MOVING FORWARD ON CERVICAL CYTOLOGY

A workshop sponsored by the National Cancer Control Initiative and the Australain Society for Colposcopy and Cervical Pathology

9 May 2001
Fremantle, WA

Workshop Summary
Moving forward on cervical cytology

The Workshop

‘Moving forward on cervical cytology’ the workshop sponsored by the National Cancer Control Initiative and the Australian Society for Colposcopy and Cervical Pathology (ASCCP) was held on 9th May 2001 at the West End Convention Centre in Fremantle, WA. The workshop followed the ASCCP’s XVII scientific meeting.

Objective

The object of this workshop was to address what could and should be done in Australia to develop cervical screening both within existing programs and in new service programs or new research.

Structure of workshop

The workshop was chaired by Associate Professor Michael Quinn.

Five topics were identified for discussion. Two speakers were invited to introduce each topic. One speaker presented the case for change and the other speaker presented the arguments against change for each topic. The speakers were asked to present either the for or against argument whether or not it was in full accordance with their own views.

An open discussion took place at the conclusion of the presentations.

Topics for discussion

Why shouldn’t we extend the current two-year screening interval?

Why shouldn’t we incorporate HPV testing in primary screening?

Why shouldn’t we use HPV testing in the triage management of abnormalities?

Why shouldn’t we use HPV testing in follow up?

Why shouldn’t we make changes within the current national publicly funded program?

Attendance

Approximately 130 people attended the workshop. The audience was comprised of cytologists, histopathologists, general practitioners, gynecologists, gynecological oncologists, scientists, nurse practitioners, members of the pharmaceutical industry, state recruitment coordinators and other cervical registry staff. Members of the National Advisory Committee on Cervical Screening attended including the chair, Dr Heather Mitchell, and the Chair of the New Technologies Working Group, Mr Robert Rome and members of state and federal government groups.

Workshop Summary

This document contains a summary of the workshop proceedings. For each presentation the main arguments raised either in support of or against change are summarised. A summary of specific issues raised during the discussion period is also included along with suggestions for development. It should be noted that the presenters were assigned the topics for discussion. The presenters do not necessarily concur with the arguments they presented. Furthermore, the presenters appeared at the workshop as individuals, not as the representatives of particular groups or on behalf of any organisation.
Why shouldn’t we extend the current two-year screening interval?

- Arguments in favour of extending the interval

Dr. Gerard Wain, Program Director NSW Cervical Screening Program, Westmead Hospital, PO Box 533, Wentworthville, NSW 2145

It is a screening program for cervical cancer

- It is not a smoking prevention campaign, it is not a domestic violence counselling campaign and it’s not a well-being campaign.
- It is a screening program that involves allocating risk categories to populations of people. It is about deciding whether a person is at low or high-risk of developing the disease. It is not a diagnostic procedure.
- The objective of the cervical screening program is to achieve optimal reductions in the incidence and mortality of cervical cancer, at an acceptable cost to the community. The objective is not to eradicate cervical cancer at whatever cost.

It is effective

- A three-year screening interval is highly effective at preventing cervical cancer and only marginally less effective than annual screening (IARC recommendations in the 1980’s).
- There has been a dramatic reduction in incidence and mortality in most countries where organised programs exist regardless of varying policies or intervals.
- Internationally cervical screening policies vary significantly. However, international results have shown similar reductions in the incidence of cervical cancer regardless of the screening intervals. That is, frequent screening with whatever interval achieves the same outcomes in most populations.

It is safe

- A US study by Sawaya et al., (2000), using 128 000 women, showed that the screening interval made very little difference to outcomes, in that, although there was a slight increase in the incidence of low-grade SILs with increasing time intervals, the incidence rate of high-grade SILs or worse was similar across the varying time intervals.
- In NSW similar findings have been seen. In women over the age of 50 years the incidence of CIN III was similar across screening time intervals ranging from 9-36 months. An increase in CIN III was only observed when the screening interval was greater than 36months.
- A consequence of doing Pap smears more frequently is the morbidity that is induced by picking up a whole range of insignificant low grade lesions.

The current program has in place:

- Aspects of recruitment
- Registers
- Good laboratory capacity
- A monitoring system built into the system

Therefore, with all these systems in place, we have all the infrastructure required to make changes to the screening program.

The resources can be used else where

- Freeing up resources spent on the cervical screening program can be used to address other issues such as issues in women’s health and issues in cancer control.
Why shouldn't we extend the current two-year screening interval?

- Arguments against extending the interval

Dr Barbara Jones, State Director RACGP Training Program, Townsville General Hospital, School of Medicine, James Cook University, Townsville, QLD 4811

- Arguments for maintaining the two-year screening interval are based on pragmatic rather than epidemiological grounds.
- On cost effectiveness alone, a three-year interval makes sense. However, clinicians, patients, journalists and lawyers think in terms of individuals, not populations.

