

HPV Triage and Test of Cure for London

**North West London Hospitals NHS
Trust and
Barts and the London NHS Trust**

HPV Triage and Test of Cure: Background, Protocol and Training

**Dr Tanya Levine
Consultant Cellular Pathologist
Director of the London Regional Cytology Training
Centre
North West London Hospitals NHS Trust**

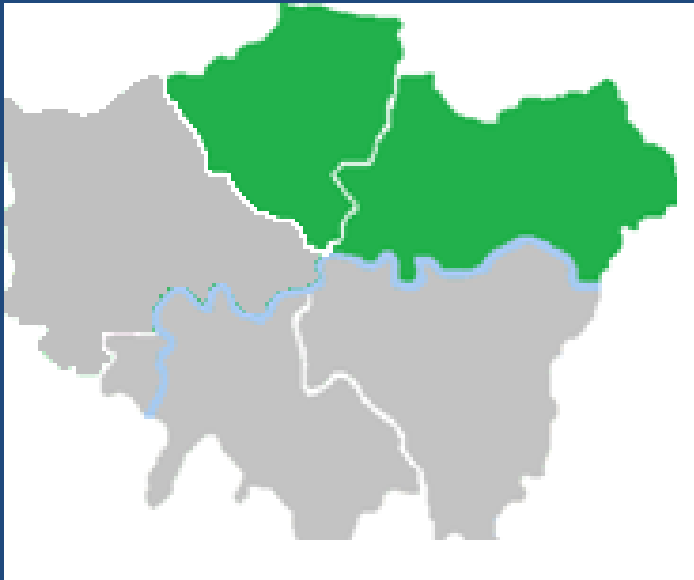
Introduction

- **NHS LBC and HPV testing pilots in 2001**
- **Sentinel sites from 2007**
- **2010 Advisory committee for cervical screening recommended roll-out of HPV testing across the programme nationally as triage and test of cure**

For London

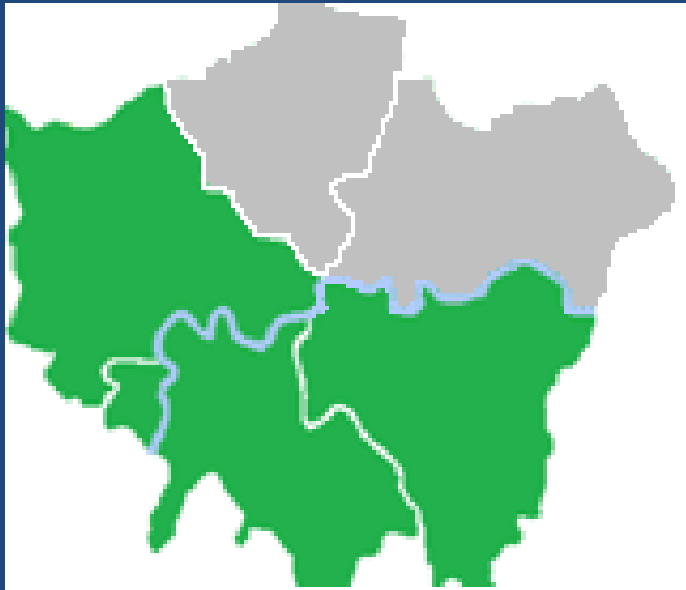
- **Bids for HPV testing submitted December 2011**
- **NHS London and PCT commissioners chose a 2 centre model for HPV testing across London**
- **NWLH Trust and Barts and the London are the successful bidders**
- **NWLH Trust will cover 3 sectors and Barts and the London 2 sectors**

Barts and The London



- Roche platform for HPV testing

Northwick Park Hospital



- **Abbott platform for HPV testing**

Key personnel

NWLH Trust

- Dr Tanya Levine
- Mr David Smith
- Mr Mark Terry
- Mr Matthew Longmate

Barts and the London

- Dr Mike Sheaff
- Mr Geoffrey Curran
- Mr Cliffe Adams
- Mr Steve Jones

Background

- >100 subtypes of HPV
- Low-risk and high-risk subtypes
- Low –risk subtypes associated with warts
- Most women will clear infection within 12-24 months
- In some women the high-risk virus integrates and can drive the “pre-cancer (CIN)– cancer sequence”
- >99% of cervical cancers contain HR HPV subtypes
- Triage and test of cure aims to identify those women who have high-risk HPV and at an increased risk of cervical cancer

Triage

- Currently you are referring all mild (previous routine recall) and women with persistent borderline changes
- Without HPV testing you cannot predict which women may or may not have the necessary drivers to push the CIN – carcinoma pathway
- Triage allows a more “intelligent referral” pathway for women than blanket referral of all milds and persistent borderline

