European Journal of Obstetrics and Gynecology xxx (xxxx) xxx-xxx

Contents lists available at ScienceDirect



European Journal of Obstetrics and Gynecology

journal homepage: www.elsevier.com

Review article

# European consensus statement on essential colposcopy

C.W.E. Redman<sup>a</sup>, V. Kesic<sup>b</sup>, M.E. Cruickshank<sup>c,</sup>, M. Gultekin<sup>d</sup>, X. Carcopino<sup>e</sup>, M. Castro Sanchez<sup>f</sup>,

M. Grigore<sup>g</sup>, M. Jakobsson<sup>h</sup>, V. Kuppers<sup>i</sup>, A. Pedro<sup>j</sup>, O. Reich<sup>k</sup>, S. Leeson<sup>1</sup>, U. Tabuica<sup>m</sup>, J. Zodzika<sup>n</sup>,

A. Ciavattini<sup>o</sup>, R. Jach<sup>p</sup>, M. Katsyuba<sup>q</sup>, R. Koiss<sup>r</sup>, P. Martin-Hirsch<sup>s</sup>, W.A. Tjalma<sup>t</sup>, P. Nieminen<sup>u</sup>On behalf of the European Federation for Colposcopy and Pathology of the Lower Genital Tract (EFC) and the European Society of

Gynecologic Oncology (ESGO)

<sup>a</sup> Past-President European Federation of Colposcopy and University Hospitals of North Midlands, Stoke-on-Trent, UK

<sup>b</sup> Faculty of Medicine, University of Belgrade, Clinic of Obstetrics and Gynecology, Clinical Center of Serbia, Belgrade, Serbia

- <sup>d</sup> Department of Obstetrics and Gynecology, Hacettepe University Faculty of Medicine, Ankara, Turkey
- e Department of Obstetrics and Gynaecology, Hôpital Nord, APHM, Aix-Marseille University (AMU), University Avignon, CNRS, IRD, IMBE UMR 7263, Marseille, France
- <sup>f</sup> Department of Obstetrics and Gynaecology, University Hospital Puerto De Hierro Majadahonda, Madrid, Spain
- <sup>g</sup> Department of Obstetrics and Gynecology, University of Medicine and Pharmacy "Grigore T. Popa" Iasi, Romania
- <sup>h</sup> HUS Hyvinkää Hospital, University of Helsinki, Finland
- <sup>i</sup> Obstetrics and Gynecology Koenigsallee 64, Duesseldorf, Germany
- <sup>j</sup> Department of Obstetrics and Gynaecology, Cuf Sintra Hospital, Sintra, Portugal
- <sup>k</sup> Department of Obstetrics and Gynecology, Medical University of Graz, Austria
- <sup>1</sup> Department of Obstetrics and Gynaecology, Ysbyty Gwynedd, Bangor, Wales, UK
- <sup>m</sup> Department of Obstetrics and Gynecology, State University of Medicine and Pharmacy, Referral Center of Colposcopy, Chisinau, Moldavia
- <sup>n</sup> Department of Obstetrics and Gynaecology, Riga Stradin<sup>§</sup> University, Riga East Clinical University Hospital, Riga, Latvia
- <sup>o</sup> Department of Woman's Health Sciences, Gynecologic Section, Polytechnic University of Marche, Ancona, Italy
- <sup>p</sup> Clinic of Endocrynologic Gynecology, University Hospital UJ CM, Krakow, Poland
- <sup>q</sup> Department of Oncology, Kazan State Medical Academy, Kazan, Russian Federation
- <sup>r</sup> Department of Obstetrics and Gynecologic Oncology, St. Stephan Hospital, Budapest, Hungary
- <sup>s</sup> Department of Obstetrics & Gynaecology, Lancashire Teaching Hospitals NHS Foundation Trust, Lancashire & Royal Preston Hospital, Preston, United Kingdom
- <sup>t</sup> Department of Obstetrics and Gynecology, Breast Clinic Unit Gynecologic Oncology, Antwerp University Hospital and University of Antwerp, Belgium
- <sup>u</sup> Department of Obstetrics and Gynecology, Helsinki University Hospital and Helsinki University, Finland

# ARTICLE INFO

Article history: Received 14 April 2020 Received in revised form 24 May 2020 Accepted 15 June 2020 Available online xxx

Keywords: Colposcopy European guideline Cervix Screening Cancer

### Introduction

This consensus statement is an up-date of the previous European guideline from 2008 and relates to colposcopy undertaken in patients identified through cervical screening and does not deal with the organisation and management of cervical screening itself [1].

