CONVEGNO NAZIONALE GISCI 2015

Complesso Monumentale di Santa Caterina
Finalborgo (SV), 21-22 maggio 2015

Il convegno è dedicato a Mario SIDERI Membro del Comitato di Coordinamento

Uno screening: due percorsi

Test HPV e PAP Test a confronto nella pratica
Valutazione e analisi della coesistenza dei due percorsi nella pratica corrente

WORKSHOP PRECONGRESSUALE

IL RUOLO DELLA COLPOSCOPIA NELLO SCRENNING CON HPV

DOPPIO TEST HPV POSITIVO E CITOLOGIA NEGATIVA: DALLE LINEE GUIDA AMERICANE AI PROTOCOLLI REGIONALI

G. MAINA
A.O CITTA' DELLA SCIENZA E DELLA SALUTE DI TORINO – PRESIDIO S. ANNA

American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology Screening Guidelines for the Prevention and Early Detection of Cervical Cancer

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Summary of Recommendations

Population	Recommended Screening Method*	Management of Screen Results	Comments
Aged <21 y	No screening		HPV testing should not be used for screening or management of ASC-US in this age group
Aged 21-29 y	Cytology alone every 3 y	HPV-positive ASC-US† or cytology of LSIL or more severe: Refer to ASCCP guidelines[2] Cytology negative or HPV-negative ASC-US†: Rescreen with cytology in 3 y	HPV testing should not be used for screening in this age group
Aged 30-65 y	HPV and cytology "cotesting" every 5 y (preferred)	HPV-positive ASC-US or cytology of LSIL or more severe: Refer to ASCCP guidelines[2] HPV positive, cytology negative: Option 1: 12-mo follow-up with cotesting Option 2: Test for HPV16 or HPV16/18 genotypes • If HPV16 or HPV16/18 positive: refer to colposcopy • If HPV16 or HPV16/18 negative: 12-mo follow-up with cotesting Cotest negative or HPV-negative ASC-US: Rescreen with cotesting in 5 y	Screening by HPV testing alone is not recommended for most clinical settingst
	Cytology alone every 3 y (acceptable)	HPV-positive ASC-US† or cytology of LSIL or more severe: Refer to ASCCP guidelines[2] Cytology negative or HPV-negative ASC-US†: Rescreen with cytology in 3 y	
Aged >65 y	No screening following adequate negative prior screening		Women with a history of CIN2 or a more severe diagnosis should continue routine screening for at least 20 y

Summary of Recommendations

Population	Recommended Screening Method*	Management of Screen Results	Comments
After hysterectomy	No screening		Applies to women without a cervix and without a history of CIN2 or a more severe diagnosis in the past 20 y or cervical cancer ever
HPV vaccinated	Follow age-specific recommendations (same as unvaccinated women)		

ASCCP

The society for lower genital tract disorders since 1964.

Algorithms

Updated Consensus Guidelines for Managing Abnormal Cervical Cancer Screening Tests and Cancer Precursors

American Society for Colposcopy and Cervical Pathology

Reprinted – April 2013

Introduction

Cytology

Since the publication of the 2006 consensus guidelines, new cervical cancer screening guidelines have been published and new information has become available which includes key cervical cancer screening and follow up, and cervical precancer management data over a nine year period among more than 1 million women cared for at Kaiser Permanente Northern California. Moreover, women under age 21 are no longer receiving cervical cancer screening and cotesting with high-risk HPV type assays, and cervical cytology is being used to screen women 30 years of age and older.

Therefore, in 2012 the American Society for Colposcopy and Cervical Pathology (ASCCP), together with its 24 partner professional societies, Federal agencies, and international organizations, began the process of revising the 2006 management guidelines. This culminated in the consensus conference held at the National Institutes of Health in September 2012. This report provides updated recommendations for managing women with cytological abnormalities. A more comprehensive discussion of these recommendations and their supporting evidence was published in the *Journal of Lower Genital Tract Disease* and *Obstetrics and Gynecology* and is made available on the ASCCP website at www.asccp.org.

