

Overtreatment cervicale in età fertile

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Nearly 30% of young women initiating first sexual activity test HPV positive within 1 year of first intercourse with a first male sex partner, and by 3 years almost half test positive

The cumulative transition probability from an HPV DNA negative state to an HPV 16 DNA positive state is greater than 30% after 24 months of first sexual exposure

Winer RL et al. Risk of female human papillomavirus acquisition associated with first male sex partner. *J Infect Dis* 2008;197(2):279-82.

L'HPV è talmente comune che praticamente quasi tutte le donne e gli uomini sessualmente attivi lo contraggono in qualche momento della propria vita

Oltre il 90% delle nuove infezioni da HPV, comprese quelle con i tipi ad alto rischio, regrediscono o non sono più rilevabili entro 12-36 mesi

CDC Atlanta - MMWR Recomm Rep 2015;64(No. RR-3):84-93.

Drivers of overdiagnosis

- Marketing
- Technology

- Politics
- Patients

- Defensive medicine
- Medicalisation
- Professional vanity

- Productivity
- Complexity

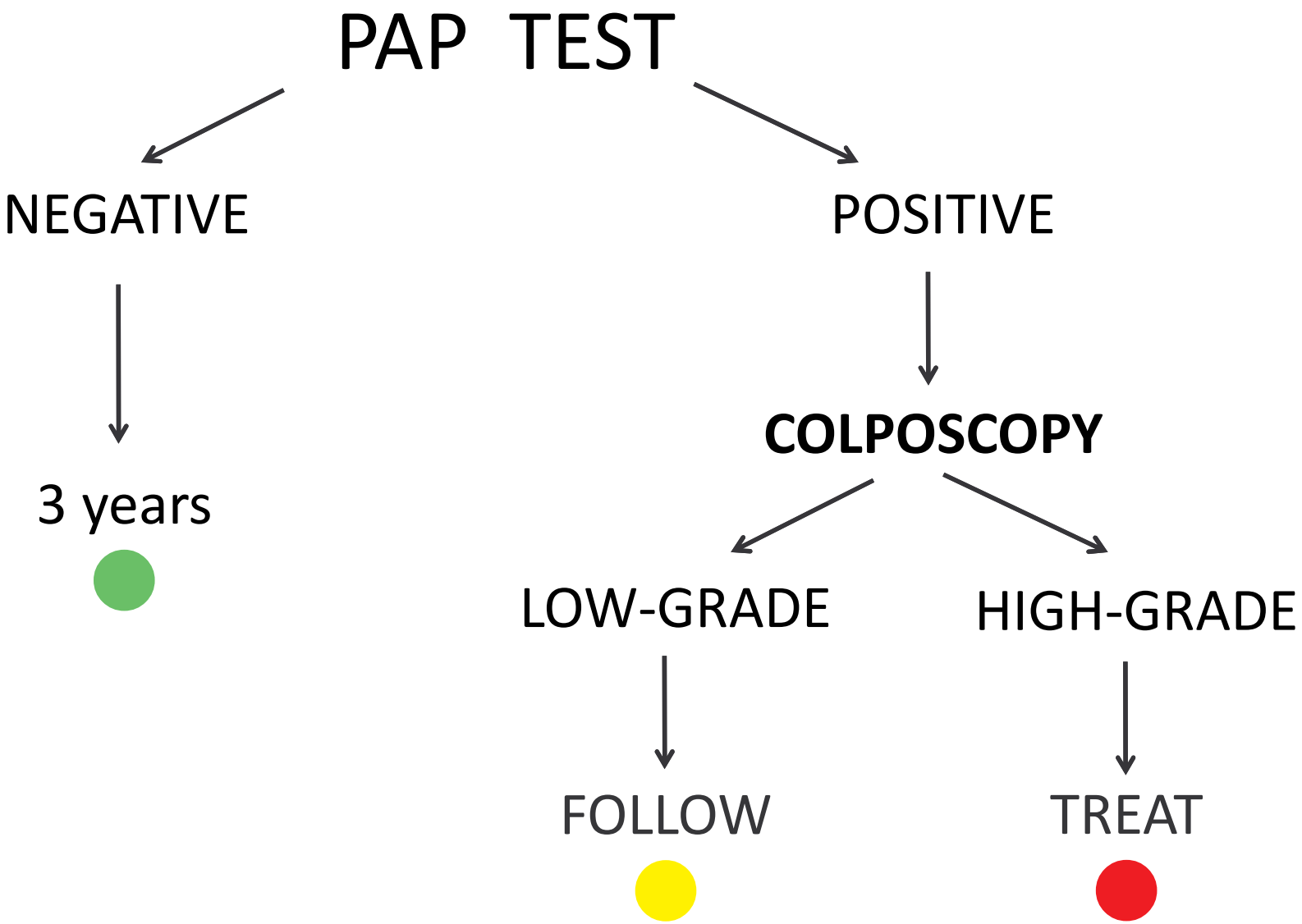
Early Human Papilloma Virus (HPV) Oncogenic Influences in Breast Cancer

Christopher Ngan[1], James S. Lawson[1], Rosemary Clay[2], Warick Delprado[2], Noel J. Whitaker[1] and Wendy K. Glenn[1]

[1]School of Biotechnology and Biomolecular Science, University of New South Wales, Sydney, Australia. [2]Douglass Hanly Moir Pathology, Sydney, NSW, Australia.