The guidance is intended for general, rather than specialist or expert colposcopists and therefore may not be appropriate in countries such as the United Kingdom or Germany where such distinctions do not exist. Although there are some differences in colposcopic practice in different parts of Europe, this statement aims to a common consensus or core of practise. This guidance provides a short but not exhaustive set of recommendations that will cover most aspects of colposcopy. Specialist advice should be sought for those topics not adequately covered, either because of complexity or lack of consensus.

In 2018, cervical cancer is still a major health issue in Europe with 61.072 diagnoses and 25.829 deaths [2]. It is with a crude incidence and mortality rate of respectively 15.9 and 6.7 per 100.000

© 2020.

<sup>&</sup>lt;sup>c</sup> Aberdeen Centre for Women's Health Research, University of Aberdeen, UK

<sup>\*</sup> Corresponding author at: Aberdeen Centre for Women's Health Research, Aberdeen Maternity Hospital, Aberdeen, AB25 2ZD, UK.

Email address: m.e.cruickshank@abdn.ac.uk (M.E. Cruickshank)

women per year, the second most common disease and cause of death in women aged between 15–44 years in Europe [2]. Primary (vaccination) and secondary prevention (screening) have the potential to reduce the world-wide cervical cancer incidence to 4 or less per 100.000 by the end of the century [3].

The World Health Organisation has called for urgent action to scale up implementation of proven measures towards achieving the elimination of cervical cancer as a global public health problem, including vaccination against HPV, screening and treatment of pre-cancer, early detection and prompt treatment of early invasive cancers, and palliative care [3].

Colposcopy is a tool to evaluate women who have an abnormal cervical screening test (including cytology and HPV tests) or to assess women with a clinically suspicious cervix.

Women who have a positive cervical screening result are at risk of having a progressive cervical neoplastic lesion, which without treatment might progress to cancer. Equally some lesions may regress spontaneously, especially in young women, and therefore treatment can be avoided. Criteria for referral to colposcopy will vary between different cervical screening programmes for a variety of reasons. Likewise, patients are informed differently about colposcopy.

An overview of digital information leaflets for colposcopy available in European countries, together with the EFC consensus leaflet for women attending a colposcopy clinic are shown respectively in Tables 1 and 2.

# The aims of colposcopy are:

- 1 To evaluate the cervical, vaginal, vulvar and perianal epithelium and to differentiate between normal and abnormal.
- <sup>2</sup> To determine the precise geographical/anatomical position of the cervical transformation zone (TZ).
- 3 To identify if there are atypical findings in squamous epithelium and enable appropriate histological assessment.
- 4 To recognize or rule out cervical glandular disease.

#### Table 1

An overview of digital information leaflets for colposcopy available in European countries.

