Prevalence of Conventional Risk Factors in Patients With Coronary Heart Disease

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Context It is commonly suggested that more than 50% of patients with coronary heart disease (CHD) lack any of the conventional risk factors (cigarette smoking, diabetes, hyperlipidemia, and hypertension). This claim implies that other factors play a significant role in CHD and has led to considerable interest in nontraditional risk factors and genetic causes of CHD.

Objective To determine the prevalence of the 4 conventional risk factors among patients with CHD.

Design, Setting, and Patients In 2002-2003, we analyzed data for 122 458 patients enrolled in 14 international randomized clinical trials of CHD conducted during the prior decade. Patients included 76 716 with ST-elevation myocardial infarction, 35 527 with unstable angina/non–ST-elevation myocardial infarction, and 10 215 undergoing percutaneous coronary intervention.

Main Outcome Measures Prevalence of each conventional risk factor and number of conventional risk factors present among patients with CHD, compared between men and women and by age at trial entry.

Results Among patients with CHD, at least 1 of the 4 conventional risk factors was present in 84.6% of women and 80.6% of men. In younger patients (men ≤55 years and women ≤65 years) and most patients presenting either with unstable angina or for percutaneous coronary intervention, only 10% to 15% of patients lacked any of the 4 conventional risk factors. This pattern was largely independent of sex, geographic region, trial entry criteria, or prior CHD. Premature CHD was related to cigarette smoking in men and cigarette smoking and diabetes in women. Smoking decreased the age at the time of CHD event (at trial entry) by nearly 1 decade in all risk factor combinations.

Conclusions In direct contrast with conventional thinking, 80% to 90% of patients with CHD have conventional risk factors. Although research on nontraditional risk factors and genetic causes of heart disease is important, clinical medicine, public health policies, and research efforts should place significant emphasis on the 4 conventional risk factors and the lifestyle behaviors causing them to reduce the epidemic of CHD.

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APPRECIATION OF THE CRUcial role of risk factors in the development of coronary heart disease (CHD) is one of the most significant advances in the understanding of this important disease. Extensive epidemiological research has established cigarette smoking,[1] diabetes,[2] hyperlipidemia,[3] and hypertension[4] as independent risk factors for CHD. In addition, treatment of these risk factors has been convincingly shown to reduce the risk of future cardiac events.[1,5] Because of the strength of evidence supporting their role in the pathogenesis of CHD, these 4 risk factors have often been labeled as "conventional" risk factors.

Although the importance of conventional risk factors is well established, it is commonly suggested that more than 50% of patients with CHD lack any of the conventional risk factors.[6-13] This implies that other factors play a significant role in the development of this disease and, furthermore, that there is a substantial void in current understanding of the pathogenesis of CHD. This perceived void has led to considerable research on nontraditional risk factors and genetic causes of heart disease. Yet, data to support this "50%" belief are limited, and some have suggested that conventional risk factors play a much more significant role.[14,15] Determining the validity of this idea is important for scientific accuracy and to guide the practice of clinical medicine, public health policies, and prioritization of research efforts. In addition, patients and physicians can better understand the impact of preventing or modifying these specific risk factors on the risk of future CHD.

We therefore sought to determine the prevalence of the 4 conventional risk

See also pp 891, 932, and 947 and Patient Page.

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factors—cigarette smoking, diabetes, hyperlipidemia, and hypertension—in a broad population of patients with CHD.

METHODS

We compiled data from 14 clinical trials involving 122 458 patients with a wide spectrum of CHD. Briefly, GUSTO I,[16] GUSTO III,[17] and GUSTO V[18] studied thrombolytic therapies in ST-elevation myocardial infarction (MI). GUSTO IIb compared hirudin with heparin in both ST-elevation MI and unstable angina/non–ST-elevation MI.[19] PURSUIT,[20] PARAGON A,[21] PARAGON B,[22] CAPTURE,[23] and GUSTO IV ACS[24] studied intravenous glycoprotein IIb/IIIa inhibitors in patients with unstable angina/non–ST-elevation MI. EPIC studied abciximab in angioplasty patients with recent MI, unstable angina, or high-risk angiographic or clinical characteristics.[25] EPILOG studied abciximab in urgent or elective percutaneous coronary intervention (PCI).[26] CAVEAT I and II compared balloon angioplasty with directional coronary atherectomy in native coronary stenoses[27] and saphenous vein graft disease,[28] respectively. Finally, IMPACT II studied the use of eptifibatide in PCI.[29]

