



Sex differences in cardiovascular risk factors and disease prevention



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ABSTRACT

Cardiovascular disease (CVD) has been seen as a men's disease for decades, however it is more common in women than in men. It is generally assumed in medicine that the effects of the major risk factors (RF) on CVD outcomes are the same in women as in men. Recent evidence has emerged that recognizes new, potentially independent, CVD RF exclusive to women. In particular, common disorders of pregnancy, such as gestational hypertension and diabetes, as well as frequently occurring endocrine disorders in women of reproductive age (e.g. polycystic ovary syndrome (PCOS) and early menopause) are associated with accelerated development of CVD and impaired CVD-free survival.

With the recent availability of prospective studies comprising men and women, the equivalency of major RF prevalence and effects on CVD between men and women can be examined. Furthermore, female-specific RFs might be identified enabling early detection of apparently healthy women with a high lifetime risk of CVD.

Therefore, we examined the available literature regarding the prevalence and effects of the traditional major RFs for CVD in men and women. This included large prospective cohort studies, cross-sectional studies and registries, as randomised trials are lacking. Furthermore, a literature search was performed to examine the impact of female-specific RFs on the traditional RFs and the occurrence of CVD.

We found that the effects of elevated blood pressure, overweight and obesity, and elevated cholesterol on CVD outcomes are largely similar between women and men, however prolonged smoking is significantly more hazardous for women than for men. With respect to female-specific RF only associations (and no absolute risk data) could be found between preeclampsia, gestational diabetes and menopause onset with the occurrence of CVD.

This review shows that CVD is the main cause of death in men and women, however the prevalence is higher in women. Determination of the CV risk profile should take into account that there are differences in impact of major CV RF leading to a worse outcome in women. Lifestyle interventions and awareness in women needs more consideration. Furthermore, there is accumulating evidence that female-specific RF are of influence on the impact of major RF and on the onset of CVD. Attention for female specific RF may enable early detection and intervention in apparently healthy women. Studies are needed on how to implement the added RF's in current risk assessment and management strategies to maximize benefit and cost-effectiveness specific in women.

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1. Introduction

Despite enormous declines in the burden of cardiovascular disease (CVD) in the past decades, mainly due to improvements in

primary and secondary prevention, CVD disease remains a main cause of premature death and disability among men and women worldwide. Statistics from the World Health Organization (WHO) show that an estimated 17.3 million people died of CVD in 2008 of which 80% occurred in low- and middle income countries [1]. About 7.3 million deaths were due to coronary heart disease (CHD) and 6.2 million were due to stroke [2]. It is expected that the number of people who die from CVD, mainly from CHD and stroke, will increase to reach 23.3 million by 2030 [1,3].

Although CVD has been seen as a men's disease for decades, it is actually more common in women. In the European population, 38% of deaths in women before the age of 75 years are due to CVD - in men this figure is 37% - a figure that is partly explained by a higher risk of competing events, i.e. the risk of dying from other causes (Fig. 1) [4]. Most of the burden of CVD can be explained by a set of traditional risk factors that affect both men and women, including elevated blood pressure, smoking, overweight and obesity, diabetes, and elevated cholesterol. Already in 1999 the American Heart Association (AHA) developed the first women-specific clinical recommendations for CVD prevention, which led to increased awareness of women's CVD risk, and to improved risk factor management and treatment of CVD in women [5]. However, despite these women-specific guidelines and accruing evidence for clinically important sex differences in the prevalence of traditional CVD risk factors, and in the effects of these risk factors on CVD outcomes sex-specific risk remains poorly understood and the prevention and management of stroke and cardiovascular risk factors is essentially still the same for men and women.

Recent evidence has emerged that recognizes new, potentially independent, CVD risk factors exclusive to women [6]. In particular, common disorders of pregnancy, such as gestational hypertension and diabetes, as well as frequently occurring endocrine disorders in women of reproductive age (e.g. polycystic ovary syndrome (PCOS) and early menopause) are associated with accelerated development of CVD and impaired CVD-free survival [7,8]. Other risk factors, although not exclusive to women, have a much higher prevalence in women than men. As an example, migraine occurs 3 times more often in women, and is associated with an increased risk of stroke [9,10]. The most recent AHA guideline (2011) and AHA/American Stroke Association (ASA) guideline (2014) for the prevention of cardiovascular complications and stroke in women recommends CVD risk assessment in women with certain reproductive manifestations of CVD risk, such as adverse pregnancy outcomes, and suggests that female-specific risk factors may improve current CVD risk assessment strategies [11,12].

