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Sex-specific temporal trends in the incidence and prevalence of cardiovascular disease in young adults: a population-based study using UK primary care data

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Aims	There is concern that cardiovascular disease (CVD) in young adults is rising. However, current trends in the UK are unknown. We investigated sex-specific trends in the incidence and prevalence of CVD in young UK adults.
Methods and results	A series of annual (1998–2017) cohort and cross-sectional studies were conducted to estimate incidence rates and prevalence in men and women aged 16–50. Joinpoint regression models were fitted to evaluate changes in trends. From 1998 to 2017, incidence and prevalence had an overall downward trend for ischaemic heart disease (IHD) and angina, while coronary revascularization, stroke/transient ischaemic attack (TIA), and heart failure (HF) had an upward trend in both sexes. Myocardial infarction (MI) trends were stable in men and increased in women. For incidence, the average annual percentage change (AAPC) for men vs. women, respectively, was IHD -2.6% vs. -3.4% ; angina -7.0% vs. -7.3% ; MI 0.01% vs. 2.3%; revascularization 1.1% vs. 3.9%; stroke/TIA 1.9% vs. 0.6%; HF 5.6% vs. 5.0% (<i>P</i> for trend <0.05 for all except MI and revascularization in men and stroke/TIA in women). For prevalence, AAPCs for men vs. women, respectively, were IHD -2.8% vs. -4.9% ; angina -7.2% vs. -7.8% ; MI -0.2% vs. 2.0; revascularization 3.2% vs. 4.1%; stroke/TIA 3.1% vs. 3.6%; HF 5.0% vs. 3.0% (<i>P</i> for trend <0.05 for all except MI and revascularization trends levelled off, while stroke/TIA and HF trends increased in both sexes.
Conclusion	Overall trends in incidence and prevalence of CVD are worsening in young adults. Factors behind unfavourable trends warrant investigation and public health intervention.
Keywords	Trends • Sex-specific • Ischaemic heart disease • Stroke • Heart failure

Introduction

Cardiovascular disease (CVD) is a leading cause of mortality globally and remains a persistent public health burden. In Europe, CVD is the leading cause of premature mortality, accounting for 31% and 26% of the total deaths in men and women under 65 years.¹ Despite commendable improvements, CVD mortality rates have declined unequally in different age groups. Age and sex-disaggregated data from trend analyses conducted in countries from the western world have revealed that the rate of decline in CVD burden was sustained in older adults but had slowed down in younger adults.^{2–8} Differences between the sexes were observed, with coronary heart disease

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(CHD) mortality trend stagnating in young women.² Factors contributing to the slowing down of CVD mortality trends in young adults are heterogenous. The prevalence of common traditional risk factors, including obesity and diabetes, has risen globally.^{9,10} This is compounded by a lack of awareness in young adults regarding CVD and associated risk factors.¹¹ In addition, biological differences in CVD risk are under-appreciated in young adults. Age and sex-specific factors, such as pregnancy complications, which are associated with premature CVD, place women at a unique disadvantage.¹² Premature CVD translates to young adults living their productive years with illhealth, persistent disability, and increased economic burden.

Studies focussing on CVD in young UK adults are scarce and limited to ischaemic heart disease mortality statistics. To address this gap, we used UK primary care data to examine contemporary trends in the incidence and prevalence of CVD in young UK adults aged 16– 50 years.

Methods

A series of cross-sectional studies were conducted on 1 January of every year from 1998 to 2017 to estimate annual prevalence of CVD. Yearly cohort studies were carried out from 1 January to 31 December over the same period to calculate annual incidence rates.

Data source

IQVIA Medical Research Data (IMRD), incorporating The Health Improvement Network (THIN), is a database of electronic health records contributed to by more than 780 general practices spread across the UK. THIN is generalizable to the UK population in terms of demographics and major condition prevalence.¹³

Practices were eligible for inclusion from the later of 1 year after the practice commenced using the Vision software system and 1 year after the practice met acceptable mortality reporting to maximize data quality.¹⁴

Study population

Participants aged 16–50 years were eligible for inclusion. Participants must have been registered with an eligible practice for \geq 1 year before study entry to ensure documentation of all important patient data. Study period was from 1 January 1998 to 31 December 2017. Study participants were eligible to enter at the latest of their 16th birthday, study start date (1 January 1998) and 1 year after joining an eligible practice. Participants were censored when they reached 50 years of age.

Case definition of cardiovascular diseases

Diagnoses and other health-related concepts are recorded in UK primary care using the Read code terminology.¹⁵ The relevant cardiovascular disease Read codes were selected through a meticulous process described in Supplementary material online, *Methods*. Cardiovascular diseases of interest included: stroke/transient ischaemic attack (TIA), heart failure (HF), revascularization procedures [coronary bypass graft (CABG) and percutaneous coronary intervention (PCI)] and ischaemic heart disease (IHD), including its subtypes angina and myocardial infarction (MI). Cardiovascular conditions are part of the Quality and Outcomes Framework and are well recorded in UK primary care.¹⁶

Analysis

A detailed description of the analysis is found in the Supplementary material online, *Methods*. Briefly, annual prevalence (per 100 000 population) and incidence rate (per 100 000 person-years) were calculated for eligible males and females separately, and separately for each cardiovascular disease. The changes in incidence and prevalence trend over time were analysed using Joinpoint software (V.4.8.0.1).¹⁷ Joinpoint software takes the trend data and fits the simplest model that the data allow.^{17,18} Bayesian information criterion was used to identify the optimal model that fitted the data best. The programme calculates annual percentage change (APC) and the corresponding 95% confidence interval (95% CI) for any identified segment to estimate the change in slope between a preceding joinpoint and the next.¹⁹ The rate of change in slope for the entire study period was summarized by the average APC (AAPC) and 95% CI.²⁰

Results

Among the registered practices, there were a total of 317 344 adults aged 16–50 at the beginning of 1998. There were 160 714 (50.6%) males and 156 630 (49.4%) females with a male to female ratio of 1.03:1. The total number of eligible adults peaked at 2 248 149 in 2013, before dropping 1 475 946 in 2017. The mean age of both men and women was 34 years and remained constant over the study period.