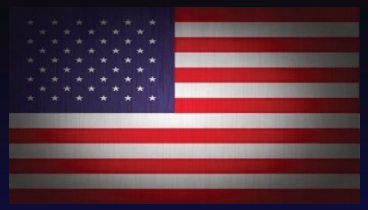
Libertas Academica
FREEDOM TO RESEARCH

Primary Cervical Screening - Cyto





Cervical cancer screening



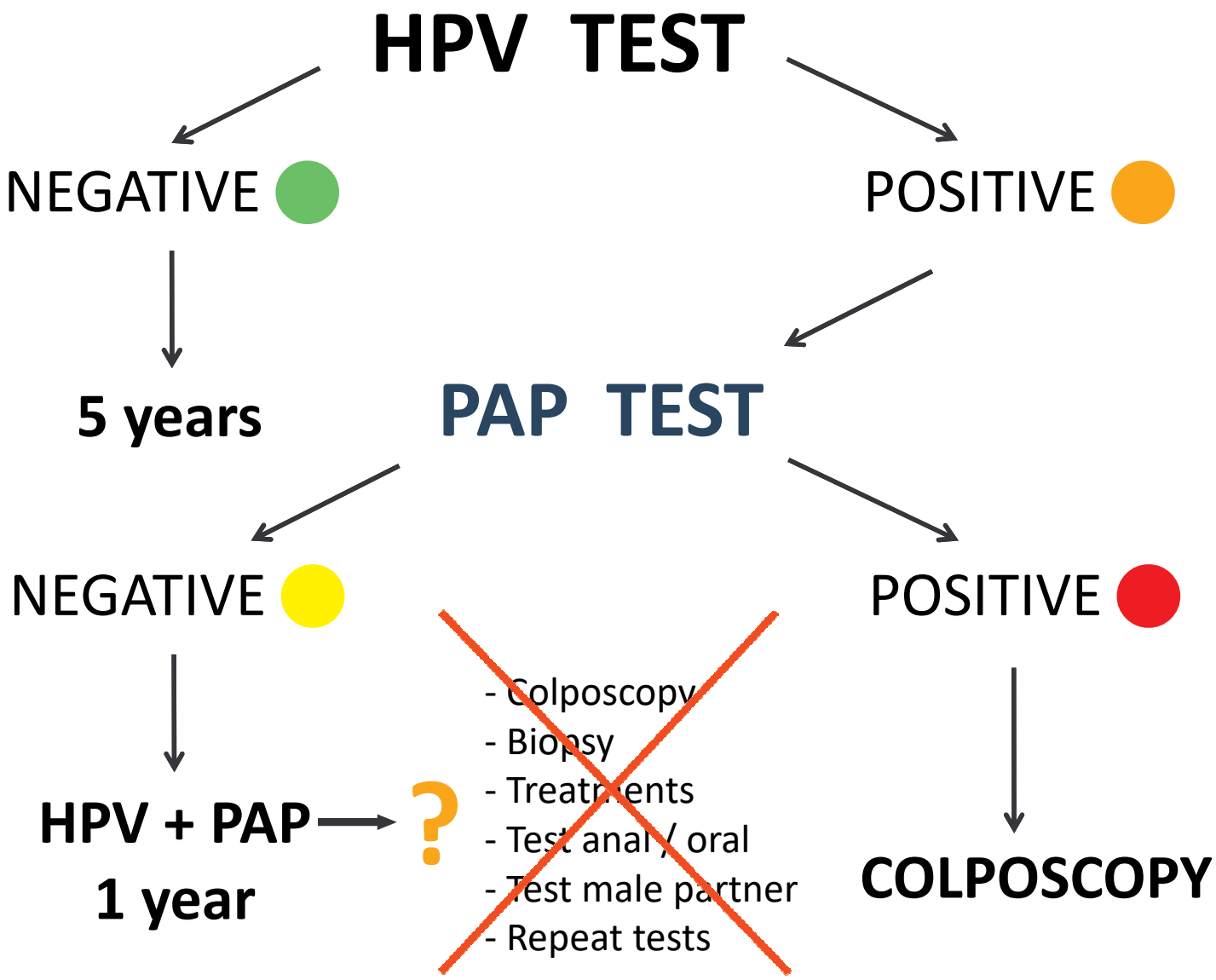
< 21 yrs No screening

21-29 yrs PAP TEST every 3 years

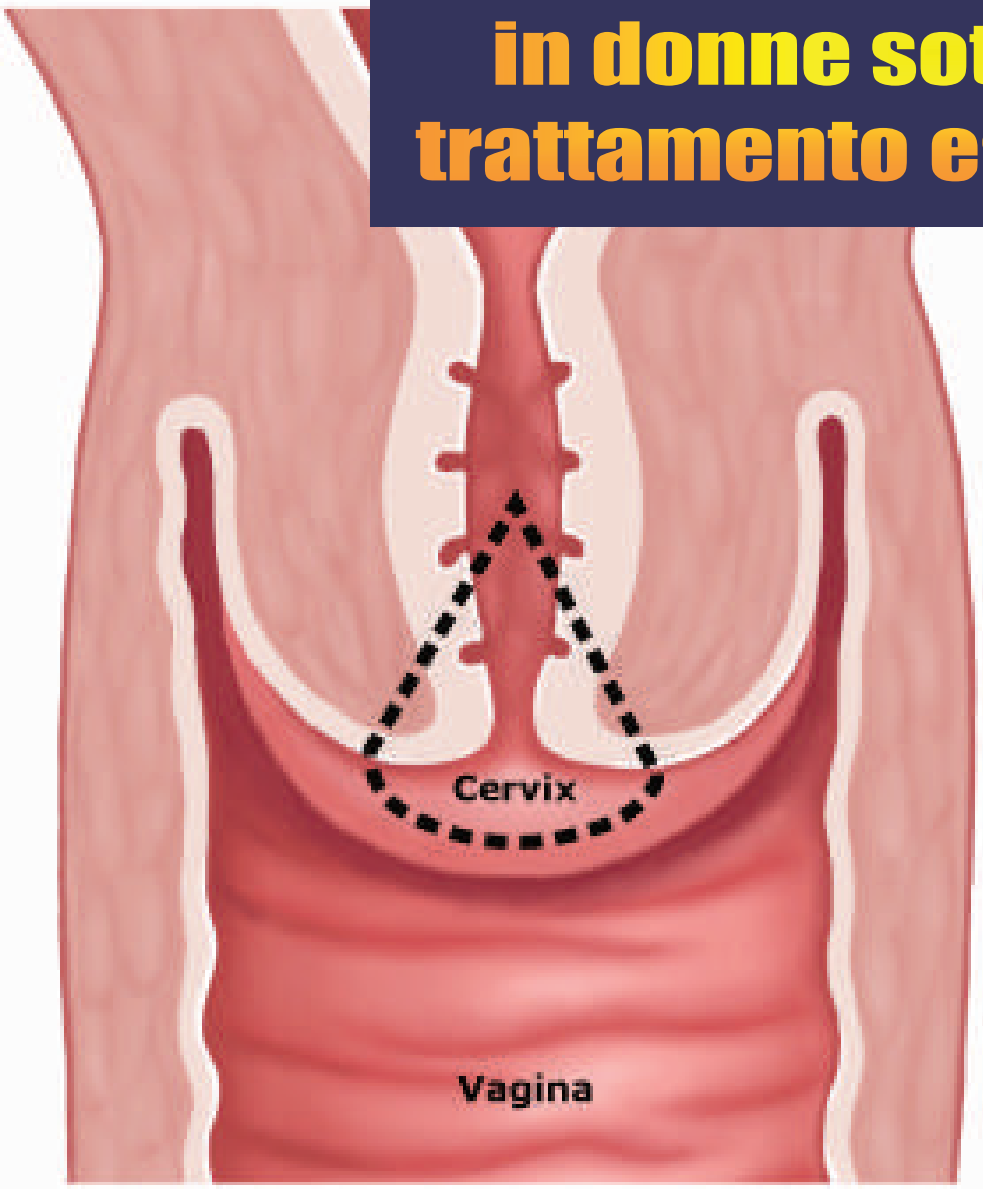
