# Pulse Pressure and Cardiovascular Disease-Related Mortality Follow-up Study of the Multiple Risk Factor Intervention Trial (MRFIT) 

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SUSTAINED ANTIHYPERTENSIVE drug treatment has reduced the incidence of cardiovascular disease mortality ${ }^{1,2}$ and has resulted in a national effort to optimize prevention, detection, evaluation, and treatment of individuals with high blood pressure. ${ }^{3}$ Previously reported data from men screened for the Multiple Risk Factor Intervention Trial (MRFIT) demonstrated the prognostic importance of both systolic blood pressure (SBP) and diastolic blood pressure (DBP). ${ }^{4-6}$ Additionally, SBP was found to be more strongly associated with cardiovascular disease-related mortality than DBP in individuals aged 45 years or older. The MRFIT data also showed that SBP was related to cardiovascular disease at every level of DBP, including lower levels, underscoring the importance of systolic hypertension. ${ }^{4,6}$ Similar results were obtained for women. ${ }^{7}$ Together, these findings were important evidence for the fifth Joint National Committee (JNC-V) revised


#### Abstract

Context The sixth Joint National Committee (JNC-VI) classification system of blood pressure emphasizes both systolic blood pressure (SBP) and diastolic blood pressure (DBP) for cardiovascular disease risk assessment. Pulse pressure may also be a valuable risk assessment tool. Objective To compare relationships of SBP, DBP, and pulse pressure, separately and jointly, with cardiovascular disease-related mortality in men. Design and Setting Data from the Multiple Risk Factor Intervention Trial (MRFIT), which screened men aged 35 to 57 years from 1973 through 1975 at 22 US centers, was used to assess cardiovascular disease-related mortality through 1996. Participants A total of 342815 men without diabetes or a history of myocardial infarction were divided into 2 groups based on their age at MRFIT screening (35- to 44-year-olds and 45- to 57-year olds). Participant blood pressure levels were classified into a JNC-VI blood pressure category based on SBP and DBP (optimal, normal but not optimal, high normal, stage 1 hypertension, stage 2-3 hypertension), and pulse pressure was calculated.

Main Outcome Measure Cardiovascular disease-related mortality. Results There were 25721 cardiovascular disease-related deaths. Levels of SBP and DBP were more strongly related to cardiovascular disease than pulse pressure. Relationships of SBP, DBP, and pulse pressure to cardiovascular disease-related mortality varied within JNC-VI category. Concordant elevations of SBP and DBP were associated with a greater risk of cardiovascular disease-related mortality for both age groups of men. Among men aged 45 to 57 years, higher SBP and lower DBP (discordant elevations) also yielded a greater risk of cardiovascular disease-related mortality.


Conclusion In both age groups, cardiovascular disease risk assessment was improved by considering both SBP and DBP, not just SBP, DBP, or pulse pressure separately. JAMA. 2002;287:2677-2683
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classification system ${ }^{8}$ of blood pressure emphasizing both SBP and DBP. ${ }^{9}$

Recently, research has focused on the relationship between cardiovascular disease and elevated pulse pressure, which

[^0]apparently reflects increased large artery stiffness. ${ }^{10-28}$ In this article, we compare the relationships of SBP, DBP, and pulse pressure with cardiovascular disease mortality in 2 age groups of men to

[^1]determine whether the inclusion of pulse pressure as risk assessment tool with the sixth JNC (JNC-VI) revised classification system ${ }^{29}$ affects prognosis.

## METHODS <br> MRFIT Design

The design and procedures of the MRFIT have been described. ${ }^{4-6}$ Of the 361662 men aged 35 to 57 years, who were screened between 1973 and 1975, a total of 353340 had complete blood pressure information. Of these men, 10525 were excluded because they reported either a prior hospitalization for myocardial infarction or current use of diabetes medication.

