THE CANCER LETTER

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Cancer Centers

Northwestern Repays Government $3 Million To Settle Claims Over Use Of NCI Grants; Researcher Bennett Now Faces Feds Alone

By Paul Goldberg

Northwestern University agreed to pay the federal government nearly $3 million to settle a whistleblower lawsuit alleging that a prominent researcher whose work focuses on harm caused by cancer drugs had diverted NCI grant money for personal use.

Settling the lawsuit last week, the university said it would return the funds to the government, but admitted no wrongdoing in administering the grants obtained by Charles Bennett, an oncologist whose best-known work focused on overuse of erythropoiesis-stimulating agents.

Now, with Northwestern having negotiated its way out of the line of fire, the U.S. Department of Justice case goes forward against Bennett alone.

According to a DOJ statement, between Jan. 1, 2003, and Aug. 31, 2010, Bennett used NCI money to pay for "family trips, meals and hotels for himself and friends, and 'consulting fees' for unqualified friends and family members, including his brother and cousin."

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Guest Editorial

What? Only a "B"?

By Christine D. Berg

The recent draft recommendations of the U.S. Preventive Services Task Force in favor of lung cancer screening with computerized tomography are an affirmation of the decision by NCI to fund and conduct the National Lung Screening Trial.

This landmark study provided solid evidence documenting a 20 percent lung cancer mortality reduction by screening high-risk individuals.

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In Brief

Wender Named ACS Chief Cancer Control Officer

RICHARD WENDER was named chief cancer control officer of the **American Cancer Society**.

The new position will lead the society's national and global cancer control initiatives. Wender will assume his duties on a full-time basis in November. Wender's role will complement that of the society's chief medical and scientific officer, Otis Brawley, the society said.

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The Cancer Letter is taking a publication break, and will return **Sept. 6, 2013.**

As Northwestern Settles, Bennett Faces DOJ Alone

(Continued from page 1)

Making enemies is an exhaustively studied side effect of probing the safety of cancer drugs, and during much of the period in question, Bennett was producing more than his standard quota of foes.

Notably, Bennett was the first researcher to use meta-analysis of ESA data to show that harm to patients—including increased mortality—was visible across all studies of ESAs (The Cancer Letter, June 1, 2007). He was subjected to pressure over his findings, and briefly recanted (The Cancer Letter, June 8, 2007). However, his results were ultimately published in the Journal of the American Medical Association in 2008.

Contacted by The Cancer Letter, Bennett said the allegations that he spent NCI money on dinners and vacations were inaccurate. He said he had encountered administrative irregularities at Northwestern and reported them to compliance officials.

"I am in active discussion to settle this matter," Bennett said.

Bennett left Northwestern's Robert H. Lurie Comprehensive Cancer Center in 2010 and is now a professor of clinical pharmacy and outcomes sciences at the South Carolina College of Pharmacy.

Should Bennett fail to convince the prosecutors—or the court—to accept his side of the story, he would face penalties that could include treble damages and fines between $5,500 and $11,000 for each violation.

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Bennett's statement about lax administration of grants at Northwestern appears to be bolstered by an aspect of the scandal that has escaped media attention even as multiple news stories in Chicago and national outlets focused on the settlement.

The Cancer Letter has learned that days before the settlement with Northwestern was announced, a former research administrator at the Division of Hematology and Oncology at the university's medical school pled guilty to felony charges stemming from administration of Bennett's NCI grants.

According to documents filed in the U.S. District Court for the Northern District of Illinois, Feyifunmi Sangoleye, the rogue administrator, set up an elaborate scheme to divert $86,000 to her personal accounts.

The proceeds financed a wedding and a honeymoon in Europe, court documents say.

Legal experts say that the final plea agreement between Sangoleye and the government would have weakened Northwestern's position in negotiating the settlement. The final version of the plea agreement with Sangoleye was filed on July 25, just five days prior to the announcement of the government's $3 million settlement with Northwestern.

Northwestern No Longer Target of Federal Action

The case against Northwestern was filed jointly by DOJ and a former university employee.

In actions of this sort, the individual plaintiff, called "relator," is usually an insider who brings forward information the government couldn't otherwise obtain. The relator is rewarded with a portion of recovered funds.

The suit was filed in 2009, but it remained under seal until July 30, when it was released in conjunction with the memorandum of settlement between the prosecutors and Northwestern.

Under the memorandum of settlement, Northwestern agrees to pay $2.93 million to resolve the suit.

The relator, Melissa Theis, a former purchasing coordinator in the Division of Hematology and Oncology, will receive $498,100 from these proceeds.

"The settlement involves no findings or admissions of wrongful conduct by Northwestern or any of its current faculty members or employees," top university officials said in a statement. "Northwestern was nonetheless disappointed to see the allegations in the complaint, because they are at odds with the University's commitment to a culture of compliance in the administration of federal research grants.

"Northwestern takes its grant administration responsibilities seriously, and fully cooperated with the government's investigation of these allegations in an effort to demonstrate their inconsistency with its institutional values."

The statement was signed by Northwestern President Morton Schapiro, Provost Daniel Linzer, and Vice President for Medical Affairs and Dean of the Feinberg School of Medicine Eric Neilson.

University officials said the settlement was limited to Bennett's grants.

"Although Northwestern expressly denied wrongdoing by any current faculty members as part of the settlement agreement, the university elected to settle the case rather than engage in protracted litigation that would divert time and resources from its primary missions of education and research," officials said.

Some outside observers question feasibility of the acts Bennett was alleged to have committed.

