Attributable Risk, Population Attributable Risk, and Population Attributable Fraction of Death Associated with Hypertension in a Biracial Population

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SUMMARY

In 1961, blood pressure was measured in the 40–69-year-old segment of the population of Evans County, Georgia. Mortality was monitored for up to ten years. The relationship found between hypertension and mortality is characterized in this report by four parameters: attributable risk, prevalence, population attributable risk, and population attributable fraction.

Attributable risk of death, a measure of the over-all impact of hypertension on those in each race-sex group with hypertension, is high in white males, black males, and black females, and is lowest in white females. Population attributable risk, a measure of the impact of hypertension on each entire race-sex group, is highest in black males and females due to the high prevalence of hypertension in blacks. It is somewhat lower in white males and lowest in white females. The fraction of all deaths attributable to hypertension (population attributable fraction) is highest in black females and lower in the other three groups. The population attributable fraction (ranging from 0.26 to 0.54 for systolic hypertension) is of such magnitude that if the 50% reduction in mortality achieved in the Veteran Administration Cooperative Study could be repeated in the general population, life expectancy after 40 years of age could be substantially increased.

THE INCREASE in risk of death in persons with hypertension compared to otherwise similar persons without hypertension is termed the *attributable risk of death* associated with hypertension. This is different from a measure of the excess deaths that occur in a community which are associated with the existence of hypertension in some members of that community, termed the *population attributable risk of death* associated with hypertension.[1] If hypertension is the cause of the excess risk with which it is associated, then the attributable risk may be considered the theoretical improvement in the death rate of persons with hypertension should hypertension and its sequelae be eliminated. Similarly, the population attributable risk may be considered the theoretical improvement in the average death rate of a population should hypertension be eliminated from that population.

In general the population attributable risk of death (AR_P) due to a condition such as hypertension is equal to the attributable risk (AR) times the prevalence (P) of the condition in the population.

$$AR_P = AR \times P$$

If the population attributable risk is divided by the over-all death rate (R_T), the result is the fraction of deaths in the population that are excess deaths associated with hypertension, or the *population attributable fraction* (AF_p).

$$AF_P = \frac{AR_P}{R_T}$$

The population attributable fraction multiplied by 100 is identical to Cole and MacMahon's population attributable risk percent.[2]

For example, if in white males aged 40–49, the ten-year death rate was 0.10 in normotensives and 0.25 in hypertensives, the attributable risk would be $0.25 - 0.10$ or $AR = 0.15$. If the prevalence P of hypertension in this group was 20%, then the population attributable risk would be 0.15×0.20 or $AR_p = 0.03$. Therefore, in each group of 100 men aged 40–49 starting the ten-year period, one would expect three excess deaths associated with hypertension. As the over-all death rate in this example would be 0.13, the population attributable fraction would be equal to $(0.03 \div 0.13)$ or 0.23, indicating that 23% of

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Received May 5, 1975; revision accepted for publication June 6, 1975.

the deaths were excess deaths associated with hypertension.

Attributable risk of death as a measure of the total impact of hypertension in an individual is a criterion in assessing the need for initiation of antihypertensive therapy and the levels of inconvenience and drug toxicity that should be tolerated in the maintenance of that therapy. Analyzing attributable risk will help in understanding the mechanisms by which hypertension interacts with other risk factors to cause coronary heart disease, hypertensive heart disease, and stroke.

Population attributable risk of death relates to public health management of hypertension. As a measure of how important an element hypertension is on a population, it is useful in deciding whether to undertake case finding and treatment in a community hypertension control program.

The purpose of this study is to estimate and compare the attributable risk from hypertension for the four race-sex groups predominant in Evans County, Georgia. The attributable risk, prevalence of hypertension, and over-all death rates in the race-sex groups are used to estimate their respective population attributable risks and population attributable fraction associated with hypertension.

Methods

Blood pressure was measured in the biracial population of Evans and Bulloch counties, Georgia, from 1960 to 1962.[3] This population has been followed for up to ten years in two stages. A second examination was conducted in 1967 to 1969.[4,5] Those successfully examined at that time have been followed with periodic interviews and field investigation of life and death status.

