Adolescent health and future cardiovascular disability: it's never too early to think about prevention

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Major improvements in medical treatments over the past half century have resulted in more people than ever surviving with cardiovascular disease (CVD). Despite these successes, however, CVD remains not only the world's largest cause of premature mortality, but also a major cause of chronic disability affect many living with the disease[1]. With estimated costs for this disability burden predicted to account for over €190million a year in the EU alone, it is clear that a focus on population-level prevention strategies – rather than attempts to simply cure end-stage disease – are essential if the increases in longevity and quality-of-life achieved in recent decades are to be maintained.

It has been estimated that over 90% of the population attributable risk for myocardial infarction alone can be attributed to a number of well-established modifiable risk factors such as high BMI, low physical activity levels, poor diet, and smoking[2]. Arguably one of the greatest risks to population health in the coming years is that of the emerging obesity crisis, the prevalence of which has doubled since 1980[3]. More alarmingly still, evidence suggests that children and adolescents are not only at the greatest risk for developing obesity, but are also highly likely to remain obese adults[4,5], resulting in a lifetime of cumulative exposure to the negative health consequences caused by increased fat mass and its accompanying metabolic complications. While developed countries have taken major steps to address this phenomenon in recent years, a burgeoning crisis in developing countries threatens to undermine the improvements in life expectancy made in recent times[6]. Childhood and adolescence may represent a crucial window of opportunity for prevention strategies aimed at changing health behaviours. However, the extent to which differences in modifiable risk factors such as BMI and cardiorespiratory fitness at this early age affect risk of disability in later-life are still poorly understood.

In the paper published today in the *European Heart Journal*, Henriksson et al report findings relating cardiorespiratory fitness, muscular strength, and obesity in adolescence with later chronic disability caused by cardiovascular disease. Using a registry of over one million Swedish men conscripted to the military between 1972 and 1994, the authors were able to investigate associations between measures of body mass and fitness carried out during their initial conscription examination and the granting of disability pension over a maximum forty years of follow-up. Furthermore, through the use of distinct ICD codes, information could also be acquired as to whether the cause of disability arose due to underlying cerebrovascular disease, ischaemic heart disease, or development of heart failure. Their findings mirror previous studies in which obesity and cardiorespiratory fitness have been related to CVD mortality[7,8],

demonstrating that increasing levels of BMI associate with a greater risk for disability from numerous types of CVD, and increasing levels of fitness with a lower risk. Also similar to previous studies, the greatest benefits from increasing fitness levels appeared to occur at the lower end of the fitness spectrum (i.e. moving from no activity to low activity), with progressive but more incremental gains then evident as fitness increased further. Some evidence of benefit was demonstrated for increased muscular strength, but this was likely confounded by overall fitness. Finally, in order to address the possibility of the controversial "fat-but-fit" phenotype, comparisons were also drawn between normal-weight and obese participants of differing fitness levels, with the authors noting that high levels of cardiorespiratory fitness in obese adolescents appeared to ameliorate much of the future risk of disability arising from cardiovascular disease.

This study has a number of major strengths. Firstly, the inclusion of over one million individuals with up to 40 years of follow-up highlights the power of 'big data' to permit large-scale and long-term studies in a real-world (albeit exclusively male in this case) population, and the use of ICD codes allowed a range of disability outcomes to be studied. Secondly, the availability of standardised exercise tests at baseline (rather than physical activity questionnaires which are often used as a proxy measure in cohort studies) removes the risk of recall bias for this exposure, and greatly strengthens the link reported between aerobic fitness and future disease. A noticeable weakness of the study, however, is the lack of data available during follow-up, and it is therefore not possible to ascertain what proportion of the observed adult risk is a result of early cardiovascular damage sustained in adolescence, and what proportion simply reflects the fact that those who were obese/unfit in childhood were more likely to remain so in later-life. Despite this, however, it is clear from the current findings that – regardless of the mechanisms involved – individuals with a high BMI and a low level of fitness during adolescence are significantly more likely to suffer from CVD disability in later life, and that prevention strategies addressing these factors in childhood are likely to provide significant lifetime benefits at a population level.

Obesity is a complex condition, and the relative contribution of genetic vs. lifestyle factors in its development (and therefore the extent to which it can be prevented) remains contentious. On the one hand, it is unarguable that genetics have a considerable role to play in the emergence of an obese phenotype, and that this phenotype is most commonly established in early life[5]. However, it is also important to note that the obesity epidemic is a relatively recent phenomenon which has emerged in an essentially unchanged genetic landscape, strongly suggesting that the presence of a modern-day 'obesogenic environment' is acting to expose a previously rarely-observed genetic susceptibility to disease. Although it has long been accepted that steps must be taken to tackle this obesogenic environment, the best way to do this has so far remained elusive. While clinicians clearly have a role to play, previous efforts at tackling lifestyle behaviors at the individual level have been largely ineffective, and can be complicated further by difficulties in addressing the topic due to the social stigma which is often attached to conditions such as obesity. In order for real gains to be made, major policy changes at a national/international level are almost certainly required in order to change the overall environment in which we live, and thereby nudge people's behavior over time towards healthier choices. The ability of this approach to produce long-term benefits has already been clearly demonstrated with respect to smoking, with the prevalence of smoking steadily declining in recent years[9]. Encouragingly, similar trends

are already emerging for other health behaviours such as alcohol intake and physical activity, with recent evidence suggesting that young people are less likely to drink and more likely to partake in structured exercise compared to previous generations[10].

It is important that future government policies maintain this welcome shift in attitudes in the young by emphasising that – when it comes to prevention – it is never too early to start. The reasons for this are numerous and compelling. Firstly, as previously mentioned, genetic susceptibility to an obese phenotype emerges in adolescence and tracks into later life, resulting in life-long exposure to the negative effects of adiposity[5]. With cumulative exposure to risk factors suggested to be the predominant driving force behind CVD risk[11], early intervention would therefore be expected to offer the greatest gains. Secondly, and as shown in the current study, increased physical fitness (and likely other health behaviours) in adolescence may attenuate much of the risk associated with obesity, and are more likely to be maintained if established in early life. Finally, significant evidence from both longitudinal and genetic studies suggests that individuals who normalize their weight status between childhood and adulthood have equivalent CVD risk to those who have never been obese, suggesting that it is the tracking of obesity across the life-course which poses the greatest risk to health, rather than early CV damage *per se*[4,12–14]. As a caveat to this final point, however, it should be noted that weight loss at any point in the lifespan has also been shown to have beneficial effects on CVD risk[15], so while it's never too early to start, it's also never too late!

In summary, findings from this long-term follow-up of over one million men clearly demonstrate an increased risk of mid-life CVD disability from multiple causes in individuals who have high levels of obesity and/or low levels of fitness in adolescence. These findings further strengthen claims that prevention strategies targeted in childhood are likely to provide the greatest benefits for lifetime cardiovascular health.

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Figure Legend:

Proposed lifetime trajectories to CVD disability and their modification by weight status and physical fitness levels. A combination of obesity and low physical fitness in adolescence are associated with the highest risk of progression to CVD disability in mid-to-late life (red line), whereas a combination of normal weight and high physical fitness are associated with the lowest risk. However, the negative effects of obesity may be at least partially offset by improved physical fitness (yellow line) or weight loss (dashed black lines representing findings from previous studies). Prevention strategies targeted at the young are therefore likely to provide the greatest benefits for lifetime cardiovascular health.