Triage continued

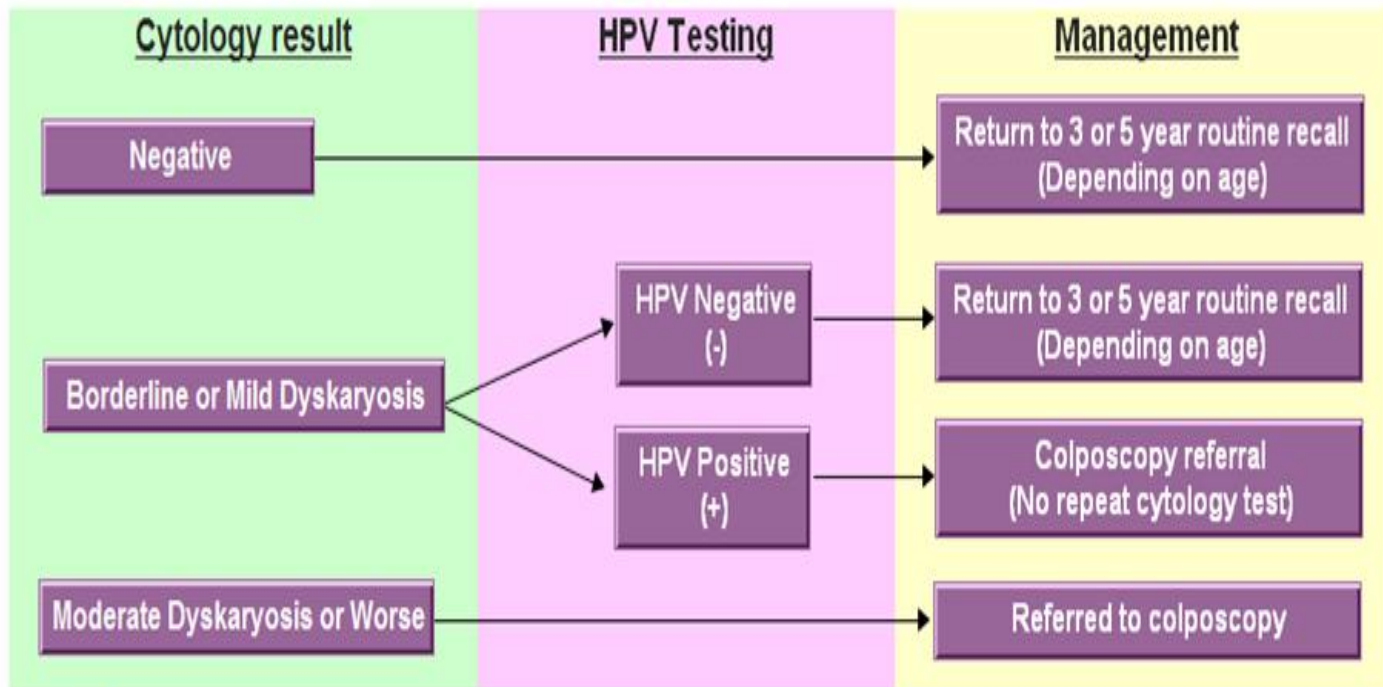
- HPV testing allows HR HPV positive with borderline or mild dyskaryosis referred to colposcopy
- These women have an increased risk of significant disease (15-20% \geq CIN II)
- Negative predictive value of HR-HPV testing 93.8-99.7%
- Borderline / mild and HR HPV negative returned to 3 or 5 yearly screening



Section Two: Why we are using HPV testing?

HPV Triage testing Flowchart

Below is a flowchart to help you remember what you've learnt from the last two pages.



Triage Protocol

Year 1

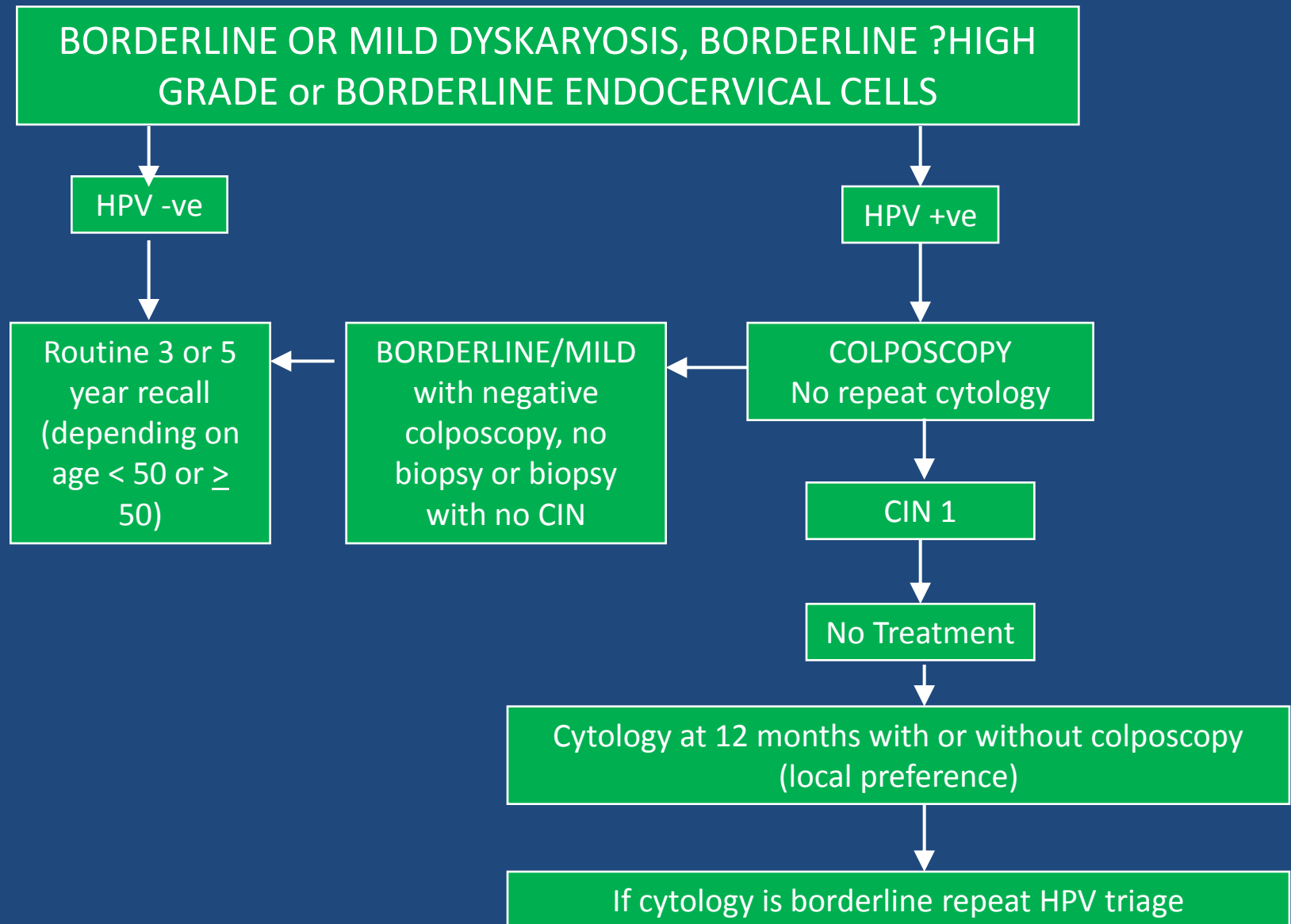
- **New first mild and borderline cases for HPV Triage Testing: previous routine recall**
- **This covers ALL borderline categories including borderline high-grade not excluded and borderline in endocervical cells**

