Epidemiological trends in acute coronary syndromes: understanding the past to predict and improve the future

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Abstract

Epidemiology of acute coronary syndrome is of major public health interest as coronary disease is the leading cause of morbidity and mortality worldwide. There are dynamic changes in the prevalence of coronary risk factors and clinically manifest coronary heart disease (CHD) across geographically-diverse communities. Decreases in cigarette smoking, cholesterol and blood pressure are counterbalanced by increases in proportion of the elderly population and absolute increases in obesity and diabetes. Additionally, interpretation of changes in this epidemiology is complicated by changes in the definition of myocardial infarction and changes in the sensitivity of biomarker assays. Nevertheless, improvements in evidence-based treatment have resulted in declining case-fatality. The reduction in event-rates has contributed to more than half of the reduction in CHD mortality and reduction in case-fatality accounted for the remainder. Despite these changes in developed economies, mortality is increasing elsewhere and CHD is likely to remain the biggest killer globally in coming years.

Key words: coronary heart disease, myocardial infarction, angina pectoris, epidemiology, mortality and morbidity.

Introduction

Acute coronary syndrome (ACS) describes a spectrum of unstable coronary artery disease from unstable angina pectoris to non-ST elevation myocardial infarction (NSTEMI) and ST elevation myocardial infarction (STEMI). A triad of clinical presentation, electrocardiographic (ECG) changes and biochemical markers are used to define ACS. Previously, myocardial infarction (MI) was defined using the World Health Organization (WHO) criteria based on symptoms, ECG abnormalities, and cardiac enzymes. However, the development of more sensitive and specific serological biomarkers allows detection of even smaller volumes of myocardial necrosis and has resulted in a revised definition of MI by the joint committee of European Society of Cardiology and American College of Cardiology [1].

The epidemiology of ACS has changed considerably over the last few decades. It is important to define these trends and their underlying reasons to inform future planning for the management of ACS. A change in epidemiological trends was first noticed in the United States in 1970s with national decline in coronary heart disease (CHD) mortality [2]. Since then many registries and surveys have described changes in CHD mortality at

national, regional and international levels. These changes in mortality could be the result of changes in incidence and/or case fatality. In turn, incidence is impacted upon by underlying demographic trends, changes in risk factor profiles, primary prevention measures and other unknown factors. Case fatality can change as a result of acute therapeutic interventions or secondary prevention measures. Both the incidence and fatality can also change as a direct result of change in natural history of the disease.

This paper systematically reviews the trends in ACS morbidity, mortality and medical care over the last three decades. It also explores key issues including the question of whether the observed changes in incidence and mortality of ACS are real and if real, whether they relate to population trends in the known coronary risk factors or due to changes in definition or case identification of patients and/or changes in management. This review does not aim to scrutinize the strengths and weaknesses of individual registries but to provide an overall picture of trends in ACS over time.

Changing epidemiology or methodology

Over the last few decades changes have been observed not only in the epidemiology of ACS but also in the methodology for measuring these trends. The first question that needs to be answered is whether this observed change in epidemiology is a true change or just a reflection of changes in diagnostic, statistical and epidemiological methods; as suggested by some critics [3]. The methodological changes may have affected the epidemiology of ACS in artificial ways, for example, an iatrogenic change in incidence and mortality seen in 1979 when the ICD-8 coding system was switched to ICD-9. Moreover changes in clinical diagnostic methods, especially more sensitive troponin assays, and changes in epidemiological criteria used to define MI have led to apparent changes in incidence and changes in hospitalisation rates and mortality in patients diagnosed with myocardial infarction [4, 5]. Changes in the diagnostic criteria for MI equated to approximately 160,000 additional myocardial infarctions per year in the United Kingdom [6]. However these changes would tend to increase the frequency of MI and do not explain the declining trends seen in many continuous registries and repeat surveys; which provide a dynamic estimate of the changing patterns of disease presentation, management and outcome [7]. Cardiovascular risk factor profile has changed in a complex manner over the last few decades. The prevalence of obesity, diabetes and metabolic syndrome has increased, while the frequency of smoking and levels of serum cholesterol and mean blood pressure have decreased. There has also been an increasing emphasis on primary and secondary prevention along with awareness and availability of better therapeutic agents. These take place in the context of societal and socio-economic changes and population migration. The technical diagnostic advancements and greater accessibility of percutaneous treatment options has revolutionised the management of ACS and contributed to changes in outcome measures. The summation of evidence suggests that both epidemiological trends and better management of patients presenting with ACS have contributed to the observed changes over the last three decades.