Three-year screening and clinicians

- A two-year screening interval hasn’t met with total acceptance from the clinicians. Research done by the college of GP’s in 1994 with 259 GP’s in SA showed that only half agreed with the two-year screening interval (Beilby et al., 1994). The remaining GP’s were using annual screening.
- In 1996 Wai et al., surveyed GP’s in NSW (N=70) and found that only 33% were comfortable with a two-year screening interval.
- In 1998 a national study by Ward et al., using 855 GP’s showed that 19% still recommended annual screening. Although these studies show a change in attitude towards annual screening, a substantial number of GP’s and gynaecologists are still recommending annual screening.
- A survey of 30 GP registrars in North Queensland revealed that 20% recommended annual screening despite being aware of the national recommendation for a two-year policy.
- Only 10% of surveyed registrars would accept a three-year screening interval.
- Clinicians are wary of less frequent screening despite understanding the epidemiological reasons for changing the screening interval. It is the clinicians that are going to implement this screening interval, not the epidemiologists or the politicians. Therefore, what is the point in having a policy that nobody is going to use?

Three-year screening and patients

- Changing to a three-year interval is going to be very hard to introduce. 
- Three years is a difficult interval to remember. If patients are older they can link a two-year interval to other screening tests such as mammography, or odd and even numbers. But three years is a difficult interval to remember. There must be a very good reminder system in place if a change to a three-year screening interval is going to work. Although a reminder system is in place it is an expensive system to introduce.
- A change in the interval may suggest to patients that the Pap smear is not really important.

Increased detection rate of abnormalities with two-year screening

- More frequent Pap smears result in a small increase in the pick up rate in abnormalities. Studies by Hakama et al., (1996) have shown a cumulative 3% reduction in incidence of cervical cancer using annual screening (cumulative incidence reduced by 93.5% in annual screening versus 90.8% in three yearly screening).
- This is significant if you are part of the three percent and believe that you could have been cured if you had been screened earlier. The courts and the media may also view it this way. In terms of cost effectiveness, one court case could be worth millions of dollars and that equates to many smears that could have been done more frequently.

Summary points

- Increasing the screening interval may be seen as a cynical cost saving exercise by the public and the clinicians.
- Increasing the interval creates public disquiet about cutting health services.
- It creates mistrust of doctors who may be perceived as being party to saving money rather than looking after the individuals health needs.
- It will probably result in an increased cost of litigation.
- It is likely to create a market for laboratories offering more or different tests at a cost to the patient. This can lead to further inequities and a waste of resources.
Why shouldn’t we incorporate HPV testing in primary screening?

-Arguments in favour of incorporating HPV testing in primary screening

Associate Professor Suzanne Garland, Director, Department of Microbiology, The Royal Women’s Hospital, 132 Grattan Street, Carlton, VIC 3053

- Cytology screening unequivocally reduces cervical cancer incidence and mortality. However, the current Pap smear has never been rigorously tested in a randomised controlled trial. In the best programs a 50-70% reduction in mortality can be seen but then the reduction in mortality plateaus.

- For a cervical screening program to be successful it must have a broad coverage of at risk women, good quality assurance, good quality control and treatment support.

- Failures in the program can be related to sample error, detection error and poor quality.

- In Australia 85% of women diagnosed with cervical cancer have an inadequate Pap smear or haven’t had a Pap smear in the last 3-5 years.

HPV as an aetiologial agent - we should test for the aetiologic agent

- From natural history studies - know that most HPV’s are transient but it is the persistent oncogenic high risk HPV’s that we should test for.
- Data from IARC has shown that the odds ratios for the development of cervical cancer for these high-risk persistent HPV’s is very high (>100-200) which is much higher than smoking and lung cancer.
- High viral load is also a marker. SIL is the viral cytopathic effect of HPV.

Optimised HPV DNA testing is objective, automated, standardised, and reproducible.

- Studies using HPV and Pap smear for the detection of high grade disease have shown that HPV DNA testing is more sensitive at detecting high-grade disease than the Pap smear (88-97% vs. 50-80% respectively).
- In terms of the specificity associated with HPV testing the issue is the age at which screening commences.
  - HPV declines with age and abnormal Pap smears plateau around the age of 30 years. Therefore, HPV testing in over 30’s is appropriate

- Need to develop clinical algorithms with the opportunity to focus on subsets of women more likely to get disease.

- Need to look at increasing the interval of the Pap smear and look at decreasing costs.

- Need to look at women who do not access services or women in areas where there isn’t access to Pap smears. There is data now that shows that patient collected samples for HPV DNA are as effective as the Pap smear.

HPV testing can be used as:

- An adjunct or a stand-alone screening test.
- As a stand alone screening test where women aren’t accessing screening services, as a self-collected sample, it may be appropriate.
- It could be used as an adjunct to a Pap smear with a biomarker for progression such as p16, or oncogenic transcripts of HPV.

HPV testing has come of age technically and can be used as a viable cervical cancer screening method.

Future research in Australia

- We should be using a more sensitive test less frequently and some of the areas we should be looking at are:
  - The performance of HPV testing.
  - Progression markers.
  - Acceptability of new technologies to the general public – how do we tell women they have an HPV which is a sexually transmitted disease.
  - Cost effectiveness models.
  - Education of the public as well as professionals.
  - Compare new tests vs. the “status quo”.