30-65 yrs HPV DNA test every 5 years

> 65 yrs No screening

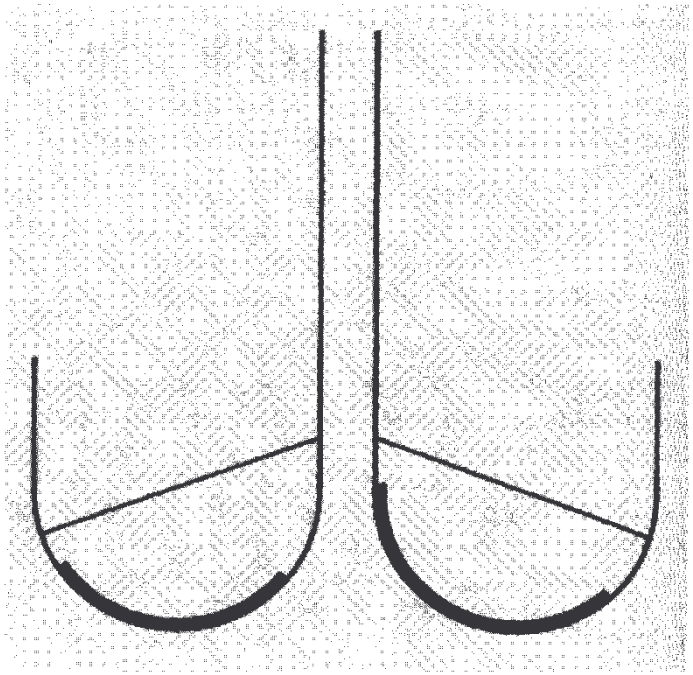
Primary Cervical Screening - HPV

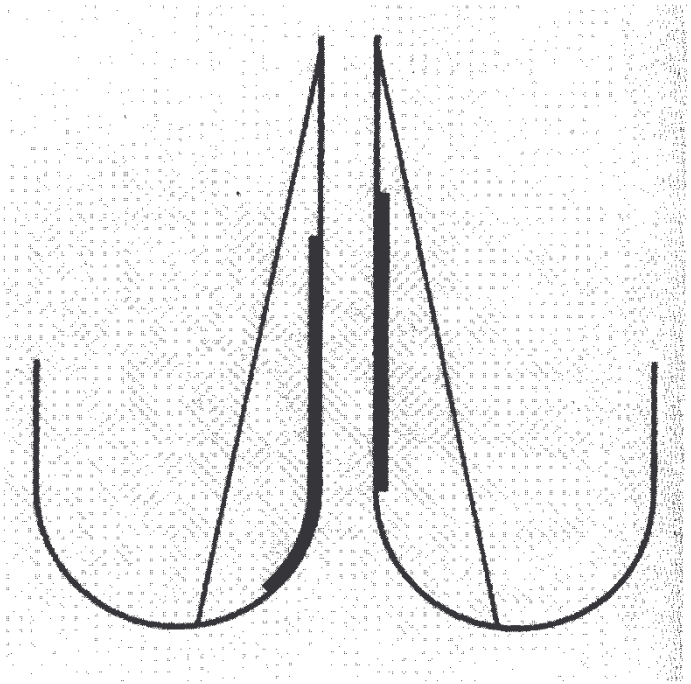


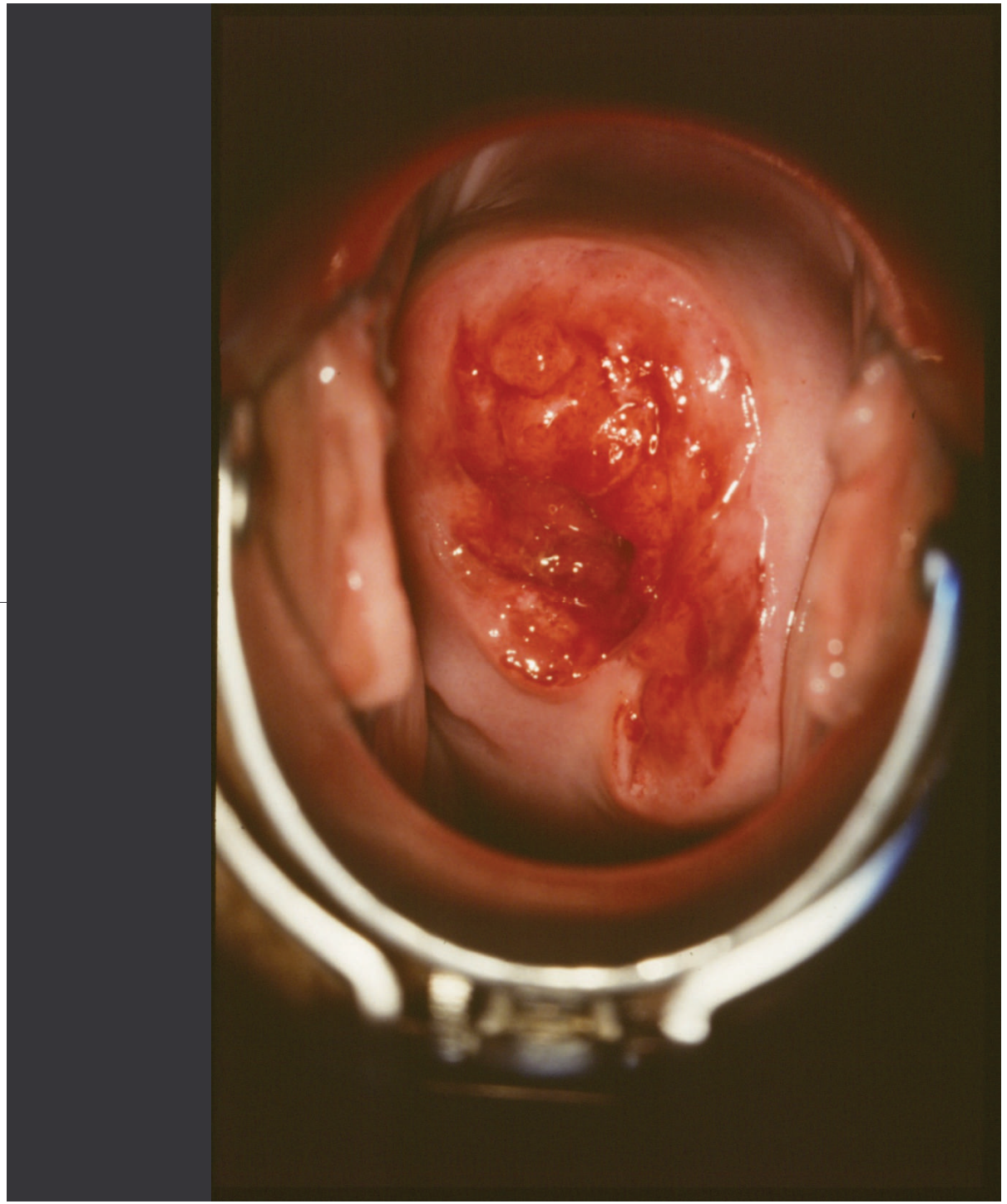
OUTCOME OSTETRICO in donne sottoposte a trattamento escissionale

