Coronary Heart Disease in Women

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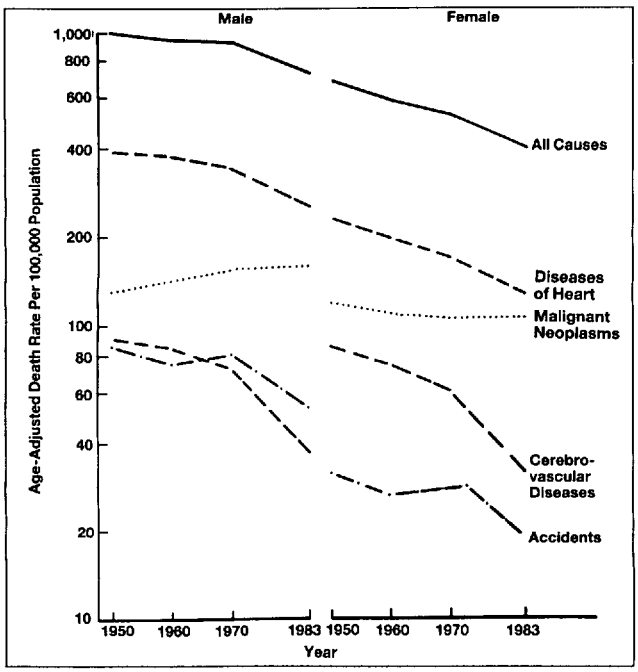
Magnitude of the Problem

Coronary heart disease is often thought of as a disease of middle-aged men, where it has a dramatic impact. Diseases of the heart, however, are the leading cause of death among women in the United States. Figure 1 shows the age-adjusted death rates per 100,000 population for men and women between 1950 and 1983.



Source; Vital Statistics of the U.S., NCHS.

Fig. 1. Death rates: United States, 1950–1983.

Diseases of the heart are the leading cause of death for both men and women, followed by malignant neoplasms, cerebrovascular disease, and motor vehicle accidents. As can be seen, there has been a steady decline in deaths due to heart disease over this time period. Between 1968 to 1978 there was a 27.3 percent decline in deaths from coronary heart disease among white women, and a 32.2 percent decline for black women. In 1983, diseases of the heart accounted for approximately 28 percent of all deaths in women.

Table 1 presents the percent decline in death rates from coronary heart disease by race and sex.

For white women the average percent decline per year was 2.7 percent from 1968 to 1978. Black women experienced the greatest decline of 3.2 percent per year. Between 1979 and 1983 white males experienced the greatest decline of 2.8 percent per year, which was on average a greater decline per year than they experienced between 1968 to 1978. The other race and sex catagories experienced less of a decline in the more recent years than previously. Black females demonstrated the smallest decline of 1 percent per year from

Tab. 1. Percent decline in death rates from coronary heart disease by race and sex.*

Sex/Race	ICD/8		ICD 9	
	1968–78	% per year	1979–83	% per year
White females	27	2.7	7	1.8
Black females	32	3.2	4	1.0
White males	24	2.4	11	2.8
Black males	23	2.3	8	2.0

* All ages, age-adjusted.
Source: U.S. Vital Statistics, NCHS.

Tab. 2. Percentage change in age-standardized death rates from ischemic heart disease between 1970 and 1972 and 1980 and 1983, age group 40 to 69 years.

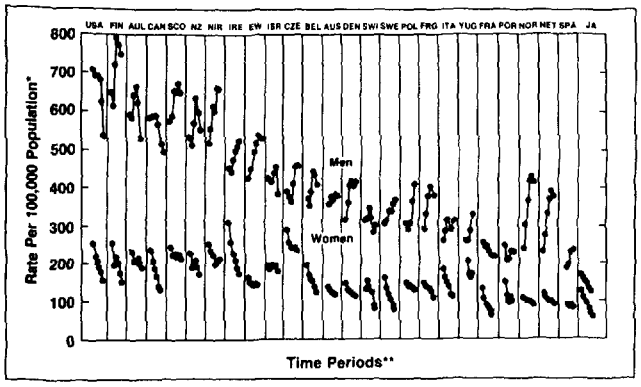
Women		Men	
Country	Change in %	Country	Change in %
U.S.A	−39	U.S.A	−36
Australia	−36	Australia	−33
Japan	−35	Belgium	−28
Belgium	−30	Canada	−28
Canada	−26	New Zealand	−23
France	−25	Japan	−22
Finland	−23	Netherlands	−20
Netherlands	−21	Finland	−13
Italy	−20	England/Wales	−12
Sweden	−19	Scotland	−10
Austria	−17	Denmark	− 9
New Zealand	−17	France	− 8
Bulgaria	−11	Federal Rep. of Germany	− 6
Norway	−11	Norway	− 5
Denmark	−11	Northern Ireland	− 1
Scotland	−10	Switzerland	0
Switzerland	−10	Austria	0
England/Wales	− 7		
Federal Rep. of Germany	− 7	Italy	+ 1
Ireland	− 5	Sweden	+ 1
		Ireland	+ 7
Czechoslovakia	+ 3	Czechoslovakia	+ 9
Hungary	+ 6	Bulgaria	+20
Yugoslavia	+13	Yugoslavia	+35
Northern Ireland	+13	Hungary	+38
Poland	+43	Romania	+53
Romania	+50	Poland	+58