Incidence

Ischaemic heart disease

The crude annual incidence rate of IHD and angina is provided in Supplementary material online, *Table S1*. The annual crude incidence rate of IHD (per 100000 person-years) decreased from 104.1 in 1998 to 64.1 in 2017 in men, compared to a decrease from 49.4 in 1998 to 24.9 in 2017 in women (Figure 1). Overall, the rate of decline of IHD incidence was steeper in women (AAPC -3.4%; 95% CI -4.1 to -2.6) compared with men (AAPC -2.6%; 95% CI -3.4 to -1.8) (Figure 3A). Changes in the magnitude and direction of the trend were detected by joinpoint analysis. Between 1998 and 2008, the decline in IHD incidence was greater in women (APC -6.7%; 95% CI -7.7 to -5.7) compared with men (APC -4.0%; 95% CI -5.1 to -2.9). After 2008, a slowing down of trend was observed in both sexes with the direction of trend sustained in men (APC -1.1%; 95% CI -2.4 to 0.2), but a reversal of trend emerged in women (APC 0.5%; 95% CI -0.8 to 1.7) (Supplementary material online, Table S2 and Figure S1). However, these later changes were not statistically different from a 0% APC.

Angina

Examination of the trend by subtypes of IHD revealed that the descending IHD incidence trend was mainly driven by falls in angina incidence. The annual incidence (per 100 000 person-years) of angina fell from 64.1 in 1998 to 15.4 in 2017 in men (AAPC -7.0%; 95% CI -9.2 to -4.8), compared to a fall from 37.5 in 1998 to 7.7 in 2017 in women (AAPC -7.3%; 95% CI -10.5 to -4.0) (*Figures 1* and 3A and Supplementary material online, *Table S2*). From 1998 to 2002, a stable trend in angina incidence was exhibited in both men (APC -1.9%; 95% CI -8.9 to 5.7) and women (APC -6.6%; 95% CI -16.1 to 4.0). This was followed by a significant decline from 2002 to 2007 with an APC of -19.9% (95% CI -25.6 to -13.8) per year in men

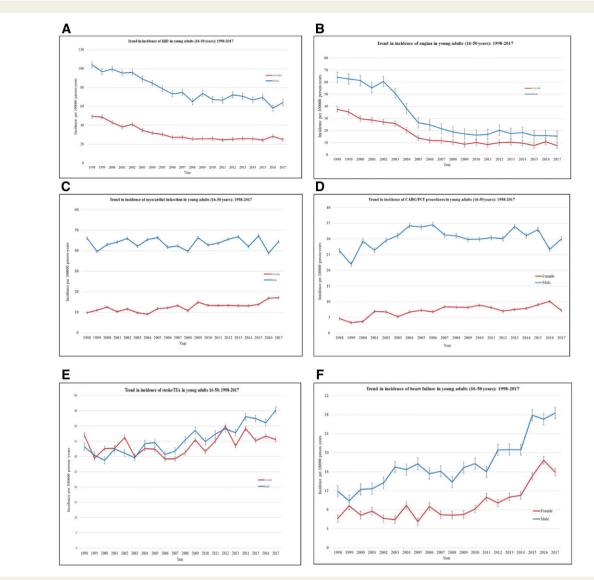


Figure I Annual incidence trend (per 100 000 person-years) of cardiovascular conditions in young men and women in the UK: 1998–2017. (A) Ischaemic heart disease. (B) Angina. (C) Myocardial infarction. (D) Revascularization procedures (coronary bypass graft and percutaneous coronary interventions). (E) Stroke and transient ischaemic attack. (F) Heart failure.

compared with an APC decrease of -17.9% per year (95% CI -26.3 to -8.6) in women. However, after 2007, the trend slowed down in both men (APC -1.9%; 95% CI -3.7 to -0.1) and women (APC -1.8%; 95% CI -4.3 to 0.9) (Supplementary material online, *Table S2* and *Figure S1*).

Myocardial infarction

Supplementary material online, *Table S3* provides the annual incidence of MI. The crude incidence (per 100 000 person-years) of MI decreased from 46.1 in 1998 to 44.5 in 2017 in men, compared to an increase from 9.8 in 1998 to 17.1 in 2017 in women (*Figure 1*). This was reflected in a significant AAPC increase of 2.3% per year (95% CI 1.4 to 3.2) in women compared with the stable trend in men (AAPC 0.01%; 95% CI –0.5 to 0.5) (*Figure 3A*). For the entire study period,

no changes in the incidence trends of MI were detected in either men or women (APC = AAPC).

Coronary revascularization

The crude annual incidence rates of revascularization procedures are provided in Supplementary material online, *Table S3*. The annual incidence (per 100 000 person-years) of revascularization procedures rose from 26.2 in 1998 to 30.0 in 2017 in men, compared to a rise from 4.6 in 1998 to 7.2 in 2017 in women (*Figure 1*). This represented an AAPC of 1.1% (95% CI –0.2 to 2.5) per year in men compared to an AAPC of 3.9% (95% CI 1.0 to 6.8) per year in women (*Figure 3A*). In men, the incidence trend of revascularization procedures increased by an APC of 5.5% per year (95% CI 1.5 to 9.7) between 1998 and 2004 before flattening after 2004 (APC –0.8%; 95% CI –2.0 to 0.4). In women, the incidence trend of revascularization

procedures increased by an APC of 8.3% (95% CI 3.4 to 13.5) per year between 1998 and 2007 before plateauing after 2007 (APC 0.01%; 95% CI -3.9 to 4.1) (Supplementary material online, *Table S2* and *Figure S1*).