Triage Protocol

Year 2

- Triage rolled-out to all women with borderline or mild changes on early repeat / cytological surveillance

HPV Triage Protocol



Test of Cure

- **Women who have had treatment for CIN II or CIN III or persistent CIN 1**
- **Cytology sample screened and if negative / borderline / mild BUT HR HPV negative can be returned to routine recall**

Test of Cure Protocol

Year 1

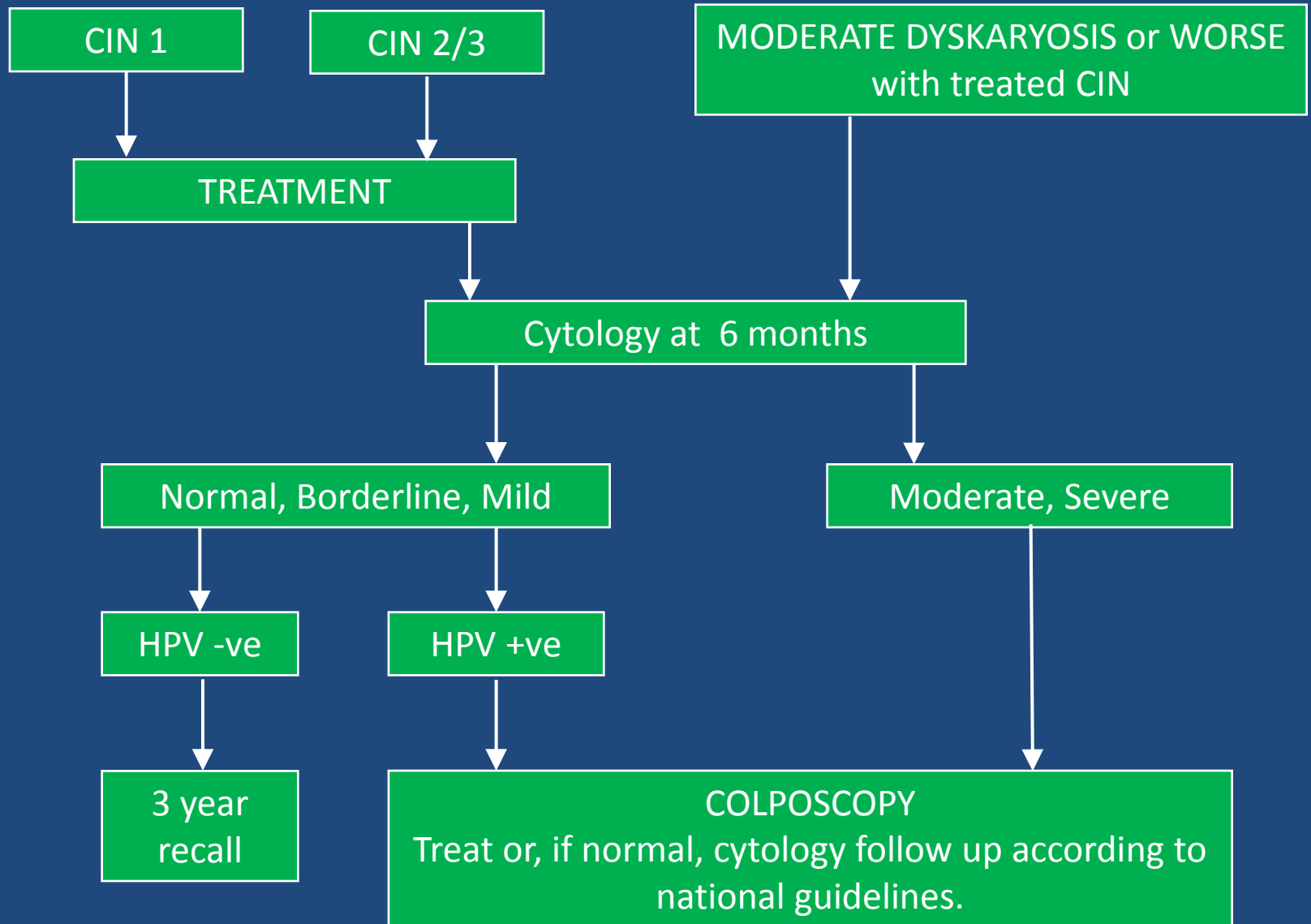
- **Women with their FIRST cervical cytology sample from April 1st following previous treatment for CIN**
- **Eligible samples will be negative / borderline / mild**

