interval of 2 years. By contrast, the 2004 International Agency for Research on Cancer (IARC) recommendations specify that women aged 25–49 years undergo screening every 3 years and those aged 50–64 years undergo screening every 5 years. These recommendations were adopted by the UK in 2003.

A comparative approach between Australia and the UK in terms of screening policies, participation rates, and outcomes with respect to cancer incidence can lead to valuable insights. Examination of the crude participation rate in Australia demonstrates a 2-year participation rate of 61% and a 5-year participation rate of 78%. The UK 3-year participation rate was 66% and the 5-year participation rate was 88%. Data from the NSW Pap Test Register show two peaks in re-screening rates, the first occurring at 1 year, and the other between 2 and 2.5 years. These data illustrate that annual screening continues to be a relatively common practice in Australia. In contrast, data from Oxfordshire show that the peak re-screening timing in the UK, prior to the implementation of the 2003 changes, was between 3 and 4 years.

Sasieni et al. 2003 has demonstrated a discontinuous relationship between time since a negative smear and risk of cervical cancer. In women below 50 years of age in the UK, the protective effect of a negative screen remains in place for approximately 3 years and then rapidly returns to levels close to baseline. In women aged over 50, the protective effect persists for approximately 5 years.

In women aged 50–64 years, the rate of cervical cancer in the UK in the years 1998–2000 was lower than that in the comparable group in Australia, even with the pre-2003 UK policy of mixed 3–5 year screening intervals. This probably reflects the longer duration of protective effect of a negative screen in this age group. In the over 65 age group, the rate of cervical cancer in the UK overtakes that in Australia, probably as a result of the UK screening program targeting women under 65, while in Australia, women up to the age of 70 continue to be included in screening programs.

Among Australian women under the age of 50 years, the rates of cervical cancer are substantially lower than in the UK. This may in part be a reflection of differences in management. Another contributing factor may be the screening interval. Peak re-screening in the UK occurs after 3–4 years which may be longer than ideal given the shorter persistence of a protective effect in this age group.

To summarise the implications for Australian screening policy, the international data suggest that screening in women aged under 25 years should be reviewed. In women aged 25–49 years, Australia could potentially afford to "shift the re-screening peak" from the current 1–3 years to 2–3 years, whilst in women aged 50–64, the screening interval could potentially be extended. The current strategy of screening until age 70 appears to be effective. However, more research is needed to examine the duration of protective effect of a negative screening test under Australian conditions, to assess the impact of recent management changes upon these conclusions, and to inform policy-makers.

Reference

TruScreen – The Australian experience

Dr David Itzkovic
Gynaecologist, Bondi Junction, NSW
Dr Deborah Cromer BSc
Statistical analysis

The Pap smear has significant shortcomings in terms of its sensitivity, but continues to perform as a very specific test. It misses a significant number of abnormalities, with data suggesting that up to 30% of cervical cancer patients may have received a normal smear result on cytology screening.

TruScreen is used in conjunction with a conventional cytological Pap tests to improve accuracy. TruScreen uses a handpiece with optical sensors that emit a number of discrete wavelengths in the visible and infrared regions of the spectrum as well as an electrical biosensor to stimulate cervical tissue. Up to 24 sites are sampled during the examination. The device then analyses backscattered light, direct reflectance and electrical response curves of the tissue and these are compared with an existing database of demographically matched tissue "signatures." Results are available instantly. TruScreen is listed on the Australian Register of Therapeutic Goods and is CE marked in Europe as an adjunct to conventional Pap testing. Recently, it has also been approved in parts of Asia.

Dr Itzkovic presented an analysis of 456 patients screened in his practice between May 2003 and December 2004. None of the women offered the test refused. Patients underwent TruScreen, a Pap screen, and if TruScreen results were abnormal, immediate colposcopy was performed. Patients with an abnormal Pap smear were also recalled for colposcopy.

Of the entire sample, 88 patients (19.3%) had abnormal TruScreen results. On colposcopy 47 (10.3%) had abnormal results, and 41 (8.9%) had normal results. Of the 13 women with CIN lesions, seven were identified only by TruScreen and two were identified only by Pap smear. Both tests identified an additional two CIN lesions, and the final two of the 13 CIN lesions were missed by both methods. Overall, the Pap smear identified only four of the 13 (30.7%) CIN patients, while combined Pap smear and TruScreen detected 11 (84.6%) cases (see Figure 1, page 11).