Stroke/transient ischaemic attack

The crude annual incidence rates of stroke/TIA are provided in Supplementary material online, *Table S4*. The annual incidence (per 100 000) of stroke/TIA ranged from 32.2 in 1998 to 45.2 in 2017 (AAPC 1.9%; 95% CI 1.0 to 2.9) in men, compared to 7.0 in 1998 to 35.5 in 2017 (AAPC 0.6%; 95% CI -0.7 to 1.9) in women (*Figures 1* and *3A*). The incidence trend of stroke/TIA remained stable between 1998 and 2006 in both males (APC 0.6%; 95% CI -1.2 to 2.5) and females (APC -1.2%; 95% CI -3.7 to 1.5). After 2006, the increase in stroke/TIA incidence was higher in males at an APC of 2.9% (95% CI 1.7 to 4.1) per year compared with an APC 1.9% (95% CI 0.2 to 3.6) per year in females (Supplementary material online, *Table S2* and *Figure S1*).

Heart failure

The crude annual incidence rates of HF are provided in Supplementary material online, *Table* S4. The annual incidence (per 100 000 person-years) of HF increased from 11.9 in 1998 to 28.3 in 2017 (AAPC 5.6%; 95% CI 2.2 to 5.8) among men, and from 6.2 in 1998 to 15.9 in 2017 (AAPC 5.0%; 95% CI 2.7 to 8.5) among women (*Figures 1* and 3*A*). In men, the incidence rate of HF increased steeply by an APC of 8.3% (95% CI 3.2 to 13.6) per year from 1998 to 2004. This was followed by a flattening of the trend from 2004 to 2009 (APC -1.8%; 95% CI -10.2 to 7.4) which was later followed by a rapid APC increase of 8.3% (95% CI 5.0 to 11.8) per year after 2009. In women, a stable trend in HF incidence was exhibited between 1998 and 2004 (APC 0.2%; 95% CI -3.0 to 3.5). However, after 2009, HF incidence rapidly increased at an APC of 11.9% per year (95% CI 6.2 to 17.9) (Supplementary material online, *Table S2* and *Figure S1*).

Prevalence

Ischaemic heart disease

The crude annual prevalence of IHD and angina is provided in Supplementary material online, Table S5. The annual prevalence (per 100 000 population) of IHD decreased from 655.8 in 1998 to 370.6 in 2017 in men, compared to a decrease from 341.6 in 1998 to 129.8 in 2017 in women (Figure 2). This translated to an AAPC of -2.8%(95% CI -3.3 to -2.3) per year in men, compared to an AAPC of -4.9% (95% CI -5.9 to -3.9) per year in women (Figure 3B). There was a significant decline in the prevalence of IHD between 1998 and 2011 in both men and women. In men, the prevalence of IHD decreased from 1998 to 2001 (APC -5.9%; 95% CI -8.5 to -3.2), followed by a slowing down in trend from 2001 to 2011 (APC -2.9%; 95% CI -3.4 to -2.4). In women, the prevalence of IHD declined from 1998 to 2002 (APC -9.1%; 95% CI -12.5 to -5.5), followed by a slowing down in trend from 2002 to 2011 (APC -4.9%; 95% CI -6.2 to -3.7). However, the period from 2011 onwards was characterized by a levelling off in IHD prevalence trends in both men (APC -0.9%; 95% Cl -1.9 to 0.0) and women (APC

-2.0%; 95% CI -4.0 to 0.1) (Supplementary material online, *Table S6* and *Figure S2*).

Angina

The prevalence (per 100 000) of angina declined from 413.8 in 1998 to 94.6 in 2017 in men (AAPC -7.2%; 95% CI -8.1 to -6.3), compared to a decrease from 243.3 in 1998 to 51.5 in 2017 (AAPC -7.8%; 95% CI -9.8 to -6.3) in women (*Figures 2* and *3B* and Supplementary material online, *Table S5*). In men, angina prevalence declined with an APC of -5.7% (95% CI -7.0 to -4.3) per year from 1998 to 2005, -10.4% (95% CI -7.4 to -4.0) per year from 2005 to 2011, and -5.7% (95% CI -7.4 to -4.0) per year from 2011 to 2017. In women, the prevalence of angina declined with an APC of -6.6% (95% CI -8.3 to -4.9) from 1998 to 2006, -12.1% (95% CI -16.6 to -7.3) per year from 2011 to 2017 (Supplementary material online, *Table S6* and *Figure S2*).

Myocardial infarction

The crude annual prevalence rates of MI are provided in Supplementary material online, *Table S7*. Prevalence (per 100 000) of MI ranged from 276.3 in 1998 to 253.2 in 2017 in men, compared to 55.5 in 1998 to 74.6 in 2017 in women (*Figure 2*). This was reflected in the stable trend (AAPC -2.0%; 95% CI -0.8 to 0.4) noted in men compared to a gradual increase (AAPC 2.0%; 95% CI 1.3 to 2.6) in women (*Figure 3B*). A closer examination of MI prevalence trend in men revealed a significant decline from 1998 to 2001 (APC -5.2%; 95% CI -8.0 to -2.3), followed by a stable trend from 2001 to 2008 (APC 0.2%; 95% CI -0.8 to 1.3), and an upward trend from 2008 onwards (APC 1.2%; 95% CI 0.6 to 1.7). In women, the prevalence of MI was stable from 1998 to 2005 (APC 0.5%; 95% CI -1.1 to 2.1), followed by an upward trend from 2005 onwards (APC 2.8%; 95% CI 2.1 to 3.5) (Supplementary material online, *Table S6* and *Figure S2*).

