

#### D COMPLICATION RATES

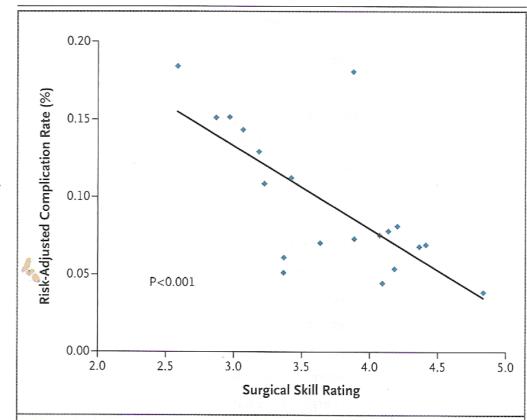


Figure 1. Relationship between Summary Peer Rating of Technical Skill and Risk-Adjusted Complication Rates after Laparoscopic Gastric Bypass.

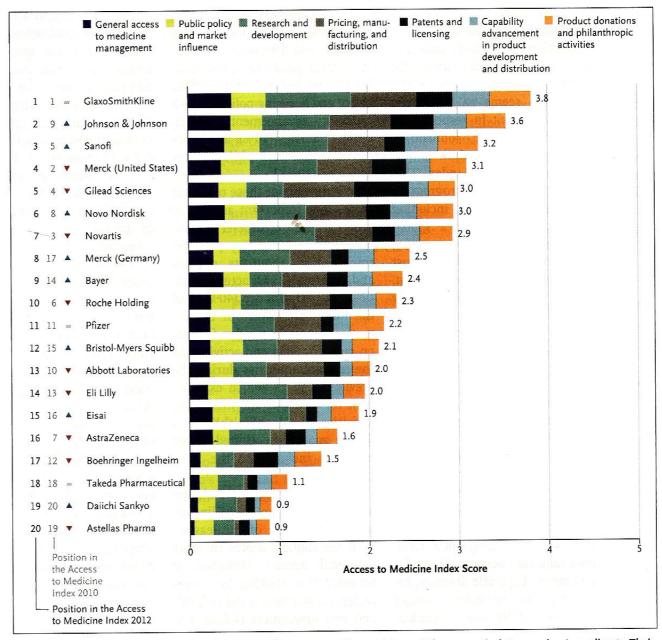
Each diamond in the scatter plot represents 1 of 20 practicing bariatric surgeons.

(Fig. 1) The 5 curgeons in the hottom quartile

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SPECTIVE

BIG PHARMA AND SOCIAL RESPONSIBILITY



Access to Medicine Index 2012 Rankings of the World's 20 Largest Research-Based Pharmaceutical Companies According to Their Efforts to Make Their Products More Available, Affordable, and Accessible in Developing Countries.

Company scores range from 0 (lowest) to 5 (highest) and are based on a weighted average of scores on 101 indicators. The indicators are divided into seven technical areas (shown in different colors); within each technical area, four aspects of implementation are measured.

### Can England's NHS Survive?

Nicholas Black, M.D.

The past few months have witnessed the most intense and prolonged criticism of England's National Health Service (NHS) in its 65-year history. Some critics have suggested that the NHS faces

a crisis that can be resolved only by altering the fundamental principle on which it was founded — provision of funding from general taxation, with care being free at the point of use. Although the criticism was sparked by a February report on an inquiry into shortcomings at one hospital,1 the problems originated in 2010, when two profound forces were unleashed on the NHS: public-sector financial austerity and administrative reorganization. Together, these three factors have created the current turmoil.

Never before has the NHS had to cope with no increase in funding for a sustained period. With rising demand, the NHS is required to improve its productivity at an unprecedented rate of 4% per year.<sup>2</sup> The government is convinced that to achieve this

improvement, two fundamental changes are needed.

The first concerns the local commissioning organizations that are responsible for purchasing hospital and community services for their geographically defined populations of 200,000 to 1 million people. The 151 existing administrative bodies called Primary Care Trusts, which were led by nonclinical managers, have been replaced by 212 Clinical Commissioning Groups that are led by primary care doctors (general practitioners [GPs]) who, the government believes, will be more effective in controlling the use of the £60 billion (approximately \$90 billion) spent on secondary and community care services. (Spending on tertiary care — £20 billion [\$30 billion] will be managed at a national level by a new entity called NHS England.) The second means of achieving better productivity is by increasing the competition among providers of hospital and community services through the greater use of non-NHS providers (including private for-profit, not-for-profit, and charity or volunteer organizations).