There were 2,033 subjects in the 40–69-year-old study population in 1969. After ten years of follow-up dating from each subject's initial examination, 362 were dead and 559 were known to be alive. The remaining, 1,112, were classified as having been "withdrawn alive" before ten years. Of these, 41 were lost to follow-up. As no life-death status date could be accurately given, they were assumed to have migrated out of Evans County or Georgia. They were assigned a date of withdrawal consistent with the estimated mean date of migration of their group. Three white males, four white females, 20 black males, and 14 black females were thus assigned. The remainder comprised two categories: those withdrawn after the 1967-69 examination during the interview period, because of refusal or unavailability, whose life or death status was known; and those completing the second interview less than ten years from the initial examination. The first was assigned a date of withdrawal at the approximate (average) time their availability and living status were determined, and the latter group was assigned a date of withdrawal equal to the date of second interview.

From these data a ten-year survival rate was calculated by a life table method[6] for groups segregated by race, sex, age (40–49, 50–59, and 60–69 years), and either systolic blood pressure ($\leq$ 139, 140–159, and $\geq$ 160 mm Hg) or diastolic blood pressure ($\leq$ 89, 90–94, and $\geq$ 95 mm Hg).

Table 1

Number of Subjects in Systolic Blood Pressure Categories

	White males	White females	Black males	Black females
≦139 mm Hg				
Age				
40–49	143	145	56	50
50–59	101	73	33	27
60–69	36	33	16	5
140–159 mm Hg				
40–49	68	59	41	36
50–59	59	60	33	26
60–69	41	53	17	22
≧160 mm Hg				
40–49	41	34	53	94
50–59	57	76	66	90
60–69	62	93	53	76

Division of this population into categories listed above gives 36 cells in both the systolic (SBP) and diastolic blood pressure (DBP) divisions. The sizes of these cells are shown in tables 1 and 2. Five persons are missing from the SBP listing and six from the DBP listing due to missing blood pressure data from the initial examination. Three cells in the SBP listing and five cells in the DBP listing contain less than 20 persons. Blacks make up all small cells.

The race-sex groups were compared for attributable risk, population attributable risk, and population attributable fraction of death associated with hypertension by means of weighted means calculated across the age categories. These are weighted by the actual age distribution or death distribution in each group. Tables showing the results following direct standardization across age categories are not presented. The small differences between the race-sex groups in age structure within the 30-year range and the lack of relationship between attributable risk and age results in only small differences following standardization. It was felt that the public health significance of the figures based on the actual population distribution outweighed the small gain in comparability afforded by direct age standardization.

The categorization of subjects by blood pressure does not insure comparable mean blood pressure levels between the different race-sex groups. Tables 3 and 4 indicate that the mean blood pressure in each category is similar within the

Table 2

Number of Subjects in Diastolic Blood Pressure Categories

	White males	White females	Black males	Black females
≤89 mm Hg				
Age				
40–49	126	137	35	41
50–59	99	92	28	29
60–69	56	71	19	21
90–94 mm Hg				
40–49	43	36	25	23
50–59	39	47	13	14
60–69	28	37	17	11
≧95 mm Hg				
40–49	83	65	90	116
50–59	79	69	91	100
60–69	55	71	50	71

Table 3

Means of Systolic Blood Pressure Groups (mm Hg)

	White males	White females	Black males	Black females
≦139 mm				
Age				
40–49	123.6	122.8	126.2	125.0
50–59	124.0	127.5	126.9	128.0
60–69	124.3	127.6	128.1	120.4
140–159 mm				
40–49	146.5	147.5	145.9	147.8
50–59	148.3	148.5	148.5	147.5
60–69	148.2	148.3	149.1	149.6
≧160 mm				
40–49	177.8	175.2	190.2	186.3
50–59	180.1	181.6	187.4	196.6
60–69	180.1	186.6	189.2	194.3

four race-sex groups for the first two categories and within the sex groups in the hypertensive category. Blacks of both sexes have higher mean blood pressures in the hypertensive categories than whites. This must be considered in the interpretation of attributable risk.

