/d of whole grains, and no more than 36 oz/wk of sugar-sweetened beverages and 1500 mg/d of sodium.

[‡] Measured as mmHg and classified according to 2004 NHLBI Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents

Prevalence* of Poor, Intermediate, and Ideal Cardiovascular Health Metrics for Adolescents ages 12–19 years according to the American Heart Association 2020 Strategic Goals [6••]

Table 2

	Poor	Intermediate	Ideal
Current Smoking	12.9	0.0	87.1
Body Mass Index*	21.4	13.9	64.7
Physical Activity	6.6	56.8	36.5
Healthy diet pattern, number of components	91.6	8.3	0.1
Total cholesterol, mg/dL	6.6	17.7	75.7
Blood pressure	1.7	16.0	82.3
Fasting plasma glucose, mg/dL	0.3	14.4	85.3

* Unadjusted prevalence as reported in the National Health and Nutrition Examination Survey 2009 to 2010. The most prevalent category for each metric is in **bold**.