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Why shouldn’t we incorporate HPV testing in primary screening?

-Arguments against incorporating HPV testing in primary screening

Dr Gabriele Medley, Victorian Cytology Service, 752 Swanston St, Carlton, VIC, 3053

Cost of HPV testing in the Australian context

- For a screening program to survive it must be cost effective. That is, the cost of screening must be less than the cost of not screening.
- The question being asked here is whether to incorporate HPV testing into the cervical screening program. What we are being asked to consider is the issue in the Australian context not in the context of developing nations. HPV testing would be an additional procedure to cytology, clearly then, cost is an issue.

Specificity of HPV testing

- Data from Costa Rica (Schiffman et al., 2000) and China (Belinson et al., 1999) shows that adding HPV testing to cytology screening increases the sensitivity of screening for high grade intra-epithelial and invasive lesions to nearly 100%. However, specificity in both these studies was in the order of 85-89% and roughly twice as many women were referred to colposcopy by this test as they were for cytology.
- In a systematic review of Human Papillomavirus Testing within a Cervical Screening Program (Health Technologies Assessment, NHS R&D HTA Programme, Cuzick et al., 1999) it was stated that HPV testing has a greater sensitivity for CIN II and III than cytology. Variability of HPV positivity rate in normal populations has been shown to range from 3-20%, or more in some studies, leading to a concern about specificity. This variability reflects a number of factors including age, extent of sexual exposure, previous disease and the type of assay used.

Cannot currently recommend HPV testing in primary screening

- Recommendations from Cuzick et al., (1999) includes a very large randomized control trial to evaluate the effect of HPV testing on cancer incidence and the length of protection afforded by a negative HPV test in conjunction with cervical cytology.
- Further discussing the health policy issues this document and other reviews of available data have expressed the concern that an appropriate screening policy must consider the balance between benefits and cost. Better health and survival outcome at the cost of provision of follow-up and treatment, the human cost of over treatment and the unnecessary physical and mental suffering of those whose positive screening results represent no threat to health.
- A quote from J T Cox (1996) “Even increased detection of high grade lesions in young women may not contribute substantially to decreasing the interval cancers that occur”.
- J Cuzick (2000) is quoted “whether widespread HPV testing is feasible or affordable, and whether it will eventually lead to fewer cases of invasive cervical cancer or reduce morbidity and mortality form the disease will require further studies”.

Direct verification for a reduction in screening incidence should be obtained before introducing a new test into the program.

- The conclusion from the Health Technologies Assessment document (Cuzick et al., 1999) “HPV testing cannot currently be recommended for wide spread implementation".
Why shouldn't we use HPV testing in the triage management of abnormalities?

– Arguments in favour of incorporating HPV testing in triage

Mr. Robert Rome, Gynaecological Oncologist, Suite 209, 320 Victoria Parade, East Melbourne, VIC 3002

Scientific
- There is mounting scientific evidence relating to the biology of HPV and the use of HPV testing from overseas studies.
- The ASCUS/LSIL triage (ALTS) study showed that HPV DNA testing using Hybrid Capture 2 has a high negative predictive value >98%.
- A publication from the ALTS study on patients with low-grade SIL (equivalent to CIN I) triaged women on the basis of the HPV test – 83% of women were referred for colposcopy. Many of these women were young and the study was terminated early. They concluded that HPV testing was not useful in the triage of low-grade SILs. They didn’t do a detailed analysis on the basis of age and they didn’t publish the cost aspects of this study.
- A second study was published on ASCUS cells (atypical squamous cells of uncertain significance) (equivalence in Australia - patients <CIN I and inconclusive). 3488 women were studied. Results showed that the sensitivity to detect CIN III was 96%. In the arm that was triaged on the basis of HPV testing 56% were referred for colposcopy after being HPV positive. Many of these women were young and detailed age, breakdown and costings are yet to be published. However, they did conclude that HPV testing was useful in the triage of ASCUS and HPV testing was better than the repeat smear.

Economic
- Cost savings can probably be made which will enable re-direction of resources into other areas such as recruitment and possibly other aspects of public health.

Costings of several management pathways can be done using the MBS schedule
- Referral to a specialist including colposcopy, biopsy and no treatment - cost $388+
- Referral to specialist, colposcopy, biopsy, treatment and follow-up – cost $599
- GP observation and repeat smears every 6 months – cost $80+
- Many women end up being treated because of persistence of abnormalities. It is estimated that about 50000 women are treated per annum with low-grade lesions and this can place a significant burden on the health budget.

HPV testing for triage
- If HPV positive (Hybrid Capture 2) triggers referral and treatment – cost $700
- If HPV negative and leads to observation by GP – cost $141
- Potential significant cost saving can be achieved by the introduction of HPV testing for the triage management of low grade abnormalities (<CIN I), inconclusive smears and in women >30 years of age.

Establishment of guidelines for the use of HPV testing
- By introducing HPV testing some guidelines will be developed for its use thereby lessening the confusion. There is a lot of confusion amongst consumers, general practitioners and specialists.