Test of Cure Protocol

Year 2

- Eligible women will be any on cytological surveillance following treatment for CIN
- Eligible samples will be negative / borderline / mild

HPV Test of Cure Protocol



Women not eligible

- Outside screening age
- Vault samples
- Treated CGIN (exempt test of cure)
- Treated invasive carcinoma (exempt test of cure)

Cases inadequate for HPV testing

Inadequate for HPV testing

- Insufficient volume for HPV testing
- Insufficient cells for HPV testing
- Bloody sample

Management

- If mild – refer to colposcopy
- If borderline - ask for repeat at 6 months and then HPV test: negative routine recall / HR HPV detected – colposcopy referral

Other exemptions to HPV testing

- Test of cure NOT indicated for histologically proven CGIN
- Follow-up as current protocol

Time Considerations

- Cytological review by the pathologist / AP needs to be regular and timely manner
- Do NOT stockpile or batch!

Training / Communication 1

PCT / Sample takers / colposcopy

- E-learning (London Regional Cytology Training Centre – Moodle training)
- Paper
- Face-to-face
- Cascade learning

Training/Communication 2

Laboratory

- Face-to-face
- Cascade learning
- E-learning (London Regional Cytology Training Centre)

Follow-up Users meetings

Telephone / email queries

Training / Communication

Colposcopy

- Yourselfes
- E-learning
- Paper
- Face-to-face

Needs joined-up communication with lab, PCT and colposcopy unit(s)

About cervical screening

- [What is cervical screening?](#)
- [What happens at a cervical screening appointment?](#)
- [What is LBC?](#)
- [Possible future developments](#)
- [What does the NHS Cervical Screening Programme do?](#)
- [Who is eligible for cervical screening?](#)
- [Why are women under 25 not invited?](#)
- [Why are women over 65 not invited?](#)
- [What about women who are not sexually active?](#)
- [When was the NHS Cervical Screening Programme started?](#)
- [How many women are screened?](#)
- [How is the programme organised?](#)
- [How much does the programme cost and how is it funded?](#)
- [Is cervical screening effective?](#)
- [Coverage of the target population](#)
- [Frequently Asked Questions \(FAQs\)](#)

What is cervical screening?

Information about cervical cancer

[Diethylstilbestrol \(DES\) exposed women](#)

[Liquid Based Cytology \(LBC\)](#)

[LBC implementation guidance](#)

[Who does what in the programme](#)

[Quality Assurance and Training](#)

[Section 60 of the Health and Social Care Act 2001](#)

[Cervical cytology training centres](#)

[Human Papilloma virus \(HPV\)](#)

[HPV Sentinel Sites implementation project](#)

[HMR101 Request/Report Form](#)

[14 day turnaround time](#)

[Research in cervical screening](#)

[NHSCSP home page](#)

[Programme publications](#) →

[About cervical screening](#)

[More information about the screening programme](#) →

[Frequently asked questions](#)

[Programme statistics](#)

[Programme news index](#)

[Useful links](#)

HPV Sentinel Sites Implementation Project

Experience gained from the HPV triage pilots has enabled the programme to move forward with HPV triage of borderline changes and mild dyskaryosis and testing will now be introduced to the programme. Data from the original pilots indicated a large initial increase in the number of referrals to colposcopy followed by a reduction in referrals, which might be particularly apparent where current practice is to refer on the second occurrence of mild dyskaryosis. Therefore, the introduction of HPV triage, initially in a small number of centres is being carefully managed.

This means that any women (where HPV triage is implemented) who have a cervical screening test result of borderline changes or mild dyskaryosis will automatically have an HPV test performed on their sample. If HPV is found they will be referred for colposcopy and if HPV is not found they will be returned to routine screening every 3 or 5 years depending on age.

In addition to HPV triage, an HPV 'Test of Cure' is being introduced for women who have undergone treatment for CIN. This means that HPV tests will be carried out on samples from women who have a normal screening test result after having treatment for CIN. If HPV is not found then the women will not be recalled for screening for a further three years. If, however, HPV is found or the screening test does show an abnormality the women will be referred again to colposcopy.

[HPV Triage & Test Flowchart](#) (PDF 417Kb)

Fact sheets: HPV testing Information for Women

This fact sheet is designed to be given to women upon invitation for screening (including early repeat testing) and to women who have undergone treatment for CIN.

- [Arabic HPV Testing Fact Sheet](#) (210Kb PDF)
- [Bengali HPV Testing Fact Sheet](#) (188Kb PDF)
- [Chinese HPV Testing Fact Sheet](#) (259Kb PDF)
- [English HPV Testing Fact Sheet](#) (162Kb PDF)
- [Punjabi HPV Testing Fact Sheet](#) (178Kb PDF)

[NHSCSP home page](#)

[Programme publications](#)



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[Useful links](#)



[NHS Breast Screening Programme](#)

[NHS Cervical Screening Programme](#)

[NHS Bowel Cancer Screening Programme](#)

[NHS Prostate Cancer Risk Management](#)

Human Papilloma virus (HPV)

- [ARTISTIC trial](#)
- [HPV testing](#)
- [Our answers to questions asked about HPV infection](#)
- [TOMBOLA study](#)
- [HPV pilots](#)
- [Evaluation of HPV triage](#)
- [HPV Sentinel Sites](#)

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Impact on the Cytology Laboratory

Identification of samples for HPV testing

- **Primary screeners**
 - Initial identification of Borderline/Mild & Test of Cure cases
 - Initial separation of “?HPV test” samples
- **Checkers**
 - Confirmation of potential HPV cases and flagged to ABMS / Pathologist
 - Segregation of Low vs High grade cases?
- **Colposcopy**
 - Test of Cure cases

Screening Practice (1)

- All cases of Borderline/Mild must be seen by a Pathologist or ABMS before going for HPV testing.
- Any Negative Test of Cure cases may be selected for HPV testing by Checker / Senior BMS
- Report must be placed in a “holding category” awaiting the outcome of the HPV test.