"As I learned when I was a young faculty member, these grants are made to institutions," wrote Roy Poses, a physician at Brown University, who runs the Healthcare Renewal blog.

"The institution that receives the grant is responsible for making all payments and disbursements related to that grant," Poses wrote. "The grant's principal investigator is responsible for the scientific conduct of the grant, but NOT payments, disbursements, business management or accounting.

"The principal investigator can request that payments be made for various things, including travel expenses and consulting work. But the principal investigator cannot directly authorize or make these payments. They are authorized, signed, and made by institutional administrators, usually in grants and contracts offices or the equivalent, and usually only after copious paperwork to justify the payments.

"So Dr. Bennett may have requested reimbursement for travel expenses, or requested the university to hire a consultant. But university managers must have made those payments, unless the university's grants administration mechanism had completely broken down. Note that given the usual ways grants are administered, it would appear that Ms. Theis, the ostensible whistle-blower, who will receive nearly one half of a million dollars from this settlement, actually may have had more direct responsibility for making the payments in question than did Dr. Bennett."

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DOJ Case Was Under Seal Since 2009

According to the memorandum of settlement, Northwestern improperly submitted claims to NIH for grant expenditures for:

• "Professional and consulting services, subcontracts to the University of Illinois, airfare and other transportation, conference registration fees, food, hotel, travel, meals, and other expenditures for items that were for the personal benefit of Dr. Charles L. Bennett, his friends, and family; and

• "Subcontracts to entities other than the University of Illinois, incentives, supplies, equipment, salaries, benefits, and associated Facilities and Administrative expenditures; that were incurred in connection with certain grants as to which Dr. Charles Bennett was a Principal Investigator. The United States further contends that these Grant Expenditures did not meet applicable NIH and Office of Management and Budget grant guidelines."

As they announced the settlement, Justice officials delivered an eviscerating critique of both Bennett and Northwestern.

"Allowing researchers to use federal grant money to pay for personal travel, hotels, and meals, and to hire unqualified friends and relatives as 'consultants' violates the public's trust," said Gary Shapiro, U.S. Attorney for the Northern District of Illinois. "This settlement, combined with the willingness of insiders to report fraud, should help deter such misconduct, but when it doesn't, federal grant recipients who allow the system to be manipulated should know that we will aggressively pursue all available legal remedies."

Court documents allege that improper expenditures were charged to the following grants: Research on Adverse Drug-Events and Reports: Novel Multiple Myeloma Drugs, NIH grant number CA125077; Research on Adverse Drug-Events and Reports, CA102713; Study of TTP: Incidence Rates and Risk Factors, HL69717; Patient Navigator, CA116875; and Multi-City Study of HIV-PCP, DA10628.

It's not clear why the original lawsuit names the Lurie Comprehensive Cancer Center Director Steven Rosen as a defendant.

Several observers were surprised to see that the relator, Theis, was never employed by the cancer center.

According to her 2009 suit, Theis came to Northwestern as a temp two years earlier, in 2007, serving as a purchasing coordinator for the Division of Hematology and Oncology. The division, which is separate from the cancer center, administered all but one of the grants in question, the NIH database shows.

After a year, in 2008, Theis was hired as a full-time employee of the Northwestern Medical Faculty Foundation. The foundation, which runs the medical practice, is also separate from the cancer center. She left Northwestern in October 2008.

"Theis specifically noted that invoices were submitted for consultants and services that were never included in the initial grant budget," the complaint states. "Invoices were submitted for consultants and services that were significantly in excess of the amount budgeted for the grant, and many of the consultants and vendors failed to provide detailed information about the actual services rendered.

"With respect to time and effort reporting on federal grants, Relator Theis noticed that the PIs would frequently draw down any excess grant funds for salary payments near the end of a budget period. Theis was also aware that PI's effort reports failed to control co-mingling and properly allocate researcher's time to a particular grant while they were working on multiple grants during a given budget period."

The civil action alleges that "defendants submitted false claims to the U.S. when Drs. Rosen and Bennett directed and authorized the spending of grant funds on goods and services that did not meet applicable NIH and Office of Management and Budget grant guidelines."

Rosen's name came up again as DOJ officials announced the settlement. Rosen was ultimately responsible for failure to institute proper financial controls, they said.

However, the final settlement document contains no allegations against Rosen.

"As the settlement makes clear, the covered conduct in the settlement involved allegations focused on Dr. Charles Bennett, and grants for which Dr. Bennett was the principal investigator," Northwestern officials said in a statement.

"The settlement does not in any way suggest or refer to any misconduct by Dr. Rosen, or relating to Dr. Rosen's grants," the statement said. "In fact, the settlement releases Dr. Rosen in the same way it releases anyone else at Northwestern who had no involvement with Dr. Bennett's grants.

"Not only does the settlement contain no findings or admissions of wrongful conduct by Northwestern or any of its current faculty members or employees, including Dr. Rosen, there are in fact no allegations about Dr. Rosen at all in the settlement agreement."

Sources close to Rosen said that until the settlement he was unaware of having been a defendant in the sealed federal lawsuit.

Administrator Pleads Guilty in Related Case

In a statement to The Cancer Letter, Bennett said that Northwestern has a history of problems with administration of grants.

"For the university to actively and accurately administer complex NIH grants, this is a very complex matter," he said. "The current settlement between the U.S. attorney and Northwestern University represents the second such multi-million dollar settlement in this area in recent years."

In an earlier whistleblower case, which was settled a decade ago, Northwestern repaid the government $5.75 million received from NIH. In the lawsuit—United States ex rel. Schwiderski v. Northwestern University—the government alleged that Northwestern inflated reimbursement by including in Institutional Base Salary researchers' income from clinical activities compensated by an affiliated faculty practice plan, while excluding those same clinical activities in calculating effort devoted to grants.

