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NCI Didn't Publish Two Bypass Budgets As Sequestration Set In and Funds Tightened

By Paul Goldberg

What's the NCI director's professional judgment of opportunities in cancer research at a time of shrinking budgets, sequestration and conclusion of the windfall of the American Recovery and Reinvestment Act?

Under ordinary circumstances, this question wouldn't have required a mind reader. The NCI director has an authority no other government executive enjoys: every year, he submits a summary of scientific opportunities directly to the White House, bypassing review by the NIH director and officials at the place ominously called "downtown," the brutalist-style HHS headquarters at the base of Capitol Hill.

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Guest Editorial

On PSA Skepticism, Rational and Irrational

By Andrew Vickers

I consider myself a prostate cancer screening skeptic. For example, in the title of the grand rounds lecture I have given for many years, I describe PSA as a "public health fiasco."

I have also [gone on the record](#) to state: "PSA testing as it is commonly practiced in the U.S. is indefensible."

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In Brief

Boyle Wins ESMO Lifetime Achievement Award

THE EUROPEAN SOCIETY FOR MEDICAL ONCOLOGY named three winners of the society's annual awards.

Peter Boyle received the **ESMO Lifetime Achievement Award** for his long-standing contribution to cancer epidemiology, education and prevention.

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Two Bypass Budgets Missing As Research Funding Dips

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This privilege, created by the National Cancer Act of 1971, has been a part of the political landscape since 1974.

Yet, today, as Congress stands poised to battle over budget priorities for fiscal 2016, the NCI bypass budgets for FY 2014 (the year gone by), and FY 2015 (the current fiscal year), are missing. They haven't been published.

Some Capitol Hill insiders say that the absence of a clearly stated vision from the NCI director is all the more disappointing since, for the first time in its history, NCI is led by a Nobel laureate, Harold Varmus.

The bypass budget is a unique authority. Under normal circumstances, government officials are precluded from asking for more money than what the president's budget proposal allots to them. The only exception to that rule is the NCI bypass budget. And, with the appropriations process on Capitol Hill getting streamlined, the bypass budget has become one of the few opportunities for the institute director to speak about the lifesaving potential of cancer research—and the ultimate price of putting cancer science on a starvation diet.

"Any document that shows the need that exists today and outlines the scientific opportunities would be very much welcomed," said a lobbyist for a major scientific organization, who spoke on condition that his name wouldn't be used. "It's an important tool to have in our tool box. We have not asked for it formally, but as an advocacy community, I think this is something we should consider doing. We should ask: 'We'd like to see the bypass budget. Is there an explanation for its absence?'"

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Peter Garrett, a spokesman for NCI, said the institute focused its efforts on defending against sequestration rather than putting together aspirational goals.

"The FY 2012 and 2013 bypass budgets required extensive involvement from the NCI director, the two chief deputies and the heads of the divisions, offices and centers," Garrett said.

"Rather than direct our efforts on proposing unrealistic increases for NCI, we have focused on holding the line with the rest of NIH, and defending against cuts.

"The next bypass budget proposal, with accompanying narrative, will be made available at the next joint meeting of the National Cancer Advisory Board and NCI's Board of Scientific Advisors on Dec. 2, 2014," said Peter Garrett, a spokesman for NCI.

"We recognize that the bypass budget is an important tool for NCI's advocacy communities. For this reason, we are working hard to make certain the the documents produced this fall for the president provide clear and compelling information that will make a strong case for the need to support cancer research vigorously in current and future fiscal years.

"The primary focus of the forthcoming bypass budget will be FY 2016, but we will also address issues that were relevant to FY 2014 and remain relevant to FY 2015.

"We remain engaged in the normal NIH budget process and contribute to the justification of the president's budget for the NCI and the NIH. We also work closely with the NIH, HHS, the White House, OMB, and our many advocates on an ongoing basis to convey the many opportunities cancer research and the resources required to support them," Garrett said.

The Role of the Bypass Budget

Veterans of the cancer program said to The Cancer Letter that they are surprised by the absence of two consecutive bypass budgets.

"The bypass budget gives NCI the opportunity to say precisely what it's able to accomplish and how it plans to go about it," said Joseph Simone, former chairman of the Institute of Medicine National Cancer Policy Board, and former director of St. Jude Children's Research Hospital, former physician-in-chief at Memorial Sloan Kettering Cancer Center and the first senior clinical director of the Huntsman Cancer Institute.

"When it's used effectively, the bypass budget speaks about the promise of research and its impact on bettering the lives of real people," Simone said. "The bypass budget is a scientific document. It is a strategic

document. And it's a political document. It gives cancer advocacy groups the messages they are able to amplify in appeals to Congress and the administration.

"It is incomprehensible why this important tool wasn't available to cancer advocates in the making of the FY 2014 and FY 2015 budgets. During unprecedented tightening of budgets and sequestration, this community needed all the help it could get."

Bruce Chabner, director of clinical research at Massachusetts General Hospital Cancer Center and former chair of the National Cancer Advisory Board, agrees with Simone.

"I understand NCI's reluctance to devote a great deal of time and thought to a document that will likely carry little weight with Congress and the Administration, burdened as they are with budget deficits and other national issues," Chabner said to *The Cancer Letter*. "However, the bypass budget serves a wider purpose, in that it provides NCI with the opportunity to present the incredible promise and potential of the field of cancer research to a national audience, and build a consensus for future action on the part of both the private and public sectors."

