



Victorian Cytology Service

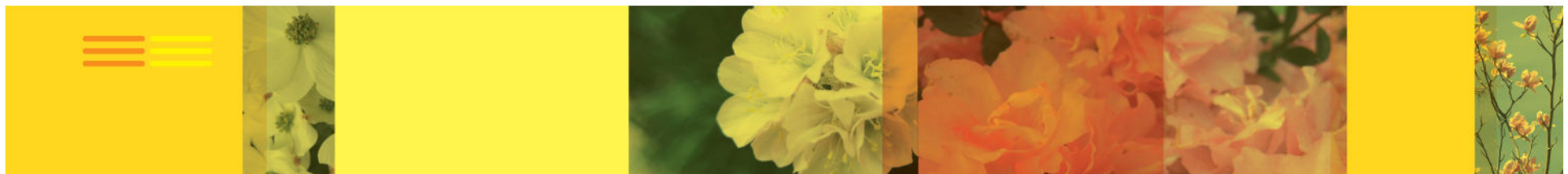
≡ The impact of National
HPV Vaccination
Program on cervical
screening



Associate Professor
Marion Saville

Impact of the HPV vaccine on the NCSP

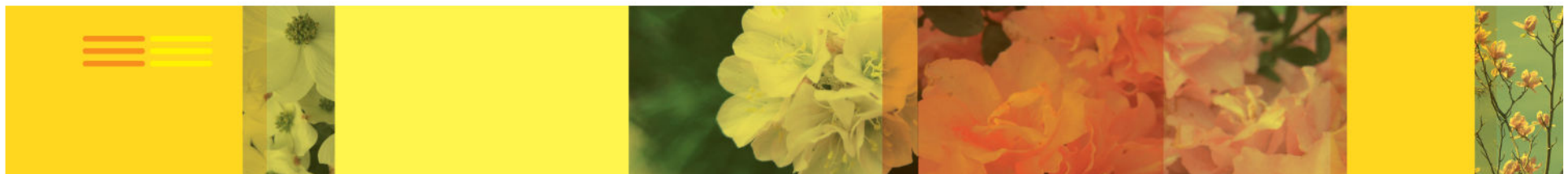
1. Confusion about the need to continue screening
2. Reduction in the numbers of abnormalities detected
3. Reduction in the number of cancers





Confusion about the need to continue screening

- Any change to screening recommendations will not affect women already being screened, so our existing programme will need to continue in some form until the youngest of these women reaches the age of stopping screening, presently 69 years

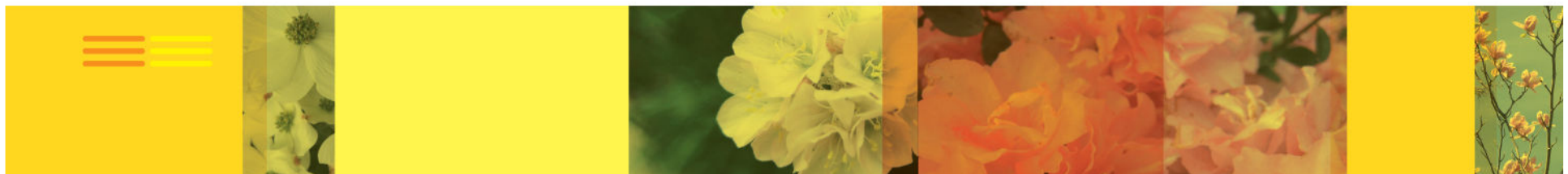




Confusion about the need to continue screening cont/..



- Because the vaccine only protects against HPV 16 and 18 related cancers some form of screening will still be required by the vaccinated cohort, albeit potentially a modified screening programme.

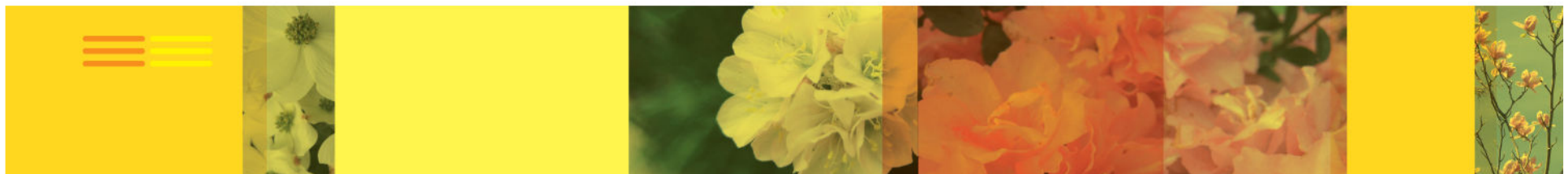




Confusion about the need to continue screening cont/..



- This is being addressed in the information provided to girls, parents and women by the vaccination program
- In Victoria, our cervical screening program has also utilised media releases to reinforce this message





At last
there's
some
good news
about
cancer.

National cervical cancer vaccinations begin April 2007.

Cervical cancer is the second most common cancer in women worldwide which is almost always caused by the human papillomavirus (HPV).

The good news is that a new vaccine, developed in Australia, can protect against HPV, the cause of up to 70% of cervical cancers.

The other good news is that the Australian Government is making the cervical cancer vaccine available free to

all females aged 12 to 26 under the National HPV Vaccination Program.

For girls at school, the program starts in April 2007. A consent form will be sent home shortly for parents to fill in and return.

For women who have left school, and are under 27, the free vaccine will be available from your GP or community immunisation clinic from July.

The vaccine doesn't prevent all cervical cancers, so regular Pap smears are still essential.

But a free cervical cancer vaccine is still very good news for women.

Help protect your daughter from cervical cancer. Sign the consent form.

For more information:
National Immunisation Hotline 1800 671 811
australia.gov.au/cervicalcancer



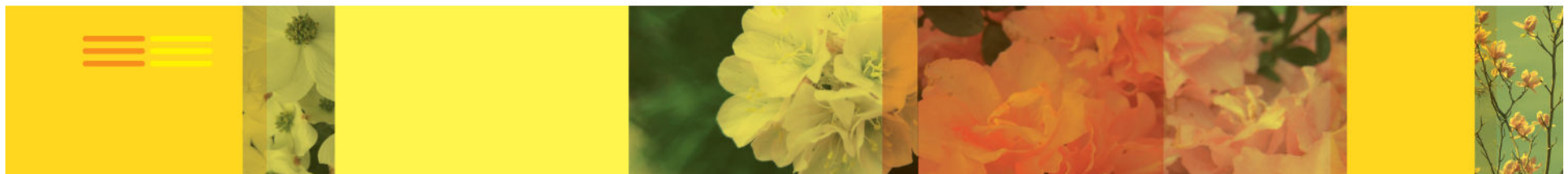
Australian Government



Confusion about the need to continue screening cont/..



