Cervical screening and colposcopy

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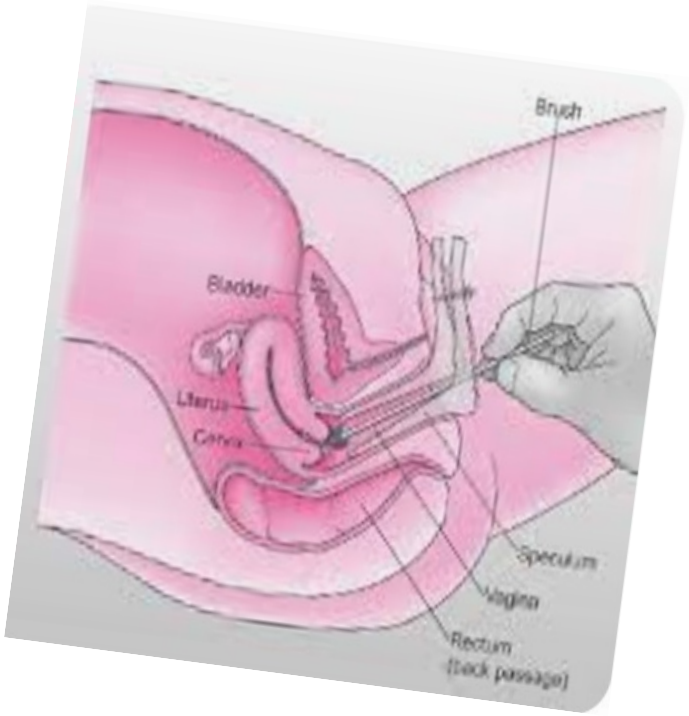
Cervical Cancer Incidence

- Lifetime risk 1:142
- 99.8% of cervical cancer in UK preventable
- 99.8% of cervical Cancer in UK caused by infections
- 21% of cervical cancer changes are caused by smoking

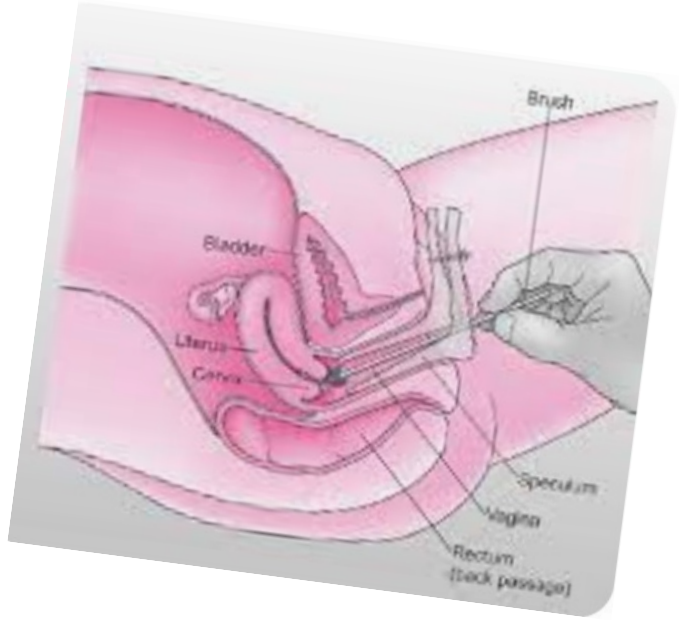
Cervical screening programme

- Reduction in Incidence of cervical cancer
- Improved survival rates
- Prevention of Advanced Stage Cancer
- Reduced Mortality



Population to be screened

- All individuals with a cervix
- Age 24.5 – 64 years
- Individuals with a cervix over the age of 65years who have not been screened since aged 50years or who have recently had an abnormal smear.



