Follow up after Tx

Why do we need FU?

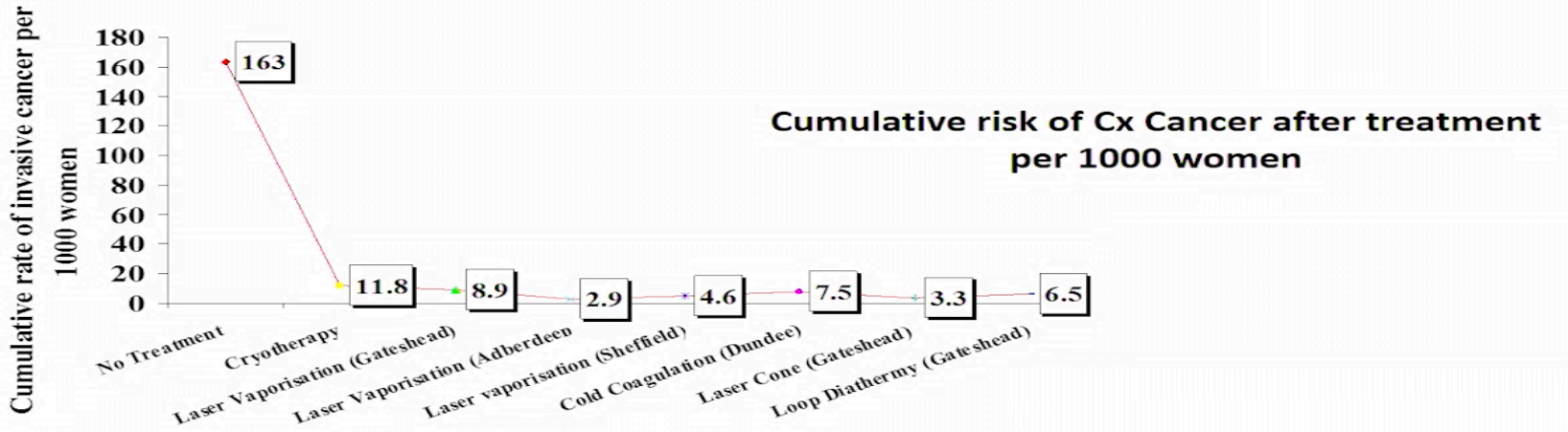
- Local CIN Treatment: highly effective (all techniques)

Martin-Hirsch Cochrane Library 2013

- Risk of Cx Cancer: 4-5x greater for 20y or a lifetime

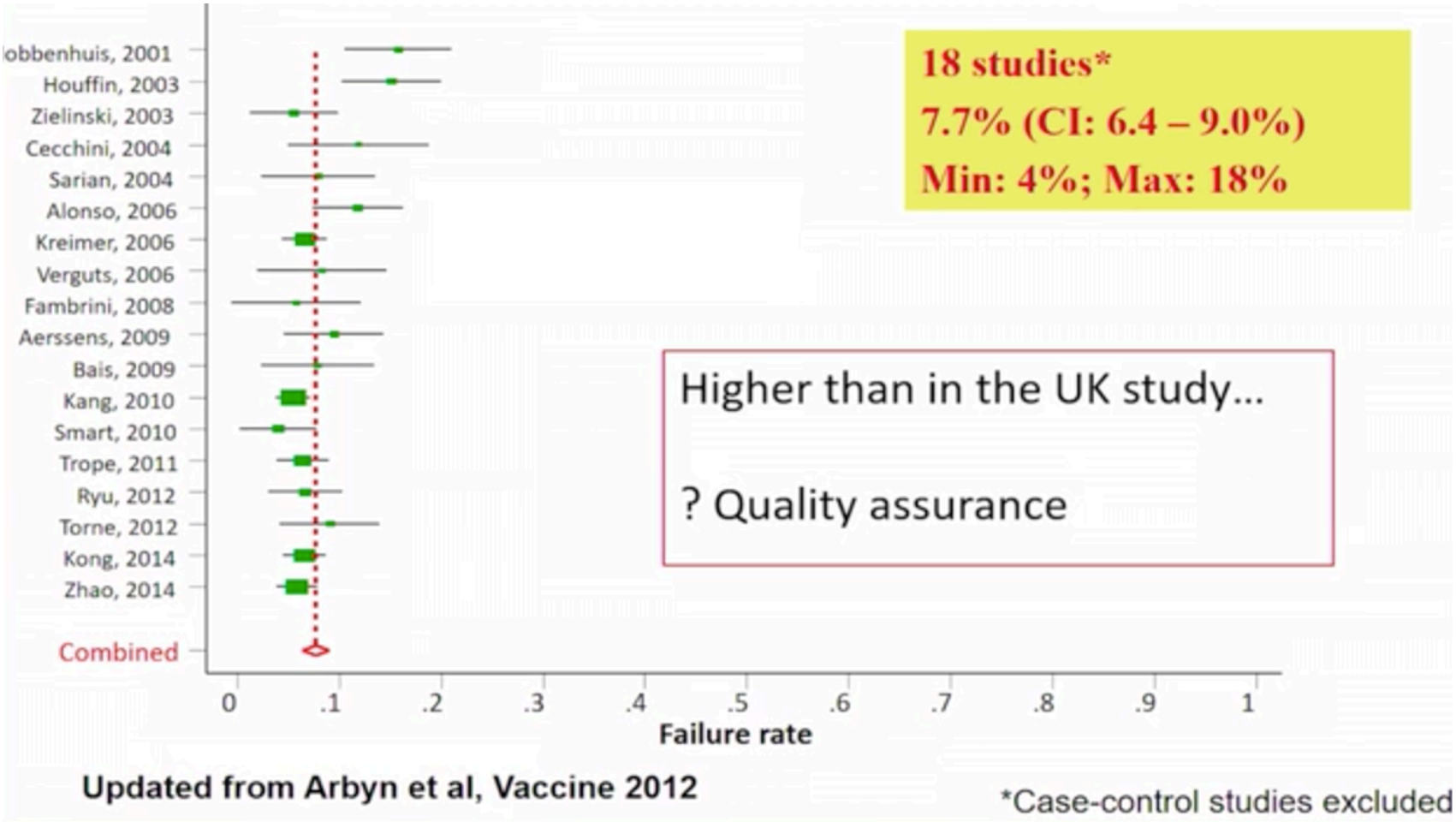
Soutter IJC 2005; Kalliala BMJ 2005; Strander BMJ 2014