"I reported administrative issues by Northwestern University with my grants to the university compliance officer in 2006, just prior to my long-term bout with cancer that was diagnosed there," Bennett said to The Cancer Letter. "I have never had a single administrative discussion about the matter with anyone. I am in active discussion to settle this matter, and my legal team continues to strongly disagree with statements that have been disseminated in the press and related press releases."

Bennett said that he saw irregularities in the actions of the research administrator who handled his Research for Adverse Drug Events and Reports and that he has alerted the administration of the Division of Hematology and Oncology.

That same administrator, Sangoleye, pled guilty to larceny and theft, admitting to having embezzled NCI funds from Bennett's program into a checking account created in the name of a fictitious contractor.

According to court documents, Sangoleye created a vendor code for a fictitious entity she called ATSDATA.

Then she created 10 false invoices from that entity and paid them with Northwestern's checks.

The checks were sent to the ATSDATA post office box, which Sangoleye had rented, and placed into a bank account she created.

Between June 29, 2007, and July 29, 2008, ATSDATA received eight Northwestern checks that added up to $86,000. "Sangoleye converted the proceeds of the ATSDATA checks to her own use and to the use of another" individual, the plea agreement states.

"I knew nothing about ATSDATA," Bennett said in response to questions from The Cancer Letter. "The administrator told me that ATSDATA was the billing address for the University of Illinois Survey Research Laboratory, a formal subcontractor. I did not know that the Survey Research Lab had any particular billing name. I have documented this to Jonathan Licht [chief of Northwestern's Division of Hematology/Oncology] in 2008."

Northwestern officials declined to discuss Sangoleye, saying only that she had been employed by the university as a research administrator from February 2006 through August 2009.

Rumors about Northwestern's inquiries into Bennett's grants started to fly shortly before his departure for South Carolina.

Asked about the circumstances of his departure, Bennett said he had "voluntarily decided to look for jobs without the turmoil."

In South Carolina, he was offered an endowed chair with $6 million in startup funds to study safety of pharmaceutical agents, he said.

The settlement agreement, the original complaint and Sangoleye plea agreement are posted on The Cancer Letter website.

Bennett's Role in ESA Debates

At Northwestern, Bennett founded the Research on Adverse Drug Events and Reports (RADAR) project in 1998, which remained at the institution after his departure.

RADAR reviews physician queries, published and unpublished clinical trials, case reports, FDA databases and manufacturer sales figures to identify serious adverse drug and device reactions.

According to a recent paper, over the years, RADAR investigators reported 43 serious ADRs. Data sources included case reports (17 sADRs), registries (five sADRs), referral centers (eight sADRs) and clinical trial reports (13 sADRs).

Correlative basic science findings were reported for ten sADRs. Thirty-seven sADRS were described as published case reports (five sADRs) or published case-series (32 sADRs). Related safety information was disseminated as warnings or boxed warnings in the package insert (17 sADRs) and/or 'Dear Healthcare Professional' letters (14 sADRs).

ESAs were the most important projects for RADAR and Bennett.

In a nutshell, the red blood cell growth factors received FDA approval based on their ability to reduce the risk of blood transfusion at a time when the blood supply was in danger of contamination with HIV.

However, the sponsors started to expand its uses beyond approved indications, even though the question of the agent's impact on hard endpoints like survival were never addressed.

As the agent's use in oncology became ubiquitous, randomized trials started to show evidence of harm, including disease progression and decreased survival (The Cancer Letter, Oct. 24, 2003).

For a researcher with Bennett's set of interests, the questions of adverse events associated with ESAs presented an opportunity of a lifetime.

The ESA issue was ultimately resolved in February 2010, when FDA made ESAs subject of a Risk Evaluation and Mitigation Strategy because eight studies pointed to their potential to cause strokes, heart attacks, and tumor progression (The Cancer Letter, Feb. 19, 2010).

REMS require additional training and certification for health care providers as well as distribution of a medication guide for patients who may be receiving these agents. Doctors are cautioned to refrain from prescribing these agents in a setting where a cure is possible, and to administer informed consent at each administration of these.

Bennett wasn't directly responsible for FDA's actions. His principal contributions to the debate consisted of pooling and analyzing data from earlier studies. While FDA doesn't make decisions based on meta-analyses, Bennett's findings created the atmosphere of caution, and his papers gave physicians another reason to pause before they reached for prescription pads. This reporter, too, frequently turned to Bennett for on-record quotes on the controversy.

Now, researchers who worked with Bennett on the ESA issues are puzzled by his legal problems.

"Charlie has been an important voice in raising concerns regarding the use of erythropoietin in patients with cancer," said Anthony Blau, co-director, Institute for Stem Cell and Regenerative Medicine at the University of Washington. "In particular, his 2008 meta-analysis, published in JAMA, heightened awareness of the issue and helped to reduce the indiscriminate use of erythropoietin in cancer patients."

Blau is a co-author on the JAMA paper.

"This doesn't really fit in his picture," said Michael Henke, a radiation oncologist in Freiburg, Germany, who was the first to stumble across potential problems stemming from overuse of ESAs.

"You might recall, we got in contact in 2003 when

our group communicated potential dismal effects of erythropoietin on cancer patients—a story not really appreciated these days because of economic interests," Henke said referring to the pioneering paper in The Lancet. Henke was the senior author on the JAMA paper.

"However, Dr. Bennett and we consistently gathered additional data that were finally reported as a meta-analysis in 2008. Consequently, erythropoietin prescriptions dramatically decreased, eventually prolonging or even saving lives of cancer patients.