Blood pressure levels were obtained by trained technicians using standard mercury sphygmomanometers. ${ }^{30}$ Three readings were taken of first and fifth Korotkoff sounds to estimate SBP and DBP. The average of the second and third reading is used here. Pulse pressure is calculated by subtracting the average DBP from the average SBP. Vital status was ascertained through 1996 by using the National Death Index and Social Security files. ${ }^{31}$ Deaths were considered cardiovascular disese-related if underlying cause received codes 390 to 459 in the International Classification of Diseases, Ninth Revision ${ }^{32}$ or I00 to I99 in the International Classification of Diseases, 10th Revision. ${ }^{33}$

## Statistical Methods

Systolic, diastolic, and pulse pressures were measured on a single occasion and cardiovascular disease-related mortality was compared by grouping each measurement into approximate quartiles and by using continuous measurements. The proportional hazards regression model was used to assess relationships of SBP, DBP, and pulse pressure with cardiovascular disease-related mortality. Ageadjusted rates were determined by the direct method using the age-distribution of all men screened as weights. Adjusted hazard ratios (HRs) for fourth vs first quartile, adjusted risks associated with 1 SD higher blood pressure, and likelihood ratio $\chi^{2}$ statistics were used to compare the prognostic significance
of SBP, DBP, and pulse pressure. Analyses were also performed with both SBP and DBP in models (or equivalently, both pulse pressure and SBP, or pulse pressure and DBP).

Additional analyses were performed with participants classified by the following JNC-VI blood pressure categories: (1) optimal: SBP lower than 120 mm Hg and DBP lower than 80 mm Hg ; (2) normal but not optimal: SBP of 120 to 129 mm Hg or DBP of 80 to 84 mm Hg ; (3) high normal: SBP of 130 to 139 mm Hg or DBP of 85 to 89 mm Hg ; (4) stage 1 hypertension: SBP of 140 to 159 mm Hg or DBP of 90 to 99 mm Hg ; and (5) stage 2-3 hypertension: SBP of 160 mm Hg or higher or DBP of 100 mm Hg or higher. ${ }^{29}$ Adjusted HRs for cardiovascular disease-related mortality were computed within each JNC-VI stratum for approximate quartiles of pulse pressure, SBP, or DBP. Quartiles 2, 3, and 4 were compared with quartile 1 (lowest quartile) and risk associated with 1 SD higher blood pressure was determined. Analyses were performed to compare cardiovascular disease risk for men with SBP and DBP levels that met both JNC-VI stratum criteria (SBP and DBP termed concordant) and for men with only 1 qualifying blood pressure level (SBP and DBP termed discordant). For these analyses, the reference group used was men who met the specific JNC-VI stratum criterion based on DBP only (lower SBP). Version 8 of SAS statistical software was used in our analyses (SAS Institute Inc, Cary, NC).

## RESULTS <br> Baseline Findings

Average SBP, DBP, and pulse pressure were lower for men aged 35 to 57 years than for men aged 45 to 57 years ( 130 vs $132 \mathrm{~mm} \mathrm{Hg} ; 84$ vs 85 mm Hg ; and 46 vs 47 mm Hg , respectively). With older age, more men are classified as hypertensive using JNC-VI criteria for elevated SBP. For example, among 33238 men aged 35 to 44 years with stage 1 hypertension, $23 \%$ are classified based on SBP alone (140-159 mm Hg with DBP $<90 \mathrm{~mm} \mathrm{Hg}$ ) vs $30 \%$ for men aged 45 to 57 years. ${ }^{6}$

## Cardiovascular Disease Mortality

SBP, DBP, and Pulse Pressure. Among the 342815 men, 25721 died from cardiovascular disease during follow-up of 22 years. In each age group, both SBP and DBP were more strongly associated with cardiovascular disease-related mortality than pulse pressure (Table 1).

For the entire cohort (both age groups), with any 2 of the 3 blood pressure variables (SBP, DBP, pulse pressure) included together in multivariable regression analyses, the coefficients were 0.0178 for SBP $(P<.001)$ and 0.0118 for $\operatorname{DBP}(P<.001)$, which is an improvement in the $\chi^{2}$ statistic of 176 compared with SBP only. The coefficients were 0.0296 ( $P<.001$ ) for SBP and -0.0118 for pulse pressure ( $P<.001$ ), which is also an improvement of 176 in the $\chi^{2}$ statistic compared with SBP only. The coefficients were 0.0296 for DBP $(P<.001)$ and 0.0178 for pulse pressure $(P<.001)$, which is an improvement of 1302 in the $\chi^{2}$ statistic compared with DBP only.