Primary human papillomavirus (HPV) screening

- Screening was previously done by cytology alone and then by cytology with HPV triage
- **Primary HPV screening has been demonstrated to be more sensitive than cytology to detect pre-invasive disease of the cervix**
- Improved sensitivity leads to reduction in incidence of both adenocarcinomas and squamous carcinomas of the cervix compared to cytology screening alone
- Improved sensitivity of high-risk HPV (hrHPV) testing and its high negative predictive value enables longer screening intervals for individuals with normal test results

Current screening programme

- **Primary HPV screening with triage by cytology**
- Due to the lower specificity of hrHPV testing, cytology is performed on all HPV positive samples to ensure colposcopy clinics are not overburdened
- hrHPV includes types 16,18, 31, 33, 45, 52 and 58

Routine screening intervals

- First invitation when an individual reaches 24.5
- 3 yearly recall until the age of 49
- 5 yearly recall from the age of 50
- Screening ceases when an individual attends for screening at or after the age of 60 where this test is negative and they have had no recent abnormal results
- People aged 65 or over who have had a previous cervical abnormality remain in recall until they have completed follow up

Cessation of screening

- People may choose to cease screening early for many reasons including –
  - Voluntary withdrawal
  - FGM
  - Vaginismus
  - Cervical stenosis
  - Physical conditions and disabilities
  - Terminal illness
  - Mental capacity
  - Prior radiotherapy to the cervix
  - Absence of the cervix
- In all these cases support should be offered and appropriate adjustments made to enable screening should the person wish to be screened

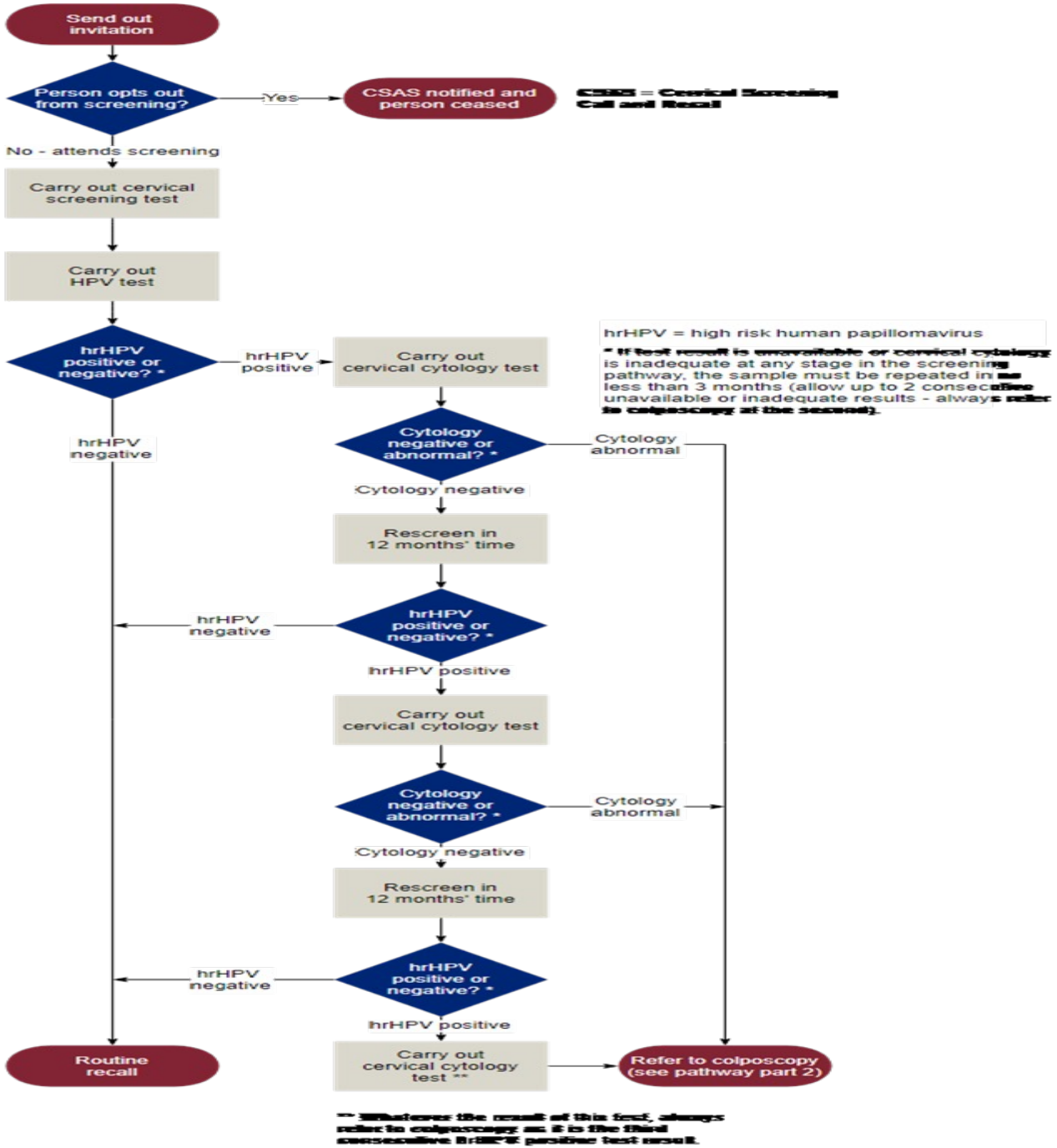
Assessment of women aged 20-24 with abnormal vaginal bleeding