Trends in acute coronary syndrome morbidity

Incidence and prevalence

Only a few registries report the true incidence and prevalence of ACS in well defined geographic regions with a known total population. Criteria have been defined to judge the strength and weaknesses of individual registries [7]. Nevertheless, examining the most robust data sources, there has been a significant and consistent trend towards decline in incidence and prevalence of ACS, especially for STEMI in industrialised countries and an increase in other regions including Eastern Europe and South Asia. Despite falls in age adjusted incidence of CHD, the burden of CHD has increased globally as a result of rising life expectation and the survival of individuals with ACS. The WHO MONICA (MONItoring trends and determinants In CArdiovascular disease) project examined the incidence of ACS in 21 countries [8]. It has shown that the incidence of coronary events is higher in Northern, Eastern and Central Europe than in Southern and Western Europe. This study also revealed that incidence of coronary events is falling rapidly in Northern and Western Europe but is not falling as fast in the populations in Southern, Central and Eastern Europe and is rising in some populations. For example incidence rate in adult men fell by 6.5% in Finland but rose by 1.2% in Lithuania from 1983 to 1996 [9]. In the CZECH registry, the calculated annual incidence of confirmed ACS (MI and unstable angina) was 3248 cases/million population. The annual incidence of hospitalized confirmed acute myocardial infarction (AMI) was 1960 cases/ million population while the annual incidence of STEMI was 661 cases/million population [10]. The calculated annual incidence of hospitalised AMI in a Danish registry was 2,612 cases/million population. A registry of the Portuguese National Health Service has shown that the number of cases of acute or sub-acute coronary events was 11,623 in 1997 and increased to 14,147 in 2001. There was also a parallel increase in number of patients with stable coronary artery disease during this time period [11].

British Heart Foundation estimated that there are about 123,000 cases of AMI per year in the UK while the incidence rate for angina is about 95,000 new cases per year. Prevalence of CHD was measured in the 1994, 1998 and 2003 health survey for England. Data from 2003 Health Survey for England suggest that the prevalence of CHD in England was 7.4% in men and 4.5% in women. Overall between 1994 and 2003, the prevalence of CHD increased from 6.0 to 7.4% in men and from 4.1 to 4.5% in women. However this increase is largely due to increase in the recognition of cases of angina (ascertainment bias) while the age-adjusted hazard of MI actually fell by 62% from 1980 to 2004 [12]. In Scotland, where there are continuous data of CHD incidence since 1996, there has been a steady decline in CHD incidence, though the incidence and prevalence rates are higher than England for each time interval [13]. Although data from the British Regional Heart Study [14], suggested that there has been no change in the prevalence rates over the period 1978-1996 these data need to be interpreted in the context of a falling incidence but increasing survival.

Hospitalisation

Admission rate

Rate of admission (sometimes referred to as hospitalisation rate or rate of hospital discharge) has been used to judge incidence and mortality of ACS. This rate has remained stable in most of the Western European countries since 1995, but rates in some Eastern European countries have increased considerably [15].

There has been a substantial reduction in the rate of hospitalisation for acute MI over last decade but there has also been an increase in hospitalisation rate for unstable angina and chest pain [16]. In the United States, rate of hospitalized definite AMI declined by ~5% between 1985 and 1990 and by ~10% between 1990 and 1995. In contrast, hospitalisation rate for unstable angina increased by 56% in men and 30% in women between 1985 and 1995. [17]. This may suggest increased awareness in population to attend hospital for chest pain, changes in the threshold for admission, and changes in diagnostic criteria for ACS. Longitudinal studies with consistent populations and consistent diagnostic criteria are required to estimate changes in the proportion of survivors of ACS.

Hospital stay

The total duration of hospital stay among the patients with ACS has decreased significantly in last two decades. In the Minnesota Heart Survey, between 1985 and 1995, the mean length of stay for definite AMI decreased by ~40%, from 8.3 days to 5 days in men and from 8.4 days to 5.5 days in women [17]. It may suggest easy availability and rapid application of definite diagnostic and treatment modalities, in the context of economic and societal pressures to reduce hospital stay.

Trends in acute coronary syndrome presentation
Demographic trends

There has been no change in the age at first presentation with ACS in both men and women over last 25 years. The median age of AMI patients in the Minnesota Heart Survey was 60, 61, and 60 years in 1985, 1990, and 1995, respectively, in men and 66, 66, and 64 years in women, respectively [17]. However women are significantly older than men (73.1 ±11.1 vs. 63.9 ±17.0) at presentation across all forms of ACS [11]. The mean age at presentation with ACS was 66 years in CZECH and Canadian ACS Registry, 67 yeas in BLITZ, 69 years in National Patient Registry Denmark and 73 years in a Danish study by Terkelsen *et al*. In the GRACE registry across 14 countries, the mean age of patients with STEMI was 64 years, with NSTEMI 68 years, and with unstable angina 66 years [18-20].

Incidence of CHD is significantly higher in men than women [21] and this sex difference has remained unchanged over decades [11]. Women presenting with chest pain are more likely to be discharged home form the emergency department [22] and are less likely to receive reperfusion or revascularisation therapy [22, 23]. Thus there are both gender related differences and gender biases and these gender related differences have changed little over time [23]. Gender related differences in treatment have been linked to a higher in-hospital mortality in women after MI [24-26] but this remains a controversial issue. Some randomized trials report greater hazard and less benefit with intervention in women [27, 28]. However, compared to men, high-risk women with ACS suffer an increased rate of refractory ischemia and re-hospitalization [29].