Coronary revascularization

The crude annual prevalence of revascularization procedures is provided in Supplementary material online, *Table* S7. The prevalence (per 100 000) of revascularization procedures increased by an AAPC of 4.1% (95% CI 3.2 to 4.9) per year in men, from 90.8 in 1998 to 150.8 in 2017, compared to an AAPC increase of 3.2% (95% CI 2.8 to 3.6) per year in women, from 20.4 in 1998 to 40.5 in 2017 (*Figures 2* and *3B*). In men, the prevalence trend of revascularization procedures was characterized by an APC increase of 5.5% (95% CI 4.7 to 6.3) per year between 1998 and 2006, followed by slowing down of trend to a 1.5% (95% CI 1.1 to 2.0) APC increase after 2006. In women, the prevalence of revascularization procedures increased by an APC of 4.7% (95% CI 4.0 to 5.5) per year from 1998 to 2011, followed by a slowing down of trend to a 2.6% (95% CI 0.3 to 5.0) APC increase after 2011 (Supplementary material online, *Table S6* and *Figure S2*).

Stroke/transient ischaemic attack

The crude annual prevalence of stroke/TIA is provided in Supplementary material online, *Table S8*. The prevalence (per 100 000) of stroke/TIA ranged from 211.6 in 1998 to 358.7 in 2017 (AAPC 3.1%; 95% CI 2.6 to 3.5) in men, and from 194.7 in 1998 to

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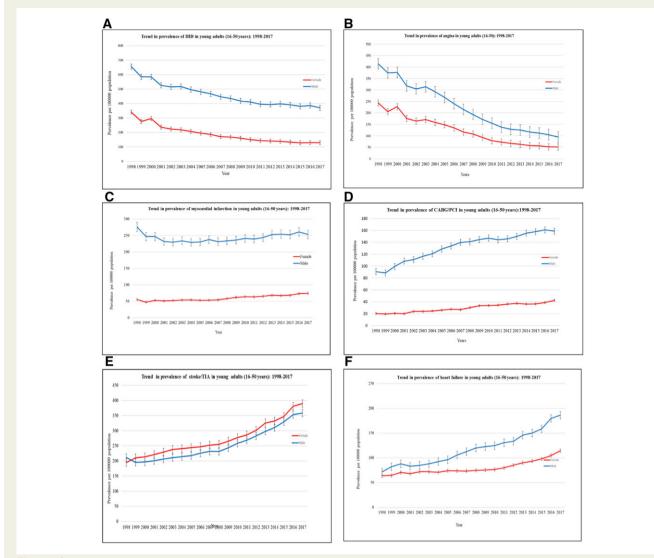


Figure 2 Annual prevalence trend (per 100 000 population) of cardiovascular conditions in young men and women in the UK: 1998–2017. (A) Ischaemic heart disease. (B) Angina. (C) Myocardial infarction. (D) Revascularization procedures (coronary bypass graft and percutaneous coronary interventions). (E) Stroke and transient ischaemic attack. (F) Heart failure.

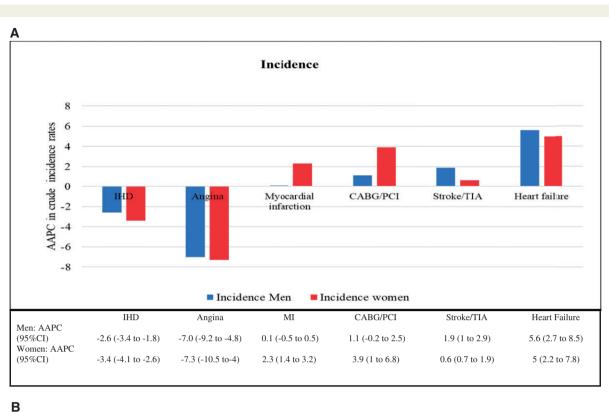
389.8 in 2017 (AAPC 3.6% 95% CI 3.2 to 4.1) in women (*Figures 2* and 3*B*). In men, the trend in stroke prevalence was stable until 2001 (APC -0.9%; 95% CI -2.9 to 1.3). This was followed by a 2.3% (95% CI 1.6 to 3.0) APC increase between 2001 and 2008 and a 5.0% (95% CI 4.6 to 5.4) APC increase after 2008. In women, the prevalence trend of stroke was characterized by a steep increase (APC 3.6%; 95% CI 2.6 to 4.7) between 1998 and 2003, followed by further acceleration of pace (APC 5.2% 95% CI 4.7 to 5.7) from 2009 onwards (Supplementary material online, *Table S6* and *Figure S2*).

Heart failure

The crude annual prevalence of HF is provided in Supplementary material online, *Table S8*. The crude prevalence (per 100 000) of HF increased from 75.6 in 1998 to 182.3 in 2017 in men (AAPC 5.0%; 95% CI 4.0 to 6.1), compared to an increase from 63.8 in 1998 to 114.4 in 2017 in women (AAPC 3.0%; 95% CI 2.4 to 3.5) (*Figures 2* and 3B). Heart failure prevalence trend in men was characterized by a steep increase (APC 4.5%; 95% CI 4.0 to 5.5) from 1998 until 2014, which subsequently doubled in magnitude (APC 8.1%; 95% CI 1.6 to 15.0) from 2014 onwards. In women, the prevalence of HF exhibited a significant increase from 1998 to 2002 (APC 2.8%; 95% CI 0.8 to 4.8), followed by a stable trend from 2002 to 2010 (APC 0.8%; 95% CI -0.1 to 1.6) and a steep upward trend after 2010 (APC 5.7%; 95% CI 4.8 to 6.5) (Supplementary material online, *Table S6* and *Figure S2*).

