Racial Differences in Myocardial Infarction Outcomes

TO THE EDITOR: Spertus and colleagues (1) confirm the findings of many other studies that black patients with heart disease receive lower-quality care than white patients. The authors document major care disparities, with black patients getting statistically significantly fewer diagnostic catheterizations and revascularizations and less discharge counseling regarding smoking cessation and exercise. Contrary to current dogma, do Spertus and colleagues believe that these interventions have no value and that the differences in health outcomes in the black and white study populations were simply due to “cardiac risk factors”? If so, we must seriously reconsider our approach to all patients with myocardial infarction. In any case, 1 of the conclusions of their research should be that medical treatment is still unequal (2) in the United States.

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Potential Conflicts of Interest: None disclosed.

References

TO THE EDITOR: Spertus and colleagues (1) concluded that black patients with myocardial infarction have worse outcomes than white patients. Although the study was potentially clinically directive, we have 2 concerns. First, because the white patients were mostly men, the findings must be extrapolated to women with caution. Furthermore, enrollment bias may have caused the difference in proportions of men between the 2 groups. Second, the fundamental question of causality between racial differences and myocardial infarction outcomes could not be answered in this observational study. Thus, before speculating about the putative mechanisms underlying the observed survival advantage of white over black persons, perhaps one should investigate the cause of the nonsignificant differences between the groups after adjustment for patient factors and site of care.

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Potential Conflicts of Interest: None disclosed.

Reference

IN RESPONSE: Dr. Webster is correct that we found disparities in quality of care by race. The differences were, for the most part, modest in absolute terms, and each measure is relevant to only a subset of the patients. Therefore, we are not surprised that differences in the quality measures did not have a dominant effect in explaining differences in outcomes among the entire cohort. This does not suggest that the indicators are unimportant to the subset of patients to whom they apply or that addressing the disparity is unimportant. But when the entire group and the differences in outcomes are considered, differences in patients’ clinical characteristics on admission explain much of the difference in outcomes. Nevertheless, we emphatically support the use of evidence-based therapies in all patients, regardless of race.

Dr. Han and colleagues raised concern about the representativeness of the enrolled patients and about the inferred assumptions of causality between race, or its associated risk factors, and outcome. With regard to recruitment bias, we reported elsewhere (1) the representativeness of the study patients by comparing their characteristics with those of the entire population of eligible patients with myocardial infarction at our enrolling centers. Although not previously described by race, 55.1% of black patients enrolled in our study were men, compared with 54.1% of the entire black population. We thus feel that enrollment bias probably did not contribute to the larger proportion of black patients who were women compared with white patients.

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Reference

Does Direct-to-Consumer Prescription Drug Advertising Do More Harm Than Good?

TO THE EDITOR: Schwartz and colleagues (1) found that including drug facts boxes in direct-to-consumer advertising (DTCA) of prescription drugs improved consumers’ knowledge of drug benefits and harms. Although this seems laudable, I have several concerns. First, the drug facts box may give more legitimacy to DTCA but is unlikely to counteract the negative effects, increasing the medicalization of everyday life and the neglect of lifestyle issues. Including drug facts boxes does not address the issue of pictures and slogans used in advertisements that may convey misleading information. For example, the picture in the Amicar advertisement used in the study strongly suggests that medicines elimi-
nate the need to change potentially harmful eating habits. Also, DTCA encourages unrealistic beliefs in the therapeutic value of new drugs. Thus, health professionals will still be pressured to prescribe advertised medicines even though alternative treatments or lifestyle changes may be more appropriate for many patients.

Second, the simplicity of drug facts boxes may be misleading, because the reality is often more complex. For example, contrary to the information in the drug facts box for clopidogrel, in many countries aspirin is still considered first-line treatment in the population targeted by the U.S. advertisement. Reasons for this are the limited extra benefit provided by clopidogrel, the fact that the benefit is mainly seen in persons with existing peripheral artery disease, and the inferior cost-effectiveness of clopidogrel compared with aspirin. Although DTCA is prohibited in all developed countries except the United States and New Zealand, it spills into other countries, particularly Canada.