Results

Comparison of the race-sex groups for over-all ten-year survival (table 5) reveals the expected male-female difference in survival, but the race differences for males are smaller than expected from calculations based on the Georgia 1959–61 Life Tables.[7] The white males have slightly poorer survival and the black males better survival than expected. The ten-year survival rates by blood pressure groups (tables 6 and 7) are the basis for the attributable risk of death for the borderline and hypertensive categories of SBP and DBP (tables 8 and 9). It is apparent that for DBP the borderline group is not different in any meaningful way from the normotensive category. For both SBP and DBP there is no consistent relationship of attributable risk to age.

The over-all relations between death rates in normotensives and hypertensives, attributable risk, prevalence of hypertension, population attributable risk, the over-all death rate, and the population attributable fraction are shown for the four race-sex groups in tables 10 and 11 for two definitions of systolic and diastolic hypertension. For SBP the white males have the highest attributable risk (0.23, 0.16 for SBP > 159 mm Hg and > 139 mm Hg respectively), the blacks are intermediate (males, 0.15, 0.17; females, 0.17, 0.14), and white females have the lowest (0.08, 0.08). However, due to the higher prevalence of hypertension in blacks, they have the highest population attributable risk (females, 0.11, 0.12; males, 0.07, 0.12). The white males have the lowest prevalence, and therefore have an intermediate population attributable risk (0.06, 0.09). White females are again lowest with an intermediate prevalence of hypertension combining with low attributable risk to give a low population attributable risk (0.03, 0.05). Calculation of population attributable fraction once again changes the order. White females, with a low over-all death rate (0.12), have approximately the same population attributable fraction as white males and black males (0.26) for systolic hypertension defined as greater than 159 mm Hg. Black females, with a high population attributable risk and an intermediate over-all death rate, have the largest population attributable fraction (0.54) (fig. 1).

For DBP, the relationships between the parameters are similar except that the very low attributable risk and prevalence of diastolic hypertension in white females results in a low population attributable risk and population attributable fraction (fig. 2).

The above data on population attributable risk confirm the general belief that black females and males suffer most from hypertension and white females the least. Attributable risk for systolic hypertension is found to be generally greater than that for diastolic hypertension. This might be explained if the cut points for systolic hypertension were relatively more extreme than those for diastolic hypertension.

Table 4

Means of Diastolic Blood Pressure Groups (mm Hg)

	White males	White females	Black males	Black females
≦89 mm Hg				
Age				
40–49	79.6	79.9	80.5	82.2
50–59	79.5	80.0	79.4	80.0
60–69	80.0	80.8	80.7	80.9
90–94 mm Hg				
40–49	91.8	91.8	91.2	91.7
50–59	92.1	91.6	91.8	92.1
60–69	92.2	91.7	91.3	92.4
≧95 mm Hg				
40–49	106.5	102.9	112.5	109.4
50–59	106.9	107.4	110.2	113.1
60–69	106.1	107.0	112.2	113.0

Table 5

Over-all Survival — Evans County. Proportion Surviving Ten Years and Standard Error by Age, Race, and Sex

Age	Proportion	SE	Proportion	SE
	White males		*White females*	
40–49	0.86	0.024	0.92	0.019
50–59	0.78	0.030	0.91	0.020
60–69	0.54	0.046	0.78	0.033
	Black males		*Black females*	
40–49	0.89	0.030	0.87	0.028
50–59	0.72	0.043	0.83	0.034
60–69	0.50	0.057	0.66	0.053

SE = standard error.