Vincent DeVita, one of Varmus's predecessors as NCI director, describes the absence of two bypass budgets as unfortunate.

"I thought the preparation of the bypass budget was still required by law?" he asked rhetorically.

The [National Cancer Act](#) sought to make cancer more visible to the White House. To accomplish this, the president appoints the NCI director and members of the two principal advisory boards dealing with cancer: the National Cancer Advisory Board and the President's Cancer Panel. The latter was intended to review the National Cancer Program and submit annual progress reports directly to the president.

No other NIH institute has all these authorities.

DeVita, who ran NCI from 1980 to 1988, used to go to the Oval Office with the chair of the President's Cancer Panel and hand the budget to the president. However, since those days, the panel has lost much of its political clout, and these days it's not clear how (or whether) the NCI bypass budget reaches its intended reader.

NCI's special authorities have been eroding for years, said DeVita, the Amy and Joseph Perella Professor of Medicine and professor of epidemiology and public health at Yale Cancer Center.

He points to one of the more puzzling moments in political history of cancer: when then-NCI Director Richard Klausner hired Harold Freeman, chair of the President's Cancer Panel at the time, to run the NCI Center to Reduce Cancer Health Disparities and serve

as an associate director of NCI while remaining on the panel (*The Cancer Letter*, [Sept 15, 2000](#)).

"Klausner actually hired the panel chair, his supervisor, as an NCI employee while he remained chair, and no one noticed," DeVita said.

Being the first in a chain of bureaucratic entities the bypass budget bypasses, NIH has been known to create obstacles to the cancer institute, DeVita said.

"NIH never liked the bypass budget or the National Cancer Act and prefers to ignore it, and most of my successors have not used the authorities provided by the act because they often put you in conflict with the NIH director," DeVita said. "But even then, if [the bypass budget] was carefully prepared and not just a blue sky document, it gave the NCI director a chance to highlight program priorities that required more money, giving congressmen a guide they could use to ask questions.

"And the director could respond more freely than would normally be allowed of a presidential appointee. I'm surprised that members of Congress haven't asked for it," DeVita said, referring to the missing bypass budgets.

"But now you have an NCI director (who is a former NIH director) who has publicly opposed the National Cancer Act reporting to an NIH director, who doesn't like it, so it's no surprise that they choose to ignore it." (*The Cancer Letter*, [June 11, 2010](#).)

"But to refuse to prepare it, if it is still required by law, is a scandal."

Varmus: Bypass Budget is NCI's Annual Report

The absence of the bypass budgets is all the more puzzling, because, as NCI director, Varmus has successfully produced two such documents.

Early in his stint as NCI director, Varmus characterized the bypass budget as a worthwhile endeavor that had the potential to benefit the institute.

"This book will be attractive," Varmus said [at the NCAB meeting Feb. 2, 2011](#). "I think of this as the NCI's annual report, the way that Memorial Sloan Kettering or other cancer centers put together an annual report for donors. Indeed, this is addressed to donors—the American public.

"There will be charts, and pretty pictures, and quotes from investigators of all types to express the enthusiasm the scientific community has for the work it does, if not for the budgets it's currently receiving."

Varmus also saw the bypass budget as an opportunity to illustrate the point that the organs where cancers are diagnosed are not as important as the tumor's genomic characteristics.

The Varmus bypass budget would focus on six cancers, he said to NCAB in 2011.

“By doing things in this way, we also highlight the intrinsic differences in various kinds of cancers,” he said.

“I think it’s an important message for everyone to learn, because when I hear folks say, ‘I want a cure for cancer,’ those of us who are in the know understand that cancers are all inherently different. Not only are types of cancer different, but individual cases of cancer within the same even narrowly defined type are different. Emphasizing these differences is what this is all about.”

Varmus’s first bypass budget, for FY 2012, profiled cancers where important gains had been made: melanoma, glioblastoma, acute myeloid leukemia, neuroblastoma, lung cancer and ovarian cancer. [The document](#), called “Changing the Conversation,” was printed in March 2011.

His second bypass budget, for FY 2013, focused on pancreatic ductal carcinoma, colorectal cancer, b-cell lymphoma, renal cell cancer and GI stromal cancer. [That document](#) was printed in November 2012.

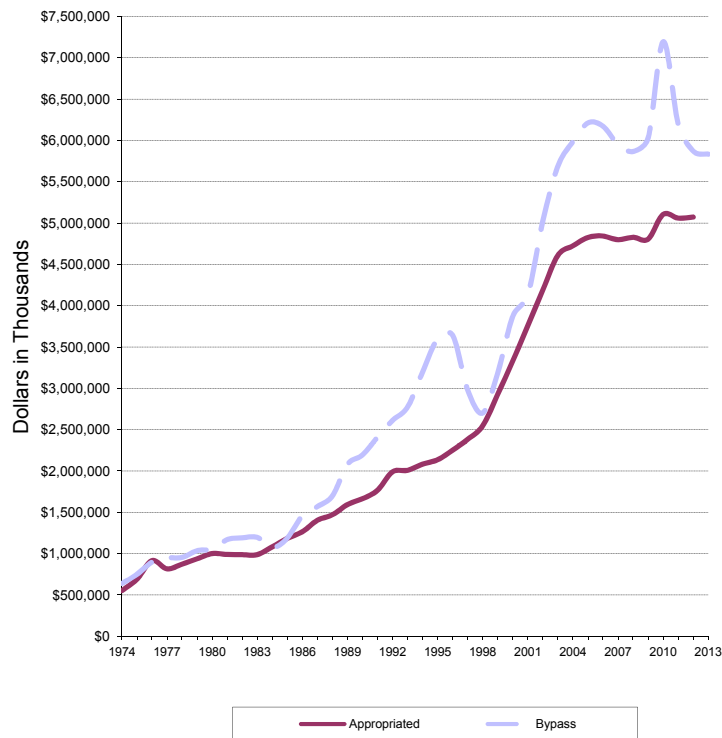
After producing these two volumes, NCI appears to have been hit by writer’s block. Insiders say that postdocs at Harvard were asked to write the cancer profiles component of the FY 2014 bypass budget. Then, NCI staff members reworked their copy. Later, an outside professional writer was hired.