Acute coronary syndrome pathophysiology and case definition

There has been an apparent shift towards an increase in number of cases with unstable angina and chest pains while the number of patients with AMI especially STEMI has decreased over the period of time. In the recently reported CZECH registry, STEMI represented only one fifth of hospitalized confirmed acute coronary syndromes [10]. Different studies have reported 10-30% decrease in rate of myocardial infarction since 1990 while at the same time there was 50-80% rise in number of angina cases [16, 17]. The rate of confirmed ACS

has decreased by 12%, though rate for suspected ACS increased by a quarter. There has also been about 110% rise in number of patients presenting with chest pains [16]. In the EuroHeart Survey (EHS) of ACS which included more than ten thousand patients from 25 countries, the initial diagnosis was ST elevation ACS in 42.3%, non-ST elevation ACS in 51.2%, and undetermined electrocardiogram ACS in 6.5%. The discharge diagnosis was Q wave MI in 32.8%, non-Q wave myocardial infarction in 25.3%, and unstable angina in 41.9% [30].

The decline in overall rate of AMI and STEMI and increase in unstable angina and NSTEMI over the period of time may be the result of all of the following factors: increased survivorship from prior acute coronary events; an alteration in the clinical course of coronary heart disease, modification of pathophysiology by use of medical treatments (anti-platelet, lipid lowering and anti-hypertensive and ACE inhibitors); better diagnostic criteria for ACS, excluding those without biomarker evidence of necrosis or ECG change, but including those with more modest extent of myocyte injury and changes in case definition.

Trends in acute coronary syndrome mortality

To analyse the outcome of ACS over a period of time, we need to compare data from various registries. However, it must be kept in mind that different registries have recruited different patients; some registries include AMI (STEMI and NSTEMI) others report together all three forms of ACS (STEMI, NSTEMI and unstable angina); some registries enrol patients with suspected ACS, while others only patients with confirmed ACS [7]. Moreover, they have reported mortality over different time scales; before hospitalisation, in-hospital, 30-day, 6 month, one year etc.

Consistently, there has been a steady decline in CHD mortality in most of the developed countries over the last three decades. The first key question is whether this decline represents change in disease incidence or change in case fatality. The trend in ACS incidence has been discussed in previous section and it is estimated that in the populations where mortality has decreased, the reduction in coronary-event rates contributed a half to two thirds and reduction in case fatality accounted for the remainder one third [8].

Overall coronary heart disease mortality

Data collected on CHD mortality showed an increase in mortality rate in the 1950s and early 1960s, but a decline started in the late 1960s in the United States and Australia, followed by other industrialised countries [31].

In the United States, the overall CHD mortality declined from 1980 through 2002 by 52% in men and by 49% in women. In the Minnesota Heart Survey, there was about 3% annual decline in 1970s, 3-4% per year through early 1980s, and about 5.5% between 1985 and 1997 [17]. The death rate from all non-cardiovascular causes remained essentially unchanged during this period. A Canadian registry of more than 5000 patients with suspected ACS revealed 6.5% one-year mortality for Q-wave MI, 10% for non Q-wave MI, and 5.4% for unstable angina [32].

In Europe, over the past 30 years, death rates have been falling in most of the Northern and Western European countries but rising in some Central and Eastern European countries. The overall mortality in Europe has changed very little in this time, however, in the countries of European Union (EU), CHD mortality declined in all the countries over a decade from 1991-2002 but not equally across the EU. Death rate almost halved in the UK, Ireland, Finland and the Czech Republic. Most of the other countries showed a decline of 20-30% with the exception of Latvia and Poland where decline was just over 10% [15]. In Finland, there has been 63% decline in CHD mortality from 1982 to 1997 [33]. In the Danish National Patient Registry, the 28-day and 1-year mortality declined steadily from 1994-2002. The 28-day mortality was 25.9% in 1994 and 17.5% in 2002 [34]. In England, data from office for National Statistics has shown that age standardised CHD death rate, in under 65 years old, has fallen from 82 deaths/100,000 population in 1970 to 24 deaths/100,000 population in 2005 [35]. In Scotland the death rate for under 75 has fallen from 115 deaths/100,000 population in 1997 to 63 deaths/100,000 population in 2006 [13]. In the GRACE registry, the case fatality between discharge and 6 months was 4.8% for STEMI, 6.2% for NSTEMI, and 3.6% for unstable angina [18-20]. In Portugal, AMI mortality was lower in 2001 (9.9% male, 19.8% female) than in 1997 (11.6% male, 22.1% female) [11]. In The BLITZ survey of nearly two thousand acute MI patients in Italy in 2001, 30-day mortality was 9.4% for all AMI, 9.5% for STEMI, and 7.1% for NSTEMI [36]. The BLITZ-2 survey of 1888 NSTE-ACS patients (half had NSTEMI and half had unstable angina), done in 2003, revealed that the 30-day mortality in this cohort was reduced to 2.4% [37] (Figure 1).

In-hospital case fatality

In-hospital mortality is significantly different in various registries owing to different time periods, difference in inclusion and diagnostic criteria and geographic variation in disease management. However, there has been a consistent decline in mortality rate for definite hospitalized AMI which has substantially improved the long-term survival of AMI.

The major proportion of reduction in case fatalities since 1985 is due to reduced in-hospital mortality in both sexes [17]. In most of the studies, the mortality was higher for STEMI as compared with NSTE-ACS. The in-hospital mortality rate for STEMI was 10.9% in a Danish registry [38], 8.6 in CZECH [10], 7.8% in GRACE [18-20], 7.4% in BLITZ [36], 7% in the EuroHeart Survey and 4.9% in Canadian Registry [32]. The mortality figures were significantly lower for NSTE-ACS (NSTEMI and unstable angina); 4.2% in the CRUSADE Registry [39, 40], 2.8% in the EuroHeart Survey [30], 2.4% in the BLITZ-2 Survey and Canadian ACS Registry [32, 37] and 2.0% in CZECH registry [10]. However, some studies did show no difference in mortality between STEMI and NSTEMI or rather worse prognosis in NSTEMI [38] (Table I).