Histopathology

Appropriate management of women with histo-pathologically diagnosed cervical precancer is an important component of cervical cancer prevention programs. Although the precise number of women diagnosed with cervical precancer each year in the U.S. is not known, it appears to be a relatively common occurence. In 2001 and 2006, the American Society for Colposcopy and Cervical Pathology and 28 partner professional societies, federal agencies, and international organizations, convened processes to develop and update consensus guidelines for the management of women with cervical precancer. Since then, considerable new information has emerged about management of young women, and the impact of treatment for precursor disease on pregnancy outcomes. Progress has also been made in our understanding of the management of women with adenocarcinoma in-situ, also a human papillomavirus (HPV)—associated precursor lesion to invasive cervical adenocarcinoma. Therefore, in 2012 the ASCCP, together with its partner organizations, reconvened the consensus process of revising the guidelines. This culminated in the September 2012 Consensus Conference held at the National Institutes of Health. This report provides the recommendations developed for managing women with cervical precancer. A summary of the guidelines themselves–including the recommendations for managing women with cervical cytological abnormalities — are published in JLGTD and Obstetrics & Gynecology.

General Comments

Although the guidelines are based on evidence whenever possible, for certain clinical situations limited high-quality evidence exists. In these situations the guidelines are based on consensus expert opinion. Guidelines should never be a substitute for clinical judgment. Clinical judgment should always be used when applying a guideline to an individual patient since guidelines may not apply to all patient-related situations. Finally, both clinicians and patients need to recognize that while most cases of cervical cancer can be prevented through a program of screening and management of cervical precancer, no screening or treatment modality is 100% effective and invasive cervical cancer can develop in women participating in such programs.

The 2001 Bethesda System terminology is used for cytological classification. This terminology utilizes the terms low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL) to refer to low-grade lesions and high-grade cervical cancer precursors respectively. For managing cervical precancer, the histopathological classification is two-tiered applying the terms cervical intraepithelial neoplasia grade 1 (CIN 1) to low-grade lesions and CIN2,3 to high-grade lesions. If using the 2012 Lower Anogenital Squamous Terminology (LAST), CIN1 is equivalent to histopathological LSIL and CIN2,3 is equivalent to histopathological HSIL. Please note that cytological LSIL is not equivalent to histopathological CIN 1 and cytological HSIL is not equivalent to histopathological CIN2,3. The current guidelines expand clinical indications for HPV testing based on studies using FDA-approved, validated HPV assays. Management decisions based on results using HPV tests not similarly validated may not result in outcomes intended by these guidelines. HPV testing should be restricted to high-risk (oncogenic) HPV types. Testing for low-risk (non-oncogenic) HPV types has no role in evaluating women with abnormal cervical cytological results. Therefore, whenever "HPV testing" is mentioned in the guidelines, it refers to testing for high-risk (oncogenic) HPV types only.

Definitions

Terms Utilized in the Consensus Guidelines

- **Colposcopy** is the examination of the cervix, vagina, and, in some instances the vulva, with the colposcope after the application of a 3-5% acetic acid solution coupled with obtaining colposcopically-directed biopsies of all lesions suspected of representing neoplasia.
- **Endocervical sampling** includes obtaining a specimen for either histopathological evaluation using an endocervical curette or a cytobrush or for cytological evaluation using a cytobrush.
- **Endocervical assessment** is the process of evaluating the endocervical canal for the presence of neoplasia using either a colposcope or endocervical sampling.
- **Diagnostic excisional procedure** is the process of obtaining a specimen from the transformation zone and endocervical canal for histopathological evaluation and includes laser conization, cold-knife conization, loop electrosurgical excision procedure (LEEP), and loop electrosurgical conization.
- **Adequate colposcopy** indicates that the entire squamocolumnar junction and the margin of any visible lesion can be visualized with the colposcope.
- **Endometrial sampling** includes obtaining a specimen for histopathological evaluation using an endometrial aspiration or biopsy device, a "dilatation and curettage" or hysteroscopy.