Source: K. Uemura and Z. Pisa (1985), Recent trends in cardiovascular disease mortality in 27 industrialized countries. World Health Statistics Quarterly, 38:142–162.

1979 to 1983. The major difference between the ICD/8 and ICD/9 is that death due to hypertensive disease is included in CHD in the eighth revision, but not in the ninth revision. The difference seen in the decline for these two time periods may be a true slowing of the decline for black and white women or may be a function of the different coding schemes.

The percent change in the age-adjusted death rates from ischemic heart disease (IHD) mortality between 1970–72 to 1980–83 is shown in table 2.

This demonstrates that the United States has experienced the largest decline in IHD mortality of the countries listed here. The Federal Republic of Germany experienced a 6 percent decline in ischemic heart disease deaths among men and a 7 percent decline among women. Figure 2 illustrates the trends in heart disease deaths in various countries.



* Age adjusted.

** Six points in time: 1950–54, 1955–59, 1960–64, 1965–69, 1970–74, 1975–78.

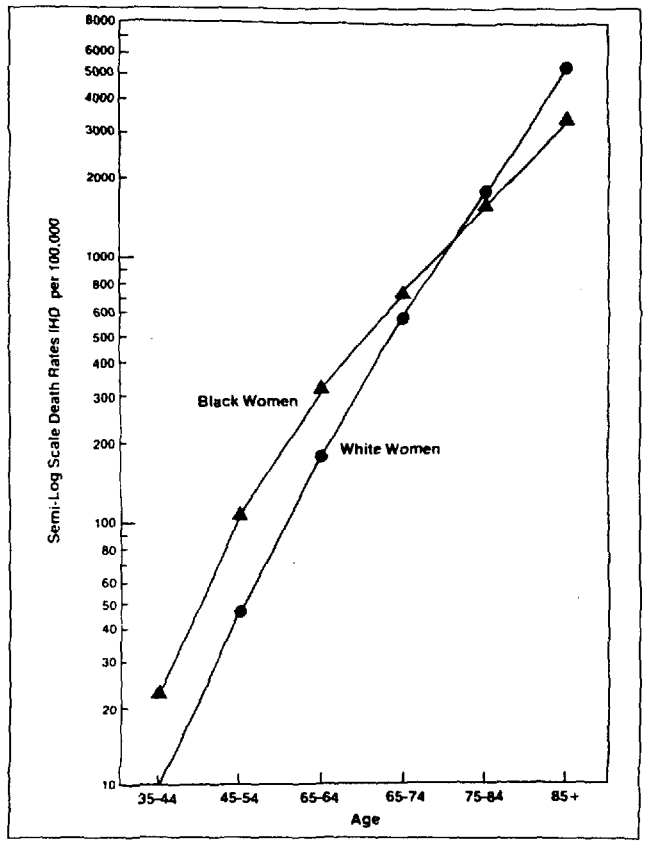
Thom, Epstein, Leaverton and Feldman (in press).

Fig. 2. Death rates for heart disease in men and women ages 45–64 years. Twenty-six countries, 1950 to 1978.

An observation from this figure is that there is substantial variation across countries in the rate of heart disease deaths among men. Among women, on the other hand, there is a more consistent pattern of low prevalence and decline in almost all the countries listed here.

When examining cause-specific mortality statistics it is important to assess the impact of death across various age groups. As women progress through their life-cycle, the risk of death from various causes changes. Figure 3 demonstrates that from a cross-sectional examination of the data, the risk of dying of heart-related causes increases steadily with age (for both men and women).