On Feb. 27, 2014, [Varmus gave the National Cancer Advisory Board the following update](#):

“NCI is obliged to provide a bypass budget. Some of you watching this closely may have noted that the FY14 bypass budget proposal has not seen the light of day. Since FY14 has happened, it will be folded into a FY15 budget request and we hope that will be done within the next few weeks, shortly after the president unveils his request for FY15.”

This promise notwithstanding, (The Cancer Letter, [March 7](#)), the two-year bypass budget didn’t materialize.

Bypass Requests and Appropriations of the NCI Fiscal Years 1974-2013



*As of publication, the FY 2014 figures were still under development. When figures are finalized they will be available online at <http://www.cancer.gov>.

The Elements of Style

For years, NCI’s friends on Capitol Hill viewed the bypass budget as an important element of the appropriations process—or at least good fodder for posturing.

Until recently, NCI directors were given separate time slots before appropriators. (Now, Harold Varmus appears as part of the retinue of the NIH director.)

With television cameras rolling and news photographers crouching beneath their lectern, legendary appropriators of yesteryear—Sens. Tom Harkin (D-Iowa) and Arlen Specter (R-Penn., and, later, D-Penn.) and Rep. John Porter (R-Ill.)—challenged NCI directors to provide solemn assurances that their bypass budgets were produced without interference from either the NIH director or HHS officials “downtown.”

Still, the bypass budget was funded fully only on three occasions: once in the mid-seventies, once during the DeVita era, and once during the Klausner-era [doubling of the NIH budget](#). During all other years, NCI directors believed they could spend more money than anyone was willing to provide.

In 2013, the last year with [a bypass budget](#), the

National Cancer Institute

At a Glance (dollars in thousands)

Fiscal Year 2012 Estimate	5,072,183
Current Services Increase	177,227
Subtotal	5,249,410
Fiscal Year 2013 Additional Resources	
Support Individual Investigators	173,000
Genomics	145,600
Clinical Trials	125,000
Translational Sciences	115,000
Provocative Questions	25,000
Subtotal	583,600
Total NCI	\$5,833,010

The Ask: FY 2013 bypass budget argues for a 15 percent boost.

institute had the estimated budget of under \$5.1 billion. Varmus was asking for \$177 million to continue current services and another \$584 million to launch new initiatives.

While Varmus at least initially viewed the bypass budget as an annual report, other NCI directors had different approaches to the document.

Samuel Broder viewed it as a serious scholarly exercise. His final bypass budget, for FY 1997, was the longest on record: 468 pages.

The following year, Klausner slashed the bypass budget down to 78 pages (The Cancer Letter, [March 29, 1996](#)).

Also, Klausner made the bypass budget glossy: “Both wonder and heartache,” the FY 1998 bypass budget began. “The wonder has come both from our success in treating certain tumors and from our astonishing new knowledge of how cancer cells work...The heartache comes from what we haven’t been able to do.”

Klausner’s successor, Andrew von Eschenbach, used the bypass budget to promote his plan to “eliminate suffering and death due to cancer” by the year 2015, seizing on the opportunity to argue that his alliterative formula of the “three Ds”—discovery, development and delivery—would make cancer into a chronic disease.

As von Eschenbach’s benchmark year approaches, suffering and death due to cancer have yet to be eliminated and the NCI bypass budget for FY 2015 remains a work in progress.

Guest Editorial

Vickers: On PSA Skepticism, Both Rational and Irrational

(Continued from page 1)

But there are two types of PSA skeptics. Those in the “fix it” camp, myself included, believe that PSA screening, as it has been implemented in the U.S., may well have done more harm than good, because of indiscriminate screening in older men and overtreatment of low-risk disease.

More rational use of PSA could result in more good than harm.

PSA skeptics in the “forget it” camp believe, conversely, that PSA screening is inherently flawed, will never be of net benefit and should be abandoned.

It turns out that “forget it” skepticism is untenable, and can only be maintained by gross misrepresentation of the evidence. As [a recent example](#), Boniol and colleagues conducted a modeling study in which they report that any beneficial effects of PSA testing on prostate cancer mortality are dramatically attenuated by deaths associated with prostate biopsy.

However, the estimate they use for biopsy mortality, 0.2 percent, is 400-fold higher than the estimate of the largest well-conducted study.

[When we pointed this out](#) to the authors, [they dismissed our concern](#) on the grounds that the study we cited lacked a control group, an unusual position for a study in which every death following biopsy was analyzed and causality assessed. The large U.S. randomized trial on PSA screening [subsequently reported](#) no deaths attributable to biopsy in many thousands of biopsies, and no difference in overall mortality, compared to a control group.