HPV testing and triage - suggestions
- There should be limited and controlled introduction of this test .
- Its potential cost effectiveness should be closely monitored and studied.
- Local trials are needed.
  - economic modeling should be done before any trial is started
  - cost benefit analysis should be undertaken
  - funding should come from the company itself
  - could and should by facilitated by the Commonwealth

- HPV testing in triage represents a research and development project for the Commonwealth’s Cervical Screening Program. A lot of effort has gone into recruitment and laboratory quality but nothing has gone into research and development.
Why shouldn’t we use HPV testing in the triage management of abnormalities?

Arguments against incorporating HPV testing in triage

Dr Ross Pagano, Obstetrician and Gynaecologist, Frances Perry House, 10th Floor, 285 Cardigan Street, Carlton, VIC 3053

Would not trust HPV testing as the sole method of assessment.
- If there is an abnormality on the Pap smear it needs to be taken further. If a patient is HPV negative but has a high-grade abnormality on their smear they are going to be referred for colposcopy and treated accordingly.

HPV testing does not offer any more than Colposcopy and / or biopsy
- If a smear test shows a high-grade abnormality, colposcopy ± biopsy is required.
- HPV testing offers no added benefit and does not change the way the clinician would manage the patient.
- If a smear test shows a low-grade abnormality, it still requires a colposcopy to show the patient that there is not abnormality on the cervix. Taking a HPV test in that situation does not offer any added benefit.
- In ASCUS smears 25% will be positive for a high risk HPV, HPV testing doesn’t add anything in this situation.
- Even if the smear is HPV negative you can’t assure the patient that she wont develop a cancer or a pre-cancerous change of the cervix.
- If a Pap smear shows HPV atypia without CIN, the patient deserves a colposcopy. Doing a HPV test doesn’t add anything. If the HPV test is negative it doesn’t reassure the patient because her Pap smear is still abnormal and if it's positive you have added an extra element of concern for the patient, especially since you can't reassure her that the HPV is going to disappear.
- If HPV negative or low risk positive, you still need to follow-up

Only value of HPV testing is to avoid colposcopy
- However, what is the point of avoiding colposcopy? Patients find colposcopy reassuring especially if they can visualise the cervix themselves.

Cost
- Cost of a colposcopy is similar to the cost of a HPV test done by the specialist.

Patient discomfort
- It is questionable as to whether a colposcopy is more uncomfortable than having a Pap smear taken.

Reassurance
- Is it reassuring to have a HPV negative test or a low grade HPV? No, patients want to be told that they are fine.

The only place for HPV testing is when it can replace the smear test by a technique of self-testing.
Why shouldn’t we use HPV testing in follow-up?

- Arguments for using HPV testing in follow-up

Dr David Allen, Gynaecologist Oncologist, Mercy Hospital for Women, 7th Floor, 126 Clarendon Street, East Melbourne, VIC 3002

- Standard follow-up after treatment of CIN – women would be seen 3 times in the first 18-24 months. The visit would involve a Pap smear ± colposcopy.
- Current recommendation by NHMRC is yearly smears for life following treatment for high grade CIN.

Reoccurrence of abnormalities and follow-up

- In clinicians own practice a 5-7% recurrence rate of disease has been observed and this rate can be up to 15% as cited in the literature.
- Often the results of these Pap smears are low grade which gives rise to a lot of follow-up and re-treatment and more investigation, colposcopies, laser, LLETZ, conization, hysterectomies etc.
- Therefore a lot of follow-up goes on after the treatment of a high-grade lesion.

HPV testing and disease reoccurrence

- Studies by Nagai et al., 2000 looked at the persistence of HPV after therapeutic conization for CIN III. The study used 58 patients with CIN III and showed that 96.6% were positive for HPV DNA. After treatment 19.6% remained positive for HPV DNA and of these HPV DNA positive patients 45.5% developed CIN recurrence. In the patients who were HPV DNA negative following treatment (80.4%) there were no recurrences of CIN.
- Kjellberg et al., 2000 looked at 108 patients with CIN 73.3% of them were HPV DNA positive. Following conization by carbon dioxide laser 97.3% were HPV negative. Furthermore, there were no recurrences of CIN in this group.
- Bollen et al., 1999 showed that all recurrent and residual CIN’s were HPV DNA positive and a HPV DNA negative test virtually rules out recurrent CIN. Furthermore, low-grade SIL on smear and HPV negative virtually rules out the ability to develop CIN and you don’t need to follow-up the patient every 6 months.
- Nobbenhuis et al., 2001 looked at 184 patients with CIN II-III – recurrence rate of 15.8% after treatment and at 3,6,9,12 and 24 months the authors undertook cytology and HPV testing and found that being HPV positive at 6 months was more predictive of CIN than cytology. The negative predictive value was 99% and the study suggested that HPV testing at 6 and 24 months after treatment is adequate.

