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Massachusetts recently joined New York, New Jersey, and Pennsylvania in reporting death rates associated with cardiac surgery for individual surgeons — another wave in the tide of public reporting that is sweeping the country. Such reporting raises questions about distinguishing the goals that define one’s work from the targets used to measure success. For hospitals and physicians, minimizing death and complications is an undisputed goal. But is zero the ideal target for measures of performance with respect to death and complications? In this era of public accountability, the answers to questions such as this turn out to be surprisingly complex.


Since April 16, when Virginia Tech student Seung-Hui Cho gunned down 27 fellow students and 5 faculty members and injured 24 other people before taking his own life, some disturbing facts about his mental health history have emerged. At various points during Cho’s college career, Virginia Tech police officers, professors, and students recognized that he was mentally troubled, but although state psychiatric evaluators once briefly committed him to a psychiatric hospital, it is unclear whether anyone from the school monitored him after his release. These discoveries have left investigators wondering whether the killings could have been prevented — and college . . .


Teleradiology has become an essential part of the practice of radiology, with broad implications for care delivery and the organization of work. The same technology that can transmit a radiograph or a computed tomographic (CT) scan obtained at night at an emergency department in Philadelphia to Bangalore, India, for reading during the day can move any digital radiograph anywhere at any time.1 Within minutes, images can appear on the desktop of a radiologist at home, in an office several floors away from a central reading room, or at another hospital. Studies can be transmitted to the referring physician, a workstation . . .


For several weeks this spring, national attention was focused on a mother’s struggle to prevent the Children’s Hospital of Austin from withdrawing life support from her infant son. Emilio Gonzales was an 18-month-old boy who had Leigh’s disease, a progressive and fatal neurometabolic disorder. He had been on life support in the intensive care unit for 5 months. The hospital had invoked the Texas Advance Directives Act, which authorized it to withdraw life support if an ethics committee had determined that further life support was medically inappropriate and provided the hospital gave the family 10 days’ notice and attempted to . . .


A recent meta-analysis raised concern regarding an increased risk of myocardial infarction and death from cardiovascular causes associated with rosiglitazone treatment of type 2 diabetes. We conducted an unplanned interim analysis of a randomized, multicenter, open-label, noninferiority trial involving 4447 patients with type 2 diabetes who had inadequate glycemic control while receiving metformin or sulfonylurea, in which 2220 patients were assigned to receive add-on rosiglitazone (rosiglitazone group), and 2227 to receive a combination of metformin plus sulfonylurea (control group). The primary end point was hospitalization or death from cardiovascular causes. Because the mean follow-up was only 3.75 years, our interim analysis had limited statistical power to detect treatment differences. A total of 217 patients in the rosiglitazone group and 202 patients in the control group had the adjudicated primary end point (hazard ratio, 1.08; 95% confidence interval [CI], 0.89 to 1.31). After the inclusion of end points pending adjudication, the hazard ratio was 1.11 (95% CI, 0.93 to 1.32). There were no statistically significant differences between the rosiglitazone group and the control group regarding myocardial infarction and death from cardiovascular causes or any cause. There were more patients with heart failure in the rosiglitazone group than in the control group (hazard ratio, 2.15;

Pregnancy rates in women of advanced maternal age undergoing in vitro fertilization (IVF) are disappointingly low. It has been suggested that the use of preimplantation genetic screening of cleavage-stage embryos for aneuploidies may improve the effectiveness of IVF in these women. We conducted a multicenter, randomized, double-blind, controlled trial comparing three cycles of IVF with and without preimplantation genetic screening in women 35 through 41 years of age. The primary outcome measure was ongoing pregnancy at 12 weeks of gestation. The secondary outcome measures were biochemical pregnancy, clinical pregnancy, miscarriage, and live birth. Four hundred eight women (206 assigned to preimplantation genetic screening and 202 assigned to the control group) underwent 836 cycles of IVF (434 cycles with and 402 cycles without preimplantation genetic screening). The ongoing-pregnancy rate was significantly lower in the women assigned to preimplantation genetic screening (52 of 206 women [25%]) than in those not assigned to preimplantation genetic screening (74 of 202 women [37%]; rate ratio, 0.69; 95% confidence interval [CI], 0.51 to 0.93). The women assigned to preimplantation genetic screening also had a significantly lower live-birth rate (49 of 206 women [24%] vs. 71 of 202 women [35%]; rate ratio, 0.68; 95% CI, 0.50 to 0.92). Preimplantation genetic screening did not increase but instead significantly reduce the rate of ongoing pregnancies and live births after IVF in women of advanced maternal age.