Finally, because patients in the drug box groups were less enthusiastic than the control participants about using the advertised medicines, Schwartz and colleagues suggested that “consumers may be insufficiently calibrated in judging what constitutes an important effect size.” Although the authors recognized that consumers may have different values, consumers’ values are at least as legitimate as those of health professionals. Medicine agencies have been criticized for approving the marketing of new drugs with minimal benefits and important or uncertain adverse effects (2). Health technology assessment bodies are recognizing the need to increase consumers’ engagement when making decisions about new medicines (3). Different presentations of medicine effects on patient choice must be evaluated to determine which ones best help people make choices that are consistent with their own values (4).

Potential Conflicts of Interest: None disclosed.

References

IN RESPONSE: We share Dr. Vitry’s concerns about DTCA of prescription drugs: It can generate exaggerated beliefs about drug efficacy and encourage the medicalization of ordinary experiences. The drug facts box directly addresses these concerns by providing balanced data about drug efficacy and harms, and by including a section called “Other things to consider doing,” highlights nondrug treatment options. The Amcid box, for example, suggests dietary changes, such as eating smaller meals or avoiding alcohol before bedtime. Our findings demonstrated that the drug facts box approach worked, even in the presence of advertising images. Enthusiasm for Amcid was much lower in the drug facts box group than in the control group: 16% versus 46% rated Amcid as “extremely” or “very” effective.

We do not agree, however, that drug facts boxes legitimize DTCA of prescription drugs. Instead, drug facts boxes ensure that advertisements have at least some educational value (given that a DTCA ban is unlikely). If boxes were written independently by U.S. Food and Drug Administration (FDA) reviewers using a transparent, reproducible process, consumers and physicians would have ready access to balanced, understandable information about prescription drug performance.

Although we studied the effect of drug facts boxes as a replacement for the current “brief summary” in DTCA, the boxes could also have an important role outside of advertisements. Boxes serve as a kind of executive summary of the FDA’s review documents and thus highlight what the FDA knew at the time of drug approval. Boxes could be posted on the Web sites of the FDA, consumers, the Centers for Medicare & Medicaid Services, and the National Library of Medicine, as well as in medical journals.

Dr. Vitry’s last points are about the role of patient values in medical decision making. To decide whether drug benefits outweigh harms, persons need more than facts: they need perspective. Physicians can and should help here. Regarding the drugs in our study, a physician could point out that clopidogrel’s minimal effect on a composite outcome is not nearly as important as the statin’s reduction in cardiovascular mortality. We hope that the drug facts boxes will enhance meaningful patient–physician discussion and foster shared decision making by making key information about what drugs do—and don’t—accessible.

Potential Conflicts of Interest: None disclosed.

Understanding the Combined Effects of Conventional Risk Factors and Genetic Loci on Diabetes Incidence

TO THE EDITOR: We read with interest the article by Cornelis and colleagues (1). Studies have evaluated the risks for diabetes associated with comorbid conditions or behavioral factors (conventional risk factors) (2) and with some genetic loci (3, 4). Cornelis and colleagues presented combined effects of conventional risk factors and genetic loci for the first time. However, the presented data were insufficient to show the whole picture of the combined effects. The authors did not explain in detail how genetic loci and conventional risk factors were related or how the effects of genetic loci were adjusted by conventional risk factors. Above all, they did not show how including body mass index (BMI) altered the effects of genetic loci. Obesity is the most important risk factor for diabetes (2). In this regard, careful examination of the patterns of adjustment of the effect of each and joint genetic loci by BMI could have given clues to how these genetic loci contribute to development of diabetes.

In addition, regarding the area under the curve for incidence of diabetes, the authors mentioned possible collinearity between con-
ventional risk factors and genetic risk score (GRS) as an explanation for marginal contribution of including GRS. However, they should have calculated the correlation if they thought collinearity was possible. The authors also suggested that the effects of GRS could have been mediated through conventional risk factors—but this is the opposite of their findings. In the Results section, they showed that the effects of GRS were significant after adjustment for age and BMI and were minimally changed by adding other risk factors.

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Potential Conflicts of Interest: None disclosed.

References

IN RESPONSE: Dr. Kim’s comments highlight some of the challenges of combining genetic and conventional risk factors. Such challenges will persist as new loci with modest effects on risk continue to be discovered.