This decline probably represents better in-hospital management of ACS patients including coronary revascularisation, medical treatment and coronary care. Clearer evidence comes from longitudinal studies that employ consistent definitions throughout, defined populations and adjustment for differences in baseline risk. In such registry studies (GRACE) clear declines in in-hospital case fatality are due to differences in management [18]. The studies have also noted improvements in other outcomes including recurrent MI, pulmonary edema, cardiogenic shock and stroke in both STEMI and NSTEMI patients [18]. The increasing survival in patients admitted to hospital suggests that the trial-based efficacy of modern therapies is now translating into population-based effectiveness [41] (Figure 2).
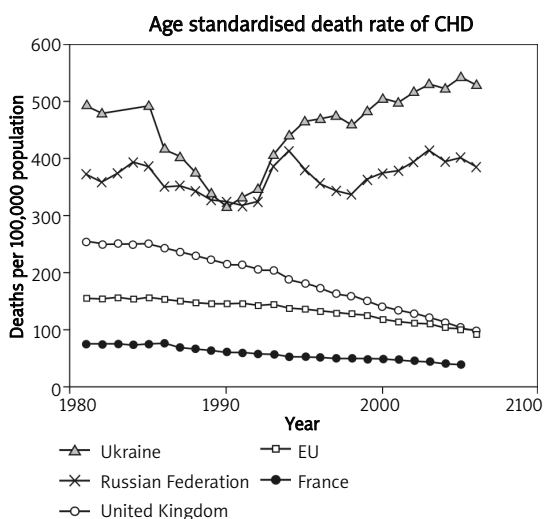

Figure 1. Trends in age standardised CHD death rates (1980-2006) in selected European countries (*Source: WHO/Europe, European HFA Database, July 2008*)

Table I. In-hospital case fatality in various registries (1994-2006)

| Diagnosis	Source	Time period	Country	Mean age	In-hospital mortality [%]
AMI	Aguado-Romeo	2000-2003	Spain	–	14.7
	Terkelsen	1999-2001	Denmark	73	13.6
	AMIS plus	1997-2002	Switzerland	65	9.9
	BLITZ	2001	Italy	67	7.4
	CZECH	2005	Czech	66	6.5
STEMI	NRMI (2-4)	1994-2000	US	66	15.5
	Terkelsen	1999-2001	Denmark	69	10.9
	CZECH	2005	Czech	65	8.6
	GRACE	1999-2006	14	64	7.8
	BLITZ	2001	Italy	66	7.5
	EHS-ACS	2000-2001	25	63	7
	Canadian ACS Registry	1999-2001	Canada	62	4.9
NSTEMI	Terkelsen	1999-2001	Denmark	75	13.3
	NRMI (2-4)	1994-2000	US	71	15.8
	GRACE	1999-2006	14	68	5.9
	CZECH	2005	Czech	68	3.3
	BLITZ	2001	Italy	68	5.2
	Canadian ACS Registry	1999-2001	Canada	67	2.5
NSTE-ACS	CRUSADE	2000-2002	US	68	4.2
	BLITZ-2	2003	Italy	68	2.4
	CZECH	2005	Czech	67	2.0
	EHS-ACS	2000-2001	25	66	2.8
	ACSIS 2002	2002	Israel	65	2.9
Unstable angina	CZECH	2005	Czech	67	1.3
	GRACE	1999-2006	14	67	0.4
	Canadian ACS Registry	1999-2001	Canada	66	2.7
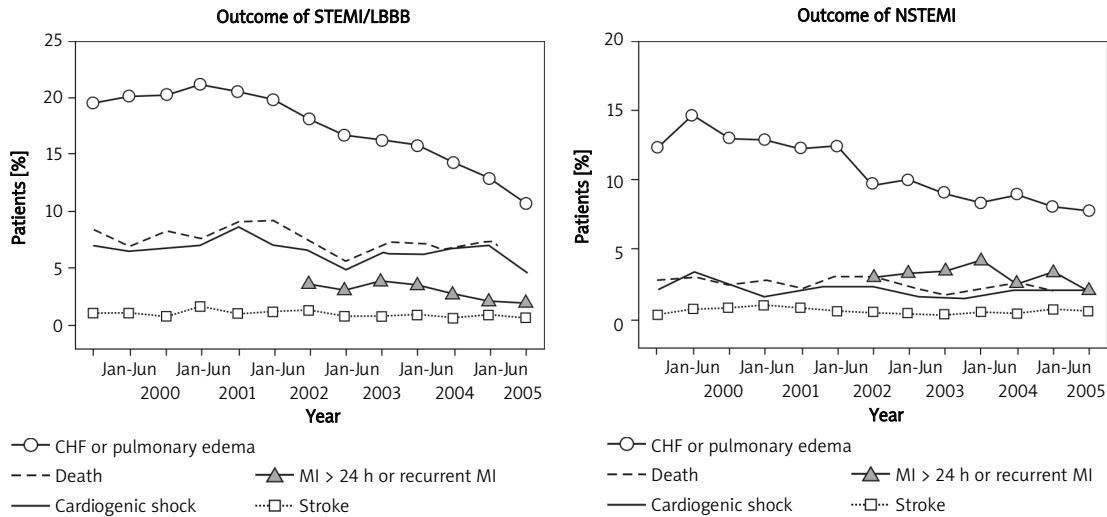
Figure 2. In-hospital outcomes in patients with STEMI/LBBB and NSTEMI. GRACE data reproduced with permission from JAMA (May 2, 2007, Vol. 297, No. 17)
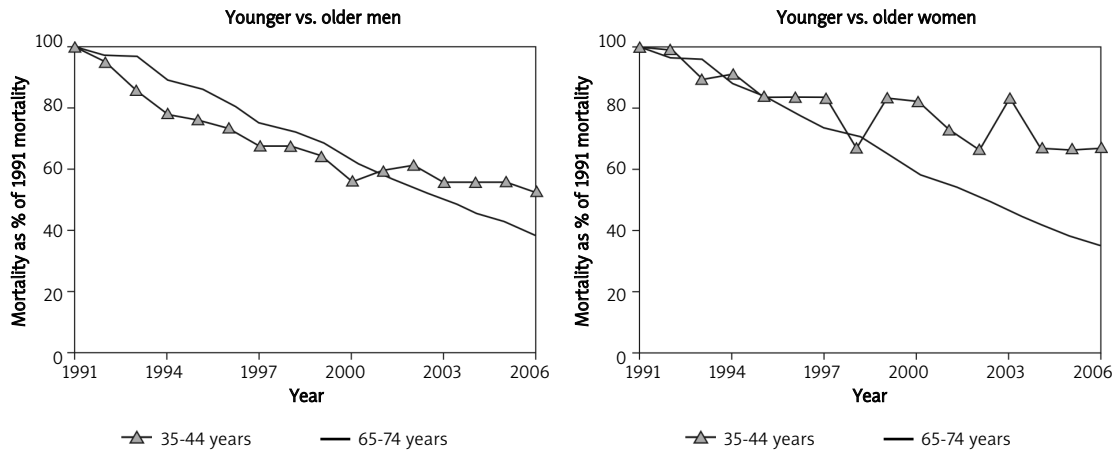*Source: GRACE Registry (JAMA, May 2007, Vol. 297)*