=> crucial to monitor for treatment failure with an accurate test



Soutter Lancet 1997

Recurrence of CIN2+ within 12 mo



Risk of recurrence

Risk of cervical and other cancers after treatment of cervical intraepithelial neoplasia: retrospective cohort study

Ilkka Kalliala, Ahti Anttila, Eero Pukkala, Pekka Nieminen

BMJ

2005

Primary site*	Observed cases	Expected cases	Standardised incidence ratio (95% CI)
Overall cancer	448	352	1.3 (1.2 to 1.4)
Anus	3	0.5	5.7 (1.2 to 17.0)
Lung or trachea	40	15	2.5 (1.9 to 3.5)
Breast	149	135	1.1 (0.9 to 1.3)
Vulva	6	1.5	4.1 (1.5 to 8.9)
Vagina	5	0.4	12.0 (3.9 to 28.0)
Cervix:			
CIN 3	3	1.4	2.2 (0.5 to 6.4)
CIN 2	3	0.8	3.7 (0.8 to 10.9)
CIN 1	8	2.6	3.1 (1.4 to 6.2)
CIN not otherwise specified	8	3.3	2.5 (1.1 to 4.9)
Overall	22	8.0	2.8 (1.7 to 4.2)
Corpus	19	20	1.0 (0.6 to 1.5)
Ovaries	21	17	1.2 (0.8 to 1.9)
Female genital organs	74	48	1.5 (1.2 to 1.9)
Other smoking related	45	26	1.7 (1.3 to 2.3)

Effect of ageing on cervical or vaginal cancer in Swedish women previously treated for cervical intraepithelial neoplasia grade 3: population based cohort study of long term incidence and mortality

OPEN ACCESS

Björn Strander *consultant*[1], Jonas Hällgren *biostatistician*[2], Pär Sparén *professor*[2]

2014

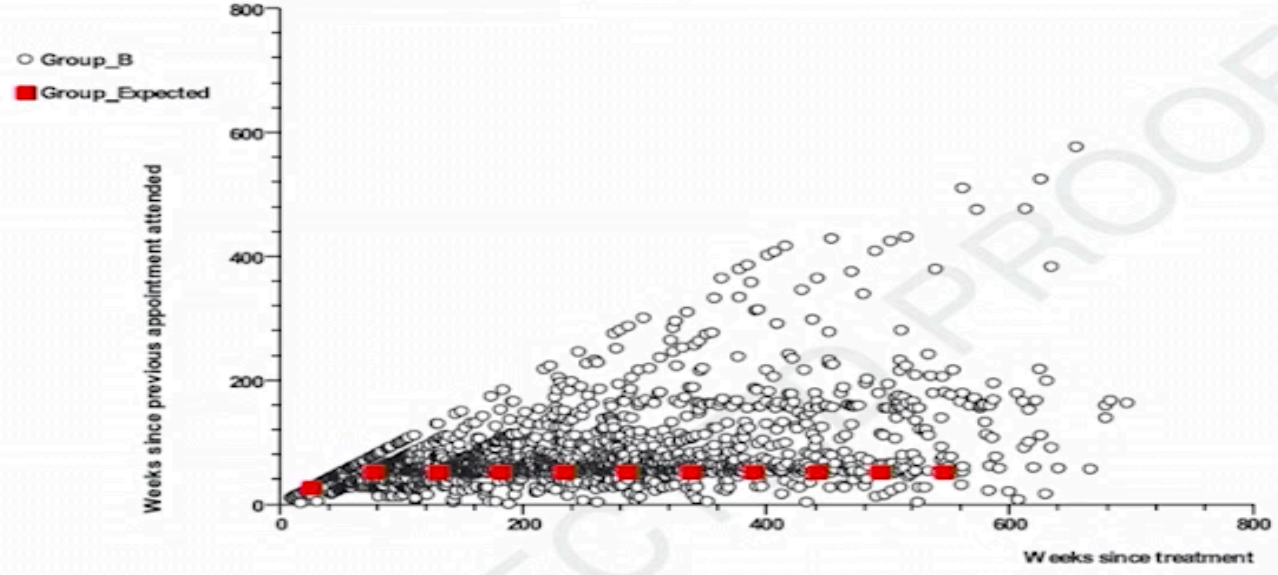
Treatment period (calendar year)								
1958-70	308	150	2.05 (1.83 to 2.30)	739 483	128	59	2.18 (1.82 to 2.60)	743 065
1971-80	388	181	2.14 (1.93 to 2.36)	1 139 381	120	53	2.25 (1.86 to 2.68)	1 144 118
1981-90	322	119	2.71 (2.42 to 3.02)	799 922	68	27	2.50 (1.94 to 3.17)	803 280
1991-2000	156	53	2.96 (2.52 to 3.47)	369 239	34	10	3.40 (2.36 to 4.76)	370 183
2001-08	62	14	4.52 (3.47 to 5.80)	100 196	5	2	2.64 (0.86 to 6.16)	100 333

Disadvantages of conventional FU

Long-term compliance with follow-up after treatment for cervical intra-epithelial neoplasia

WILLIAM PATRICK SOUTTER[1], BRONWEN MOSS[1], KAREN PERRYMAN[2], MARIA KYRGIOU[1,2], KATERINA PAPAKONSTANTINOU[2] & SADAF GHAEM-MAGHAMI[1,2]

AOGS 2012
Acta Obstetricia et Gynecologica Scandinavica



Compliance with FU falls with time and may increase the risk of Cervical Cancer after RX

HPV Test of Cure

Persistence of HR HPV type is the most significant prognostic factor:

