Teaching Health Centers and the Primary Care Workforce Crisis for the Underserved

TO THE EDITOR: One of the proposed models for national health care is to expand into the natural adjacency of the Medicare and Medicaid systems. However, the influx of new patients will cause an even greater burden on a failing system, and the current workforce of physicians and nonphysician providers will be unable to properly care for these patients. The model proposed by Rieselbach and colleagues (1) seems viable and operationally sound, but the funding mechanism remains a challenge.

A plausible funding mechanism would be to allocate a portion of recoveries from the Recovery Audit Contractor (RAC) program to this primary care initiative. Although it is operationally impractical to prevent all improper payments, a January 2008 report by the Office of Management and Budget (2) indicated that Medicare is among the top 3 federal programs with improper payments (not fraud), with an estimated total of $10.8 billion in 2007 (2). The Centers for Medicare & Medicaid Services performed a 3-year pilot RAC program in 3 states. The RACs corrected more than $1.03 billion in improper Medicare payments (2). Conservative estimates suggest that the recoveries from the mature program will exceed $35 billion per year.

The Medicare program currently uses payment bonuses to encourage care based on high-quality evidence (3). Increasing quality-based bonuses to recruit primary care physicians and to diminish the variance between cognitive and procedural physicians makes good sense. In addition, the bonus payments will negate the reimbursement issues associated with rural and community health care.

Many community health centers (CHCs) do not have adequate facilities to attract physicians, much less patients. The RAC recoveries could augment funds already designated for electronic health records, state-of-the-art diagnostic tools, and high-quality multimedia educational facilities that would be a “health care destination.” This prestige is cherished by patients and physicians alike.

The model proposed by Rieselbach and colleagues solves 2 major health care problems: the diminishing pool of primary care physicians and the rapidly expanding patient population, which could dramatically increase if national health care requires the expansion of Medicare and Medicaid. Access to high-quality health care in a sustainable system remains a very high priority. I propose a novel funding mechanism that uses money recouped from overpayments to Medicare providers. Expansion of the RAC program into Medicaid and Medicare Parts C and D would provide even greater recoupments. All U.S. residents deserve the highest-quality health care available, and this is one way to provide it.

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Potential Conflicts of Interest: None disclosed.

References

TO THE EDITOR: Rieselbach and colleagues (1) proposed strengthening the link between primary care graduate medical education and care for the underserved by increasing resident training in CHCs. This should also include the education of medical students: The authors’ arguments may be analogously applied to student-run health clinics.

Given recent progress toward universal health coverage, it is imperative to guarantee access for underserved populations and to enhance primary care education. One potential threat to the achievement of true universal health coverage is the shortage of primary care physicians, as seen in Massachusetts health care reform (2). Secondary goals of reform should be to enhance training in primary care and to attract a larger primary care physician workforce.

Student-run clinics have been shown to provide quality health care to those without insurance or a regular health care provider. Although more qualitative and quantitative data are needed to fully assess quality of care, initial research findings are positive. Clinical rates of diabetes quality-of-care indicators at a student-run clinic in East Harlem were similar to or better than averages described elsewhere for similar uninsured populations (3). Furthermore, student-run clinics provide a safety net by flexibly operating in nontraditional settings (churches, mobile vans, homeless shelters) and during nontraditional hours, appealing to and allowing better access for a broad range of patients (4).

Student-run clinics enhance primary care education for medical students and may provide a potential recruitment base for a shrinking workforce of primary care physicians. By providing primary care under a supervising faculty physician to underserved populations, participation in student-run clinics is often an influential early clinical experience. According to National Residency Matching Program data from 1978 to 1982 (5), 96.5% of Clinica Tepati participants at University of California, Davis, School of Medicine entered primary care specialties, with 55.2% entering family medicine, diverging drastically from the specialty choices of their peers. Although this trend may be dated or produced by student self-selection, such statistics should not be overlooked.

As a unique opportunity to fill 2 concurrent needs, student-run clinics provide care to the underserved and allow students to confront the realities of access, cost, and quality in the U.S. health care system. This experience will reveal that the shortage of primary care physicians is an alarming problem that needs to be addressed. Thus, student-run clinics should be added to the arsenal of approaches to remedy the primary care workforce crisis.