This smooth linear increase with age in women has been interpreted as showing that menopause, as distinct from age, has no effect on death from CHD. In other words, there is no observed threshold effect at around the age of menopause (approximately 50 years of age). When the death rates from ischemic heart disease (IHD) are compared for white and black



Source: Vital Statistics from NCHS.

Fig. 3. Death rates from ischemic heart disease (410–414) among black and white women age 35–85+: U.S. 1980 (Rates/100,000).

women (figure 3), it can be seen that black women have a higher rate of death from IHD until the age of 75 and over. The overall age-adjusted death rate from white women is 129.3 per 100,000 and for black women 198.7 per 100,000 for women between the ages of 35–74 years.

Another way to compare the death rates for CHD among women by race and to compare women to men is to look at the ratio of death rates. The first column of table 3 shows that young black women (prior to the age of 55 years) have over twice the death rate due to CHD as compared to their white counterparts.

Tab. 3. Ratio of death rates from coronary heart disease by age, race, and sex. United States, 1982.

Age	Females Black:With	Male:Female All races
35–44	2.7	4.5
45–54	2.4	4.0
55–64	1.7	3.0
65–74	1.2	2.2
75–84	0.9	1.6
85+	0.7	1.2

Source: Vital Statistics of the U.S., National Center for Health Statistics.

Men in the same age group have four times the death rate as females.
An indication of the impact a disease has on a population is the medical care received and various procedures performed that involve therapeutic value. Table 4 presents the change in selected medical procedures in men and women from 1979 to 1984.

Tab. 4. Number of selected surgical procedures in men and women: United States, 1979, 1984.

Type of surgery	Year	Number in 1000s		% in women
		Men	Women	
Coronary artery bypass graft	1979	93	21	18
	1984	156	46	23
Pacemakers	1979	90	82	48
	1984	110	98	47
Cardiac catheterization	1979	196	103	34
	1984	372	198	35

Source: National Hospital Discharge Survey, National Center for Health Statistics.

As can be seen cardiac catheterization increased 47 percent in men and 48 percent in women from 1979 to 1984. Surgery for pacemakers increased 18 percent for men and 16 percent for women from 1979 to 1984. Coronary artery bypass surgery increased by 40 percent for men and 54 percent for women between 1979 and 1984. By 1984 almost one-fourth of coronary artery by-pass surgeries were performed on women.

Risk Factors for Coronary Heart Disease in Women
The recognized risk factors for coronary heart disease in men are high blood pressure, high blood cholesterol, and cigarette smoking. Other risk factors include diabetes and obesity. The Framingham Study permits the examination of risk factors for coronary heart disease in both men and women. Table 5 presents the prediction of the ten year incidence of CHD among women aged 50 to 59 at baseline.
The left-hand section of the table represents the multiple logistic regression equation for the first manifestation of coronary heart disease which includes angina pectoris, myocardial infarction, coronary insufficiency and CHD death. The significant risk factors for CHD where angina is included are increased systolic blood pressure, relative weight, and serum cholesterol. For example, a woman with a systolic blood pressure of 160 mm Hg is at 26 percent higher risk of developing CHD as compared to a woman with a systolic blood pressure of 140 mm Hg. The equation on the right is the prediction of the ten year incidence of CHD where angina pectoris is excluded from the diagnosis. Relative weight drops out as a significant risk factor which is not surprising since other analyses from Framingham have shown that longer periods than 10 years of follow-up are needed before relative weight is associated in multivariate analysis with definite CHD endpoints. Cigarette smoking and glucose intolerance are significant predictors of subsequent CHD in women aged 50 to 59 years of age. In previous analyses of heart disease among women in Framingham, the relationship of cigarette smoking to CHD had been weak and it was thought by some that smoking was not a strong risk factor for women. From this analysis it is quite evident that cigarette smoking is strongly related to the hard CHD endpoints. The lack of association before was probably an anomaly of a cohort effect. That is, the older women in 1950 were less likely to smoke and the youngest were the heaviest smokers. As these young women grow older, their smoking behavior is shown to be related to their risk of heart disease.
The risk factors are compared separately for men and women in table 6.

Tab. 5. Framingham Study: Ten-year incidence of CHD among women aged 50 to 59 years. Multiple logistic regression analysis.