Acute mountain sickness occurs in some unacclimatized persons who travel to terrestrial altitudes at which barometric pressures are the same as those in commercial aircraft during flight. Whether the effects are similar in air travelers is unknown. We conducted a prospective, single-blind, controlled hypobaric-chamber study of adult volunteers to determine the effect of barometric pressures equivalent to terrestrial altitudes of 650, 4000, 6000, 7000, and 8000 ft (198, 1219, 1829, 2134, and 2438 m, respectively) above sea level on arterial oxygen saturation and the occurrence of acute mountain sickness and discomfort as measured by responses to the Environmental Symptoms Questionnaire IV during a 20-hour simulated flight. Among the 502 study participants, the mean oxygen saturation decreased with increasing altitude, with a maximum decrease of 4.4 percentage points (95% confidence interval, 3.9 to 4.9) at 8000 ft. Overall, acute mountain sickness occurred in 7.4% of the participants, but its frequency did not vary significantly among the altitudes studied. The frequency of reported discomfort increased with increasing altitude and decreasing oxygen saturation and was greater at 7000 to 8000 ft than at all the lower altitudes combined. Differences became apparent after 3 to 9 hours of exposure. Persons older than 60 years of age were less likely than younger persons and men were less likely than women to report discomfort. Four serious adverse events, 1 of which may have been related to the study exposures, and 15 adverse events, 9 of which were related to study exposures, were reported. Ascent from ground level to the conditions of 7000 to 8000 ft lowered oxygen saturation by approximately 4 percentage points. This level of hypoxemia was insufficient to affect the occurrence of acute mountain sickness but did contribute to the increased frequency of reports of discomfort in unacclimatized participants after 3 to 9 hours.


Some features of breast cancer in women with a BRCA1 mutation suggest that hereditary breast cancer has a poor outcome. We conducted a
national population-based study of Israeli women to determine the influence, if any, of a BRCA1 or a BRCA2 mutation on the prognosis in breast cancer. We obtained data on all incident cases of invasive breast cancer that were diagnosed from January 1, 1987, to December 31, 1988, and recorded in the Israel National Cancer Registry. We requested a paraffin-embedded tumor block or an unstained slide and the corresponding pathological and clinical records for all such cases. DNA extracted from the tumor specimens was analyzed for the three founder mutations in BRCA1 and BRCA2. For each subject, available pathological and oncologic records were reviewed. We were able to retrieve a pathological sample from 1794 of 2514 subjects (71%). Among those women, we obtained medical records for 1545 (86%). A BRCA1 or BRCA2 mutation was identified in 10% of the women who were of Ashkenazi Jewish ancestry. The adjusted hazard ratios for death from breast cancer were not significantly different among carriers and noncarriers (hazard ratio among BRCA1 carriers, 0.76; 95% confidence interval [CI], 0.45 to 1.30; P=0.31; hazard ratio among BRCA2 carriers, 1.31; 95% CI, 0.80 to 2.15; P=0.28). Among women who were treated with chemotherapy, the hazard ratio for death among BRCA1 carriers was 0.48 (95% CI, 0.19 to 1.21; P=0.12). Breast cancer–specific rates of death among Israeli women are similar for carriers of a BRCA founder mutation and noncarriers.


