

Special Article

RELATION OF RACE AND SEX TO THE USE OF REPERFUSION THERAPY
IN MEDICARE BENEFICIARIES WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

Background There are few reports describing the combined influence of the race and sex of a patient on the use of reperfusion therapy for acute myocardial infarction.

Methods To determine the relation of race and sex to the receipt of reperfusion therapy for myocardial infarction in the United States, we reviewed the medical records of 234,769 Medicare patients with myocardial infarction. From these records we identified 26,575 white or black patients who met strict eligibility criteria for reperfusion therapy. We then performed bivariate and multivariate analyses of prevalence ratios to determine predictors of the use of reperfusion therapy in four subgroups of patients categorized according to race and sex: white men, white women, black men, and black women.

Results Among eligible patients, white men received reperfusion therapy with the highest frequency (59 percent), followed by white women (56 percent), black men (50 percent), and black women (44 percent). After adjustment for differences in demographic and clinical characteristics, white women were as likely as white men to receive reperfusion therapy (prevalence ratio, 1.00; 95 percent confidence interval, 0.98 to 1.03). Likewise, black women were as likely as black men to receive reperfusion therapy (prevalence ratio, 1.00; 95 percent confidence interval, 0.89 to 1.13). However, black women were significantly less likely to receive reperfusion therapy than white men (prevalence ratio, 0.90; 95 percent confidence interval, 0.82 to 0.98), as were black men (prevalence ratio, 0.85; 95 percent confidence interval, 0.78 to 0.93).

Conclusions After adjustment for differences in clinical and demographic characteristics and clinical presentation, differences according to sex in the use of reperfusion therapy are minimal. However, blacks, regardless of sex, are significantly less likely than whites to receive this potentially lifesaving therapy. (N Engl J Med 2000;342:1094-100.)

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EVERY year, more than 1 million patients in the United States have acute myocardial infarction, and almost half these patients have myocardial infarction with ST-segment elevation. Guidelines on myocardial infarction issued by the American College of Cardiology and the American Heart Association¹ recommend prompt restoration of antegrade coronary blood flow as the main goal of treatment in such patients. Thrombolytic therapy is the most common method used to restore flow,² and primary angioplasty has been accepted as an alternative method of reperfusion.³⁻⁵ However, there is increasing evidence that reperfusion may be underused among blacks,⁶⁻⁸ women,⁹⁻¹⁴ and the elderly.¹⁵⁻¹⁷

The effect of race on the risk and incidence of ischemic heart disease and its associated mortality differs between men and women.^{18,19} For example, among men, the prevalence of the risk factor of cigarette smoking is higher in blacks than in whites, but among women, the opposite is true.¹⁹ Similarly, the effect of sex on the risk and incidence of ischemic heart disease and its associated mortality differs between blacks and whites.¹⁹ For instance, among blacks, the prevalence of the risk factor of obesity is markedly higher in women than in men, whereas among whites, the prevalence of obesity is slightly higher in men.¹⁹ These observations have prompted other investigators to pay careful attention to the interactions of race and sex in epidemiologic studies of ischemic heart disease and its risk factors, frequently analyzing subgroups of patients categorized according to race and sex when sufficient numbers of subjects are available.^{18,19}

The Cooperative Cardiovascular Project is an ongoing national project, sponsored by the Health Care Financing Administration, that is designed to improve the treatment and outcomes of Medicare beneficiaries who have had acute myocardial infarction. The project has a large clinical data base that includes information on patients of all races, both sexes, and all

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ages who have had myocardial infarction. Our primary objective was to examine the potential interaction of race and sex with respect to the rate of use of reperfusion therapy in a sample of patients who are primarily older than 65 years of age.

METHODS

Study Sample

We retrospectively identified patients with a principal diagnosis of myocardial infarction (code 410) according to the *International Classification of Diseases, 9th Revision, Clinical Modification*,²⁰ from codes designating discharge diagnoses, excluding the codes with a fifth digit of 2, which designates a subsequent episode of care. Copies of the complete medical records of these patients were sent to a study center for the abstraction of clinical data by trained chart abstractors. A random sample of the entire Medicare cohort with myocardial infarction from February 1994 to July 1995 was selected, and the charts from 234,769 patients hospitalized at 6684 hospitals in the United States were reviewed. A complete description of the methods used has been published elsewhere.²¹ Because all study data were fully encrypted and we had no way of identifying individual patients and providers, approval by the institutional review board and informed consent were not required.