	CHD including angina[1]			CHD excluding angina[2]		
Variable	coeff.	RR*	p-value	coeff.	RR*	p-value
Systolic blood pressure	0.01	1.26	<0.001	0.01	1.24	<0.01
Relative weight	0.01	1.24	<0.01	0.01		n.s.
Serum cholesterol	0.00	1.22	<0.05	0.01	1.28	<0.05
Cigarette smoking	0.19		n.s.	0.62	1.85	<0.01
Glucose intolerance	0.46		n.s.	1.15	3.17	<0.001

[1] 2017 women, 177 cases. [2] 2017 women, 79 cases. * Relative risks for the differences: Systolic blood pressure: 20 mm Hg. Metropolitan relative weight: 20%. Serum cholesterol: 50 mg/100 ml. Cigarette smoking: smokers vs. nonsmokers. Glucose intolerance: yes vs. no. n.s. = not significant.

Tab. 6. Framingham Study: Ten-year incidence of CHD excluding angina pectoris among men and women aged 50–59 years. Multiple logistic regression analysis.

	Women[1]			Men[2]		
Variable	coeff.	RR*	p-value	coeff.	RR*	p-value
Systolic blood pressure	0.01	1.24	<0.01	0.02	1.46	<0.001
Relative weight	0.01		n.s.	0.00		n.s.
Serum cholesterol	0.01	1.28	<0.05	0.01	1.34	<0.001
Cigarette smoking	0.62	1.85	<0.01	0.59	1.80	<0.001
Glucose intolerance	1.15	3.17	<0.001	0.25		n.s.

[1] 2017 women, 79 cases. [2] 1545 men, 188 cases. * Relative risks for the differences: Systolic blood pressure: 20 mm Hg. Metropolitan relative weight: 20%. Serum cholesterol: 50 mg/100 ml. Cigarette smoking: smokers vs. nonsmokers. Glucose intolerance: yes vs. no. n.s. = not significant.

Systolic blood pressure, serum cholesterol and cigarette smoking are all significant risk factors for both men and women. The relationship of smoking to CHD is as strong for women as it is for men. The same is true for serum cholesterol. The one difference noted here is that glucose intolerance is a highly significant risk factor for women, but is not related to the incidence of heart disease in men. When the coefficients for men

and women were compared (not shown here), the only significant difference between men and women was glucose intolerance.

The next question is whether the standard risk factors account for the differences in CHD rates between men and women. Table 7 shows that after controlling for systolic blood pressure, relative weight, serum cholesterol, cigarette smoking, and glucose intolerance, men still have over 3.5 times the risk of developing CHD as compared to women.

Tab. 7. Framingham Study: Ten-year incidence of CHD excluding angina pectoris, men and women combined[1], aged 50–59 years. Multiple Logistic Regression Analysis.

Variable	Coefficient	RR*	p-value
Systolic blood pressure	0.02	1.37	<0.001
Relative weight	0.00		n.s.
Serum cholesterol	0.01	1.35	<0.001
Cigarette smoking	0.61	1.84	<0.001
Glucose intolerance	0.56	1.75	<0.001
Gender	−1.33	3.78	<0.001

[1] 3562 men and women, 267 cases. * Relative risks for the differences. Systolic blood pressure: 20 mm Hg. Metropolitan relative weight: 20%. Serum cholesterol: 50 mg/100 ml. Cigarette smoking: smokers vs. nonsmokers. Glucose intolerance: yes vs. no. n.s. = not significant.

At examination number eleven lipoprotein cholesterol were collected in the Framingham Study making it possible to assess their impact on CHD in the most recent 10 years of follow-up (1970–1980). The women included in the analyses of lipoproteins represent about one-third of the sample when all three decades are examined. The third multiple logistic equation in table 8 demonstrates the independent inverse association of high density lipoprotein to CHD.

The second equation shows the more modest but significant positive association of low density lipoproteins and CHD and the first equation includes the ratio of total cholesterol: high density lipoproteins which is also significant.

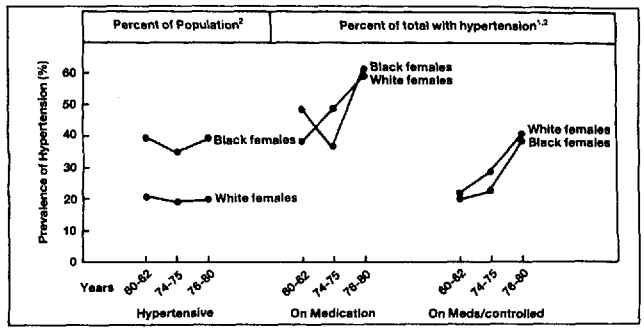
Tab. 8. Framingham Study: Ten-year incidence of CHD excluding angina pectoris among women aged 50–59 years at examination 11. Multiple Logistic Regression Analysis.

