A Bill to 'Eliminate Prostate Cancer Misdiagnosis'

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Larry Bucshon, MD, a cardiac surgeon and US Congressman from Indiana (R), wants to put an end to prostate biopsy results that are misdiagnosed as positive for cancer.

More than 1 million prostate biopsies are performed each year in the United States, and most are triggered by a blood test with an elevated prostate-specific antigen (PSA) level, which may indicate the presence of cancer.

A small percentage of the results are false positive, in which the biopsy results indicate cancer but are wrong because of human error — namely, specimen mix-ups or cross-contamination with other tissue. These are known as specimen provenance complications.

"It is estimated that 1.3% of patients are erroneously told they have prostate cancer when they do not," Dr Bucshon told *Medscape Medical News* in an email, referring to the frequency of specimen provenance complications among positive biopsies.

As a remedy for these mix-ups, Dr Bucshon is sponsoring the Prostate Cancer Misdiagnosis Elimination Act of 2017, which calls for Medicare to reimburse labs $200 for DNA testing that compares and matches the patient's biopsy tissue with cells from the inside the cheek that are taken with a cotton swab to ensure both came from the same person.

Medicare paid for 148,000 prostate biopsies in 2016, but it does not pay for DNA tests to double-check the identity of the biopsy.

Experts agree that DNA testing would reduce troublesome specimen complications.

"It's a fundamental way to assure that the biopsy material that shows cancer is from the same patient who gave the cheek swab," said Thomas Wheeler, MD, who is chair of the Department of Pathology and Immunology at Baylor College of Medicine in Houston, Texas, and was asked to comment.

But there is a caveat, said Dr Wheeler: "The result is going to be 100% accurate — but only if both the biopsy tissue and the cheek swab are from that patient."

Genetics labs can mix up samples, too, he added. In other words, the potential for human error exists in every lab.

Furthermore, DNA testing will not eliminate prostate cancer misdiagnoses because the problem is bigger than specimen complications, Dr Wheeler told *Medscape Medical News* in an interview.

Another problem that is "at least as significant," said Dr Wheeler, is when pathologists wrongly diagnose cancer, often because "the tissue mimics cancer." The medical literature indicates that pathologists' interpretive errors can occur at rates as high as 2%, he added.

If legislators want to reduce prostate cancer misdiagnoses, then they should consider further investing in second opinions, argued Dr Wheeler. "Getting a second opinion by an expert pathologist on everything that is called cancer would probably do as much or more good to correct overtreating cancer than doing some kind of identity test."
Medicare currently will pay for second opinions, and this costs "a lot less than $200 [the proposed reimbursement] for the DNA test," he added.

Deepak Kapoor, MD, a urologist, already uses DNA testing. He is chairman of Integrated Medical Professionals in the metropolitan New York City area, which is the largest urology group practice in the United States.

He emphasized that the DNA test ensures that a prostate cancer diagnosis is given to the correct person.

"These errors are frighteningly common," testified Dr Kapoor before the US House of Representatives' Committee on Energy and Commerce, which conducted a hearing about the bill in July. He said provenance errors (ie, switching and contamination) occurred at a rate of 1.28% among all prostate biopsy specimens that are positive for cancer, echoing Dr Bucshon.

The DNA test "definitively rules out" these errors, said Dr Kapoor, who is also a clinical professor of medicine at the Icahn School of Medicine at Mt Sinai Hospital in New York City.

He added that 60,000 DNA tests are used on biopsied prostate tissue each year in the United States.

The value of DNA testing for prostate cancer is partly based on its projected cost-effectiveness, according to its advocates.

Perhaps surprisingly, Dr Bucshon's bill would decrease Medicare's direct net spending — by more than $7 million from 2018 to 2027, according to the Congressional Budget Office (CBO). That's because the cost of the test for tens of thousands of men annually (estimated at $46 million over 10 years) would be recouped by the savings associated with avoiding treatment of men who did not have prostate cancer.

But Baylor's Dr Wheeler has doubts about that assessment.

While acknowledging that DNA testing would correct some cases of specimen mix-ups, he points out that the total number of prostate cancers does not change. Thus, there is no reduction in savings from treatment.

Dr Wheeler also believes the assumed rate of errors in the CBO's calculations is questionable. They estimated that 1.5% of all biopsy results among Medicare beneficiaries were false positive because of specimen mix-ups or contamination. Both the 1.5% and 1.3% rates (cited by Dr Bucshon) are too high, he argued.

Medscape Medical News asked the American Urological Association (AUA), which has endorsed the bill in a letter to Congress and cited the 1.3% rate, what the source of the number was, but there was no answer at the time this article was published.