Limited space did not allow us to provide details on how genetic loci and conventional risk factors were related. Obesity is an important risk factor to consider in understanding the mechanism by which these loci contribute to diabetes development. None of the 10 loci included in the GRS were related to BMI or the remaining conventional risk factors (age, smoking, alcohol use, physical activity, menopausal status, and family history of diabetes) (data not shown). In women, adjustment for BMI slightly strengthened the association for GRS, but additional adjustment for other covariates did not appreciably alter the results (Table). Results were similar in men (data not shown). The study design and the modest effect of each locus on risk impedes our ability to postulate potential mechanisms by which each locus contributes to risk. Nevertheless, our primary purpose was not to uncover mechanisms but to evaluate the combined effects of these loci and conventional risk factors on risk for the disease and on our ability to discriminate between patients with and those without diabetes.

Dr. Kim may have misinterpreted our discussion on the discriminative value of the GRS. We were not suggesting that collinearity may have explained the minimal improvement we observed. We were referring to previous studies (1, 2) that incorporated fasting glucose levels or other measures of insulin sensitivity in their clinical risk models and that observed the least-discriminative improvement with the addition of genetic information. We observed no correlation between GRS and conventional risk factors in our study. Although the mechanism by which these loci contribute to risk has not been established, some loci may act via pathways similar to those of conventional risk factors, whereas others may act by novel pathways. Our GRS would not capture interactions between individual loci and conventional risk factors regardless of whether they exist, a limitation we highlighted in our article. Although a score that accounts for all possible interactions will perform better than a score that does not, designing and validating such a score will be a challenge.

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Potential Conflicts of Interest: None disclosed.

References

Ultrasonography to Guide Duration of Anticoagulation in DVT

TO THE EDITOR: Prandoni and colleagues (1) showed that basing the duration of anticoagulation on ultrasonography findings can lead to better outcomes. However, the study participants had surprisingly high rates of residual thrombus after completing the recommended

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**Table. SNP Loci, GRS, and Risk for Type 2 Diabetes in Women***

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Model 1</td>
</tr>
<tr>
<td>GRS Quintile 1</td>
<td>1.15 (1.12–1.19)</td>
</tr>
<tr>
<td>GRS Quintile 2</td>
<td>1.06 (0.86–1.33)</td>
</tr>
<tr>
<td>GRS Quintile 3</td>
<td>1.62 (1.31–2.01)</td>
</tr>
<tr>
<td>GRS Quintile 4</td>
<td>2.06 (1.69–2.52)</td>
</tr>
<tr>
<td>GRS Quintile 5</td>
<td>2.07 (1.70–2.51)</td>
</tr>
</tbody>
</table>

GRS = genetic risk score; SNP = single-nucleotide polymorphism. *Models are adjusted for age (model 1); age and body mass index (5 categories) (model 2); and age, body mass index (5 categories), family history of diabetes (yes or no), smoking (never, past, or current), menopausal status (pre- or postmenopausal [never, past, or current hormone use]; women only), alcohol (5 categories), and quintiles of physical activity (h/wk) (model 3).
The reader must validate the results from the number of events presented in Table 2, which does not provide evidence for a significant difference between flexible- and fixed-duration therapy based on Fisher exact test statistics ($P = 0.084$ for unprovoked DVT, 0.80 for secondary DVT, and 0.087 for both combined).

Although information on the ideal anticoagulation duration is needed, we doubt that Prandoni and colleagues’ study will clarify this issue or help us treat patients with DVT.

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Potential Conflicts of Interest: None disclosed.

References

TO THE EDITOR: Prandoni and colleagues (1) compared a fixed duration of anticoagulation with a flexible duration in patients with proximal DVT. Fixed-duration anticoagulation was defined according to guidelines as 3 months for secondary DVT and 6 months for unprovoked DVT, whereas flexible-duration anticoagulation was prolonged until complete recanalization occurred for up to 12 months for secondary DVT and 24 months for unprovoked DVT. The topic is interesting, especially because current guidelines (2) recommend reevaluation of patients with DVT after 3 months of anticoagulation but give no clear recommendations about how reevaluation should be performed.