- Cervical cancer is rare in women aged 20-24
- Abnormal vaginal bleeding is common in this age group
- Women with postcoital bleeding (PCB) or persistent intermenstrual bleeding (IMB) should be offered speculum examination
- If the cervix appears abnormal or suspicious this should trigger an urgent suspected cancer referral for colposcopy
- If the cervix appears normal, a pregnancy test and testing for cervical infection should be performed

Screening under the age of 25

- The following people are eligible for screening under the age of 25
  - People within 6 months of the 25th birthday
  - People screened elsewhere in the UK who are subject to routine or non-routine recall as a result of their previous test
  - People who have been previously screened privately and who require a follow-up non-routine recall as a result of their previous test

Screening flow chart – sample taking, HPV testing and cytology triage



Inadequate samples

- When the hrHPV test result is unavailable or cytology is inadequate the sample must be repeated in no less than 3 months
- Individuals with 2 consecutive HPV unavailable or inadequate cytology results are referred to colposcopy
- If colposcopy is normal and adequate, follow up screening should be offered at 12 months
  - If this is normal, the individual will return to routine recall
- If colposcopy is inadequate, repeat screening and colposcopy should be offered at 12 months
  - If this is normal, the individual will return to routine recall
- If colposcopy is abnormal, management will depend on the abnormality

hrHPV negative results

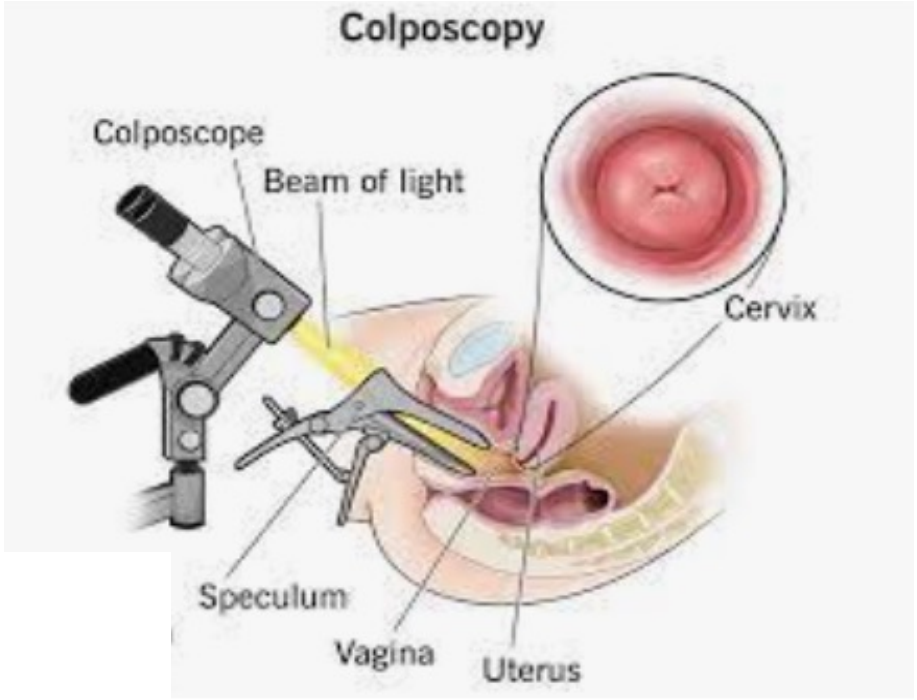
- A hrHPV negative result can be safely returned to routine recall unless on –
  - The test of cure pathway
  - The untreated CIN1 pathway
  - Follow up for incompletely excised CGIN/SMILE or cervical cancer
  - Follow up for borderline changes in endocervical cells