Patients infected with hepatitis C virus (HCV) genotype 2 or 3 have sustained virologic response rates of approximately 80% after receiving treatment with peginterferon and ribavirin for 24 weeks. We conducted a large, randomized, multinational, noninferiority trial to determine whether similar efficacy could be achieved with only 16 weeks of treatment with peginterferon alfa-2a and ribavirin. We randomly assigned 1469 patients with HCV genotype 2 or 3 to receive 180 µg of peginterferon alfa-2a weekly, plus 800 mg of ribavirin daily, for either 16 or 24 weeks. A sustained virologic response was defined as an undetectable serum HCV RNA level (≤50 IU per milliliter) 24 weeks after the end of treatment. The study failed to demonstrate that the 16-week regimen was noninferior to the 24-week regimen. The sustained virologic response rate was significantly lower in patients treated for 16 weeks than in patients treated for 24 weeks (62% vs. 70%; odds ratio for 16 weeks vs. 24 weeks, 0.67; 95% confidence interval, 0.54 to 0.84; P<0.001). In addition, the rate of relapse (a detectable HCV RNA level during follow-up in patients who had undetectable HCV RNA at the end of treatment) was significantly greater in the 16-week group (31%, vs. 18% in the 24-week group; P<0.001). The sustained virologic response rates in patients with a pretreatment serum HCV RNA level of 400,000 IU per milliliter or less was 82% with the 16-week regimen and 81% with the 24-week regimen. Among patients with a rapid virologic response (an undetectable HCV RNA level by week 4), sustained virologic response rates were 79% in the 16-week group and 85% in the 24-week group (P=0.02). Treatment with peginterferon and ribavirin for 16 weeks in patients infected with HCV genotype 2 or 3 results in a lower overall sustained virologic response rate than treatment with the standard 24-week regimen.


In 1998, folic acid fortification of a large variety of cereal products became mandatory in Canada, a country where the prevalence of neural-tube defects was historically higher in the eastern provinces than in the western provinces. We assessed changes in the prevalence of neural-tube defects in Canada before and after food fortification with folic acid was implemented. The study population included live births, stillbirths, and terminations of pregnancies because of fetal anomalies among women residing in seven Canadian provinces from 1993 to 2002. On the basis of published results of testing of red-cell folate levels, the study period was divided into prefortification, partial-fortification, and full-fortification periods. We evaluated the relationship between baseline rates of neural-tube defects in each province and the magnitude of the decrease after fortification was implemented. A total of 2446 subjects with neural-tube defects were recorded among 1.9 million births. The prevalence of neural-tube defects decreased from 1.58 per 1000 births before fortification to 0.86 per 1000 births during the full-fortification period, a 46% reduction (95% confidence interval, 40 to 51). The magnitude of the decrease was proportional to the prefortification baseline rate in each province, and geographical differences almost disappeared after fortification began. The observed reduction in rate was greater...
for spina bifida (a decrease of 53%) than for anencephaly and encephalocele (decreases of 38% and 31%, respectively). Food fortification with folic acid was associated with a significant reduction in the rate of neural-tube defects in Canada. The decrease was greatest in areas in which the baseline rate was high.

**REVIEW ARTICLE**


Overexpression of human epidermal growth factor receptor type 2 (HER2, also referred to as HER2/neu or ErbB-2), a 185-kD receptor first described more than two decades ago, occurs in 20 to 30% of invasive breast carcinomas. In general, patients with breast-cancer cells that overexpress this receptor or that have a high copy number of its gene have decreased overall survival and may have differential responses to a variety of chemotherapeutic and hormonal agents. Thus, strategies to target HER2 appear to be important in treating breast cancer. One such medication is trastuzumab (Herceptin, Genentech), a humanized monoclonal antibody. Trastuzumab binds to . . .

