COMMENTS AND RESPONSES

Sex Differences in Revascularization

TO THE EDITOR: The excellent study of sex and coronary revascularization by Ghali and colleagues (1) highlights an important question facing those who use observational data to investigate ethnic and gender disparities: Are administrative databases sufficiently detailed to control for potential confounders in the relationship of ethnicity and sex to health outcomes? Ghali and colleagues found that the addition of two essential clinical predictor variables (extent of coronary disease and ejection fraction) to a multivariate analysis of administrative data produced an unbiased assessment of the effect of sex on revascularization. Although this demonstrates the inadequacy of some administrative data for the assessment of a particular disease–outcome relationship, it does not necessarily imply that all disparity studies based on administrative data are inherently flawed. Rather, if any database contains adequate information on all reasonable covariates, outcomes analyses based on such data may produce useful results.

A fundamental issue, therefore, is how to identify whether a particular database, administrative or clinical, has adequate detail for a multivariate analysis of outcomes. In the case of coronary revascularization, it should have been clear that analyses failing to control for the extent of coronary disease would probably produce biased results (2, 3). Researchers in sex and ethnic disparities should be vigilant in identifying and reporting the absence of important covariates from their databases. Readers of such studies should verify that all reasonable factors that may influence the frequency of clinical outcomes were incorporated in multivariate analyses (4). Inevitably, even analyses based on highly detailed clinical databases will occasionally fail to include important covariates and will lead to erroneous conclusions. It is also likely that many sparse but sufficient administrative databases contain all the information necessary to accurately advance the understanding of ethnic and sex disparities in medical care.

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IN RESPONSE: Dr. Groeneveld is correct to suggest that administrative data can often be used to generate useful information on disparities in access to care. He is also correct in highlighting that the need for detailed clinical information may not apply to all administrative databases nor to all potential research questions on issues of access and disparity of care. Given these valid comments, the challenge for researchers and readers then becomes how to know when an analysis is applying sufficiently detailed data to make meaningful conclusions.

Dr. Groeneveld has made two concrete recommendations: 1) Researchers should vigilantly identify and report the absence of potentially important covariates from their databases, and 2) readers of such studies should verify that all factors that may influence outcomes were incorporated in multivariate analyses. To these, we would add the following: 3) Readers and researchers should look for consistency of conclusions across studies and data sources (not seen in the issue of sex differences in access to cardiac care) because such consistency may increase the probability of valid findings, and 4) the developers of new clinical databases should strive to include as many relevant clinical predictors as possible and should also attempt to capture more information on newly recognized social determinants of health and health care delivery, such as income, education, housing, and social support. Greater attention to the latter factors will almost certainly enhance our understanding of disparities in health and health care.

Administrative data continue to be a valuable tool in this type of research, and researchers should not be discouraged from continuing to use these data to generate at least preliminary information on health care delivery and outcomes. This information can then be interpreted with attention to the points we and Dr. Groeneveld have raised and followed up with confirmatory research with more detailed clinical data sources, such as that used in our recent research.

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Emergency Contraception

TO THE EDITOR: In their review on emergency contraception (1), Grimes and Raymond claim that emergency postcoital contraception is fundamentally different from early abortion of an established pregnancy. In so doing, they have created a distinction without a difference.

Hormonally mediated contraception, whether pre- or postcoital, is well recognized as having a dual mechanism of action. Sometimes conception itself is prevented and sometimes implantation of an already conceived embryo is prevented, thus precipitating an early abortion. The use of the term *abortion* is appropriate for this type of procedure because a human embryo is genetically a distinct individual from the moment of conception. Implantation simply changes its home and its mode of nutrition.

Artificial distinctions that are not based on fundamental genetic differences will only lead to flawed ethical recommendations. Emergency postcoital contraception (or, by obvious inference, precoital contraception), when it prevents implantation and thereby destroys an already conceived embryo, remains abortifacient despite the authors' apparently veiled attempt at obfuscation.