- Micro-foci of residual disease
- Risk of developing new disease

HPV –ve: very low risk of developing new disease within 3 years

FU post-treatment HPV test

Accuracy CIN2+ recurrence

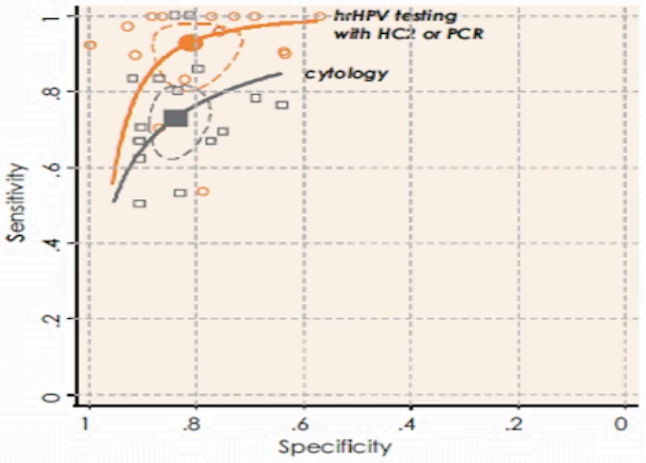
- Sensitivity

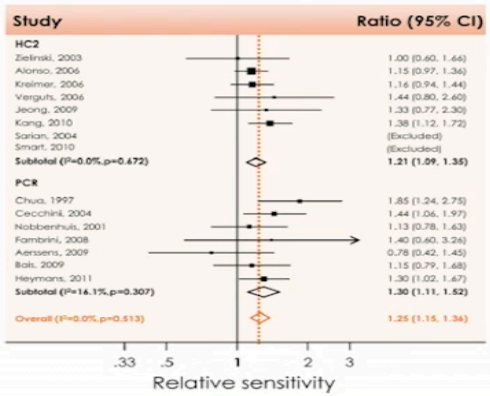
HPV test > than cytology (93 v 72%)

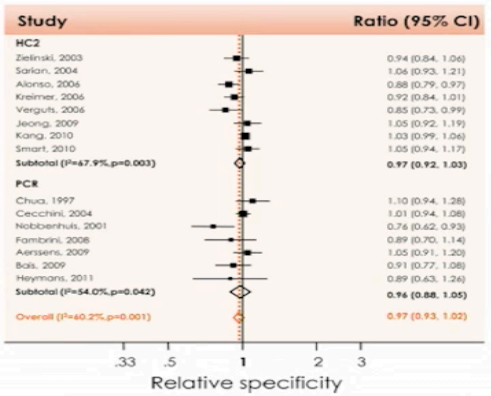
- Specificity

HPV test = cytology

'Test of cure'