When we wrote to Dr. Boniol asking whether he had changed his mind in the light of the new evidence, he said that he now believed the true mortality rate to be 0.1 percent rather than 0.2 percent.

When asked to justify that number, given zero biopsy related deaths in over 18,000 reviewed cases in two large randomized trials, he declined to provide an explicit answer, stating only that he planned a subsequent modeling paper.

As another example, in [a guest editorial in The Cancer Letter](#), the noted PSA skeptic Richard Ablin wrote:

“One fact remains irrefutable: Only 3 percent of all men diagnosed with prostate cancer will die of the disease; the other 97 percent will die of another cause, such as old age. The lasting damage done to 97 percent

of men in an effort to save 3 percent using a procedure with uncertain benefits is simply unconscionable.”

But Ablin’s “irrefutable” fact is completely erroneous.

About 235,000 U.S. men are [diagnosed with prostate cancer each year](#) with close to 30,000 deaths, a death rate of 12 percent, not 3 percent.

Sometimes skeptics make claims that, while erroneous, require detailed knowledge to understand. A meta-analysis [published in the British Medical Journal](#) concluded that evidence from trials does not support PSA screening, at least partly because the major trial reporting benefit to screening had “substantial methodological limitations.”

The specific claim was that the method of randomization in the trial might have led to selection bias. But anyone with knowledge of how randomization was implemented in the trial would know that this was completely untrue.

When I confronted the senior author on this point, explaining the trial methodology, he accepted that he had misunderstood and that his criticism of the trial had been mistaken. It is hardly a trivial problem when a meta-analysis in one of the top medical journals of the world claims that a major trial supporting PSA is flawed when it is not.

Such gross errors have also crept into decision aids for patients. For instance, [one decision aid](#) states “there are two types of prostate cancer—harmless and dangerous...and doctors can’t tell which one a man has...[moreover] treatment may or may not help men with dangerous prostate cancer.” Such claims can only be seen as bizarre given the [strong prognostic value of Gleason grading](#), the incorporation of risk stratification algorithms [into clinical guidelines](#) and [clear evidence](#) that treatment is of most benefit for patients [with higher risk disease](#).

The apotheosis of “forget it” skepticism [is the USPSTF](#), which concluded that there is “moderate or high *certainty* of no benefit” from prostate cancer screening. Gross errors in the USPSTF report have been [well documented](#), as but one example, they overestimate mortality after radical prostatectomy at least five fold. The chair of the USPSTF [has gone on record](#) to state that PSA “cannot tell the difference between cancers that will and will not affect a man during his natural lifetime.” This clearly [contradicts scientific data](#) that PSA is [a very strong predictor](#) for the risk of aggressive disease, indeed, discrimination is far higher for prostate cancer death than for prostate cancer incidence.

So what is the scientific evidence? In brief, PSA

screening does prevent death from prostate cancer. The only [large randomized trial](#) comparing PSA screening to no screening demonstrated reduced prostate cancer mortality. Prostate cancer mortality in the U.S. has fallen by about 40 percent since the introduction of PSA, an effect difficult to attribute entirely to a cause [other than screening](#). On the other hand, current U.S. practice predominately involves [screening older men](#) who are highly unlikely to die from a screen-detected cancer, widespread overtreatment of low risk disease and, perhaps ironically, [undertreatment of aggressive cancer](#). Moreover, [despite clear data](#) suggesting lower complication rates and better oncologic outcomes in high volume surgeons, most surgeons who treat prostate cancer conduct [three or fewer cases a year](#). What [is needed](#) is radical reform of clinical practice, with more selective screening, biopsy and treatment, and regionalization of care.

Yet tell urologists that biopsy mortality is 400 times greater than it is, overestimate the dangers of surgery five-fold or underestimate the number of men dying from prostate cancer by a factor of four, and no-one is going to listen.

And that is the real tragedy of skeptics like Boniol, Ablin and the USPSTF: their work has the effect of shutting down the conversation, with everyone retreating to their established positions without any change in clinical practice.

Ensuring that prostate cancer screening does no more harm will require abandoning the old sterile, adversarial debates, with grossly erroneous statistics used as weapons, and instead start to focus on best evidence.

The author is an attending research methodologist at the Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center.

Conflicts of Interest: Vickers is a co-inventor of a test, the 4kscore, to inform the decision to conduct a prostate biopsy. He may receive royalties from sales of this test.

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UT Board Announces Support For MD Anderson Tenure System

By Matthew Bin Han Ong

The University of Texas System Board of Regents has—in response to the threat of censure by an external group—voted to continue support of MD Anderson Cancer Center’s seven-year term tenure system.

The board convened a special meeting Oct. 3 to address an investigation of MD Anderson by the American Association of University Professors, an academic freedom and governance group that has criticized the institution’s lack of a lifetime tenure system (The Cancer Letter, [Sept. 19](#)).

The motion, made by Regent Bobby Stillwell and seconded by Regent Wallace Hall, reads:

“In recognition of the unique mission and international leadership of The University of Texas MD Anderson Cancer Center in the fight against cancer, I move that the Board voice strong support for the outstanding work of the institution’s faculty, staff and administration.

“I also move that the Board acknowledge appreciation for the work of the students, residents, and fellows in training and for the trust shown by the patients receiving care at UT MD Anderson.