JNC-VI Strata. As previously reported, risk of cardiovascular diseaserelated mortality was progressively greater according to JNC-VI stratum. ${ }^{6}$ The additional prognostic information provided by blood pressure levels varied by JNC-VI stratum and age (Table 2 and Table 3). Level of SBP, DBP, and pulse pressure provided little or no significant additional prognostic information regarding risk of cardiovascular disease for men aged 35 to 44 years in the categories of optimal and normal but not optimal. For older men in these same strata, SBP and pulse pressure were positively associated with cardiovascular disease.

For men in the categories of high normal or stage 1 or stage 2-3 hypertension, the associations of DBP and pulse pressure with cardiovascular diseaserelated mortality varied by age. For example, for those with high normal blood pressure, the DBP coefficient was $0.0181(P<.01)$ for men aged 35 to 44 years and -0.0092 ( $P<.01$ ) for men aged 45 to 57 years. The pulse pressure coefficient was larger for older men (0.0116) than younger men (-0.0023). Similar dif-
ferences between the 2 age groups for DBP and pulse pressure coefficients were evident for those with stage 1 hypertension and stage 2-3 hypertension. The SBP coefficients were positive for each JNC-VI stratum for both age groups. For those with high normal blood pressure, the association between SBP and cardiovascular disease was stronger for men aged 45 to 57 years ( 0.0198 ) than men aged 35 to 44 years (0.0071).

SBP and DBP Levels Within JNC-VI Strata. The JNC-VI strata include individuals with either concordant or discordant patterns of SBP and DBP. For men aged 35 to 44 years in each JNC-VI stratum, the greatest cardiovascular disease risk was found with both SBP and DBP at high levels (concordant) (Figure A and Table 4). For ex-
ample, among men with high normal blood pressure, age-adjusted cardiovascular disease risk ranged from 12.1 per 10000 person-years for men with SBP of less than 120 mm Hg and DBP of 85 to 89 mm Hg to 18.4 for men with SBP of 130 to 139 mm Hg and DBP of 85 to 89 mm Hg .

In contrast, for men aged 45 to 57 years with high normal blood pressure (Figure B), the age-adjusted mortality rate for cardiovascular disease was greatest among men with SBP of 130 to 139 mm Hg and DBP lower than 80 mm Hg (discordant) (53.5 per 10000 person-years). Cardiovascular diseaserelated mortality risk was $28 \%$ ( $95 \%$ confidence interval [CI], 16\%-40\%) higher for men with SBP of 130 to 139 mm Hg and DBP lower than 80 mm Hg
vs men with SBP lower than 130 and DBP of 85 to 89 mm Hg (elevated DBP only) ( $P<.001$ ). Similarly, cardiovascular disease-related mortality risk was $23 \% ~(95 \%$ CI, 13\%-35\%) higher for men with SBP of 130 to 139 mm Hg and DBP of 85 to 89 mm Hg vs men with SBP lower than 130 mm Hg and DBP of 85 to 89 mm Hg (elevated DBP only) ( $P<.001$ ). Likewise, among men aged 45 to 57 years with stage 1 hypertension and stage 2-3 hypertension, those with concordant elevations of SBP and DBP had greater risks of cardiovascular disease-related mortality by $47 \%$ ( $95 \%$ CI, $35 \%-61 \% ; P<.001$ ) and $70 \%$ (95\% CI, 47\%-95\%; P<.001) compared with the subgroup meeting JNC-VI criterion for DBP only (ie, with lower SBP). Cardiovascular disease-

| Table 1. Association of Systolic and Diastolic Blood Pressure and Pulse Pressure With Cardiovascular Disease-Related Mortality* |
| :--- | :--- | :--- | :--- | :--- |