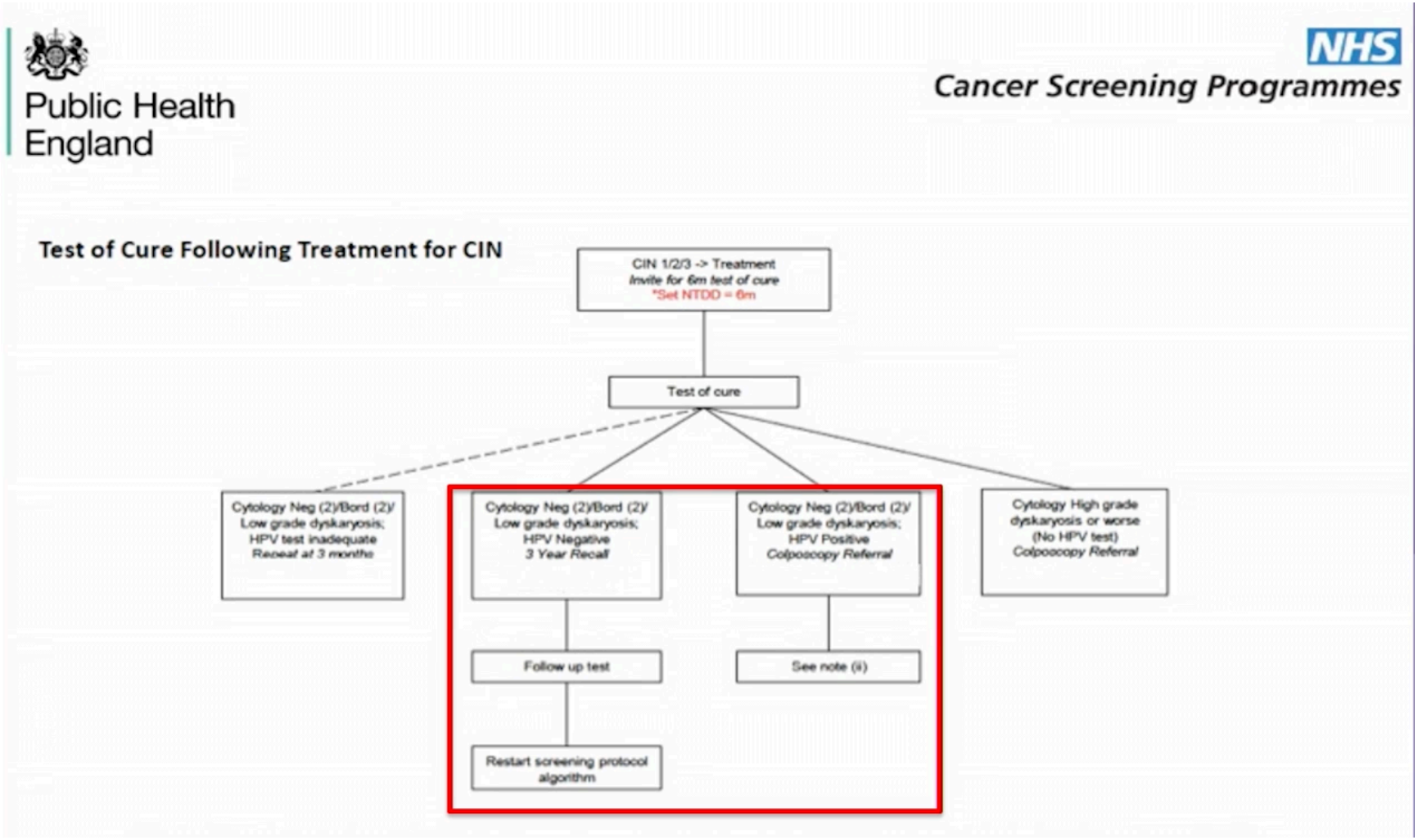






Arbyn Vaccines 2012

UK Test of Cure after Rx for CIN



What happens elsewhere

ASCCP

Co-testing: HPV test + cytology
12 & 24 months

-ve: Screening >20y

+ve: Colposcopy

+ve margins: cytology 4-6m

Scotland

HPV + cytology at 6 & 12m

Sweden

Cytology 6m & HPV 12m

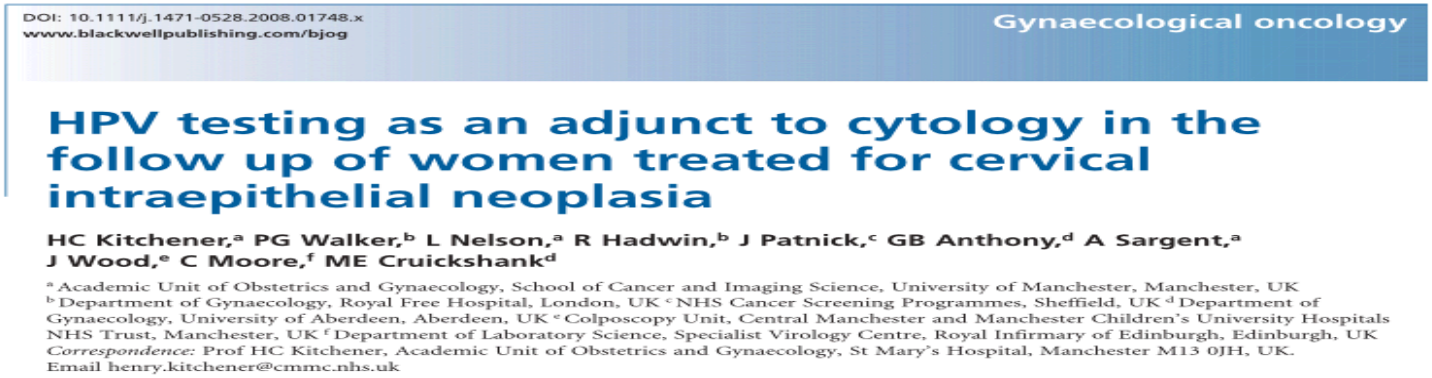
Ireland

HPV + cytology 6 & 18m

Australia and New Zealand

HPV + cytology 12 & 24m

NHS CSP HPV Post Tx Study



DOI: 10.1111/j.1471-0528.2008.01748.x
www.blackwellpublishing.com/bjog

Gynaecological oncology

HPV testing as an adjunct to cytology in the follow up of women treated for cervical intraepithelial neoplasia

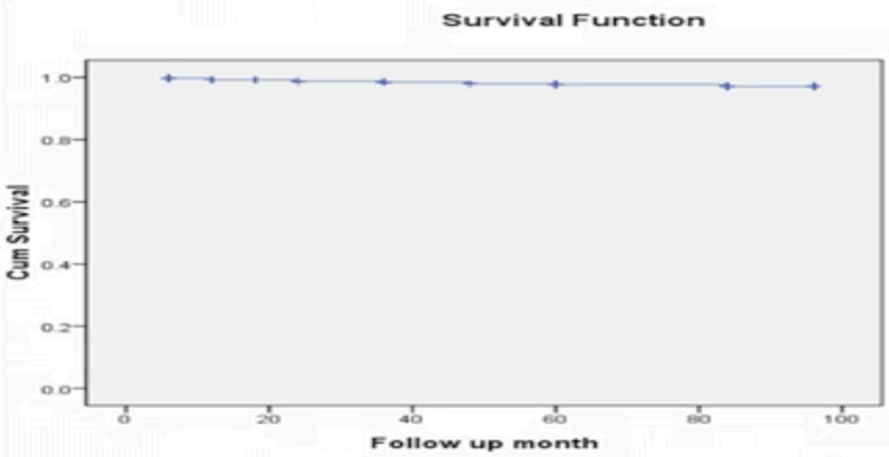
HC Kitchener,[a] PG Walker,[b] L Nelson,[a] R Hadwin,[b] J Patnick,[c] GB Anthony,[d] A Sargent,[a] J Wood,[e] C Moore,[f] ME Cruickshank[d]

[a] Academic Unit of Obstetrics and Gynaecology, School of Cancer and Imaging Science, University of Manchester, Manchester, UK [b] Department of Gynaecology, Royal Free Hospital, London, UK [c] NHS Cancer Screening Programmes, Sheffield, UK [d] Department of Gynaecology, University of Aberdeen, Aberdeen, UK [e] Colposcopy Unit, Central Manchester and Manchester Children's University Hospitals NHS Trust, Manchester, UK [f] Department of Laboratory Science, Specialist Virology Centre, Royal Infirmary of Edinburgh, Edinburgh, UK
Correspondence: Prof HC Kitchener, Academic Unit of Obstetrics and Gynaecology, St Mary's Hospital, Manchester M13 0JH, UK.
Email henry.kitchener@cmmc.nhs.uk