Prolonged financial stringency and a reorganization were challenging enough without a highprofile report suggesting that NHS hospitals may not be safe.1 The Francis Report on the inquiry into the Mid Staffordshire NHS Foundation Trust told a sad and troubling story of a hospital in which the humanity of care in some wards was appalling and in which the proportion of deaths deemed avoidable may have been higher than the 5% observed elsewhere in England and in other high-income countries. Despite uncertainty about the appropriateness of allowing public inquiries to influence policy,3 the government has responded by announcing sever-

## The Thousand-Dollar Pap Smear

Cheryl Bettigole, M.D., M.P.H.

me to say that she'd been billed more than \$600 for her Pap smear, I was sure it was a mistake. The second time, I was less sure, and these days I am no longer surprised to find laboratory charges of \$1,000 or more for a test that until recently cost only \$20 or \$30.

Cervical-cancer screening is

one of the 20th century's true public health successes. The incidence of a disease that once caused more deaths among American women than any other form of cancer has decreased dramatically since the introduction of routine Pap smears in the 1970s. In the modern era, most deaths due to cervical cancer occur among women who have never

been screened or who have gone decades without screening. One of the main factors in helping to conquer this once-dreaded disease has been the availability of a cheap, effective screening test that can detect disease early, while it's still very treatable. Yet increasingly, in my roles as the chief medical officer of a community health center and as a family

# **Tobacco Use among Homeless People** — Addressing the Neglected Addiction

Travis P. Baggett, M.D., M.P.H., Matthew L. Tobey, M.D., and Nancy A. Rigotti, M.D.

Although the prevalence of smoking in the United States has declined, vulnerable and marginalized groups continue to use tobacco at high rates. One such group is the 2.3 to 3.5 million people nation-

wide who are homeless in any given year. Approximately three quarters of homeless adults are cigarette smokers1 - a prevalence 4 times that in the U.S. adult population and 2.5 times that among impoverished Americans in general. The coexisting psychiatric and addictive conditions and life circumstances of homeless smokers have long fueled a fatalistic attitude among health care professionals toward addressing tobacco use in this population. We believe that this approach should change.

Smoking-related deaths among homeless and marginally housed people occur at double the rate seen among more stably housed people and account for a considerable fraction of the absolute mortality disparities between these groups.2 In our study of more than 28,000 adults seen at the Boston Health Care for the Homeless Program in 2003 through 2008, cancer was the secondleading cause of death overall and the leading killer among adults 45 years of age or older. Malignant neoplasms of the trachea, bronchus, and lung caused more than one third of these deaths. a finding that underscores the excess burden of lung-cancer mortality in this population that has been documented elsewhere.2

Studies have also shown higher rates of death due to circulatory and respiratory diseases among homeless people than among people with homes.

A number of factors create challenges for reducing tobacco use and its consequences in this population. Homeless smokers have a high burden of nicotine dependence, psychiatric symptoms, and coexisting substanceuse disorders.<sup>3</sup> They are more likely than homeless nonsmokers to have experienced physical or sexual trauma.<sup>1</sup> Many homeless people lack health insurance and a usual source of care, which limits their access to smoking-cessation therapies.

The circumstances of homelessness add to these barriers. Whereas most homeless shelters no longer permit smoking indoors, smoking around shelters is com-

### Toward Patient-Centered Drug Development in Oncology

Ethan Basch, M.D.

As an oncologist, when I sit with patients to disdiscuss starting a new chemotherapy regimen, their first questions are often "How will it make me feel?" and "How did patients like me feel with

this treatment?" Regrettably, this information is generally missing from U.S. drug labels and from published reports of clinical trials—the two information sources most commonly available to people trying to understand the clinical effects of cancer drugs.

In 2011, 15 hematology—oncology drugs were approved by the U.S. Food and Drug Administration (FDA). In only one case — that of ruxolitinib for the management of myelofibrosis — was symptom information included in the portion of the label that manufacturers can legally use for marketing purposes. In fact, ruxolitinib was the first cancer therapeutic in more than a decade for which symptom information was included in a U.S. drug label.

Cancer-drug labels stand in

sharp contrast to labels for other types of drugs, about 25% of which list the drugs' effects on patients' symptoms or functioning.¹ That disparity is surprising, given how common symptoms and functional impairment are in patients with cancer and how toxic oncology drugs can be.