Table 6

Proportion Surviving Ten Years and Standard Error by Race, Sex, Age, and Systolic Blood Pressure

	Normotensive ≤ 139 mm Hg		Borderline 140–159 mm Hg		Hypertensive ≥ 160 mm Hg	
	P	SE	P	SE	P	SE
Age 40–49						
WM	0.95	0.019	0.82	0.055	0.65	0.082
WF	0.94	0.022	0.90	0.046	0.89	0.060
BM	0.98	0.018	0.85	0.072	0.79	0.066
BF	0.96	0.028	0.90	0.053	0.81	0.047
Age 50–59						
WM	0.82	0.042	0.81	0.057	0.69	0.063
WF	0.95	0.028	0.93	0.033	0.85	0.041
BM	0.89	0.064	0.71	0.099	0.63	0.062
BF	0.96	0.037	0.88	0.065	0.77	0.050
Age 60–69						
WM	0.72	0.075	0.67	0.082	0.36	0.070
WF	0.89	0.062	0.82	0.060	0.72	0.048
BM	0.55	0.127	0.60	0.129	0.45	0.072
BF	0.80	0.179	0.86	0.077	0.59	0.066

Abbreviations: P = proportion surviving; SE = standard error; WM = white male; WF = white female; BM = black male; BF = black female.

However, the population attributable risk for systolic hypertension is also consistently greater than that for diastolic hypertension, and this cannot be explained by differences in cut points. This suggests that the level of systolic blood pressure is more closely related to the pathogenic processes leading to death than is the level of diastolic blood pressure.

Discussion

Sources of Error

Misclassification of Hypertension

The blood pressure in this study was measured at one point in time, and misclassifications could have occurred in both directions. This would tend to decrease both attributable risk and population attributable risk.

Table 7

Proportion Surviving Ten Years and Standard Error by Race, Sex, Age and Diastolic Blood Pressure

	Normotensive ≤ 89 mm Hg		Borderline 90–94 mm Hg		Hypertensive ≥ 95 mm Hg	
	P	SE	P	SE	P	SE
Age 40–49						
WM	0.93	0.025	0.90	0.046	0.75	0.054
WF	0.93	0.024	0.91	0.049	0.90	0.044
BM	0.94	0.040	0.92	0.055	0.85	0.046
BF	0.95	0.034	1.00	—	0.81	0.041
Age 50–59						
WM	0.81	0.044	0.80	0.068	0.74	0.053
WF	0.90	0.033	0.96	0.030	0.88	0.039
BM	0.75	0.092	0.92	0.074	0.68	0.054
BF	0.96	0.035	0.85	0.100	0.79	0.045
Age 60–69						
WM	0.68	0.067	0.53	0.110	0.43	0.068
WF	0.76	0.057	0.95	0.037	0.72	0.054
BM	0.56	0.119	0.57	0.123	0.44	0.077
BF	0.73	0.121	0.73	0.134	0.63	0.065

For abbreviations see table 6.

Failure of Reclassification

As prevalence of high blood pressure is known to increase with age in the United States population, and does so in the Evans County data, some individuals would become hypertensive during the study time interval but still remain in the normotensive classification for their age groups. Similarly, blood pressure in hypertensives could increase and this change would not be reflected by reclassification. Therefore, the total impact of developing hypertension on this population is undoubtedly underestimated.

Failure of Follow-up

Vital statistics for the black population are underreported in this county, and there is every possibility that those lost to follow-up were in fact unreported deaths. The loss of these deaths would contribute to the higher survival rate seen as compared to Georgia Life Tables.[7] Attributable risk and population attributable risk would be falsely lowered by the percentage of deaths missed if there were no relation between reporting of deaths and the presence or absence of hypertension. Under this assumption, population attributable fraction would not be affected. The worst possible estimate would assume all those lost to follow-up had died. The reduction would be 20/108 or 19 percent for black males, 14/86 or 16 percent for black females, 3/135 or 2 percent for white males, and 4/74 or 5 percent for white females. Correction for these hypothesized false reductions in attributable risk does not cancel the race differences in male attributable risk, and would inflate the observed race differences in population attributable risk.

