

## Exercise Stress Testing for Older Persons Starting an Exercise Program

**To the Editor:** Dr Gill and colleagues<sup>1</sup> stated that few older persons are capable of achieving maximal effort on a stress test, defined as a respiratory exchange ratio of 1.10 or greater, but it is unclear if the authors suggest that patients undergoing stress testing should attempt to achieve maximal effort. It is also important to differentiate between stress testing for screening purposes and maximal exercise testing to determine functional capacity.

Most elderly people are able to achieve maximal effort during a maximal exercise test, depending on the protocol used. Ramp treadmill protocols rather than stage protocols use more gradual increases (eg, every 30-60 seconds) in work rate toward maximal effort, are better tolerated by older persons of varying fitness and health, and may be a better tool to determine maximal performance. Determination of functional capacity is important for older adults,<sup>2,3</sup> and stress testing to determine functional capacity can guide the prescription of exercise and its monitoring in older adults.<sup>4</sup>

The authors' choice of prospective studies of exercise among older persons may not have been appropriate. The groups of patients in these studies may comprise frail (rather than sedentary) elderly persons, who represent a greater proportion of the elderly at risk from inactivity. The studies included outcomes such as falls and general lower extremity function, rather than functional capacity or cardiorespiratory outcomes. It is not clear what purpose determination of cardiorespiratory function would serve in such individuals, although stress testing might be appropriate to determine their functional capacity.

The article by Gill et al should stimulate a much-needed debate and development of evidence-based guidelines for screening and safety monitoring in independent healthy and dependent older adults who begin formal (and informal) exercise. Of perhaps greater importance is how to encourage physicians and other health care professionals to promote and prescribe physical activity behavior change among older adults who could benefit most from increased physical activity.

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1. Gill TM, DiPietro L, Krumholz HM. Role of exercise stress testing and safety monitoring for older persons starting an exercise program. *JAMA*. 2000;284:342-349.
2. Myers J, Froelicher VF. Optimizing the exercise test for pharmacological investigations. *Circulation*. 1990;82:1839-1846.
3. Simons-Morton DG, Calfas KJ, Oldenburg B, Burton NW. Effects of interventions in health care settings on physical activity or cardiorespiratory fitness. *Am J Prev Med*. 1998;15:413-430.
4. Petrella RJ, Pedersen L, Cunningham DA, Koval JJ, Paterson DH. Physician contact with community dwelling older patients: is there a relation to fitness, health status and lifestyle? *Prev Med*. 1999;29:571-576.

**To the Editor:** Dr Gill and colleagues have offered a set of recommendations regarding exercise stress testing for older persons prior to starting an exercise program.<sup>1</sup> However, in our litigious society, physicians may be reluctant to suggest an exercise program without prior exercise stress testing. An additional problem may be a high rate of false-positive exercise stress test results, which will then require coronary arteriograms with more expense and risk.<sup>2</sup> This may be a significant problem in a population with a somewhat lower incidence of significant coronary artery disease, if the concept of the Bayes theorem is considered. More research is needed concerning the precise incidence of false-positive stress test results in older individuals without clear evidence of symptomatic coronary artery disease.

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1. Gill TM, DiPietro L, Krumholz HM. Role of exercise stress testing and safety monitoring for older persons starting an exercise program. *JAMA*. 2000;284:342-349.
2. Finestone AJ. A case report: in some geriatric patients is stress testing a Hobson's choice? *J Am Dir Assoc*. 2000;1:223.

**In Reply:** Dr Petrella asserts that most persons aged 75 years and older can satisfactorily complete an exercise stress test. However, Hollenberg et al<sup>1</sup> found that 68% of a large sample of community-living persons aged 75 years and older did not attempt or were excluded from performing the exercise stress test for physical or medical reasons. Among the remaining subgroup, only 26% achieved maximal exercise effort, despite a protocol that increased the work rate gradually, in 2-minute increments. Interestingly, the study by Petrella et al<sup>2</sup> actually supports these conclusions. Among another representative sample of community-living persons aged 75 years and older, less than 20% were able to complete an exercise stress test.<sup>3</sup>

The randomized controlled trials of successful exercise interventions that we cited included a wide spectrum of persons aged 75 years and older (ie, those who were healthy and those who were frail) and functional outcomes that are particularly

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**Letters Section Editors:** Stephen J. Lurie, MD, PhD, Senior Editor; Phil B. Fontanarosa, MD, Executive Deputy Editor.

relevant to this population. Of note, at least 1 of these studies excluded potential participants based on a positive exercise stress test result.<sup>4</sup>

We agree with Dr Finestone that current recommendations for routine exercise stress testing among persons aged 75 years and older could lead to a cascade of increasingly invasive cardiac procedures. However, because the prevalence of asymptomatic coronary artery disease in this population is high,<sup>5</sup> the rate of false-positive test results may be lower than Finestone indicates.