The FDA has taken several recent steps toward encouraging inclusion of the patient perspective in drug development. It issued highly influential guidance on the use of patient-reported outcomes (PROs) in drug development,<sup>2</sup> collaborated with the Critical Path Institute and industry to form the PRO Consortium with the aim of developing robust symptom-measurement tools, and obtained support from Congress in the fifth reauthorization of the Prescription

Drug User Fee Act (PDUFA) to expand its internal expertise on the methodology of measuring PROs. (Unfortunately, allocated PDUFA funds have been withheld, which substantially impairs the FDA's ability to implement planned patient-centered programs.)

These FDA efforts are evident in the ruxolitinib label and in the label for abiraterone acetate, approved this year for metastatic prostate cancer, which describes beneficial delays in time to the development of pain and the need for opioid use. Yet in preapproval trials in patients with cancer, symptom or functional-status evaluations that meet the FDA's standards remain rare.

Some experts have argued that the FDA has raised the methodologic bar too high, whereas others accuse the pharmaceutical industry of paying too little attention to patients' experiences. The bottom line is that both regulators and industry continue to prioritize survival-based end points rather



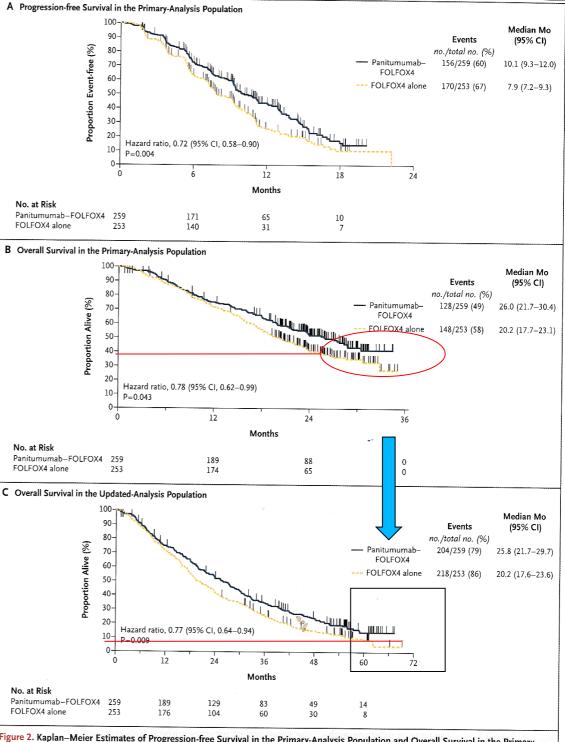


Figure 2. Kaplan—Meier Estimates of Progression-free Survival in the Primary-Analysis Population and Overall Survival in the Primary-Analysis and Updated-Analysis Populations, According to Treatment Group.

Elizabeth G. Phimister, Ph.D., Editor

#### Mapping the Journey to an HIV Vaccine

Margaret Ackerman, Ph.D., and Galit Alter, Ph.D.

"Universal" vaccines that elicit cross-reactive and broadly neutralizing antibodies (bNAbs) are the ultimate goal of efforts to provide protective immunity against both the influenza virus and the human immunodeficiency virus (HIV). Infection with either virus leads to the induction of abundant strain-specific antibodies that are easily evaded by subsequent viral variants. However, the circulating diversity of HIV is greater than that of influenza by orders of magnitude, posing a tremendous challenge to the achievement of vaccine-mediated protection.

New hope for a universal sterilizing HIV vaccine arose several years ago with the evidence that bNAbs emerge in 10 to 30% of infected persons.1 Because these bNAb responses typically appear after 2 to 3 years of infection, they fail to control established infection: the kinetics of the evolving B-cell response lag behind the rapidly diversifying virus, and they cannot "catch up" to control established infection. However, these bNAbs have provided protection from infection at remarkably low doses in animals, suggesting that vaccine-induced bNAbs could provide sterilizing immunity if they were present before infection. Translating our current knowledge of bNAbs into a vaccine remains a daunting challenge, since the mechanism by which such antibodies are induced remains enigmatic.