Acknowledgments

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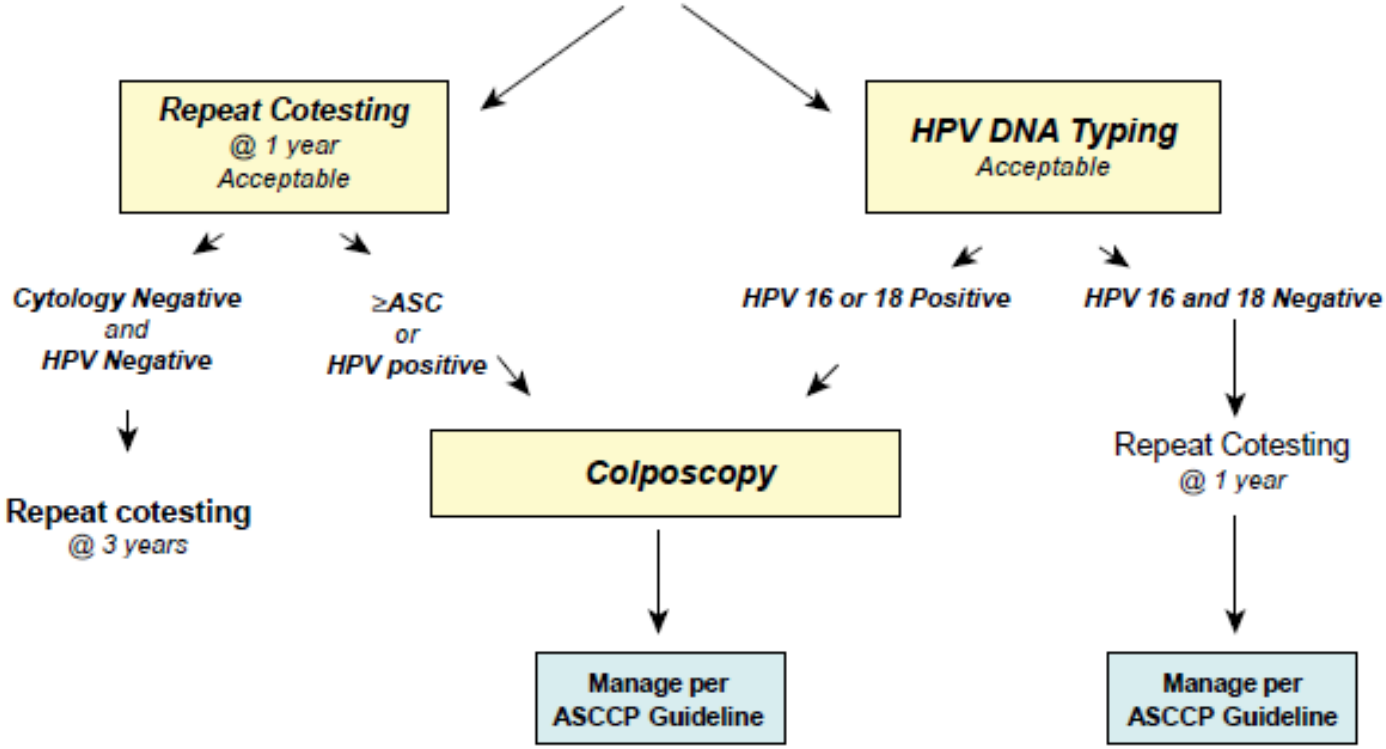
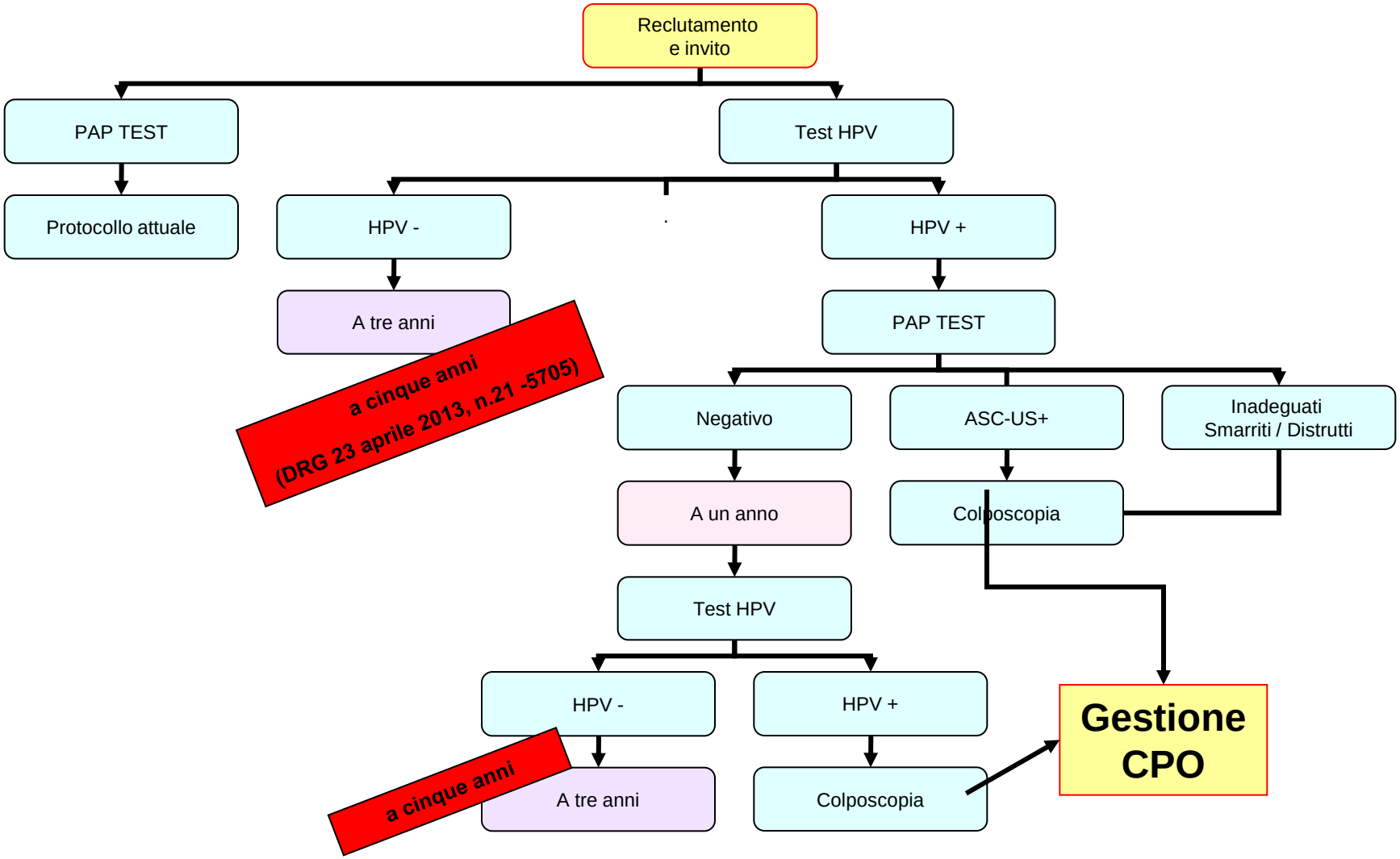
Management of Women ≥ Age 30, who are Cytology Negative, but HPV Positive