Variable	Coefficients Equation I	Equation II	Equation III
Systolic blood pressure	0.02*	0.02*	0.02*
Glucose intolerance	0.67	0.78	0.67
Metropolitan relative weight	−0.00	−0.00	−0.00
Cigarette smoking	1.45**	1.48**	1.42**
Ratio (total/HDL)	0.04**		
Low density lipoproteins		0.01*	
High density lipoproteins			−0.04**

* $0.01 < p <= 0.05$.
** $0.001 < p <= 0.01$.
*** $p <= 0.001$.

Trends in Risk Factors for Coronary Heart Disease in Women

The National Health and Nutrition Surveys during the most recent follow-up found that 20 percent of adult white women and 40 percent of adult black women over the age of 18 years were hypertensive (figure 4). Hypertension was defined as systolic blood pressure of at least 160 mm Hg or a diastolic blood pressure of at least 95 mm Hg or current use of antihypertensive medication.

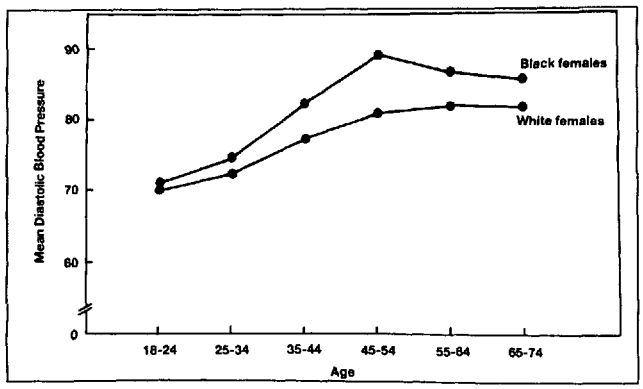


[1] Elevated blood pressure (SBP > 160 mmHg, DBP > 95 mmHg) or taking medication.
[2] Age adjusted by direct method to the population at midpoint of 1976–80 NHANES.

Fig. 4. Prevalence rates of hypertension[1] for women aged 25–74 years by race: United States, 1960–62, 1974–75, and 1976–80.

Of women defined as hypertensive, 59 percent of white women and 61 percent of black women were currently taking antihypertensive medications. As can be seen, the prevalence of hypertension has not substantially altered from 1960 to 1980. However, the number of women who are taking antihypertensive medication and have controlled their blood pressure below 160/95 mm Hg has steadily increased from 1960 to 1980; approximately a two- fold increase for both black and white women over the two decades.

The cross-sectional association of diastolic blood pres-



Source: Vital and Health Statistics, NCHS.

Fig. 5. Mean diastolic blood pressure of women 18–74 years of age by race and age: United States, 1976–80.

sure to age among black and white females is illustrated in figure 5.
Women aged 45 to 54 have the highest diastolic blood pressure; it then levels off for both black and white women. It is evident from this figure that black women have higher diastolic blood pressure than white women, especially in the older age groups. Figure 6 shows the average age trends in diastolic pressure levels in men and women.

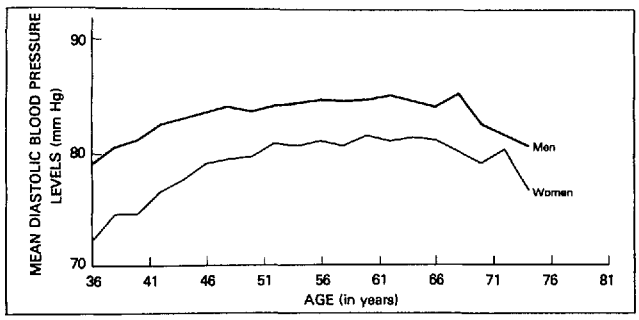


Fig. 6. Average age trends in diastolic blood pressure levels for cohort data: Framingham Study, exams 3–10.

This shows that diastolic blood pressure rises until about the age of 55 in women, levels off and then decreases after about the age of 65 years.
The cross-sectional relationship of serum cholesterol to age in white and black women is presented in figure 7.