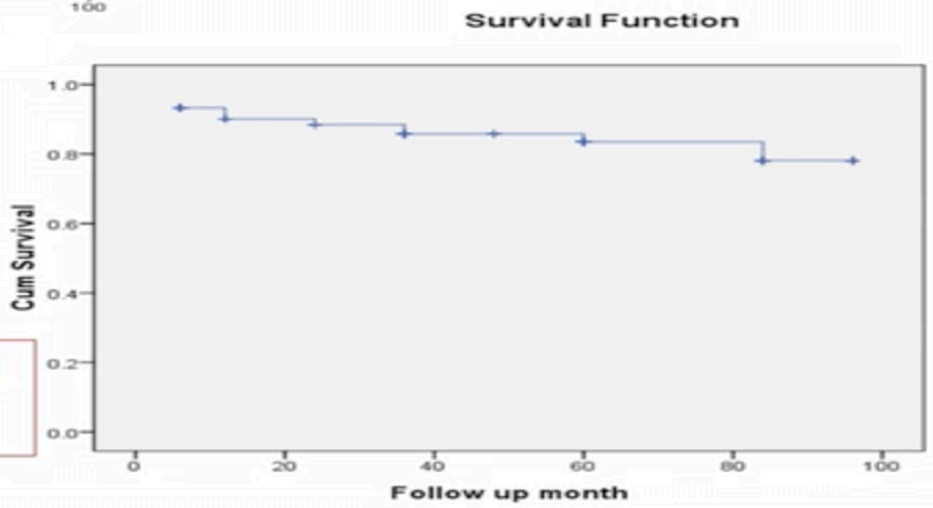
HPV –ve at 6 mo can:

- Identify low risk women
- Rapid return to recall
- Reduce intensive follow-up
- Reassurance