PROTOCOLLO PROGETTO PILOTA



2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors

L. Stewart Massad, MD, Mark H. Einstein, MD, Warner K. Huh, MD, Hormuzd A. Katki, PhD, Walter K. Kinney, MD, Mark Schiffman, MD, Diane Solomon, MD, Nicolas Wentzensen, MD, and Herschel W. Lawson, MD, for the 2012 ASCCP Consensus Guidelines Conference

From Washington University School of Medicine, St. Louis, Missouri; Albert Einstein College of Medicine, New York, New York; University of Alabama School of Medicine, Birmingham, Alabama; Division of Cancer Epidemiology and Genetics and Division of Cancer Prevention, National Cancer Institute, Bethesda, Maryland; The Permanente Medical Group, Sacramento, California; and Emory University School of Medicine, Atlanta, Georgia

2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors

Box 1. Essential Changes From Prior Management Guidelines*

- Cytology reported as negative but lacking endocervical cells can be managed without early repeat.
- CIN 1 on endocervical curettage should be managed as CIN 1, not as a positive ECC.
- Cytology reported as unsatisfactory requires repeat even if HPV negative.
- Genotyping triages HPV-positive women with HPV type 16 or type 18 to earlier colposcopy only after negative cytology; colposcopy is indicated for all women with HPV and ASC-US, regardless of genotyping result.
- For ASC-US cytology, immediate colposcopy is not an option. The serial cytology option for ASC-US incorporates cytology at 12 months, not 6 months and 12 months, and then if negative, cytology every 3 years.
- HPV-negative and ASC-US results should be followed with co-testing at 3 years rather than 5 years.
- HPV-negative and ASC-US results are insufficient to allow exit from screening at age 65 years.