Given the compelling evidence supporting the benefits of physical activity and exercise among older persons, it is essential that potential impediments to exercise be identified, critically evaluated, and eliminated or modified. We hope that our article will spur investigators to address the many unanswered questions regarding the role of exercise stress testing and safety monitoring among older persons so that evidence-based guidelines for exercise prescription can be developed.

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1. Hollenberg M, Ngo LH, Turner D, Tager IB. Treadmill exercise testing in an epidemiologic study of elderly subjects. *J Gerontol A Biol Sci Med Sci.* 1998;53:B259-B267.

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4. Buchner DM, Cress ME, de Lateur BJ, et al. The effect of strength and endurance training on gait, balance, fall risk, and health services use in community-living older adults. *J Gerontol A Biol Sci Med Sci.* 1997;52:M218-M224.

5. Rautaharju PM, Manolio TA, Furberg CD, et al. Ischemic episodes in 24-h ambulatory electrocardiograms of elderly persons: the Cardiovascular Health Study. *Int J Cardiol.* 1995;51:165-175.

## Long-term Prognosis of Hepatitis C Virus Infection

**To the Editor:** Dr Thomas and colleagues<sup>1</sup> present the results of 9 years of follow-up in a cohort of injection-drug users with hepatitis C virus (HCV) infection. The primary outcome measures were viral clearance and end-stage liver disease (ESLD). Since injection drug use now accounts for 60% of cases of new HCV infections in the United States,<sup>2</sup> this work is a valuable prospective study of a high-risk population in which the natural history of infection has great public health consequences. The design avoids the referral bias that limits the validity of retrospective studies, and the study population is demographically distinct from previous study cohorts, which have tended to be older and sicker (such as transfusion-infected persons<sup>3</sup>) or younger and healthier (such as immune globulin recipients<sup>4</sup>). Nonetheless, these data do not answer several important questions.

First, it is not clear that the follow-up periods are sufficiently long to identify those who will develop ESLD. The authors use a proxy time of infection, defined as time from first injection drug use, which may overestimate the duration of HCV infection. They evaluated patients after a median of 13.7 years of drug use plus a median of 8.8 years follow-up, estimating a median duration of HCV infection greater than 15 years for 75% of patients. Even if their estimates are correct, this may not be long enough to rule out the development of ESLD in the majority of patients. Given the broad range of estimated infection times within the cohort, it would have been of greater interest to report the incidence of ESLD in those infected for 20 to 30 years as compared with the rest of the cohort.

Second, the study outcomes of gross clinical stigmata of ESLD or death due to ESLD occur very late in liver disease. Biopsy evidence of cirrhosis is a far more sensitive marker. Liver histology was reported for 2 subsets of patients and showed cirrhosis in 1% (2/210) of those with no apparent liver disease and 7% (5/71) of those dying from a nonhepatic cause. Again, it would have been useful to report the estimated duration of infection in patients with cirrhosis.

Finally, it is not clear why serum liver enzyme levels, which were measured, were not reported. It would be interesting to know how transaminase levels correlated with viral clearance, histology (when known), and ESLD incidence.

It has been estimated that 15% to 20% of those with chronic HCV will develop cirrhosis and ESLD.<sup>5</sup> Prospective information on homogeneous cohorts is badly needed. Additional information on this cohort would be of great interest.

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1. Thomas DL, Astemborski J, Rai RM, et al. The natural history of hepatitis C infection: host, viral, and environmental factors. *JAMA.* 2000;284:450-456.

2. Centers for Disease Control and Prevention. Recommendations for prevention and control of hepatitis C virus (HCV) infection and HCV-related chronic disease. *MMWR Morb Mortal Wkly Rep.* 1998;47(RR-19):1-39.

3. Seeff LB, Buskell-Bales Z, Wright EC, et al, for the National Heart, Lung, and Blood Institute Study Group. Long-term mortality after transfusion-associated non-A, non-B hepatitis. *N Engl J Med.* 1992;327:1906-1911.