*CI indicates confidence interval; HR, hazard ratio.
†The HR for 1 SD higher blood pressure adjusted for age, race (black or nonblack), serum cholesterol level, and reported number of cigarettes consumed per day. $\ddagger$ The order of blood pressure is systolic, diastolic, and pulse pressure.
related mortality risk was also higher for those with discordant elevations (higher SBP and lower DBP): 45\%
higher (95\% CI, 28\%-64\%; $P<.001$ ) for those with stage 1 hypertension and $51 \%$ higher ( $95 \%$ CI, $25 \%-83 \%$;
$P<.001$ ) for those with stage 2-3 hypertension compared with the subgroup meeting JNC-VI criterion for DBP only.

Table 2. Relationship of Systolic and Diastolic Blood Pressure and Pulse Pressure With Cardiovascular Disease (CVD) Mortality Among Men Aged 35 Through 44 Years $(n=148204)^{*}$

| Joint National Committee High Blood Pressure Stratum | Blood Pressure |  |  |  |  |  |  |  | Pulse Pressure |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Systolic |  |  |  | Diastolic |  |  |  |  |  |  |  |
|  | No. of Men | No. of CVD Deaths | Age Adjusted Rate | Adjusted HR | No. of Men | No. of CVD Deaths | Age Adjusted Rate | Adjusted HR | No. of Men | No. of CVD Deaths | Age Adjusted Rate | Adjusted HR |
| Optimal Blood Pressure |  |  |  |  |  |  |  |  |  |  |  |  |
| Quartiles |  |  |  |  |  |  |  |  |  |  |  |  |
| 1 | 6589 | 111 | 8.0 | 1.00 | 7280 | 118 | 7.8 | 1.00 | 7595 | 130 | 8.0 | 1.00 |
| 2 | 7913 | 131 | 7.8 | 0.92 | 6636 | 129 | 9.2 | 1.22 | 7716 | 153 | 9.3 | 1.11 |
| 3 | 7996 | 139 | 8.2 | 0.97 | 8421 | 142 | 7.9 | 1.04 | 6899 | 117 | 8.0 | 0.97 |
| 4 | 9148 | 204 | 10.7 | 1.22 | 9309 | 196 | 9.9 | $1.30 \dagger$ | 9436 | 185 | 9.5 | 1.07 |
| Average blood pressure (IQR), mm Hg | 112 (108-116) |  |  |  | 72 (69-76) |  |  |  | 40 (36-43) |  |  |  |
| Coefficient | 0.0079 |  |  |  | 0.0128 |  |  |  | -0.0032 |  |  |  |
| Normal Blood Pressure |  |  |  |  |  |  |  |  |  |  |  |  |
| Quartiles |  |  |  |  |  |  |  |  |  |  |  |  |
| 1 | 8794 | 211 | 11.2 | 1.00 | 8899 | 199 | 10.9 | 1.00 | 8420 | 205 | 11.4 | 1.00 |
| 2 | 9194 | 245 | 12.8 | 1.10 | 7712 | 195 | 12.1 | 1.08 | 10017 | 284 | 13.4 | 1.03 |
| 3 | 9834 | 246 | 12.0 | 1.04 | 12264 | 340 | 13.1 | 1.18 | 10649 | 297 | 13.2 | 1.11 |
| 4 | 12602 | 349 | 13.2 | 1.12 | 11549 | 317 | 12.9 | 1.15 | 11338 | 265 | 11.3 | 0.97 |
| Average blood pressure (IQR), mm Hg | 122 (120-125) |  |  |  | 79 (76-82) |  |  |  | 43 (38-48) |  |  |  |
| Coefficient | 0.0078 |  |  |  | 0.0040 |  |  |  | 0.0016 |  |  |  |