"While collaborating, I did learn him as extraordinarily active, alert-eyed colleague who strictly adhered to serious scientific conduct and to the well-being of patients."

Henke confesses to wondering whether the many powerful enemies Bennett made in the pharmaceutical and biotechnology industries have struck back.

"We shouldn't feed paranoia," Henke said. "However, given the exclusively positive experience when collaborating with his group, makes me wonder whether this litigation might follow some very particular other issues."

The paper that eventually ended up in JAMA found that ESAs were associated with increased risk of venous thromboembolism and mortality. The researchers didn't have access to patient charts. A later patient-level analysis by the Cochrane Collaboration, which had access to proprietary data Bennett couldn't obtain, came up with a very similar result.

"Charlie is an aggressive investigator who is driven by the story's outcome," said Howard Ozer, director of the University of Illinois Cancer Center and the Heidrick Professor of Medicine, whose research is focused on growth factors. "With ESAs, he seemed intent to get to the result before anyone else—and ultimately he was on the correct side of the outcome."

Bennett's papers also examined the motivations and conflicts of interest of his colleagues as they studied and prescribed ESAs. And, sources say, he was occasionally consulted by reporters and attorneys tracking the case.

Last December, Amgen Inc., the sponsor of the ESA agent Aranesp, pled guilty to charges of illegally introducing a misbranded drug into interstate commerce.

The plea was part of a global settlement with the U.S. government, in which Amgen agreed to pay $762 million to resolve criminal and civil liability.

This largest-ever criminal settlement involving a biotechnology company was obtained under the same law that another team of prosecutors is invoking against Bennett: the False Claims Act.

Guest Editorial

NLST Co-Principal Investigator Begs to Differ with USPSTF Lung Cancer Screening Grade

(Continued from page 1)

This was the first time this aggressive, heterogeneous disease was shown to be amenable to early detection with subsequent surgical resection being curative in a fraction of the cases. Even though many lung cancers are aggressive, some can be detected and cured at a phase where metastases have not developed.

This has clear public health importance as, unfortunately, lung cancer remains the leading cause of cancer death even in the face of substantial declines in smoking prevalence.

Why is the recommendation only a B: moderate certainty for moderate benefit? The primary results of the NLST documented a 20 percent decrease in lung cancer specific mortality (95% CI, 6.8 to 26.7; P=0.004).

This result was statistically significant adjusted for interim analyses in this well-powered study.

In fact, the data and safety monitoring board recommended that the study be halted early, results announced and all of the participants informed.

Nonetheless, five-year lung cancer survival in the CT arm is 54 percent. Therefore, almost half of the patients are still dying of their lung cancer by five years and it is reasonable to classify the benefit as moderate.

Clearly, additional research to improve early detection modalities with imaging and/or biomarkers is warranted. The USPSTF did err in reporting on a presentation made at the joint BSA/NCAB meeting in June 2013, which stated that the mortality reduction had declined to 16 percent. First, inclusion of this presentation violates the USPSTF own guidelines for only peer-reviewed publications contributing to the systematic review. Secondly, and more importantly, this is NOT the trial result.

The presented analysis included more follow-up with continued dilution with deaths from lung cancer occurring in patients whose lung cancers occurred after screening ended. Also, it was NOT a change from adjudication as The Cancer Letter erroneously reported (Aug. 2, 2013).

A well-powered, well-conducted study with a solid, highly stable result—which is the gold standard in clinical research—only merits a description of moderate certainty? This study involved 53,454 participants enrolled at 33 sites with satellites and required that

a hard-working, large, multi-disciplinary team work diligently from 1999 to 2012.

It also cost $256 million. It is very reasonable to accept the NLST result as solid and definitive. It makes no sense to consider that if a screening question of equal import arises we should launch TWO identical studies simultaneously.

The published screening studies from Europe were appropriately analyzed by the USPSTF with cautionary comments about size, unequal follow-up across arms and in one study uneven randomization.

Results from the other ongoing studies, particularly NELSON from the Netherlands and Belgium, the largest of them, are eagerly awaited. However, the total enrollment across all studies in Europe is only 34,000. The control groups in these studies did not get screened with CXR.

But the NLST and PLCO results do not show that a posterior-anterior chest x-ray as a screening tool lowers lung cancer specific mortality. A very small benefit of CXR remains possible and could have been missed.

Nonetheless, even a meta-analysis of all of the European studies when they are completed may be underpowered. There is much additional valuable information to be gained from these studies and they should be completed.

These additional issues include frequency of screening and the effect of varying definitions of a positive screen on outcomes.

The USPSTF guidelines recommend annual screening of individuals aged 55 to 80 who meet the NLST criteria of 30 pack-years of smoking and 15 years from smoking cessation. So, an individual may not need continued annual screening 15 years from smoking cessation.

However, Michael LeFevre, co-vice chair of the USPSTF, states that overall this screening regimen would lower lung cancer mortality by only 14 percent.

What can be done with the current CT technology to improve upon this?

The criteria for entry into screening assessed by the Cancer Intervention and Surveillance Modeling Network that led to this recommendation are straightforward: age, pack-years smoked, and years since quitting.

This does lead, however, as documented by Kovalchik et al. (N Engl J Med 2013; 369:245-254), to individuals at rather low risk of lung cancer death with correspondingly low risk of benefit being screened.

Also, there are individuals with a high risk of lung cancer outside of the NLST criteria who would benefit from screening.