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Reference

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IN RESPONSE: Dr. Miller apparently disagrees with the internationally accepted definition of the beginning of pregnancy that we used in our review. Major medical organizations (1) as well as the federal government (2) concur that implantation defines the beginning of pregnancy. Fertilization is a necessary but insufficient step toward establishing pregnancy.

An in vitro fertilization example may help to clarify this point. Assume that a woman from Dr. Miller's hometown of Hickory has successful in vitro fertilization in a medical center in Charlotte, North Carolina, 64 miles distant. An egg and sperm unite in a Petri dish, leading to a unique new genetic complement. Can the woman announce to her neighbors that she is pregnant? Should her obstetrician in Hickory begin providing prenatal care? Her fertilized ovum resides in a different city. Clearly, not until the fertilized ovum successfully implants in her uterus (or elsewhere) is she pregnant. Similarly, with in vivo fertilization in the fallopian tubes, a woman is not pregnant until the ovum implants.

Contrary to Dr. Miller's claim, this is a distinction with a difference: Emergency contraception prevents a pregnancy from starting, and abortion interrupts a pregnancy already established. Whether emergency contraception acts by inhibition of ovulation or by interference with implantation, no pregnancy exists and thus no abortion can occur. Stated alternatively, regardless of its mechanism of action, emergency contraception is not abortifacient.

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Urinary Catheters: A One-Point Restraint?

TO THE EDITOR: In their timely editorial, Saint and colleagues (1) drew attention to the widespread problem of excessive and inappropriate use of urinary catheters in U.S. hospitals and suggested several important measures that could reduce this practice. The health care establishment in the United States is currently focusing on reducing medical errors, improving pain management, reducing nosocomial infections, and controlling antimicrobial resistance. Unnecessary urinary catheter placement exemplifies all of these factors. Inappropriate catheterization should be considered a medical error that results in unnecessary patient discomfort and places the patient at increased risk for serious morbidity and mortality from resistant nosocomial infection.

Although akin to a single-point restraint, inappropriate catheterizations are not limited to the elderly or to patients with functional or cognitive impairment. In fact, the risk for inappropriate catheterization appears to be independent of these factors (2). An often ignored aspect of this practice is the element of patient disclosure. Many patients agree to undergo this embarrassing and discomforting procedure because they believe it is important to their recovery and are generally unaware of the increased risk for serious infection. The medical community is well attuned to the practice of informed consent with full disclosure for other common medical procedures. The same standards and sense of accountability should also apply for placement of urinary catheters.

An informed consumer is the best defense. It would be difficult for medical professionals to continue with the practice of inappropriate catheterization if they are required to inform and document the indication for the procedure and its infectious complications (3). Ethical, professional, and regulatory standards should mandate that informed consent with full disclosure be required for the placement of urinary catheters in nonemergency situations.

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IN RESPONSE: We appreciate the letter by Dr. Munasinghe and colleagues and their contribution to this field (1). We are, however, unclear about what they mean by "informed consent with full disclosure." If they are recommending that patients receiving nonemergent indwelling urinary catheters should be required to sign a consent form, we disagree. Such a policy is less likely to have the desired effect than it is to serve as a deterrent to doctors' placing or ordering urinary catheters. Whether the deterrent would decrease inappropriate use without compromising appropriate use is a matter for empirical investigation. One could extend Munasinghe and colleagues' argument to intravenous catheters and even to certain medications that can have adverse effects (for example, aminoglycosides and amiodarone), thereby making the practice of medicine even more bureaucratically unwieldy. Furthermore, patients and research participants often view the informed consent form as a formality even when they can understand it (2). We agree with other observers that true consent is a dialogue, not a signature (3).

If Dr. Munasinghe and colleagues mean that patients should understand the risks and benefits of, alternatives to, and rationale for placing a catheter, this is the current standard for any clinical intervention, albeit one that is frequently not met. Requiring "informed consent with full disclosure" merely restates what should already be the case. For the case of urinary catheters, the problem may be that physicians, unaware of the extent of the risk involved, may not be motivated or able to communicate this information to patients. A previous study indicated that the problem is less with the inappropriateness of initial insertion and more with inertia: Use of urinary catheters is not discontinued when it is no longer needed (4). Thus,

other organizational efforts, such as automatic stop orders, are likely to be more effective (5).

