

Double whammy is Exactly the wrong prescription for Cologuard



[Jacob Plieth](#)

Cologuard, Exact Sciences' stool-based colorectal cancer diagnostic, was always going to walk a fine line between price and accuracy. And its feet have now slipped off the tightrope as a US expert panel decided that it was not, after all, good enough to be a recommended test.

The company was doubly unlucky for the spotlight to fall on Cologuard's cost effectiveness just when healthcare pricing is entering the political debate and causing panic after four years of a bull market. Exact's stock crashed by 46% yesterday, putting it 67% off its June peak, and back to where it had stood in 2013.

The problem was revealed with the publication of draft colorectal cancer screening guidance by the US Preventive Services Task Force (USPSTF). This unexpectedly relegated Cologuard – an assay applied to a stool sample that a patient has mailed through the post – to a mere “alternative screening test”, which private payers might not be mandated to cover.

Under the USPSTF's previous 2008 recommendations Cologuard had stood in a separate category along with computed tomographic colonography. Instead, these two approaches are now alternatives “in select clinical circumstances that the USPSTF did not define”, Exact's chief executive, Kevin Conroy, said on a call yesterday.

The USPSTF's main category of recommended tests for people aged 50 to 75 includes faecal immunochemical testing (FIT) as well as 10-yearly colonoscopy, the current gold standard.

Sensitivity vs specificity

Colorectal cancer diagnostics prove themselves in terms of sensitivity – ability to pick out actual cancers – and specificity, or the accuracy in ruling out cancer.

Pricing also plays a key part in terms of real-world pharmacoeconomics. Thus it is key that expensive and invasive colonoscopy is super-accurate, while FIT is notoriously less so, but – crucially – it is much cheaper.

The contention with Cologuard is that its specificity is too low. Put simply, Cologuard identifies too many negatives as positives, and the risk is that its widespread use would drive many of these false positive patients to undergo unnecessary confirmatory colonoscopy, driving up healthcare costs.

Still, compliance with routine colonoscopy is low, at roughly 60% in the US, and one economic case for Cologuard, hardly a cheap test, was that it could increase compliance; at least this was the argument once Exact abandoned the idea of pitching Cologuard as an alternative to colonoscopy.

Until now all seemed to be going well as Cologuard secured FDA approval and reimbursement from the Centers for Medicare & Medicare Services ([Exact Sciences set for US reimbursement after Cologuard approved, August 12, 2014](#)). Exact says its 2014 launch has been strong, with over 100,000 tests ordered by 20,000 doctors.

Arch rival

If the USPSTF has thrown a serious spanner in the works Exact's arch rival, the struggling German group Epigenomics, can hardly celebrate either.

Epigenomics' blood-based colorectal cancer test, Epi Procolon, might be cheaper and more convenient than Cologuard, but its specificity and sensitivity are worse, and it has been knocked back by the US regulator. The pharmacoeconomic argument is far from proven for either assay.

Mr Conroy said Exact would continue to push Cologuard, arguing for raising US colonoscopy compliance and modelling the theoretical life years saved with its assay. There is precedent for the USPSTF changing its mind between public consultation and final recommendation, which happened with [hepatitis C screening guidelines](#) two years ago.

Exact's strongest case might be that the USPSTF cites a false positive rate of 16% annually with Cologuard, which the company says is erroneous because it considers all polyps and advanced adenomas as false positives; the correct number is 10% every three years, says Mr Conroy.

Still, in a population with colorectal cancer incidence of 0.5% a 10% false positive rate still means that, for every 100 samples Cologuard identifies as positive, 95 will turn out incorrect on confirmatory colonoscopy.

At a time when healthcare costs are under the spotlight this will continue to be a tough issue to overcome.

To contact the writer of this story email Jacob Plieth in London at jacobp@epvantage.com or follow [@JacobPlieth](https://twitter.com/JacobPlieth) on Twitter

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