As compared with other antibodies, bNAbs have unusual characteristics, including odd physical structures (e.g., elongated antigen-binding loops) and remarkably high levels of mutation

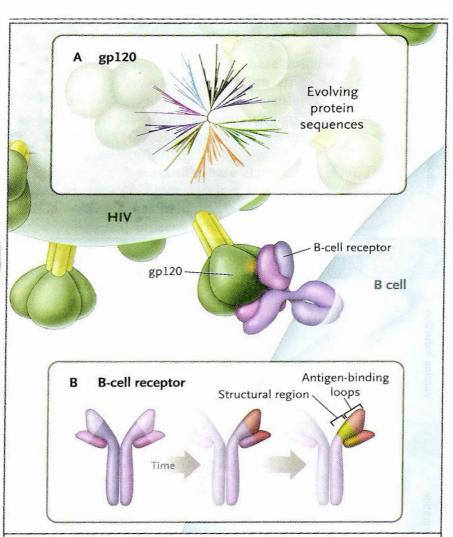
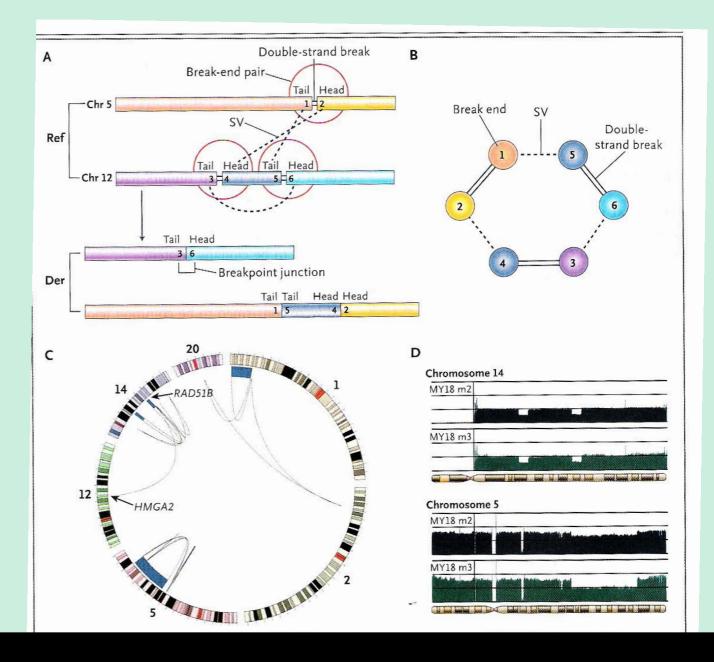
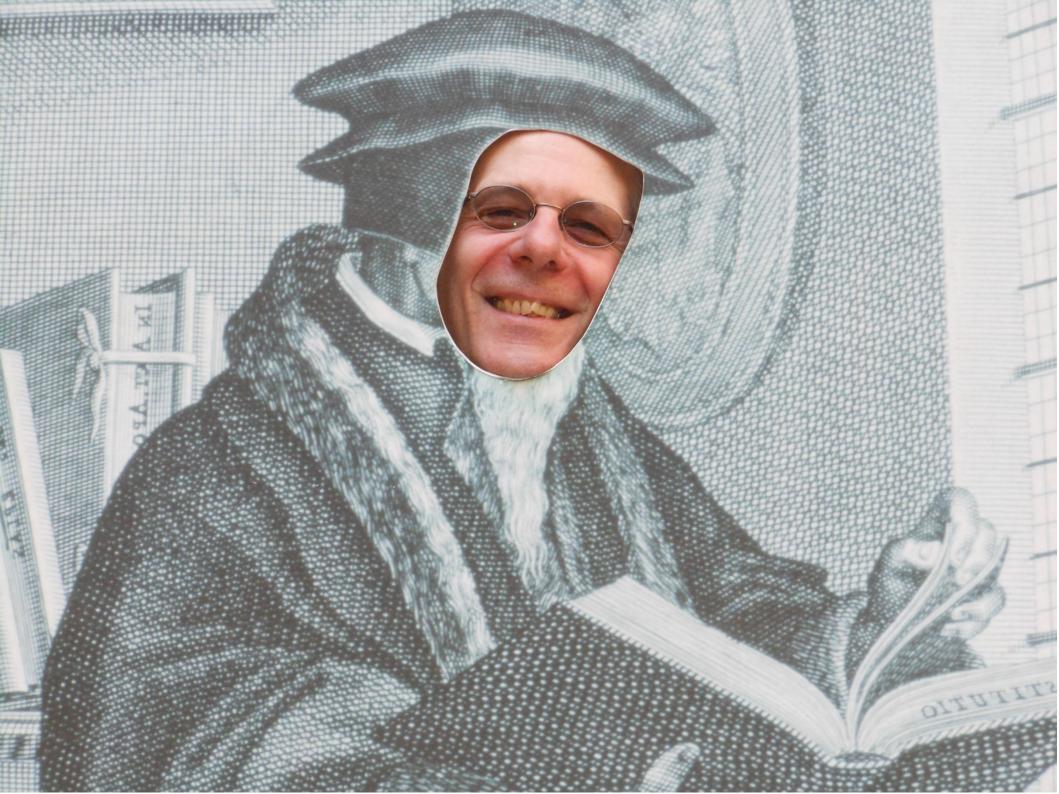