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TO THE EDITOR: The ongoing debate on health care reform centers on reforming health care finance to provide the laudable goal of universal health care. The basis of any fiscally responsible health care delivery system is improved access to quality primary care. The shortage of primary care physicians is one of the key obstacles, but no concentrated effort has been made to address this shortage. Rieselbach and colleagues (1) state that the decrease in primary care resident graduates is due to deficient reimbursement, debt, lifestyle preferences, and the current problematic structure of primary care practice. Unfortunately, because many of the best medical graduates over the past decade have chosen non–primary care specialties as career paths, there is a shortage of good, young primary care teaching physicians to serve as role models for current medical students. As an academic internist and geriatrician, I see the dwindling interest of medical students in primary care medicine and geriatrics as career options. It is appalling that less than 1% of internal medicine residents consider geriatrics as a career option when they start residency training. The lure of more lucrative reimbursements attracts many primary care resident physicians to subspecialty training (2). This is partly because many program directors and heads of departments of internal medicine in academic medical centers are subspecialists, not primary care physicians or geriatricians.

No meaningful discussion on health care reform is complete without discussion of health care for elderly persons. Today, U.S. residents are living longer, and fewer are dying of acute diseases. Chronic diseases are now the major cause of illness, accounting for 75% of all deaths and 80% of health resources used. In addition, the changing needs of the geriatric population mean that more than half of the outpatient visits by geriatric patients are to non–primary care specialists. Despite this, 70% of the graduate medical education specialties do not have specific geriatric curriculum requirements (3).

Finally, we need more primary care physicians to voice their opinions on health care reform and suggest meaningful solutions. If we do not, we will have to accept reform that has input from politicians and from the insurance, hospital, and pharmaceutical industries but little input from physicians. If that happens, we will have no one to blame but ourselves.

TO THE EDITOR: We applaud Rieselbach and colleagues’ (1) call for practical solutions to improve care for the underserved while bolstering the primary care workforce through teaching health centers. The need for such programs is urgent in California, the state with the most uninsured residents. In 2005, the University of California, Davis, Internal Medicine residency program partnered with the Sacramento County Department of Health and Human Services to develop a teaching health center in our county’s largest community clinic. The TEACH (Transforming Education and Community Health) program successfully places residents into primary care and medically underserved communities and improves care for medically underserved persons. The program is supported by a Title VII Health Resources and Services Administration Residency Training in Primary Care grant (D58HP05139-04-00).

Each year, 5 residents spend their final year of residency in the TEACH Program, caring for a cohort of uninsured patients in a county clinic and on a dedicated inpatient service. Patients discharged from this service are followed by the residents in the TEACH clinic, which provides continuity of care. The inpatient team includes 1 resident, 1 third-year medical student, and a supervising TEACH faculty. During a typical month, residents spend 1 week on the inpatient service and 3 weeks in the county ambulatory setting, at 4 continuity clinics and a variety of subspecialty clinics. Including the current graduating class of 2010, 25 residents have completed the TEACH Program. In the year after graduation, 80% of TEACH graduates practice general internal medicine (compared with 33% nationally) (2, 3), 68% practice primary care, and 52% practice in medically underserved settings. Anecdotally, TEACH residents report “better continuity of care and stronger bonds with patients” and “exposure to more patients with undiagnosed illness” but also “burdensome paperwork, lack of an electronic health record, difficulty obtaining specialty care referrals, and lack of exposure to a geriatric population.”

As measured by an American Board of Internal Medicine’s Practice Improvement Module (4), compared with 2007 Healthcare Effectiveness Data Information Set quality metrics TEACH residents outperformed managed care plans in both process (testing hemoglobin A₁c level and fasting lipid levels) and outcome (hypertension control and management of hemoglobin A₁c and low-density lipo-protein) measures for diabetes care.

The TEACH program provides high-quality longitudinal care for the underserved in the setting of a rewarding primary care train-

Acknowledgment: The author thanks Rebecca Berman, MD, for her gracious assistance with and support of this letter.

Potential Conflicts of Interest: None disclosed.