hrHPV positive results with negative cytology

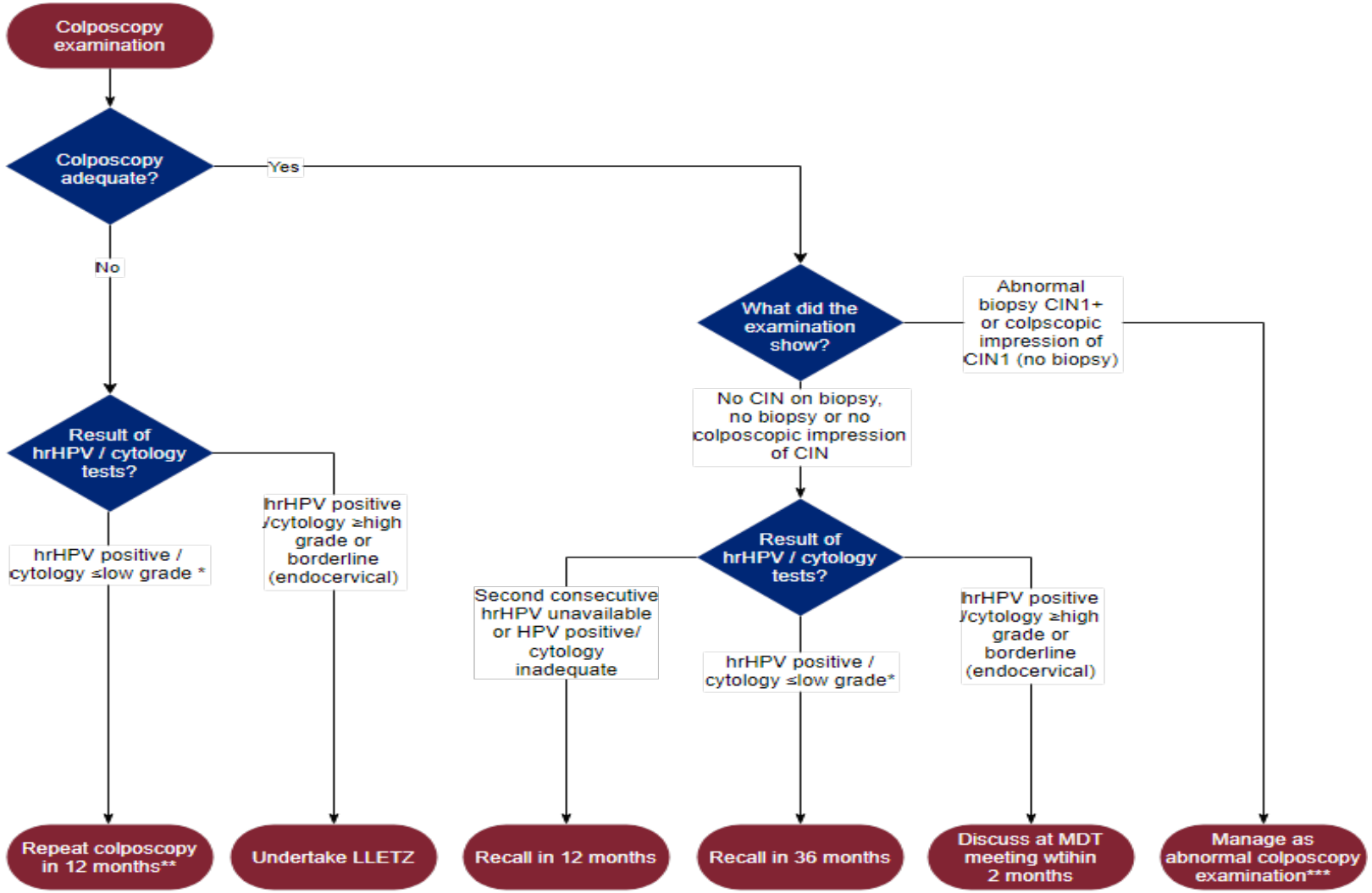
- If the patient is on routine screening, they should have the HPV test repeated at 12 months
  - If HPV testing is negative at 12 months – return to routine recall
  - If hrHPV positive with negative cytology at 12 months – repeat HPV test in a further 12 months
- Individuals who remain hrHPV positive, cytology negative or inadequate at 24 months should be referred to colposocpy
- If the patient is on the TOC pathway, they should be referred to colposocpy