The high survival rate of black males in a

Table 8

Attributable Risk of Mortality Due to Systolic Hypertension by Age, Race, and Sex

Age	WM	WF	BM	BF
	Normotensive vs Borderline (≦139 mm Hg) (140–159 mm Hg)			
40–49	0.13	0.04	0.13	0.06
50–59	0.01	0.02	0.18	0.08
60–69	0.05	0.07	−0.05	−0.06
	Normotensive vs Hypertensive (≦139 mm Hg) (≧160 mm Hg)			
40–49	0.30	0.05	0.19	0.15
50–59	0.13	0.10	0.26	0.19
60–69	0.36	0.17	0.10	0.21

Negative values indicate 10-year mortality of the borderline category was less than that of the normotensive category.

Table 9

Attributable Risk of Mortality due to Diastolic Hypertension by Age, Race, and Sex

Age	WM	WF	BM	BF
	Normotensive vs Borderline			
	≦89 mm Hg	90–94 mm Hg		
40–49	0.03	0.02	0.02	−0.05
50–59	0.01	−0.06	−0.17	0.11
60–69	0.15	−0.19	−0.01	0.00
	Normotensive vs Hypertensive			
	≦89 mm Hg	≧95 mm Hg		
40–49	0.18	0.03	0.09	0.14
50–59	0.07	0.02	0.07	0.17
60–69	0.25	0.04	0.12	0.10

Negative values indicate 10-year mortality of the borderline category was less than that of the normotensive category.

longitudinal study compared to estimates based on vital statistics and census reports has been found elsewhere.[8] This may be due in part to under ascertainment of black males in the census contributing to a falsely lowered survival rate.

The finding that the survival rate in white males in Evans County is less than that for white males in the state of Georgia as a whole may be explained by the location of Evans County in a region of high cardiovascular mortality for white males.[9]

Life Table Method of Calculating Ten-year Survival

The life table method utilizes the information on each individual as long as he is in the study. It assumes the experience is the same for those withdrawn from the study as those who remain in it. It is dependent on decisions based on independent evidence for the handling of persons completely lost to follow-up, like any other method of survivorship calculation.

Medical Care

Better medical care for white females could conceivably influence their lower attributable risk. As it is doubtful that the medical care after a life-threatening event such as stroke or myocardial infarction differs significantly between white males and white females, any effect of medical care differential would have to be effective before such events, i.e., control of blood pressure. To have the effect seen, this would mean white females would have to have experienced a remarkable improvement in hypertension control relative to the other race-sex groups after 1962. Given the low levels of effective hypertension treatment prevalent in the United States and having no reason to suspect that Evans County was different in this respect during the period of observation, better medical care is an unlikely explanation for the lower attributable risk found in white females.

Associated Risk Factors

Other risk factors for death such as social class, smoking, obesity, or cholesterol levels could, if positively associated with hypertension and themselves powerfully associated with death, exaggerate the attributable and population risks ascribed to hypertension. The other risk factors might affect the race-sex comparisons if their association with hypertension varied among the race-sex groups. In the present data

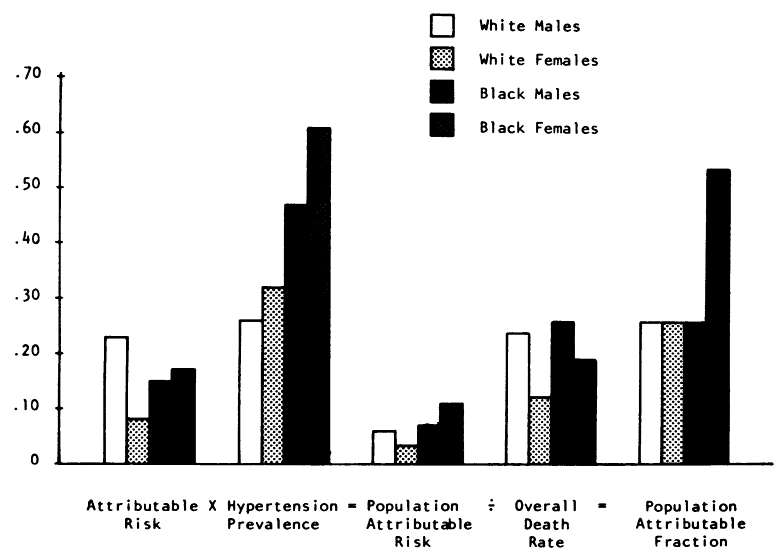

Figure 1

Parameters of mortality associated with systolic hypertension (> 159 mm Hg) in Evans County, Georgia.