References

None disclosed.

Potential Conflicts of Interest: None disclosed.

References
letters

ing program. It is a potential model for improving care of the underserved and increasing the primary care workforce.

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References

TO THE EDITOR: Rieselbach and colleagues (1) highlight the urgent workforce shortage in CHCs and the increasing interest in the “health center” concept. Current language in the health reform bill provides funding for support and creation of health centers as a potential solution to the workforce shortage for the underserved.

As the authors acknowledge, the idea of health centers is not new, and family medicine residencies have partnered extensively with CHCs for more than 25 years. These partnerships can help inform the health center model and bring to light crucial policy attributes necessary to best support fully functional health centers.

The authors’ proposal builds on work done by the Education Health Center Initiative (EHCI), a partnership of the Northwest Regional Primary Care Association and the University of Washington’s Department of Family Medicine and Family Medicine Residency Network, which has studied partnerships between family medicine residencies and CHCs since 2005. This work has shown that physicians trained in CHCs are nearly 3 times more likely to work in underserved areas after completing their residency (2) and describes the high satisfaction of trainees in this model (2), the number and type of these affiliations in the United States in 2007 (3), and the barriers and facilitators to these collaborations (4). Current policies hinder CHC training partnerships, because of the administrative challenges with funding of graduate medical education, residency training regulations, and health center funding and operation. The greatest challenges facing these partnerships are the competing missions of service and training versus financing.

Regardless of the outcome of the health reform legislation, the EHCI has collected a library of reference material on funding, legal considerations, educational requirements, and CHC requirements (5). Last year, the EHCI sponsored a “Residency–CHC Collaboration Nuts and Bolts” workshop attended by representatives from residencies and CHCs throughout the nation.

The teaching health center will need not only adequate financing and legislative action, but also broad-based, community-oriented support to succeed. We welcome the interest of other primary care specialties in this collaborative effort.

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Potential Conflicts of Interest: The authors are affiliated with the Education Health Center Initiative, a nonprofit partnership to promote collaboration between residency training programs and health centers.

References

Sex Differences in Career Development Awardees’ Subsequent Grant Attainment

TO THE EDITOR: Jagi and colleagues (1) found a sex disparity in the achievement of National Institutes of Health (NIH) R01 awards by past career development (that is, K) awardees and raised concerns about the progression of women in research careers. Several of their conclusions deserve additional scrutiny and discussion.

Of greatest importance, as the authors acknowledged, they did not have information about application rates. Analyses by the NIH indicate that the rates at which K awardees subsequently apply for research grants are higher for men than for women. Among K08 recipients from 1995 to 1998, for example, 74% of men and 67% of women applied for an R01 award within 10 years (P = 0.015). Those disparities also were evident in the broader category of research project grants, in which 80% of male and 74% of female K08 recipients applied within 10 years (P = 0.029).

However, NIH data show that when female K08 awardees apply for new R01 awards, they are equally or more successful than their male peers who hold the same types of degrees (specifically, we compared male and female MDs, including those with MD/PhDs). In addition, in the total pool of applicants for type 1 R01s, success rates for men and women
are equivalent (2). These data suggest that sex disparities in receiving NIH awards are more attributable to differences in application rates than differences in success.

Furthermore, it often takes several years to completely transition to research independence after receiving a K award. Over the long history of the K08 award, 55% of awardees who receive a subsequent R01 award do so within 5 years; the percentage increases to 76% for 8 years and to 83% for 10 years. As a result, Jagsi and colleagues’ analyses (which, in some cases, were limited to 5 years of follow-up) probably excluded many K awardees who will later receive an R01 award. Data from the NIH, however, do support the authors’ finding that women progress from K awards to research awards more slowly than men, at least in the beginning of their careers. To help women—and men—who need more time to transition to research independence, the NIH introduced new policies to allow career development awardees to pursue their projects part-time and new investigators to request an extension to their status as early-stage investigators if they have had a lapse in research due to family or other responsibilities (3, 4). We expect these policies to foster continued participation in research by many investigators.