NPV of HPV-ve at 6 mo

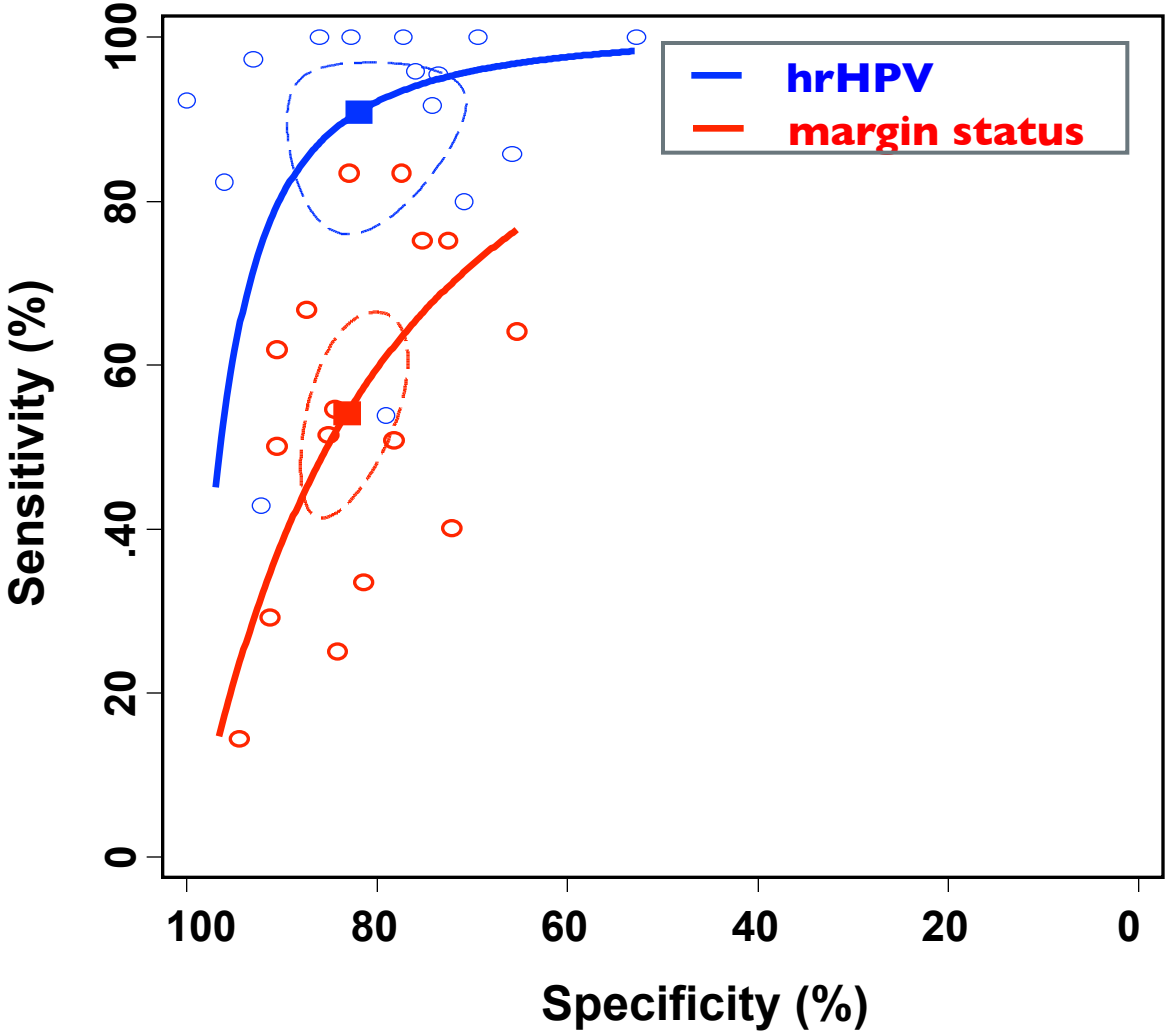


HPV –ve at 6m months - n =783
No of CIN2+



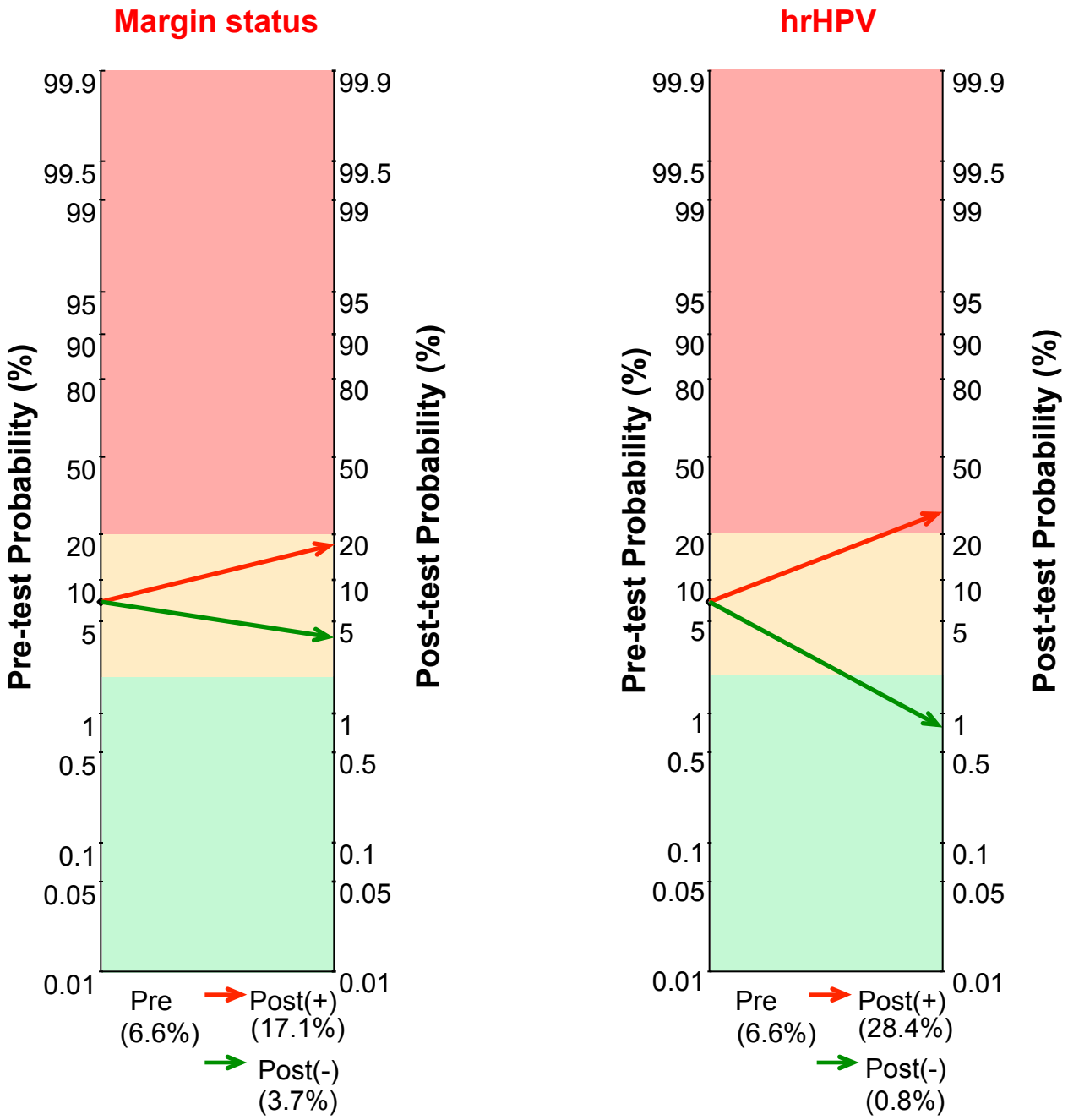
HPV +ve at 6m months - n =134
No of CIN2+

Accuracy of margin status and post-treatment HPV testing to predict treatment failure



	Sensi	Speci
Margins	55.8%	84.4%
HPV	91.0%	83.8%

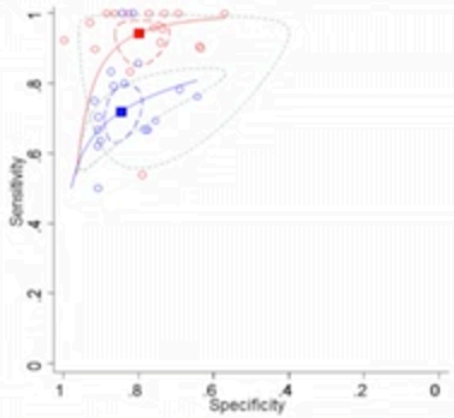