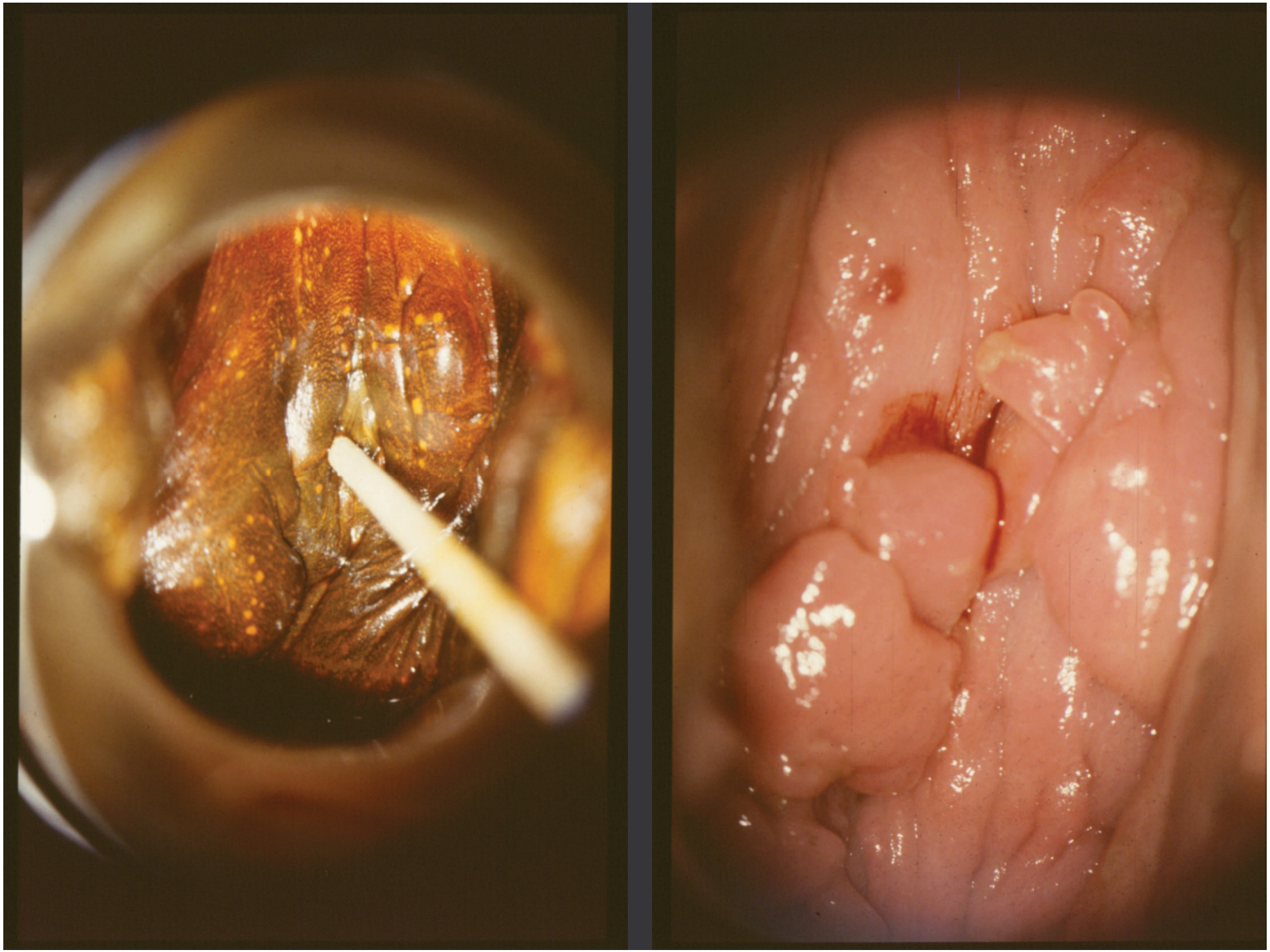


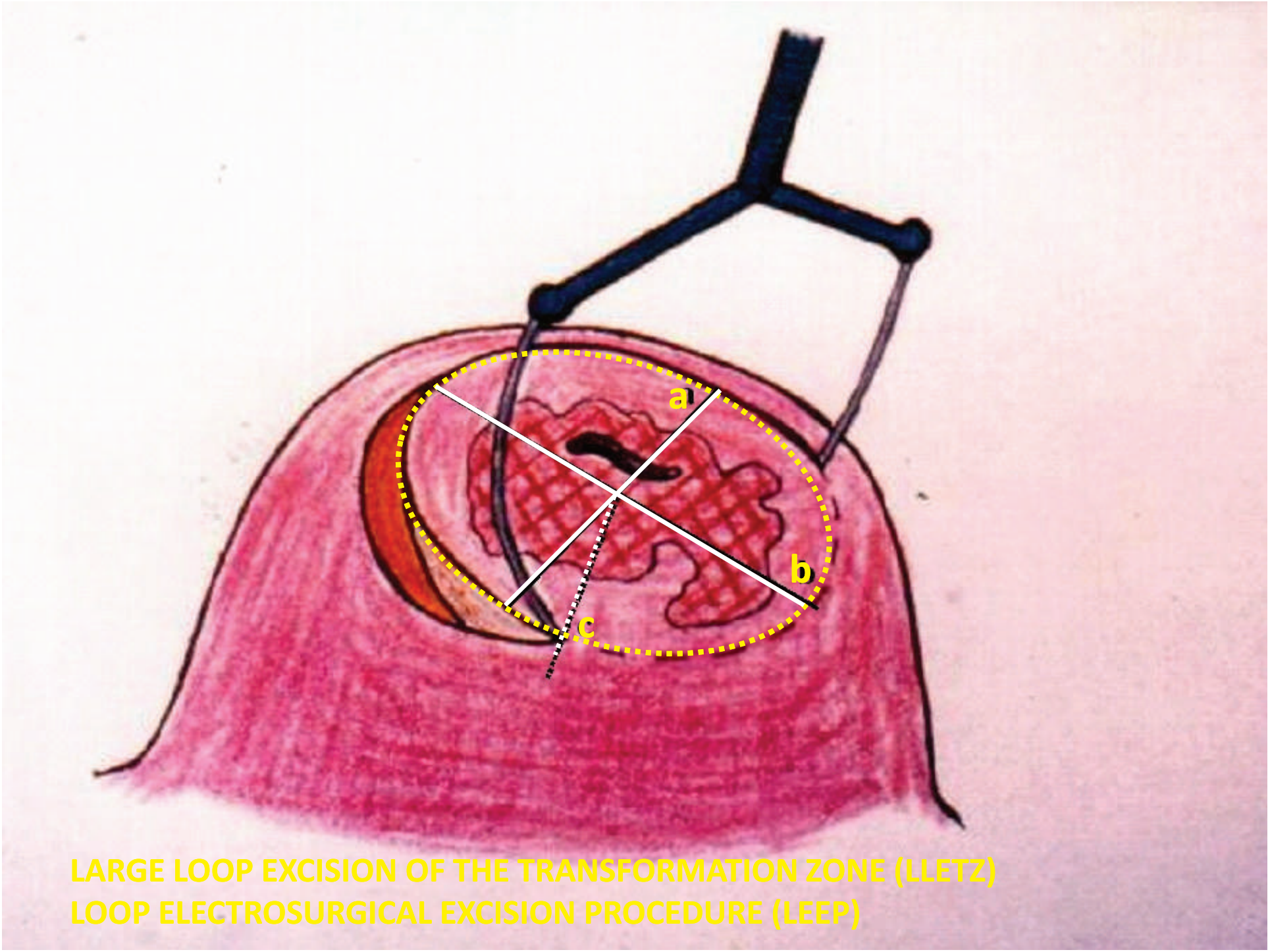






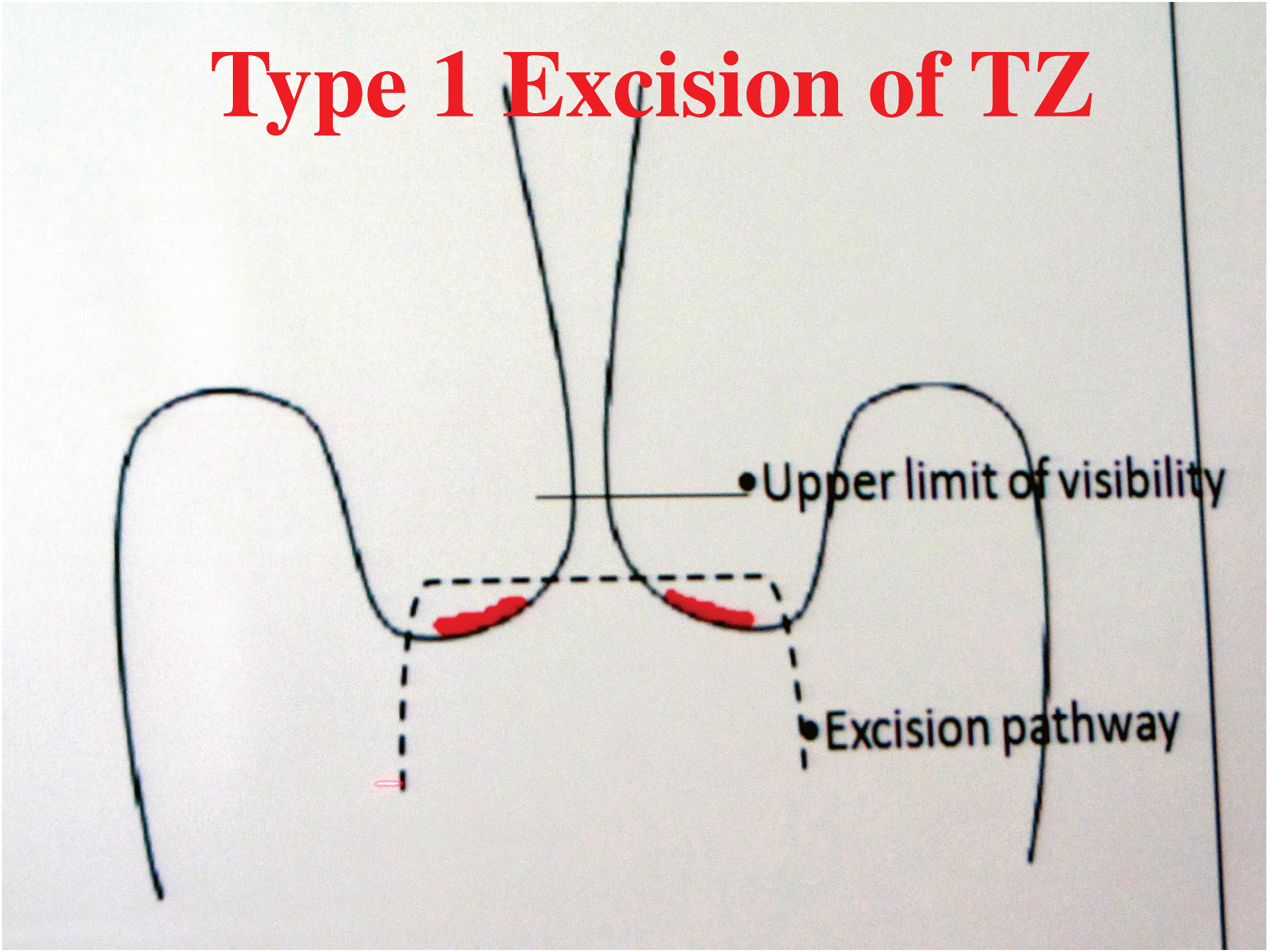