Tammemagi et al. (N Engl J Med 2013; 368:728-736) developed a more complex risk model with a larger number of variables that can more precisely estimate risk. This model is available for all to use at http://www.brocku.ca/lung-cancer-risk-calculator. They utilized an earlier version of this model in the Pan-Canadian Early Lung Cancer Detection Study demonstrating that they needed to screen fewer people to get more lung cancers than using the NLST criteria.

Other models are also available and straightforward to use, such as the Bach model at http://www.mskcc.org/cancer-care/adult/lung/screening-decision-tool. These models are a step forward, and, as stated by the USPSTF, "future improvements in risk assessment tools will help clinicians better individualize patients' risks."

There are several limitations of screening with CT that also contribute to a result of moderate benefit. One is the high rate of positive examinations that require additional imaging and at times invasive evaluation for what turns out to be benign disease.

This increases costs and radiation exposure. Exciting work has been done in evaluating positive examinations and incorporating baseline lung cancer risk factors to estimate risk of malignancy, and this research may be available soon. The frequency of screening should also be studied; those with normal initial scans may not need to be screened annually to get benefit.

Radiation exposure is another concern. CISNET modeled radiation risk and they still concluded that, in a high-risk group, the benefits of the screening outweighed the radiation-induced cancer harms.

The benefits occur in the near term while the induced cancers are few in number and occur later. There are groups in whom the risks of radiation-induced cancers are not outweighed by the screening benefits.

This is particularly true in younger, non-smoking individuals (Berrington de González A, Kim KP, Berg CD. J Med Screen. 2008;15(3):153-8). Harms of interventions from screening are also more severe in those with serious co-morbid conditions and the oldest of the elderly—who may have little to gain from finding a tumor they may die with, rather than from. Healthcare providers need to incorporate these cautionary comments when advising patients.

Implementation of lung cancer screening will be a challenge as it is not population-based, like mammography screening. Careful attention to assessment of lung cancer risk will be required. The worried-well who will not benefit from screening will

also need reassurance.

The most critical item, though, is that screening must not detract from continued public health efforts to lower the rates of cigarette smoking with the manifold benefits of cessation.

Wouldn't it be wonderful if only 15 more years of lung cancer screening were needed as the lung cancer epidemic fades away?

The author is the co-principal investigator of the National Lung Screening Trial and former chief of the Early Detection Research Group at the NCI Division of Cancer Prevention.

The Cost of Healthcare

GAO Report Finds Increase In Self-Referred Pathology Services

The Government Accountability Office found that self-referred anatomic pathology services increased at a faster rate than non-self-referred services between 2004 and 2010.

The watchdog agency's report, released July 15, states that the number of self-referred anatomic pathology services more than doubled nationwide, growing from 1.06 million services to about 2.26 million services—while non-self-referred services grew about 38 percent, from about 5.64 million services to about 7.77 million services.

Similarly, the growth rate of expenditures for self-referred anatomic pathology services was higher than for non-self-referred services.

Three provider specialties—dermatology, gastroenterology, and urology—accounted for 90 percent of referrals for self-referred anatomic pathology services in 2010.

Self-referral occurs when providers refer patients to entities in which they or their family members have a financial interest. The practice is prohibited under the Stark Law.

However, an exception allows physicians to bill for some medical services where an ownership interest exists. It was intended to apply to services provided at the time of an office visit as a convenience to patients.

Over time, these services started to include pathology, advanced diagnostic imaging, and intensity modulated radiation therapy (The Cancer Letter, April 13, 2012).

GAO has looked at impact of the self-referral law in the past, producing a report titled "Higher Use of Advanced Imaging Services by Providers Who Self-Refer Costing Medicare Millions."

Based on Medicare data, GAO estimates that in 2010, self-referring providers likely referred over 918,000 more anatomic pathology services than if they had performed biopsy procedures at the same rate as and referred the same number of services per biopsy procedure as non-self-referring providers. These additional referrals for anatomic pathology services cost Medicare about $69 million.

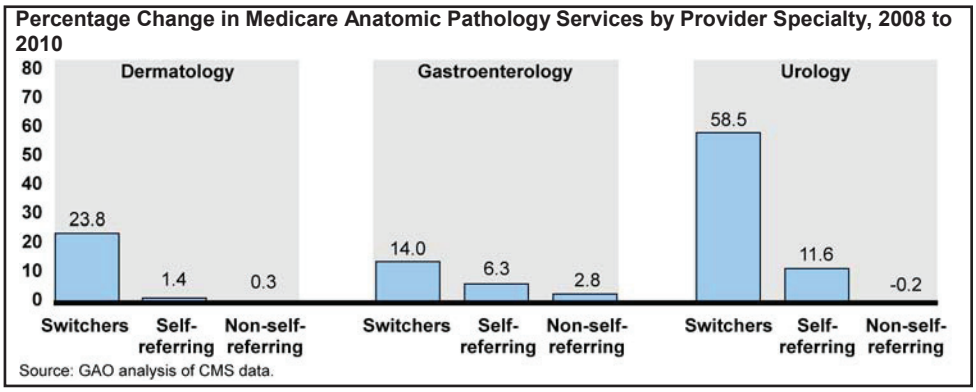
The report says that financial incentives for self-referring providers were likely a major factor driving the increase in referrals.

The agency found that referrals for anatomic pathology services by dermatologists, gastroenterologists, and urologists substantially increased the year after they began to self-refer.

Providers that began self-referring in 2009—referred to as switchers in the GAO report—had increases in anatomic pathology services that ranged on average from 14.0 percent to 58.5 percent in 2010 compared to 2008, the year before they began self-referring, across these provider specialties.