Our analysis involved only patients who were eligible for reperfusion therapy. To be eligible, patients had to present to the hospital after at least 30 minutes but less than 12 hours of chest pain and had to have ST-segment elevation of at least 1 mm on two contiguous leads on the initial electrocardiogram. Patients were excluded from the analysis if they were older than 80 years of age, if they had been transferred from another hospital, if there was documentation that thrombolysis had been considered by the physician but was declined by the patient or otherwise decided against, if the patients were not white or black or their race was not known, or if they had any known absolute or relative contraindication to the administration of thrombolytic therapy.²¹

Statistical Analysis

We categorized patients in four subgroups according to race and sex — white men, white women, black men, and black women — and compared their demographic and clinical characteristics, including their presenting characteristics at the hospital. An analysis of prevalence ratios was performed to ascertain the association of race and sex with the receipt of acute reperfusion therapy (the dependent variable). We computed the adjusted probability of undergoing reperfusion for blacks and whites separately, using multiple logistic-regression models to adjust for potential confounders. We then used these adjusted probabilities of reperfusion to compute the adjusted prevalence ratios among the subgroups of patients.²² To determine the 95 percent confidence intervals, statistical differentials were used to approximate the variance for the prevalence ratios.²³ In addition, potential confounders were entered into a regression model in which the main independent variables were the subgroups of patients, represented by three dummy variables, with white men as the reference group.

For all multivariate models, predictive variables that may have influenced the receipt of reperfusion therapy were entered into a series of models to provide us with better understanding of the additive effects of the following confounding factors: age (as a continuous variable), medical history, clinical presentation, and characteristics of the hospital. Variables were entered sequentially, but all variables were kept in the final models; almost all coefficients were significant (P values of less than 0.05 were considered to indicate statistical significance).

To ascertain more precisely the differences in the use of acute reperfusion therapy according to race and sex, we developed additional multivariate models, as follows: women only, in which the main independent predictor was race; men only, in which the main independent predictor was race; blacks only, in which the main in-

dependent predictor was sex; and whites only, in which the main independent predictor was sex. Age, medical history, clinical presentation, and characteristics of the hospital were also included as independent variables in each of these models. An additional multivariate model with two dichotomous independent variables (race and sex) and a term for their interaction (rather than the dummy variables for each subgroup) was also studied, but it yielded no additional insight. Finally, we performed separate analyses that included an adjustment for the clustering of patients in hospitals by correcting for overdispersion.²⁴ The results remained consistent with our previous findings and therefore are not reported here. All initial statistical analyses were performed with the use of Stata statistical software (version 4.0, Stata Corporation, College Station, Tex.) and were independently verified with SAS software (version 6.12, SAS Institute, Cary, N.C.).

RESULTS

Demographic and Clinical Characteristics

Of the 234,769 Medicare patients with acute myocardial infarction whom we identified, 26,575 (11 percent) met the criteria for inclusion in the study and had been eligible for reperfusion therapy (Table 1). On average, white women were older (mean age, 72.1 years) and black men were younger (mean age, 66.0 years) than the patients in the other subgroups. The prevalence of diabetes, hypertension, prior myocardial infarction, and prior renal failure was higher in black men and women than in white men and women. The highest rate of current smoking was among black men, and the greatest frequency of limited mobility was among black women. A history of percutaneous transluminal coronary angioplasty or coronary-artery bypass surgery was most frequent among white men and least frequent among black women.

Characteristics at Presentation and Characteristics of the Hospitals

Black women had the highest mean systolic blood pressure (151.0 mm Hg) and the highest mean heart rate (86.6 beats per minute) (Table 2). White men were the most likely to present in Killip class I (63.6 percent), and black women the least likely (51.4 percent). Black patients were more likely than white patients to present at large hospitals (with more than 400 beds), those with an urban location and teaching affiliations, and those with cardiac catheterization facilities.