4. Kenny-Walsh E. Clinical outcomes after hepatitis C infection from contaminated anti-D immune globulin. *N Engl J Med.* 1999;340:1228-1233.

5. Liang TJ, Reherman B, Seeff LB, Hoofnagle JH. Pathogenesis, natural history, treatment, and prevention of hepatitis C. *Ann Intern Med.* 2000;132:296-305.

**In Reply:** In response to Dr Behrman, we followed up 1667 HCV-infected persons for a median of 8.8 years, and their estimated median duration of HCV infection was 13.7 years at enrollment. Data from some prior studies indicate that the infection duration profile of the cohort was ideal for detecting ESLD. For example, in 1 study 20% of persons with HCV infection following blood transfusion had cirrhosis 1.5 to 16 years later and 10% developed ESLD.<sup>1</sup> On the other hand, our data and those recently reported by others indicate that the ESLD incidence can be much lower, underscoring the importance of factors that modify disease expression.<sup>2,3</sup> Longer duration of

infection, older age, and heavy alcohol use appear to be especially unfavorable prognostic factors.<sup>4</sup> Thus, while it is difficult to predict the rate of disease progression for a given HCV-infected person, rates are best surmised from the experience of persons with similar risk profiles.

The incidence of ESLD in persons infected for 20 to 30 years is similar to what we presented for those infected for 18 or more years: the upper quartile. In those with an estimated duration of infection of 20 or more years, there were 13 instances of ESLD during 2492 person-years, an incidence of 5.22 per 1000 person-years. In this cohort, age is highly correlated with time from first drug use and thus could not be simultaneously considered in the multivariate analysis. However, both age and time from first drug use were associated with ESLD after adjusting for alcohol ingestion. The estimated duration of infection for the 2 patients with cirrhosis in the subset who underwent biopsy was 16.5 and 20 years, respectively.

In this cohort, routine serum liver enzyme testing began in 1995. Since this represented only a small fraction of the observation time (two thirds of the instance of ESLD had already occurred), the data were judged to be too incomplete to warrant analysis against that outcome. A complete analysis of liver-related studies vs liver biopsy results is ongoing.

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## Estimating the Risk of Cancer in Children With AIDS

**To the Editor:** Dr Biggar and colleagues<sup>1</sup> recently reported elevated risks of cancer in children with AIDS (acquired immunodeficiency syndrome). As contributors of data to this study, we have several concerns about the authors' conclusions.

First, the authors did not measure the effect of perinatal antiretroviral therapy exposure on the relationship between HIV (human immunodeficiency virus) infection and cancer. However, some AIDS registries contain data on perinatal antiretroviral exposure. Evaluation of these data would help confirm that cancer incidence is not related to antiretroviral exposure.

Second, Biggar et al overestimate the relative risks, which were calculated using the observed and expected number of cancer cases. In a significant departure from previous analyses of matched AIDS and cancer data,<sup>2-5</sup> the study's observed cancer cases were derived from patients with cancers recorded in the cancer registry that matched an AIDS case or cancer cases that appeared in only the AIDS registry. For some sites, such as the brain, the majority of cases (61%) were derived from only the AIDS registry.

The calculation of expected cases was also inaccurate. While the cancer cases from only the AIDS registry were added to the number of observed cases, they are not recorded in the cancer registry, and therefore would not contribute to the population-based cancer incidence. Because the expected cases are derived from the population cancer incidence multiplied by the person-time at risk, the authors underestimate the expected number of cases. Using an inflated numerator and deflated denominator results in a substantial overestimation of risk.

Third, the analysis of cancer incidence by risk factors in this study must be interpreted with caution. Biggar et al ascertained risk using the Centers for Disease Control and Prevention (CDC) AIDS case hierarchy. Although patients may have multiple risks for the acquisition of HIV infection, they may appear to have a single risk factor when the CDC hierarchy is used. Use of the summary risk variable does not fully describe every patient's known risks. In New York State's pediatric AIDS cohort, approximately 250 infants have 2 risks recorded, and approximately 50 have 3 risks (approximately 24% of the entire cohort have multiple risks). For children whose mothers were infected through contact with a bisexual man, a group of interest in this study, 12 infants had this risk recorded on the AIDS registry, although the CDC risk hierarchy classified them as having other risks.