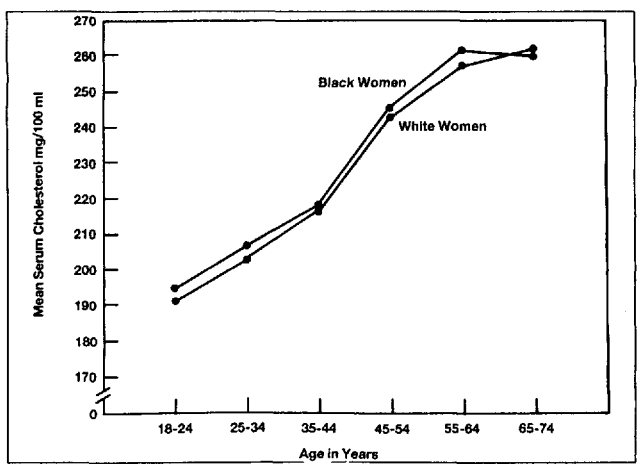


Fig. 7. Mean serum cholesterol levels of women aged 18–74 years, by race and age: United States, 1971–74.

The United States national data demonstrates that there is a very close concordance between white and black women at each age category for mean cholesterol level. Figure 8 shows the cohort data from the Framingham Study for men and women. Prior to the age of 45, the total cholesterol level in women averages 220 mg/dl.
As women age cholesterol rises sharply to levels of 240

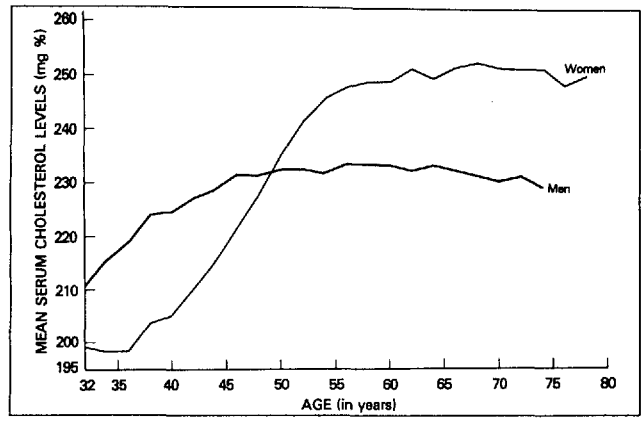
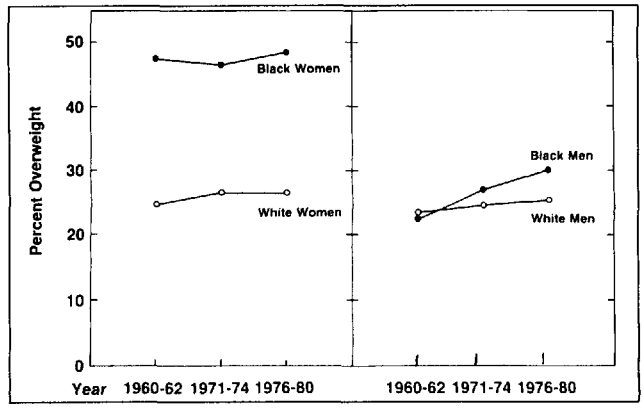


Fig. 8. Average age trends in serum cholesterol levels for cohort data: Framingham Study, exams 1–10.

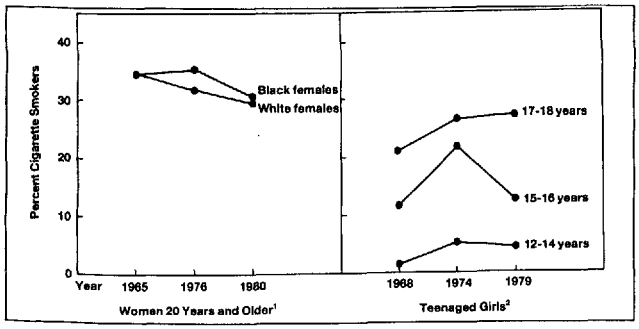
to 260 mg/dl. Between the ages of 45 to 55 (roughly the age of menopause) the average cholesterol level of women rises higher that the average level in men. It is estimated that over 23 percent of adult women in the United States have a total cholesterol level over 260 mg/dl. To the extent this rise in total cholesterol is a function of menopause or simply the aging process is not known.
Figure 9 shows the percent overweight persons from 1960 to 1980.



[1] Age adjusted by the direct method to the 1970 civilian noninstitutionalized population 25–74 years of age, using 5 age groups.

Fig. 9. Percent overweight persons 25–74 years of age[1] by race and sex: United States 1960–62, 1971–74, 1976–80.

