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by Leo Twiggs

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# Is colposcopy and/or biopsy always necessary?

LuViva® Advanced Cervical Scan is designed as a new non-invasive test that has the potential to significantly improve the early detection of cervical precancers

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In the 1950s, cytology-based cervical cancer screening methods were first widely introduced to reduce mortality. As a result, the incidence rate of cervical cancer has declined between 50 and 80%<sup>1,2</sup> in countries with available screening infrastructure.

Although clinical practice and screening recommendations vary from country to country, the majority of developed countries generally follow the same basic guidelines. The typical screening programme includes a woman receiving a periodic Pap test. If abnormal cells are found, she is recalled for a follow-up procedure. In some cases the recall visit may involve a confirmatory Pap test and/or a visual inspection of the cervix, or colposcopy. During the colposcopy

examination, various solutions (Lugol's solution and/or acetic acid) may be applied to the cervix to highlight any lesions on its surface. If a lesion is visible, a biopsy is taken or a sample from the distal endocervix is taken. The biopsy is then generally sent to a laboratory for review and a pathology result is given.

*“If used in the recall system for triage after screening, LuViva has shown the ability to reduce unnecessary procedures by 35–40%”*

The number of women going onto recall colposcopy with biopsy, while dependent on the population screened, is approximately 6–10% of the screening population. Of that number, only 20–35% have disease that requires treatment,<sup>3,4</sup> resulting in a large proportion of women receiving unnecessary procedures and creating an unnecessary burden on

the financial and human resources of healthcare systems.

Unnecessary referrals from Pap screening tests increase the resource burden, leading to psychological and financial problems faced by the patients and their families with potential for medical complications from treatment.

The consequences of women going through a recall procedure for an abnormal Pap test may have a negative emotional impact. A number of studies have reviewed the psychological aspects of women after being informed of an abnormal Pap test result. Women commonly feel stressed and anxious, irrespective of the severity of the result.<sup>5</sup>

Table 1: Percentage of women reporting various after-effects of procedures post- abnormal screening result<sup>6</sup>

Follow-up procedure	Number of women reporting	Pain		Bleeding		Discharge		Changes to first menstrual period post-colposcopy
		Any	Moderate/severe	Any	Moderate/severe	Any	Moderate/severe	
Cytology only	884	15%	NA	16%	NA	7%	NA	NA
Colposcopy only	401	18%	5%	14%	3%	15%	5%	29%
Colposcopy/biopsy	165	53%	28%	79%	21%	46%	14%	43%
Colposcopy/LLETZ	185	67%	33%	87%	53%	63%	42%	71%

In a 2008 study by Hellsten and colleagues, it was suggested that these emotions are long lasting and are present up to two years after the abnormal Pap test.<sup>6</sup>

Additionally, a series of studies reported the frequency of after-effects due to follow-up cytology, colposcopy, biopsy and loop excision of the transformation zone (LLETZ).<sup>7,8</sup> Their data, summarised in Table 1, demonstrated that cervical punch biopsy carries a substantial risk of after-effects. For example, of the 165 women that underwent colposcopy and punch biopsy, 28% reported moderate-to-severe pain and 21% reported moderate-to-severe bleeding. In addition, 43% reported changes in their first menstrual period post-colposcopy and biopsy. The American Cancer Society, the American Society for Colposcopy and Cervical Pathology and the Society for Clinical Pathology, all consider the potential after-effects sufficiently serious to accept increases in the delay of diagnosing cervical intraepithelial neoplasia (CIN)2, CIN3 and cancer.<sup>9</sup>

In addition to these reported complications,<sup>9,10</sup> there may be an increased risk of severe adverse pregnancy outcomes from treating the cervix, including preterm delivery, low birth weight and premature rupture of the membranes.

Beyond the emotional impact the patient endures, there is the additional potential burden of having to miss work, arrange for childcare, and/or transportation costs associated with the additional appointments.<sup>9</sup>

### New guidelines

In order to relieve the burdens incurred by the patient and the payors, governments around the world have begun implementing new guidelines to reduce the rate of over-referral of women to recall and potential over-treatment. The two predominant techniques are increasing the age that cervical screening is initiated and lengthening the screening intervals. In most developed countries, guidelines for when screening should begin have changed from when the woman becomes sexually active to age 21 in the US or age 25+ in many European countries. The screening interval has changed from a yearly exam to once every three-to-five years.



The LuViva® Advanced Cervical Scan

In addition to the changes in frequency, the introduction of the human papilloma virus (HPV) test has been gaining in popularity because of its ability to identify a patient's active HPV infection.<sup>1,2</sup> Although this test provides the added knowledge that the patient has an active infection, it has been limited in the screening venue to women over the age of 30 years.<sup>11</sup>

### Current screening strategies

Despite the changes made in screening programmes over the past few years to reduce the number of women receiving unnecessary treatment, current screening strategies are not able to effectively identify true disease and a significant proportion of women are still unnecessarily incurring the emotional, financial and physical effects. The question that emerges is:

can we confidently reduce the number of women receiving costly and unnecessary examinations within current screening guidelines without decreasing the ability to identify disease?

### A promising solution

A promising solution for this global issue is the LuViva® Advanced Cervical Scan developed by Guided Therapeutics Inc (Norcross, Georgia, USA). LuViva is a fast and painless scan of the cervix that indicates the likelihood of CIN2 and higher (CIN2+) in a population referred onto further investigation from screening. LuViva evaluates cervical tissue, including the distal endocervix, in a painless process that combines fluorescence and reflectance spectroscopy to produce an immediate result on a three-point scale (low, moderate and high) without a tissue sample.<sup>12</sup>

LuViva provides an immediate result at the point of care, and is designed to reduce false positive results and accelerate care for patients with a higher likelihood of CIN2+. In a prospective, multicentre study, 1330 patients were evaluated with LuViva after referral from abnormal Pap results or other risk factors associated with cervical disease, such as positive HPV result or previous dysplasia. The clinical trial demonstrated that as the results increased in magnitude on the three-point scale, so did the likelihood of CIN2+, as documented by quality-controlled, multi-reader histopathology results.<sup>13</sup>

According to the pivotal clinical trial results, a patient with CIN2+ is approximately four-times more likely to be in the high category than the low category, and a patient with CIN3+ (including cancer) is approximately seven-times more likely to be in the high category than the low category. A patient in either the low or moderate category is least likely to harbour a CIN2+ lesion.

Perhaps most importantly, LuViva's Negative Predictive Value of 99% indicates that a patient with a low LuViva result has only a 1% chance of a CIN3+ lesion.<sup>14</sup>

Including LuViva into the current cervical screening models after, or in conjunction with initial screening tests, but before colposcopy, would not only give physicians more confidence in determining if actual disease is present, but

would also eliminate unnecessary follow up tests, biopsies and other procedures on healthy patients from 35–44%.<sup>12,15</sup> The emotional and physical burden that the patient incurs will be reduced significantly. Returning the patient to her normal screening intervals sooner would reduce the emotional and physical trauma and the financial burden for both the patient and the payor.

### Conclusions

Despite substantial reductions in the incidence and subsequent mortality of cervical cancer worldwide, ongoing screening programmes, although proven to be effective, subject many women to unnecessary procedures with known complications and create an unnecessary burden on national health care resources. If inserted into the recall system for triage after screening, LuViva has shown the ability to reduce unnecessary procedures by 35–40%, thus significantly reducing health care expenditures in the field of cervical precancer and improving the patient's experience. ♦

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