Good medical practice requires explaining all clinical interventions and their rationale to patients, including disclosure of risks, benefits, burdens, and alternatives. We are not in favor, however, of requiring written informed consent for patients undergoing urinary catheterization. Improved use of these catheters will more likely be accomplished by automated systems that aid providers to remember and rethink the need for these helpful and harmful devices.

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Reports of Drug-Induced Thrombocytopenia

TO THE EDITOR: We previously systematically reviewed all English-language reports, published up to 31 December 1999, on drug-induced thrombocytopenia (1, 2). Our goal for continuing to update our database is to provide an accessible resource (http://moon.ouhsc.edu/jgeorge) for all reports of drug-induced thrombocytopenia, describing the level of evidence for a causal role for each drug as well as clinical outcomes (1). This letter describes our continuing systematic review for the period from 1 January 2000 to 1 August 2002.

In addition to the review of individual-patient data, current publications required additional methods to assess drug-induced thrombocytopenia presented only as group data in case series and clinical trials (**Table**). Through a MEDLINE search, using our previously described strategy (1), we retrieved 84 articles; we identified 72 additional articles by searching the bibliographies of the retrieved articles. Forty of the 72 additional articles had been published since 1966 but had not been identified in our previous searches (1, 2), again demonstrating the incompleteness of literature searches. Using our previously published criteria (1), two of the authors independently reviewed each patient case report to establish the level of evidence for a causal role of the drug in thrombocytopenia. These articles contained 149 case reports of individual-patient data, of which 41 were excluded because they did not meet previously defined criteria (1). The remaining 108 patient case reports involved 51 drugs; 5 had level I (definite) evidence, and 27 had level II (probable) evidence. Of these 32 drugs, 9 had not been documented in our previous reviews as causing thrombocytopenia, defined by at least one report with level I evidence or two reports with level II evidence (1). One additional drug was identified as having definite evidence for causing thrombocytopenia based on group data rather than individual-patient data. The **Table** lists the three drugs with level I evidence and the seven drugs for which the causal relation to thrombocytopenia was validated by at least two reports with level II evidence, none of which were included in our previous reports (1, 2).

Table. **Drugs Causing Thrombocytopenia***

Drug	Case Reports, *n*	
	Level I Evidence	Level II Evidence
Individual-patient data		
Octreotide	1	0
Lotrafiban	0	5
Naproxen	0	3
Sulfamethoxypyridine	0	3
Abciximab	0	2
Chlorpropamide	0	2
Roxifiban	0	2
Sulfapyridine	0	2
Group data		
Abciximab	1	0
Eptifibatide	1	0

* These nine drugs were not reported in the initial two systematic reviews (1, 2) as having definite or probable evidence supporting a causal relation to thrombocytopenia. For individual-patient data, definite evidence (level I) required reexposure to the drug that resulted in recurrent thrombocytopenia or validation of the causal relation to thrombocytopenia by at least two patient case reports with probable evidence (level II), requiring all criteria except reexposure to the drug. For group data, definite evidence (level I) was defined as a significantly increased rate of thrombocytopenia associated with the drug compared with a control group in a randomized clinical trial. Probable evidence (level II) was defined as a significantly increased rate of thrombocytopenia in a controlled but nonrandomized study. Possible evidence (level III) was defined as the occurrence of thrombocytopenia in a case series without controls. A causal relation of the drug to thrombocytopenia was assessed as unlikely (level IV) if a controlled trial demonstrated no significant difference in the rate of thrombocytopenia between the drug and control groups. The full list of articles reviewed, the definitions of levels of evidence, the complete database, and the previous reviews are available at http://moon.ouhsc.edu/igeorge.

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