Use of Reperfusion Therapy

Overall, only 57 percent of the study patients who were eligible to receive reperfusion therapy received such therapy. White men were most likely to receive reperfusion therapy (59 percent of them did), followed by white women (56 percent), black men (50 percent), and black women (44 percent) (Table 3). In each group, the predominant method of restoring anterograde flow in an infarct-related coronary artery was thrombolytic therapy (range, 87.6 to 92.3 percent of those who received reperfusion therapy). After stratification according to geographic region, black

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE PATIENTS.

CHARACTERISTIC	WHITE MEN (N=15,018)	WHITE WOMEN (N=10,026)	BLACK MEN (N=799)	BLACK WOMEN (N=732)	P VALUE*
Mean age (yr)	69.8	72.1	66.0	69.3	<0.001
Diabetes (%)	20.9	27.5	29.7	45.1	<0.001
Hypertension (%)	34.5	43.5	52.1	59.0	<0.001
Current smoking (%)	23.0	23.0	37.4	23.4	<0.001
Prior myocardial infarction (%)	31.0	22.9	32.8	31.8	<0.001
Prior heart failure (%)	25.8	32.1	31.2	38.0	<0.001
Prior percutaneous transluminal coronary angioplasty (%)	18.2	16.2	13.4	13.0	<0.001
Prior coronary-artery bypass surgery (%)	8.3	5.3	5.1	5.2	<0.001
Prior stroke (%)	0.7	0.7	1.0	0.7	0.80
Prior renal failure (%)	2.7	2.5	7.3	9.3	<0.001
Dementia (%)	1.3	1.9	1.6	2.2	0.001
Limited mobility (%)	5.8	9.2	8.8	16.5	<0.001

*The P values are for comparisons among the four groups.

TABLE 2. PRESENTING CHARACTERISTICS OF THE PATIENTS AND CHARACTERISTICS OF THE HOSPITALS.

CHARACTERISTIC	WHITE MEN (N=15,018)	WHITE WOMEN (N=10,026)	BLACK MEN (N=799)	BLACK WOMEN (N=732)
Presenting				
Mean systolic blood pressure (mm Hg)	143.6	144.1	147.6	151.0
Mean diastolic blood pressure (mm Hg)	83.3	80.3	86.6	84.6
Mean heart rate (beats/min)	80.8	84.1	84.1	86.6
Killip class I (%)	63.6	57.6	57.7	51.4
Onset of symptoms ≤6 hr before presentation (%)	88.3	86.4	87.6	85.0
Anterior myocardial infarction (%)	50.1	51.1	54.6	54.1
Hospital				
No. of beds (%)				
<200	37.7	38.3	27.9	25.3
200–400	40.8	41.3	45.2	38.6
>400	21.6	20.4	26.9	36.1
Urban (%)	78.5	78.7	85.4	84.3
Teaching affiliation (%)	36.1	36.2	50.9	53.8
Cardiac catheterization facilities (%)	76.0	75.5	80.4	83.2

men and women were less likely to receive reperfusion therapy than white men and women, regardless of geographic region (data not shown).

After stepwise adjustment for differences in age, medical history, clinical presentation, and hospital characteristics, the differences according to both race and sex in the probability of receiving reperfusion therapy were attenuated, but the racial differences re-

TABLE 3. PROBABILITY OF RECEIVING REPERFUSION THERAPY.*

ANALYSIS	WHITE MEN	WHITE WOMEN	BLACK MEN	BLACK WOMEN
Unadjusted	0.59	0.56	0.50	0.44
Sequentially adjusted				
Age	0.59	0.57	0.47	0.44
Age and medical history	0.59	0.58	0.50	0.59
Age, medical history, and clinical presentation	0.59	0.59	0.50	0.52
Age, medical history, clinical presentation, and characteristics of the hospital	0.59	0.59	0.50	0.53

*Variables in the analysis of medical history were current smoking, diabetes, hypertension, prior angina, prior myocardial infarction, prior percutaneous transluminal coronary angioplasty, prior coronary-artery bypass surgery, prior heart failure, peripheral vascular disease, dementia, and limited mobility. Variables in the analysis of clinical presentation were heart rate, systolic blood pressure (per millimeter of mercury), Killip class II (vs. I), Killip class III (vs. I), Killip class IV (vs. I), anterior myocardial infarction, Q-wave myocardial infarction, and onset of symptoms within six hours before presentation. Variables in the analysis of characteristics of the hospitals were cardiac catheterization facilities, urban location (vs. rural), small size (vs. large), medium size (vs. large), Southeast (vs. West), Midwest (vs. West), and Northeast (vs. West).

