

Correspondance

The merits of new alternatives to the Papanicolaou test

The claim by Eduardo Franco and colleagues that "nearly half of specimens [cervical smears] yield false-negative results" is misleading, as are several of their claims regarding the value of liquid-based and automated cytology.¹ Most studies quote a false-negative rate of approximately 1–5%.^{2–4} Any laboratory with a 50% false-negative rate would be shut down.

Liquid-based preparations are not free of drawbacks, including the loss of necroinflammatory background that can be a clue to malignancy. Although it is true that "virtually all cellular material is made available to the laboratory," only a small proportion of this material is placed on the slide for screening. Conventional preparations contain many more cells. The newer methodologies are also very expensive and tightly controlled by a few companies, drawbacks that are not just "perceived." Their claims of improved false-negative rates are questioned by a recent meta-analysis, which concluded that most of the studies of liquid-based preparations and automation were "severely limited by design, inadequate reference standards, and incomplete verification of cytological diagnoses."⁵ Finally, none of these technologies will reduce the number of false-negative cases that are due to suboptimal sam-

pling or interval disease progression.

If the jury is still out on the statistical value of these methodologies, the societal value is even less certain. Traditional cervical smears have been successful because they are inexpensive, easy to perform and generally accurate. Because of slow progression to malignancy, yearly smears will detect almost all serious disease even if it is missed on one specimen. The greatest gain in cervical cancer control is in first-time screening, and the increase in cost associated with new techniques will reduce access by underserved populations. Increased costs will also follow the inevitable rise in false-positive tests.

There is a social cost in quoting questionable statistics about false-negative cervical smears, eroding both patients' and clinicians' confidence in a test that is fundamentally sound. Calculated from 8 representative studies,³ the predictive value of a negative smear for significant disease is 99.96%. It's hard to improve on that.

Erin Ellison
Histoctyopathologist
Laboratory Medicine Program
Lakeridge Health Corporation
Oshawa, Ont.

References

1. Franco EL, Duarte-Franco E, Ferenczy A. Cervical cancer: epidemiology, prevention and the role of human papillomavirus infection. *CMAJ* 2001;164(7):1017–25.
2. Lemay C, Meisels A. 100% Rapid (partial) re-screening for quality assurance. *Acta Cytol* 1999; 43:86–8.
3. Arbyn M, Schenck U. Detection of false negative Pap smears by rapid reviewing, a metaanalysis. *Acta Cytol* 2000;44:949–57.
4. Appendix A. False negative and false negative rates (FNRS): a review. In: Regulatory closure of cervical cytology laboratories. Recommendations for a public health response. *MMWR* 1997; 46(RR17):16–8.
5. Broadstock M. Effectiveness and costs effectiveness of automated and semi-automated cervical screening devices: a systematic review. *NZTA Rep* 3(1). Christchurch (N.Z.): New Zealand Health Technology Assessment Clearing House; 2000.

[The authors respond:]

Erin Ellison has challenged our contention that the false-negative rate for conventional Papanicolaou (Pap) smears is much higher than it is generally perceived to be.¹ A recent meta-analysis conducted in primary screening settings indicated an average sensitivity of 51% (95% confidence interval 0.37–0.66).² This figure will be shocking to anyone, like Ellison, whose knowledge base includes studies that were plagued by verification bias (also known as diagnostic workup bias) or involved the triage of equivocal or minor abnormalities, which are situations with a high prevalence of lesions. Screening sensitivity in studies affected by verification bias is invariably overestimated³ and should not be included in pooled overviews, a precaution that was taken in the aforementioned meta-analysis.² In fact, it has been recommended that cost-effectiveness models of cervical cancer screening should be revised to use more conservative estimates of Pap test sensitivity.⁴

Ellison's arguments about the draw-

backs of liquid-based cytology notwithstanding, this technique does represent an improvement over conventional smear techniques. The few studies that satisfy today's stringent criteria for quality of evidence have found liquid-based cytology to be significantly more sensitive than the conventional Pap test.^{2,5}

The evidence for the effectiveness of the Pap test as a cancer control measure was obtained in an era before the randomized controlled trial paradigm became widespread. Newer techniques are being judged by criteria that are far more stringent than the ones used to place the Pap test on its current pedestal. Well-designed studies with suitable end points are expensive and take many years. Privileged observers of the cervical cancer screening scene, such as Ellison, should take this into account before prematurely repudiating new methods.

We agree that it is unfortunate that reliance on new technologies may limit the practice of cervical cancer screening to a few commercial interests. However, as these technologies gain ground, competition is likely to ensue and the present monopolies will disappear.