Screening Practice (2)

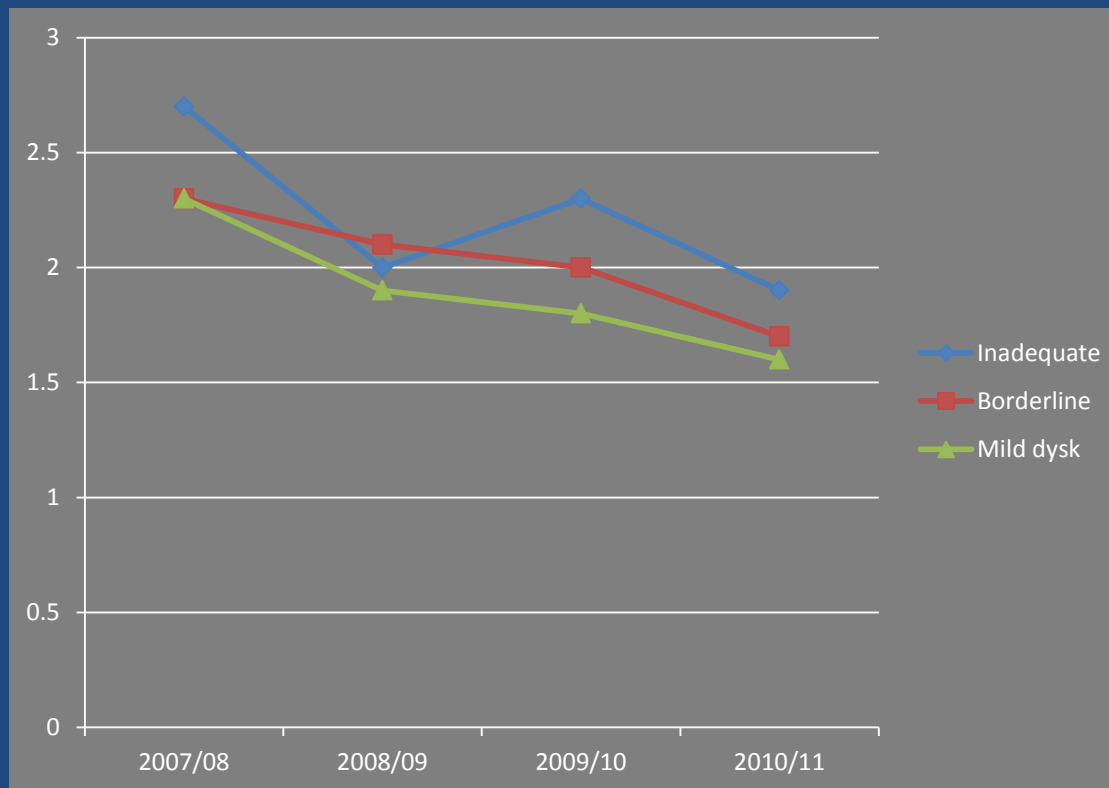
- Final report of Triage cases including the HPV test must be authorised by the Pathologist / ABMS or on their behalf by an agreed Senior BMS.
- Negative Test of Cure cases with a Negative HPV result may be signed out by Checker / Senior BMS
 - If HPV Positive pass to Pathologist

Sorting of samples

- Daily retrieval of vials for HPV testing
- Check remaining volume in vial
- Packaging of samples
- Laboratory database of samples sent
- Chasing up results
- Need to manage workforce effectively

Impact on Screening

- Workload – decrease by 10%
- Reporting profiles:



REMOVE TAPE STRIP AND SEAL TRANSPORT BAG FIRMLY

H.P.V SAMPLES ONLY

Deliver to:
Cytology Department
Level 4, St Marks Building
Northwick Park Hospital
Watford Road
Harrow
HA1 3UJ

Telephone 0208 869 3314

**"BIOLOGICAL SUBSTANCE,
CATEGORY B"**



**CYTOLOGY SAMPLES
METHANOL BASED, BUFFERED
PRESERVATIVE SOLUTION**

**HAZARDS
TOXIC BY INHALATION, EYE
CONTACT AND INGESTION**



FLAMMABLE



TOXIC HAZARD

Packaging Instructions:

- Screw sample container cap correctly to prevent leakage
- Put sample in primary specimen bag with accompanying paperwork
- Seal specimens in primary bag
- Place multiple specimens into this bag and seal

DO NOT REMOVE ABSORBANT PAD

Packaging and transport

Labelling of sample

- **Unique number series per lab for Northwick Park users**
- **Common number series for Barts and the London users (supplied in lots of 1000)**
- **Label vial with supplied bar code**
 - **1st on sample length ways**
 - **2nd keep for internal use in your laboratory**
 - **3rd label (NWP users – return label to NWP)**

Spread sheet data

- We will supply a pro forma spread sheet to be completed with:
 - Referring laboratory name
 - Date vials dispatched
 - Signature of person completing sheet
 - HPV bar code number
 - Date of birth
 - NHS number
 - Triage or test of cure
 - 1st borderline or 1st mild dyskaryosis
 - Recent treatment