Box 1. Essential Changes From Prior Management Guidelines*

- The pathway to long-term follow-up of treated and untreated CIN 2+ is more clearly defined by incorporating co-testing.
- More strategies incorporate co-testing to reduce follow-up visits. Pap-only strategies are now limited to women younger than 30 years, but co-testing is expanded even to women younger than 30 years in some circumstances. Women aged 21-24 years are managed conservatively.

CIN, cervical intraepithelial neoplasia; ECC, endocervical curettage; HPV, human papillomavirus; ASC-US, atypical squamous cells of undetermined significance.
**Prior management guidelines were from the "2006 Consensus Guidelines for the Management of Women With Abnormal Cervical Screening Tests" (6). Prior guidelines not changed were retained.*

Box 2.

A recent consensus conference (the Lower Anogenital Squamous Terminology [LAST] Project convened by the College of American Pathologists and the American Society for Colposcopy and Cervical Pathology) adopted a two-tier terminology that incorporates ancillary tests and other criteria to distinguish indeterminate lesions as high grade or low grade. Until a comprehensive evidence review and consensus guidelines development process can be conducted, histopathology results reported as low-grade squamous intraepithelial lesions (LSIL) should be managed as cervical intraepithelial neoplasia (CIN) 1 and those reported as high-grade squamous intraepithelial lesions (HSIL) should be managed as CIN 2,3 (14).

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Primary cervical cancer screening with human papillomavirus: End of study results from the ATHENA study using HPV as the first-line screening test☆

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HIGHLIGHTS

- A negative HPV results at baseline predicts one-half the risk of CIN3 + over 3 years than a negative cytology result.
- HPV primary screening with triage using 16/18 genotyping and cytology increases sensitivity to detect CIN3 + 28% over cytology.
- Cytology failed to detect approximately 50% of CIN3 + in women 25–29 years.

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ABSTRACT

Objectives. ATHENA evaluated the cobas HPV Test as the primary screen for cervical cancer in women ≥25 years. This reports the 3-year end-of-study results comparing the performance of HPV primary screening to different screening and triage combinations.

Methods. 42,209 women ≥25 years were enrolled and had cytology and hrHPV testing. Women with abnormal cytology (≥atypical squamous cells of undetermined significance) and those HPV positive were referred to colposcopy. Women not reaching the study endpoint of CIN2 + entered the 3-year follow-up phase.

Results. 3-year CIR of CIN3 + in cytology-negative women was 0.8% (95% CI; 0.5–1.1%), 0.3% (95% CI 0.1–0.7%) in HPV-negative women, and 0.3% (95% CI; 0.1–0.6%) in cytology and HPV negative women. The sensitivity for CIN3 + of cytology was 47.8% (95%CI; 41.6–54.1%) compared to 61.7% (95%CI; 56.0–67.5%) for the *hybrid strategy* (cytology if 25–29 years and cotesting with cytology and HPV if ≥30 years) and 76.1% (95% CI; 70.3–81.8%) for *HPV primary*. The specificity for CIN3 + was 97.1% (95% CI; 96.9–97.2%), 94.6% (95% CI; 94.4–94.8%), and 93.5% (95%CI; 93.3–93.8%) for cytology, *hybrid strategy*, and *HPV primary*, respectively. Although *HPV primary* detects significantly more cases of CIN3 + in women ≥25 years than either cytology or *hybrid strategy*, it requires significantly more colposcopies. However, the number of colposcopies required to detect a single CIN3 + is the same as for the *hybrid strategy*.

Conclusions. HPV primary screening in women ≥25 years is as effective as a hybrid screening strategy that uses cytology if 25–29 years and cotesting if ≥30 years. However, HPV primary screening requires less screening tests.

Introduction

Persistent infection with a high-risk human papillomavirus (HPV) genotype is required for the development of high-grade cervical neoplasia (cervical intraepithelial neoplasia [CIN] grade 3, adenocarcinoma in-situ, and invasive cervical cancer (CIN3 +) [1]. Molecular tests that detect HPV demonstrate increased sensitivity but lower specificity than cytology for detecting women with CIN3 + [2]. Currently in the United States (U.S.) HPV testing is recommended to triage women with atypical squamous cells of undetermined significance (ASC-US) and as an adjunct to cytology when screening women ≥30 years (i.e., "cotesting") [3–5]. In Europe, guidelines recommend the use of HPV testing to triage women with ASC-US, for surveillance after treatment of CIN, and as a stand-alone primary screening test without cytology

☆ This study is registered with ClinicalTrials.gov (NCT00709891).