In comparison, increases in anatomic pathology referrals for providers who continued to self-refer or never self-referred services during this period were much lower.

Thus, the increase in anatomic pathology referrals for switchers was not due to a general increase in use of these services among all providers. The GAO's examination of all providers that referred an anatomic pathology service in 2010 showed that self-referring



A chart showing the changes in Medicare anatomic pathology services in three specialties, from 2008 to 2010. *Source: GAO*

providers of the specialties we examined referred more services on average than non-self-referring providers.

The agency recommended that CMS identify self-referred anatomic pathology services and address their higher use. The Department of Health and Human Services agreed with GAO's recommendation that CMS address higher use of self-referral through a payment approach, but disagreed with GAO's other two recommendations to identify self-referred services and address their higher use.

"The GAO's assertion that urologists and other specialists are utilizing ancillary services for financial gain is both fundamentally wrong and offensive," the American Urological Association said in a statement.

"To label an entire profession by proposing that urologists are performing unnecessary or inappropriate biopsies to boost their bottom lines not only disparages urologists, but does a great disservice to patients. Urologists should be involved in all aspects of a prostate cancer patient's care, including referral, diagnosis, and management of the disease. Patient access to in-office ancillary services, including laboratory services, allows for prompt treatment and ensures continuity of care while simultaneously allowing for optimal patient management by the urologist."

The College of American Pathologists said the GAO report documents millions of dollars in wasteful health care spending by physicians who self-refer anatomic pathology services, and called on Congress to take immediate action outlawing this business practice.

"GAO issued a report today with irrefutable evidence that physician self-referral is a national problem," said CAP President-elect Gene Herbek, "It contributes to widespread abuses, increased medical costs and over utilization, and it allows physicians to exploit a loophole that permits them to bill Medicare for certain additional services they provide to patients at the time of the office visit. However, this provision was never intended to protect self-referral of anatomic pathology services because unlike clinical laboratory services they can almost never be performed at the time of an office visit," Herbek said.

CAP drew attention to the problem in anatomic pathology by co-sponsoring the first independent research published last year on the impact of self-referral of anatomic pathology services on utilization, patient care, and health care costs.

The research was conducted by health care economist Jean Mitchell and published in Health Affairs.

Mitchell's paper compared Medicare billing practices for anatomic pathology services related to prostate biopsies by self-referring and non-self-referring urologists, and using Medicare's own data showed that self-referring urologists billed Medicare for 72 percent more prostate biopsy specimens compared to non-self-referring physicians, with no increase in cancer detection.

Self-referring urologists had a 40 percent lower cancer detection rate than those who didn't self-refer, despite billing for nearly twice as many specimens.

Data suggest that in IMRT, incentives similarly appear to drive overutilization.

In a paper that appeared in the Journal of the

American Medical Association June 25, Bruce Jacobs and his colleagues analyzed treatment data for 55,947 prostate cancer patients aged 66 years or older in the Surveillance, Epidemiology and End Results Medicare database from 2004 to 2009.

The study, "Use of Advanced Treatment Technologies Among Men at Low Risk of Dying from Prostate Cancer," found that the use of advanced treatment technologies increased from 32 to 44 percent among men with low-risk prostate cancer, from 36 to 57 percent among men with high risk of non-cancer mortality, and from 13 to 24 percent among men unlikely to die from prostate cancer.

In discussion, the paper raises questions about "aggressive direct-to-consumer marketing and incentives associated with fee-for-service payment may promote the use of advanced treatment technologies."

Michael Steinberg, chairman of the American Society for Radiation Oncology board of directors, said the study reaffirms the society's commitment to closing the self-referral loophole for radiation therapy.

While ASTRO supports the use of IMRT, it should be "carefully considered along with other effective treatments and management options," ASTRO said in a statement.

"Treatment decisions should not be based on the physician's potential for profit, yet we believe profit-motivated IMRT overuse is rampant due to the proliferation of urology ownership of radiation therapy centers," the society's statement said. "The abuse of this expensive technology is allowed by a loophole in the federal physician self-referral law.

"We agree with Dr. Jacobs's concerns that financial incentives may be negatively impacting treatment decisions, which we believe are compounded by ownership arrangements protected under the self-referral loophole."

"Cumulatively, all of these studies demonstrate that self-referral abuse drives overutilization of expensive technologies. ASTRO agrees and urges Congress to act this year.

"All evidence confirms that the self-referral loophole must be closed to protect every patient and to preserve the Medicare program," Steinberg said.

"This loophole endangers patients and erodes their trust in us as physicians. In addition, self-referral abuse wastes our nation's already stretched financial resources."

In Brief

Wender Named First ACS Chief Cancer Control Officer

(Continued from page 1)

While Brawley will focus on epidemiologic and peer-reviewed cancer research programs and their translation to clinical practice, Wender will focus on consumer and clinical guidance on cancer prevention and early detection, and their implementation through evidence-based cancer control interventions.

Wender serves as alumni professor and chair of the Department of Family and Community Medicine at the Jefferson Medical College of Thomas Jefferson University and Hospital. He has been an ACS volunteer for 26 years.

In 2006, Wender became the first primary care physician to be elected society president. He has served as chair of the Incidence and Mortality Committee and has been a member of the editorial advisory boards for the society's peer reviewed journal, CA: A Cancer Journal for Clinicians. He chairs the Cancer Screening Guideline Group.

Wender's academic focus has been on cancer prevention and screening. In collaboration with the Centers for Disease Control and Prevention and the National Colorectal Roundtable, Wender helped develop many of the tools used across the country to promote colorectal cancer screening. Wender is one of the lead authors on several of the society's cancer screening guidelines, including the recent lung cancer screening guideline.