“I move that the UT System Board of Regents vote to confirm its continued support for the authorization to award 7-year term tenure to faculty at The University of Texas MD Anderson Cancer Center, as the award of term tenure has helped to successfully elevate the institution to international recognition and success in delivering the best possible treatment and prevention against cancer.

“And, I further move that the Board support the position taken by UT MD Anderson in response to the recent challenge to the institution’s implementation of policies approved by the Board.”

UT System officials did not respond to questions from The Cancer Letter.

AAUP’s criticism is secondary to two internal tenure dispute cases. The association’s investigation was triggered by refusal on the part of the MD Anderson administration to provide public justification for denying tenure renewals to two faculty members.

The faculty members in question—Kapil Mehta and Zhengxin Wang—received unanimous votes in favor of renewal from the Faculty Senate Promotions & Tenure Committee, but MD Anderson’s president Ronald DePinho ultimately decided not to extend their tenure (The Cancer Letter, [April 25](#)).

A two-day visit by a four-member independent committee—the first phase of AAUP’s formal investigation of the MD Anderson executive leadership—concluded Sept. 19. If the committee finds MD Anderson at fault, the institution could face censure by the association.

AAUP officials declined to comment on the statement from the Board of Regents.

“The chair of our investigating committee informs us that the investigation went well,” Gregory Scholtz, associate secretary and director of the AAUP Department of Academic Freedom, Tenure and Governance, said to The Cancer Letter. “I cannot predict when the report will be published. Much depends on how long it will take the committee to produce a draft.”

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- ADVERTISEMENT -

Study: Drug Discounts Used For Wealthier Patients In Many 340B-Enrolled Hospitals

By Matthew Bin Han Ong

Hospitals that qualified for the 340B drug pricing program in 2004 or later were more likely to serve wealthier communities with higher rates of health insurance coverage, according to a study published Oct. 6 in the journal *Health Affairs*.

The primary purpose of the 340B program—established by Congress in 1992—was to provide significantly discounted outpatient drugs to low-income and uninsured patients.

“The 340B program is being converted from one that serves vulnerable patient populations to one that enriches hospitals and their affiliated clinics,” wrote study authors Rena Conti and Peter Bach. “These results suggest that the expansions among 340B DSH hospitals run counter to the program’s original intention.”

Conti is an assistant professor of health policy and economics in the Departments of Pediatrics and Health Studies at the University of Chicago, and Bach is a pulmonologist, health systems researcher, and director of the Center for Health Policy and Outcomes at Memorial Sloan Kettering Cancer Center.

Conti and Bach [matched data for 960 hospitals](#) and 3,964 affiliated clinics registered with the 340B program in 2012 with the socioeconomic data of their communities from the U.S. Census Bureau.

“Beginning around 2004, newly registered 340B DSH hospitals have tended to be in higher-income communities, compared to hospitals that joined the 340B program earlier,” the authors wrote. “Other recent analyses have suggested that hospitals receiving DSH payments are shifting some specialty care from the inpatient to the outpatient setting, where drug discounts gained from participation in the 340B program may generate increased profits.”

The 340B program has grown dramatically in recent years, increasing from 591 participating hospitals in 2005 to 16,572 covered entities in 2011, according to a policy statement by the American Society of Clinical Oncology.

About a third of the country’s non-federal hospitals qualify for the program, and 340B now accounts for about 2 percent of the \$325 billion U.S. retail spending on prescription drugs.

There are no regulations directing hospitals and clinics as to how they should use 340B discounts—raising concerns among policymakers, payers, manufacturers,

and healthcare providers about whether the program is serving its original purpose of incentivizing healthcare for uninsured, underinsured and Medicaid patients.

According to critics, the 340B program is poorly defined, and is increasingly abused by entities that don’t need help from the government—leading to calls by industry to re-evaluate and reform the program (*The Cancer Letter*, [June 13](#)).

“More broadly, our findings suggest that gaining access to 340B drug discounts may act as one motivating rationale for the affiliations and mergers among hospitals and outpatient physician practices that are becoming increasingly common in the United States,” Conti and Bach wrote.

According to the authors, hospitals that gain access to 340B discounts improve payer mix, avoid competition from specialist-owned ambulatory surgery centers, increase leverage with health plans, and reduce physicians’ financial risks.

“In this context, the potential for profit derived from 340B drug purchases should be most concentrated among specialty outpatient practices—including those in oncology, neurology, and ophthalmology—that heavily use costly prescription drugs to care for their patients,” Conti and Bach wrote. “It is beyond the scope of our analysis to test this hypothesis empirically.

“However, we surveyed the trade literature on documented shifts in care and in merger and acquisition activities among outpatient specialty care providers,” they wrote. “We found evidence that supported the hypothesis for oncologists.”

According to a 2012 report by Elaine Towle et al., the share of physician-owned private practices in oncology declined 10 percentage points between 2010 and 2011, while merger and acquisition activities between community oncology practices and hospitals increased substantially.

Conti and Bach called for more studies to systematically assess the impact that the expansion of 340B-qualified hospitals may be having on medical care spending, access, and quality.

“In previous work we argued that these expansions are likely raising chemotherapy spending and prices for patients and insurers, and providing limited gain to the poor and uninsured,” they wrote. “The pursuit of timely, transparent, and national assessments of whether and how the activities of 340B hospitals and their affiliated clinics are benefiting the populations originally targeted by the Veterans Health Care Act is an important policy goal.”

Adam Fein, an expert on pharmaceutical economics and the drug distribution system, lauded the study.