Study End Points

Information regarding cigarette smoking, diabetes, hyperlipidemia, and hypertension had been prospectively recorded at trial entry in all studies. Information regarding family history of CHD was not collected in CAPTURE, GUSTO III, and GUSTO IV ACS. Information regarding body mass index was not collected in GUSTO IV. Current smoking was noted if the patient smoked at the time of the index event; however, EPIC, EPILOG, CAPTURE, and GUSTO IV ACS noted whether the patient had smoked in the previous year. Diabetes, hyperlipidemia, and hypertension were documented if a diagnosis had been made prior to randomization and were identified through physician interview and by patient self-report.

The prevalence of each risk factor was calculated. Patients were categorized according to their number of risk factors. Subgroups included age, sex, geographic location, and absence of prior CHD. Prior CHD was noted with history of MI, prior PCI, or prior coronary artery bypass graft surgery. Three further subgroups included ST-elevation MI (GUSTO I, GUSTO IIb [ST-elevation group], GUSTO III, and GUSTO V); unstable angina/non–ST-elevation MI (GUSTO IIb [non–ST-elevation group], PURSUIT, PARAGON A, PARAGON B, CAPTURE, and GUSTO IV ACS); and PCI (EPIC, EPILOG, CAVEAT I, CAVEAT II, and IMPACT II), which enrolled primarily those with stable/unstable angina but also a small number with ST-elevation MI (EPIC and IMPACT II). Furthermore, we determined the relationship between number of conventional risk factors and mean age at trial entry.

Statistical Methods

We had access to the original raw data for all of the clinical trials, and these data were combined to perform the analyses. Categorical data are presented as percentages and continuous data are presented as means (SDs). Frequencies were analyzed by χ^2 tests and continuous variables were analyzed by Wilcoxon 2-sample tests. We used SAS version 8 software (SAS Institute Inc, Cary, NC) to analyze all data. All comparisons were considered significant at $P<.05$.

RESULTS

Overall among patients with CHD, the prevalence of those with at least 1 of the 4 conventional risk factors was 84.6% in women and 80.6% in men (TABLE 1). For all risk factors except cigarette smoking, the prevalence was significantly higher in women than in men. However, women aged 65 years or younger had nearly identical rates of smoking as similarly aged men (TABLE 2).

The prevalence of the 4 conventional risk factors was related to age. The majority (85%-90%) of patients with premature CHD had at least 1 conventional risk factor, with cigarette smoking being the most common.

Table 1. Prevalence of Conventional Risk Factors by Sex*

	Women (n = 34 589)	Men (n = 87 869)
ST-elevation MI, No.	19 513	57 203
Unstable angina/non–ST-elevation MI, No.	12 367	23 160
Percutaneous coronary intervention, No.	2709	7506
Age, mean (SD), y	66.1 (11.2)	59.9 (11.6)
Current smoking, No. (%)†	10 107 (29.5)	36 301 (41.6)
Diabetes, No. (%)†	7989 (23.2)	13 424 (15.3)
Hyperlipidemia, No. (%)†	13 335 (39.6)	29 252 (34.1)
Hypertension, No. (%)†	19 271 (55.9)	33 624 (38.4)
No. of risk factors, No. (%)†		
0	5118 (15.4)	16 454 (19.4)
1	12 348 (37.2)	36 539 (43.0)
2	11 025 (33.2)	23 622 (27.8)
3	4310 (13.0)	7558 (8.9)
4	437 (1.3)	787 (0.9)

Abbreviation: MI, myocardial infarction.
*All differences between women and men are statistically significant at $P<.001$.
†Denominators differ slightly for these numbers because of lack of complete data. For No. of risk factors, 33 238 women and 84 960 men had complete data.