Finally, Jagsi and colleagues concluded that K awards are smaller for women than for men by comparing average total costs for all K awards. Because the entire pool of K awards includes mentored awards to junior investigators, individual awards to mid-career and senior investigators, and institutional awards to established investigators, true similarities—or differences—in direct costs between men’s and women’s awards were probably obscured. Furthermore, because individual K awards largely consist of salary support, any observed differences could be due to differences in institutional salary structure. The NIH continues to study these and other issues related to women in research and urges others to do the same (5, 6).

The transition to research independence will continue to be shaped by personal circumstances for both women and men. Nevertheless, we hope that concerns about sex-related differences in NIH funding are allayed and that all potential investigators will be encouraged to pursue NIH support. In most cases, applying for independent research funding is a critical first step on which scientific careers are built.

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Potential Conflicts of Interest: None disclosed.

References

IN RESPONSE: Dr. Pohlhaus and colleagues have provided useful data supporting our identification of a leakage problem, especially for women, in the academic pipeline. However, we wish to clarify a few points.

First, there is no reason to expect that female K awardees have less research desire or talent than male peers; thus, the lower rate of R01 applications among women is a cause for concern. We need to understand why a lower proportion of promising women reach the point of applying for an R01 award.

Second, the rates of R01 attainment we presented were calculated through actuarial analysis, censored to account for follow-up. Dr. Pohlhaus and colleagues have shown no evidence that we “excluded many K awardees who will later receive an R01 award.” In fact, if one extrapolates from the information they share—that over the long history of the K08 award, 55% of awardees who receive a subsequent R01 do so within 5 years and 83% within 10 years—one concludes, on the basis of both the 5-year and 10-year rates we observed, that about one half of K awardees in this cohort will never receive R01 funding.

As noted in our article, “Women . . . may have a longer time course to R01 receipt, given the exigencies they face with regard to childbearing.” Nevertheless, the actuarial curves in our study showed no sign of convergence, increasing the likelihood that the sex differences we observed will persist even with further follow-up. Another point deserves repeating: “ . . . the duration of follow-up in our study spans the time period in which most medical schools require research faculty to apply for tenure.”

Third, when we speculated about the potential effect of career award size, we could only refer to published data that pooled 472 K02 and K04 awardees with 2956 K01, K08, and K23 awardees. This pooling may have obscured differences across award type. We encourage Dr. Pohlhaus and colleagues to consider analyzing these data further (or sharing their data with us), including whether there are, as they speculate, differences in K award size due to sex differences in salary. This would be a great opportunity to explore associations of salary with institution type and specialty and to assess whether sex disparities exist between similarly situated male and female biomedical researchers.

Finally, we applaud the NIH for developing policies to allow grantees to pursue their projects part-time or to extend their status. We hope such initiatives lead to the retention of more promising researchers in biomedical careers.

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Potential Conflicts of Interest: None disclosed.
Co-infection With Pandemic H1N1 and Seasonal H3N2 Influenza Viruses

Background: One immediate concern about the current influenza pandemic is whether the virus will further reassort with other cocirculating influenza subtypes in humans or an intermediate host (1, 2). However, despite annual cocirculation of different subtypes of influenza A viruses, dual infection has rarely been reported (3). In Hong Kong, there are 2 seasonal peaks of influenza activity. In 2009, the summer peak for seasonal influenza coincided with the first wave of the pandemic (4).

Objective: To report the first documented dual infection of pandemic (H1N1) 2009 and seasonal H3N2 viruses in a human.

Case Report: We managed a 38-year-old woman who received a renal transplant and was taking tacrolimus, prednisolone, and azathioprine. She presented with fever, rhinorrhea, sore throat, and cough in mid-September 2009. Her temperature was 37.7 °C, and she had normal blood pressure and oxygen saturation. Chest radiography showed no pneumonic changes. Nasopharyngeal aspirate collected at presentation was positive for influenza A antigen by an immunofluorescence assay, and pandemic (H1N1) 2009 infection was confirmed by specific real-time polymerase chain reaction (PCR) assay. We put the patient on droplet precautions and treated her with oseltamivir, 75 mg/d, adjusted for renal function. Her symptoms resolved, and we discharged her 48 hours later. We continued treatment for a total of 5 days.