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HIGHLIGHTS

- **A NEGATIVE HPV RESULTS AT BASELINE PREDICTS ONE-HALF THE RISK OF CIN 3 + OVER 3 YEARS THAN A NEGATIVE CYTOLOGY RESULT**
- **HPV PRIMARY SCREENING WITH TRIAGE USING 16/18 GENOTYPING AND CYTOLOGY INCREASES SENSITIVITY TO DETECT CIN 3 + 28% OVER CYTOLOGY**
- **CYTOLOGY FAILED TO DETECT APPROXIMATELY 50% OF CIN 3 + IN WOMEN 25-29 YEARS**

Programma Regionale di Screening per il Cervicocarcinoma Prevenzione Serena

REGIONE PIEMONTE

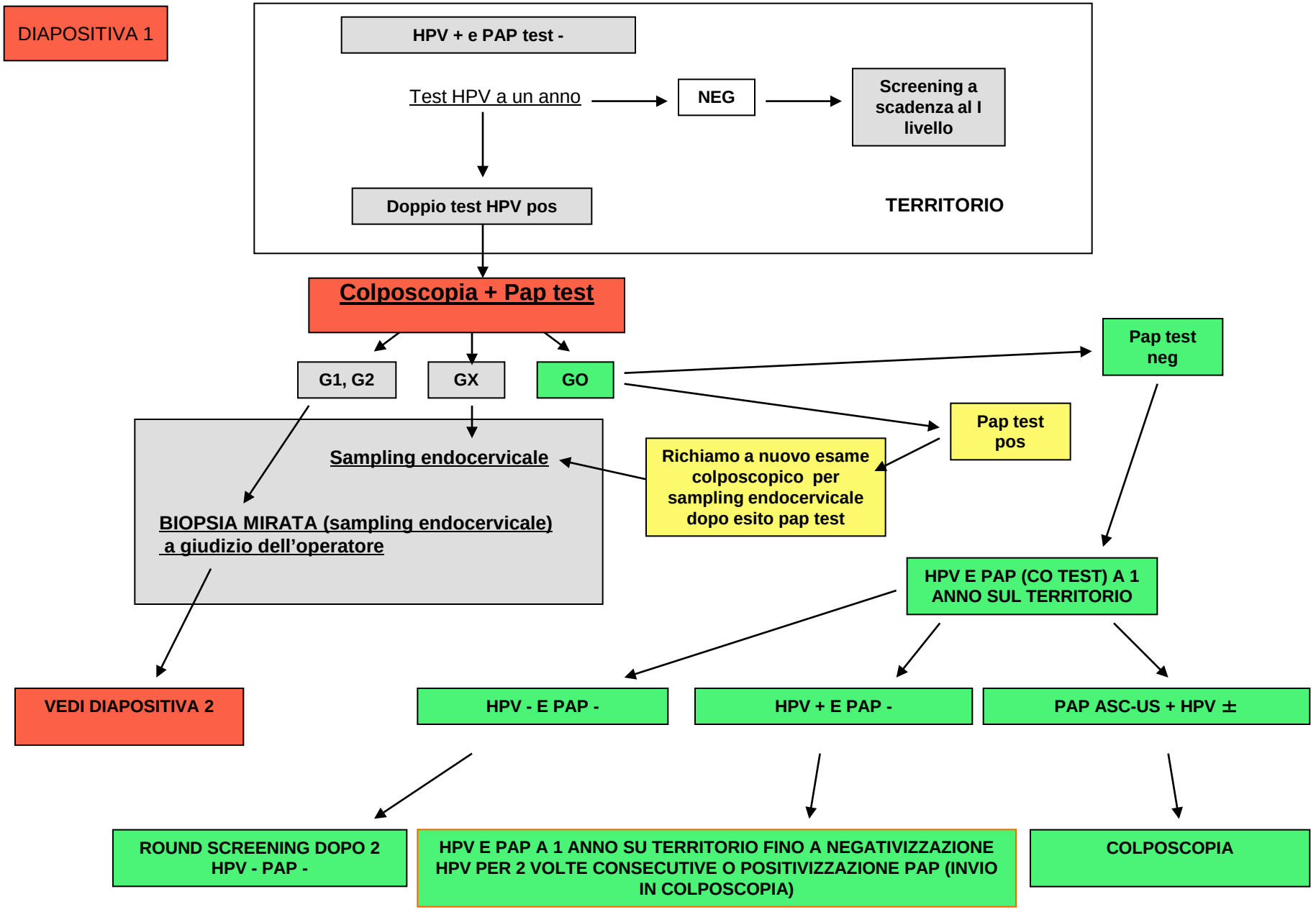
PROTOCOLLO DIAGNOSTICO COLPOSCOPICO E POST-COLPOSCOPICO NELLE DONNE CHE FANNO SCREENING CERVICALE BASATO SUL TEST HPV