Packaging

- **Print spread sheet**
- **Complete spread sheet**
 - **Check vials against spread sheet**
 - **Sign and date spread sheet**
 - **Place spread sheet and any spare labels in sealable bag**
- **Place each vial in sealable bag**
- **Place all bags in lilac Midco bag**
- **Seal Midco bag**

Transport

- **Take to van collection point**
 - One collection per site per day in the morning
 - Delivery arrives at HPV testing site early afternoon
- **E mail spread sheet to HPV testing site**
 - **NHS.net accounts**

HPV testing laboratory processes

- **Unpack vials**
- **Check vials against spread sheet**
- **Enter onto HPV testing site LIMS**
- **Aliquot sample**
- **DNA extracted**
- **DNA amplified**
- **Result entered on to HPV testing site LIMS**
- **Spread sheet updated with result**
- **Spread sheet e-mailed to sender laboratory via NHS.net within 48 hrs**

Receipt of HPV results

Receipt of HPV results

- HPV results will be added to submitted spread sheet

HPV number	Date of birth	NHS number	Triage or Test of cure (TOC)	1st BNA	1st mild	Recent treatment	HPV result
12C000001	09/03/1985	123 456 7890	Triage	Y		N	Positive
							Negative
							Positive

- E-mailed back to spoke laboratory

Handling HPV results in spoke laboratory

- Need to incorporate HPV result in to cytology report

High risk HPV DETECTED by test

or

High risk HPV NOT DETECTED by test

Please note

- **Must remove any terms relating to cytological evidence of HPV from reports**
- **The only mention of HPV should be in regards of whether the HPV test was positive or negative.**

MILD DYSKARYOSIS
Koilocytic changes seen
suggestive of HPV
infection

MILD DYSKARYOSIS
High risk HPV DETECTED
by test

MILD DYSKARYOSIS
High risk HPV DETECTED
by test

Changes to reporting codes

- **Borderline**

High risk HPV +ve	
8R6	B9S
8R3	
8S	
High risk HPV -ve	
8R6	B0A
8R3	
8S	

Changes to reporting codes

- Mild dyskaryosis

High risk HPV +ve	
3R6	M9S
3S	
High risk HPV -ve	
3R6	M0A
3S	

Changes to reporting codes

- Test of cure

High risk HPV +ve	
2R6	N9S
8R6	B9S
3S	M9S
High risk HPV -ve	
2R6	N0R36
8R6	B0R36
3S	M0R36