- Workforce implications in cytology
 - Informally we are seeing some hesitation on behalf of students in the lab science degree at RMIT to select cytology as a major subject and to enter this field of study and employment

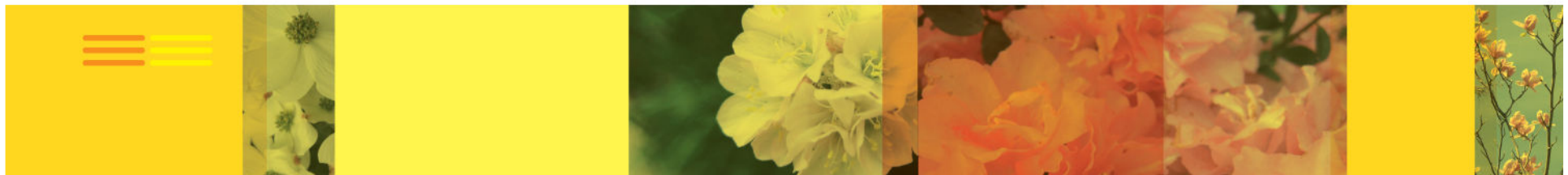




Confusion about the need to continue screening cont/..



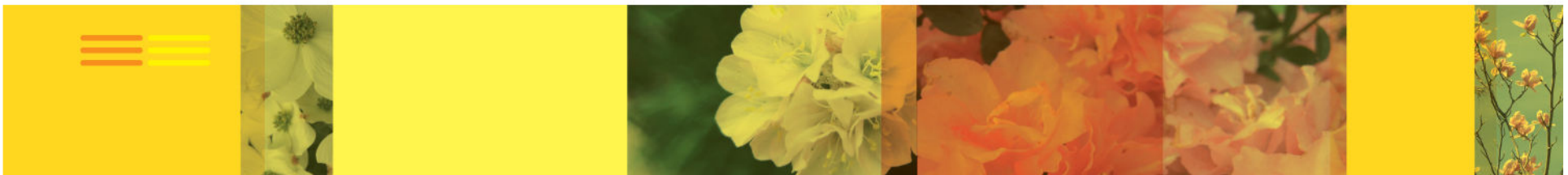
- Workforce implications in cytology
 - This may mean that there is a substantial decline in capacity to report Pap smears that precedes any significant decline in demand





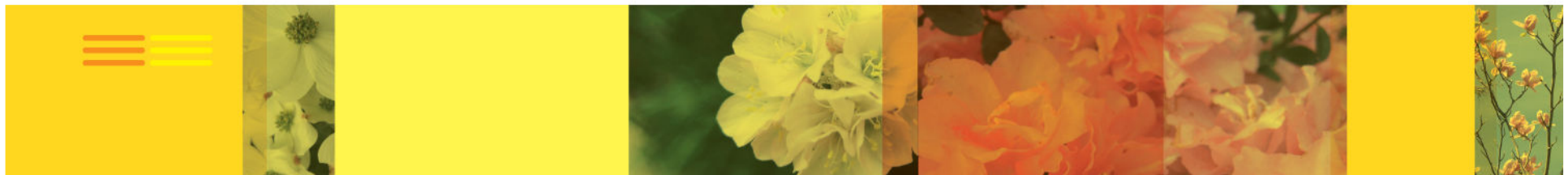
Impact of the HPV vaccine on the NCSP

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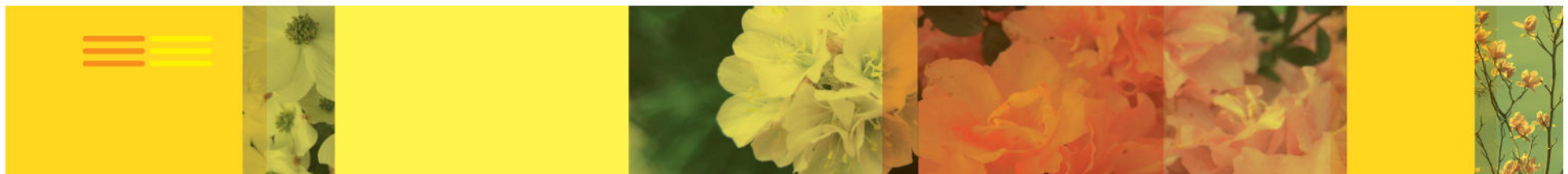
Reduction in the number of abnormalities detected in Pap tests

- ↓ in LSIL, estimate of around 20%
- ↓ in HSIL, estimate of around
 - 40% for those vaccinated against 16/18 and
 - 50% for those vaccinated against 6/11/16/18



Reduction in the number of abnormalities detected in Pap tests cont/...

- It is unclear how long these reductions will take
- However, given the extent of the publicly funded catch up program, this will occur sooner in Australia than elsewhere.



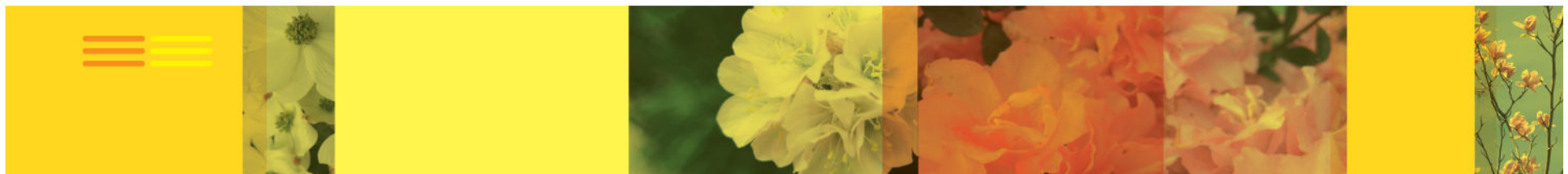


Reduction in the number of abnormalities detected in Pap tests cont/...



- The implications of a reduction in LSIL and HSIL are:
 - Firstly a reduction, in the need to work up these abnormalities and a reduction in associated financial, time and psychosocial costs.