L. Pasero e G. Maina

SSCVD COLPOSCOPIA E LASERCHIRURGIA

P.O. SANT'ANNA – CITTA' DELLA SALUTE E DELLA SCIENZA DI TORINO

- GRUPPO DI LAVORO Guglielmo Ronco , Mansueto Pavesi , Corrado Magnani Raffaella Ribaldone , Laura Pasero , Giovanni Maina Leonardo Micheletti , Maggiorino Barbero Bruno Ghiringhello ,Bruno Inaudi


DIAPOSITIVA 1
HPV + e PAP test -
Test HPV a un anno
NEG
Screening a scadenza al I livello
Doppio test HPV pos
TERRITORIO
Colposcopia + Pap test
G1, G2
GX
GO
Pap test neg
Pap test pos
Sampling endocervicale
Richiamo a nuovo esame colposcopico per sampling endocervicale dopo esito pap test
BIOPSIA MIRATA (sampling endocervicale) a giudizio dell'operatore
HPV E PAP (CO TEST) A 1 ANNO SUL TERRITORIO
VEDI DIAPOSITIVA 2
HPV - E PAP -
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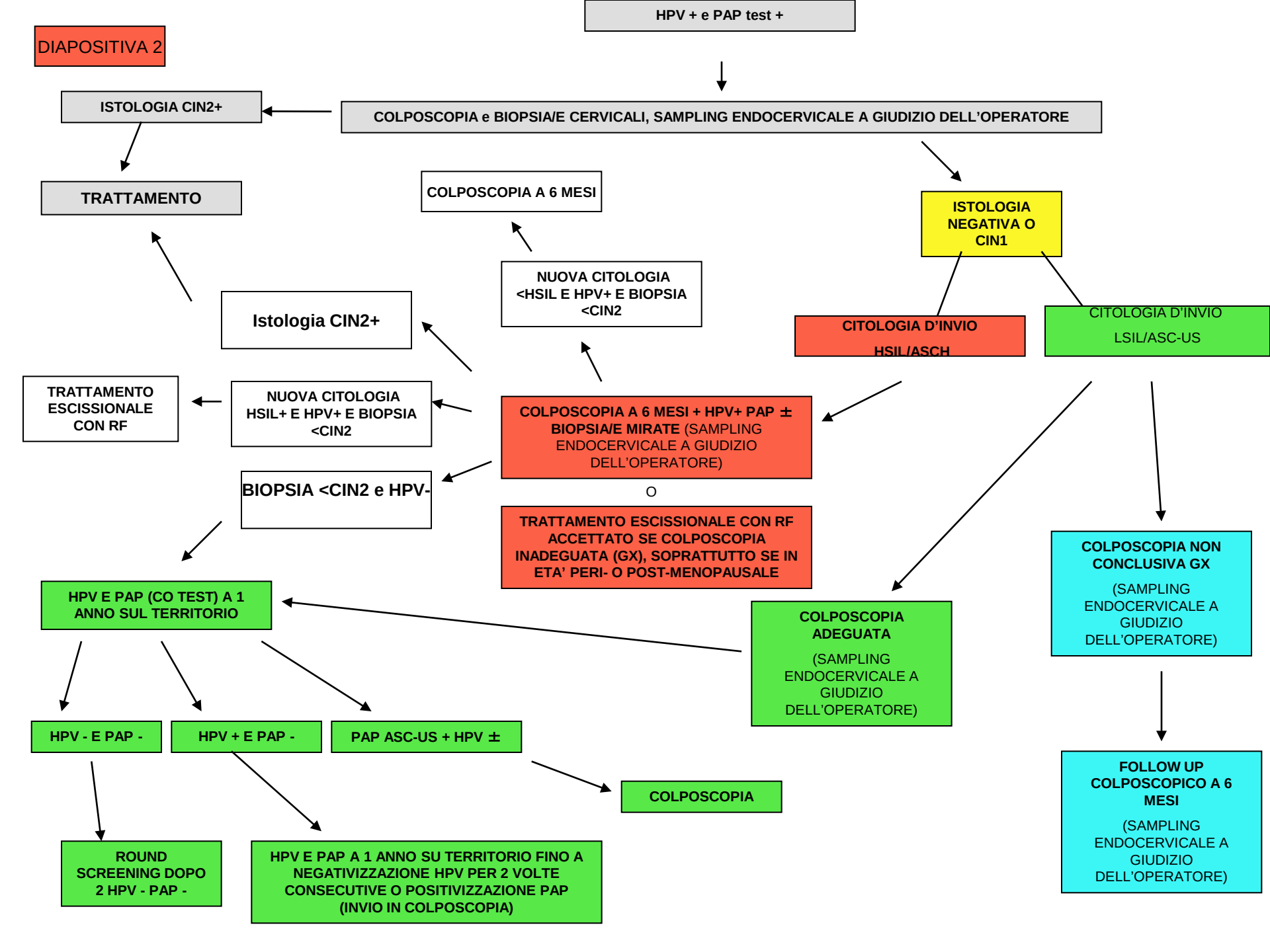
HPV E PAP A 1 ANNO SU TERRITORIO FINO A NEGATIVIZZAZIONE HPV PER 2 VOLTE CONSECUTIVE O POSITIVIZZAZIONE PAP (INVIO IN COLPOSCOPIA)
COLPOSCOPIA