Advantages of HPV testing after treatment

- Sensitivity for patients with recurrent disease is 100%.
- Positive predictive value of 50%.
- Negative predictive value of 100% - this negative predictive value makes this testing valuable in a secondary setting.
- Persistent HPV DNA positivity after treatment indicates incomplete excision in about half the cases but HPV DNA negativity virtually rules out residual CIN.
- HPV DNA positive – these patients would require Pap smear colposcopy and appropriate treatment.
- HPV DNA negative after treatment – repeat HPV DNA test every 3-5 years and this would eliminate the yearly Pap smear after treatment of CIN II or III. This would result in far fewer colposcopies and other interventions.
- Less stress for women.
- Financial benefit to community.
- Way around the medico-legal minefield.
Why shouldn’t we use HPV testing in follow-up
– Arguments against using HPV testing in follow-up

Dr. Jeffrey Tan, Gynaecologist, Frances Perry House, 10th Floor, 285 Cardigan Street, Carlton, VIC 3053

The sensitivity for detecting high-grade SIL is 76.2% with a Pap test, 89.2% with a HPV Hybrid Capture test and 96.9% with the HPV and Pap test combined (Manos et al., 1999).

Study at the Royal Women's Hospital, Carlton, Victoria, between 1/7/1998 and 31/12/2000: Follow-up of 1300 women who presented for follow-up after laser ablation and Loop Excision of cervix (LEEP).

Incidence of abnormal pap smears at first post-operative visit (3-4 months post-surgery)
- 21% of these women had an abnormal pap smear at the first post-operative visit
- 2.8% were reported as high-grade abnormalities

Of the patients that had a negative Pap smear at the first post-operative assessment, at the subsequent follow-up:
- 3.4% had low-grade SILs
- 0.5% had high-grade SILs
- Pap smear alone missed 26% of these low-grade SILs but detected all high-grade SILs
- Pap smear together with colposcopy still missed 7% of low-grade SILs

As the likelihood of high-grade SILs in this group is no higher than the screened population, there is a case to follow-up with Pap smears alone and not with colposcopy or HPV testing, as is the case in women undergoing routine screening.

Subsequent follow-up of low-grade persistent abnormalities – place for HPV testing?
- 9.3% of patients had persistent low-grade abnormalities after first follow-up.
- We could expect 80% of these women to be HPV Hybrid capture positive

The Pap test alone missed 18% of these low-grade abnormalities.
The Pap test together with colposcopy missed 1% of low-grade SILs.
Therefore, Pap test together with colposcopy will detect most low-grade SILs at follow-up.
The only application of HPV testing would be to reduce the frequency of follow-up colposcopy in women with low-grade SILs, perhaps by up to 20% if they are HPV test negative.

In following the low-grade SILs detected at first follow-up visit, 36% remain as low-grade, with 5.4% progressing to high-grade SILs.

Subsequent follow-up of high-grade persistent abnormalities – place for HPV testing?
- 1.8% of patients had persistent high-grade abnormalities at subsequent follow-up.
- One would expect 93% of these to be HPV positive using Hybrid Capture 2.

The Pap test alone missed 16% of these high-grade SILs.
The Pap test and colposcopy detected all high-grade SILs.
Therefore, there is no need to employ new technologies to improve diagnostic accuracy of high-grade SILs, as theoretically, some of these patients will be missed using HPV testing alone.

More research would need to be conducted into follow-up with HPV testing to determine the benefits before it introducing HPV testing as a routine test for follow-up.
Why shouldn't we make changes within the current national publicly funded program?

-Arguments for making changes to the current national publicly funded program

Professor Mark Elwood, Director, National Cancer Control Initiative, 1 Rathdowne Street, Carlton, VIC 3053

We should be prepared to review and modify the cervical screening program

- Any program that costs 200 million dollars of tax payers’ money and affects 2.7 million women should constantly be reviewed in light of the best scientific evidence and consideration should be given to both major and minor changes to the program that will achieve optimal efficiency.

Cervical screening in Australia has low cost efficiency

- The cervical screening program in Australia is effective but by international standards the current policy of two yearly screening from ages 18 to 70, giving 25 smears in a lifetime is very intensive. For example, most European countries use three yearly screening with a higher starting age, and Finland and the Netherlands have a policy requiring only six screens in a lifetime and very low mortality rates.

- Better targeting of screening, perhaps linking an increased screening interval with a more sensitive test by the use of better technology and perhaps HPV testing, could reduce over screening, reduce the morbidity associated with over screening and unnecessary investigations, and free up some funds for other initiatives, such as concentration on reaching women who have not been screened recently.

How the system can be changed

- Give greater priority to women at risk – mainly unscreened women.

- Bigger efforts in the Aboriginal community – possibly the use of new technologies or the redirection of funds from low risk women.

Research and development

- Decide whether to evaluate liquid based preparations, computer reading and HPV applications in Australia or review, contribute to and apply international trials.

- Research and development should be an integral part of any screening program with a budget. By industrial standards, the budget should be around 5% of the program budget. This money should be different to NHMRC money, as it is to deal with clinically relevant questions looking at practical issues.
Why shouldn’t we make changes within the current national publicly funded program?