Discussion

We examined sex-specific temporal trends in the incidence and prevalence of CVD in young adults using UK primary care data. Generally, trends were similar between men and women, with the burden of CVD greatest in men compared with women. Overall,



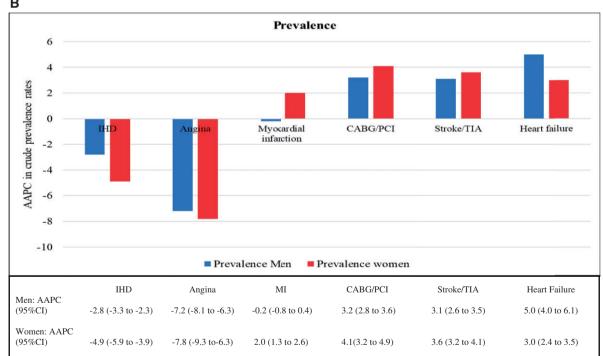


Figure 3 Average annual percentage change in crude incidence (A) and prevalence (B) of cardiovascular disease in young UK adults (16–50 years), 1998–2017.

from 1998 to 2017, for both incidence and prevalence analyses, IHD exhibited descending trends while revascularization procedures, stroke/TIA, and HF showed ascending trends. Examination of trends by subtypes of IHD revealed that the fall in angina rates was the

principal driver of IHD trend. Myocardial infarction exhibited an upward trend in women but remained stable in men.

Joinpoint analyses captured several notable changes in the magnitude and direction of trends in recent years. In both men and women,

the period after 2008 was characterized by a slowing down of angina and IHD incidence trends with a small albeit non-significant reversal of IHD trend detected in women. A flattening of incidence trends was detected for revascularization procedures after 2004 and 2007 in men and women, respectively. For stroke/TIA, the period after 2006 was characterized by a significant rise in incidence trends in both men and women compared to the stable trends noted before this period. For HF, the period after 2009 was characterized by steep increases in incidence trends in both men and women. Overall, prevalence trends paralleled incidence trends for all cardiovascular conditions except stroke/TIA prevalence rates which were marginally higher in women compared with men.

Literature on incidence and prevalence trends in CVD in young UK adults is sparse. Supplementary material online, Table S9 highlights the comparisons of trends with findings from selected existing literature. Direct comparisons are challenging due to methodological differences in the definition of young adults, disparities in the source population (community vs. hospital setting), and differences in study periods. The declining IHD observed in this study aligns with the overall findings from existing UK literature.^{21,22} Between 2000 and 2010, among UK adults aged >30 years, Bhattarai et $al.^{21}$ noted similar trends in the incidence of IHD in both sexes. Additionally, our study observed a slowing down in IHD trends in recent years. These findings complement reports from studies from the USA and Western Europe which noted similar decelerations in IHD trends (Supplementary material online, Table S9).^{2,3,6,23} Moreover, Bhattarai et al.²¹ reported that between 2000 and 2010, there was a significant decline in the incidence of angina, while the incidence of MI and revascularization procedures remained unchanged. Our study provides additional evidence that the falling angina rates were the principal drivers of IHD trends. This study identified that the incidence and prevalence of MI significantly increased in women and remained stable in men. These findings echo similar ominous trends observed among women from Australia, Canada, and the USA (Supplementary material online, Table S9).^{24–28}

Studies examining sex-specific trends in revascularization procedures in young adults are limited. Recent studies conducted in the USA noted that there was a downward trend in incidence of coronary revascularization procedures.^{29–31} Dani *et al.* reported that between 2004 and 2008, the volume of CABG procedures was on a downward trend among US adults aged 18–45. The greater burden of revascularization procedures among women compared with men in this study may be attributable to the concurrent rise in the incidence of MI (Supplementary material online, *Table S9*).

We noted that men had slightly higher incidence rates of stroke/ TIA overall, while women had reported higher prevalence rates of stroke/TIA. Studies examining sex-specific temporal trends in stroke report inconsistent results, with some studies reporting no difference. Other studies noted differences in particular age categories, while some studies report a higher incidence in specific genders.³² A study examining stroke incidence in young adults from 15 European countries noted a female predominance below 34 years, while male predominance was noted at ages 40–49 years.³³ A Dutch study noted that the incidence of stroke in young adults was higher in females than in males.³² Despite inconsistent results on sex differences in the burden of stroke, our study concurs with the reports of increased stroke incidence in young adults noted in previous literature (Supplementary material online, *Table* S9).^{32–35}

This study supports findings of rising HF incidence rates noted in cohorts from Denmark, Sweden, and the USA. However, these studies were limited by a lack of sex-specific data (Supplementary material online, *Table S9*).^{36–38}

The factors behind unfavourable trends in CVD among young UK adults are unclear but are possibly multifactorial. The risk of CVD increases with increasing age. Throughout the study period, the mean population age remained constant. Therefore, the unfavourable trends observed in this study are unlikely to be attributable to population ageing. The latest data from Health Survey England shows that the prevalence (1993-2019) of obesity and diabetes mellitus is on an upward trend, while smoking and alcohol consumption are on a downward trend in men and women aged over 16 years.³⁹ Also, the proportion of adults with untreated hypertension has been on a downward trend since 2003. The unfavourable trends in cardiovascular conditions noted in the present study parallel the rising prevalence of obesity and diabetes mellitus. Examination of recent reports on CVD morbidity trends reveals that the incidence and prevalence trends (2005-17) for all cardiovascular conditions are on a downward trend in older adults (>65 years).⁴⁰ Although strategies for the primary prevention of cardiovascular disease are the same across all age groups, the disparities in CVD morbidity trends between older adults and young adults warrants investigation. The unfavourable trends reported in this study suggest that young adults are less responsive to strategies for primary prevention of CVD. The variations in the impact of traditional risk factors may explain differences between sexes. Age, total cholesterol, low-density lipoprotein, and hypertension have a more significant effect on men. Diabetes, smoking, systolic arterial hypertension, triglycerides, and high-density lipoprotein levels have a greater impact in women.⁴¹ During the study period, we observed a stable trend in MI in men and an upward trend in women. A study conducted using UK Biobank data showed that diabetes mellitus (type 1 or 2), current smoking, and systolic blood pressure were associated with an excess risk of MI in women.⁴² Socioeconomic deprivation could also be a key factor in young adults. A large perspective cohort study conducted in 20 low-, middle-, and high-income countries found that low levels of education rather than household wealth was the marker of socioeconomic status associated with major cardiovascular events in all the countries studied.⁴³ O'Flaherty et al.⁴⁴ noted that the flattening of CHD mortality trends in young Scottish adults was restricted to the most deprived groups. The adverse trends reported in this study may be partly influenced by young materially-deprived adults who not only lead unhealthy lifestyles but have a low level of awareness or education regarding primary prevention of CVD.