Among women and men aged 45 years or younger, the prevalence of patients without any of the 4 conventional risk factors was only 9.4% and 11.4%, respectively. There was a gradual increase with age in the prevalence of patients lacking any of the conventional risk factors. Only among women older than 75 years and men older than 65 years did the prevalence of patients lacking any of the 4 conventional risk factors exceed 20%. Older patients had much lower rates of cigarette smoking but typically higher rates of diabetes and hypertension.

Few young patients (≤65 years) lacked any of the 4 conventional risk factors, irrespective of trial entry criteria (TABLE 3). Fewer older patients (>65 years of age) presenting with unstable angina/non–ST-elevation MI or for PCI lacked any of the conventional risk factors than those presenting with ST-elevation MI. Patients presenting with ST-elevation MI had higher rates of cigarette smoking but lower

rates of diabetes, hyperlipidemia, and hypertension than those with either unstable angina/non–ST-elevation MI or PCI. Patients presenting for PCI had intermediate rates of cigarette smoking but the highest prevalence of diabetes, hyperlipidemia, and hypertension. The overall pattern of conventional risk factors existed irrespective of geographic origin (TABLE 4). Patients without prior CHD (74.4% of women and 69.7% of men) had slightly higher rates of cigarette smoking and slightly lower rates of hyperlipidemia, hypertension, and diabetes compared with those with prior CHD (data not shown). The overall prevalence of patients without prior CHD who lacked any of the 4 conventional risk factors remained largely unchanged (17.2% in women and 20.7% in men).

The inclusion of a family history of CHD and obesity (body mass index [calculated as weight in kilograms divided by the square of height in meters] ≥30) as risk factors further reduced the prevalence of patients without risk factors to 8.5% in women and 10.7% in men.

As the number of conventional risk factors increased, the mean age at the time of CHD event (at trial entry) decreased by a decade (FIGURE 1), primarily because of cigarette smoking in both sexes (FIGURE 2).

COMMENT

Our study indicates that in patients with CHD, conventional risk factors were present at a much higher prevalence than commonly believed, with only 15% to 20% of patients lacking any of the conventional risk factors for the disease. In younger patients (men ≤55 years and women ≤65 years) and most patients presenting with either unstable angina or for PCI, the prevalence of conventional risk factors was even higher, with only approximately 10% to 15% of patients lacking any of the 4 conventional risk factors. This overall pattern was largely independent of sex, geographic region, or entry criteria of the trial. Thus, in direct contrast with conventional thinking, only a small minority of patients with CHD lacks conventional risk factors.

Cigarette smoking played a critical role in the development of premature CHD, reducing the age at trial entry by about 1 decade in every risk factor subgroup. In addition, more than 70% of the 12 154 patients aged 45 years or younger were current cigarette smokers. Although cigarette smoking is harmful at any age, the increase in relative risk of coronary events in young persons is particularly magnified given their baseline low risk. Furthermore, cigarette smoking acts synergistically with other conventional risk factors, greatly increasing the baseline risk associated with each risk factor individually.[30] Thus, elimination of cigarette smoking is of dramatic public health importance because it could delay the onset of CHD by a decade.

Overall, the prevalence of risk factors was greater in women than in men. Because CHD typically presents 10 years later in women than in men, higher risk factor prevalence in women is necessary to lead to the development of CHD at the same age as in men.[31] The higher prevalence of diabetes in women than in men is consistent with other studies that have shown that diabetes is a powerful risk factor in women, virtually negating the usual protection women have against cardiac disease.[32] The only risk factor with a lower prevalence in women was cigarette smoking. However, younger women (≤65 years) smoked at a virtually identical rate to men, reflecting widespread adoption of smoking among