THE AMERICAN SOCIETY OF CLINICAL ONCOLOGY outlined a strategy to reduce premature deaths due to **tobacco use**.

The society's policy statement, published in the Journal of Clinical Oncology, focuses on public policy needs, provider education and research on tobacco cessation and control interventions.

ASCO also announced its endorsement of the proposed Tobacco Tax Equity Act, which would close tax loopholes by taxing pipe and cigarette tobacco equally. Research has shown that smokers are price sensitive, and are more prone to quitting tobacco use as the price of products rise.

ASCO recommends strengthening education of healthcare providers during medical school and

through continuing medical education programs on proven strategies for tobacco cessation counseling, and educating oncologists about the critical impact of persistent smoking by patients during their cancer care. Patients have longer progression-free and overall survival if they are not smoking during their cancer treatment.

The policy statement supports legislative and regulatory efforts—excise tax increases, clean indoor air policies to avoid second-hand smoke, and graphic warning labels on cigarette packages.

The statement also supports providing health plan coverage (with no co-pay or deductible) and appropriate provider reimbursement for evidence-based tobacco cessation services, including counseling and quitlines, as well as FDA-approved cessation medications; and increasing funding for research on tobacco control and more effective cessation interventions, as well as including tobacco use as a core data element in oncology clinical trials.

THE BIG TEN CANCER RESEARCH CONSORTIUM selected **Forte Research Systems** to provide the consortium's clinical trials software infrastructure.

Hoosier Oncology Group, the consortium's administrative headquarters, selected Forte's OnCore Enterprise Research system to support its clinical trials portfolio. The system will include financial management and electronic data capture.

The Big Ten Cancer Research Consortium, launched in June, is a network of 12 academic cancer centers and research universities that will collaborate and conduct translational oncology trials. The consortium has access to more than 30,000 new patients each year.

GlaxoSmithKline announced that it will discontinue the manufacture and sale of the **Bexxar therapeutic regimen** February 20, 2014.

The Bexxar regimen (tositumomab and iodine I-131 tositumomab) is approved in the U.S. and Canada for the treatment of patients with CD20-positive relapsed or refractory, low grade, follicular, or transformed non-Hodgkin lymphoma who have progressed during or after rituximab therapy, including patients with rituximab-refractory non-Hodgkin lymphoma.

Bexxar was approved for use in the U.S. in 2003 and in Canada in 2005. The use of Bexxar has been extremely limited and is projected to continue to decline, according to GlaxoSmithKline, which says it will continue to provide support services for patients and treatment centers over the next six months.

Funding Opportunities

National Lung Cancer Partnership Announces Grant Competition

The National Lung Cancer Partnership announced its 9th annual **research grant competition**. Several two-year, $100,000 awards are available to post-doctoral fellows and junior faculty.

The partnership is seeking research applications in the following areas of interest: improving outcomes for patients with early stage cancer—proposals that have near-term potential to make a dramatic improvement in early stage cures; and in improving outcomes for patients with unresectable lung cancer—proposals describing innovative strategies to address challenges in treating locally advanced, oligometastatic, and disseminated metastatic patients.

Pre-clinical, translational, and clinical proposals are eligible for funding, and all proposals must clearly identify how the work will lead to increased survival for lung cancer patients.

At the time of application, an applicant must hold a doctoral degree and be a post-doctoral fellow, or be in the first five years of their first faculty appointment at a not-for-profit institution in the U.S. or Canada.

Complete application eligibility and instructions are available on the partnership's website: www.nationallungcancerpartnership.org. The application deadline is Oct. 22. Awards will be announced on or before March 1, 2014.

FDA News

FDA Grants Orphan Designation To E7777 in T-Cell Lymphoma

FDA granted orphan drug designation to an investigational compound, **E7777**, developed by Eisai Inc., for cutaneous t-cell lymphoma.

The compound is designed to have an improved purity profile and manufacturing process. It is being studied in a phase III trial.

The Orphan Drug Act allows FDA to grant orphan status to a drug which has the potential for the treatment, diagnosis, or prevention of a rare disease or disorder that affects fewer than 200,000 people in the U.S.

CTCL begins in the white blood cells and attacks the skin. It is one of several types of lymphoma collectively called non-Hodgkin lymphoma.

FDA approved the Aptima HPV assay for use on the automated Panther system, both developed by Hologic Inc.

The test is performed with a ThinPrep liquid cytology specimen, which are routinely used for Pap testing, and can be tested before and after it has been processed for cytology testing on the ThinPrep 2000 system.

The mRNA based assay is a nucleic acid amplified test that detects 14 high-risk strains of human papillomavirus associated with cervical cancer and precancerous lesions, and has demonstrated significantly improved specificity with no compromise in disease detection. The addition of the Aptima HPV assay to the Panther system allows low to high-volume laboratories to run multiple tests from a single specimen, on a flexible and automated molecular testing platform.

The Aptima HPV assay has been approved for two uses: to screen women 21 years and older with atypical squamous cells of undetermined significance to determine the need for referral to colposcopy; and to use adjunctively with cervical cytology to screen women 30 years and older to assess the presence or absence of high-risk HPV types.

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An Appreciation

Long-time NCI Spokesman Paul Van Nevel Dies at 75

By Jerry D. Boyd

Paul Van Nevel had a tough job, but he made it seem easy.

Van Nevel, who died Aug. 4 at age 75, was the director of the NCI Office of Cancer Communications. The period which NCI insiders call "the Paul Van Nevel Years" stretched for over a quarter century, from 1973 to 2000.