In a 2013 study, researchers prospectively looked at a databank of 13,000 prostate biopsy specimens obtained at 54 labs in the United States. The combined rate of specimen mix-ups and cross-contamination errors was 0.93%. In other words, it was less than 1% (*Am J Clin Pathol.* 2013;139:93-100).

Another study using data from the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) prostate cancer risk reduction trial, which required biopsies from all participants, also indicated a combined rate of less than 1% (*J Clin Oncol.* 2011; 29:1744-1749).

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Using the 1.5% rate of specimen provenance complications, the CBO estimates that the number of Medicare beneficiaries who would not be wrongly treated for prostate cancer thanks to DNA testing would be 60 in 2019 and rise to 450 in 2027, as the test becomes increasingly used.

Dr Wheeler believes that DNA testing has utility, but perhaps not en masse via Medicare.

He recalled a case at his institution, where a patient was "convinced" he did not have prostate cancer despite biopsy findings. "He refused to believe it. The DNA test is very useful in such circumstances because it provides an element of reassurance that the cancer sample is yours."

Other pathologists say that DNA testing has evolved and improved in recent years, which has led to its use beyond specimen mix-up detective work.

"Testing is now performed in the absence of any direct indication that a specimen mix-up or contamination has occurred, namely when pathologic findings are unexpected or the clinical setting is atypical," write the authors of a 2015 review paper, led by John Pfeifer, MD, professor of pathology and immunology at Washington University in St Louis, Missouri (*Am J Clin Pathol.* 20115;135:132-138).

In a recent *New York Times* article, Dr Pfeifer advocated for DNA testing of all cancer biopsy specimens. "All the process improvement in the world does not get rid of human errors," he said. "Millions get biopsies every year. Is society going to say, 'Yeah, mistakes happen but we're not going to look for them?'"

Dr Wheeler argued that pathologists have put many safeguards in place and that errors, especially in prostate cancer, are rare.

He finds one innovation at Baylor to be especially helpful: putting the same colored ink on the slides of all 12 prostate tissue cores from a single patient. At the same time, the pathologists will indicate that specific color in the case description. "When I look at a slide, I make sure the colors match up," he said.

Medicare Has Previously Rejected Reimbursement

In their letter to Congress this past July, the AUA and its co-signers, such as the Men's Health Network and Prostate Health Education Network, urged Congress to pass the Prostate Cancer Misdiagnosis Elimination Act of 2017, saying that the DNA Specimen Provenance Assay was "standard of care" with "widespread adoption."
However, the National Comprehensive Cancer Network (NCCN) clinical practice guidelines for the diagnosis and treatment of prostate cancer do not mention the DNA Specimen Provenance Assay or any other type of DNA testing. Nor do the AUA's clinical guidelines for the early detection of prostate cancer.

Furthermore, in 2013, the Centers for Medicare & Medicaid ruled that this DNA testing does not explicitly diagnose or treat disease and therefore did not qualify as a Medicare benefit.

The AUA and its fellow letter writers disagree with this interpretation. "To deprive Medicare beneficiaries of access to an important test which eliminated medical errors is contrary to the best interests of patients," reads the letter.

However, the US courts later agreed with Medicare.

In 2015, a US judge in Indiana found that the DNA Specimen Provenance Assay from Strand Diagnostics was not covered by Medicare because it was not "reasonable and necessary for diagnosis or treatment" of prostate cancer, as required by Medicare, according to a news report.

Despite the setbacks with Medicare and US courts in recent years, Strand Diagnostics offers their *Know Error* DNA Specimen Provenance Assay kit online directly to men with prostate cancer diagnoses for $299.

Strand Diagnostics is also the sole company lobbying for the Prostate Cancer Misdiagnosis Elimination Act of 2017.

The company, which is headquartered in Indianapolis — about 165 miles away from Dr Bucshon's home in Newburgh, Indiana — spent $40,000 from April through September of this year on lobbying members of Congress about the bill, according to OpenSecrets.org, the website of the Center for Responsive Politics.

The bill is still in the legislative process, having passed unanimously through the Energy and Commerce Committee earlier this year, but still needs a "path" to full passage in the House of Representatives, said Dr Bucshon.
The bill has bipartisan support, with additional sponsors from both the Republican and Democratic parties.

However, the bill's passage in the House and then the Senate is not guaranteed. In fact, a similar bill was introduced in the House in 2016 by Dr Bucshon. Thus, the Prostate Cancer Misdiagnosis Elimination Act of 2017 is at least a second legislative go-round for the idea.

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