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1. Biggar RJ, Frisch M, Goedert JJ. Risk of cancer in children with AIDS. *JAMA*. 2000;294:205-209.
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**In Reply:** We did not analyze the effect of therapy because of limited data. Most US children with AIDS were born between 1987 (when therapy first became available) and 1994, before the era of highly active therapy. Thus, most children had the opportunity to receive antiretroviral therapy of some type. However, AIDS registries are not reliable sources of information about individual therapy.

Mr Gallagher and Dr Wang question our inclusion of brain lymphomas in the analysis when these were reported only in the AIDS registry data. As explained in our article, we were presented with an unusual finding in the analysis. More than half (12) of the 23 cases of primary brain lymphoma recorded in children were known only from the AIDS registry data. For 2 other cases, the diagnosis was primary brain lymphoma in the AIDS registry but the cancer registry information simply listed non-Hodgkin lymphoma. Among the remainder, 5 cases were known from both AIDS and cancer registry data, and 4 cases were known only from the cancer registry. Thus, had we restricted diagnoses of primary brain lymphoma to the cancer registry data, we would have used only 39% of the reported cases. In contrast, among children with AIDS who had known nonbrain lymphomas, 71% of cases were found in the cancer registries, a proportion similar to that found in adults with AIDS.

We felt that it was reasonable to accept all reports as valid because the reporting of brain lymphomas in children might represent a special circumstance. Diagnosing primary brain lymphoma requires invasive techniques, which clinicians might have been reluctant to undertake in children dying with AIDS. Few children with AIDS would have had autopsies. Cancer registries often obtain much of their data from pathology departments and medical record review, sources that might be incomplete in children with terminal AIDS illnesses. It is possible that the diagnosis of lymphoma might be incorrect in some cases, since conditions such as toxoplasmosis and other infections can mimic primary brain lymphoma. However this error seems unlikely since these diagnoses are uncommon in children with AIDS. Furthermore, it seems unlikely that clinicians would err in specifying the brain as the site in a case diagnosed as lymphoma; it is more likely they would neglect to provide the site, thus understating the true frequency of cases.

Expected values for primary brain lymphoma were derived from 32 children with such tumors who were not identified as having AIDS. In this group, diagnostic procedures probably would have been more aggressive, and, with more complete evaluations, the records would be more likely to come to the attention of the cancer registry data collectors. Furthermore, some of these patients could have had unreported AIDS. If the background rate in children without AIDS is high because of these factors, our estimates of the relative risks in children with AIDS would be too low.

We stressed that the risks we reported in our article were imprecise for a number of reasons, including those described here. However, whether cases listed only in AIDS registries are included or excluded, children with AIDS are at exceptional risk of primary brain lymphoma.

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## Helping Patients Integrate Research Evidence

**To the Editor:** In their article on integrating research evidence with the care of the individual patient, Dr McAlister and colleagues<sup>1</sup> state, "Since your radiology department, in a recent audit, demonstrated that their ultrasonographic interpretations are highly correlated with angiographic results,<sup>2</sup> you feel confident about their findings that both patients have moderate [carotid] stenoses. . . ." This conclusion is not supported by the cited reference, which concludes that "the results indicate that the accuracy of ultrasonography is moderate when flow parameters are used to assess the degree of stenosis. Ultrasonography should be used as a screening tool to exclude patients with no carotid artery disease from further testing. Conventional angiography remains an essential investigation before assigning the risk of stroke and deciding appropriate treatment. . . ."<sup>2</sup>

By excluding the diagnostic process from the discussion, the authors ignore a basic principle in decision analysis: treatment decisions are always made with uncertainty. The choice of treatment depends on many factors, including the probability of having moderate instead of severe stenosis. The level of certainty of diagnosis should be made explicit to the patient because it may play a role in individual decision making. For example, a patient who prefers medical treatment for moderate stenosis might choose endarterectomy in case of severe stenosis. If, on the basis of clinical examination and ultrasonography, the chance of moderate stenosis is 80% and severe stenosis is 20%, such a patient probably would ask for additional testing (eg, conventional angiography or magnetic resonance angiography).

In general, the question of whether the patient will benefit from additional testing depends on the prior probability of disease, the accuracy of testing, and the risks and benefits of the diagnostic procedure and treatment.<sup>3</sup> Whether to perform additional diagnostic tests involves judgments about whether the potential increased information justifies the costs and risks. I appreciate that the discussion of McAlister et al was simplified in the interest of clarity. However, although patients often do not want to be involved in the diagnostic process,<sup>4</sup> I would like to emphasize that both diagnosis (including screening) and therapy should be subject to informed consent and patient participation.