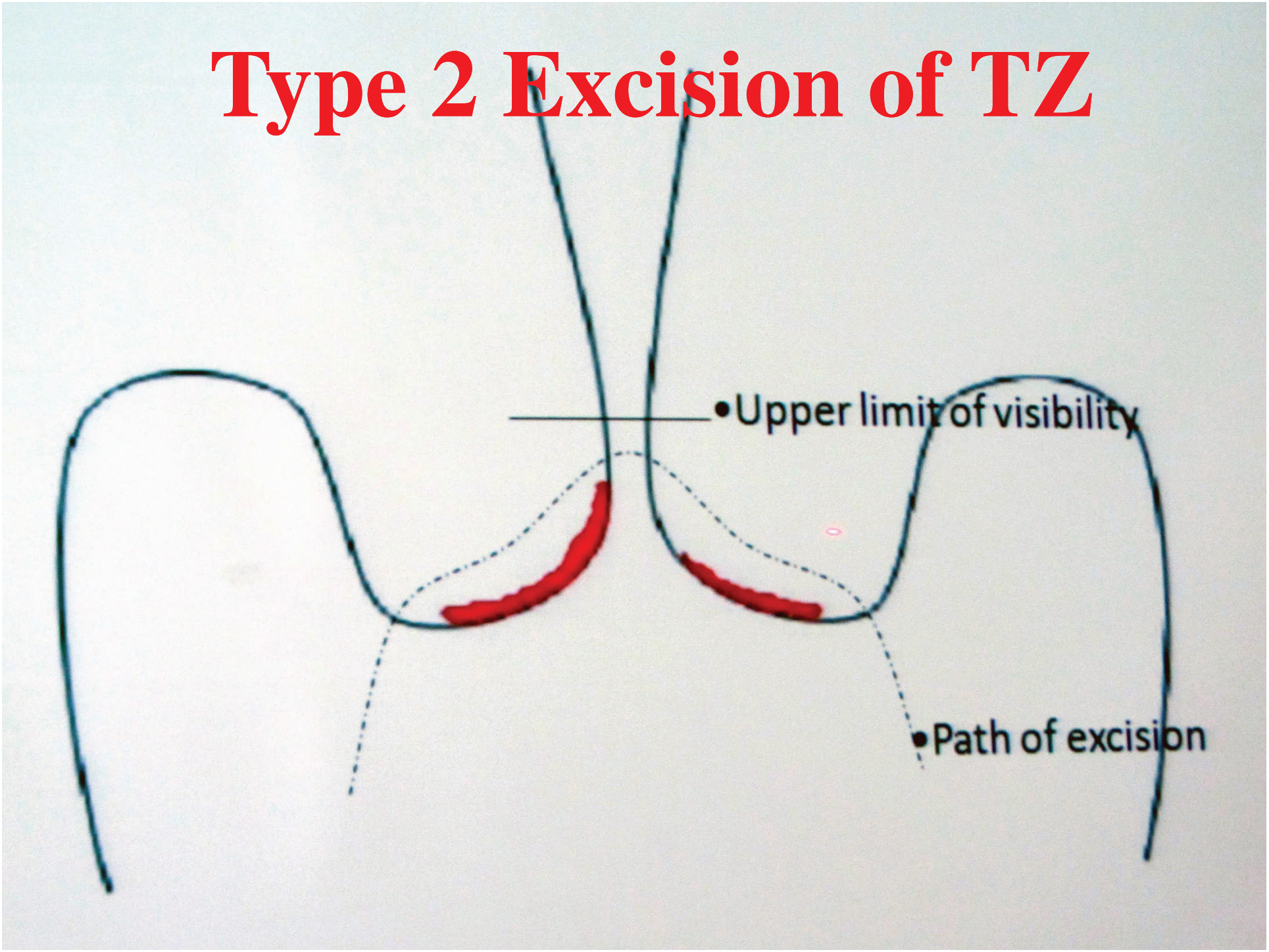


LARGE LOOP EXCISION OF THE TRANSFORMATION ZONE (LLETZ)
LOOP ELECTROSURGICAL EXCISION PROCEDURE (LEEP)