Although the study was a randomized trial, it has some drawbacks that seriously threaten the validity of the results. First, mean duration of anticoagulation was 4.7 months in the fixed-duration group versus 7.4 months (almost double) in the flexible-duration group. The risk for thromboembolic recurrence is highest shortly after a first event and after cessation of anticoagulation and diminishes with time (3, 4). Therefore, prolongation of anticoagulation in 1 study group inevitably leads to a decreased event rate, independent of the criteria used for deciding on prolongation. This means that even completely unrelated criteria would lead to a decreased event rate in the prolonged-treatment group, which invalidates the authors’ conclusion. The fact that the cumulative incidence rates differ primarily during the first 10 to 12 months and become parallel later indicates such an effect.

In addition, the authors do not provide $P$ values for their primary results and did not perform log-rank tests to ensure that the Kaplan–Meier analysis shown reaches the required significance level.

The reader must validate the results from the number of events presented in Table 2, which does not provide evidence for a significant difference between flexible- and fixed-duration therapy based on Fisher exact test statistics ($P = 0.084$ for unprovoked DVT, 0.80 for secondary DVT, and 0.087 for both combined).

Although information on the ideal anticoagulation duration is needed, we doubt that Prandoni and colleagues’ study will clarify this issue or help us treat patients with DVT.

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Potential Conflicts of Interest: None disclosed.

References
tion of anticoagulation. The advantage of our approach lies in the identification of a subgroup of patients who can benefit from prolonging anticoagulation without exposing many people who are less likely to develop recurrent VTE to the risk of anticoagulants. Our decision model, which stipulates continuation or cessation of anticoagulation in response to ultrasonography results over time, reflects increasing understanding that postbaseline variables may be as important as (or more important than) baseline characteristics, such as sex, thrombophilia, and type of DVT, for predicting risk for VTE recurrence. As far as the statistical approach is concerned, we performed the primary analysis with a Cox proportional hazards model, which allows adjustment for confounders. The P value in Kaplan–Meier log-rank analysis showed similar results (P = 0.047).

**Potential Conflicts of Interest:** None disclosed.

**References**


Is Lifelong Anticoagulation Worth the Risk in Patients With Unprovoked DVT?

**TO THE EDITOR:** Goldhaber and colleagues (1) state that, based on the PREVENT (Prevention of Recurrent Venous Thromboembolism) trial (2), indefinite anticoagulation with warfarin should be standard practice in unprovoked DVT. This conclusion could be challenged for several reasons. PREVENT showed a statistically significant decrease in recurrent DVT, but not in overall mortality. Of the 8 deaths in the placebo group, only 2 were due to pulmonary embolism. Furthermore, 9 placebo recipients but only 4 warfarin recipients developed cancer, indicating that the slight increase in mortality in the placebo group may be due to neoplasia. Therefore, the risk for death from stopping anticoagulation seems to be less than 1% during the approximately 2-year median follow-up in the trial, probably the same as the risk for hemorrhagic death from anticoagulation. Lifelong anticoagulation is risky, is associated with significant morbidity and mortality, and may not be appropriate for all patients with unprovoked DVT.

**Potential Conflicts of Interest:** None disclosed.

**References**


In response: PREVENT studied the optimal management of patients with an initial idiopathic and unprovoked VTE. Although PREVENT was not powered to assess mortality, the data monitoring and safety board terminated the study early because of the marked reduction in recurrent VTE in the low-intensity warfarin group (target international normalized ratio, 1.5 to 2.0) compared with the placebo group. I am not aware of any cancer risk with warfarin, which has been available in the United States since 1954. The long-term risk for recurrent VTE after an initial DVT or pulmonary embolism is high, about 30% 10 years after discontinuation of anticoagulation. Therefore, patients managed without anticoagulation after unprovoked VTE have substantial long-term risk for a recurrent event. The take-home message from PREVENT is to consider long-term anticoagulation with low-intensity warfarin after an initial 3 to 6 months of standard anticoagulation in patients with idiopathic VTE.

**Potential Conflicts of Interest:** None disclosed.

**CORRECTION**

**Correction: In the Clinic: Community-Acquired Pneumonia**

On page 2 of the In the Clinic on community-acquired pneumonia (1), the section “Who should receive pneumococcal vaccination and when should they receive it?” contains an error. In the list of chronic diseases for which pneumococcal vaccination is indicated, asthma is specifically excluded. In fact, patients with asthma should receive pneumococcal vaccination.

**Reference**