mained significant (Table 4). After adjustment, white women were as likely as white men to receive reperfusion therapy (prevalence ratio, 1.00; 95 percent confidence interval, 0.98 to 1.03). However, black women were significantly less likely than white men to receive reperfusion therapy (prevalence ratio, 0.90; 95 percent confidence interval, 0.82 to 0.98), as were black men (prevalence ratio, 0.85; 95 percent confidence

TABLE 4. PREVALENCE RATIOS FOR RECEIPT OF REPERFUSION THERAPY ACCORDING TO SUBGROUP.*

ANALYSIS	WHITE WOMEN VS. WHITE MEN	BLACK WOMEN VS. WHITE MEN	BLACK MEN VS. WHITE MEN
	prevalence ratio (95% CI)		
Unadjusted	0.94 (0.92–0.96)	0.75 (0.69–0.81)	0.84 (0.78–0.90)
Sequentially adjusted			
Age	0.97 (0.94–0.99)	0.79 (0.72–0.86)	0.74 (0.67–0.80)
Age and medical history	0.98 (0.95–0.99)	0.85 (0.78–0.92)	0.85 (0.79–0.92)
Age, medical history, and clinical presentation	1.00 (0.98–1.03)	0.89 (0.81–0.96)	0.85 (0.77–0.92)
Age, medical history, clinical presentation, and characteristics of the hospital	1.00 (0.98–1.03)	0.90 (0.82–0.98)	0.85 (0.78–0.93)

*White men served as the reference group. Variables in the analysis of medical history were current smoking, diabetes, hypertension, prior angina, prior myocardial infarction, prior percutaneous transluminal coronary angioplasty, prior coronary-artery bypass surgery, prior heart failure, peripheral vascular disease, dementia, and limited mobility. Variables in the analysis of clinical presentation were heart rate, systolic blood pressure (per millimeter of mercury), Killip class II (vs. I), Killip class III (vs. I), Killip class IV (vs. I), anterior myocardial infarction, Q-wave myocardial infarction, and onset of symptoms within six hours before presentation. Variables in the analysis of characteristics of the hospitals were cardiac catheterization facilities, urban location (vs. rural), small size (vs. large), medium size (vs. large), Southeast (vs. West), Midwest (vs. West), and Northeast (vs. West). CI denotes confidence interval.

interval, 0.78 to 0.93). When the analysis was repeated with only the patients who presented within six hours after the onset of symptoms included in the models, the results did not change substantially (data not shown).

To determine more precisely the magnitude of the differences according to race and sex in the likelihood of receiving reperfusion therapy, we analyzed four separate multivariate models (Table 5). When patients were stratified according to sex, race remained an important predictor of the receipt of acute reperfusion therapy. However, when patients were stratified according to race, sex was not significantly associated with the probability of receiving therapy. These models confirm that among Medicare beneficiaries with myocardial infarction who were eligible for reperfusion therapy, race, but not sex, was important in predicting the receipt of such therapy.

DISCUSSION

In this national sample of 26,575 Medicare beneficiaries with acute myocardial infarction who were eligible for reperfusion therapy, white women were as likely as white men to receive reperfusion therapy after adjustment for differences in age and clinical and presenting characteristics. However, blacks, regardless of sex, were significantly less likely than whites to receive this potentially life-saving therapy.

The reasons for the lower rate of use of reperfusion therapy in blacks in this study are not readily apparent, but they may include the following: the preferences of the patient, the expertise and preferences

TABLE 5. ADJUSTED PREVALENCE RATIOS FOR RECEIPT OF REPERFUSION THERAPY IN FOUR LOGISTIC-REGRESSION MODELS STRATIFIED ACCORDING TO RACE AND SEX.*

MODEL	PREVALENCE RATIO (95% CI)	P VALUE
1: Women only — black vs. white†	0.89 (0.81–0.97)	0.005
2: Men only — black vs. white†	0.85 (0.78–0.93)	<0.001
3: Blacks only — women vs. men‡	1.01 (0.89–1.13)	0.92
4: Whites only — women vs. men‡	1.00 (0.98–1.03)	0.53

*The other predictive variables included in these models are listed in Table 4. CI denotes confidence interval.