Figure 3. Trends in CHD mortality (1991-2006) in younger (35-44 years) and older (65-74 years) groups expressed as percentage of mortality seen in 1991
Source: BHF Statistics (www. heartstats.org)

Demographic variations

The in-hospital mortality figures are higher in older age groups for all types of ACS (1.9% for 55-64, 3.7% for 65-74, 6.2% for 75-84 and 14.5% for 85+) [42]. It is important to note that in recent years, the mortality in younger age groups is not declining as fast as in older age groups and in some cases it is even rising. In England and Wales, the data from 1984 to 2004 revealed that among men aged 35-44 years, CHD mortality rates increased for the first time in 2002, despite a decline in the overall age-adjusted mortality rate [43]. Similar trend has also been noticed in the United States [44]. The mortality rate also seems to be slowing in both men and women aged 45-54 [45]. This unfavourable trend in younger age group is probably due to rise in risk factors for CHD, specifically obesity and diabetes [46] (Figure 3).

The decline in ACS mortality has been greater in higher socioeconomic groups [47]. This observed difference may be due to earlier and better risk factor modification in higher socioeconomic groups or availability of differentially better treatment options in some health care systems.

Geographical variations

While the rate of CHD mortality has been falling in most of Western Europe, America and Australia, the countries of Eastern and Central Europe (most notably the countries of former USSR) have experienced a substantial increase in CHD mortality. In the Ukraine, for example, the death rate from CHD rose by over 60% between 1990 and 2000. According to WHO statistics 2002 the lowest documented CHD death rate (400/million population) was observed in Dominica, Kuwait, Korea,
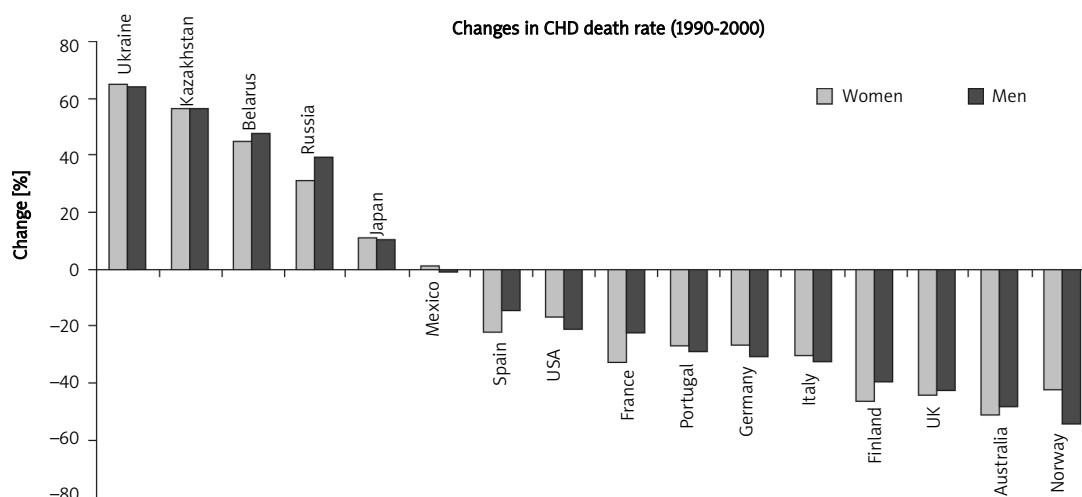
Figure 4. Geographic trends in change in CHD death rates (1990-2000) in selected countries around the world
Source: World Health Organisation 2004

