

# Quantity and quality in medicine: lessons from the humble Pap



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It has been almost 75 years since Drs George N. Papanicolaou and Andrew A. Marchetti<sup>1</sup> published in the pages of the *American Journal of Obstetrics and Gynecology* their seminal paper on the use of endocervical and endometrial smears for the detection of uterine cancer. Dr Papanicolaou's pioneering work was initially rejected by the establishment, as many revolutionary ideas are.<sup>2</sup> It was not until over a decade after the appearance of the initial reports that the promise of cervical cytology for the detection and, later on, the prevention of cervical cancer received wide recognition. In the time since its introduction into clinical practice in the 1950s, the "Pap smear" has been responsible for a phenomenal improvement in health outcomes. Cervical cancer was once the most important cause of cancer deaths among US women, with an incidence of close to 40 cases per 100,000 in 1958.<sup>3</sup> The Centers for Disease Control and Prevention reports that by 2012 (the latest year for which data are available), the incidence had dropped to about 7.4 per 100,000, ranking it 14th among cancers in women.<sup>4</sup> The majority of cervical cancers worldwide now occur in those who have never been screened or are screened inadequately.<sup>5,6</sup>

These statistics are not on the tip of my patients' tongues, but they get the gist. It is therefore no surprise that some feel uneasy when I inform them that they do not need an annual Pap.

There is an important lesson here for the practice of medicine: sometimes when something is really good, the less you have of it the better.

How can that be? How can less information be better than more?

In statistical terms, overtesting does not increase sensitivity (the probability of detecting a disorder if it is present), but it does increase the number of false positives (abnormal test results when there is in fact no disorder). This effect is magnified for conditions like cervical cancer, where the prevalence of disease is low. And there are some real drawbacks to false-positive results, among which are the generation of unnecessary anxiety and expense, and the

performance of excisional or destructive procedures on the cervix. Such procedures are associated with cervical incompetence and pregnancy loss or preterm delivery, sequelae that fortunately are uncommon. The same drawbacks exist even for true-positive Pap smears, as most mild abnormalities will regress spontaneously without treatment. It is best not to know of these mild abnormalities, thus sparing doctors from the almost irresistible urge to fix what ain't broke.

Current recommended testing intervals were based on concerns for the consequences of false-positive diagnoses, along with modeling that demonstrated miniscule or no improvements in rates of detection and/or prevention of cancer or high-order dysplasia compared to annual screening.<sup>7</sup> It takes decades for most forms of cervical cancer to develop from the precursor abnormalities the Pap smear is designed to identify. Though the optimal testing interval can and has been debated,<sup>8</sup> it is clear that for the vast majority of women, annual screening, particularly screening that combines liquid-based cytology with human papillomavirus testing, is simply too frequent.

I find that patients often confuse the ordering of tests with quality and caring. My own 83-year-old mother, defying me all the way, heaped praise on her doctor for ordering an unnecessary \$7000 test (positron emission tomography [PET] scan) as a follow-up to an unnecessary \$1000 test (computed tomography scan), which was a follow-up to an unnecessary \$600 test (ultrasound), as follow-up to an unnecessary \$150 test (Ca-125), ordered after she acknowledged in answer to a question that she had some bloating, for which the most appropriate response would have been some words of reassurance (\$0) and an over-the-counter laxative (\$6.99 for 6 doses). (Medicare paid for everything except the laxative. And you wonder why American health care is so expensive?).

"Congratulations!" her physician announced cheerfully over the phone from Florida. "Mom's PET scan was negative!" I shared his enthusiasm, but it was less for the I-told-him-so negative PET scan than for the cessation in the onslaught of medical care and my mother's narrow escape from the unintended consequences of invasive diagnostic testing, medical treatment, and surgery.

Assessment of the utility of a medical test is a complex process in which the performance characteristics of the test and the natural history of the disease are only two relevant factors. In the end the facts must be subjected to a value judgment about risks and benefits made by human beings. In the case of the Pap smear this calculus is relatively easy. With mammography it is less so. When in 2009 the US Preventive Services Task Force panel of experts recommended after a

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Received June 8, 2016; accepted June 22, 2016.

The author reports no conflict of interest.

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0002-9378/free

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<http://dx.doi.org/10.1016/j.ajog.2016.06.042>

scholarly review of the scientific literature to start screening mammography for average-risk women at age 50 years (instead of 40 years) and to perform the test only every 2 years (instead of annually) it caused an uproar. The ensuing debate tended to minimize the fact that what is really needed to improve breast health is not more mammography but a test that is better than mammography.

Some experts have predicted that the Pap smear is approaching the end of its natural life span and may be replaced in coming years by molecular testing for human papillomavirus (the virus that causes the majority of cervical cancers).<sup>9</sup> Shed no tears for Dr Papanicolaou if that occurs. His name is etched in history for preventing the deaths of millions of women with his beautifully simple intervention.

And what of the annual visit at which I inform my patients that they do not need an annual Pap? Should it continue to exist or be thrown out as medical waste? Ah, but that is a matter for a different time. ■

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