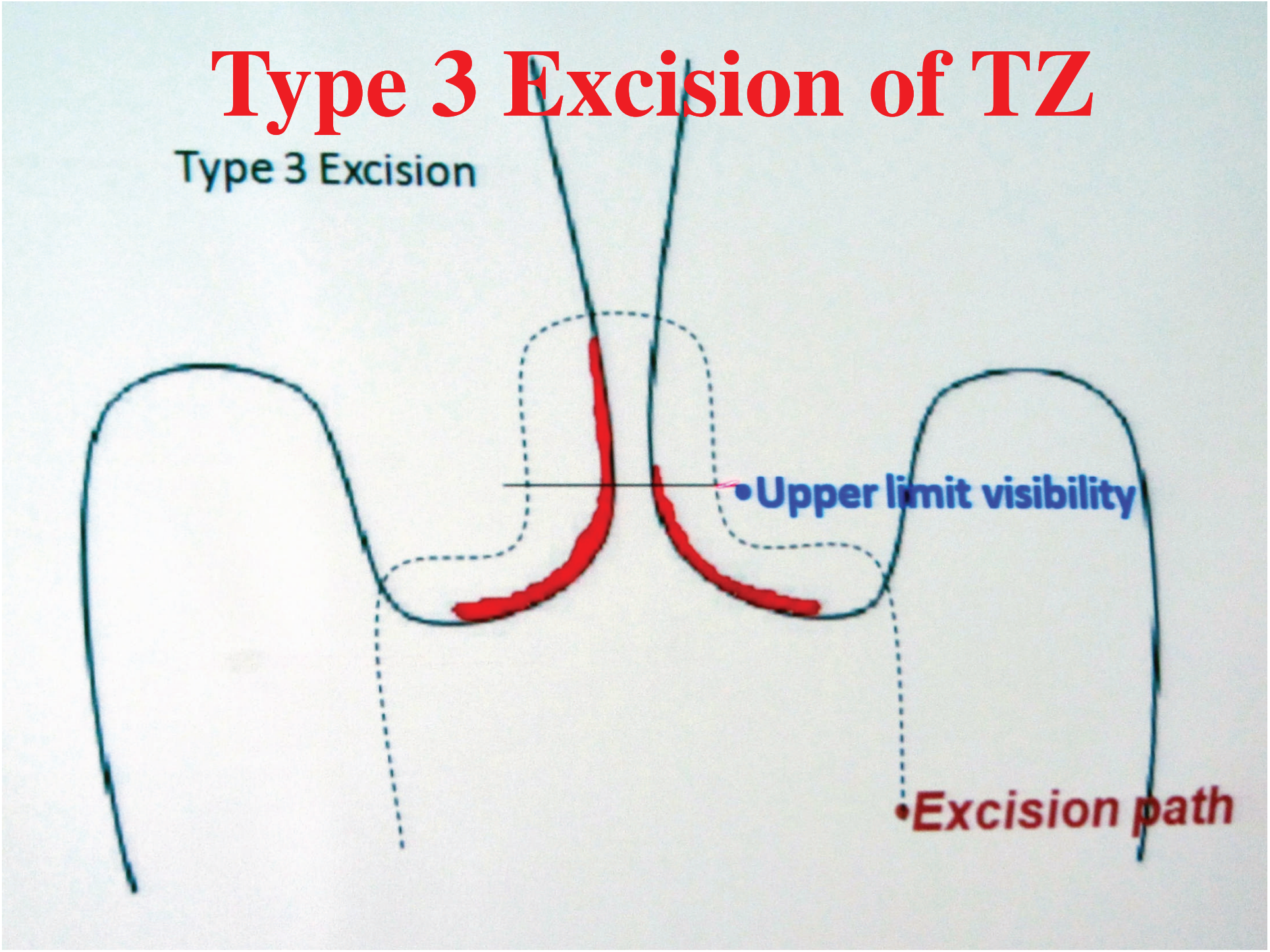
Type 1 Excision of TZ



Type 2 Excision of TZ



Type 3 Excision of TZ

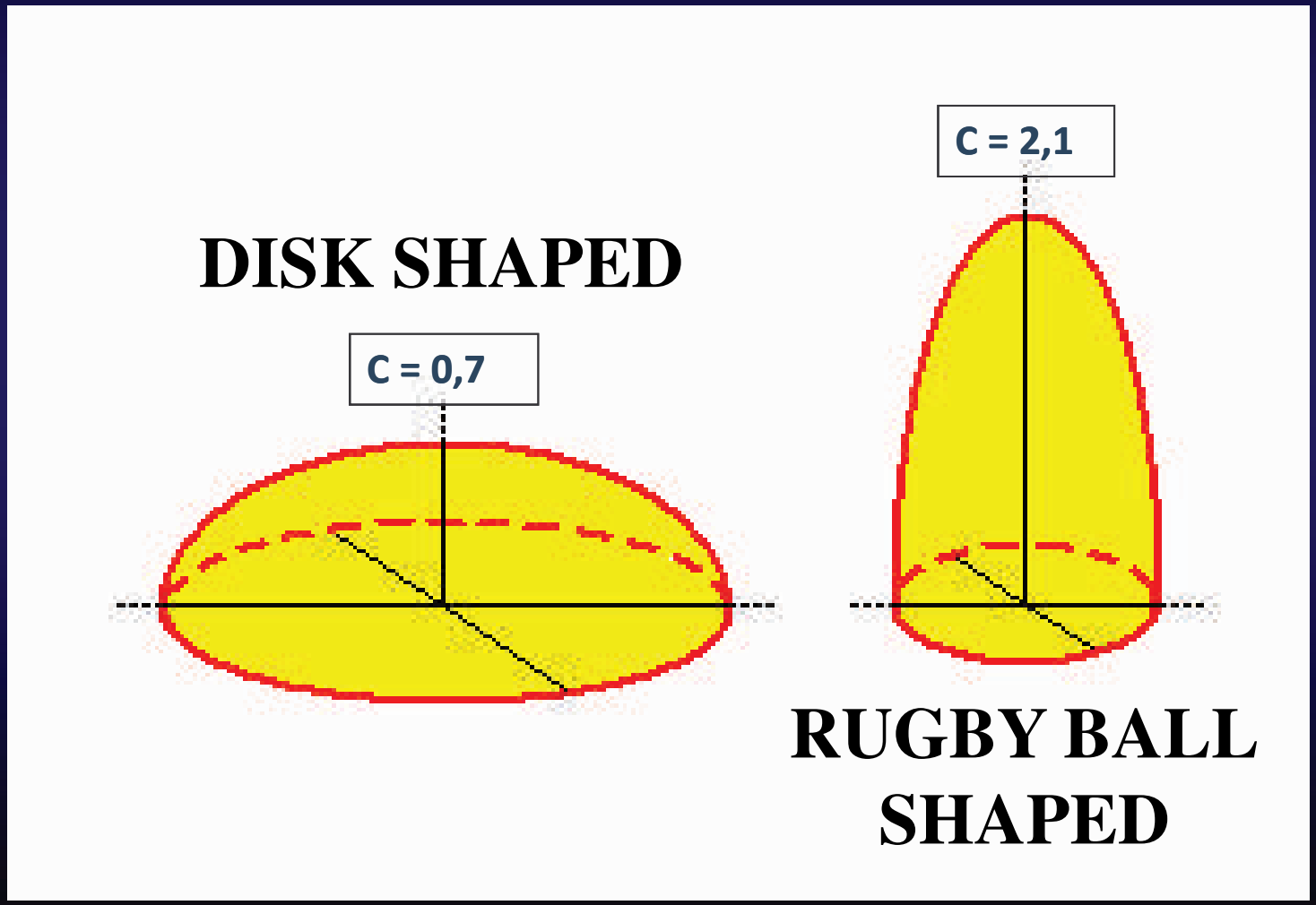


LUNGHEZZA DEL CONO ESCISSO E RISCHIO DI PARTO PRETERMINE

- Aumentando la *lunghezza* del cono asportato si ha un aumento del rischio del 6% per ogni millimetro addizionale di tessuto escisso

- Nelle donne con lunghezza del frammento escisso superiore a 1,7 cm il rischio di pPROM aumenta di ben tre volte

RAPPRESENTAZIONE SCHEMATICA DI DUE EMIELLISSOIDI CON IDENTICO VOLUME, MA DIVERSE LUNGHEZZE E DIAMETRI (TRASVERSO E LONGITUDINALE)



66.215 parti 2000-2009 (**61.730** parti singoli)

608 donne sottoposte a LEEP per CIN 2-3

Parti < 37 sett. = 3.875 (6.3%)
= 15 nelle LEEP (2.4%)

- Volume mediano del tessuto escisso = **2,8 cm^3**
- Lunghezza mediana = **1,2 cm**

Liverani CA et al. Length but not transverse diameter of the excision specimen for high-grade cervical intraepithelial neoplasia (CIN 2-3) is a predictor of pregnancy outcome. *Eur J Cancer Prev* 2016;25(5):416-22.