Brunei Darussalam, Guatemala and Kiribati. The highest documented CHD dearth rate (4000/million population) was seen in former USSR states including Ukraine, Belarus, Georgia, Russia, Estonia, Moldova and Latvia (Figure 4).

Marked differences are also present in various regions of same country. In the United Kingdom, for example, death rates from CHD are highest in Scotland and Northern England, lowest in South England and intermediate in Wales and Northern Ireland [43]. Socio-economic factors interact with diet, smoking, exercise and medical management and within countries such socio-economic factors are powerfully related to the regional variations in death rates from CHD [43].

Ethnic variations

Different ethnic groups living in same geographic area show difference in CHD prevalence and mortality. South Asians living in the UK have a higher CHD death rate than average population. The difference in the death rates between those born in South Asia and general population increased in the 1970s and 1980s.This was because the death rate from CHD did not fall as fast in South Asian groups as in the rest of the population. From 1971 to 1991 the mortality rate for the whole population fell by 29% in men and 17% for women whereas in people born in South Asia it fell by 20% for men and 7% for women [48]. National Registry of Myocardial Infarction (NRMI) in the US also revealed that in-hospital mortality was higher among African American women compared with white women and it has remained unchanged over time [23]. Data from the Auckland Coronary or Stroke (ARCOS) study for the years 1983 to 1992 revealed that the mortality rate was consistently higher among

people from Maori and Pacific Islands than in those of European origin living in New Zealand [49].

These ethnic differences may be substantially accounted for by differences in coronary risk factor profile and difference in disease pathophysiology in different ethnic groups though there is also some evidence of differences in access to medical care in certain groups, but hospital care is usually similar in all groups [49].

Is change in outcome attributable to changes in cardiovascular risk factors?

The risk factors for ACS can be broadly classified into modifiable and non-modifiable factors. INTER-HEART study, which looked at the potentially modifiable risk factors associated with MI in 52 countries, found that cigarette smoking, abnormal lipid profile, high blood pressure, diabetes, abdominal obesity, stress, lack of fruits and vegetables consumption and lack of daily exercise account for more than 90% risk of MI worldwide in both men and women [50]. INTERHEART also calculated population attributable risks (PAR), the relative risk associated with a given factor in the context of the prevalence of the condition within a population. Population attributable risks was 35.7% for smoking, 49.2% for raised ApoB/ApoA1 ratio, 17.9% for hypertension, 20.1% for abdominal obesity, 32.5% for psychosocial factors, 13.7% for lack of fruit and vegetable consumption and 12.2% for lack of regular physical activity [50]. Other studies have also found that cigarette smoking, blood pressure, and total blood cholesterol are most consistently and powerfully correlated with CHD [9, 51, 52]. These major risk factors explain at least 75% of new cases of cardiovascular disease [53].

The epidemiological studies from 1950 onwards, have shown substantial reductions in coronary heart disease from changes in major risk factors [54]. Studies using the IMPACT model [55] suggested that population-wide change in risk factors contributed approximately 60% towards the decline in CHD mortality that occurred in Scotland between 1975 and 1994 [55] and about 58% of the CHD mortality decline in England and Wales between 1981 and 2000 [56]. In New Zealand, nearly 50% fall in CHD mortality can be attributed to reductions in major cardiovascular risk factors [57]. In Finland, from 1982 to 1997, risk factor modification explained about 53-72% of the mortality reduction [33]. Studies from US have shown approximately 44% CHD death reduction attributable to changes in risk factors [58].

Since mid 1980s, there has been steady but cumulatively substantial reduction in coronary risk factors in western population, notably reduction in cigarette smoking prevalence, mean systolic blood pressure, mean non-HDL cholesterol levels (with an increase in HDL cholesterol) and physical inactivity [9, 12]. However there has been an increase in body mass index and prevalence of diabetes [46, 58]. The changes in cigarette smoking and cholesterol profile can each explain half of the reduction seen in MI incidence where as the fall in blood pressure (13%) and physical inactivity (5%) can explain the remainder, although these reductions are partially offset by increases in the body-mass index and the prevalence of diabetes [12, 58].

Risk factor reductions help in reducing mortality in patients with CHD (secondary prevention) as well as in individuals without recognised CHD (primary prevention). It is estimated that a half to two thirds

of the reduction in CHD death may be attributed to primary prevention and remainder attributed to acute treatment and secondary prevention [59]. A meta-analysis of twenty studies has shown a 36% reduction in crude relative risk of mortality for those CHD patients who quit smoking compared with those who continue to smoke [60].