Austria	www.Kolposkopie.at
Belgium	https://www.vvog.be/sites/default/files/patientenbrochures/
	afwijkend baarmoederhalsuitstrijkje 0.pdf
Finland	https://www.terveyskyla.fi/naistalo/gynekologinen-terveys/
	kohdunsuun-irtosolumuutokset-papa/kudosmuutokset-ja-niiden-
	hoitaminen.
France	www.societe-colposcopie.com
Germany	https://www.ag-cpc.de/wp-content/uploads/2019/09/Patninfo.pdf
Hungary	www.cancerscreening.hscni.net/pdf/Cervical screening
0,1	colposcopy_edit_2_HUNGARIAN_FINAL.pdf
Italy	http://www.colposcopiaitaliana.it/newsletter inc.asp
Latvia	http://kolposkopija.lv/kolposkopija
Moldova	https://paptest.md
Poland	kolposkopia.info
Portugal	https://www.cuf.pt/marcacoes/exames/colposcopia; https://www.
Ũ	hospitaldaluz.pt/pt/guia-de-saude/dicionario-de-saude/C/165/
	colposcopia; https://rotasaude.lusiadas.pt/prevencao-e-estilo-de-
	vida/saude-da-familia/colposcopia-para-que-serve-e-cuidados-a-
	adotar/; https://hff.min-saude.pt/saude-da-mulher-exames-
	preventivos-que-precisa-fazer/
Romania	https://www.clinicamicomi.ro/?page_id=124; http://
	patologiacolului.ro/examenul-colposcopic/
Russian	https://ncagp.ru/index.php? t8=251
Federation	
Scotland	https://www.bsccp.org.uk/women/frequently-asked-questions/
	#about-colposcopy
Serbia	http://www.ukcps.rs/
Spain	http://www.aepcc.org/pacientes/
Turkey	no link
United-	https://www.bsccp.org.uk/women/frequently-asked-questions/
Kingdom	#about-colposcopy
Wales	http://www.cervicalscreeningwales.wales.nhs.uk/sitesplus/
	documents/1032/colposcopy%20booklet%20eng%20no%20crop.
	pdf

# Table 2

EFC consensus leaflet for women attending a colposcopy clinic.

#### What is colposcopy?

- A colposcopy is an examination to check the health of your cervix (neck of the womb).
- A specialist doctor (called a colposcopist) looks at your cervix using a colposcope. This looks like a pair of binoculars on a stand. It does not go inside you. **Why do I need a colposcopy?**
- Your cervical screening test has shown that the human papillomavirus (HPV) is present, which can cause cell changes; or
  - You have had symptoms of bleeding after sex or between your period
  - You cervix showed some alteration and your doctor wanted you to have a closer examination of your cervix

#### What does 'cell changes' mean?

- Your smear sample may be checked for HPV virus as well as for changes in the cells that covers the cervix. If changes are seen in the cells taken at your screening test, there is a chance they will need to be treated.
- Most 'low grade' changes do not need treating, but your colposcopist needs to see you to make sure.
- If you have 'high grade' changes, these might need to be treated, to stop them becoming cervical cancer. Most women who have a colposcopy do not have cervical cancer.

### What is HPV?

- The human papilloma virus (HPV) is a common virus. Today, more than 200 different types of HPV are known. Of these, at least 40 can cause genital infection and 13 of these 40 are high-risk HPV types with the ability to cause cervical precursor changes and cancer. According to studies, more than 80 % of people have had a papillomavirus infection in their lifetime.
- There is no medical treatment for an HPV infection. This virus infection itself is not cancer or any of its preliminary stages; yet HPV is a necessary factor in the development of precancer stages in the cervix. These premalignant lesions can be effectively treated. In non-serious cases, monitoring through Pap tests is sufficient, since most of these changes and infections heal on their own.

### What will happen at the clinic?

The colposcopist will explain why you are at the clinic and what they will do. You can ask them any questions. It is helpful to know the date of your last period. The colposcopist will check if you are happy to go ahead with the examination.

#### What happens during the colposcopy examination?

- You will need to get onto a special couch. A nurse will help you and stay with you. A speculum (the same instrument used when you had your smear taken) is gently put inside your vagina. The colposcopist will put some liquid onto your cervix. Sometimes this can feel cold or can tingle. Most colposcopists use a combination of diluted acetic acid and Schiller's iodine tests:
- Acetic acid is a very weak acidic liquid. It is sometimes called diluted vinegar. The colposcopist gently applies it to your cervix using a cotton wool ball or with a spray. It shows cell changes by turning them white.
- Schiller's iodine test uses an iodine solution. It stains normal cervical tissue dark brown. Cell changes may not stain, so the colposcopist can see them. Some people are allergic to iodine or sea food. If you are, please tell your colposcopist
- The colposcopist might take a small piece of skin from your cervix for a biopsy (examination) if they think there are cell changes. This is sometimes called a punch biopsy. You will be contacted with your results. These will confirm if you need treatment or not.

The examination takes 10-20 min.