Remember

- HR HPV +ve cases must be screened and reported by Pathologist

Changes to reporting codes

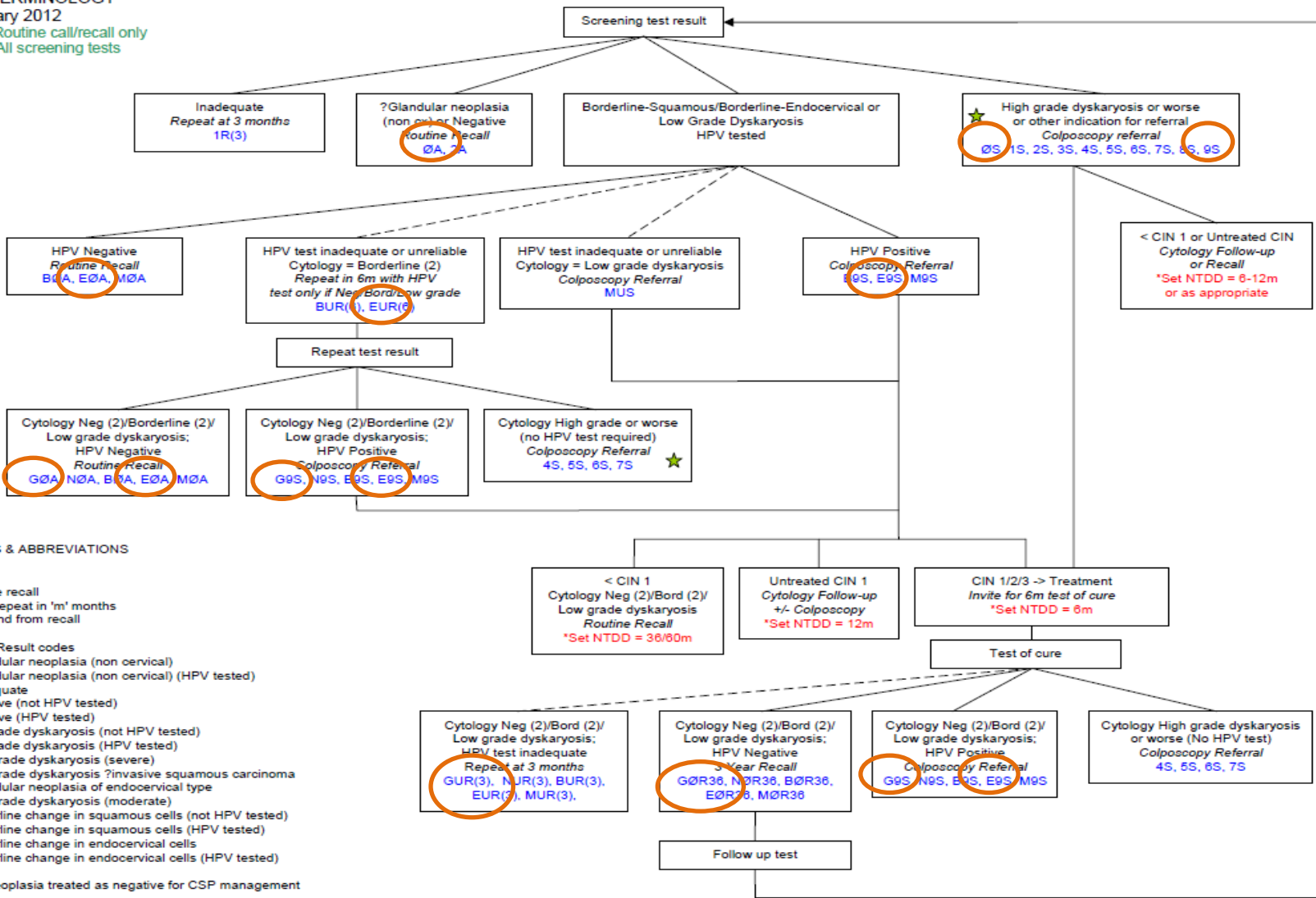
- Unavailable / unreliable

Borderline triage case	
8R6	BUR6
8R3	
8S	
Mild dyskaryosis triage cases	
MR6	MUS
MS	
Test of cure cases	
2R6	NUR3
8R6	BUR3
8S	
3R6	MUR3
3S	

Reporting process

- Final report including the HPV test must be authorised by the Pathologist / ABMS or on their behalf by an agreed Senior BMS
- Use of dedicated logins
 - Reported by Dr ??????, verified by ?????

HPV TRIAGE PROTOCOL
 INCL ABC3 TERMINOLOGY
 DRAFT January 2012
 YEAR ONE – Routine call/recall only
 YEAR TWO – All screening tests



KEY TO CODES & ABBREVIATIONS

Action codes
 A routine recall
 Rm early repeat in 'm' months
 S suspend from recall

PROVISIONAL Result codes
 Ø ?glandular neoplasia (non cervical)
 G ?glandular neoplasia (non cervical) (HPV tested)
 1 inadequate
 2 negative (not HPV tested)
 N negative (HPV tested)
 3 low grade dyskaryosis (not HPV tested)
 M low grade dyskaryosis (HPV tested)
 4 high grade dyskaryosis (severe)
 5 high grade dyskaryosis ?invasive squamous carcinoma
 6 ?glandular neoplasia of endocervical type
 7 high grade dyskaryosis (moderate)
 8 borderline change in squamous cells (not HPV tested)
 9 borderline change in squamous cells (HPV tested)
 E borderline change in endocervical cells
 E borderline change in endocervical cells (HPV tested)
 * non-cervical neoplasia treated as negative for CSP management

Infection codes
 Ø (zero) HPV negative
 9 (nine) HPV positive
 U HPV result inadequate/unreliable

Miscellaneous
 NTDD Next Test Due Date
 BLUE indicates codes used on NHAIS in format
 Cytology result – HPV infection code – Action code
 RED indicates manual action required to reset NTDD
 ★ colposcopy referral without HPV test

Transmission to PCT

S01+1'
NAD+SRC+1:ZZZ'
NAD+SND+0189:ZZZ'
NAD+GP+0189:ZZZ'
S02+2'
PNA+PAT++++SU:ZZTEST22-FS:PATIENT22'
DTM+329:13011916:951'
S03+3'
TST+RCD+B:ZZZ+SNO:08090013+S:ZZZ'
DTM+119:20080206:102'
HEA+INM+g:ZZZ'
S01+1'
NAD+SRC+1:ZZZ'
NAD+SND+0189:ZZZ'
NAD+GP+0189:ZZZ'
S02+2'
PNA+PAT++++SU:ZZTEST24-FS:PATIENT24'
DTM+329:15031938:951'
S03+3'
TST+RCD+M:ZZZ+SNO:08090014+S:ZZZ'
DTM+119:20080206:102'
HEA+INM+g:ZZZ'
S01+1'
NAD+SRC+1:ZZZ'
NAD+SND+0189:ZZZ'
NAD+GP+0189:ZZZ'
S02+2'
PNA+PAT++++SU:ZZTEST26-FS:PATIENT26'
DTM+329:17051960:951'
S03+3'
TST+RCD+B:ZZZ+SNO:08090015+R:ZZZ'
DTM+119:20080206:102'
HEA+INM+g:ZZZ'
QTY+961:06'

Borderline. Refer to Colposcopy
HPV positive

Mild dyskaryosis. Refer to
Colposcopy
HPV positive

Borderline. Repeat in 6 months
HPV negative

PCT

- **Need to make sure the file loads correctly in to Exeter system**
- **Correct letters generated**

Finance

Assumptions on Practice and Sentinel Site Experience

- **Based on NHS CSP Publication 20 “Colposcopy Programme management” 2004**
 - No sites should be referring on second mild dyskaryosis
 - All commissioners should have funded conversion to referral on first mild
- **We identified a need for support of Colposcopy and Histology as a pilot site**
 - Only marginal increases in activity can be attributed to this initiative

Our Commitment to Support for Colposcopy and Histology

- **Colposcopy services can invoice for up to £50 towards each attributable additional Colposcopy**
- **Histology services will receive £30 for 40% of the volume of colposcopies claimed**
- **The Colposcopy service will need to make arrangements to distribute the funding to the appropriate Histology services based on local agreement**

Important Messages to Take Away

- Increased activity is marginal
- Colposcopy to receive £50 per additional referral and Histology £30 per additional case
- If you refer on second mild not first mild and you think this will have financial implications the you need to speak to your commissioners
- London QA has written to commissioners to remind them of their responsibility

To all PCT Cluster Commissioners
Screening commissioners
Lead Colposcopists
HBPCs

27th February 2012

Dear Colleague

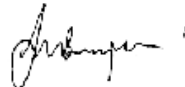
RE: Referring on first mild dyskaryotic sample and implementation of HPV testing for triage and test of cure.

