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EDITORIAL

Double hazard of smoking and alcohol on vascular function in adolescents

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This editorial refers to 'Early vascular damage from smoking and alcohol in teenage years: the ALSPAC study'†, by M. Charakida *et al.*, on page 345.

The cardiovascular risk factor smoking is known to adversely affect vascular function, and there is a clear dose–response relationship, which mean the more you smoke the greater the vascular damage.[1,2] The situation is less clear with respect to alcohol intake. The dose–response relationship more closely follows a J-shaped curve, which means that lower alcohol intake may be beneficial while higher alcohol intake may be disadvantageous for vascular function and therefore cardiovascular risk.[3,4] Importantly, from the pathophysiological point of view, alcohol and smoking induce endothelial dysfunction and this is probably secondary to increased oxidative stress in vascular tissue.[5,6] Thus, in theory, the combination of alcohol and smoking should have additive negative effects on vascular function.

The life expectancy of smokers is ∼20 years less compared with non-smokers,[7] demonstrating that smoking also carries a significant socioeconomic burden of ∼US$6.6 billion of lost productivity.[8] Smoking also directly affects the health of others via the harmful effects of second-hand smoke. Second-hand smoke exposure kills >600 000 non-smokers globally per year, many (31%) of whom are children, as indicated in the global estimate of the burden of disease from second-hand smoke.[9] Children exposed to second-hand smoke in the home are also more likely to initiate smoking in the future and ∼25% initiate smoking by the age of 13.[10]

Adolescent alcohol use is a major public health concern in many European countries. One-fifth of young people aged 15 years and over in Europe report heavy episodic drinking (five or more drinks on one occasion), the highest rate in the world. The prevalences of weekly drinking and drunkenness (defined as having been drunk on two or more occasions) are very low at age 11 but increase significantly by 15 for boys and girls in almost all countries and regions. Increases are particularly large between ages 13 and 15.[10]

Adolescents in many cultures perceive drinking alcohol and smoking as a normal part of adult life, using them to fulfil social and personal needs, intensify contacts with peers, and initiate new relationships.[10]

So far it has remained to be established whether smoking and alcohol use up to the age of 17 years may have both independent and additive associations with arterial stiffness, a marker of vascular damage that predicts later cardiovasculaar disease and events.[11,12]

In the present study in this issue of the journal, Charakida *et al.* provide data on the cardiovascular health risks of cigarette and alcohol use during adolescence and highlight the additive effects when both lifestyle risk factors are present.[13] The authors assessed smoking habits and alcohol use by questionnaires in a cohort of 1266 teenagers of the Avon Longitudinal Study of Parents and Children (ALSPAC) at the age of 13, 15, and 17 years, and established a correlation with carotid to femoral pulse wave velocity (PWV) as a read-out for arterial stiffness. Importantly, these associations remained significant even when adjusting for other cardiovascular risk factors including blood pressure, gender, age, family history of cardiovascular disease, LDL-cholesterol, high-sensitivity C-reactive protein, parental smoking, physical (in)activity, and socioeconomic status. The important results were that tobacco use and more frequent alcohol intake had additive effects on arterial stiffness, a parameter that reflects endothelial function. It is important to note that the early stages of atherosclerosis are characterized by endothelial dysfunction while the later stages result in arterial stiffness,[12] a parameter that also reflects vascular nitric oxide bioavailability and has a clear impact on cardiovascular prognosis.[11]

The observation that smoking and alcohol may have additive adverse effects on endothelial function and therefore arterial stiffness, as assessed by PWV, are somewhat surprising. Since the numbers of

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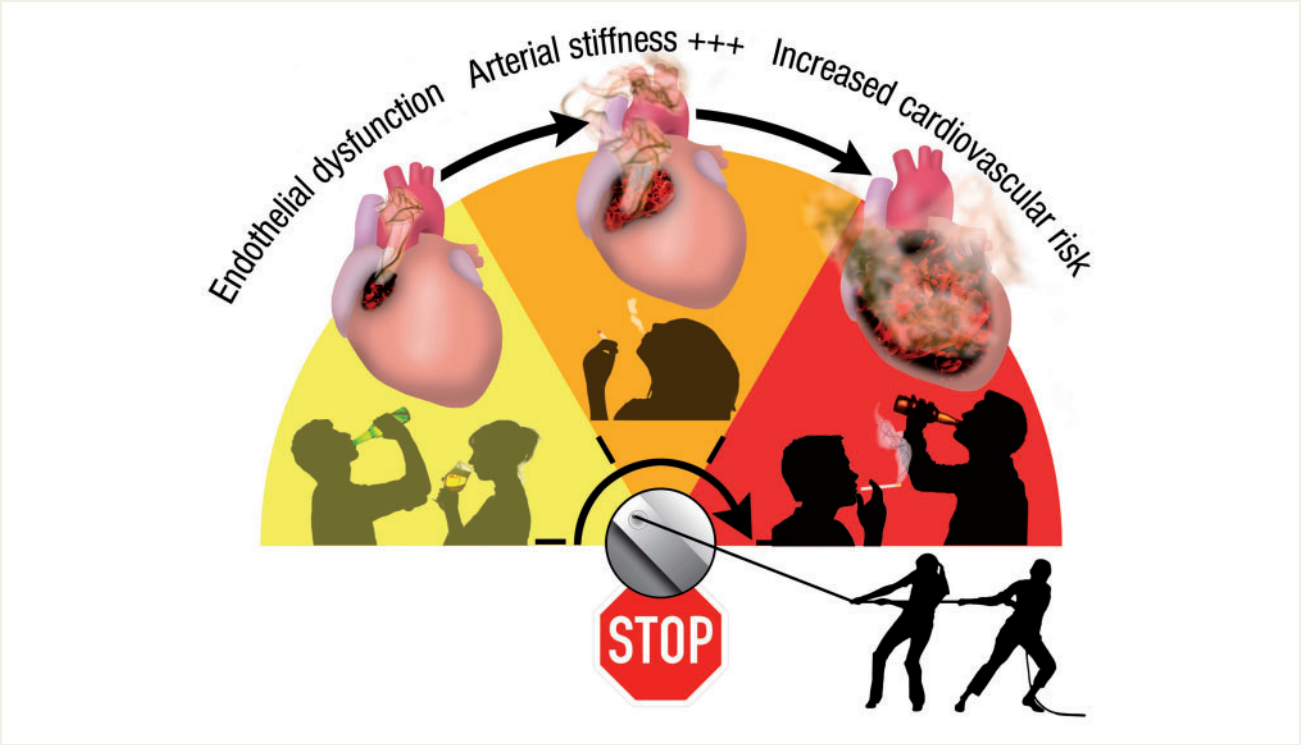