Methods and Findings: Virus isolation performed by the National Influenza Centre in Hong Kong (4) grew both pandemic (H1N1) 2009 and seasonal H3N2 viruses. A specific reverse-transcription PCR (RT-PCR) assay for H3N2 virus confirmed its presence in the original sample. We then estimated the burdens of the respective viruses. First, we measured the total virus concentration in the original sample by using 1-step real-time RT-PCR that targeted the consensus region of the matrix gene for influenza A viruses (Appendix, available at www.annals.org). We used the primers 5’-AAGACCAATTCCCTCAGCTCTCTTA-3’ (forward) and 5’-CAGAGGCTTCACGTGAGTTC-3’ (reverse), which amplify a 74-base pair fragment in the matrix gene. Second, we estimated the relative titers of both viruses by using end-point dilution comparison. In brief, we used RT-PCR with primers 5’-CCACAGGAATCTCCGCTCT-3’ (forward) and 5’-CCTTGGCATGTTTTTCTAGCTGCTTC-3’ (reverse) to amplify a 432-base pair fragment in the hemagglutinin gene of pandemic H1N1, and we used 5’-ATGGGACCTTTTRTYGAACGCAGCA-3’ (forward) and 5’-CCCKAGGAGGCAATTAGATTCCCTGCTG-3’ (reverse) to amplify a 519-base pair hemagglutinin fragment of seasonal H3N2. We prepared serial 10-fold dilutions of the extracted RNA preparation and ran them in parallel with the pandemic H1N1-specific and H3N2-specific PCR assays to obtain the end point (Appendix). The combined viral concentration was 7.64 log_{10} RNA copies per μL, which was above the 75th percentile for adults hospitalized for pandemic H1N1 infection in our hospital (124 patients; median, 6.19 [interquartile range, 4.80 to 7.06]). The titer of H3N2 virus was 1000-fold higher than that of the pandemic H1N1 virus (Figure).

Discussion: In theory, infection with 1 virus interferes with subsequent infection. Our case, however, confirms that co-infection by 2 influenza subtypes with viral shedding in high titers is possible, raising concerns about further genetic reassortment of the pandemic H1N1 virus in humans. There are several implications. First, managing patients in 1 location with respiratory illnesses caused by different subtypes of influenza A may not be advisable, especially if they are immunocompromised. Second, multivalent vaccines that cover all cocirculating influenza strains should be considered to minimize the possibility of co-infection (5). Finally, co-infection may be underrecognized. Therefore, it may be worthwhile to use rapid diagnostic tests that can diagnose and differentiate influenza A subtypes. That way, patients with co-infection can be properly isolated and antiviral resistance patterns for different subtypes can be identified.

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Potential Conflicts of Interest: None disclosed.
Respiratory Failure Caused by 2009 Novel Influenza A/H1N1 in a Hematopoietic Stem-Cell Transplant Recipient: Detection of Extrapulmonary H1N1 RNA and Use of Intravenous Peramivir

**Background:** Data on the manifestations and optimum management of H1N1 infection in immunocompromised patients are sparse (1, 2).

**Objective:** To report a case of H1N1-associated pneumonia in a hematopoietic stem-cell transplant recipient with extrapulmonary H1N1 RNA detection who was treated with intravenous peramivir.

**Case Report:** A woman in her 40s (body mass index, 31.8 kg/m²) with multiple myeloma had outpatient autologous hematopoietic stem-cell transplantation with myeloablative conditioning in May 2009. Two days after transplantation, she was hospitalized with fever, nausea, diarrhea, and minimally productive cough. Chest radiography was normal, neutrophil count was 1.42 × 10⁹ cells/L, and no lymphocytes were present. Despite receiving empirical broad-spectrum antibiotics, the patient developed increased tachypnea and hypoxia. Chest computed tomography on hospital day 3 showed bilateral ground-glass opacities with central nodules. Nasal swab was positive for influenza A/H1N1 by a real-time RT-PCR assay developed at our center by using primers and a probe targeting a 102-base-pair fragment of the virus. Intravenous influenza antiviral drugs may be useful or required for critically ill patients with severe novel influenza A/H1N1 infection, particularly if viral RNA is detectable in plasma. Whether peramivir was responsible for our patient’s recovery cannot be determined with certainty; lymphocyte reconstitution in addition to aggressive antiviral treatment may be required for successful management of influenza pneumonia in this setting (5).