### What about treatment?

- You may be offered treatment at your first visit, if you have high grade changes and if you agree, to get rid of cell changes. This will be explained to you at the time. There are different ways of treating cell changes. You may have heard of 'loop treatment' as this is the commonest way of treating CIN today. The full name for the procedure is 'Large Loop Excision of the Transformation Zone' or LLETZ. The abnormal area is removed using a wire loop through which an electric current is passed. This can be performed after you are given local anaesthetic to 'numb' the cervix. LLETZ is a simple and safe technique which gives excellent results. Very few women may need a general anaesthetic and you will discuss this with your colposcopist.
- Another form of treatment is ablation which destroys the abnormal cells. If you have ablation, you will have a punch biopsy first and return for treatment under local anaesthetic.
- You will not need sick leave or pain medication after treatment. Minor mucous, bloody discharge will occur following the procedure for a few weeks. Taking a bath, swimming and having sexual intercourse are not recommended for 4 weeks due to a risk of inflammation and discharge. Some this there is an odour, if so contact your doctor.
- Cervical cytological changes or their possible treatment do not cause infertility. Recent studies show that LLETZ-treatment may slightly increase the risk of preterm delivery.
- Not all cell changes need to be treated. Cell changes are usually treated if they do not go back to normal or are more than low-grade changes.
- Treatment is nearly always successful. A small number of women might need to be treated again. It is very important to attend for any follow-up tests

### What else do I need to know?

- If you are having your period on the day of your appointment, please ring the clinic. They may tell you to keep your appointment, especially if your periods are not regular.
- A colposcopy can be done safely during pregnancy. If you need treatment this is usually delayed until three months after your baby is born.
- If you have a coil (IUD) there is a small chance that it might need to be taken out at your appointment. If the coil is removed install a new one or check the risk of pregnancy.
- What if I have problems after the colposcopy?
- Please contact the clinic or follow the advice the colposcopy clinic gave you, if you notice:
  - heavy bleeding (not your period)
  - vaginal discharge with or without an odour that is not normal for you
  - pain that doesn't get better with your usual painkillers
  - that you feel hot and cold, or shivery
- 5 To recognize or rule out invasive cancer.
- 6 To facilitate treatment of intra-epithelial lesions. Colposcopy must be systematically performed prior to treatment of suspected or confirmed intra-epithelial disease
- 7 To monitor progression or regression of intra-epithelial lesions.

# **Conduct of colposcopy:**

- 1 Colposcopy should only be performed by trained, and preferably certified, colposcopists or by trainees under appropriate supervision.
- <sup>2</sup> Every woman should be offered verbal information during colposcopy and be sent written information before colposcopy to facilitate informed consent.

# Technique of colposcopy

Colposcopy is a diagnostic procedure to visualize the epithelia of the lower genital tract with magnification and adequate illumination before and after application of acetic acid and Lugol's iodine.

The colposcopic examination should be adequately documented, using the International Federation of Cervical Pathology and Colposcopy (IFCPC) nomenclature [4] (See Table 3). The Swede Score [5] can be helpful to evaluate lesion grade and guide appropriate management (See Table 4).

Colposcopically directed punch biopsies:

- Should provide interpretable material
- Sensitivity is improved if at least two are taken
- Are not representative when there is a TZ 3
- LSIL cytology and grade 1 or negative colposcopic findings do not require biopsies in every case, but are recommended [6,7]
- Reasons for not performing a biopsy should be recorded
- If biopsies are reported as inadequate, then biopsy should be repeated if there is a residual colposcopic lesion.

Excisional biopsy such as Large Loop Excision of the Transformation Zone (LLETZ) is recommended in the following circumstances:

- When invasion is suspected colposcopically
- When the squamo-columnar junction (SCJ) is not visible (TZ 3) but histology is required.

An excisional biopsy/LLETZ can be considered when there is HSIL cytology and colposcopic grade 2 findings  $% \left( {{{\rm{D}}_{{\rm{B}}}} \right)$ 

Endocervical curettage can be considered:

- When the SCJ is not visible but histology is required
- When glandular disease is suspected.

#### Table 3

Documentation of a colposcopic examination; IFCPC 2011 colposcopic terminology of the cervix (4).