Table 2. Prevalence of Conventional Risk Factors by Age and Sex*

	Age, y									
	≤45		46-55		56-65		66-75		>75	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Individual Risk Factors										
No.	1623	10 531	4608	21 632	8858	25 666	12 285	22 215	7215	7825
Current smoking	72.0	71.7†	57.9	58.7†	38.9	39.8†	19.1	23.3	7.9	11.8
Diabetes	17.8	7.4	19.7	12.1	24.1	16.9	25.2	19.2	22.0	18.4
Hyperlipidemia	33.2	37.0‡	41.0	38.5‡	45.0	36.3	42.2	30.7	29.1	20.4
Hypertension	37.1	25.3	46.8	33.6	54.6	40.5	60.1	45.1	60.2	43.1
Total No. of Risk Factors										
No. with complete data	1569	10 251	4453	20 996	8524	24 817	11 807	21 411	6885	7485
No. of risk factors										
0	9.4	11.4	10.7	13.3	12.0	18.4	15.8	24.6	23.3	35.5
1	41.9	48.0	35.5	44.4	34.5	41.8	36.4	41.5	41.7	40.7
2	30.8	29.8	35.1	30.1	34.7	29.2	34.6	26.0	28.1	19.3
3	15.2	9.9	16.3	10.8	16.7	9.5	12.4	7.4	6.7	4.2
4	2.7	0.9	2.5	1.3	2.0	1.1	0.8	0.6	0.2	0.2

*All data are expressed as percentages unless otherwise specified. Risk factor prevalence differences between women and men are statistically significant at $P<.001$ unless otherwise noted.
†Risk factor prevalence differences between women and men are nonsignificant.
‡Risk factor prevalence differences between women and men are statistically significant at $P<.01$.

this generation of women. Cigarette smoking has a similar effect on increasing the risk of CHD in both men and women.[33] Therefore, reductions in the prevalence of diabetes and smoking cessation have the potential to dramatically reduce the burden of CHD in women.

Our observation of a steadily decreasing prevalence of conventional risk factors with age may be explained by 3 reasons. First, clinical trials have a selection bias limiting enrollment to a healthier subset of the elderly population.[34] Second, age steadily increases the absolute baseline risk of CHD independent of the conventional risk factors[35]; therefore, patients without risk factors will tend to present at a much later age once their baseline absolute risk increases sufficiently to cause a significant prevalence of disease. Third, this decreasing prevalence reflects an inherent survivor bias because patients with conventional risk factors die at a much younger age.[15] Conventional risk factors increase the risk of coronary events in elderly persons at a similar magnitude to that of middle-aged individuals.[36] Thus, given their increased absolute baseline risk, the benefit of preventing or treating conventional risk factors in elderly patients is greater in absolute terms than the benefit in younger patients.[37]

Although widely asserted,[6-13] the belief that more than 50% of patients with CHD lack conventional risk factors is not supported by primary data. A related assertion is that the conventional risk factors explain less than 50% of the incidence of CHD.[38] Yet, there are inaccuracies in the interpretation of the primary data that have been referenced to support this claim.[14] In fact, 2 studies have shown that lack of hypertension, hyperlipidemia, and cigarette smoking was associated with a 77% to 92% reduction in cardiovascular mortality,[15] findings similar to other studies.[14,30] In essence, patients without conventional risk factors are unlikely to develop CHD.

Table 3. Prevalence of Conventional Risk Factors According to Trial Entry Criteria*