**Conclusion:** Although the importance of extrapulmonary influenza viral RNA detection is not clear and the benefit of intravenous antiviral therapy in such patients is speculative, we hypothesize that viral RNA in plasma may be associated with severe influenza disease. Further investigation is needed to replicate this finding because this easy-to-measure biomarker could be used to determine patients who

She had sustained detection of H1N1 RNA in plasma and respiratory secretions for at least 9 and 11 days, respectively, which resolved with lymphocyte recovery and antiviral therapy (Figure). H1N1 recurred in nasal wash on hospital day 34, prompting a second 10-day course of oral oseltamivir, 150 mg twice daily. There was no oseltamivir resistance (H275Y mutation) in viral RNA from bronchoalveolar lavage on hospital day 7 or from nasal wash on hospital day 34 (IntelligentMDx, Cambridge, Massachusetts).

**Discussion:** Novel influenza A/H1N1 may cause rapidly progressive disease after hematopoietic stem-cell transplantation, as in this obese patient with respiratory failure who had influenza viral RNA detected in extrapulmonary samples, including plasma and stool. Viral RNA has been detected in blood and extrapulmonary tissues in fatal cases of avian influenza A/H5N1 and, rarely, of seasonal human influenza in immunocompromised patients (3, 4). Our finding of viral RNA in the plasma of this patient is novel and may indicate hematologic dissemination of the virus. Influenza B virus is more common in immunosuppressed patients, but we did not find influenza B virus in nasal wash. Viral loads in plasma were high, suggesting that RNAemia may be important in severe cases. The limit of reverse-transcription polymerase chain reaction assay detection is 3 log₁₀ viral copies/mL. Bronchoalveolar lavage on hospital day 7 and blood culture on hospital day 29 were also positive for *Saccharomyces cerevisiae*. The patient received a short course of intravenous micafungin initially. Positive blood culture was treated with line removal and intravenous micafungin followed by oral voriconazole. BAL = bronchoalveolar lavage.

**Figure.** Time course of novel influenza A/H1N1 infection in a hematopoietic stem-cell transplant recipient.

<table>
<thead>
<tr>
<th>Hospital Day</th>
<th>Viral Load, log₁₀ copies/mL</th>
<th>Lymphocyte Count, × 10⁹ cells/L</th>
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<tr>
<td>0</td>
<td>10</td>
<td>1</td>
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<tr>
<td>5</td>
<td>9</td>
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</table>

The limit of reverse-transcription polymerase chain reaction assay detection is 3 log₁₀ viral copies/mL. Bronchoalveolar lavage on hospital day 7 and blood culture on hospital day 29 were also positive for *Saccharomyces cerevisiae*. The patient received a short course of intravenous micafungin initially. Positive blood culture was treated with line removal and intravenous micafungin followed by oral voriconazole. BAL = bronchoalveolar lavage.
will benefit most from aggressive intravenous or combination approaches to antiviral therapy.

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References

Correction

Correction: In the Clinic: Breast Cancer Screening and Prevention

In the April issue of In the Clinic (1), the following errors were made.

On page 1, the physician writer’s name should be “Ann B. Nattinger, MD, MPH.”

On page 2, line 8 of the introduction should say “… decreases the risk for breast cancer by 30% to 50%.” Starting on line 11, the phrase “… although other modalities are useful” should be deleted. On line 13, the sentence should begin “Women of average…” instead of “All women of average…” On the left column, line 13 should say “45% of cases…” and line 14 should say “65 years or older.” On the right column, starting on line 10, the phrase “can have breast cancer” should say “have high risk for breast cancer.”

On page 3, left column, starting on line 12 of the first full paragraph, the phrase “a specific type of estrogen called estrone…” and insulin-like growth factor (IGF)-1” should just say “estrogen and other compounds.” On the right column, line 17 of the second full paragraph, the phrase “and it underestimates risk in African-American women” should be deleted.