Pregressa chirurgia cervicale

Previous cold knife cone is associated with delivery prior to 34 weeks, while LEEP and ablative procedures are not.

Cold knife cone should be carefully considered and avoided when possible in reproductive age women.

Ehsanipoor RM. et al. The relationship between previous treatment for cervical dysplasia and preterm delivery in twin gestations. *J Matern Fetal Neonatal Med* 2014;27(8):821-4.

Pregressa chirurgia cervicale

- Women with CIN: higher baseline risk for prematurity
- Excisional and ablative treatment: further increases risk
- Frequency and severity of adverse sequelae increases with increasing cone depth and is higher for excision than for ablation

The results should be interpreted with caution as they were based on low or very low quality observational studies, most of which were retrospective

Kyrgiou M et al. Obstetric outcomes after conservative treatment for cervical intraepithelial lesions and early invasive disease. *Cochrane Database Syst Rev* 2017;11:CD012847

Farmaci: contraccezione E/P [redacted]

VACCINO HPV: NO

PAP TEST 03/2011 = **LSIL**
PAP TEST 05/2011 = **LSIL**
Biopsia cervice 05/2011 = cervicite cronica
PAP TEST 09/2011 = **LSIL**
Biopsia cervice 12/2011 = **CIN 1**
PAP TEST 04/2012 = **LSIL**
PAP TEST 05/2012 = **LSIL** (HPV DNA test 10/2012 = **pos. 59**)
PAP TEST 03/2013 = **LSIL**
HPV DNA test 10/2013 = **pos. HR** (I.E.O. Milano)
Cono cervicale 10/2013 = **CIN 1** (I.E.O. Milano)
PAP TEST 03/2014 = **LSIL**
HPV DNA test 04/2014 = **pos. HR** (Melegnano)
Biopsia cervice 04/2014 = **CIN 1/HPV** (Melegnano)
PAP TEST 09/2014 = **LSIL**
LEEP nel 2014 per **CIN 1** (I.E.O. Milano)
PAP TEST 01/2015 = **LSIL** (HPV DNA test **pos. 16**)
Dual staining 12/2015 = **p16/Ki67 negative**
PAP TEST 10/2016 = negativo
PAP TEST 12/2017 = **ASC-US**
PAP TEST 01/2018 = **ASC-US** (HPV DNA test **pos. 61**)

NOTIZIE CLINICHE

Paziente di 21 anni

- Non patologie concomitanti
- No allergie
- Fumo: 1 sigaretta/die

PAP TEST 12/2015 = ASC-US

HPV TEST 01/2016 = positivo alto rischio

Biopsia cervice 03/2016 = CIN 1 - CIN 2

Inviata per LEEP

Intervento e materiale inviato

Conizzazione cervicale LEEP

Esocervice

Descrizione macroscopica

Cono cervicale di cm 1,8 x 1,8 x 0,6.

Diagnosi istopatologica

Cervice: intensa flogosi erosiva con focali atipie citologiche di significato reattivo.

Esami precedenti: 16-I-16154

Test genetico per la ricerca di HPV ad alto e basso rischio oncogeno.

Estrazione del DNA virale eseguita separatamente da:

tampone faringeo, tampone anale esterno e tampone anale interno.

Amplificazione mediante PCR con oligo specifici
per ceppi di HPV ad alto e basso rischio.

RISULTATO:
Tampone faringeo NEGATIVO.
Tampone anale esterno NEGATIVO.
Tampone anale interno POSITIVO per ceppi HPV ad alto rischio e per ceppi HPV 6,11 a basso rischio

SEZIONE DI BIOTECNOLOGIE
ANALISI HPV - DNA

IN ESAME: materiale cervicale.

Ricerca HPV mediante P.C.R. (Polymerase Chain Reaction) e ibridazione inversa [kit "INNO-LiPA HPV Genotyping"]:

HPV basso rischio:
Tipo 6 : negativo
Tipo 11 : negativo
Tipo 40 : negativo
Tipo 53 : negativo
Tipo 54 : negativo
Tipo 70 : negativo

HPV alto rischio:
Tipo 16 : negativo
Tipo 18 : negativo
Tipo 31 : negativo
Tipo 33 : negativo
Tipo 45 : negativo
Tipo 51 : negativo
Tipo 58 : negativo
Tipo 59 : negativo
Tipo 66 : negativo
Tipo 68 : negativo

HPV X (HPV non tipizzabile): POSITIVO

mo (w949/3)

Esame n° **16-T-39419** **Data** 19/12/2016

Cognome nome

Telefono

Notizie cliniche

Anni 57
Allergie non riferite
Non fuma
Appendicectomia a 25 anni
P.D. (V.E.) AT nel 1990
Menopausa a 50 anni
Pap test 2015 = **ASC-US** (**HPV DNA test negativo**)
Pap test 09/2016 = **ASC-US**
Biopsia cervice 11/2016 = **CIN 3**

C. M. Esame n° 17-T-39847 del **19-01-2017**

- Pap test 07/2016 = HSIL
- HPV TEST = NEGATIVO
- Pap test 11/2016 = HSIL
- Colposcopia = epitelio bianco ispessito a livello della parete vaginale destra

Biopsia vagina = VaIN di alto grado

Am J Transl Res 2012;4(4):452-457
www.ajtr.org /ISSN:1943-8141/AJTR1209006

Brief Communication

High risk HPV DNA subtypes and E6/E7 mRNA expression in a cohort of colposcopy patients from Northern Italy with high-grade histologically verified cervical lesions

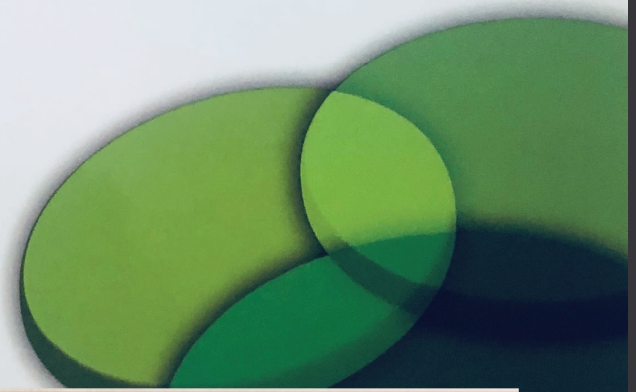
Liverani CA[1], Ciavattini A[2], Monti E[1], Puglia D[1], Mangano S[1], Di Giuseppe J[2], Zizzi A[3], Goteri G[3], Bolis G[1]

[1]II Institute of Obstetrics and Gynaecology, University of Milan, Milan, Italy; [2]Section of Woman's Health, Department of Clinical Sciences, Polytechnic University of Marche Region, Ancona, Italy; [3]Department of Biomedical Sciences and Public Health, Section of Pathologic Anatomy and Histopathology, Polytechnic University of the Marche/United Hospitals, Torrette (Ancona), Italy