“Conti and Bach have published one of the first peer-reviewed examinations of the 340B program’s many problems,” Fein, president of Pembroke Consulting and author of the Drug Channel’s blog, said to *The Cancer Letter*. “The results support the more informal observations from industry observers.

“Unfortunately, Conti and Bach are now being attacked by the program’s hospital advocates, who oppose modernizing and updating this important program.”

Trade Groups Respond

Safety Net Hospitals for Pharmaceutical Access, a trade group for 340B-enrolled hospitals said Conti and Bach neglected to mention that 340B DSH hospitals provide twice as much uncompensated care. <http://www.snhpa.org/news/snhpa-responds-to-health-affairs-article-on-340b>

“First, Conti and Bach misconstrue the 340B program’s intent,” SNHPA, which represents over 1,000 hospitals, said in a statement. “340B is not—and never was—a direct assistance program for the poor.

“Congress specifically designed the program to help 340B providers ‘stretch their scarce resources’ and reach more patients.

“The fact remains that 340B DSH hospitals support heavy caseloads of Medicaid and low-income Medicare patients—regardless of where their outpatient clinics are located. Savings from the program are essential in helping [sic] all safety-net hospitals treat vulnerable populations.”

The American Hospital Association criticized Conti’s and Bach’s findings.

“The uncompensated care provided by hospitals in the 340B program represented 62 percent of all uncompensated care provided by America’s hospitals in 2012,” AHA [said on its blog](#). “This report does a real disservice to this important program that has a proven track record in helping patients get the medicines they need.”

PhRMA Files Lawsuit on Orphan Drugs

In related news, the Pharmaceutical Research and Manufacturers of America, a trade group representing U.S. pharmaceutical research and biotechnology companies, has filed a lawsuit against HHS “to challenge its second attempt to issue a rule conflicting with the plain language of the statute.”

The complaint is posted [on *The Cancer Letter* website](#).

Over the past several years, many key players in oncology have been questioning the program’s

expansion and its eligibility criteria. All of these disparate interests—those who love 340B and those who hate it—have been waiting for the federal Health Resources and Services Administration to issue a “mega-rule,” which is expected to define who should qualify for 340B discounts.

The mega-rule appears to have been postponed, thanks to a ruling by a judge at the Federal District Court of the District of Columbia.

Judge Rudolph Contreras challenged HRSA’s authority to engage in legislative rulemaking on May 23, invalidating the agency’s attempt to expand the discount program to include uses of orphan drugs.

However, the agency defended its position on the Affordable Care Act orphan drug exclusion in July, and labeled its rule “interpretive.” (*The Cancer Letter*, [June 20](#).)

HRSA released a statement on its website June 18, reaffirming its original interpretation, regardless of the court ruling:

“The Court did not invalidate HRSA’s interpretation of the statute. HHS/HRSA continues to stand by the interpretation described in its published final rule, which allows the 340B covered entities affected by the orphan drug exclusion to purchase orphan drugs at 340B prices when orphan drugs are used for any indication other than treating the rare disease or condition for which the drug received an orphan designation.”

Mit Spears, executive vice president and general counsel for PhRMA, said the ACA exempts manufacturers from having to provide 340B discounts on orphan drugs to newly eligible providers.

“At issue is the HRSA’s interpretation of the 340B orphan drug exemption, enacted as part of the Affordable Care Act,” Spears said in a statement. “While we value the hard work and efforts of all agencies, it is important federal agencies recognize and work within the bounds set by Congress.”

SNHPA condemned PhRMA’s move, calling it an attempt to “quash” a federal regulation that significantly lowers the cost of orphan drugs for hospitals and patients.

“Once again, Big Pharma is trying to increase its prices at the expense of rural and cancer hospitals and their patients,” said Ted Slafsky, SNHPA president and CEO. “These providers depend on 340B savings to serve needy patients and, in many cases, to keep their doors open.”

In Brief

Peter Boyle Receives ESMO Lifetime Achievement Award

(Continued from page 1)

Carsten Bokemeyer will receive the **ESMO Award** for his commitment to accelerate the transition of cancer discovery into real benefit.

Heikki Joensuu was acknowledged with the **Hamilton Fairley Award** for his significant contribution to improve breast cancer and GIST diagnostics and care.

Boyle became the first non-medical oncologist elected to full membership of ESMO in 2006. He is currently a professor of global public health at the University of Strathclyde and holds honorary or visiting professorships at Glasgow and Yale Universities.

Boyle is founder and president of the World Prevention Alliance and inaugural director of the University of Strathclyde Institute of Global Public Health at iPRI. He led the EUROCAN+PLUS project for the European Parliament which developed priorities for coordination of cancer research in Europe and was Editor of the World Cancer Report 2008 and the State of Oncology 2013 which highlighted the growing global cancer crisis.

Bokemeyer's discoveries include identifying the early stages of malignant germ cell transformation and the mechanisms of resistance of germ cell tumors to chemotherapy. He has also developed therapeutic concepts with cytostatic drugs and immunotherapy in solid tumors. He is currently director of the University Cancer Center Hamburg.

In 2000, Joensuu and colleagues discovered that imatinib was effective for most advanced GIST and, in 2011, he found that as adjuvant treatment it improved recurrence-free survival and possibly overall survival.