| High Normal Blood Pressure |  |  |  |  |  |  |  |  |  |  |  |  |
| Quartiles |  |  |  |  |  |  |  |  |  |  |  |  |
| 1 | 7670 | 241 | 14.7 | 1.00 | 7767 | 243 | 15.2 | 1.00 | 7438 | 242 | 15.2 | 1.00 |
| 2 | 8606 | 286 | 15.8 | 1.02 | 5828 | 209 | 16.8 | 1.13 | 8630 | 314 | 17.1 | 1.07 |
| 3 | 7217 | 254 | 16.6 | 1.07 | 9045 | 302 | 15.7 | 1.09 | 7716 | 285 | 17.4 | 1.07 |
| 4 | 9902 | 378 | 18.1 | 1.13 | 10755 | 405 | 17.6 | $1.22 \dagger$ | 9611 | 318 | 15.8 | 0.96 |
| Average blood pressure (IQR), mm Hg | 130 (126-134) |  |  |  | 84 (81-87) |  |  |  | 46 (39-52) |  |  |  |
| Coefficient | 0.0071 |  |  |  | $0.0181 \ddagger$ |  |  |  | 0.0023 |  |  |  |
| Stage 1 Hypertension |  |  |  |  |  |  |  |  |  |  |  |  |
| Quartiles |  |  |  |  |  |  |  |  |  |  |  |  |
| 1 | 7544 | 313 | 19.3 | 1.00 | 7770 | 383 | 23.5 | 1.00 | 8178 | 364 | 20.9 | 1.00 |
| 2 | 8750 | 437 | 23.5 | $1.16 \dagger$ | 6191 | 290 | 21.8 | 0.97 | 7702 | 385 | 23.5 | 1.10 |
| 3 | 7487 | 378 | 23.9 | 1.15 | 8472 | 440 | 24.3 | 1.07 | 8605 | 492 | 26.8 | $1.20 \dagger$ |
| 4 | 9467 | 593 | 29.5 | $1.38 \S$ | 10815 | 608 | 26.5 | $1.16 \dagger$ | 8763 | 480 | 26.1 | $1.15 \dagger$ |
| Average blood pressure (IQR), mm Hg | 138 (131-144) |  |  |  | 90 (90-94) |  |  |  | 48 (39-56) |  |  |  |
| Coefficient | $0.0136 \S$ |  |  |  | 0.0137 $\ddagger$ |  |  |  | $0.0048 \dagger$ |  |  |  |
| Stage 2-3 Hypertension |  |  |  |  |  |  |  |  |  |  |  |  |
| Quartiles |  |  |  |  |  |  |  |  |  |  |  |  |
| 1 | 2293 | 149 | 30.8 | 1.00 | 1307 | 94 | 34.7 | 1.00 | 2191 | 162 | 35.3 | 1.00 |
| 2 | 2248 | 191 | 40.1 | 1.22 | 2697 | 203 | 35.4 | 1.08 | 2340 | 210 | 42.2 | 1.14 |
| 3 | 2351 | 239 | 48.7 | $1.50 \S$ | 3081 | 285 | 43.8 | $1.30 \dagger$ | 2573 | 287 | 53.3 | $1.47 \S$ |
| 4 | 2599 | 345 | 64.4 | 2.01§ | 2406 | 342 | 69.5 | $2.09 §$ | 2387 | 265 | 53.7 | $1.44 \S$ |
| Average blood pressure (IQR), mm Hg | 154 (143-162) |  |  |  | 104 (100-108) |  |  |  | 51 (39-60) |  |  |  |
| Coefficient | 0.0160 $\ddagger$ |  |  |  | $0.0317 \S$ |  |  |  | $0.0061 \S$ |  |  |  |
| *IQR indicates interquartile range; HR, hazards ratio. The coefficient is the proportional hazards regression coefficient for blood pressure measure after adjustment for age, race (black or nonblack), serum cholesterol level, and reported number of cigarettes consumed per day.$\begin{aligned} & \dagger P<.05 \\ & \ddagger P<.01 . \\ & \S P<.001 . \end{aligned}$ |  |  |  |  |  |  |  |  |  |  |  |  |