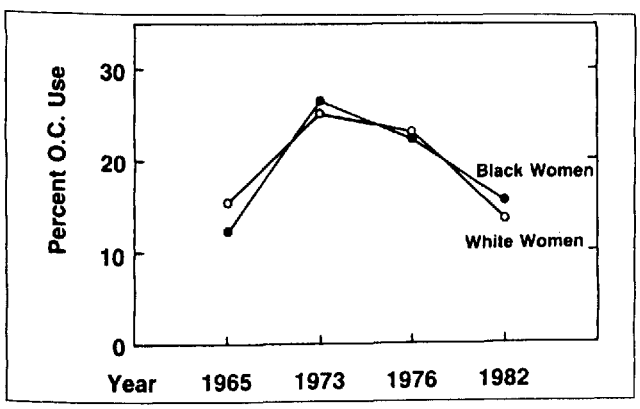
Overweight is defined for men as body mass index greater than or equal to 27.8 kilograms/meter^2, and for women as body mass index greater than or equal to 27.3 kilograms/meter^2. These cut points were used because they represent the sex-specific 85th percentiles for persons 20–29 years of age in the 1976–80 National Health and Nutrition Examination Survey (pregnant women excluded from all calculations). There has been virtually no change over time for women in the percentage defined as overweight. Almost twice as many black as compared to white women are defined



[1] Data based on household interviews of a sample of civilian noninstitutionalized population.
Source: Division of Health Statistics, NCHS: NHIS.
[2] Data based on telephone interviews of samples of the noninstitutionalized population.
Source: Green, D.E.: Teenage Smoking and Long-Term Patterns, 1979.

Fig. 10. Current smoking status of teenagers and women 20 years of age and older by race: United States, 1965, 1976, 1980 (Current smokers).

as overweight. Slightly more black men as compared to white men were defined as overweight in the latest follow-up from 1976–80. Approximately 25 percent of white women and 50 percent of black women are defined as overweight by these criteria.
In 1980 almost 30 percent (over 25 million) of all adult women in the United States smoke cigarettes. The left portion of figure 10 demonstrates that between 1965 and 1980 there was a 14 percent decline in cigarette smoking among white women aged 20 years or more and a 10 percent decline for black women of the same age.
There was very little change between 1980 to 1983 for smoking. From 30.0 to 29.8 percent for white women and a slight increase for black women from 30.6 to 37.5 percent. The trends in female teenage smoking are shown on the right. Overall, there has been a 31 percent increase in teenage girls smoking between 1965–1980. There is a three-fold increase in girls aged 12 to 14 years old, a 12 percent increase in girls 15 to 16 years old and a 29 percent increase among 17 to 18 year old teenage girls.
Another characteristic of women shown to be a risk factor for coronary heart disease and thrombolytic disease in women is use of oral contraceptives. Figure 11 shows the secular trend in oral contraceptive use from 1965 to 1982 in black and white women.
Usage is remarkably similar in both groups of women with peak use in 1973. Usage in 1982 was very similar to usage in 1965.



Source: NCHS, National Surveys of Family Growth, National Fertility Study, 1965.

Fig. 11. Oral contraceptive pill use among currently married women aged 15–44 years: U.S. 1965, 1973, 1982.

Workshop on Coronary Heart Disease in Women
In January 1986 a Workshop was sponsored by the National Heart Lung and Blood Institute to review the research and information on coronary heart disease in women. One session was devoted to the epidemiology of heart disease in women. One of the intents of the Workshop was to summarize the risk factor for CHD in women from some selected longitudinal cohort studies. The studies represented at this workshop included: the Federal Women's Study, Charleston County, Rancho Bernardo, Nurses' Health Study, Framingham Study, Lipid Research Clinics, Alameda County, and the Tecumseh Community Health Study. Across almost all of these studies several risk factors consistently predicted coronary heart disease in women in multivariate equations. These risk factors included: age, high blood pressure, hypercholesterolemia, diabetes or glucose intolerance, cigarette smoking, and an inverse relationship with high density lipoproteins. There were some predictors that were found in some but not all studies, either because they were not significant or because they were not measured across all studies. These included: vital capacity, physical activity, membership in groups (protective relationship), chest pain, previous heart disease, treated hypertension, triglycerides, and family history of CHD.
For characteristics that are specific to women it was concluded that current use of oral contraceptives constitutes a risk factor for CHD and the risk increases synergistically with cigarette smoking. The relationship of menopause to the risk of CHD is not clear. Some studies show a relationship while others do not. Because menopause is so strongly associated with age it is difficult to separate out the effect of aging as opposed to menopause per se. Examining women with early surgical menopause presents the problem of a possible biased sample. The evidence that the use of noncontraceptive hormones in women is related to heart disease is sparse and conflicting in case-control and cohort studies, although the general direction of the association is toward the protective side.