Clinical utility of a test: PPP plot (pretest-posttest probability)



HPV, cytology and margins

Relative accuracy to predict residual/recurrent CIN2+

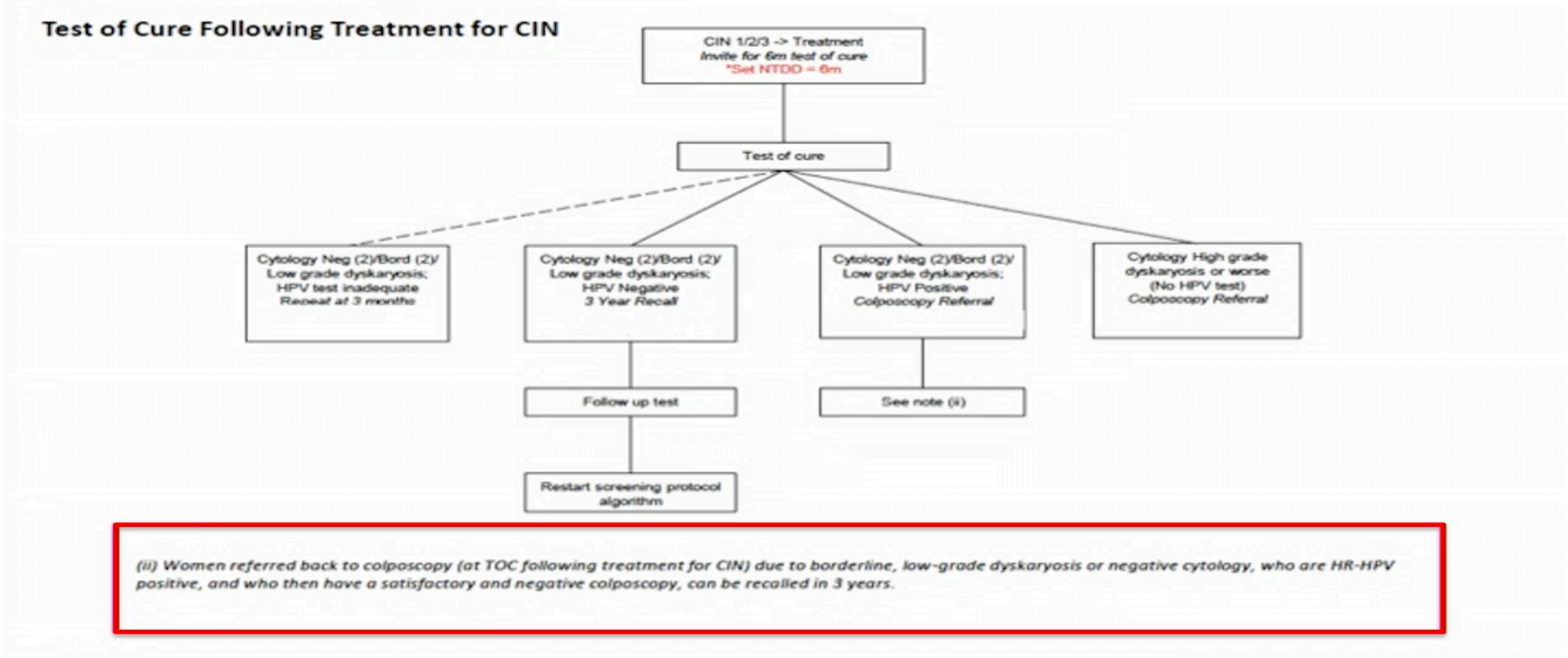
	Sensitivity ratio		Specificity ratio		
HPV test vs Cytology	1.25	(1.12-1.39)	0.96	(0.92-1.00)	=
HPV test vs Margins	1.48	(1.29-1.70)	1.00	(0.96-1.06)	=
HPV/Cytology vs HPV	1.07	(0.97-1.17) =	0.93	(0.88-0.97)	↓