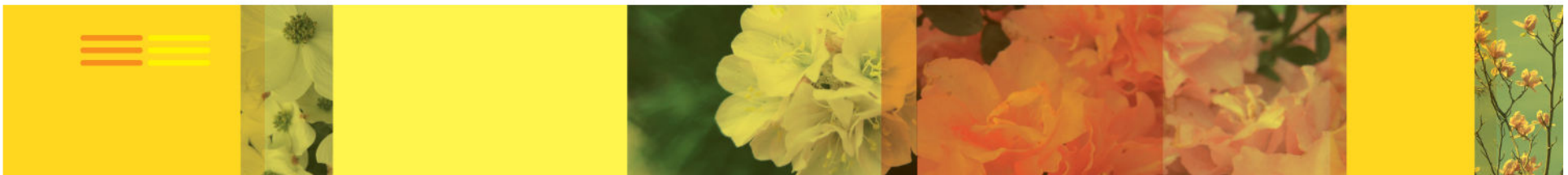
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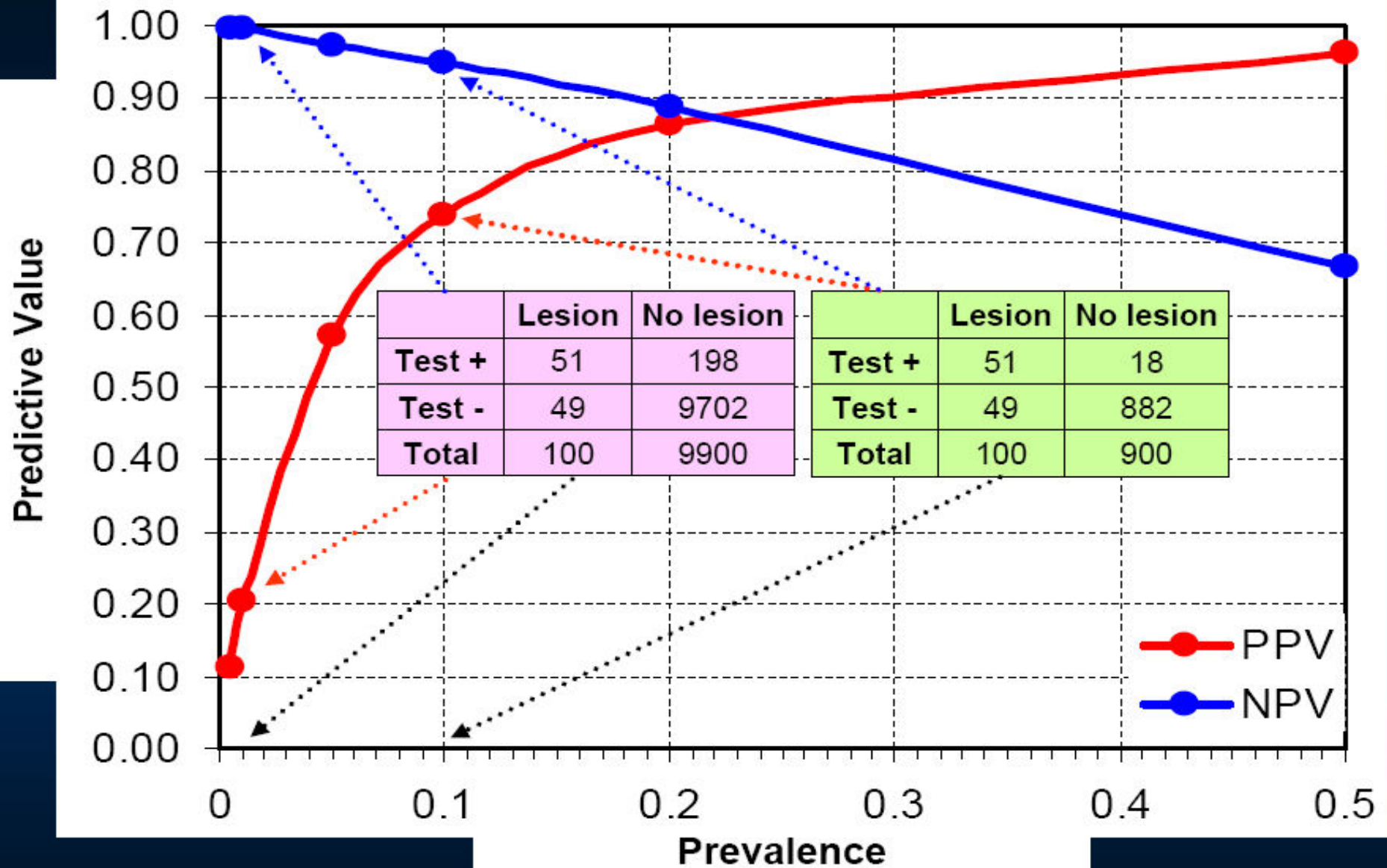




Reduction in the number of abnormalities detected in Pap tests cont/..

- Fewer abnormalities seen by scientists may lead to reduced expertise
- The reduced prevalence of these abnormalities will mean a reduction in the positive predictive value (PPV) of these diagnoses





Assumptions: constant 51% sensitivity and 98% specificity (as per Nanda et al., 2000)

Franco et al., Vaccine 2006



Reduction in the number of abnormalities detected in Pap tests cont/..



- There are implications for laboratory performance measures
 - Std 1: Unsatisfactory rate
 - Std 2: HGA detection rate
 - Std 3: PPV of HGA predictions
 - Std 4: “False Neg” rate
- NPAAC will need to review these measures in view of the predicted fall in the prevalence of HGAs

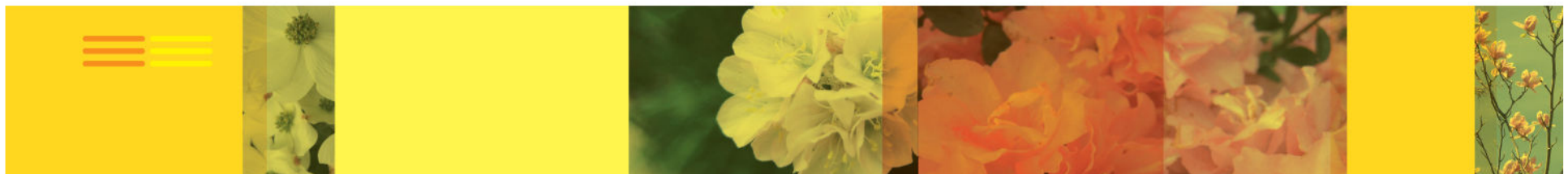
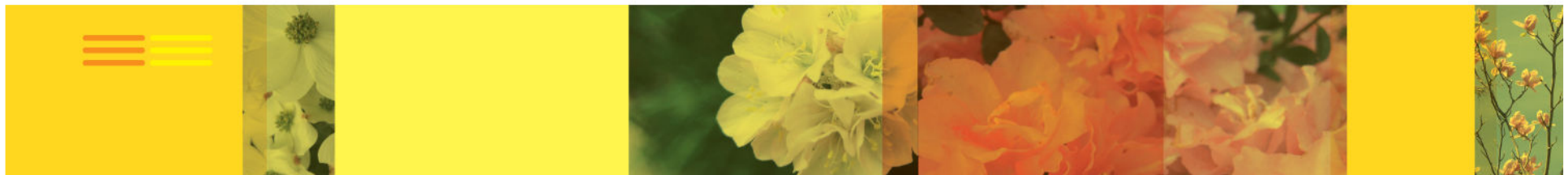


Image assisted LBC

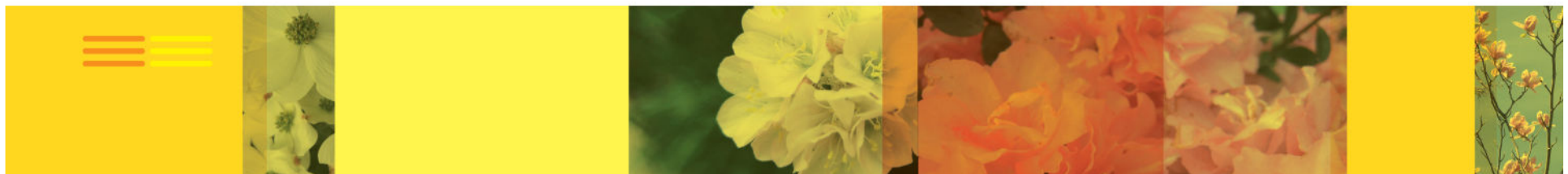


- May have two strategic advantages not captured by classical cost effectiveness analysis
 - The increased productivity may be needed if our capacity to report cytology falls below demand in the next 5 to 10 years
 - The increased productivity (approx doubling) could compensate for the reduced prevalence of abnormalities and thus the absolute number of abnormalities seen by scientists could be maintained