Dr Itzkovic explained that patients felt reassured by the increased accuracy available through combined use of TruScreen and conventional Pap testing. The immediate
availability of results provided by Truscreen was an additional advantage and allowed further investigations (e.g. colposcopy) to be performed at the same time. He concluded that as an adjunct to Pap testing, Truscreen is a significant improvement in the detection of CIN lesions compared to use of the Pap smear alone. Patients are very accepting of the combined Truscreen and Pap testing approach. More investigation is required to accurately define the potential of the Truscan.

Figure 1

![Diagram of Truscreen and Pap detection of CIN lesions]

**Cervical histology - The gold standard?**

Huw Llewellyn  
Staff Pathologist, ACT Pathology, The Canberra Hospital, ACT

Traditional diagnostic criteria for the evaluation of cervical cytology have been in place for approximately 30 years. A significant part of the problem with existing Bethesda classification of abnormal cytology lies in the presence of multiple processes being under way at different cervical sites, including productive viral replication, pre-neoplastic transformation, immature neoplasia and reactive changes.

Morphological diagnosis tends to be subjective, and anecdotal evidence suggests that the natural desire to avoid missing high-grade squamous intraepithelial lesions (HSIL) may result in "over-calling". This approach does not accommodate the range of reactive changes that may be present, and immature metaplasia may confound classification.

In low-grade squamous intraepithelial lesions (LSIL), HPV changes are only observed in the upper endotheleum and HPV DNA is only expressed in this upper endotheleum. In HSIL, the HPV genome is integrated into the basal epithelium stem cell genome, and uncontrolled epithelial proliferation occurs with the nuclear abnormalities present in basal stem cells persisting upward through the cervical epithelial cells.

Studies of the diagnostic framework for cervical cancer proposed by Dr Christopher Crum of the Brigham and Women's Hospital in Boston demonstrate a higher level of intra- and inter-observer reproducibility of results compared to observers using the Bethesda system. Molecular studies also support the use of Dr Crum's system.

Histology remains the gold standard for the evaluation of cervical cytology, and will remain so for the foreseeable future. However, traditional diagnostic criteria are suboptimal. The diagnostic criteria developed by Dr Christopher Crum warrant further consideration as their use improves the characterisation of true high grade disease as high risk HPV types preferentially segregate into the HSIL category. Dr Crum has published a comprehensive monograph illustrating his work and he continues to refine his classification system.

**Reference:**


**Session 2**

**HPV Testing - Where are we?**

**Professor Henry Kitchener**  
Professor of Gynaecological Oncology, St Mary's Hospital, Manchester, UK

Professor Henry Kitchener commented on the potential place of HPV testing in the analysis of cervical cytology. He discussed the ongoing ARTISTIC (A Randomised Trial of HPV Testing in Primary Cervical Screening) trial which is investigating the use of HPV testing as a primary screening tool.

ARTISTIC involves 29,000 women aged 20-64 years attending general practices for routine cervical screening and who consent to having an HPV test. It began in June 2001 with full results expected in 2007-8. The study has been designed to provide clear evidence on the costs, medical effects and psychological impact of combining HPV testing with cervical cytology. It will also evaluate the effectiveness of stand-alone HPV testing, and its impact on sensitivity, specificity and the rate of inadequate smears.

After providing consent, subjects were randomised (3:1) to having the HPV result either revealed or concealed to both women and investigators. Women in the revealed arm who are HPV positive with a negative smear will undergo repeat testing at 12 months, and colposcopy will be offered to those who are still HPV positive.

All participating women will be re-screened after 3 years to determine whether, as a result of HPV testing, there is a reduced incidence of pre-cancers at this time point. Another important objective is to determine the psychological impact of HPV testing, given that it is sexually transmitted and may cause women to feel anxious or embarrassed. The third key outcome is to determine whether HPV testing is cost effective, i.e. whether the additional cost of the test is satisfied by higher detection rates or has the potential to save costs elsewhere in the programme. The final results will be published in 2007.