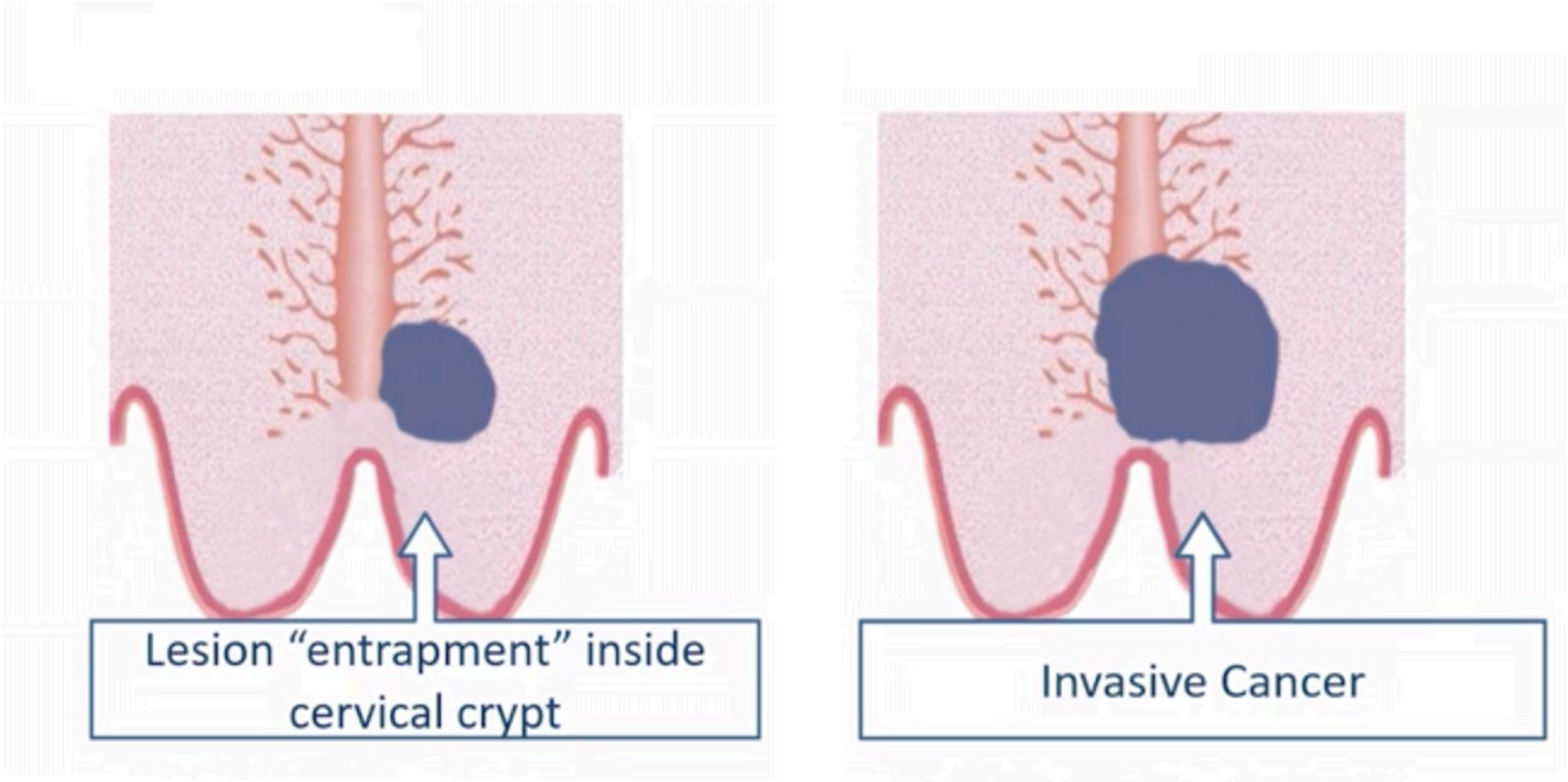
Role of colposcopy

Public Health England

NHS Cancer Screening Programmes



Cervical crypt theory



Micro invasive disease

NHS Cervical Screening Programme

Colposcopy and Programme Management

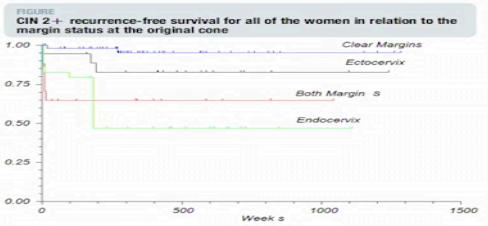
NHSCSP Publication number 20

Third Edition March 2016

- Cytology 6 and 12 months & annually for 9 years
- Then routine recall till 65

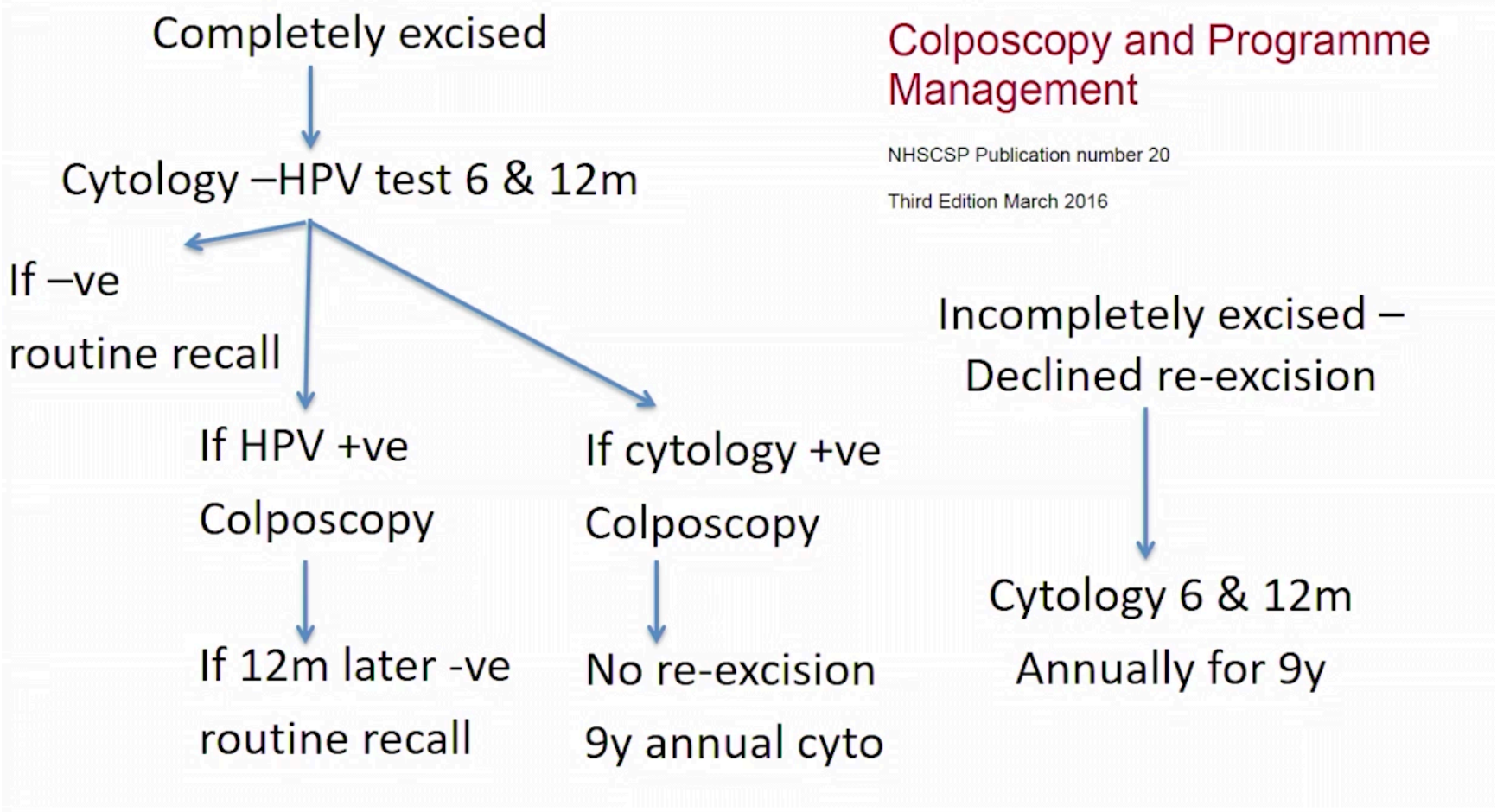
Management of stage Ia1 squamous cervical cancer and the importance of excision margins: a retrospective study of long-term outcome after 25 years of follow-up AJOG 2014

Katerina Papakonstantinou, PhD; Maria Kyrgiou, MSc, PhD, MRCOG; Deidre Lyons, MRCOG; William P. Soutter, MD, FRCOG; Sadaf Ghaem-Maghami, PhD, MRCOG



- 111 women
- Margins affected risk of CIN2+ recurrence +ve: 6.4% & -ve: 2.7%
- Resurgery: +ve: 31% & -ve 11.1%

Glandular Disease



After hysterectomy

VAIN after hysterectomy

VAIN: 1-4% - invasion: 0.6%

Hysterectomy vs cone:
Risk recurrent intra-epithelial neoplasia lower
Risk recurrent invasion similar

- No CIN – routine recall: no cytology
- Completely excised CIN: 6 and 18m
- Incompletely excised CIN:
  CIN1: 6, 12, 24m
  CIN2/3: 6, 12, annual for 9 years
- Subtotal: as normal screening

HPV test may be of use in the future…

NHS Cervical Screening Programme

Colposcopy and Programme Management

NHSCSP Publication number 20

Third Edition March 2016

Summary

- Detection of residual/recurrent disease
- hrHPV test: high sensitivity and NPV
- vs cytology: more sensitive, less specific
- Co-testing: more sensitive and slightly less specificity

Considerations

Why different algorithms?

Does we need cytology?

Sensitivity of colposcopy when HPV +ve?

Need for larger and longer FU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FOR COLPOSCOPY
6th
Satellite Meeting
and Training the Trainers
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