Sex-specific factors disadvantage women. Female reproductive complications including adverse pregnancy outcomes and reproductive endocrine factors enhance the risk of premature cardiovascular disease.^{12,45} Results from an exploratory analysis of ecological data found that countries with higher rates of pre-term delivery had higher rates of stroke (correlation coefficient; r = 0.65).⁴⁶ The prevalence of several of these reproductive factors is on an upward trend in high-income countries and may influence the rising trend of CVD in young women.^{47,48} It is commonly accepted that endogenous oestrogen delays onset of CVD in premenopausal women; ovarian dysfunction may therefore impact CVD in women aged >45. However, evidence on the cardioprotective effects of oestrogen is debated and epidemiological evidence does not support an acceleration of CVD risk in women at menopause.^{49,50} Furthermore, the average age of onset of menopause is 51, which is after the upper age cut-off for our study.

Strengths and limitations

This study has several strengths. The long-term follow-up covering 20 years allowed detailed analysis of the changes in CVD morbidity trends. Compared to qualitative descriptions, the use of joinpoint regression is an unbiased quantitative technique used to detect changes in trend. Analysis of temporal trends was based on a primary care database that is representative of the UK population. However, some potential limitations need highlighting. First, although diagnoses for MI and other cardiovascular conditions are well-recorded in UK primary care, the sole use of primary care data compared with linked primary and secondary care data underestimates crude incidence rates.⁵¹ Second, our analysis is descriptive in nature. The relationship between risk factors and cardiovascular disease trend was beyond the scope of this study. Third, analysis of temporal trends in this study was limited to young adults. Comparisons with older populations were beyond the scope of this study.

Implications for policy and future research

The adverse trends in this study suggest an increased burden of CVD in the future as the young UK population ages. Future research should focus on identifying factors behind unfavourable trends in CVD morbidity. Public health interventions are needed to stem the ominous trends.

Conclusion

From 1998 to 2017, among young UK adults, the incidence and prevalence of IHD and angina exhibited a downward trend, while revascularization procedures, stroke/TIA, and HF exhibited an overall upward trend. Myocardial infarction trends remained stable in men but significantly increased in women. Several noteworthy changes in trend were detected over the period. In recent years, in both sexes, a levelling off in trends of IHD and revascularization procedures was detected, while stroke/TIA and HF trends exhibited significant increases. The factors behind the unfavourable trends warrant urgent investigation and intervention.

Patient and public involvement

No patients or the public were involved in the study.

Supplementary material

Supplementary material is available at *European Journal of Preventive Cardiology* online.

Ethical approval

IQVIA Medical Research Data (IMRD) incorporates data from The Health Improvement Network (THIN) a Cegedim database. Reference made to THIN is Reference made to THIN is intended to be descriptive of the data asset licensed by IQVIA. Anonymized data were used throughout the study provided by the data provider to the University of Birmingham Studies using IMRD-UK database have had initial ethical approval from the NHS South-East Multicentre Research Ethics Committee subject to prior independent scientific review. The Scientific Review Committee (IQVIA) approved the study protocol (SRC Reference Number: 17THIN060).

Data availability statement

The data used in this study were provided by IQVIA Medical Research Data (IMRD) under licence/by permission. Data may be shared on request to the corresponding author with permission of IMRD.

Conflict of interest: The authors declare no conflicts of interest .

References

- Wilkins E, Wilson L, Wickramasinghe K, Bhatnagar P, Leal J, Luengo Fernandez R, Burns R, Rayner M, Townsend N. European cardiovascular disease statistics 2017. European Heart Network, Brussels 2017.
- Wilmot KA, O'Flaherty M, Capewell S, Ford ES, Vaccarino V. Coronary heart disease mortality declines in the United States from 1979 through 2011: evidence for stagnation in young adults, especially women. *Circulation* 2015;**132**: 997–1002.
- O'Flaherty M, Ford E, Allender S, Scarborough P, Capewell S. Coronary heart disease trends in England and Wales from 1984 to 2004: concealed levelling of mortality rates among young adults. *Heart* 2008;**94**:178–181.
- Wu WY, Berman AN, Biery DW, Blankstein R. Recent trends in acute myocardial infarction among the young. *Curr Opin Cardiol* 2020;35:524–530.
- Shah NS, Molsberry R, Rana JS, Sidney S, Capewell S, O'Flaherty M, Carnethon M, Lloyd-Jones DM, Khan SS. Heterogeneous trends in burden of heart disease mortality by subtypes in the United States, 1999-2018: observational analysis of vital statistics. *BMJ* 2020;**370**:m2688.
- Meirhaeghe A, Montaye M, Biasch K, Huo Yung Kai S, Moitry M, Amouyel P, Ferrières J, Dallongeville J. Coronary heart disease incidence still decreased between 2006 and 2014 in France, except in young age groups: results from the French MONICA registries. *Eur J Prev Cardiol* 2020;**27**:1178–1186.
- Hussain A, Lee M, Rana J, Virani SS. Epidemiology and risk factors for stroke in young individuals: implications for prevention. *Curr Opin Cardiol* 2021;36:565–571.
- Yang J, Biery DW, Singh A, Divakaran S, DeFilippis EM, Wu WY, Klein J, Hainer J, Ramsis M, Natarajan P, Januzzi JL, Nasir K, Bhatt DL, Di Carli MF, Blankstein R. Risk factors and outcomes of very young adults who experience myocardial infarction: the partners YOUNG-MI registry. *Am J Med* 2020;**133**:605–612.e1.
- Yatsuya H, Li Y, Hilawe EH, Ota A, Wang C, Chiang C, Zhang Y, Uemura M, Osako A, Ozaki Y, Aoyama A. Global trend in overweight and obesity and its association with cardiovascular disease incidence. *Circ J* 2014;**78**:2807–2818.
- Khan MAB, Hashim MJ, King JK, Govender RD, Mustafa H, Al Kaabi J. Epidemiology of type 2 diabetes—global burden of disease and forecasted trends. J Epidemiol Glob Health 2020;10:107–111.
- Trejo R, Cross W, Stephenson J, Leigh EK. Young adults' knowledge and attitudes towards cardiovascular disease: a systematic review and meta-analysis. J Clin Nurs 2018;27:4245–4256.
- Okoth K, Chandan JS, Marshall T, Thangaratinam S, Thomas GN, Nirantharakumar K, Adderley NJ. Association between the reproductive health of young women and cardiovascular disease in later life: umbrella review. *BMJ* 2020;**371**:m3502.
- Blak BT, Thompson M, Dattani H, Bourke A. Generalisability of The Health Improvement Network (THIN) database: demographics, chronic disease prevalence and mortality rates. *Inform Prim Care* 2011;**19**:251–255.
- Maguire A, Blak BT, Thompson M. The importance of defining periods of complete mortality reporting for research using automated data from primary care. *Pharmacoepidemiol Drug Saf* 2009;**18**:76–83.