†The main independent predictor was race.

‡The main independent predictor was sex.

of the physician, hospital-related factors, and residual racial differences in clinical presentation that were not captured in our data. Given the extensive clinical information collected in the Cooperative Cardiovascular Project and used in these analyses, the latter is perhaps the least plausible explanation. Our analysis was confined to patients with myocardial infarction who met strict eligibility criteria for reperfusion therapy. Patients were excluded if there was sufficient documentation that they had declined reperfusion therapy. Therefore, the preferences of the patient are not likely to provide a full explanation of the observed differences. Furthermore, in our analysis we adjusted for differences in the characteristics of the

hospital — such as number of beds, urban as compared with rural location, teaching affiliations, and the availability of cardiac catheterization facilities. Thus, many measurable hospital-related factors were accounted for. Also, the analysis involved only Medicare patients; thus the ability of a patient to pay for medical care should not have been a factor.

A more likely explanation for our findings is that the decisions of physicians, as a result of clinical ambiguity, lack of adequate training, insufficient knowledge, or physicians' own preferences or biases, contributed to the racial differences we observed in this study. A recent study by Borzak et al.⁸ has suggested that blacks may have clinical characteristics that differ from those of whites, thus making diagnosis and a decision to treat with thrombolytic therapy more difficult. The authors reported that physicians were more likely to admit white patients than black patients to the coronary care unit with a confirmed diagnosis of myocardial infarction, and that physicians were more likely to admit black patients than white patients with a diagnosis of suspected myocardial infarction. However, their study was limited to findings from a single institution and did not include a cohort of patients who were eligible for reperfusion therapy.

In another study, Taylor et al.⁷ reported that black patients with a confirmed myocardial infarction were significantly less likely to present with chest pain than white patients with such a diagnosis. This difference in clinical presentation may be important, because the absence of chest pain was shown in the data of the National Registry of Myocardial Infarction 2 to be one of the most important determinants of withholding reperfusion therapy.⁹ Although only patients who presented with chest pain were included in our analysis, it is possible that other clinically related factors may have decreased suspicion on the part of the physician that a black patient was having a myocardial infarction.

Taylor et al.⁷ found that blacks were more likely than whites to have nondiagnostic electrocardiograms, despite retrospective confirmation of myocardial infarction. For example, blacks may have more electrocardiographic confounders, such as changes in the electrocardiogram due to early repolarization (which can mimic the appearance of acute ST-segment elevation) or patterns of left ventricular strain (which may make the interpretation of ST segments more difficult), thus affecting the differential diagnosis. Regional discrimination based on race may be possible, although this is not a likely explanation, especially because racial differences in the receipt of reperfusion therapy were found in all regions of the United States.

Lastly, cultural barriers may have contributed to racial disparities in the administration of reperfusion therapy. For example, in a recent paper, Schulman et al.²⁵ attempted to ascertain the influence that race and sex may have on patterns of referral for cardiac cath-

eterization. Physicians were found to refer blacks (especially black women) less frequently than whites for coronary angiography in the evaluation of chest pain, even after adjustment for differences in symptoms, clinical characteristics, and the physicians' estimates of the probability of coronary disease. Clearly, additional studies are warranted to address the factors that lead to racial disparities in the administration of acute reperfusion therapy.

In our study, race was an important determinant of the receipt of reperfusion therapy, although sex was not. Our results are in marked contrast to those of some studies, which have shown that women are less likely than men to receive thrombolytic therapy after acute myocardial infarction,⁹⁻¹⁴ but other studies have found no difference according to sex.^{17,26,27} However, many of the previous studies that examined differences according to sex in the receipt of thrombolytic therapy did not adjust for the presence of generally recognized eligibility criteria for the use of reperfusion therapy in patients with myocardial infarction (such as duration of symptoms, electrocardiographic criteria, and the absence of contraindications to thrombolytic therapy) or a patient's decision not to undergo therapy. Also, most studies had sample sizes that were inadequate for determining the interactions of race and sex. Therefore, it is unclear whether previously reported differences in terms of sex were due to confounding by other factors known to influence the rate of use of reperfusion therapy or were the result of true sex differences. Furthermore, in contrast to many of the previous studies, our study involved primarily older patients.