## COMMENT

Among men screened for MRFIT, pulse pressure was not as strong a predictor of
cardiovascular disease-related mortality as SBP and DBP. Any combination of 2 of the 3 blood pressure measures pro-
vided more information about cardiovascular disease risk for both age groups than any single measure. Since pulse pres-

Table 3. Relationship of Systolic and Diastolic Blood Pressure and Pulse Pressure With Cardiovascular Disease (CVD) Mortality Among Men Aged 45 Through 57 Years $(n=194611$ )*

| Joint National Committee High Blood Pressure Stratum | Blood Pressure |  |  |  |  |  |  |  | Pulse Pressure |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Systolic |  |  |  | Diastolic |  |  |  |  |  |  |  |
|  | No. of Men | No. of CVD Deaths | Age Adjusted Rate | Adjusted HR | No. of Men | No. of CVD Deaths | Age Adjusted Rate | Adjusted HR | No. of Men | No. of CVD Deaths | Age Adjusted Rate | Adjusted HR |
| Optimal Blood Pressure |  |  |  |  |  |  |  |  |  |  |  |  |
| Quartiles |  |  |  |  |  |  |  |  |  |  |  |  |
| 1 | 6737 | 312 | 23.4 | 1.00 | 6501 | 346 | 27.3 | 1.00 | 7675 | 349 | 23.1 | 1.00 |
| 2 | 7595 | 353 | 23.6 | 0.97 | 6866 | 374 | 27.5 | 1.05 | 7857 | 410 | 26.3 | 1.12 |
| 3 | 7871 | 434 | 28.3 | 1.13 | 8516 | 413 | 24.5 | 0.92 | 6832 | 372 | 27.5 | 1.14 |
| 4 | 8970 | 555 | 31.2 | $1.23 \dagger$ | 9290 | 521 | 28.6 | 1.06 | 8809 | 523 | 30.3 | $1.22 \dagger$ |
| Average blood pressure (IQR), mm Hg | 111 (108-116) |  |  |  | 72 (69-76) |  |  |  | 39 (36-43) |  |  |  |
| Coefficient | $0.0140 \dagger$ |  |  |  | 0.0010 |  |  |  | $0.0113 \dagger$ |  |  |  |
| Normal Blood Pressure |  |  |  |  |  |  |  |  |  |  |  |  |
| Quartiles |  |  |  |  |  |  |  |  |  |  |  |  |
| 1 | 8785 | 534 | 31.5 | 1.00 | 10855 | 849 | 39.2 | 1.00 | 10286 | 653 | 32.9 | 1.00 |
| 2 | 9788 | 662 | 34.4 | 1.05 | 6955 | 538 | 38.9 | 1.00 | 11566 | 811 | 35.8 | 1.04 |
| 3 | 13894 | 1064 | 38.6 | $1.17 \dagger$ | 13601 | 888 | 33.1 | 0.89 $\ddagger$ | 9906 | 786 | 39.9 | $1.14 \ddagger$ |
| 4 | 11470 | 938 | 41.0 | $1.21 \S$ | 12526 | 923 | 38.2 | 1.02 | 12179 | 948 | 38.8 | 1.09 |
| Average blood pressure (IQR), mm Hg | 122 (120-126) |  |  |  | 78 (77-82) |  |  |  | 43 (39-48) |  |  |  |
| Coefficient | $0.0134 \S$ |  |  |  | 0.0004 |  |  |  | $0.0056 \dagger$ |  |  |  |
| High Normal Blood Pressure |  |  |  |  |  |  |  |  |  |  |  |  |
| Quartiles |  |  |  |  |  |  |  |  |  |  |  |  |
| 1 | 10237 | 761 | 38.9 | 1.00 | 10260 | 1072 | 51.5 | 1.00 | 10229 | 754 | 38.6 | 1.00 |
| 2 | 8089 | 757 | 47.1 | $1.19 \S$ | 8404 | 803 | 47.6 | 0.94 | 9681 | 872 | 45.4 | $1.17 \S$ |
| 3 | 12706 | 1152 | 45.1 | $1.12 \ddagger$ | 11085 | 937 | 43.2 | $0.88 \S$ | 11627 | 1123 | 48.1 | 1.22 § |
| 4 | 11744 | 1294 | 54.8 | $1.36 \S$ | 13027 | 1152 | 45.2 | 0.93 | 11239 | 1215 | 53.3 | $1.31 \S$ |
| Average blood pressure (IQR), mm Hg | 131 (128-135) |  |  |  | 84 (81-87) |  |  |  | 47 (41-53) |  |  |  |
| Coefficient | $0.0198 \S$ |  |  |  | -0.0092† |  |  |  | $0.0116 \S$ |  |  |  |