- 15. Nick B. What are the read codes. Health Libr Rev 1994;II:177-188.
- Digital.nhs.uk. Frequently Asked Questions NHS Digital [Internet]. https://digital.nhs. uk/data-and-information/publications/statistical/quality-and-outcomes-frame work-achievement-prevalence-and-exceptions-data/2019-20/frequently-askedquestions (31 May 2021).
- Surveillance.cancer.gov. Joinpoint Regression Program [Internet]. https://surveillance. cancer.gov/joinpoint/ (1 June 2021).
- 18. Surveillance.cancer.gov. Joinpoint Help Manual 4.8.0.1. (1 June 2021)
- Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. *Stat Med* 2000;19:335–351.
- Clegg LX, Hankey BF, Tiwari R, Feuer EJ, Edwards BK. Estimating average annual per cent change in trend analysis. *Stat Med* 2009;28:3670–3682.
- Bhattarai N, Charlton J, Rudisill C, Gulliford MC. Coding, recording and incidence of different forms of coronary heart disease in primary care. *PLoS One* 2012;7:e29776.
- Davies AR, Smeeth L, Grundy EMD. Contribution of changes in incidence and mortality to trends in the prevalence of coronary heart disease in the UK: 1996 2005. Eur Heart J 2007;28:2142–2147.
- Vancheri F, Tate AR, Henein M, Backlund L, Donfrancesco C, Palmieri L. Time trends in ischaemic heart disease incidence and mortality over three decades (1990–2019) in 20 Western European countries: systematic analysis of the Global Burden of Disease Study 2019. Eur J Prev Cardiol 2021;zwab134, https: //doi.org/10.1093/eurjpc/zwab134
- Towfighi A, Zheng L, Ovbiagele B. Sex-specific trends in midlife coronary heart disease risk and prevalence. Arch Intern Med 2009;169:1762–1766.
- Arora S, Stouffer GA, Kucharska-Newton AM, Qamar A, Vaduganathan M, Pandey A, Porterfield D, Blankstein R, Rosamond WD, Bhatt DL, Caughey MC. Twenty year trends and sex differences in young adults hospitalized with acute myocardial infarction. *Circulation* 2019;**139**:1047–1056.
- Nedkoff LJ, Briffa TG, Preen DB, Sanflippo FM, Hung J, Ridout SC, Knuiman M, Hobbs M. Age- and sex-specific trends in the incidence of hospitalized acute coronary syndromes in Western Australia. *Circ Cardiovasc Qual Outcomes* 2011;4:557–564.
- Izadnegahdar M, Singer J, Lee MK, Gao M, Thompson CR, Kopec J, Humphries KH. Do younger women fare worse? Sex differences in acute myocardial infarction hospitalization and early mortality rates over ten years. J Women's Heal 2014;23:10–17.
- Guo X, Li Z, Vittinghoff E, Sun Y, Pletcher MJ. Trends in rate of acute myocardial infarction among patients aged. *Nat Rev Cardiol* 2018;**15**:119.
- Gerber Y, Gibbons RJ, Weston SA, Fabbri M, Herrmann J, Manemann SM, Frye RL, Asleh R, Greason K, Killian JM, Roger VL. Coronary disease surveillance in the community: angiography and revascularization. J Am Heart Assoc 2020;9:e015231.
- Alkhouli M, Alqahtani F, Kalra A, Gafoor S, Alhajji M, Alreshidan M, Holmes DR, Lerman A. Trends in characteristics and outcomes of hospital inpatients undergoing coronary revascularization in the United States, 2003-2016. JAMA Netw Open 2020;3:e1921326.
- 31. Dani SS, Minhas AMK, Arshad A, Krupica T, Goel SS, Virani SS, Sharma G, Blankstein R, Blaha MJ, Al-kindi SG, Nasir K, Khan SU. Trends in characteristics and outcomes of hospitalized young patients undergoing coronary artery bypass grafting in the United States, 2004 to 2018. J Am Heart Assoc 2021;10:21361.
- Ekker MS, Verhoeven JI, Vaartjes I, Van Nieuwenhuizen KM, Klijn CJM, De Leeuw FE. Stroke incidence in young adults according to age, subtype, sex, and time trends. *Neurology* 2019;92:e2444–e2454.
- 33. Putaala J, Yesilot N, Waje-Andreassen U, Pitkäniemi J, Vassilopoulou S, Nardi K, Odier C, Hofgart G, Engelter S, Burow A, Mihalka L, Kloss M, Ferrari J, Lemmens R, Coban O, Haapaniemi E, Maaijwee N, Rutten-Jacobs L, Bersano A, Cereda C, Baron P, Borellini L, Valcarenghi C, Thomassen L, Grau AJ, Palm F, Urbanek C, Tuncay R, Durukan-Tolvanen A, van Dijk EJ, de Leeuw F-E, Thijs V, Greisenegger S, Vemmos K, Lichy C, Bereczki D, Csiba L, Michel P, Leys D, Spengos K, Naess