– The argument against making changes to the current national publicly funded program

Dr Heather Mitchell, Medical Director, Victorian Cervical Cytology Registry, PO Box 161, Carlton South, VIC 3053

Program has had too much change recently

- The current screening policy has been released.
- Pap test registries have been implemented.
- Adopted the Australian version of the Bethesda system.
- NHMRC guidelines have been released.
- Introduction of mandatory reporting against quantified standards for laboratories reporting Pap smears
- Liquid based cytology.
- Starting to work on early re-screening.
- Changes at this time will only lead to confusion amongst women and practitioners.

Self interest

- Changing the screening interval will mean less smears for laboratories to report and thus, less money for pathology laboratories.
- Shifting from colposcopy to HPV testing we will see a major shift of funds from gynaecologists to pathology laboratories.

Sort out existing problems e.g. terminology issues

- Need to sort out our terminology issues before making changes to the program.
- Continued use of terms CIN I, II and III, mild, moderate and severe dysplasia which straddle the low grade and high grade abnormalities is detracting from getting the right understanding of the biology of cervical neoplasia.
- Low-grade category in Australia is problematic. Currently trying to subcategorise low-grade abnormalities into atypia, warty change and CIN I. There is concern about how repeatable those subcategories are and there is comment about how confusing it is to have three different management streams coming in under one heading.

Lack of appropriate Australian evidence

- In regard to the screening interval, the PBMA has been said by some to be methodologically limited.
- In relation to HPV testing in triage and follow-up of abnormalities – commented that people are not convinced by overseas trials and do not see how the results apply directly to Australia.

Lack of confidence that cost savings will be achieved

- With regard to the screening interval and enforcing a restricted payment schedule whereby the HIC pays for Pap smears only at the agreed screening interval – commented that it may be easy to make the policy decision but making it work in practice will be a lot harder.
- Point raised - how will the women or the practitioner know whether a smear will receive government funding or not?
- The question was asked - to achieve the cost saving will the government deny the consultation fee to the GP or the specialist as this comprises half the cost saving to be made? How will the government know what to pay for and what not to pay for?
- The question was also posed as to whether the two current item numbers in the schedule can be validly used? –There was comment that there is no confidence on this point.

In terms of changing the interval from 2-3 years concerns have been raised that an artificial change will just confuse, and it doesn’t make sense to change the interval if it isn’t going to be enforced. Therefore, leave the screening interval as it is.

In relation to HPV testing in regard to triage and management, widely expressed concerns that there is no fixed budget for managing women with abnormal Pap smears and the fee for service system that we have means that HPV testing could become an additional test, not a replacement test for colposcopy.
Research

The question was raised as to whether Australia needs to carry out its own research and duplicate or supplement the good quality research carried out overseas.

The point was raised that there hasn't been enough good research associated with some of the new technologies such as automated screening and other adjunctive tests.

It was discussed that we can not always translate overseas research into the Australian context as the quality and terminology of cytology varies between Australia and elsewhere, and therefore Australian research may need to be carried out.

A comment was made that if we are going to make changes on a national level we will need to do some Australian research in order instigate change and have the support of general practitioners, gynaecologists and pathologists.

It was commented that in terms of early re-screening and studies on Aboriginal women we don't need to do much more research. Similarly, in terms of quality assessment, the point was made that more research is not required, but rather, ownership of accreditation and re-accreditation is required.

There was some support for research into progression markers. Discussion surrounding this issue raised that point that p16 could be looked at as a progression marker, and HPV markers such as oncogenic transcripts are currently available and come in an ELISA format with a swab test. It was discussed that it would be valuable to undertake research to find something visible or detectable that would differentiate between high-grade lesions that will progress into cancers and high-grade lesions that aren't going to progress. It was stated that it was an important future need to be able to detect lesions that were going to progress into invasive cancers.

HPV

Comment was called for regarding HPV testing and whether there was any reason to repeat studies carried out in Europe and North America. In response, it was suggested that any introduction of molecular biology techniques will be compared to current gold standard cytology and since quality and terminology of the cytology varies between Australia and elsewhere, HPV testing in Australia with an Australian population is needed.

The suggestion was made that HPV research could be carried out in the areas of triage and post-treatment care of women.

There was discussion on the developing HPV vaccine and the need to carry out high-risk HPV prevalence studies in Australia. The point was raised that evidence shows that different countries can have a different prevalence of different types of HPVs and it was suggested that the prevalence of different types of HPVs in the normal population and in cervical cancer in Australian needs to be known prior to using the HPV vaccine. The point was raised that we need to know whether there was going to be a shift in prevalence of HPV types in Australia post-vaccination. In reply, the comment was made that knowing the prevalence of particular HPVs types would not affect policy and prevalence studies would purely be of academic interest.

The question was raised as to whether as a community we need to address the fact that HPV is a sexually transmitted infection (STI). In response, it was discussed that we need to be honest with people and inform them that HPV is a STI in the vast majority of instances. Further comment was made of the importance of what patients with an abnormal Pap smear are told in relation to HPV. It was suggested that HPV be discussed with patients in the context of cancer prevention but mention should
be made that HPV doesn't fit into the same STI model as gonorrhea and chlamydia. The point was also made that explaining the concept that HPV is an STI to patients is not distressing for the patient providing you are honest and take the time to talk to the patient about it. The alternate view was also expressed and it was felt by some that the fact that HPV is a STI should be downplayed to patients. Particular mention was made of the fact that there should be care taken in the terminology used and the explanations provided to the patients.