The purpose of this review is to examine the available literature regarding the prevalence and effects of the traditional risk factors

on the risk for CVD in men and women. Furthermore, the impact of the female specific risk factors on the occurrence of CVD is examined.

2. Major risk factors that affect both men and women

2.1. Elevated blood pressure

Elevated blood pressure is a major public-health challenge worldwide; it is estimated to be responsible for an annual 7.5 million deaths, about 12.8% of the total of all deaths and to account for 57 million disability adjusted life years (DALYS), about 3.7% of all DALYS [14]. The prevalence of hypertension is broadly similar in men and women, and is projected to increase with population growth and aging in both sexes. In 2000, nearly a billion adults, 27% of all men and 26% of all women, had hypertension; these estimates are projected to increase to 1.5 billion adults, 29% of men, and 30% of women, in 2025 [14,15,16].

The Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group recently conducted large-scale analyses to estimate the global trends in systolic blood pressure (SBP) levels between 1980 and 2008 [17]. In 2008, the age-standardized systolic blood pressure worldwide was 4 mmHg higher in men than in women; men on average had an SBP of 128.1 mmHg compared to 124.4 mmHg in women. Between 1980 and 2008, global levels of mean SBP had decreased by 0.8 mmHg in men and by 1.0 mmHg per decade in women and the prevalence of uncontrolled hypertension had fallen from 33% in 1980 to 29% in 2008 in men and from 29% to 25% in women. These trends, however, varied markedly among men and women living in different regions of the world. Where SBP levels had fallen considerably by about 3–4 mmHg per decade in men and women living in higher-income countries, most likely due to successful implementation of lifestyle and therapeutic interventions [18], opposite trends were seen in many lower and middle-income countries including countries in Oceania, east Africa, and south and southeast Asia where SBP levels rose with 0.8–1.6 mmHg per decade in men and 1.0–2.7 mmHg per decade for women, with no evidence that trends were curbing [17].

Studies have reported conflicting results on whether the strength of the association between increments in SBP and future risk for CVD is the same for men as for women [19,20,21,22]. A recent pooled analysis that included data from prospective cohort studies on more than 1.2 million individuals and over 50,000 cardiovascular events systematically examined whether the magnitude of the association between SBP and risk of CHD and stroke was similar in women and men [23]. After consideration of differences in other major cardiovascular risk factors, every 10 mmHg

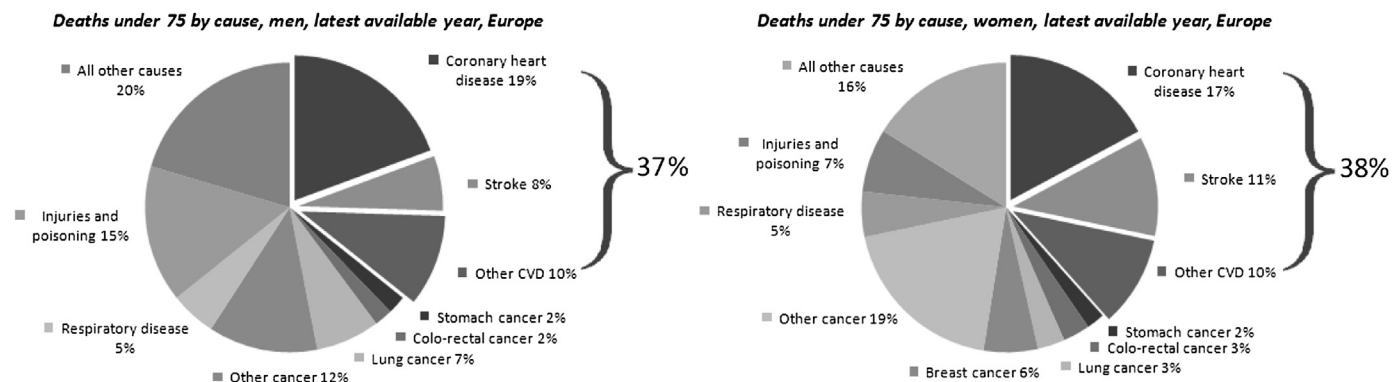


Fig. 1. Death rates in Europe 2012. Death rates in Europe, men and women <75 years of age; latest available year (2012), reprinted with permission from the World Health Organization [13].

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