| Stage 1 Hypertension |  |  |  |  |  |  |  |  |  |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| Quartiles 1 | 12937 | 1248 | 50.3 | 1.00 | 12408 | 1800 | 70.3 | 1.00 | 13380 | 1352 | 52.8 | 1.00 |
| 2 | 14587 | 1764 | 61.5 | $1.21 \S$ | 12881 | 1526 | 59.6 | 0.88§ | 13324 | 1529 | 58.7 | $1.11 \dagger$ |
| 3 | 13381 | 1793 | 66.8 | $1.29 \S$ | 12868 | 1553 | 61.2 | 0.91† | 13178 | 1897 | 72.1 | $1.33 \S$ |
| 4 | 14189 | 2380 | 82.9 | $1.59 \S$ | 16937 | 2306 | 70.1 | 1.06 | 15212 | 2407 | 77.3 | $1.40 \S$ |
| Average blood pressure (IQR), mm Hg | 141 (135-148) |  |  |  | 90 (88-94) |  |  |  | 51 (42-59) |  |  |  |
| Coefficient | $0.0191 \S$ |  |  |  | 0.0003 |  |  |  | $0.0113 \S$ |  |  |  |
| Stage 2-3 Hypertension |  |  |  |  |  |  |  |  |  |  |  |  |
| Quartiles |  |  |  |  |  |  |  |  |  |  |  |  |
| 2 | 5579 | 986 | 92.8 | $1.23 \S$ | 4908 | 838 | 88.9 | 0.88† | 5469 | 981 | 94.8 | $1.17 \S$ |
| 3 | 5490 | 1085 | 101.5 | $1.30 \S$ | 5385 | 940 | 91.4 | 0.89 $\ddagger$ | 5359 | 1146 | 111.0 | $1.34 \S$ |
| 4 | 5568 | 1504 | 146.9 | 1.87§ | 5931 | 1346 | 124.3 | 1.25§ | 5479 | 1360 | 131.3 | $1.53 \S$ |
| Average blood pressure (IQR), mm Hg | 161 (150-170) |  |  |  | 102 (100-107) |  |  |  | 59 (46-71) |  |  |  |
| Coefficient | $0.0141 \S$ |  |  |  | $0.0120 \S$ |  |  |  | 0.0092 § |  |  |  |

[^2]sure is simply the difference between SBP and DBP, given predictive information from SBP and DBP considered together, pulse pressure cannot add further information. Also, given the various ways a
specific pulse pressure can be calculated, it was anticipated and was in fact shown to be the weaker predictor of cardiovascular disease-related mortality vs SBP. For example, a pulse pressure of 70

Figure. Age-Adjusted Cardiovascular Disease Mortality Rate by Systolic and Diastolic Blood Pressure Level Used to Define Each JNC-VI Stratum


JNC-VI indicates sixth Joint National Committee classification system.
mm Hg can result from the following combinations of SBP and DBP: (1) 120 and 50 mm Hg ; (2) 130 and 60 mm Hg ; (3) 140 and 70 mm Hg ; or (4) 160 and 90 mm Hg .