Only the studies by Maynard et al. (the western Washington trial of tissue plasminogen activator),¹⁰ Krumholz et al. (the Connecticut cohort of the Cooperative Cardiovascular Project pilot study),¹⁷ McLaughlin et al. (a study of 37 hospitals in Minnesota),¹¹ and Barron et al. (National Registry of Myocardial Infarction)⁹ used generally accepted criteria for eligibility for acute reperfusion therapy to select the study population. However, the study by Maynard et al.,¹⁰ which found that women were less likely than men to receive reperfusion therapy, did not adjust for differences in clinical and presenting characteristics. In the Connecticut Medicare cohort of the Cooperative Cardiovascular Project pilot study, a preliminary study conducted before the national Cooperative Cardiovascular Project that was the source of our data, Krumholz et al.¹⁷ demonstrated that every increase of one year in age independently predicted an 8 percent reduction in the rate of use of thrombolytic therapy. However, sex and race were not reported to be statistically important predictors of the use of such therapy, although the power of the study was insufficient to detect differences according to sex and race, given the small number of blacks and women in the study.

McLaughlin et al.¹¹ and Barron et al.⁹ both found that, after adjustment for important clinical differences, women were significantly less likely than men to receive acute reperfusion therapy. However, the study by McLaughlin et al. pertained only to Minnesota residents and did not account for patients who were referred for primary angioplasty, and the study by Barron et al. was not restricted to Medicare beneficiaries. Finally, neither of the studies examined the interaction of race and sex. In our analysis, we used an extensive clinical data base to adjust more completely for potential confounders, we included strict criteria for eligibility for acute reperfusion therapy, and equally important, we rigorously analyzed the interaction of race and sex.

Our analysis was limited to Medicare patients who were primarily elderly, and we excluded patients who were not black or white, therefore limiting the generalizability of our results with respect to race. Also, we were not able to adjust directly for socioeconomic status, which could be an important confounder of the associations we observed. As in any observational study, unknown factors may have influenced the use of reperfusion strategies. Race was determined from a review of medical charts but was not directly confirmed. However, prior studies have demonstrated the validity of the racial designation in Medicare codes.^{21,28-30} Furthermore, we performed our own validation study of the concordance of race as listed in the Medicare charts of the Cooperative Cardiovascular Project with race as ascertained from Medicare claims from Alabama; we found that the agreement was 99.74 percent and that the kappa was extremely high, at 0.9795. Random misclassification of patients according to race would have biased our results toward confirming the null hypothesis, and there is no reason to believe that any misclassification was not random. The data in the Cooperative Cardiovascular Project did not contain information on the specialty of the attending physician, but this limitation alone is unlikely to have changed our main findings significantly.

Only widely accepted clinical criteria were used to determine eligibility for reperfusion therapy in this cohort of patients who had acute myocardial infarction with ST-segment elevation. These strict eligibility requirements were developed to increase the specificity of the analysis and thus minimize the possibility that controversial indications for reperfusion would decrease the importance of our findings. For example, age alone, the absence of chest pain, or the presence of left bundle-branch block is not necessarily accepted as an indication for withholding reperfusion therapy. In addition, many patients with contraindications to thrombolytic therapy (an exclusion criterion for our analyses) may have been referred for primary angioplasty.

In summary, we have shown that racial differences in the use of reperfusion therapy for myocardial in-

farction persisted after adjustment for sex and multiple clinical variables, as well as for characteristics of the hospitals. On the other hand, within each racial group, unadjusted sex differences in the use of such therapy were markedly reduced, if not eliminated, after adjustment. Thus, we found that in Medicare beneficiaries with myocardial infarction who were eligible for reperfusion therapy, race, but not sex, was important in predicting the receipt of such therapy. Our findings emphasize the need to continue searching for explanations of racial differences in the risk factors for, incidence of, mortality associated with, and treatment of ischemic heart disease. Understanding these differences will provide the key to reducing racial disparities.

Supported in part by grants from the National Institutes of Health, National Center for Research Resources (RR00032), and the Agency for Healthcare Research and Quality (HS08843 and HS09446). The content of this article does not necessarily reflect the views or policies of the Department of Health and Human Services.

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