Take home figure Combined adverse and additive negative effects of tobacco and alcohol use on vascular function during adolescence. Teenagers shift their cardiovascular risk to a critical level (when projected to adulthood) by consuming too much alcohol and too many cigarettes. In particular, when both risk factors are present, arterial stiffness, an established marker of vascular dysfunction and future cardiovascular risk, is increased.

cigarettes smoked by teenagers are far below those considered harmful in adults (0–19, 20–99, and >100 cigarettes during the whole of life or at least the last 5 years in the present study vs. 'pack-years' = 20 cigarettes/day for 1 year in studies on adults), the data are even more worrisome. Thus, an interpretation would have been easier if the authors would had measured, for example, the serum levels of the nicotine degradation product cotinine, as an analytical and objective read-out of tobacco use in addition to the rather subjective questionnaire-based assessment that largely depends on the compliance of the subjects. As the data stand now, it may be debatable whether the unexpected moderate adverse or even slightly protective effects that were observed in the moderate lifetime smoking exposure group (20–99 cigarettes during the whole of life or at least the last 5 years) are based on so far uncharacterized beneficial processes induced by moderate tobacco use (e.g. by activation of 'conditioning-like' protective, antioxidant and/or anti-inflammatory pathways) or simply reflect poor compliance of some of the subjects when answering the questionnaires. At least this issue was better solved for alcohol use, since this lifestyle habit was also controlled by measurement of serum levels of alanine aminotransferase (ALT), a clinical marker for liver damage, which significantly correlated with frequent alcohol intake and the induction of arterial stiffness by alcohol use.

What are the consequences for politicians and healthcare providers? How can we sufficiently protect our children from smoking- and alcohol-driven vascular damage?

The political willingness to change laws in Europe in order to protect our children from active smoking and from second-hand smoke damage varies greatly in Europe. For example, in 2011 the UK banned cigarette vending machines, having realized that ~35 million cigarettes are sold illegally through vending machines to children every year. In contrast, Germany still has 350 000 cigarette vending machines, which means that almost one in three cigarette machine in Europe is located in Germany. Although sales are prohibited under the age of 18 and although machines must provide an age verification system in the form of identity (ID) cards, a European driving licence, or electronic cash cards, we know that 10–15% of adolescents will still get cigarettes via these machines by using ID cards from older friends, parents, and older siblings.

We also have to take into account the danger arising from second-hand smoke. The introduction of banning tobacco smoking from public areas in Germany led, for example, to a dramatic reduction of ST-segment elevation myocardial infarction (STEMI) by 26% in non-smokers, while the STEMI rate in smokers remained the same.[14] The UK is taking into account the increased cardiovascular risk arising from passive smoking and accordingly in 2016 introduced a smoking ban in cars to prevent damaging effects of second-hand smoke. In contrast, in Germany, all the initiatives by the German Center for Cancer Research to introduce such a ban have failed so far.

Germany has only a few healthcare adverts to warn about smoking-induced disease, but it is more common to see cigarette advertising. Thus, it is a real scandal that Germany remains the only country in Europe that allows public advertising of cigarettes after Bulgaria opted out in 2016, reflecting the success of strong lobbying of the cigarette industry.

Thus, action plans are urgently needed to reduce the harmful use of alcohol and smoking in adolescents since, as demonstrated by

Charakida *et al.*,[13] the combination of these lifestyle habits has additive adverse effects on vascular function and therefore increased cardiovascular risk (*Take home figure*).

Thus, (i) we have to strengthen policies that reduce the availability of alcohol and cigarettes, such as age limits for purchasing, that are effective in decreasing access. Age limits of 18 years or older for buying any alcohol and cigarette products including E-cigarettes and hookahs have to be implemented, and there should be a ban for cigarette vending machines in every European country. (ii) We have to limit the number of shops and to reduce opening hours for sale of alcohol and cigarettes. (iii) Since adolescents are very sensitive to prices of alcohol and cigarettes, a higher price will always lead to a substantial reduction in the frequency of use of both drugs. (iv) Cigarette advertising must be forbidden immediately in every country in Europe. (v) Alcohol and cigarette advertising often target young people, with the practice of promoting these products through social media to circumvent bans and restrictions on advertising. (vi) Finally, we also have to protect our children more efficiently from passive smoking, in order to have a tobacco- and alcohol-free generation.

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Corrigendum

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In the original version of this article, due to a miscommunication, the name of co-author Bo Xu was incorrectly presented as 'Xu Bo'. This has now been corrected online and in print.