hrHPV positive results and abnormal cytology

- All individuals who are hrHPV positive and have abnormal cytology must be referred to colposcopy



Colposcopy flow chart 1



* excludes borderline change in endocervical cells

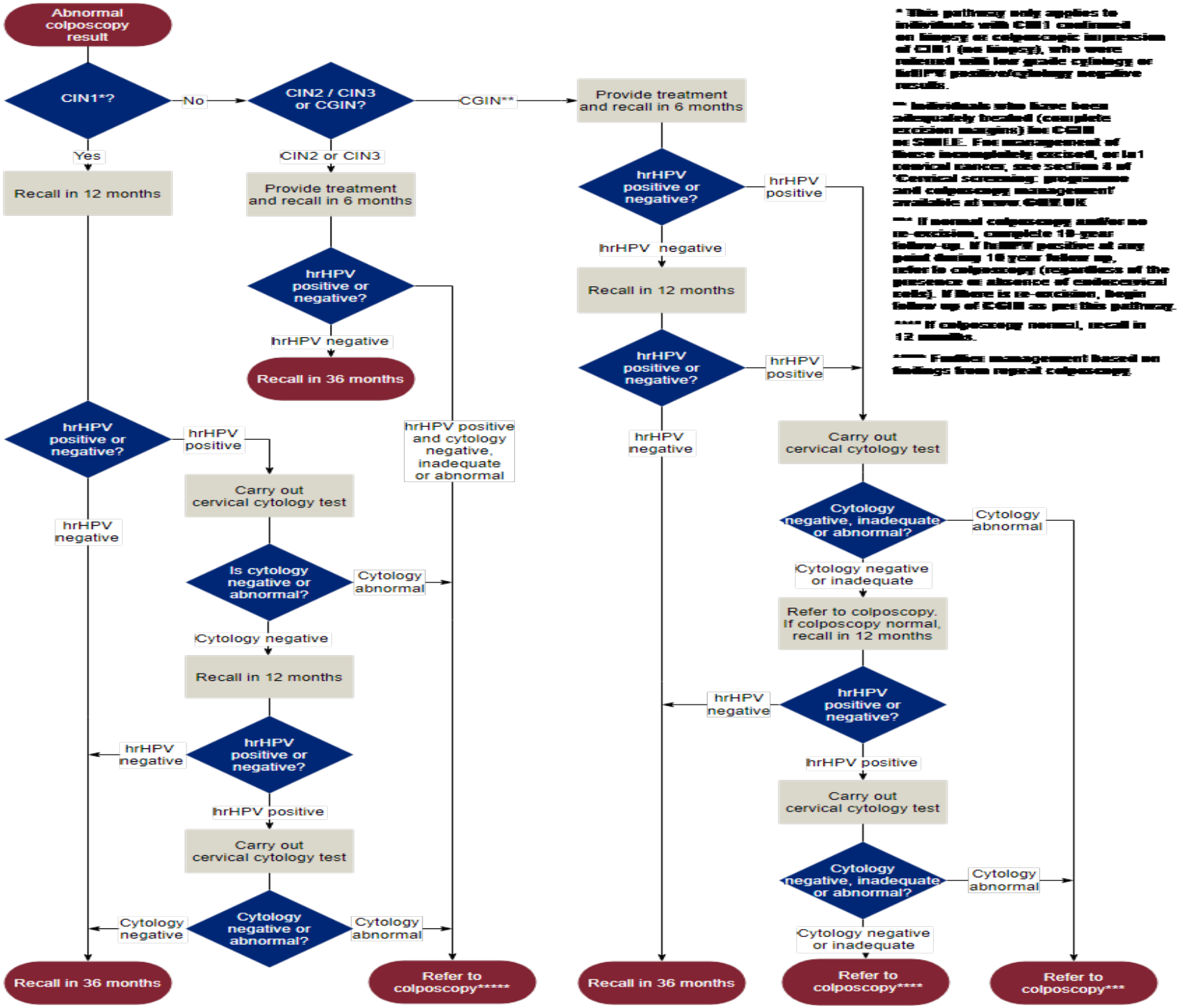
** if repeat colposcopy examination has inadequate outcome, consider LLETZ patient choice