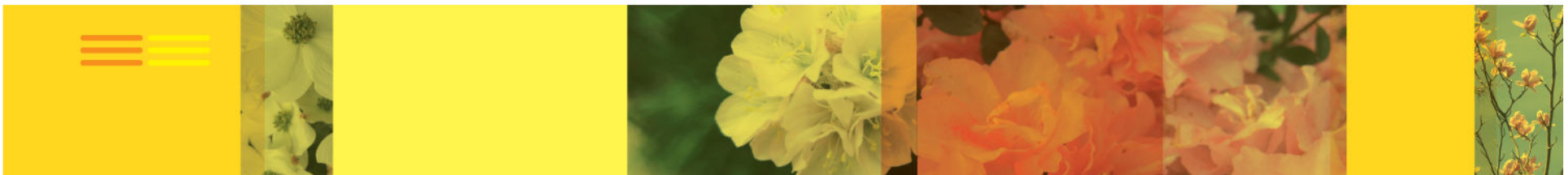
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Reduction in the number of cervical cancers

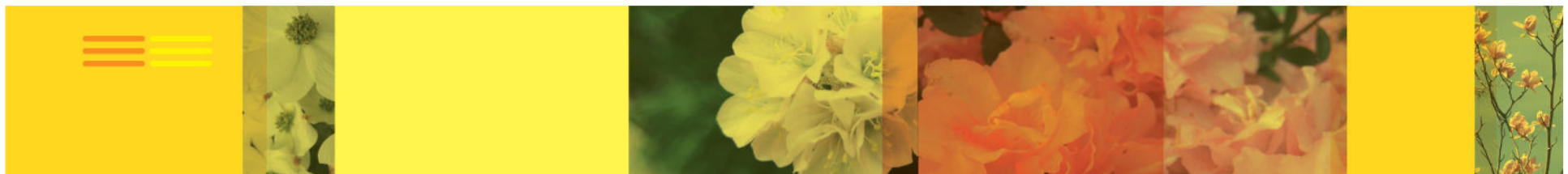
- Worldwide HPV 16/18 account for 70% of all cancers
- Australian specific data suggests that HPV 16/18 may account for closer to 80% of cancers.



Reduction in the number of cervical cancers



- These reductions will take decades.
- The reduction in cancer burden through primary prevention will make our existing screening programme much less cost effective.

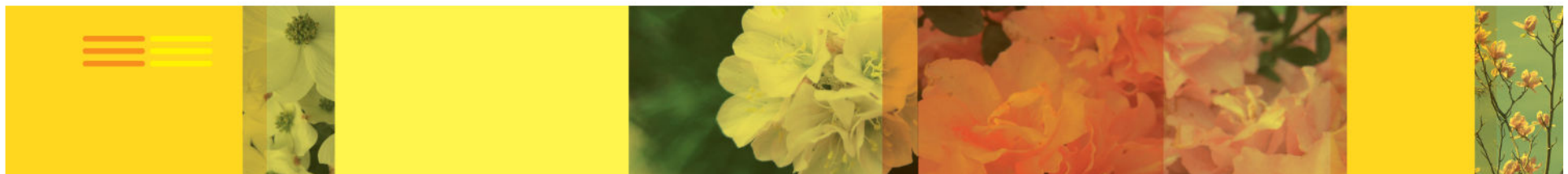




Cervical screening in the era of HPV vaccination



- Do we have different screening programmes for vaccinated and unvaccinated women?
 - **too complex**
 - Will practitioners contact a register on a woman by woman basis before collecting a Pap smear?
 - Will practitioners rely on women's recall?

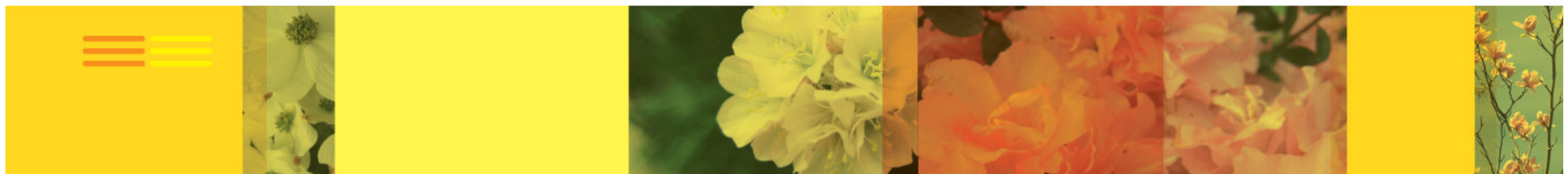




Cervical screening in the era of HPV vaccination cont/..



- Do we screen all women less intensively?
 - equity issues
 - This approach will compound the differences in outcomes between those inclined to be vaccinated and those who are less likely to be vaccinated



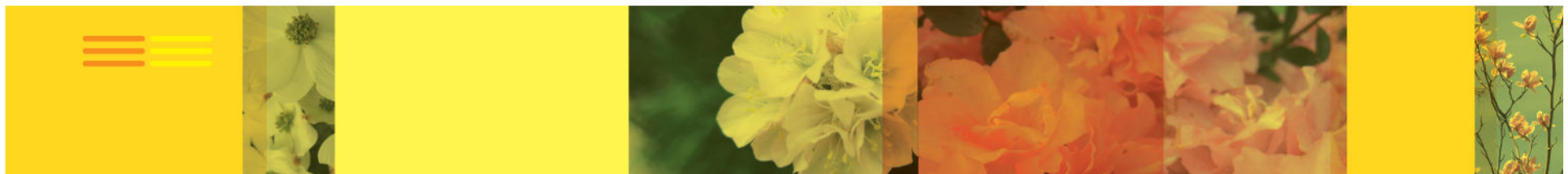
Why might a women in a vaccinated cohort develop cancer?