In summary, about one half to two thirds of the decline seen in ACS mortality can be attributed to changes in population risk status. Furthermore, in the countries where coronary mortality is increasing, for example some countries in Eastern Europe, deterioration in coronary risk profile is the likely culprit. Figure 5 shows the population trends in cigarette smoking and this closely reflects the CHD burden in these countries.

Thus, the "environmental" impact of changing risk factors interacts with underlying genetic traits that have their phenotypes in hypertension, hyperlipidaemia and diabetes and the result manifests as occult and symptomatic coronary and peripheral arterial disease. A vigorous approach towards earlier identification, better treatment and primary prevention of these risk factors is required to achieve CHD targets globally.

Has management of acute coronary syndrome changed and has it contributed to decline in case fatality?

There are widespread differences in the management of ACS patients depending on healthcare system and available resources. Studies evaluating AMI treatment in the United States and Canada, for example, have demonstrated substantially higher rates of coronary interventions in the United States [61, 62]. The practice also varies substantially according to geographic regions within the United States [63]. Patients with MI in New England have higher rates of medical therapy use and lower 30-day mortality rates than patients in other US regions [64]. There are also gender differences in the treatment of ACS which have been reviewed by Gold and Krumholz in 2006 [65]. In some registries significantly fewer women than men received aspirin, clopidogrel, GP IIb/IIIa antagonists, β-blockers and ACE inhibitors [66]. National Registry of Myocardial Infarction also revealed that in the United States, racial differences between white and African American populations exist for rates of reperfusion therapy and coronary angiography and this difference remained unchanged between 1994 and 2002 [23]. Despite these variations there is a general trend towards increased usage of evidence based therapeutic agents. In Auckland, New Zealand, approximately 50% fall in CHD mortality rate can be attributed to medical therapies [57]. In Finland, from 1982 to 1997, improved treatments explained approximately 23% of the
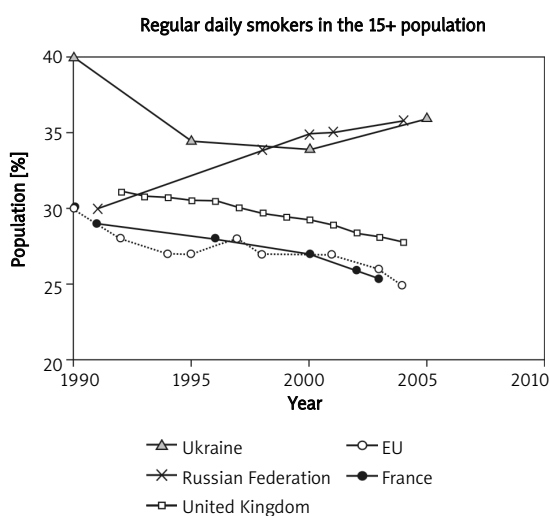
Regular daily smokers in the 15+ population

Figure 5. Trends in smoking (1990-2006) expressed as percentage of regular smokers among adult (15+) population in selected European countries
Source: WHO/Europe, European HFA Database, July 2008

mortality reduction [33]. Similarly in GRACE, a multi-national observational study, improvement in treatment of ACS patients was associated with better outcome and reduced complications at 6 months [18].

Medication

There has been a significant change in the usage of medications in the acute phase of ACS and for secondary prevention following ACS. There has been increased use of β-blockers, ACE inhibitors, aspirin, anti-thrombins and statins. However, consistent with the guidelines, the routine use of calcium channel blockers and lidocaine has decreased over the period of time [17].

In Europe, surveys conducted in mid 1990s (EUROASPIRE-1) and 2000 (EUROASPIRE-II), showed significant increase in usage of all evidence based ACS treatments; the use of anti-platelet drugs increased from 81% in 1990s to 90% in 2000, β-blockers from 54 to 66%, lipid lowering therapy from 32 to 43% and ACE inhibitors from 30 to 38%, respectively [67, 68]. In EHS-ACS, the use of aspirin, β-blockers, ACE inhibitors, and heparins for patients with ST elevation ACS were 93.0, 77.8, 62.1, and 86.8%, respectively, with corresponding rates of 88.5, 76.6, 55.8, and 83.9% for non-ST elevation ACS patients [30]. The GRACE registry also showed increase in use of aspirin, β-blockers, statins, ACE inhibitors, LMWH and GP IIb/IIIa inhibitors from 1999 to 2005 [69]. In likely consequence this change in evidence based treatment has resulted in significant reductions in CHD case fatality [58, 59] (Table II).

Reperfusion for ST elevation myocardial infarction

Thrombolysis

Thrombolysis for AMI was the mainstay of treatment in 1980s and 90s. The use of thrombolytic therapy increased from 1985 to 1990 but showed little change from 1990 to 1995 [17]. Thereafter the use of thrombolytic therapy has declined as more and more patients with AMI are being treated with percutaneous coronary intervention (PCI) [17]. In the GRACE registry, use of fibrinolytic therapy decreased from 41% in 1999 to 16% in 2005. The median time for fibrinolysis also declined significantly over this time, though one-third of potentially eligible patients still received no reperfusion therapy [70]. AMIS plus registry (1997-2005) also revealed a marked reduction in the use of thrombolysis (47 to 6%) and also in the proportion of patients who did not receive any reperfusion treatment (45 to 20%) [71].