*** see pathway part 3

LLETZ = large loop excision of the transformation zone

MDM = multidisciplinary team

Abnormal colposcopy result management



Low grade cytology

- Low grade dyskaryosis or borderline change in squamous cells on cytology
- Adequate and normal colposcopy
  - Low risk of developing cervical cancer
  - Return to 3-year recall
- Colposcopic low grade CIN or biopsy proven CIN1
  - Repeat smear in 12 months
- Persistent CIN1
  - Offer annual surveillance or treatment
- Persistent hrHPV positive with no evidence of disease on colposcopy should not be treated

High grade cytology

- Moderate or severe dyskaryosis
- Significant risk of CIN2 or CIN3
- Requires biopsy
- If high grade disease is not seen on colposcopy, MDT discussion is indicated
- Treatment should be excisional rather than ablative
- If no treatment is carried out, close surveillance with colposcopy and repeat cervical screening every 6 months is advised

Conservative management of CIN 2

- Consider if –
  - CIN3 and invasive disease has been excluded
  - The patient is amenable to 6 monthly colposcopy including repeat cervical screening and biopsy
- Treatment must be offered if CIN 2 has not resolved within 24 months
- All cases must be discussed at MDT

Benign endometrial cells in cervical samples

- Only reported in samples tested as HPV positive in individuals aged 45 or over
- Significance and management will depend on:
  - The phase of the menstrual cycle
  - Menopausal status
  - Medication
  - Clinical history
  - Age

Individuals with symptoms

- Individuals presenting with symptoms of cervical cancer (PCB, IMB, persistent vaginal discharge, etc.) are not candidates for screening
- Infection and contraceptive causes should be ruled out
- Speculum examination should be performed
- Referral to colposcopy if appearances suspicious of cervical ca.