HPV + e PAP test +
DIAPOSITIVA 2
ISTOLOGIA CIN2+
COLPOSCOPIA e BIOPSIA/E CERVICALI, SAMPLING ENDOCERVICALE A GIUDIZIO DELL'OPERATORE
TRATTAMENTO
COLPOSCOPIA A 6 MESI
ISTOLOGIA NEGATIVA O CIN1
NUOVA CITOLOGIA <HSIL E HPV+ E BIOPSIA <CIN2
Istologia CIN2+
CITOLOGIA D'INVIO HSIL/ASCH
CITOLOGIA D'INVIO LSIL/ASC-US
TRATTAMENTO ESCISSIONALE CON RF
NUOVA CITOLOGIA HSIL+ E HPV+ E BIOPSIA <CIN2
COLPOSCOPIA A 6 MESI + HPV+ PAP ± BIOPSIA/E MIRATE (SAMPLING ENDOCERVICALE A GIUDIZIO DELL'OPERATORE)
BIOPSIA <CIN2 e HPV-
O
TRATTAMENTO ESCISSIONALE CON RF ACCETTATO SE COLPOSCOPIA INADEGUATA (GX), SOPRATTUTTO SE IN ETA' PERI- O POST-MENOPAUSALE
COLPOSCOPIA NON CONCLUSIVA GX (SAMPLING ENDOCERVICALE A GIUDIZIO DELL'OPERATORE)
HPV E PAP (CO TEST) A 1 ANNO SUL TERRITORIO
COLPOSCOPIA ADEGUATA (SAMPLING ENDOCERVICALE A GIUDIZIO DELL'OPERATORE)
HPV - E PAP -
HPV + E PAP -
PAP ASC-US + HPV ±
COLPOSCOPIA
FOLLOW UP COLPOSCOPICO A 6 MESI (SAMPLING ENDOCERVICALE A GIUDIZIO DELL'OPERATORE)
ROUND SCREENING DOPO 2 HPV - PAP -
HPV E PAP A 1 ANNO SU TERRITORIO FINO A NEGATIVIZZAZIONE HPV PER 2 VOLTE CONSECUTIVE O POSITIVIZZAZIONE PAP (INVIO IN COLPOSCOPIA)

Grazie
per l'attenzione