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1. McAlister FA, Straus, SE, Guyatt, GH, Haynes RB. Users' guides to the medical literature, XX: integrating research evidence with the care for the individual patient. *JAMA*. 2000;283:2829-2836.

2. Eliasziw M, Rankin RN, Fox AJ, Haynes RB, Barnett HJ. Accuracy and prognostic consequences of ultrasonography in identifying severe carotid stenosis. *Stroke*. 1995;26:1747-1752.

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4. Deber RB, Kraetchner N, Irvine J. What role do patients wish to play in treatment decision making. *Arch Intern Med*. 1996;156:1414-1420.

**To the Editor:** Dr McAlister and colleagues<sup>1</sup> present a method for choosing between surgical and medical treatment for patients with carotid stenosis. Whether busy clinicians in practice will use this cumbersome method remains to be seen. However, I am concerned that these calculations may lead clinicians to make decisions that are not in the best interest of their patients.

First, the article leaves the impression that receiving benefits from surgery in terms of avoiding stroke is like buying a ticket in a lottery: 1 in 20 wins a big prize (the number needed to treat [NNT] is 20). However, another interpretation is that most patients derive little benefit. It is conceivable that the effect of treatment is to slow the stenosing process and delay strokes in many patients. The absolute risk reduction and hence the NNT would be the same whether a small number of patients (eg, 1 in 20) totally avoid a stroke or whether all patients experience a small delay in onset. Patients' preferences for therapy, however, may depend on the mode of action (lottery or small delays). The calculation of the "likelihood of being helped vs harmed" makes no sense unless the mode of action is identical to a lottery.

Second, in eliciting preferences for the different outcomes, McAlister et al propose to ask patients to value "stroke" and "death within 30 days of surgery." Although death and stroke are health states, "death within 30 days" entails a combination of a time dimension and a health state. Patients may be misled if clinicians make decisions without taking duration of the health states into consideration.

The NNT and proposed valuation of outcomes fail to capture the crucial time dimension in preventing strokes. Similar arguments may be relevant for a series of other interventions aimed at slowing disease processes and delaying bad outcomes such as death, myocardial infarction, and fractures. Clinicians may do well to look into the rich scientific literature on medical decision making instead of using simple—but misleading—tools such as the "likelihood of being helped vs harmed."

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1. McAlister FA, Straus SE, Guyatt GH, Haynes RB. Users' guides to the medical literature. XX: integrating research evidence with the care for the individual patient. *JAMA*. 2000;283:2829-2836.

**In Reply:** We agree with Dr Jager that our description of the accuracy of ultrasonographic interpretations of carotid disease in our institution is simplified. Our aim, as he points out, was to present various methods of individualizing evidence about therapy with simple clarity for our patients. We could have included more information about the accuracy of the diagnostic process and the morbidity associated with angiography, but we chose to present a simple model that could be easily understood.

We agree with Dr Kritiansen that the NNT of 20 is for the average patient reported in the trial and that these numbers may

not apply to individual patients whom we studied in our article. We emphasized that these numbers may not be directly applicable to an individual patient because of differences in baseline risk and relative risk reduction across subgroups. We also discussed how this can be individualized.

Ideally, we would like to be able to conduct a clinical decision analysis (including formal utility assessment) for every patient rather than using the informal method of assessing patients' values that we describe. However, given the time this requires for complex medical decisions, we have not found it to be feasible. Indeed, we recently had a decision analyst join our clinical service for a month to determine if clinical decision analysis could be done. We were unsuccessful in our efforts because of the complexity of the cases and time constraints. As a result, we (and others) are struggling to find other methods to achieve shared decision making that can be completed at the bedside and in the clinic and that are intelligible and easy to use. As we mentioned, much research in this area needs to be done, and we welcome readers to offer other potential solutions to this challenge.

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## RESEARCH LETTERS

### Knowledge of Ethical Standards in Genetic Testing Among Medical Students, Residents, and Practicing Physicians

**To the Editor:** As genetic technology evolves, physicians will find themselves called on to counsel patients about a rapidly increasing number of diseases for which genetic testing is available. The increased availability of testing raises new and complex ethical issues. Lack of familiarity with these issues may lead to profound and lifelong negative effects on patients, particularly children.