Treatment options

- Large loop excision of transformation zone (LLETZ)
- Knife cone biopsy
- Laser conisation
- Laser ablation
- Cryotherapy
- There is no obviously superior conservative surgical technique for treating and eradicating CIN

Ablative treatment techniques

- Should only be used when –
  - There is an established histological diagnosis within 3 months of treatment
  - The entire transformation zone is visualised
  - There is no evidence of glandular abnormality
  - There is no suspicion of invasive disease
  - There is no major discrepancy between cytology and histology
  - There is no history of PCB or IMB
  - There is no gland crypt involvement on biopsy
  - There is no history of previous treatment
  - The patient is under the age of 50
- Cryocautery should only be used for low grade CIN

Repeat excision

- High grade CIN extending to the excision margins results in a higher risk of recurrence
- Routine repeat excision is not justified provided –
  - There is no evidence of glandular abnormality
  - There is no evidence of invasive disease
  - The individual is under 50 years old

Local excision of microinvasive squamous cancer FIGO stage Ia1

- Stage Ia1 cervical cancer can be managed by local excision if –
  - The endocervical and deep lateral excision margins are free of both CIN and invasive disease
  - The gynaecological cancer centre pathologist and multidisciplinary team (MDT) have reviewed the histology
- If the invasive lesion is excised but CIN extends only to the deep lateral and endocervical excision margin, then a repeat excision should be performed to confirm complete excision of the CIN and to exclude further invasive disease

Investigation of glandular abnormalities

- ?glandular neoplasia of endocervical type
  - Denotes that cytology shows features of CGIN or endocervical adenocarcinoma
  - Should be referred to colposcopy and seen within 2 weeks
  - Requires excisional biopsy rather than punch biopsy
- Borderline changes in endocervical cells
  - Should be referred to colposcopy and seen within 2 weeks
  - Where colposcopy is normal all cases should be discussed at MDT and followed up after 6 months
  - Requires excisional biopsy rather than punch biopsy
- ?glandular neoplasia (non-cervical)
  - Should be referred to gynaecology as urgent suspected cancer
  - Endometrial biopsy is indicated

Management of glandular abnormalities

- CGIN
  - Deep excisional biopsy –
    - In patients wishing to conserve fertility where the squamo-columnar junction (SCJ) is visible, to a depth of 10mm above the SCJ
    - In patients over the age of 50 or where the SCJ is not visible, to a depth of 20-25mm
  - If excision margins are not free from CGIN -
    - repeat excision should be offered
  - If repeat excision is declined -
    - hrHPV testing should be performed in colposcopy at 6 months after treatment
    - If hrHPV negative – repeat hrHPV testing 6 months later (12 months after treatment) then annually for a further 9 years

SMILE

- Stratified mucin producing intraepithelial lesion of the cervix
- Usually found in conjunction with CIN and CGIN
- Can occur in isolation
- Cytological appearance is poorly understood
- Should be managed as per guidance for CGIN

Hysterectomy for CGIN

- Simple hysterectomy may be considered if –
  - Fertility is not required
  - There are positive margins after adequate excisional procedure
  - Treatment by excision is followed by further high grade cytological abnormality
  - The patient is unwilling to undergo conservative management
  - Adequate screening follow up has not been possible eg: in cases of cervical stenosis
  - The patient has other clinical indications for hysterectomy
  - Invasive disease has been confidently excluded

Treatment follow up - CIN

- Test of cure (TOC) should be performed 6 months after treatment irrespective of excision margin status
  - TOC hrHPV negative - repeat cervical sample in 3 years, irrespective of age
    - Where the 3 year test is hrHPV negative, the individual can return to routine recall
  - TOC hrHPV positive - refer directly to colposcopy
  - TOC hrHPV unavailable – repeat testing after 3 months

Treatment follow up - CGIN

- If CGIN has been completely excised (excision margins are clear)
  - TOC should be performed 6 months after treatment
  - TOC hrHPV negative – second TOC 12 months later (18 months after treatment)
  - If both 6 and 18 month samples are hrHPV negative – return to recall in 3 years
  - If either sample is hrHPV positive or has abnormal cytology – refer directly to colposcopy
  - If either sample shows abnormal cytology, colposcopy is normal and re-excision is not appropriate – annual hrHPV testing for 10 years

- If CGIN has been incompletely excised and re-excision has been declined
  - hrHPV testing at 6 months after treatment should be performed in colposcopy
  - If hrHPV negative – repeat hrHPV testing 6 months later (12 months after treatment) then annually for a further 9 years