2011 IFCPC colposcopic termi	2011 IFCPC colposcopic terminology of the cervix1					
General assessment	Adequate/inadequate for	the reason (i.e.:				
	cervix obscured by int scar)					
	<ul> <li>Squamo-columnar junction visibility: com- pletely visible, partially visible, not visible</li> </ul>					
	<ul> <li>Transformation zone type</li> </ul>					
Normal colposcopic findings	Transformation zone type	, 2, 5				
inding5	Original squamous epithelium					
	• Mature					
	Atrophic					
	Columnar epithelium					
	• Ectopy					
	Metaplastic squamous epithelium					
	Nabothian cysts					
	• Crypt (gland) openings					
	Deciduosis in pregnancy					
Abnormal General		Location of the lesion: Inside or outside the T-				
colposcopic principles	zone, Location of the lesion by clock position					
findings	Sine of the Locient Mumber	- f				
	Size of the lesion: Number the lesion covers, Size of the	*				
	of cervix	e teston in percentage				
Grade 1	Thin aceto-white	Fine mosaic, Fine				
(Minor)	epithelium, Irregular,	punctation				
	geographic border	о ·				
Grade 2 (Major)	Dense aceto-white epithelium, Rapid	Coarse mosaic, Coarse punctuation,				
(Wajor)	appearance of	Sharp border, Inner				
	acetowhitening; Cuffed	border sign, Ridge				
	crypt (gland) openings	sign				
Non	Leukoplakia (keratosis, hyp					
specific	Lugol's staining (Schiller's	test): stained/non-				
Suspicious for invasion	stained Atypical vessels					
Suspicious for invasion	Additional signs: Fragile ve	essels Irregular				
	surface, Exophytic lesion, Necrosis, Ulceration					
	(necrotic), tumor/gross neoplasm					
Miscellaneous finding	Congenital	Stenosis,				
	transformation zone,	Congenital				
	Condyloma, Polyp (Ectocervical/	anomaly, Post treatment				
	endocervical)	consequence,				
	Inflammation,	Endometriosis				

Colposcopy in postmenopausal women:

• Colposcopic examination and adequacy can be improved from the use of topical hormone replacement therapy.

Colposcopy in pregnancy:

- Should only be undertaken by an experienced, trained colposcopist
- Should be performed, if indicated, and not deferred because of pregnancy
- Primarily aims to detect or exclude invasive disease. If invasive disease is not suspected, then punch biopsy or treatment is deferred until post-partum
- Should not include endocervical curettage
- · Enables excisional biopsy/ LLETZ if invasion is suspected
- If colposcopy has been performed for an abnormal cytology or biopsy-proven CIN during pregnancy, postpartum assessment is essential.

### Management and treatment

Cervical screening aims to reduce cervical cancer incidence and mortality by the detection and treatment of HSIL (CIN 2,3). The aim

Table	e 4
-------	-----

Swede Score				
	0	1	2	Score
Aceto uptake	Zero or transparent	Shady, Milky (not transparent; not opaque)	Distinct, opaque white	
Margins/Surface	Diffuse	Sharp but irregular, jagged, 'geographical' satellites	Sharp and even, difference in surface level, including 'cuffing'	
Vessels	Fine, regular	Absent	Coarse or atypical	
Lesion size	<5mm	5–15 mm or 2 quadrants	>15 mm or 3–4 quadrants/ endocervically undefined	
Iodine staining	Brown	Faintly or patchy yellow	Distinct yellow	
Total score (maxir	num 10)	1 55		
Interpretation of S	wede Score			
Overall Swede Score		poscopic prediction	of probable histology	,
0–4		Low grade/normal CIN 1		
5–6		High grade/non invasive cancer CIN 2+		
7–10		High grade/suspected invasive cancer CIN 2+		

of treatment is to remove or ablate the premalignant epithelium in its entirety.