- Not vaccinated
- Missed some doses
- Vaccine failure
- Other oncogenic types

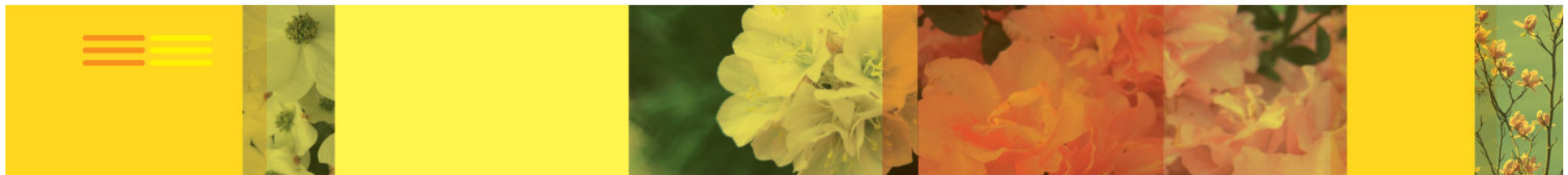
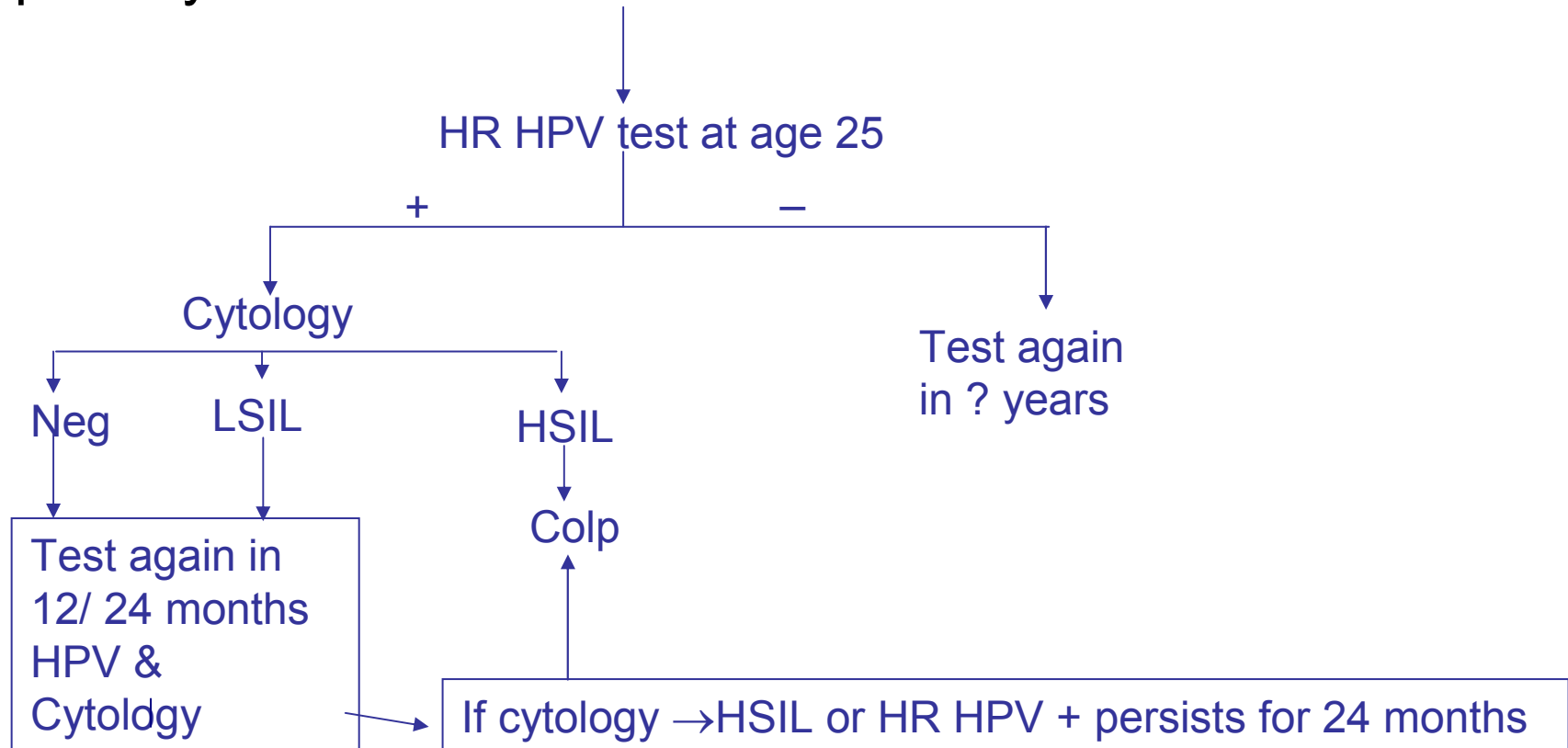


All will have acquired high risk HPV infections and developed persistence



Proposed screening algorithm

Start with all women who are of an age to be offered publicly funded vaccination.





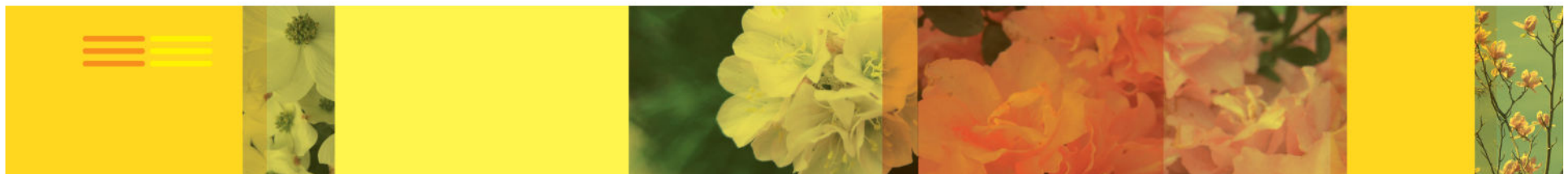
Cervical screening in the era of HPV vaccination




This “inverse screening” has been the subject of a number of trials overseas that are currently reaching conclusion.

The main drawback of this strategy in the current environment is that @ 25 years about 20% of women can be expected to test positive.

However, if almost all women were vaccinated then the proportion of women testing positive to HR HPV can be expected to dramatically decline.



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- Long term predictive value of cytology and human papillomavirus testing in cervical cancer screening: joint European cohort study

– *BMJ* 2008; 337; a1754

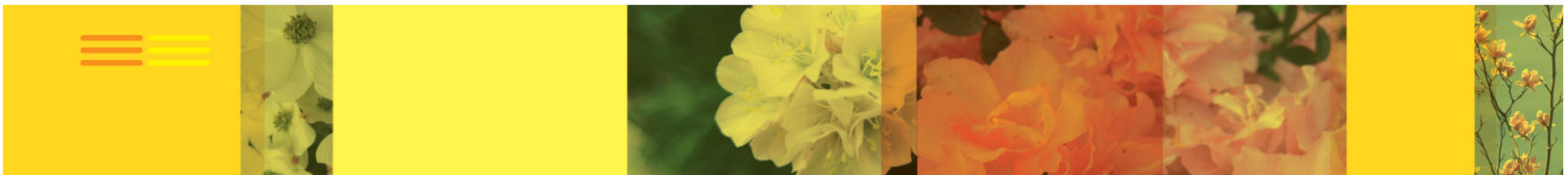


Table 1 | Study characteristics of seven European human papillomavirus (HPV) screening studies