**SPECIAL ARTICLE**


Previously uninsured adults who enroll in the Medicare program at the age of 65 years may have greater morbidity, requiring more intensive and costlier care over subsequent years, than they would if they had been previously insured. We used longitudinal data from the nationally representative Health and Retirement Study to assess self-reported health care use and expenditures from 1992 through 2004 among 5158 adults who were privately insured or uninsured before Medicare coverage began at the age of 65 years. We used propensity-score methods to compare health care use and expenditures for previously insured and uninsured beneficiaries who were similar across numerous characteristics at 59 to 60 years of age and adjusted for differences in supplemental and prescription-drug coverage after 65 years of age. Among 2951 adults with hypertension, diabetes, heart disease, or stroke diagnosed before 65 years of age, previously uninsured adults who acquired Medicare coverage at the age of 65 reported significantly greater increases in the numbers of doctor visits (P<0.001) and hospitalizations (P=0.001) and in total medical expenditures (P=0.02) than did previously insured adults. Significant differential increases were not evident among the 2207 adults without these conditions (P>0.12 for all comparisons). In analyses adjusted for supplemental and prescription-drug coverage, previously uninsured adults with these conditions reported more doctor visits (13% relative difference, P=0.04), more hospitalizations (20% relative difference, P=0.04), and higher total medical expenditures (51% relative difference, P=0.09) from ages 65 to 72 years than did previously insured adults. The costs of expanding health insurance coverage for uninsured adults before they reach the age of 65 years may be partially offset by subsequent reductions in health care use and spending for these adults after the age of 65, particularly if they have cardiovascular disease or diabetes before the age of 65 years.

**IMAGES IN CLINICAL MEDICINE**


A 56-year-old woman with diabetes mellitus complicated by retinopathy and mild nephropathy and managed with glyburide (glibenclamide) and metformin reported having abdominal pain and fever for the past 48 hours. On admission she was short of breath, hypotensive, and in shock. Her white-cell count was 25,900 per cubic millimeter and she had disseminated intravascular coagulation. She was treated with mechanical ventilation, blood products, hemodynamic support with dopamine and norepinephrine, and broad-spectrum antimicrobial therapy. The next day cyanosis developed in three fingers of the right hand (Panels A and B) and in five toes of the right foot (Panels C and . . .


A 23-year-old woman presented to the emergency department with a 3-day history of a painful, erythematous, blistering rash across her sun-exposed skin. Before the onset of the rash, the patient had spent 2 days at the beach, where she had prepared mojitos (a cocktail of rum, mint, sugar, water, and limes). During the subsequent 24 hours, a burning erythema developed and later blistered. Physical examination revealed tender skin (Panel A) with vesicles (arrow) and tense bullae (arrowhead) atop erythematous, edematous plaques on her dorsal hands, forearms, and chest.
Symmetric, discrete, erythematous patches studded with tiny vesicles were found on her . . .

**CLINICAL PROBLEM-SOLVING**


In this Journal feature, information about a real patient is presented in stages (boldface type) to an expert clinician, who responds to the information, sharing his or her reasoning with the reader (regular type). The authors’ commentary follows. A 35-year-old woman presented to the emergency department with a 2-day history of progressive swelling and pain in her left leg, without antecedent trauma. Her pain worsened acutely during the morning before her arrival. She felt warm but reported no fever or chills. She also reported mild dyspnea during the previous day, with no associated chest discomfort. She reported no recent trauma . . .

**CLINICAL PRACTICE**


This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors’ clinical recommendations. A healthy 33-year-old woman comes to establish care. She reports no breast symptoms, her age at menarche was 14, and she has no children. She notes a family history of early-onset breast cancer in her sister (whose condition was diagnosed at the age of 35 years and who is alive at 39 years), mother (diagnosed at 37 years and alive at 60 . . .