When to treat:

- When HSIL confirmed histologically or highly probable on basis of cytology and colposcopic findings. Treatment of histological LSIL should be avoided
- Not every non-pregnant woman with a histological HSIL needs treatment. Expectant management can be considered, if women are young (aged ≤30), have small HSIL/CIN2 lesions with a completely visualised TZ and can be carefully monitored [8]
- The woman should be adequately counselled, and consent obtained. Treatment methods:
- 1 All women needing treatment must have had a colposcopic assessment
- 2 Treatment modalities for histological HSIL include local treatments (excision or ablation) and, rarely, hysterectomy
- 3 There is no obviously superior conservative technique for treating SIL [9]
- 4 Ablative techniques are only suitable when:
- The entire TZ is visualised
- There is no evidence of glandular abnormality
- There is no evidence of invasive disease
- There is an established histological diagnosis
- There is no major discrepancy between cytology and histology
- There has been no previous treatment
- 5 Cryocautery should not be used to treat HSIL.

Methodology

- Local treatments should be performed, wherever possible, in outpatients and with local analgesia
- The treatment should be done using a colposcope
- Treatment at first visit to colposcopy with ASCUS or LSIL cytology should not be offered

- · Excisional treatments should aim for complete excision of CIN
- Excisional treatments should have a length of at least 8 mm (NHSCSP, 2016) and be tailored to the size of the cervix and TZ status.

# Initial management of women with ASCUS

Women with ASCUS can be referred to colposcopy in one of a number of scenarios, depending on the agreed arrangements in that screening programme. Referral after a single ASCUS result is felt to be sub-optimal. Indications for colposcopy include:

- If reflex high-risk HPV (hrHPV) testing is positive
- Persistent cytological abnormality on follow up.

Management is dependent on findings:

- If colposcopy is normal, and the TZ completely visualised, then the woman can return to recall
- If grade 1 abnormalities are observed, colposcopic biopsy is not mandatory but often recommended to confirm or exclude CIN. If not biopsied then a further cervical test (e.g. cytology +/- hrHPV) should be performed in 12 months
- If there is biopsy-proven histological LSIL lesion, a repeat cervical test (cytology +/- hrHPV test) should be performed in 12 months
- If the lesion has not resolved within 2 years of initial referral to colposcopy, then a biopsy should be taken
- If there are grade 2 changes then biopsy is mandatory.

# Initial management of women with LSIL

Women with LSIL can be referred to colposcopy in one of a number of scenarios, depending on the agreed arrangements in that screening program. These include:

- Direct referral to colposcopy after a single LSIL result
- When hrHPV test is positive
- Persistent cytological abnormality on follow-up.
- Colposcopic management and follow-up is as for ASCUS.

### Initial management of women with HSIL

Biopsies should be taken in non-pregnant women.

- If histological HSIL is confirmed, then treatment should usually be performed but expectant management can be considered in young women (≤30 years) with a small area HSIL/CIN 2 lesion, with a fully visible transformation zone [9]
- If treatment is not undertaken, then close surveillance with colposcopy and cytology is recommended with 6 monthly intervals. If at follow-up HSIL cytology persists over 24 months, then excisional treatment is recommended
- If HSIL cytology cannot be explained on biopsy and vaginal intraepithelial neoplasia has been excluded, then such cases should be discussed at multidisciplinary meetings. Multiple directed biopsies or loop excision should have been taken. If histological LSIL or less is confirmed, then colposcopic follow-up with cytology and biopsies at 6 months is recommended
- If invasion is suspected at colposcopy, then an excisional biopsy/ LLETZ is indicated. If cancer is confirmed on histology, then the case should be reviewed in a gynaecological oncology unit.

# Management of women with glandular abnormalities

• Expert cytological and colposcopic assessment is essential. Women with AGC should be seen and assessed only by expert colposcopists.

## Follow-up after treatment for CIN

Follow-up after treatment is essential as treated women are between two to five times more likely to develop cervical cancer in at least the next 20 years. The following are recommended:

- hrHPV testing at 6 months (test of cure, TOC), either alone or in conjunction with cytology is recommended [2,10]
- Women with a cytological sample that has been reported as negative or as showing LSIL or less and whose hrHPV test is negative should be recalled in 3 years
- Women with a cytological sample that has been reported as negative or as showing LSIL or less and whose hrHPV test is positive should be referred for colposcopy
- Women with a HSIL, ASC-H or AGC cytology should be referred to colposcopy.

### Follow-up of following treatment for early stage cervical cancer

In these cases, follow-up is likely to be determined by the management policy of the treating gynaecological oncologist. In general terms, if conservative treatment has been performed, leaving a residual cervix, then regular long-term follow-up with cytology follow-up or hrHPV testing is recommended.