On page 4, left column, line 20 of the first full paragraph, the word “additional” should be replaced with “specific.” On line 28, the sentence “Genetic testing is usually performed first” should be deleted. On the right column, line 4 of the first full paragraph, “… by about 30%…” should say “… by 30% to 50%…”

On page 5, left column, line 2 of the second full paragraph, it should say “34%” not “38%.”

On page 6, right column, line 11 of the second full paragraph, a new sentence, “Neither drug improves 5-year survival,” should appear before the sentence that starts “Raloxifene does not…” On line 16, the words “seems to be” should be replaced with “is.” On line 2 of the third paragraph, the phrase “the choice of agents depends mainly on…” should say “the choice of agents for postmenopausal women depends mainly on…”

On page 8, left column, last line, “diagnosis” should be “early diagnosis.” On the right column, starting at the top line, the sentence should end “prevent death.” The phrase “because some breast cancers…” should be deleted.

On page 10, left column, line 5 from the top, “for most women…” should say “for the 88% of women…” On line 4 of the first full paragraph, the word “through” should be replaced with “for.” In Table 4, the results of screening-detected invasive cancer should be “7.0,” not “70.0.”

On page 11, left column, there should be a citation for reference 29 at the end of the last line of the second full paragraph. On the right column, line 2 of the last paragraph, “best-studied” should say “best-supported.”

On page 12, right column, line 9 of the last paragraph, the word “somewhat” should be deleted.

On page 15, under “Who should get screened?” line 4 should say “… and continuing to age 74 or for as long as…”

Finally, in reference 25, the authors should be “Nelson HD, Tyne K, Naik A, et al.”

These corrections have been made to the online version.

Reference
APPENDIX

RNA Extraction

We extracted viral RNA from the nasopharyngeal aspirate sample by using the PureLink Viral RNA/DNA kit (Invitrogen, Carlsbad, California) according to the manufacturer’s instructions. In brief, we added 25 μL of proteinase K to 200 μL of specimen. We added 200 μL of lysis buffer containing 5.6 μg carrier RNA to the mixture, vortexed it for 15 seconds, then incubated it at 56 °C for 15 minutes. We added 250 μL of 100% ethanol and further incubated the mixture at room temperature for 5 minutes. We added the mixture to a spin column and centrifuged it at 6800 g for 1 minute. We then washed the column twice with the wash buffer provided. We eluted the RNA in 60 μL of sterile RNase-free water after incubating it for 1 minute in the column.

Real-Time RT-PCR for the Consensus Region of M Gene

We used a 1-step real-time RT-PCR targeting the consensus region of the matrix (M) gene for universal detection of group A influenza viruses to quantitate the total amount of influenza virus in the nasopharyngeal aspirate sample. The primers used were 5’-AAGACCAATCCTGTCACCTCTGA-3’ (forward) and 5’-CAAAGCGTCTACGCTGCAGTCC-3’ (reverse), which amplify a 74-base pair fragment in the M gene. We carried out reverse transcription by mixing 10 μL of extracted RNA with 50 ng of random-hexamer and 0.5 mM of dNTP for a 5-minute incubation at 65 °C, then equilibrating at 4 °C. This mixture was topped up to a final volume of 20 μL with 2U of RNaseOUT, 1X first strand buffer, 5 mM DTT and 10U Superscript III Reverse Transcriptase (Invitrogen), which was then incubated at 50 °C for 1 hour, and then at 70 °C for 15 minutes. In the RT-PCR assays, 2 μL of the neat or diluted complementary DNA preparation were amplified in each 25-μL reaction mix containing 0.2 mM of dNTP, 1X PCR Buffer, 1.25 U of HotStarTaq Plus DNA polymerase (Qiagen, Hilden, Germany), and 0.4 μM of each type-specific primer. The primers were used to amplify a 432–base pair fragment in the hemagglutinin (HA) gene of pandemic H1N1, and 5’-ATGGGACCTT TTTRTYGAACGCAGCA-3’ (forward) and 5’-CCTTGGCATGTTTTTATGCTGGCTTC-3’ (reverse) were used to amplify a 519–base pair fragment of seasonal H3N2.