Study	No initially screened	No analysed*	Age	Entry criteria	HPV test	Follow-up†	Histology
Germany-Hannover	4699	4107	≥30	No history of abnormal smear result, CIN, or treatment for cervical disease in past year and not pregnant	HCII	If cytology+ or HPV+ immediate and an annual colposcopy‡ for 5 years. 5% of cytology-/HPV- to colposcopy after 5 years	Blinded central review
Germany-Tubingen	672	670	≥30	No history of abnormal smear result, CIN, or treatment for cervical disease in past year and not pregnant	HCII	Cytology-/HPV- to new tests after 5 years and if either positive referred to colposcopy	Blinded central review
Sweden	6448	5671	32-38	Participating in organised screening	GP5+/6+ PCR	Cytology-/HPV+ invited for new test >1 year later, if persistent HPV+ referred to colposcopy. Similar number of women randomly referred to colposcopy. Database linked with regional pathology registries	Regional pathology labs§
Denmark	2287	2274	20-29	No current evidence of cervical neoplasia	HCII	Study data base linked with the National Pathology Registry	Regional pathology lab§
UK	2720	2322	≥35	No previous cervical treatment or abnormal smear result within past 3 years	SHARP-PCR, HCI, HCII	SHARP-PCR+ or cytology+ referred to colposcopy	Blinded central review
France	17 247	7935	No age limits	No abnormal smear result or untreated cervical lesion in past 2 years. Not HIV positive	HCII	If cytology-/HPV+ new tests after 6-12 months and if persistent HPV+ referred to colposcopy. 15% cytology-/HPV- referred to colposcopy	Blinded central review
Spain	2012	1316	Matched to general population	Population registry or attending screening	HCII	Follow-up tests 1 and 5 years later. Persistently HPV+ referred to colposcopy	Regional pathology lab§

HCII=hybrid capture II; CIN=cervical intraepithelial neoplasia; PCR=polymerase chain reaction.

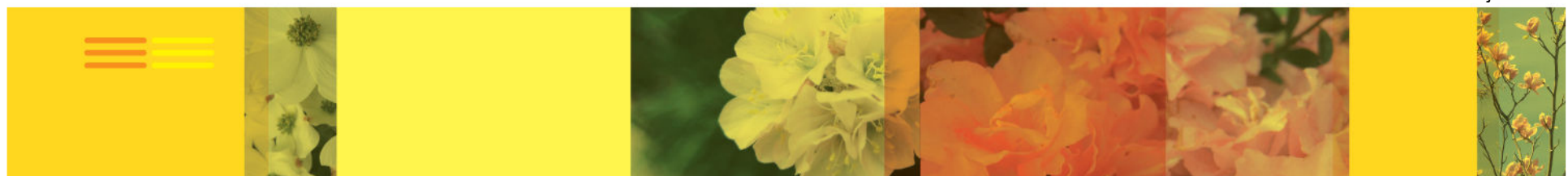
*Women with at least one follow-up cytology or histology.

†Follow-up procedures performed in addition to routine clinical practice.

‡Assessment by colposcopy.

§Blinded to HPV status.

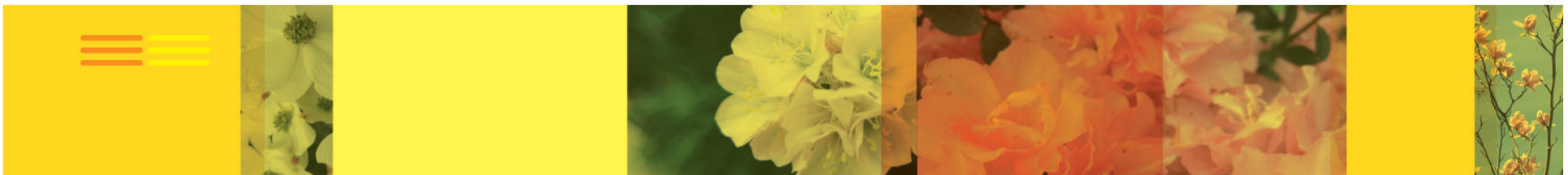
BMJ 2008;337:a1754
doi:10.1136/bmj.a1754





Victorian Cytology Service

- 24,295 Women
- 6 Years follow-up
- 381 Developed CIN 3 +



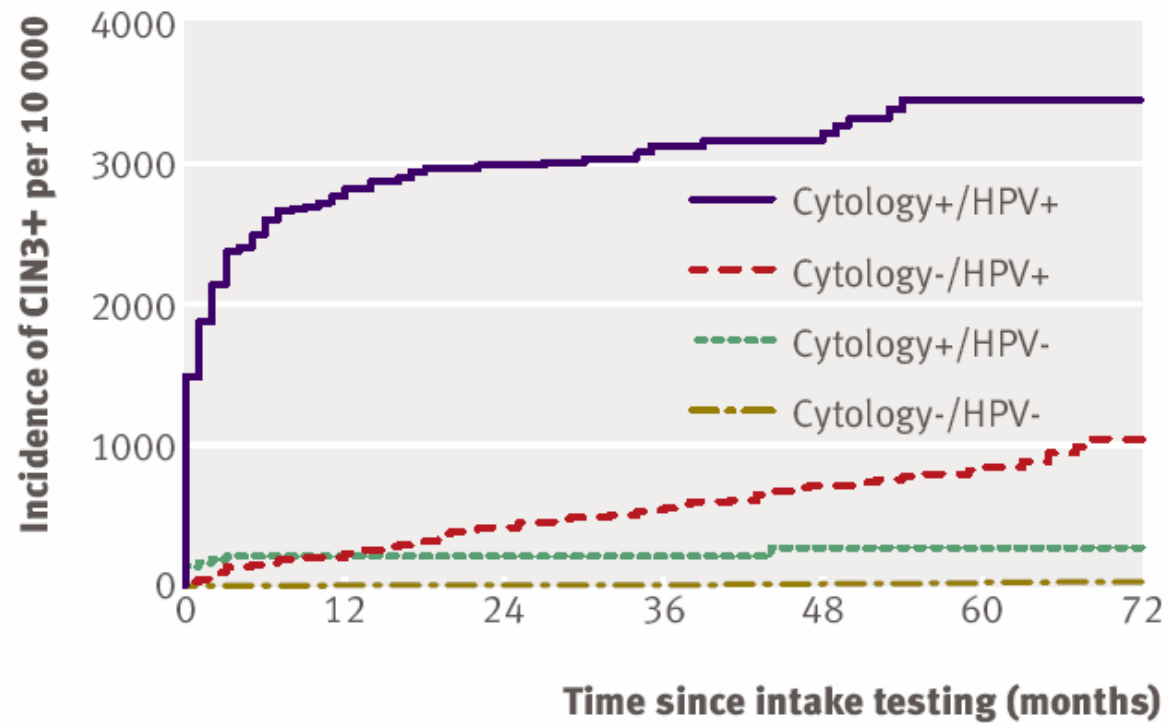


Fig 1 | Kaplan-Meier plots of cumulative incidence rate for CIN3+ for women according to baseline test results in the first 72 months of follow-up in all seven countries