# **Declaration of Competing Interest**

The authors report no declarations of interest.

### References

 J. Jordan, M. Arbyn, P. Martin-Hirsch, U. Schenck, J.-J. Baldauf, D. Da Silva, et al., European guidelines for quality assurance in cervical cancer screening: recommendations for clinical management of abnormal cervical cytology, part 1, Cytopathology [Internet] 19 (6) (2008) 342–354, https://doi.org/10.1111/j.1365-2303.2008.00623.x, Dec [cited 2020 Feb 13], Available from:.

- [2] L. Bruni, G. Albero, B. Serrano, M. Mena, D. Gómez, J. Muñoz, et al., IIC on H and C (HPV IC). Human papillomavirus and related diseases in the world, Summ Rep (2019) 1–306, 17 June 2019 [Internet], Available from: https://www. hpvcentre.net/statistics/reports/XWX.pdf.
- [3] K.T. Simms, J. Steinberg, M. Caruana, M.A. Smith, J.-B. Lew, I. Soerjomataram, et al., Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020-99: a modelling study, Lancet Oncol [Internet] 20 (3) (2019) 394–407, Mar [cited 2019 Dec 22], Available from: https://linkinghub.elsevier. com/retrieve/pii/S1470204518308362.
- [4] J. Bornstein, J. Bentley, P. Bösze, F. Girardi, H. Haefner, M. Menton, et al., Colposcopic terminology of the international federation for cervical pathology and colposcopy, Obstet Gynecol [Internet] 120 (1) (2011) 166–172, 2012 Jul [cited 2020 Feb 13], Available from: http://insights.ovid.com/crossref?an=00006250-201207000-00026.
- [5] B. Strander, A. Ellstrom-Andersson, S. Franzen, I. Milsom, T. Radberg, The performance of a new scoring system for colposcopy in detecting high-grade dysplasia in the uterine cervix, Acta Obstet Gynecol Scand [Internet] 84 (10) (2005) 1013–1017, Oct [cited 2020 Feb 13], Available from: http://www.ncbi.nlm.nih. gov/pubmed/16167921.
- [6] J.-J. Baldauf, M. Dreyfus, J. Ritter, E. Philippe, An analysis of the factors involved in the diagnostic accuracy of colposcopically directed biopsy, Acta Obstet Gynecol Scand [Internet] 76 (5) (1997) 468–473, Jan [cited 2020 Feb 13], Available from: http://www.ncbi.nlm.nih.gov/pubmed/9197451.
- [7] M.H. Jones, D. Jenkins, A. Singer, Regular audit of colposcopic biopsies from women with a mildly dyskaryotic or borderline cervical smear results in fewer cases of CINIII, Cytopathology [Internet] 7 (1) (1996) 17–24, Feb [cited 2020 Feb 13], Available from: http://www.ncbi.nlm.nih.gov/pubmed/8833870.
- [8] K. Tainio, A. Athanasiou, K.A.O. Tikkinen, R. Aaltonen, J. Cárdenas, Hernándes, et al., Clinical course of untreated cervical intraepithelial neoplasia grade 2 under active surveillance: systematic review and meta-analysis, BMJ [Internet] 360 (2018) k499, https://doi.org/10.1136/bmj.k499, Feb 27 [cited 2020 Feb 13], Available from:.
- [9] P.P. Martin-Hirsch, E. Paraskevaidis, A. Bryant, H.O. Dickinson, Surgery for cervical intraepithelial neoplasia, Cochrane Database Syst Rev [Internet] (12) (2013), CD001318, Dec 4 [cited 2020 Feb 13], Available from: http://www.ncbi. nlm.nih.gov/pubmed/24302546.
- [10] J. Jordan, P. Martin-Hirsch, M. Arbyn, U. Schenck, J.-J. Baldauf, D. Da Silva, et al., European guidelines for clinical management of abnormal cervical cytology, part 2, Cytopathology [Internet] 20 (1) (2009) 5–16, https://doi.org/10.1111/j. 1365-2303.2008.00636.x, Feb [cited 2020 Feb 13], Available from:.