	Age, y									
	≤45		46-55		56-65		66-75		>75	
Trial Entry Criteria	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
ST-Elevation MI										
Individual risk factors										
No.	1009	7736	2520	14 601	4877	16 683	6755	13 442	4352	4741
Current smoking	79.4	74.2	68.2	61.9	48.5	43.0	24.5	26.1‡	9.9	13.2
Diabetes	15.9	6.5	18.3	11.0	21.7	15.2	21.9	17.0	19.7	15.6
Hyperlipidemia	27.1	32.6†	37.3	33.6	39.3	31.3	36.2	25.7	25.5	15.9
Hypertension	30.4	21.8	40.6	28.9	47.5	35.8	54.0	40.1	56.0	37.9
Zero risk factors										
No. with complete data	977	7547	2441	14 203	4715	16 167	6490	12 948	4138	4521
Zero risk factors	8.4	12.0	8.4	14.3	12.5	20.3	18.6	27.5	26.3	40.6
UA/NSTEMI										
Individual risk factors										
No.	453	1908	1608	4930	3149	6650	4585	7005	2572	2667
Current smoking	60.0	67.2†	44.1	55.8	26.1	36.6	12.3	20.3	4.5	9.8
Diabetes	16.8	9.0	18.6	12.8	25.0	19.9	28.7	22.2	25.8	22.3†
Hyperlipidemia	37.2	42.6‡	40.4	44.4†	48.9	42.5	47.4	36.0	33.0	26.0
Hypertension	45.5	32.9	52.8	40.7	61.7	47.6	67.1	51.5	66.1	50.4
Zero risk factors										
No. with complete data	441	1869	1572	4825	3060	6504	4479	6843	2498	2589
Zero risk factors	12.9	10.8	15.5	11.9	12.6	15.2	13.3	20.7	19.4	28.2
Percutaneous Coronary Intervention										
Individual risk factors										
No.	161	887	480	2101	832	2333	945	1768	291	417
Current smoking	59.2	58.2§	49.7	42.9†	30.9	25.6†	13.5	13.3§	6.8	7.7§
Diabetes	32.3	12.0	31.0	17.7	34.9	20.6	31.7	24.3	22.3	25.4§
Hyperlipidemia	60.6	63.0§	62.2	58.8§	64.6	55.0	60.7	47.8	47.3	34.7†
Hypertension	55.0	40.2	59.0	49.4	68.7	53.7	69.7	57.5	70.4	54.9
Zero risk factors										
No. with complete data	151	835	440	1968	749	2146	838	1620	249	375
Zero risk factors	6.0	7.4	5.9	9.9	6.8	14.0	7.3	17.5	11.6	23.7

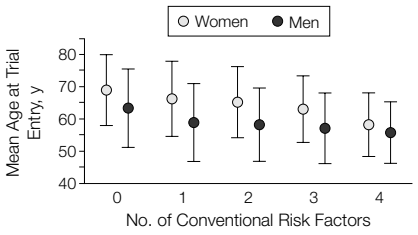
Abbreviations: MI, myocardial infarction; UA/NSTEMI, unstable angina/non–ST-elevation myocardial infarction.
*Data are expressed as percentages unless otherwise specified. Risk factor prevalence differences between women and men are statistically significant at $P<.001$ unless otherwise noted. Trials that used each entry criterion are as follows: ST-elevation MI: GUSTO I, GUSTO IIb (ST-elevation group), GUSTO III, GUSTO V; UA/NSTEMI, CAPTURE, GUSTO IIb (excluding ST-elevation group), GUSTO IV ACS, PARAGON A, PARAGON B, PURSUIT; percutaneous coronary intervention, CAVEAT I, CAVEAT II, EPIC, EPILOG, IMPACT II.
†Risk factor prevalence differences between women and men are statistically significant at $P<.01$.
‡Risk factor prevalence differences between women and men are statistically significant at $P<.05$.
§Risk factor prevalence differences between women and men are nonsignificant.

Table 4. Prevalence of Conventional Risk Factors According to Geographic Region of Origin*