H, Bahar SZ, Tatlisumak T. Demographic and geographic vascular risk factor differences in European young adults with ischemic stroke: the 15 cities young stroke study. *Stroke* 2012;**43**:2624–2630.

- Bejot Y, Daubail B, Jacquin A, Durier J, Osseby G-V, Rouaud O, Giroud M. Trends in the incidence of ischaemic stroke in young adults between 1985 and 2011: the Dijon stroke registry. J Neurol Neurosurg Psychiatry 2014;85:509–513.
- Béjot Y, Duloquin G, Thomas Q, Mohr S, Garnier L, Graber M, Giroud M. Temporal trends in the incidence of ischemic stroke in young adults: Dijon stroke registry. *Neuroepidemiology* 2021;55:239–244.
- Vasan RS, Zuo Y, Kalesan B. Divergent temporal trends in morbidity and mortality related to heart failure and atrial fibrillation: age, sex, race, and geographic differences in the United States, 1991–2015. J Am Heart Assoc 2019;8(8):e010756.
- Christiansen MN, Køber L, Weeke P, Vasan RS, Jeppesen JL, Smith JG, Gislason GH, Torp-Pedersen C, Andersson C. Age-specific trends in incidence, mortality, and comorbidities of heart failure in Denmark, 1995 to 2012. *Circulation* 2017; 135:1214–1223.
- Barasa A, Schaufelberger M, Lappas G, Swedberg K, Dellborg M, Rosengren A. Heart failure in young adults: 20-year trends in hospitalization, aetiology, and case fatality in Sweden. *Eur Heart* J 2014;35:25–32.
- hscicgov.uk. England's Changing Health Since the 1990s [Internet]. http://healthsurvey. hscic.gov.uk/data-visualisation/data-visualisation/explore-the-trends.aspx (29 May 2021).
- Bhf.org.uk. Heart & Circulatory Disease Statistics 2020. BHF [Internet]. https:// www.bhf.org.uk/what-we-do/our-research/heart-statistics/heart-statistics-publica tions/cardiovascular-disease-statistics-2020 (29 May 2021).
- Locorotondo LG. Gender differences in cardiovascular disease prevention. J Integr Cardiol 2015;1:20–22.
- Millett ERC, Peters SAE, Woodward M. Sex differences in risk factors for myocardial infarction: cohort study of UK Biobank participants. BMJ 2018;363:k4247.
- 43. Rosengren A, Smyth A, Rangarajan S, Ramasundarahettige C, Bangdiwala SI, AlHabib KF, Avezum A, Bengtsson Boström K, Chifamba J, Gulec S, Gupta R, Igumbor EU, Iqbal R, Ismail N, Joseph P, Kaur M, Khatib R, Kruger IM, Lamelas P, Lanas F, Lear SA, Li W, Wang C, Quiang D, Wang Y, Lopez-Jaramillo P, Mohammadifard N, Mohan V, Mony PK, Poirier P, Srilatha S, Szuba A, Teo K, Wielgosz A, Yeates KE, Yusoff K, Yusuf R, Yusufali AH, Attaei MW, McKee M, Yusuf S. Socioeconomic status and risk of cardiovascular disease in 20 lowincome, middle-income, and high-income countries: the Prospective Urban Rural Epidemiologic (PURE) study. Lancet Glob Heal 2019;**7**:e748–e760.
- 44. O'Flaherty M, Bishop J, Redpath A, McLaughlin T, Murphy D, Chalmers J, Capewell S. Coronary heart disease mortality among young adults in Scotland in relation to social inequalities: time trend study. *BMJ* 2009;**339**:b2613.
- Peters SAE, Woodward M. Women's reproductive factors and incident cardiovascular disease in the UK Biobank. *Heart* 2018;**104**:1069–1075.
- Kaul P, Sia WW. Pregnancy as oracle: what it augurs for women's health. Circulation 2021;143:2045–2048.
- Lavery J, Friedman A, Keyes K, Wright J, Ananth C. Gestational diabetes in the United States: temporal changes in prevalence rates between 1979 and 2010. *BJOG* 2017;**124**:804–813.
- Ananth CV, Keyes KM, Wapner RJ. Pre-eclampsia rates in the United States, 1980-2010: age-period-cohort analysis. BMJ 2013;347:f6564.
- Tunstall-Pedoe H. Myth and paradox of coronary risk and the menopause. Lancet 1998;351:1425–1427.
- Boardman HMP, Hartley L, Eisinga A, Main C, Roqué I Figuls M, Bonfill Cosp, Sanchez RG, Knight B. Hormone therapy for preventing cardiovascular disease in post-menopausal women. *Cochrane Database Syst Rev* 2015;3:CD002229.
- 51. Herrett E, Shah AD, Boggon R, Denaxas S, Smeeth L, van Staa T, Timmis A, Hemingway H. Completeness and diagnostic validity of recording acute myocardial infarction events in primary care, hospital care, disease registry, and national mortality records: cohort study. *BMJ* 2013;**346**:f2350.