Joensuu became professor of oncology at the University of Helsinki in 1994 at the age of 37, and acted as medical director of the Department of Oncology at Helsinki University Central Hospital from 1995 to 2009. He is currently an academy professor at the University of Helsinki and research director at the Helsinki Comprehensive Cancer Centre.

PHOENIX CHILDREN'S HOSPITAL and **Patrick Soon-Shiong** formed **The Chan Soon-Shiong Children's Precision Medicine Institute**.

The institute will use genomic and proteomic technology to identify precision diagnoses and treatments for young patients.

Soon-Shiong is the founder of Nantworks, which

explores genomic and proteomic analysis studies to translate diagnoses. To date, his efforts have been focused on the adult population.

Phoenix Children's will house a dedicated supercomputer for genomic sequencing and analysis. Patients will be able to undergo full genome sequencing and proteomics analysis in seven days. A bank of pediatric patient data is planned, via a consortium of children's hospitals led by Phoenix Children's.

C. PARKER GIBBS Jr. was appointed deputy director of medical affairs for the **University of Florida Health Cancer Center**.

Gibbs also serves as the Eugene L. Jewett professor of orthopaedic surgery and chief of the UF College of Medicine division of musculoskeletal oncology.

He will also serve as chairman for UF Health's Cancer Interdisciplinary Clinical and Academic Program, which sets standards for cancer care across all of UF Health's campuses in Gainesville, Jacksonville and Orlando. He also will oversee the integration of cancer research in UF Health's clinical enterprises in support of the UF Health Cancer Center's quest for an NCI cancer center designation.

Gibbs is considered an expert at limb-salvage surgery to treat bone and soft tissue sarcomas. He also directs the NIH-funded Musculoskeletal Oncology and Stem Cell Laboratory at the University of Florida.

He will report to senior UF Health administrators including Paul Okunieff, director of the UF Health Cancer Center; Edward Jimenez, interim chief executive officer for UF Health Shands Hospital; and Timothy Flynn, senior associate dean for clinical affairs in the UF College of Medicine and chief medical officer for Shands Hospital.

MD ANDERSON CANCER CENTER'S Sheikh Khalifa Bin Zayed Al Nahyan Institute for Personalized Cancer Therapy launched a fellowship program to advance personalized cancer treatments, and named two scholars and four fellows.

The Khalifa Scholars were selected from faculty level physicians and researchers at MD Anderson and will receive one to two years' salary to support independent research projects. Khalifa Fellows were selected from among trainees and junior faculty; each recipient will receive support to subsidize costs associated with a specific project in personalized cancer therapy.

The two inaugural scholars are: **Lauren Byers**, assistant professor in Thoracic/Head and Neck Medical

Oncology; and **Humaid Al-Shamsi**, assistant professor in Gastrointestinal Medical Oncology.

The four fellows are: **Jianjun Gao**, assistant professor in Genitourinary Medical Oncology; **Aubrey Carhill**, assistant professor in Endocrine Neoplasia and Hormonal Disorders; **Mitchell Frederick**, assistant professor in Head and Neck Surgery; and **Ana Beatriz Korngold**, postdoctoral fellow in Pediatrics Research.

The program was established as part of a \$150 million grant by the Khalifa Bin Zayed Al Nahyan Foundation in 2011.

The foundation's gift is also funding the construction of the Sheikh Zayed Bin Sultan Al Nahyan Building for Personalized Cancer Care, a 600,000-square-foot building nearing completion on approximately five acres of MD Anderson's main campus.

The Zayed Building will integrate delivery of basic and clinical research, and will house the Khalifa Institute for Personalized Cancer Therapy and the Sheikh Ahmed Bin Zayed Al Nahyan Center for Pancreatic Cancer Research.

MD ANDERSON CANCER CENTER and **VolitionRx** Limited announced a study collaboration within the center's Department of Genitourinary Medical Oncology. The study will examine the competency of VolitionRx NuQ assays to distinguish anaplastic prostate cancer from typical castration-resistant prostate cancer.

The retrospective study will include samples obtained from two previous clinical trials, one that selected men with CRPC who met one of seven anaplastic clinical criteria, and a second that included unselected men with non-anaplastic CRPC. The samples will be assessed using VolitionRx's assays for specific histone modifications of circulating nucleosomes.

Patterns and changes in histone modifications are used to indicate certain cancers and this method will assess the competency of VolitionRx's assays to identify anaplastic CRPC.

THE OHIO STATE UNIVERSITY, Cardinal Health and **State of Ohio Third Frontier Commission** completed a five-year-long project to create a \$13 million molecular imaging pharmaceuticals center focused imaging agents.

The 27,000-square-foot facility, called the Translational Research Center for Molecular Imaging Pharmaceuticals at the Wright Center of Innovation in Biomedical Imaging, will combine the Wright Center's research capabilities with Cardinal Health's

developmental, manufacturing and commercialization experience with molecular imaging agents. An endowed faculty position as the Ohio Molecular Imaging Pharmaceutical Scholar have been added to the faculty and staff of Ohio State's Department of Radiology.

ANDREW BRENNER received a \$1.62 million, four-year orphan disease grant from **FDA** to continue to study how the drug TH-302 may treat glioblastoma.

Brenner is a neuro-oncologist at the Cancer Therapy & Research Center. The grant will fund phase II clinical trials and supporting studies to try to predict patient benefit.

"We've seen preliminary evidence of benefit in patients with glioblastoma whose tumors have grown despite the use of Avastin. By that stage it is a horrible disease with a median survival of about four months," said Brenner.