	Region															
	United States		Western Europe		Canada		Eastern Europe		Australia/ New Zealand		Middle East		Latin America/ Mexico		Africa	
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men
Individual Risk Factors																
No.	14 559	35 975	10 559	29 751	2458	6456	3351	4934	2010	5340	1090	4203	356	698	146	459
Current smoking	35.6	40.3	25.4	43.9	34.3	40.7	18.7	41.7	25.7	31.9	23.5	50.0	17.7	45.0	29.5	49.8
Diabetes	26.2	17.3	20.4	12.6	20.7	16.3	23.6	16.3	13.6	11.3†	28.9	18.7	25.8	20.9‡	30.8	18.7†
Hyperlipidemia	46.9	40.9	34.1	29.5	34.0	31.7§	32.0	24.5	43.9	37.1	26.3	21.3	40.0	39.1‡	20.4	20.0‡
Hypertension	58.6	44.5	49.9	32.5	50.8	32.9	67.6	46.4	51.5	36.1	54.1	27.3	71.9	54.0	62.3	29.4
Total No. of Risk Factors																
No. with complete data	13 877	34 567	10 312	29 116	2363	6190	3170	4696	1901	5067	1058	4124	355	698	142	449
No. of risk factors																
0	11.1	16.4	20.2	22.0	17.4	21.2	14.7	17.3	18.4	23.6	18.9	20.8	11.5	13.0	13.4	19.6
1	33.0	39.1	40.6	45.7	39.6	45.4	40.0	46.4	38.7	44.0	41.2	49.4	36.1	34.2	40.8	51.4
2	36.5	31.8	29.0	24.8	30.9	25.1	34.3	27.2	33.4	25.3	28.9	22.3	38.0	35.2	37.3	21.4
3	17.1	11.5	9.7	6.8	10.8	7.2	10.5	8.4	8.9	6.6	10.3	6.8	14.4	15.6	8.5	6.9
4	2.3	1.2	0.5	0.7	1.4	1.0	0.4	0.7	0.6	0.5	0.7	0.7	0.0	1.9	0.0	0.7

*Data are expressed as percentages unless otherwise specified. Risk factor prevalence differences between women and men are statistically significant at $P<.001$ except as noted.
†Risk factor prevalence differences between women and men are statistically significant at $P<.01$.
‡Risk factor prevalence differences between women and men are nonsignificant.
§Risk factor prevalence differences between women and men are statistically significant at $P<.05$.

Figure 1. Relationship Between Age at Trial Entry and Number of Conventional Risk Factors



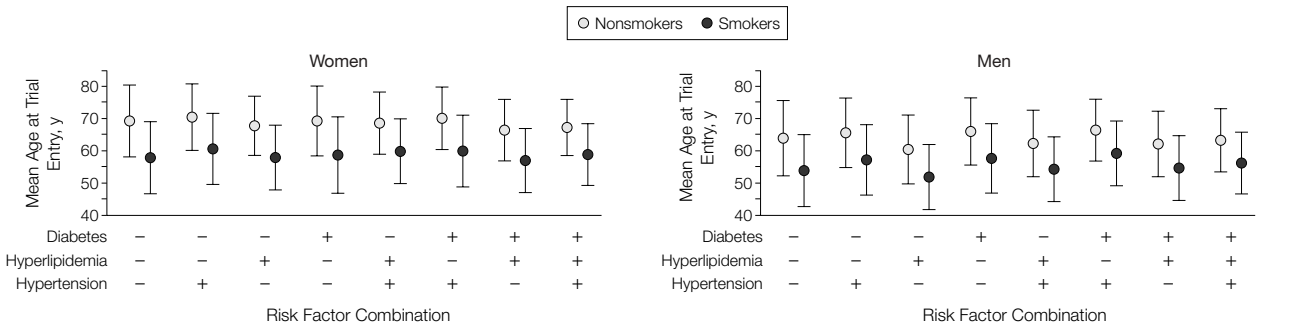
An increasing prevalence of conventional risk factors reduced the age at trial entry by about 1 decade in both sexes ($P<.001$ for all comparisons). Error bars indicate SDs.

Much attention has recently focused on the identification of genetic factors that play a role in the development of CHD. Although genetic differences may explain an individual's propensity to develop CHD in the setting of conventional risk factors, it is doubtful that the populationwide prevalence of CHD is explained by genetic factors. Epidemiological studies have convincingly shown that the risk of CHD in various populations is largely dependent on the prevalence of conventional risk factors and other environmental factors, such as diet.[3,39] Furthermore, the prevalence can vary dramatically as environmental conditions change over short periods, as seen in Japanese migration studies[40] and, more recently, in country-specific data from the World Health Organization.[41] In fact, a family history of CHD, traditionally believed to be due to a shared genetic predisposition, may simply represent a shared exposure to a higher prevalence of conventional risk factors.[42] All of these studies underscore the crucial importance of environmental influences and conventional risk factors in the development of CHD, even in populations with similar genetic profiles.