Table 10

Parameters of Mortality Associated with Systolic Hypertension (> 159 mmHg or > 139 mmHg) in Evans County, Georgia

Race/Sex	SR Normotensives	SR Hypertensives	AR	P	AR_P	R_T	AF_P
	(BP ≤ 159 mm Hg)	*(BP > 159 mm Hg)*					
WM	0.83	0.60	0.23	0.26	0.06	0.24	0.26
WF	0.91	0.83	0.08	0.32	0.03	0.12	0.26
BM	0.80	0.65	0.15	0.47	0.07	0.26	0.26
BF	0.91	0.74	0.17	0.61	0.11	0.19	0.54
	(BP ≤ 139 mm Hg)	*(BP > 139 mm Hg)*					
WM	0.85	0.69	0.16	0.54	0.09	0.24	0.36
WF	0.93	0.85	0.08	0.60	0.05	0.12	0.42
BM	0.85	0.68	0.17	0.71	0.12	0.26	0.45
BF	0.92	0.78	0.14	0.81	0.12	0.19	0.61

Abbreviations: BP = blood pressure; SR = survival rate; AR = attributable risk; P = prevalence; AR_P = population attributable risk; R_T = death rate; AF_P = population attributable fraction.

set the latter does not occur to a meaningful degree. There is however a consistent, weakly positive association between the Quetelet index of obesity (weight/height^2) × 100), and a somewhat inconsistent positive association between lower social class and hypertension. However, neither of these in the present study are strong positive risk factors for death by themselves. Therefore, they would not greatly exaggerate the attributable risk of hypertension.

Significance of Results

Total mortality as an outcome variable representing the total impact of hypertension was chosen for several reasons. Death has the advantage of being a definite clearly significant endpoint. Indeed, the presence of coronary heart disease or hypertension in the living is clinically significant primarily because each of these diseases portends death. There is also evidence that hypertension as a risk factor has a different relation to mortality than to coronary heart disease morbidity. The Framingham Study indicates that not only does the over-all incidence of coronary heart disease increase with blood pressure, but that the proportion of coronary heart disease cases which present initially with a fatal episode also increases with increased blood pressure.[10]

Finally, although the study of the relationship of hypertension to specific diseases or specific causes of death may be important for determining disease mechanisms, total mortality is a more appropriate measure of the over-all significance of hypertension. The reduction of cardiac reserve associated with the presence of hypertension must surely influence case mortality in those illnesses which put special stress on the cardiovascular system, such as chronic lung disease, sepsis, acute trauma involving blood loss, pulmonary embolism, burns, or severe metabolic disturbances. In this manner, hypertension may be a prognostic risk factor in disorders for which it is not an incidence risk factor.

Table 11

Parameters of Mortality Associated with Diastolic Hypertension in Evans County, Georgia

Race/Sex	SR Normotensives	SR Hypertensives	AR	P	AR_P	R_T	AF_P
	(≤94 mm Hg)	*(>94 mm Hg)*					
WM	0.81	0.67	0.14	0.36	0.05	0.24	0.21
WF	0.89	0.84	0.05	0.33	0.02	0.12	0.15
BM	0.80	0.69	0.11	0.63	0.07	0.26	0.26
BF	0.89	0.76	0.14	0.67	0.09	0.19	0.47
	(≤89 mm Hg)	*(>89 mm Hg)*					
WM	0.83	0.71	0.12	0.54	0.07	0.24	0.27
WF	0.87	0.87	0.00	0.52	0.00	0.12	0.00
BM	0.78	0.72	0.07	0.78	0.05	0.26	0.19
BF	0.90	0.78	0.12	0.79	0.10	0.19	0.49

For abbreviation see table 10.