The importance of considering both SBP and DBP for assessing risk is evident from analyses within JNC-VI strata. For example, among men aged 35 to 44 years, cardiovascular disease risk was greatest for those with elevated SBP and DBP levels (concordant). In men aged 45 to 57 years, in the categories of high normal, stage 1 hypertension, and stage 2-3 hypertension, higher cardiovascular disease risk was associated with either the discordant pattern of elevated SBP and low DBP (highest pulse pressure) or with the concordant pattern of elevated SBP and DBP (Figure, B). This pattern of risk within JNC-VI strata among older men supports the practical inference that in such men lower DBP and higher pulse pressure may be markers of end-organ damage. This inference is not amenable to testing in this MRFIT data set, since only limited assessment was made of target organ status at first screening.This limitation aside, it is clear from these data that men with elevated SBP who have either low or high DBP (and correspondingly have either low or high PP) should be vigorously treated.

Our results are generally consistent with findings from other studies ${ }^{10-28}$; however, they lead us to broader emphases: from age 45 years or older, SBP becomes an increasingly important measure of cardiovascular disease risk compared with DBP, but both SBP and DBP give information relevant for risk assessment. Specifically, in older people with adverse SBP and DBP levels (high normal, stage 1 hypertension, and stage 2-3 hypertension), cardiovascular disease risks are higher for individuals with concordant SBP and DBP (high on both, with lower pulse pressure) and for individuals with discordant SBP and DBP (high SBP and low DBP, with higher pulse pressure). For the latter individuals, low DBP and higher pulse pressure serve as markers not only of greater cardiovascular disease risk, but also of pos-

Table 4. Number of Men and Cardiovascular Disease-Related Deaths by Systolic and Diastolic Blood Pressure Levels*

## Diastolic Blood Pressure, mm Hg

| SBP, mm Hg | $<80,$ <br> No. of Deaths/Men | 80-84, <br> No. of Deaths/Men | $\begin{gathered} \text { 85-89, } \\ \text { No. of Deaths/Men } \end{gathered}$ | 90-99, <br> No. of Deaths/Men | $\geq 100,$ <br> No. of Deaths/Men |
| :---: | :---: | :---: | :---: | :---: | :---: |
| Men Aged 35 Through 44 Years |  |  |  |  |  |
| <120 | 585/31646 | 211/8794 | 65/2488 | 23/659 | 1/25 |
| 120-129 | 394/16611 | 446/15019 | 326/9243 | 227/5380 | 11/177 |
| 130-139 | 170/5875 | 282/7720 | 316/8069 | 500/10255 | 85/1256 |
| 140-159 | 88/1760 | 102/2478 | 193/3532 | 588/9184 | 414/4678 |
| $\geq 160$ | 13/134 | 9/138 | 11/207 | 61/828 | 319/2048 |
| Men Aged 45 Through 57 Years |  |  |  |  |  |
| <120 | 1654/31 173 | 534/8785 | 172/2437 | 54/680 | 2/15 |
| 120-129 | 1387/17810 | 1277/17342 | 793/10263 | 536/5678 | 21/203 |
| 130-139 | 808/7435 | 1067/11229 | 1124/11412 | 1460/13443 | 199/1406 |
| 140-159 | 478/3057 | 726/5195 | 1142/8002 | 2789/19 039 | 1193/7519 |
| $\geq 160$ | 99/365 | 103/482 | 191/867 | 763/3693 | 1709/7081 |

*SBP indicates systolic blood pressure. Age-adjusted rates are given in the Figure.
sible end-organ damage related to greater cardiovascular disease risk.

In summary, our results support the conclusion that the expansion in focus in the early 1990s from DBP only for cardiovascular disease risk assessment to both SBP and DBP ${ }^{8,9,29}$ was an important and useful advance. A broad focus, taking into consideration all blood pressure components as predictors, is fully warranted by the findings in older people that higher cardiovascular disease risk is associated with either elevated SBP and DBP, or elevated SBP and low DBP (high pulse pressure).

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[^2]:    *IQR indicates interquartile range; HR, hazards ratio. The coefficient is the proportional hazards regression coefficient for blood pressure measure after adjustment for age, race (black or nonblack), serum cholesterol level, and reported number of cigarettes consumed per day.
    $\dagger P<.01$.
    $\ddagger P<.05$.
    $\S P<001$.