Figure 1. The Coevolution of Virus and Antibody.

Given that the B-cell receptor is simply a membrane-bound antibody, Liao et al.<sup>3</sup> hypothesized that the parallel sequencing of B-cell receptors and viral diversity could elucidate the interplay of host and pathogen, evasion and adaptation, that resulted in a broadly neutralizing antibody. Specifically, as the virus evolves (Panel A), so does the B-cell receptor (Panel B), resulting







## Dr L. Alexandre

Nano Bio Informatique Cognitive....



http://vimeo.com/8424976

Les gènes qui gênent...

https://www.youtube.com/watch?v=HPIHLAS4gCL

### Force-Feeding, Autonomy, and the Public Interest

Michael L. Gross, Ph.D.

I unger striking is a nonviolent act of political protest. It is not the expression of a wish to die, nor is it akin to the decision of a terminally ill patient to discontinue food and fluid intake. Rather, it is brinkmanship. Faced with hunger-striking detainees, prison authorities have three choices: force-feed the hunger strikers, let them die, or accede to their demands.

As the World Medical Association (WMA) suggests, most bioethicists unequivocally oppose force-feeding. Enteral feeding through a nasogastric tube while a detainee is strapped to a chair violates a mentally competent patient's right to refuse treatment and is physically violent. The WMA is less categorical about artificially feeding unconscious or delirious hunger strikers through their abdominal wall. Under these

circumstances, physicians may permissibly weigh their patient's best interests and prior expressions of intent before deciding about continued treatment.

Physicians who care for hunger-striking detainees weigh autonomy and best interests; rarely must they consider security interests. Local authorities, however, do not have this prerogative. Whereas bioethicists are keen to uphold autonomy and avoid forcefeeding, public officials are bound to maintain public order and prevent the deaths of detainees. Those responsibilities leave officials only two choices: forced or artificial feeding, or accommodation. Accommodation deserves first consideration because it may be a reasonable choice. Faced with hunger-striking Palestinian detainees in 2012-2013, for example, Israeli officials satisfied some prisoners by improving prison conditions or modifying their prison terms. Similarly, the Turkish government met some hunger strikers' demands last year. In each case, the hunger strike ended. Strikers played their hands deftly, carefully choosing realistic aims and employing nonviolent protests to gain symbolic but important concessions. Local medical organizations also played a role: the Israeli Medical Association instructed its members to comply with WMA guidelines, thereby pushing public officials to earnestly explore accommodation.2

The situation at Guantanamo deserves similar creativity. The detainees' demands are not monolithic. Prisoners who are cleared for release require expedited repatriation, whereas others may be satisfied with customary legal proceedings, better prison con-

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### **UK carers suffering due to lack of support**

#### Carers Week 2013 10th – 16th June - Prepared to Care?

New research from Carers Week of over 2,100 carers has revealed that carers are being woefully let down by a lack of support when they first take on a caring role. The findings from the report, **Prepared to Care?** show that support is not being made available to new carers with often devastating consequences.

Released to coincide with the launch of Carers Week 2013, the findings show that 75% of carers were unprepared for all aspects of caring. A further 81% of carers say they were not aware of the support available and 35% believe they were given the wrong advice about the support on offer<sup>2</sup>.

#### Impact of caring

The survey shows that carers often struggle to balance work and their caring responsibilities, with **45% of carers** saying they had to give up work. The results also highlight how carers' physical, emotional and mental wellbeing can suffer. **61% of carers** have experienced depression and **nearly all carers surveyed (92%)** say they feel more stressed because of their caring role