NHS CSP Publication No 20 "Colposcopy and Programme Management" published in 2004 advocated that referring a woman to colposcopy following a first instance of a mild dyskaryotic result was best practice. This policy has been adopted by many of the colposcopy services across London. However there are some places where referral to colposcopy does not occur until the second 'mild' result.

Changing practice to refer on the first mild dyskaryotic result has an impact on colposcopy workload and clinics that have implemented this practice have seen an increase in workload of up to 30% over a six month period, after which time the workload stabilises.

The impact on colposcopy workload of HPV testing is dependant on the referral policy that was in place prior to its introduction. One of the assumptions that has been made when considering the costings for implementing HPV for triage and test of cure has been that referral on a first mild dyskaryotic result is already being commissioned at all trusts. Therefore women with first mildly dyskaryotic samples who are HPV positive requiring referral to colposcopy will not be eligible for additional colposcopy funding from HPV testing implementation monies.

Yours sincerely



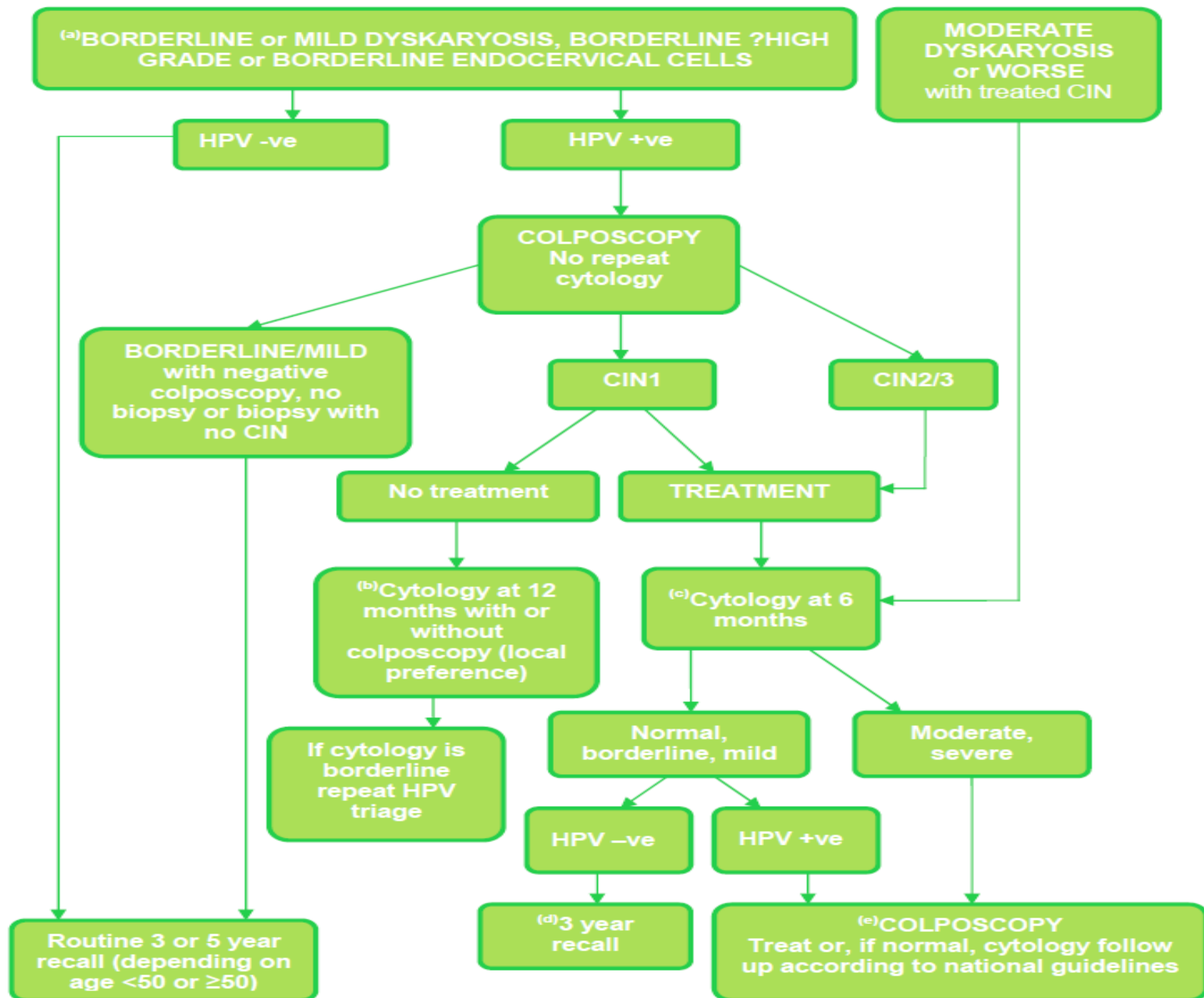
Dr Kathie Binysh
QA Director
London

Cc Jane Moore NHS London

C:\Documents and Settings\matthewlo\Local Settings\Temporary Internet Files\Content.Outlook\4NVPC4LC\Letter to Sector Leads.doc

Summary and Roll out

HPV triage and test of cure protocol



Key points

- Why we are doing this
- Year 1 triage eligibility criteria
- Year 1 test of cure eligibility criteria
- Year 2 triage eligibility criteria
- Year 2 test of cure eligibility criteria
- How the service will work
- Funding
- Communication

Roll-out

- Needs to commence by March 31st 2012 to secure funding
- Local sector implementation by March 31st 2012
- Thereafter rolled-out as soon as possible to all sites
- Timetable currently being developed with London QA
- Definite timelines early April 2012