Treatment follow up – early-stage cervical cancer

- Stage Ia1
  - Conservative treatment leaving residual cervix
  - TOC hrHPV screening at 6 and 12 months after treatment and then annually for a further 9 years

- Stage Ia2/Ib1
  - Simple or radical trachelectomy or total hysterectomy
    - Follow up determined by the gynae-oncology MDT

Follow up after simple hysterectomy

- For individuals on routine recall and with no CIN in their hysterectomy specimen
  - No further vaginal vault sample is required

- Individuals who undergo hysterectomy and have completely excised CIN
  - Vaginal vault sample at 6 months post op
    - hrHPV negative – discharge
    - hrHPV positive – refer to colposcopy to rule out VaIN

- Individuals who undergo hysterectomy and have incompletely excised CIN
  - CIN1 – vault smears at 6, 12 and 24 months
  - CIN2/3 – vault smears at 6 and 12 months, then annually for 9 years
  - Continue follow up until 65 years old or 10 years after surgery (whichever is later)
  - If any sample if hrHPV positive, referral to colposcopy is indicated

Cervical screening during pregnancy

- Routine screening should be deferred until after pregnancy
- An individual referred with abnormal screening test should undergo colposcopy in the late 1st or early 2nd trimester
- If a previous colposcopy was abnormal and in the interim the individual becomes pregnant, colposcopy should not be delayed
- If an individual is due a TOC screen following treatment, this may be delayed until after pregnancy

Colposcopy during pregnancy

- The primary aim is to exclude invasive disease and to defer biopsy or treatment until after delivery
- Repeat colposcopy at the end of the 2nd trimester may be indicated if CIN2 or CIN3 is suspected
- If excisional biopsy clinically indicated -feasible and safe
  - Risk of miscarriage is 0.8%
  - No significant increased risk of haemorrhage when compared to excisional biopsy outside of pregnancy

Use of contraceptives

- An abnormal screening result should not influence the choice of contraception
- Intra-uterine systems do not necessarily need to be removed in order to perform local treatment
- Condom use may promote hrHPV clearance and CIN1 regression in conservative management

Menopause and use of HRT

- The use of systemic HRT is not known to alter the risk of cervical disease
- Colposcopic examination and adequacy can be improved with use of topical HRT
- Postmenopausal bleeding is not an indication for cervical screening in an adequately screened individual

Immunosuppressed individuals

- Renal failure requiring dialysis
  - Need a cervical screening sample at or shortly after diagnosis if not already up to date
- Patients undergoing organ transplantation
  - Need a cervical screening sample within the previous year
- Patients on maintenance immunosuppression post-transplantation
  - Routine screening
  - Drugs increase the risk of contracting hrHPV but do not impact the rate of progression through hrHPV and CIN to cervical cancer
- Multifocal disease
  - Must be managed in a centre with appropriate skill and expertise
  - Consider 6 monthly screening, colposcopy, vulvoscopy, anoscopy and biopsy

Immunosuppressed individuals

- Other individuals with immunosuppression
  - No indication for increased surveillance for individuals receiving
    - Chemotherapy for non-genital cancers
    - Ioestrogen antagonists such as tamoxifen
    - Alemtuzumab
    - Cytotoxic drugs for rheumatological disorders or biologic agents for other disorders
- Individuals exposed to diethylstilbestrol (DES)
  - Daughters of individuals exposed to DES are at increased risk of clear cell cancer of the cervix and vagina but not other forms of cervical cancer
    - Routine call and recall is appropriate
  - DES daughters with the stigmata of DES exposure require individualised plans – usually annual colposcopy

Immunosuppressed individuals

- HIV positive individuals
  - Annual screening, ideally with initial colposcopy
  - CIN should be managed as per national guideline
  - Higher cervical treatment failure rate
  - Screening can be ceased at 65 if it has been normal

Any Questions?