Eduardo L. Franco

Departments of Oncology and Epidemiology
McGill University
Montreal, Que.

Eliane Duarte-Franco

Department of Oncology
McGill University
Montreal, Que.

Alex Ferenczy

Department of Pathology
McGill University
Montreal, Que.

References

1. Franco EL, Duarte-Franco E, Ferenczy A. Cervical cancer: epidemiology, prevention and the role of human papillomavirus infection. *CMAJ* 2001;164(7):1017-25.
2. McCrory DC, Matchar DB, Bastian L, Datta S, Hasselblad V, Hickey J, et al. *Evaluation of cervical cytology*. Evidence report/technology assessment no 5; AHCPR publ no 99-E010. Rockville (MD): Agency for Health Care Policy and Research; 1999.
3. Franco EL. Statistical issues in human papillomavirus testing and screening. *Clin Lab Med* 2000;20:345-67.
4. Nanda K, McCrory DC, Myers ER, Bastian LA, Hasselblad V, Hickey JD, et al. Accuracy of the Papam Nicolaou test in screening for and follow-up of cervical cytologic abnormalities: a systematic

5. review. *Ann Intern Med* 2000;132:810-9.
- Hutchinson ML, Zahniser DJ, Sherman ME, Herrero R, Alfaro M, Bratti MC, et al. Utility of liquid-based cytology for cervical carcinoma screening: results of a population-based study conducted in a region of Costa Rica with a high incidence of cervical carcinoma. *Cancer* 1999; 87:48-55.

Support groups for people carrying a *BRCA* mutation

The study by Lisa Di Prospero and colleagues on the psychosocial impact of genetic testing for *BRCA1* and *BRCA2* mutations is important and one of the first to explore the perceptions of tested women in Canada.¹ We believe, however, that it may be premature to state that the "organization of support groups for people found to have the gene mutation should be a priority" for clinical programs providing testing.

We are currently conducting a prospective study describing a range of outcomes of *BRCA1* and *BRCA2* testing among Quebecers during pretest genetic counselling and 1 month, 1 year and 3 years after result disclosure. Nearly half the projected consecutive series of 900 participants have been recruited to date. Participation exceeds 85%. Our data indicate relatively low interest in support groups in this population. Of the 91 subjects questioned to date at 1 year after they learned their test result, 27% of the people with a *BRCA* mutation (10/37), 20% of people with inconclusive results (2/10) and 14% of people without a *BRCA* mutation (6/44) expressed moderate or great interest in having access to support groups. Recent research among breast cancer patients suggests that peer discussion groups may be harmful to women who already have high levels of support.² This is an important point, as 75% of the participants in the study by Di Prospero and colleagues felt that support from family and friends was meeting their needs.

We believe that psychosocial interventions for people undergoing genetic testing for breast cancer susceptibility are justified, given the current consensus that all people should have access to psychosocial care. However, given that our present state of knowledge is based on data from small numbers of tested

people, more research may be needed before a clear-cut recommendation can be made concerning support groups.

Michel Dorval

Assistant Professor
Faculty of Pharmacy
Laval University
Quebec City, Que.

Elizabeth Maunsell

Professor
Department of Social and Preventive Medicine
Laval University
Quebec City, Que.

Michel J. Dugas

Assistant Professor
Department of Psychology
Concordia University
Montreal, Que.

Jacques Simard

Professor
Department of Anatomy and Physiology
Laval University
Quebec City, Que.

References

1. Di Prospero LS, Seminsky M, Honeyford J, Doan B, Franssen E, Meschino W, et al. Psychosocial issues following a positive result of genetic testing for *BRCA1* and *BRCA2* mutations: Findings from a focus group and a needs assessment survey. *CMAJ* 2001;164:1005-9.
2. Helgeson VS, Cohen S, Schulz R, Yasko J. Group support interventions for women with breast cancer: Who benefits from what? *Health Psychol* 2000;19:107-14.

[The authors respond:]

We thank Michel Dorval and colleagues for their interest in our study¹ and agree with their statement that the majority of people carrying a *BRCA1* or *BRCA2* mutation do not need support groups. By no means were we trying to suggest that all people carrying one of these mutations should be encouraged to join support groups. Genetic testing populations are heterogeneous and one would not expect a single intervention to address the psychosocial needs of all people carrying a *BRCA* mutation.

What we did say was that "a significant minority of [people carrying a *BRCA* mutation] desire such a service." This "significant minority" was 9 of the 24 patients who participated in our study (38%); this is not statistically sig-