**HEALTH POLICY REPORTS**


Efforts by the 110th Congress, which is commanded by Democrats eager to reduce the record number of people without health insurance, coupled with other federal and state initiatives,1,2,3 have thrust health care reform into the political limelight for the first time in 12 years. Not since 1994, when the comprehensive proposal of the administration of President Bill Clinton was rejected, has the erosion of private insurance coverage and the continuing rise in health care expenditures aroused such intense interest among policymakers. Adding an impetus to this renewed interest are other proposals that have been unveiled by an unusual collection of . . .

**CLINICAL IMPLICATIONS OF BASIC RESEARCH**


For the past three decades, researchers have been studying the interactions between hematopoietic stem cells and the surrounding cells of the bone marrow. The area where these interactions occur is called the hematopoietic microenvironment.1 Such interactions are key to the maintenance of hematopoietic stem cells and do not occur randomly in the bone marrow cavity; instead, they are preferentially located in different places within this space — hence the phrase “stem-cell niche.”2 A stem-cell niche is an accumulation of hematopoietic stem cells in a particular place that sustains the survival and function of the cells through cell–cell and cell–matrix interactions . . .

**IMAGES IN CLINICAL MEDICINE**


A 57-year-old man who had end-stage renal disease was admitted to the hospital because of infection of a left-upper-extremity fistula. Vancomycin was started empirically, and blood cultures grew methicillin-resistant Staphylococcus aureus. Several days after admission, he reported new pain, redness, and decreased visual acuity in his right eye. Visual acuity was assessed by the ability to count the number of fingers held up by the examiner at a distance of 10 in. (25 cm). Visual inspection revealed marked subconjunctival hemorrhage (short arrow) and a small hypopyon (long arrow). Ophthalmologic examination showed vitreous debris and retinal traction, which were consistent . . .


A 70-year-old man was admitted to the hospital for evaluation of thickening of the skin. Four years earlier, he had undergone kidney transplantation for hypertension-induced end-stage renal disease.
Two months before this admission, hemodialysis was reinitiated because of allograft failure. At that time, magnetic resonance angiography of the transplanted kidney with gadolinium enhancement showed no evidence of renal-artery stenosis. Examination revealed flexion contracture of his right elbow with prominent induration of the skin. The skin of his legs and lower abdomen was also affected, but that of his upper abdomen, chest, left (dominant) arm, and face was spared. Biopsy revealed . . .

CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL


Dr. Kevin N. Sheth (Neurology): A 58-year-old right-handed woman with type 1 diabetes was admitted to the hospital because of a 2-week history of increasing fatigue and word-finding difficulties and a 2-day history of right-arm weakness. She had been in her usual state of health until 3 years before admission, when an episode of word-finding difficulty occurred, associated with headache and mild right-sided facial weakness. She was admitted to a local hospital, where computed tomography (CT) of the head revealed no abnormalities. Magnetic resonance imaging (MRI) revealed a punctate subcortical lesion in the left parietal white matter; magnetic resonance angiography . . .

CLINICAL DECISIONS


In mid-May, we introduced Clinical Decisions — a new interactive feature designed to help us understand how our readers would manage a given clinical case. Our opening case1 involved how to tailor the care of a 30-year-old woman with mild persistent asthma who, although only intermittently symptomatic while receiving treatment with inhaled beclomethasone at a dose of 160 µg twice a day, desired to cut back her treatment. Among the three options offered to you, the most popular — receiving 2281 votes (37.5% of the 6085 votes cast) — was to switch the patient’s treatment to a corticosteroid and a . . .


In 2004, the United Kingdom committed £1.8 billion ($3.2 billion) to a new pay-for-performance contract for family practitioners.1 During the first year, the levels of achievement exceeded those anticipated by the government, with an average of 83.4% of the available incentive payments claimed.2 However, the quality of care in English family practices had already begun to improve in response to a wide range of initiatives,3,4,5,6 including national standards for the treatment of major chronic diseases and a national system of inspection (Table 1). Family practitioners already had some experience with financial incentives from the limited use of incentive . . .