**Methods.** A 2-page survey to evaluate awareness of ethical issues related to genetic testing was developed and mailed to all medical students (n=417) and primary care residents (n=161) at the University of Massachusetts Medical School, Worcester, as well as 1000 randomly selected primary care

**Table 1.** Total Response to Clinical Scenario Survey

	Agree to Test, No. (%)	Not Agree to Test, No. (%)	Unsure, No. (%)
Scenario 1	433 (49.6)	235* (26.9)	181 (20.7)
Scenario 2	308 (35.3)	325* (37.2)	215 (24.6)
Scenario 3	401* (46)	144 (16.5)	297 (34)

\*Normatively correct response.

**Table 2.** Incorrect Responses by Level of Training

	Medical Student, No. (%)	Resident, No. (%)	Practitioner, No. (%)	$\chi^2$ Value
Scenario 1	76 (31.4)	39 (43.8)	315 (61.5)	59.3*
Scenario 2	62 (25.5)	27 (30.3)	214 (42)	35.6*
Scenario 3	25 (10.4)	6 (6.7)	112 (22.1)	33.5*

\* $P < .001$ .

physicians (250 pediatricians, obstetrician-gynecologists, family practitioners, and internists, respectively). The survey included 3 scenarios regarding requests for genetic testing:

(1) "Would you agree to order cystic fibrosis carrier testing on 3 healthy young children at the request of the father who recently discovered he was a carrier?" (There is a consensus among geneticists and ethicists that genetic testing should not be performed in minors unless there is a defined medical benefit that will occur during childhood.<sup>1,2</sup>)

(2) "Would you agree to order pre-symptomatic Huntington Disease testing on the 6-year-old daughter of a man recently diagnosed with the disease at the request of her parents?" (Presymptomatic testing for Huntington disease status may have a profound and long-lasting negative effect on a child who is tested without consent. A consensus of geneticists, the International Huntington Association, and the World Federation of Neurology all agree that minors should not be tested for Huntington disease status at the parents' request.<sup>1,3,4</sup>)

(3) "Would you agree to prenatal testing for a Duchenne Muscular Dystrophy carrier who does not want to inform her husband of the pregnancy because he would not agree with her decision to abort if the test were positive?" (By consensus, geneticists, ethicists, and obstetrician-gynecologists would preserve the mother's right to privacy and autonomy and not require that the husband be informed.<sup>5,6</sup>)

**Results.** The overall response rate was 53% for practitioners (n=532), 56% for residents (n=90), and 59% for medical students (n=247). For all 3 scenarios, a minority of the sample provided the normatively correct response (TABLE 1), and practitioners were significantly more likely to provide incorrect responses to each of the 3 items than were residents and medical students (TABLE 2).

**Comment.** This study demonstrates a disturbing lack of familiarity with the ethical principles involved in genetic testing. In each scenario, practitioners were less likely to conform to expected standards than were trainees. While medical schools have made innovative curriculum changes to increase awareness of genetic testing and its ethical implications, future edu-

cational efforts need to expand to include training of practicing physicians.

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## Exhaustion of Prescription Benefits and Medicare Beneficiaries' Disenrollment From Managed Care

**To the Editor:** Rector<sup>1</sup> recently reported that enrollees in Medicare health maintenance organizations who had exhausted their capped prescription benefits were more likely than those who had not exhausted their capped benefit to disenroll from their health plan. We reexamined this relationship during a 2-year period for 3 plans varying in cap amount and administration of benefits.

**Methods.** Prescription and eligibility data were obtained from January 1, 1997, through December 31, 1998, for 3 Medicare health maintenance organization plans with capped prescription benefits. All plans were located in markets with moderate to high Medicare managed care penetration. Plan markets were located in West South Central (2 plans) and South Atlantic states (1 plan).

In 1997, annual capped benefits were \$600 (plan A), \$1000 (plan B), and \$1500 (plan C) and were administered on a quarterly basis (ie, only one fourth of the annual cap amount was available each quarter). In 1998, all plans had annual capped benefits of \$1000, administered quarterly in plans A and C and annually in plan B. Enrollment in 1997 and 1998 for plan A was 5434 and 6769, respectively; for plan B, it was 8667 and 10372; and for plan C, it was 2961 and 3731.