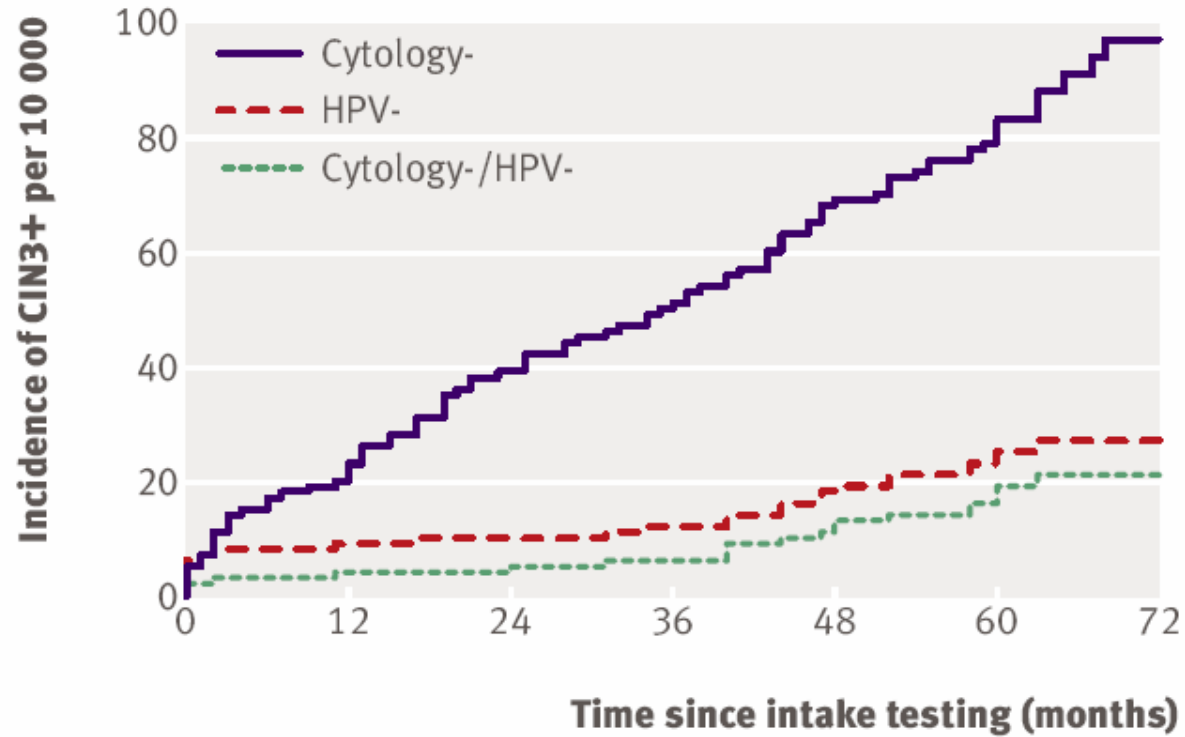
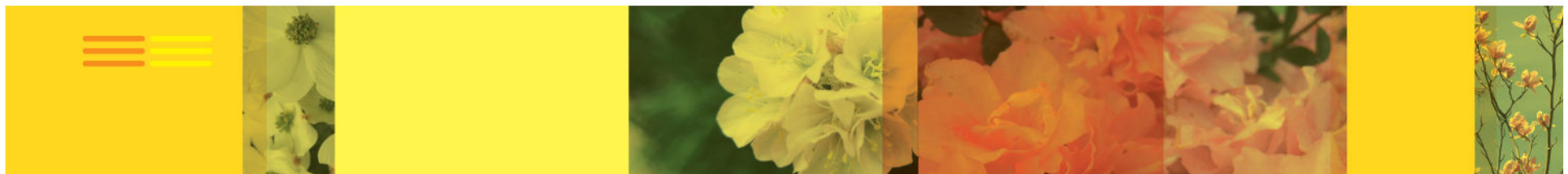


Fig 2 | Kaplan-Meier plots of cumulative incidence rate for CIN3+ for women according to baseline test results in first 72 months of follow-up, excluding Denmark and Tübingen

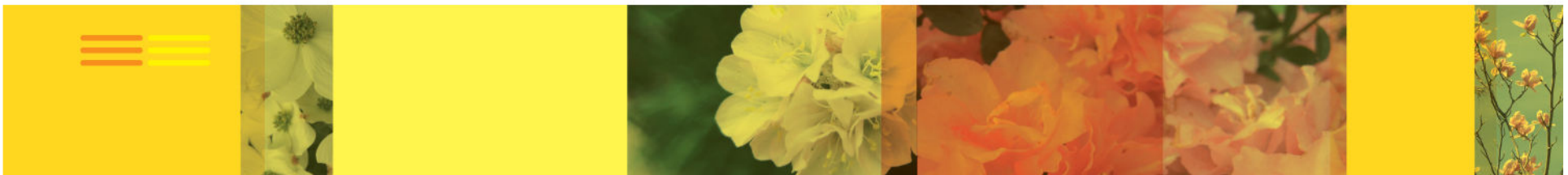
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PPV for CIN3 +



HPV -	0.27%	(0.12 to 0.45%)	6 years
CYTO -	0.97%	(0.53 to 1.34%)	6 years
CYTO -	0.51%	(0.23 to 0.77%)	3 years

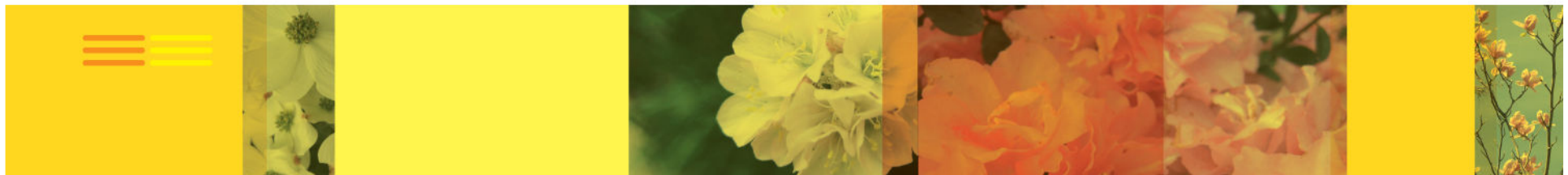




Concerns about adopting HPV testing in cervical cancer screening



- Modifications to existing screening programmes will be costly and will require extensive changes in workforce
- At present, the unit cost for HPV testing is higher than that for conventional cytology
- Screening for HPV will create a dependence on commercial interests
- Health education issues