Percutaneous coronary intervention and primary percutaneous coronary intervention

There has been a marked overall rise in the number of percutaneous coronary procedures since 1990, though there are huge geographical variations. For example, since 1990 rates of PCI have increased 20 fold in Hungary, 15 fold in Italy and 12 fold in Finland. More recently, the biggest increase in the rates of PCI have been in the Eastern European countries and Baltic States, for example a 12 fold increase in Latvia between 1995 and 2000 [15]. The data from the British Cardiovascular Intervention Society showed that there was 7 fold increase in cases of PCI from 1991 to 2005. In the GRACE registry, there was an increasing trend in use of primary PCI from 15% in 1999 to 44% in 2006 for patients with ST elevation or left bundle-branch block MI [70]. AMIS plus registry (1997-2005) also revealed significant increase in the proportion of patients treated by primary PCI (8 to 74%) [71]. In EHS-ACS, PCI was performed in 40.4% of ST elevation ACS and 25.4% non-ST elevation ACS (Figure 6) [30].

Coronary artery bypass graft

Coronary artery bypass graft (CABG) is seldom an acute ACS treatment, but has a definite role in later management of ACS and may impact upon long term survival. Data from the UK cardiac surgical registrar shows that the number of CABG operations increased rapidly from early 1980s to mid 90s but has remain unchanged since then. The rapid rise seen in 80s and early 90s was more marked in men than in women [17]. In the EuroHeart Survey, CABG was performed 3.4% for STEMI and 5.4% for NSTEMI [30]. In the United states the CABG rates increased in 1980s and early 90s remained stable in late 90s and substantially

Table II. Change in therapy for STEMI and NSTE-ACS (1999-2005)

Therapy	STEMI [%]		NSTE-ACS [%]	
	1999	2005	1999	2005
Aspirin	95.1	96.7	93.3	95.9
β-Blockers	83.6	94.3	80.0	90.0
Ca⁺-channel blockers	21.1	11.1	37.3	25.0
Statins	37.3	85.4	40.0	82.5
ACE-I/ARB	64.3	85.8%	52.6	75.1
LMWH	42.8	62.9%	48.1	70.8
Un-fractionated heparin	62.8%	42.4	52.6	33.7
Thienopyridine	29.5	78.2	19.8	71.1
GP IIb/IIIa antagonist	15.6	39.2	9.0	19.6
Fibrinolytics	49.5	27.8	–	–
PCI	32.4	63.5	16.9	34.6
pPCI	16.1	52.7	–	–
CABG	3.2	2.7	6.8	5.1

Source: GRACE registry

decreased then onwards [72]. There was a modest decline in number of patients undergoing CABG in GRACE registry [18].

Future trends

Based upon current trends mortality from ACS will continue to decline in the developed countries as a consequence of better primary and secondary prevention and better management of acute coronary disease. However, there are warning signs that the decline may be attenuated or even reversed, as a late consequence of the rising prevalence of obesity and diabetes [73]. Evidence that the decline in mortality has attenuated is already apparent in the younger (35-44 years) age group [70]. The WHO estimates that CHD mortality will remain the number one killer worldwide in next decades (12.2% deaths attributable to CHD in 2004 vs. 14.3% projected in 2030). It is estimated that 7.5 million people died from coronary heart disease in 2005 and nearly 10 million people will die from CHD in 2015, maintaining coronary disease as the single leading cause of death [74].

Epidemiological trends in acute coronary syndromes provide insights into the impact of risk factors on disease incidence and the impact of acute and subsequent care on case fatality and other important measures of outcome including re-infarction and heart failure. However, robust multinational longitudinal studies are required to reliably determine changes in disease morbidity and mortality. Such studies allow health care providers to make reliable decisions on the distribution of resources for the diagnosis, prevention and treatment of ACS. Furthermore, studies provide

a "real world" context to interpret clinical trials and to devise novel therapeutic strategies for testing in randomised trials.

Conflict of interest

KAAF is co-chair for GRACE Registry and on the Steering Committee of the ESC Euroheart Regisrty on ACS.

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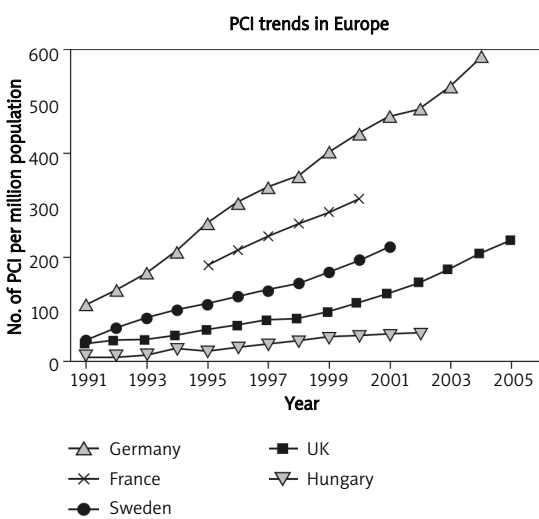
Figure 6. Trends in percutaneous coronary interventions (1991-2005) in selected European countries
Source: European cardiovascular disease statistics 2008

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