Individuals with enrollment in the first 3 months of each year were included in the analysis. For all beneficiaries who reached

the cap, whether in quarterly or annually capped plans, we identified the first month of the year in which the capped limit was exceeded. Unlike Rector, we were not able to identify and exclude members who disenrolled nonvoluntarily. Like Rector, we used an extended Cox model with the internally defined time-dependent variable of reaching the cap to analyze the relationship between reaching the cap and disenrollment from the health plan.<sup>2</sup> Models were estimated for each plan and each year controlling for participant age, sex, and chronic disease score.<sup>3</sup>

**Results.** The percentages of members reaching their annual prescription cap for plans A, B, and C, respectively, were 22.6%, 0.7%, and 1.6% in 1997 and 12%, 4.1%, and 3.9% in 1998. Disenrollment rates among those enrolled in the first 3 months of each year for plans A, B, and C, respectively, were 19.3%, 28.9%, and 6.8% in 1997 and 10.4%, 22.9%, and 14.0% in 1998. Among those disenrolling in 1997, 21%, 7%, and 7%, respectively, re-enrolled in 1998.

The risk of disenrollment across all plans and both years was significantly associated with older age, greater disease burden (ie, higher chronic disease score), and reaching the cap. In 1997, the relative risks (RRs) of disenrollment in any given month for those reaching the cap for the 3 plans were 2.62 (95% confidence interval [CI], 2.15-3.19), 2.21 (95% CI, 1.70-2.88), and 2.24 (95% CI, 1.43-3.50); in 1998, the RRs of disenrollment were 3.04 (95% CI, 2.40-3.86), 1.79 (95% CI, 1.12-2.86), and 2.30 (95% CI, 1.86-2.86) in plans A, B, and C, respectively.

**Comment.** Exhaustion of prescription coverage, whether administered on a quarterly or annual basis, was associated with a 2- to 3-fold increase in the RR of disenrollment. These findings expand on those of Rector and suggest that this relationship holds under various scenarios including variation in underlying use, cap amounts, and cap administration.

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1. Rector TS. Exhaustion of drug benefits and disenrollment of Medicare beneficiaries from managed care organizations. *JAMA*. 2000;283:2163-2167.
2. Crowley J, Hu M. Covariance analysis of heart transplant data. *J Am Stat Assoc*. 1977;72:27-36.
3. Clark DO, Korff MV, Saunders K, Baluch WM, Simon GE. A chronic disease score with empirically derived weights. *Med Care*. 1995;33:783-795.

## CORRECTIONS

**Incorrect Unit of Measure and Numbers:** In the Original Contribution entitled "Cognitive-Behavioral Therapy, Imipramine, or Their Combination for Panic Disorder" published in the May 17, 2000, issue of THE JOURNAL (2000;283:2529-2536), the units of measure for imipramine and desipramine should be ng/mL instead of ng/dL on page 2532 and ng/mL instead of mg/mL on page 2535. On page 2530 under "Study Design" patients randomized to CBT+placebo should number 5 per block of 24, not 25. In the "Treatment Conditions" section on page 2531, near the end of the third paragraph, ". . . the dosage [of imipramine] could be increased up to 300 mg/d by week 5" should read "week 7."

**Author Omitted:** In the Caring for the Critically Ill Patient article entitled "Ketoconazole for Early Treatment of Acute Lung Injury and Acute Respiratory Distress Syndrome" published in the April 19, 2000, issue of THE JOURNAL (2000;283:1995-2002), an author was inadvertently omitted from the ARDS Network listing on page 2002. Brian Christman, MD, should have been listed with the Vanderbilt University group and identified as an author.

**Acknowledgment Omission:** In the Original Contribution entitled "Menopausal Estrogen and Estrogen-Progestin Replacement Therapy and Breast Cancer Risk" published in the January 26, 2000, issue of THE JOURNAL (2000;283:485-491), acknowledgments were omitted. The authors wish to thank the Breast Cancer Detection Demonstration Project study participants as well as Susan Englehart, Cathy Ann Grundmayer, and the staff at Westat Inc, Rockville, Md, for conduct of the Breast Cancer Detection Demonstration Project Follow-up Study.

**Incorrect Data in Table:** In the Original Contribution entitled "Estrogen Replacement Therapy for Treatment of Mild to Moderate Alzheimer Disease: A Randomized Controlled Trial" published in the February 23, 2000, issue of THE JOURNAL (2000;283:1007-1015), incorrect data appeared in Table 3 on page 1013. In the placebo group column, the mean (SD) changes in scores at 12 months for the Emotional Face Recognition Test and the Grooved Pegboard Test should have been -5.7 (22.4) and -5.2 (42.4), respectively.