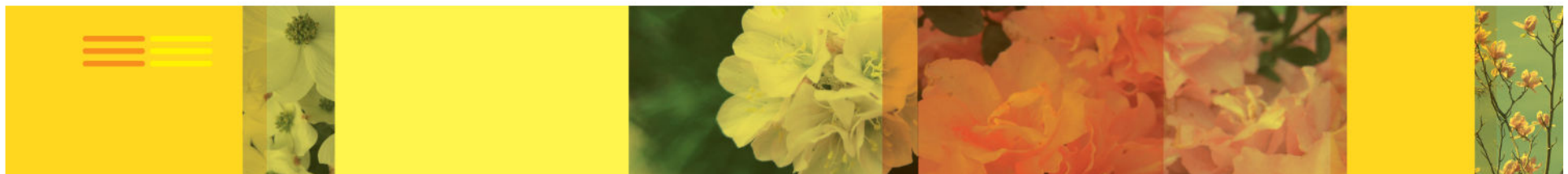


Other benefits from the HPV-Pap screening algorithm

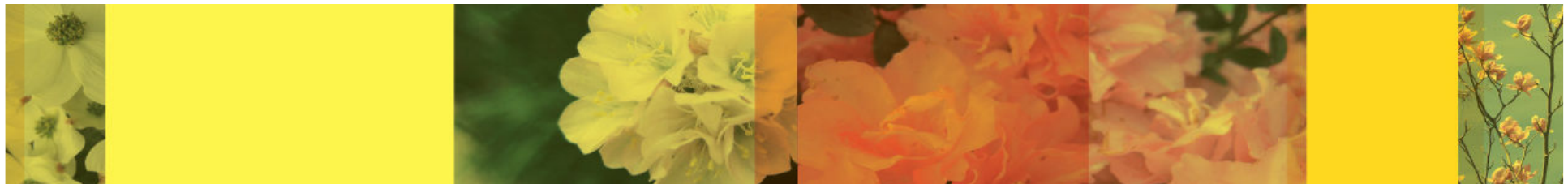
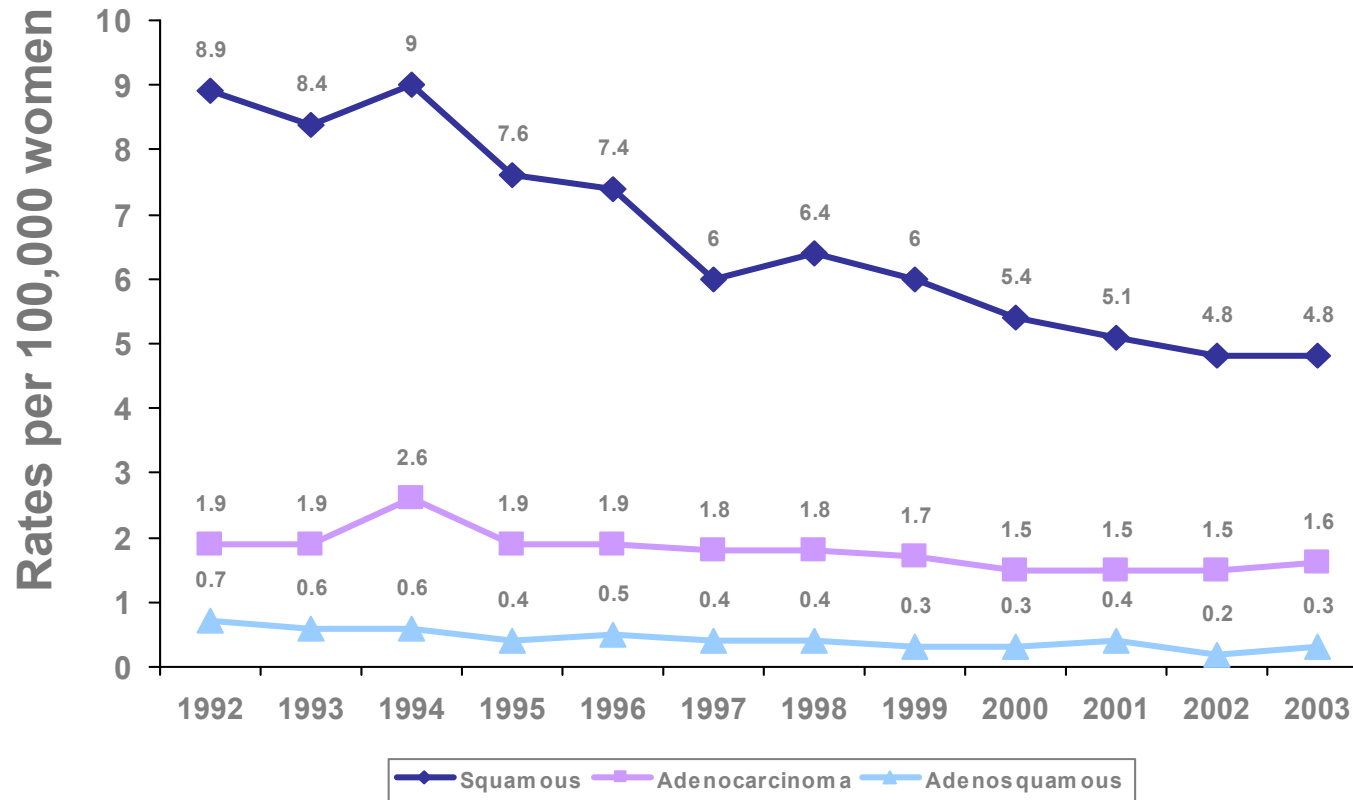


- Rational approach to address concerns that frequency of screening must not be changed to avoid missing lesions caused by other oncogenic HPV types
- Improved detection of glandular lesions

Franco et al., Vaccine, 2006



Incidence Rates for Cervical Cancer 1992 - 2003



**Screening history of Victorian women diagnosed with an invasive cervical cancer for the period
1 January 2002 and 31 December 2004.**

Screening History	Squamous cell carcinoma		Other invasive cervical cancer*		Total	
	Number	%	Number	%	Number	%
A. Women never screened	78	31%	56	39%	134	34%
B. Women with inadequate screening	155	63%	49	34%	204	52%
C. Women with some screening history**	15	6%	39	27%	54	14%
Total	248	100%	144	100%	392	100%

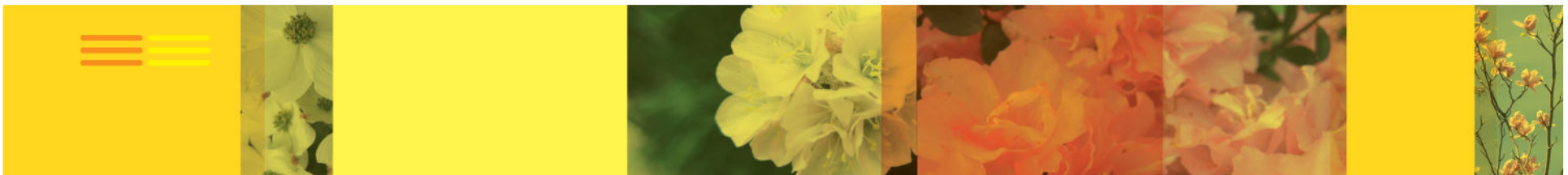
* Other cervical cancers include small cell carcinoma, mixed adenosquamous and Adenocarcinoma.

** Requires further review



The future of cervical screening

- Primary HPV test
- Reflex LBC
- Start at age 25
- Test every 5 years



Next steps



- Formal review of evidence regarding primary screening with HR HPV
- Model proposed screening pathways
- Implement modified screening
- Assess the outcomes through post-vaccination surveillance using vaccination and Pap test registers