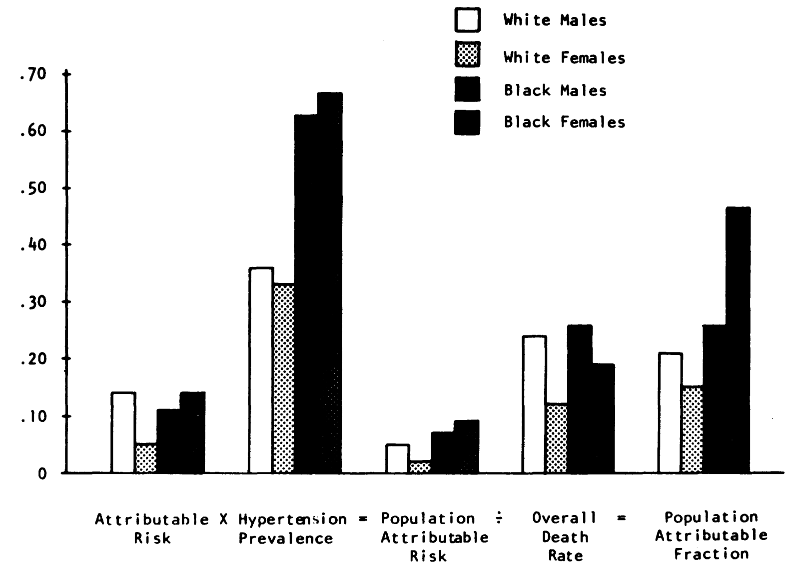

Figure 2

Parameters of mortality associated with diastolic hypertension (> 94 mm Hg) in Evans County, Georgia.

Failure to distinguish among attributable risk, prevalence, population attributable risk, and population attributable fraction frequently confuses discussions about the significance of hypertension. For instance, it is commonly stated in clinical discussions that a black male with a given level of high blood pressure is more likely to manifest severe or fatal complications as a result than is an otherwise similar white male patient. At issue is which group has the higher attributable risk associated with hypertension. In Evans County, white males with hypertension had a higher attributable risk than black males, in contrast to the general belief, even though the mean level of their high blood pressure was slightly lower. To answer the question of whether hypertension has a greater over-all impact on white or black males, both attributable risk and the prevalence of hypertension must be considered simultaneously. Black males are far more likely to have hypertension than are white males. This high prevalence, multiplied by the attributable risk, gives a population attributable risk which is higher for black males than for white males.

White females are said to tolerate hypertension well (low attributable risk) in comparison with white males. At the same time, it is argued that hypertension is responsible for the same proportion of morbid or death events in white males and females (population attributable fraction). Both of these are true. White females do tend to tolerate hypertension comparatively well, but because of very low mortality from all other causes as well, have an elevated population attributable fraction of death.

Black females are commonly left out of discussions on the effects of hypertension. However, when one considers the high attributable risk, prevalence, population attributable risk and population attributable fraction, black females have as much, if not more to be concerned about than do the other three groups. The difference in attributable risk of death between white males and females does not occur in blacks. Differences of distribution of cholesterol, obesity, smoking or social class do not explain this finding.

If hypertension causes the excess mortality with which it is associated in Evans County, the population attributable risk and population attributable fraction can be used to estimate the maximum benefit theoretically possible from hypertension control programs. The actual benefit achieved is dependent on the efficacy of available control methods and their acceptance by the population. The Veterans Administration Cooperative Study Group on Antihypertensive Agents demonstrated that a reduction of approximately 50% in the death rate of persons with diastolic blood pressures of 90–114 mm Hg could be achieved by control of blood pressure. However, their population consisted of cooperative male patients who were free of severe secondary effects of hypertension or other serious pre-existing illness.[11, 12] Our ability to achieve similar results in the general population is unproven. The Hypertension Detection and Follow-up Program is attempting to demonstrate whether hypertension screening and pharmacologic management is more effective in reducing mortality in the general population compared to the usual sources of medical care.[13] If this approach is successful in reducing the attributable risk of death associated with hypertension and the population attributable fraction by half, the effect would be a substantial reduction in the over-all death rate and an increase in life expectancy for persons over 40 years of age.

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