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BMJ EVIDENCE-BASED MEDICINE

EXPERTISE VALUES EVIDENCE



Preventing Overdiagnosis Abstracts, August 2018, Copenhagen

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HUMAN PAPILLOMAVIRUS (HPV) INFECTION OF THE ANOGENITAL TRACT DETECTED THROUGH MOLECULAR TESTS LEADS TO OVERTREATMENTS AND WASTE OF RESOURCES

Carlo Liverani*, Ermelinda Monti, Giada Libutti. *Reference Center for the prevention, diagnosis and treatment of HPV related genital pathology. Department of Mother and Infant Sciences, University of Milan. Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy*

10.1136/bmjebm-2018-111070.29

ebm.bmj.com

BMJ

1) To assess

emotional, relational, sexual aspects

in women screened through HPV DNA test

2) To document whether

clinicians respect recommended guidelines

1) Data from a survey on 421 gynecologists, to assess knowledge, attitudes and practice

- 26.5% recommend HPV re-screening within 1-3 yrs

- 45.1% recommend sexual partner testing in women with low grade lesions HPV pos.

POD Conference 2016

2) Observational, prospective, quantitative case-control study in 90 HPV pos. women interviewed compared to 61 controls through questionnaires

Women who tested HPV pos. experienced:

- anxiety, fear, anger, shame, depression, regret, overestimation of cancer risk, concerns on sexual partners: loss of reproductive functions, infidelity, changes in physical intimacy or sexual refusal
- urgent need for treatment

POD Conference 2018

I’m trying to cope with this, but it’s really rough.

Feeling like all hope is lost and feeling like love will never find its way to me.

HPV has ruined my life.

HPV testing

L'uso inappropriato dei test HPV aumenta i costi senza offrire benefici e potenzialmente espone le donne a sovratrattamenti inutili se non dannosi

Solomon D et al. Statement on HPV DNA Test Utilization.

- *Arch Pathol Lab Med* 2009;133(8):1276-7.
- *J Low Genit Tract Dis* 2009;13(3):135-6.
- *Acta Cytol* 2009;53(3):247-48 (discussion: 249-52)
- *Am J Clin Pathol* 2009;131(6):768-9.
- *Diagn Cytopathol* 2009;37(7):542-3.
- *Cancer Cytopathol* 2009;117(3):154-6.

HPV test NOT recommended

- routine screening in women aged < 30 yrs
- more often than every 5 yrs for women > 30 yrs
- adolescents/young adults (< 25 yrs) with any abnormality
- initial triage or management of LSIL < 30 yrs
- initial triage of ASC-H, HSIL, AGC/AIS
- testing for low-risk HPV types

Davey DD et al. 2013 Statement on Human Papillomavirus DNA Test Utilization on behalf of the Cytopathology Education and Technology Consortium (CETC).
Cancer Cytopathol 2014;122(2):83-86. & *Am J Clin Pathol* 2014;141(4):459-61.

L'HPV test (inclusi i ceppi oncogeni e i test per HPV 16/18) NON deve essere eseguito nelle situazioni seguenti:

- decidere se vaccinare o meno contro l'HPV
- nello screening per le MTS in uomini e donne a rischio per MTS
- nella gestione di pazienti affetti da condilomatosi florida genitale o nei loro partner
- nello screening per il cancro cervicale come unico test
- nello screening di routine di donne < 30 anni
- in sedi differenti da quella cervicale (orale o anale)

CDC Atlanta - MMWR Recomm Rep 2015;64(No. RR-3):84-93.

March 4th 2018 was International HPV Awareness Day – an IPVS initiative to increase worldwide understanding of HPV and how it affects us all.

The "Give Love Not HPV" campaign called on everyone to take action to protect their family, friends and partners whether that is by getting informed, getting vaccinated or getting screened for HPV.



HPV IS EVERYWHERE. FORTUNATELY, LOVE IS STRONGER.

Over 80% of people will get HPV at some point in life.
Protecting ourselves and loved ones requires both
detection and prevention.

GiveLoveNotHPV.com



Primary testing for oncogenic HPV outside an organized population-based programme is **NOT** recommended

von Karsa L, Arbyn M, DeVuyst H et al. European guidelines for quality assurance in cervical cancer screening. Summary of the supplements on HPV screening and vaccination. Second edition – Supplements (September 2015)


TOMMY LEE
JONES
JAVIER
BARDEM
JOSH
BROLIN
NON È UN PAESE
PER VECCHI
UN FILM DEI FRATELLI COEN
NON SI PUÒ MAI SCAPPARE FACILMENTE

OVERTESTING → money



↓

OVERDIAGNOSIS → anxiety



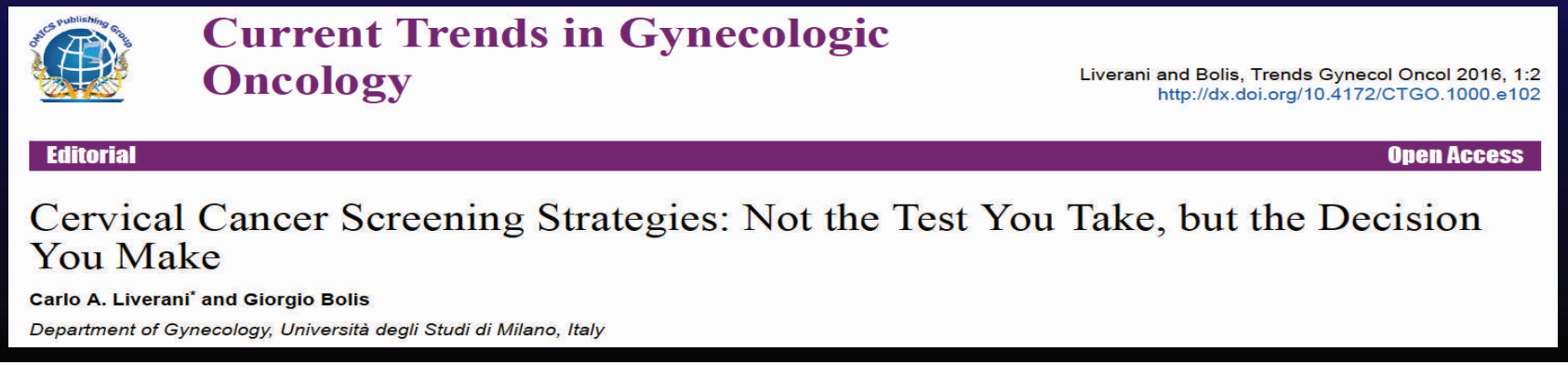
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OVERTREATMENT → harm



L'overtreatment cervicale in età fertile

- effetti negativi dal fatto di risultare "etichettati"
- danni dovuti a test e trattamenti non necessari:
  - MPP ?; elevate recidive/persistenze; stenosi; ematometra;
  - follow-up inadeguato; stress
- spreco di risorse
- distrazione da altri compiti importanti



Current Trends in Gynecologic Oncology

Liverani and Bolis, Trends Gynecol Oncol 2016, 1:2
http://dx.doi.org/10.4172/CTGO.1000.e102

Editorial Open Access

Cervical Cancer Screening Strategies: Not the Test You Take, but the Decision You Make

Carlo A. Liverani* **and Giorgio Bolis**

Department of Gynecology, Università degli Studi di Milano, Italy


Grazie