Glioblastoma is considered an orphan disease by FDA. This study combines Avastin with TH-302, which attacks cells in a low-oxygen environment. Threshold Pharmaceuticals, the company that developed the drug, is supplying it for the clinical trial. Dana-Farber Cancer Institute and UT Austin will also participate in the study.

Drugs and Targets

FDA Approves Oral Akynzeo For Treatment-Related Nausea

FDA approved Akynzeo (netupitant and palonosetron) to treat nausea and vomiting in patients undergoing cancer chemotherapy.

Akynzeo is a fixed combination capsule comprised of two drugs. Oral palonosetron, approved in 2008, prevents nausea and vomiting during the acute phase after the start of cancer chemotherapy. Netupitant, a new drug, prevents nausea and vomiting during both the acute phase and delayed phase after the start of cancer chemotherapy.

Akynzeo's effectiveness was established in two clinical trials of 1,720 participants receiving cancer chemotherapy. Participants were randomly assigned to receive Akynzeo or oral palonosetron. The trials were designed to measure whether the study drugs prevented any vomiting episodes in the acute, delayed and overall phases after the start of cancer chemotherapy.

Results of the first trial showed that 98.5 percent, 90.4 percent and 89.6 percent of Akynzeo-treated participants did not experience any vomiting or require rescue medication for nausea during the acute, delayed and overall phases, respectively.

In contrast, 89.7 percent, 80.1 percent and 76.5 percent of participants treated with oral palonosetron did not experience any vomiting or require rescue medication for nausea during the acute, delayed and overall phases, respectively. The second trial showed similar results.

Akynzeo is distributed and marketed by Eisai Inc. under license from Switzerland-based Helsinn Healthcare S.A.

FDA granted Orphan Drug Designation for DNX-2401, a conditionally-replicative oncolytic adenovirus for malignant glioma. Under the designation, companies are provided with development and commercial incentives for designated compounds. DNX-2401 has already been granted fast track status and is currently being evaluated in clinical studies in the U.S. and Europe.

Oncolytic virus therapy is based on the concept of using live viruses to selectively infect and replicate in cancer cells, with minimal destruction of normal tissue. Moreover, there is evidence for a long-lasting anti-glioma immune effect that can lead to durable tumor destruction and long-term survival in some patients.

CARIS LIFE SCIENCES launched a pilot program with the **U.K.'s National Health Service** that will offer patients with ovarian and rare gynecological cancers access to comprehensive tumor profiling.

Caris Molecular Intelligence will be made available to approximately 120 women for the first time in England. NHS England will support this evaluation through the Regional Innovation Fund, which aims to facilitate rapid evaluation of healthcare technologies. Caris Molecular Intelligence is currently available privately in the U.K. and via this pilot program.

The pilot will include cancer patients at Leeds St James' Hospital, Bradford Royal Infirmary, Huddersfield Royal Infirmary and Airedale General Hospital. The data generated through the pilot will be independently evaluated by the NIHR Diagnostics Evidence Cooperative at Leeds.

THE MAYO CLINIC Center for Individualized Medicine has partnered with **Second Genome Inc.** to develop therapeutic products for multiple disease indications, starting with inflammatory bowel disease, metabolic disorders, and colorectal cancer.

"The microbiome is an important area of medical research for Mayo Clinic, and this collaboration represents a broad and significant effort in our

attempt to develop therapeutics targeting microbiome-mediated pathways," says Heidi Nelson, director of the Microbiome Program in the Mayo Clinic center.

Second Genome will identify up to eight clinical indications where the microbiome has a potential role in disease and will collaborate on microbiome research with Mayo Clinic investigators who specialize in each of the designated disease areas. Mayo Clinic will provide human clinical samples from patients in targeted disease areas, and Second Genome will use its proprietary microbiome discovery platform to identify biological pathways implicated in disease.

BRISTOL-MYERS SQUIBB and **MD Anderson Cancer Center** will collaborate to evaluate multiple immunotherapies, including Opdivo (nivolumab), Yervoy (ipilimumab) and three early-stage clinical immuno-oncology assets from Bristol-Myers Squibb, as potential treatment options for acute and chronic leukemia and other hematologic malignancies.

The aim of the agreement is to focus numerous clinical trials using multiple agents, in mono and combination regimens, on a specific disease target.

The collaboration will launch up to 10 phase I and II clinical trials conducted by MD Anderson, focused on evaluating investigational immune-based approaches for acute myeloid leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia, myelodysplastic syndrome and myelofibrosis. Additional studies will be determined by the collaboration at a later date.

Opdivo is an investigational PD-1 immune checkpoint inhibitor currently approved in Japan for the treatment of patients with unresectable melanoma, and Yervoy is a CTLA-4 immune checkpoint inhibitor approved in the U.S. and more than 40 countries for patients with unresectable or metastatic melanoma.

Pharmaceutical research companies in the U.S. are currently developing nearly 800 new medicines and vaccines for cancer, according to **Pharmaceutical Research and Manufacturers of America**.

[In its report](#), the organization also details how researchers are identifying ways to use existing medicines, either alone or in combination with other therapies, to treat various types of cancers more effectively than current standards of care.

Of the 771 medicines and vaccines either in clinical trials or awaiting review by FDA, there are 98 for lung cancer, 87 for leukemia, 78 for lymphoma, 73 for breast cancer, 56 for skin cancer and 48 for ovarian cancer.