**Screening**
With reference to changing the screening interval and the age of screening, the audience was informed that a further evaluation is already underway: the National Cervical Screening Program is reviewing the screening policy in terms of age range and screening interval between tests. It was mentioned that a contract has been let to repeat the analysis that was in the 'options for change' book. It was further stated that the analysis would be extended to current expenditure to provide an idea of what the savings would be if the interval was changed and what the costs would be in terms of additional cancers that may have been prevented with a different screening regimen. It was noted that the results of the study should be known by early 2002 and will subsequently feed into a policy review framework.

**Changing the screening interval**
It was commented that the decision to adopt a two-year screening interval was a pragmatic decision as opposed to a scientific decision. It was discussed that a two-year screening interval was agreed to providing various infrastructure safeguards were in place. Further comment was made that we have all the infrastructure in place and people could be reassured that we could increase the screening interval further. The point was raised that we haven't been successful in encouraging women to adopt a two-year screening interval as it has been shown that between 35-40% of women are screened more frequently than every two years.

The opinion was also expressed that changing the screening interval from two to three-years may not improve the compliance with the interval.

The point was raised that there is an argument to be made for basing the screening policy on rational scientific grounds and the current scientific evidence so there is a clear policy that makes sense and is best for the patients and protects the clinician from litigation. The comment was also made that we will have to continue to pay for women to have more frequent smears because there are pragmatic problems with trying to convince everybody to change their current practices.

The comment was made that changing from a two-year to a three-year screening interval has costs associated with it. It was further discussed that a lot of public education and public money would be needed to change behavior as there would have to be media campaigns, on-the-ground community development and multi-layered strategies implemented in order to effectively make this change.

The question was raised as to what a shift in screening interval to every three years would do to women who are currently screened more than every three years?
In reply it was stated that there is not much evidence that women who are told to attend cervical screening every two years attend every three years and even if women are currently attending screening every three years, when asked to attend every two years, this it is not a majority action.

The question was asked as to whether it would be acceptable to women to promote a change in screening interval with the savings made being re-directed to other areas of women's health. The question was also raised as to whether the redirection of savings back to women's health would be acceptable to the Commonwealth. In response it was stated that it was difficult to say what would actually happen to any savings made, however, the suggestion was made that the National Advisory Committee (NAC) to the National Cervical Screening Program and the NCCI could make
recommendations for the redirection of savings into other aspects of the screening program or other cancer initiatives. Mention was also made that the federal government has a range of activities that it funds and there would be no guarantee that the funds saved would go back to health care.

**Individualised screening intervals**

The question was raised as to whether registries would be able to individualize screening intervals based on the patient’s screening history. The example was made that we have a mammography register that informs women when they need to have their next breast screen so why can’t we have a system that tells women when they can come in for their next Pap smear? In response it was commented that it would be a very useful idea to have different intervals for women with different risks, however, in terms of a public education campaign different screening intervals for different women would be hard to promote. The point was made that it would be difficult to tell some older women that they don’t need to be screened often whilst trying to recruit the women who are not being screened. The point was raised that there would be a great risk of sending out mixed messages and confusing the public.

**Age of commencement of screening**

Discussion was initiated around the age of commencement of screening. It was noted that a slide shown during the presentations showed no change in age-adjusted mortality in women less than 35 years. Discussion was held around the topic ‘can we propose a later start to screening?’ The point was raised that cervical cancer in women under the age of 35 years is extremely rare. Discussion around an increasing understanding of the role of HPVs and the natural history of the disease led to the issue of how significant is HPV infection in women in their teens and twenties in terms of the development of cervical cancer. Further comment was made that adopting an overly aggressive approach to women in that age group is not serving them well. The point was also raised that in countries where cervical screening is not done in these age groups there is no difference in mortality and there is a large cost to the national budget by managing abnormalities in this age group with very little gain.

The question was then raised as to whether screening should commence at 25, 30 or 35? In reply it was suggested that this issue needs to be looked at and agreement needs to be made. It was commented that it was a simplistic approach to say that abnormalities exist in women in their teens and twenties and therefore women in this age group need to be screened.

**Over-screened and under-screened women**

Regarding the number of unscreened women diagnosed with cervical cancer in Australia the question was put forward as to why there isn’t a focus on education services or recruiting the unscreened women into the service. The comment was made that eventually the screening program will plateau at a certain level and this will include women who have never been screened who present with cervical cancer. The point was then raised that focusing on screening will reduce the incidence and mortality of cervical cancer.

The point was also made that we should be concentrating on reducing over-screening and investing money in under-screened women.

It was commented that of the unscreened women who develop cervical cancer in Australia many of these women are indigenous women. It was further discussed that there are significant problems in reaching indigenous women for primary screening and follow-up and it was suggested that some money could be invested in this area.

Further discussion was held surrounding the under-screened aboriginal population. It was commented that there may not be a way of increasing the amount of cervical cytology in this population unless it is incorporated into a much larger program of women’s health. Further comment was made that trying to
screen remote aboriginal communities without addressing all the other matters associated with health provision is not going to work and we may need to incorporate cervical screening into a larger program.