Summary
The results presented above indicate that the risk factors associated with the development of coronary heart disease in women are not that different than those identified for men. It is encouraging to note

that while the prevalence of hypertension in women has not changed over that past twenty years, the proportion of treated hypertensive women has increased dramatically and the proportion with controlled blood pressure has doubled since 1960. It is also encouraging to note that the number of adult women who smoke cigarettes has decreased since 1960, but the number of young girls who smoke has increased at an alarming rate. It has been noted by researchers that among women who smoke, the number of cigarettes smoked per day has increased from the 1950s to the present. From the Framingham data it can be seen that womens' serum cholesterol level increases substantially with age and women should take steps to eat a healthy low-saturated fat, low cholesterol diet in order to maintain a low blood cholesterol level.

It has been shown from the Framingham Study data that although the same risk factors operate in men and women, the standard risk factors do not explain the marked differences in morbidity and mortality from heart disease between the two sexes. We must continue to study the epidimiology and biology of coronary heart disease in women both to better understand the disease process in women and to understand the large sex differential for CHD in most westernized countries.

Zusammenfassung

Koronare Herzkrankheiten bei Frauen

Die Risikofaktoren der koronaren Herzkrankheit bei Frauen sind nicht wesentlich verschieden von denen bei Männern.

Während sich die Hypertonieprävalenz bei Frauen in den letzten 20 Jahren nicht verändert hat, hat der Anteil der behandelten Hypertonikerinnen dramatisch zugenommen und der Anteil mit kontrollierten Blutdruckwerten hat sich seit 1960 verdoppelt. Die Zahl der erwachsenen Frauen, die Zigaretten rauchen, hat seit 1960 abgenommen, aber die Zahl der jungen Mädchen, die rauchen, hat sehr stark zugenommen. Unter den Raucherinnen hat die Zahl der pro Tag gerauchten Zigaretten von 1950 bis heute zugenommen. Aus der Framingham-Studie wird ersichtlich, dass die Serumcholesterinspiegel bei Frauen mit dem Alter stark zunehmen. Frauen sollten Nahrungsmittel mit einem niedrigen Gehalt an gesättigten Fetten und Cholesterin zu sich nehmen, um einen niedrigen Blutcholesterinspiegel zu erreichen.

Die Daten der Framingham-Studie haben gezeigt, dass bei Männern und Frauen dieselben klassischen Risikofaktoren wirksam sind. Allerdings können die klassischen Risikofaktoren nicht die ausgeprägten Unterschiede in der Morbidität und Mortalität an koronarer Herzkrankheit zwischen beiden Geschlechtern erklären. Wir müssen weiterhin die Epidemiologie und Biologie der koronaren Herzkrankheit bei Frauen studieren, um den Krankheitsprozess bei Frauen besser zu verstehen und den grossen Unterschied in der Häufigkeit der Erkankung zwischen Männern und Frauen in den meisten westlichen Ländern besser erklären zu können.

Résumé

Maladies coronariennes chez les femmes

Alors que la prévalence de l'hypertension chez les femmes n'a guère changé durant les 20 dernières années, la proportion d'hypertensives traitées a augmenté considérablement, de même que celle des patients dont l'hypertension est contrôlée (la proportion a doublé depuis 1960). Le nombre de femmes adultes fumant la cigarette a diminué, mais le nombre de jeunes fumeuses a fortement augmenté. Parmi les fumeuses, le nombre moyen de cigarettes par jour a augmenté depuis 1950. L'étude de Framingham a montré que le taux sanguin de cholestérol augmente avec l'âge des femmes. Elles devraient consommer des aliments contenant moins de graisses animales saturées, de façon à diminuer les taux sanguins de cholestérol.

Les données de Framingham ont montré que les mêmes facteurs de risques agissent chez les femmes et les hommes. Ce sont les différences de prévalence de ces facteurs entre les sexes qui expliquent les différences de mortalité et de morbidité liées aux maladies coronaires. Il faut étudier plus à fond l'épidémiologie et la biologie de ces maladies chez les femmes, de façon à mieux comprendre les processus à l'œuvre dans l'apparition de la maladie.

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