**Photo Misidentification:** In the Medical News & Perspectives article entitled "Psychiatrists Help Survivors in the Balkans" published in the March 8, 2000, issue of THE JOURNAL (2000;283:1277-1278), the photo on page 1278 identified as Ismet Ceric, MD, should have been identified as Vlado Jukić, MD.

**Acknowledgment Omission:** In the Original Contribution entitled "Vaginal Misoprostol Administered 1, 2, or 3 Days After Mifepristone for Early Medical Abortion: A Randomized Trial" published in the October 18, 2000, issue of THE JOURNAL (2000;284:1948-1953), an acknowledgment was omitted. The authors wish to acknowledge the contributions of Larry Lader, president of the Abortion Rights Mobilization, for making the study possible.

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**CORRECTIONS**

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**Incorrect Affiliation Description:** In the Letters entitled "Outcomes of a Trial of HIV-1 Immunogen in Patients With HIV Infection" published in the May 2, 2001, issue of THE JOURNAL (2001;285:2191), the author affiliation description was incorrect. On page 2191, the sentence that read "ASG Inc is a provider of information technology consulting services" should have read "ASG is a provider of clinical research, data management, and statistical services to the pharmaceutical industry."

**Error in Text and Table:** In the Original Contribution entitled "Long-term Effects of an Early Childhood Intervention on Educational Achievement and Juvenile Arrest: A 15-Year Follow-up of Low-Income Children in Public Schools" published in the May 9, 2001, issue of THE JOURNAL (2001;285:2339-2346), there was an error in the text and in the table. On page 2342, in Table 2, the zeros in the last 2 columns of the last 2 rows should have been  $P < .001$ . In the third column of the text, the paragraph above the heading "Outcome Variables," the last sentence that reads "The mean per child expenditures in 1996 for 1 year of preschool and 1 year of school-age participation are \$4350 and \$15.00." should read "The mean per child expenditures in 1996 for 1 year of preschool and 1 year of school-age participation are \$4350 and \$1500."

**Incorrect Word:** In the Letters entitled "Overuse of Administrative Data to Measure Underuse of Care" published in the February 14, 2001, issue of THE JOURNAL (2001;285:735-736), an incorrect word, "biannual," was placed in the text. On page 735, the sentence that read "Nonetheless, a recent cost-effectiveness analysis concluded that biannual eye examinations were appropriate for low-risk individuals with type 2 diabetes.<sup>1</sup>" should have read "Nonetheless, a recent cost-effectiveness analysis concluded that biennial eye examinations were appropriate for low-risk individuals with type 2 diabetes.<sup>4</sup>"

**Reference Incorrectly Cited:** In the Original Contribution entitled "Policy Analysis of Cervical Cancer Screening Strategies in Low-Resource Settings: Clinical Benefits and Cost-effectiveness" published in the June 27, 2001, issue of THE JOURNAL (2001;285:3107-3115), the reference was cited incorrectly. On page 3114, reference 9, "Visual inspection with acetic acid for cervical-cancer screening: test qualities in a primary-care setting: University of Zimbabwe/JHPIEGO Cervical Cancer Project. *Lancet*. 1999;353:869-873." should be "University of Zimbabwe/JHPIEGO Cervical Cancer Project. Visual inspection with acetic acid for cervical-cancer screening: test qualities in a primary-care setting. *Lancet*. 1999;353:869-873."

**Incorrect Wording:** In the Letters entitled "Industry Support of Researchers in Universities and Academic Medical Centers" published in the May 9, 2001, issue of THE JOURNAL (2001;285:2324-2325), there was incorrect wording in a sentence. On page 2324, in the second column, third paragraph, the sentence that read "The economics of low-margin computer chip markets are forcing companies to scale back their basic university-supported research and they are focusing on increasing productivity." should have read "The economics of low-margin computer chip markets are forcing companies to scale back their university-supported basic research and they are focusing on increasing productivity."

**Incorrect Spelling of Author's Last Name:** In the Letters entitled "Helping Patients Integrate Research Evidence" published in the November 22/29, 2000, issue of THE JOURNAL (2000;284:2595), the author's last name was misspelled. On page 2595, the author's last name "Kritiansen" should have been "Kristiansen."