The true prevalence of the conventional risk factors is certainly higher than identified in our study. Approximately 32% of patients with hypertension are unaware that they are hypertensive.[43] Higher rates of unawareness, approaching 50%, have been documented for hyperlipidemia and diabetes.[44,45] More stringent cutoffs for abnormal blood pressure, lipid levels, and blood glucose levels have been increasingly recommended as evidence accumulates supporting lower targets. In addition, physicians typically underdiagnose conventional risk factors.[46] Moreover, the index cardiac event may lead to the diagnosis of previously unknown risk factors. For example, nearly one third of nondiabetic patients presenting with ST-elevation MI are found to have diabetes by formal glucose tolerance testing.[47] Thus, detailed assessment for conventional risk factors using contemporary targets will almost certainly lead to higher prevalence rates than those reported in our study.

Our study has several limitations. We did not have a control group without CHD for comparison, although the prevalence of conventional risk factors noted in our patients with CHD is substantially greater than the prevalence in the general population.[48] Our analyses were limited to a clinical trial population. However, because clinical trials enroll healthier patients with fewer comorbidities than those found in the general community, our findings almost certainly overestimate the prevalence of patients lacking conventional risk factors.[49] Our study also has a survival bias because only patients with CHD who survived to hospitalization were included. Yet, the conventional risk

Figure 2. Relationship Between Age at Trial Entry and Conventional Risk Factor Combinations Stratified by Smoking Status



For every risk factor combination, smoking reduced the age at trial entry by about 1 decade in both sexes ($P<.001$ for all smoking vs nonsmoking). Error bars indicate SDs.

factors have been shown to be predictive of sudden cardiac death[50] and of all-cause mortality,[30] making it quite likely that our findings would also pertain to these patients. We acknowledge that the mere presence of a particular risk factor in an individual patient with CHD does not guarantee that it plays a causal role and may suggest a role for both nontraditional risk factors and genetic causes at the individual level. However, the causal role of conventional risk factors at the population level is incontrovertible.

Our study largely consisted of patients with acute coronary syndromes, making its relevance to subclinical manifestations of atherosclerosis unclear. However, because the conventional risk factors predict subclinical atherosclerosis, such as carotid intima-media thickness, our findings are applicable to this population.[51] Our study also relied on patient self-report of risk factors, which may not accurately compare with more objective measurements involving physical examination and laboratory testing. Self-report of cardiac risk factors has been shown to systematically underestimate the true prevalence of risk factors as measured objectively, further reducing the prevalence of patients without any conventional risk factors.[52] Our study failed to account for low levels of high-density lipoprotein cholesterol, a potent conventional risk factor[53] that is not typically considered hyperlipidemia. However, the inclusion of high-density lipoprotein cholesterol would diminish the number of patients without conventional risk factors. Finally, our study consisted of a largely white, Western population. However, the risk factor patterns outside of North America and Western Europe were similar to that found in the study as a whole (Table 4). In addition, the recent Inter-Heart study showed that conventional risk factors also are predictive of the risk of MI in non-Western populations.[54]

It is increasingly clear that the 4 conventional risk factors and their resulting health risks are largely preventable by a healthy lifestyle.[55] The continued emphasis on patients lacking conventional risk factors, a situation that we have shown occurs only in a small minority of patients with CHD, fails to acknowledge the important insights that have been made in current understanding of the relationships among lifestyle, conventional risk factors, and CHD. These insights indicate that intense focus on the 4 conventional risk factors and the lifestyle behaviors causing them has great potential to decrease the worldwide epidemic of CHD.

Author Contributions: The authors designed and performed this study, had full access to the data, prepared the final manuscript, and controlled the decision to publish independently of the sponsors.
Study concept and design: U. Khot, M. Khot, Topol.
Analysis and interpretation of data: U. Khot, M. Khot, Bajzer, Sapp, Ohman, Brener, Ellis, Lincoff, Topol.
Drafting of the manuscript: U. Khot.
Critical revision of the manuscript for important intellectual content: U. Khot, M. Khot, Bajzer, Sapp, Ohman, Brener, Ellis, Lincoff, Topol.
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