During that time, with unflappable demeanor and on a budget that seems modest by today's standards, Van Nevel steered NCI's public relations away from the reefs.

His job required managing a staff of 10 to 20 people, trying diplomatically to give counsel to his immediate bosses (the institute directors), seeking to exercise some degree of influence over NCI's 2,000 employees, thousands of grantees and contractors, the plethora of nongovernmental board members and members of scientific review committees.

Massaging egos on Capitol Hill was also a part of the job. Meanwhile, the National Cancer Act of 1971 and subsequent revisions piled more responsibilities onto OCC, making it the prime source for cancer related information nationwide.

PVN (this is how he signed his memos) organized the first U.S. government-supported cancer patient education program. OCC produced and distributed millions of copies of books, pamphlets, booklets and other informational material throughout the country, setting the pattern for similar efforts in other countries. And he developed the news section of the Journal of the National Cancer Institute and served as its editor.

Van Nevel also represented NCI at nongovernmental activities. As a member of the American Cancer Society's Communications Committee; as communications consultant to Howard Hughes Medical Institute; as a member of the U.S. National Committee of the International Union Against Cancer; and as chair of the Association of American Medical College Group on Public Affairs.

In 1999, Van Nevel was selected by President Bill Clinton for the Presidential rank of Meritorious Executive, given annually to a small number of senior federal executives. He also received that year the award for Distinguished Service to Journalism and Mass Communications from the University of Wisconsin-Madison, his alma mater.

J. Paul Van Nevel was born April 26, 1938, in New Richmond, Wis. His parents, Frank and Frances Davin Van Nevel, had nine children. Paul was the oldest.

He graduated from UW-Madison with a degree in journalism. He served in the Army for two years on the faculty of Fort Slocum, N.Y., which imparted journalism skills to Armed Forces recruiters as well as to staff members of military base newspapers.

He returned to his job as director of public information at UW-Madison, then, four years later, left to become director of public relations at Johns Hopkins University and Hospital.

He moved to NCI in 1973, first as deputy director of OCC, and a year later, became director. His formal title was associate director of NCI for cancer communications.

I first met him in 1973, when I was a reporter with the "Blue Sheet," a newsletter that covered health-related issues in Congress and the executive branch.

Van Nevel was the newly hired deputy director of OCC, whose duties frequently included answering questions from the press. With my limited exposure to biomedical research, I needed all the help I could get.

Van Nevel helped familiarize me with NIH, told me how the various NCI offices and programs worked, who did what. When we (my journalist wife Julie and I), started The Cancer Letter in 1973, Van Nevel helped with advice, mailing lists, phone numbers, and countless other details. He was equally cooperative, as far as I know, with all members of the media.

NIH, like any government organization, has the annoying tendency to withhold information that we in the media feel is important. A reporter's job is to get through the veil of obfuscation. For that, you need sources.

When he dealt with reporters, Van Nevel was sympathetic but cautious. He played by the rules. With complicated issues, he patiently explained, helping when he could, clamming up with a smile when he could not.

Taxpayers probably get more for their money from NIH than any other part of the federal government. That was especially the case with the Office of Cancer Communications when Van Nevel ran it.

The budget was usually $10-20 million. The office's budget in recent years has been as high as $68.1 million (The Cancer Letter, March 1).

Van Nevel's OCC also helped NCI staff members write speeches and respond to media inquiries, requests from Congress. The staff reported on scientific meetings around the country.

In the first 15 to 20 years after the American Society of Clinical Oncology was founded, OCC staff members ran the pressroom at ASCO's annual meeting, distributed news releases, and organized press conferences.

Van Nevel ran an efficient, bare-bones operation—with the full cooperation and guidance of directors Frank Rauscher Jr., Arthur Upton, Vincent DeVita, and Samuel Broder. Subsequently, OCC's budget was grossly inflated by their successors, some of whom were more devoted to enhancing their own stature than in helping in the battle against cancer.

NCI Director Harold Varmus is appropriately reducing the institute's PR budget.

I have been in the news business for nearly 70 years (the last 20 of which was mostly unpaid), and have been in contact one way or another with thousands of public relations people. Most of them have been fine professionals; Paul Van Nevel the finest of all.

DeVita, who retired in 1988 after eight years as NCI director and more than 25 years at NCI, knew Van Nevel as well as anyone.

"He was one of my favorite people," DeVita said in a phone conversation this week. "He was always honest with the press. He lived by that rule.

"There were times, however, when he had to stretch the truth, trying to please his bosses, who may have preferred avoiding the truth completely," DeVita said. "Nothing pained him more, but the press knew he was doing his best to be honest with them.

Van Nevel died after a five-year battle with progressive supranuclear palsy, a brain disorder with symptoms similar to Parkinson's disease.

He is survived by his wife, Lois Anderson Van Nevel, whom he married in 1962 just before going into the Army; daughters Catherine Van Nevel of Gaithersburg, Md., and Kari Buckard of St. Michaels, Md.; grandchildren Keara, Bridget, Cailin, Paul and Nick Van Nevel and Jack and Ellie Buckard; eight brothers and sisters, and numerous nieces and nephews.

The family suggested that contributions could be made to the Frances Van Nevel Memorial Fund at the Carbone Cancer Center, Univ. of Wisconsin School of Medicine and Public Health; 600 Highland Ave., K4/658, Madison, WI 53792-61264.

A celebration of his life will be held from 11 a.m.-3 p.m. Saturday, Aug. 17, at St. James Episcopal Church in Potomac, Md. A short, informal program at the beginning will be followed by a luncheon.

The author is the founding editor of The Cancer Letter.