Discussion was held around the topic as to what strategies we would like to see or are currently seeing for over-screened and under-screened women. In reply it was commented that a lot of quantitative research has been done with both women and general practitioners looking at why women are being over-screened. It was noted that it was both the provider and the woman that were contributing to that decision. However, when given sufficient information to support a change, women were comfortable changing from annual to two-yearly screening. It was commented that this decision had to be supported by providers.

**Economics**

A comment was made that it was important to use Australian data to make decisions based on the economic aspects of altering the screening interval or changing the age of first screening. It was explained that undertaking marginal analysis that does not use Australian data to analyze costs and benefits of changing the current guidelines is a dangerous practice as is the comparison of cost effectiveness ratios derived from studies that are conducted in different countries at different points of time. It was further pointed out that one of the critical issues in cost effectiveness analysis is to make sure that the costs that are being measured, as well as the outcome data, are relevant to the economy being looked at otherwise the results can not be easily trusted. It was concluded that this is the purpose for conducting another Australian cost effectiveness analysis of the proposed changes. A cost effective analysis is currently looking at optimal intervals for screening and optimal age ranges.

The suggestion that we should be concentrating on reducing over-screening and reinvesting the saved monies into under-screened women was made.

Comment was called for on whether the Cervical Screening Program should have a research and development budget within the program and, if so, what would be the priorities? Would the NAC decide the priorities? There was agreement that the National Cervical Screening Program should have its own budget. It was discussed that most of the money spent on Pap smear screening and associated investigations in Australia is billed under a fee-for-service under Medicare. The actual amount of program money that is outside Medicare is only 10-12 million dollars per annum and from that money the registries with the reminder system are run, media recruitment strategies are paid for and the NAC is convened. The comment was made that there isn't a large amount of money that could be partitioned off for research and development with out compromising other existing services. It was mentioned that the Cervical Screening Program costs about 150-160 million dollars a year and almost all of that is billed to Medicare. This raised the question as to the logistics of raising a research budget and whether the Pap smear and colposcopy fee would be reduced by 10% so that money could be allocated to research and development. Examples of other programs such as the National Immunization Program and the National Breast Screen Program were raised and the comment was made there is little, if any, money allocated in these programs for research and development.

The question was then asked as to whether we should be lobbying to ensure such programs have a research and development budget in addition to an infrastructure budget. In reply the point was made that the Commonwealth Government may argue that they already fund research and development through the NHMRC. It was discussed that the NHMRC funds fundamental research, however, the NHMRC will not fund initiatives such as changing the management or clinical guidelines or other aspects of the program, yet, these issues could have considerable consequences for the performance or the cost of the program. It was also pointed out that obtaining a research and development budget may not be achieved quickly, however, if Australian research on a topic is required there should be provision made for it.
The suggestion was made that Medicare should have a research and development budget.

It was commented that we shouldn't get caught up in whether the research funds come from NHMRC or are associated with the program budget, but rather, we should be advocating more targeted and strategic research. It was suggested that the Strategic Research Development Committee may be one avenue through which strategic policy based research could be funded.

**General**

Discussion on the follow-up of patients with treated abnormalities was introduced. The question was asked whether women go back to the same risk as the general population following the successful treatment of pre-cancerous abnormalities and if they do, why do we recommend annual screening in this group of women? In response, it was discussed that women after treatment do not go back to the same risk level as women who have not had cervical intraepithelial neoplasia (CIN), rather, these women still carry a three to four fold higher risk for a recurrence of high grade histology. However, it was acknowledged that even if a woman was at higher risk of developing a lesion it did not mean that this later lesion would develop any faster than a first lesion. It is not known whether this higher risk is consistent or diminishes with time. The point was raised that the origin of the 12-month repeat was a pragmatic decision to acknowledge the concerns of gynaecologists and there isn't an epidemiological or scientific basis for a repeat at a 12-month time frame. The point was also made that the screening interval has more to do with the sensitivity of the test and the rate of progression from non-invasive to invasive disease and there is no evidence to show that women with recurrent lesions have an accelerated rate of progression.
Suggestions for development

1. Negotiation of a separate research and development budget within the National Cervical Cancer Screening Program

2. Undertake targeted policy related research, with priorities determined by NAC and other stakeholders

3. Undertake an analysis of women with many consecutive negative smears, estimate their risk of developing cervical cancer and build that into the screening program in terms of changing screening intervals

4. Development of tests which give insight into the malignant potential of high grade lesions

5. Undertake research around issues of over-screening and under-screening

6. Further assessment of the benefits and risks of changing the screening interval

7. Develop Australian research on HPV

General Comments
The meeting was thought to be a valuable by those present, and wider consultation and discussion on cervical screening was felt useful.
There was recognition of the rapid development in the field, and general agreement that Australian research and policy should be in accord with scientific advances. The general impression from the discussion was that changes in screening policy should be considered if the evidence supported them.

Note.
No formal recommendations or votes were planned and none asked for. The above comments reflect the overall impressions from the meeting.


