

Εξατομικευμένη αντιμετώπιση γυναικών με παθολογία
τραχήλου στον 21^ο αιώνα.

Γιατί είναι σημαντική και πως επιτυγχάνεται;

Νεότερα δεδομένα

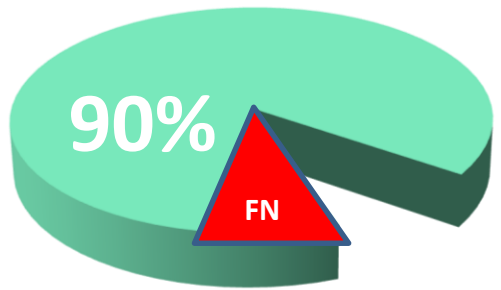
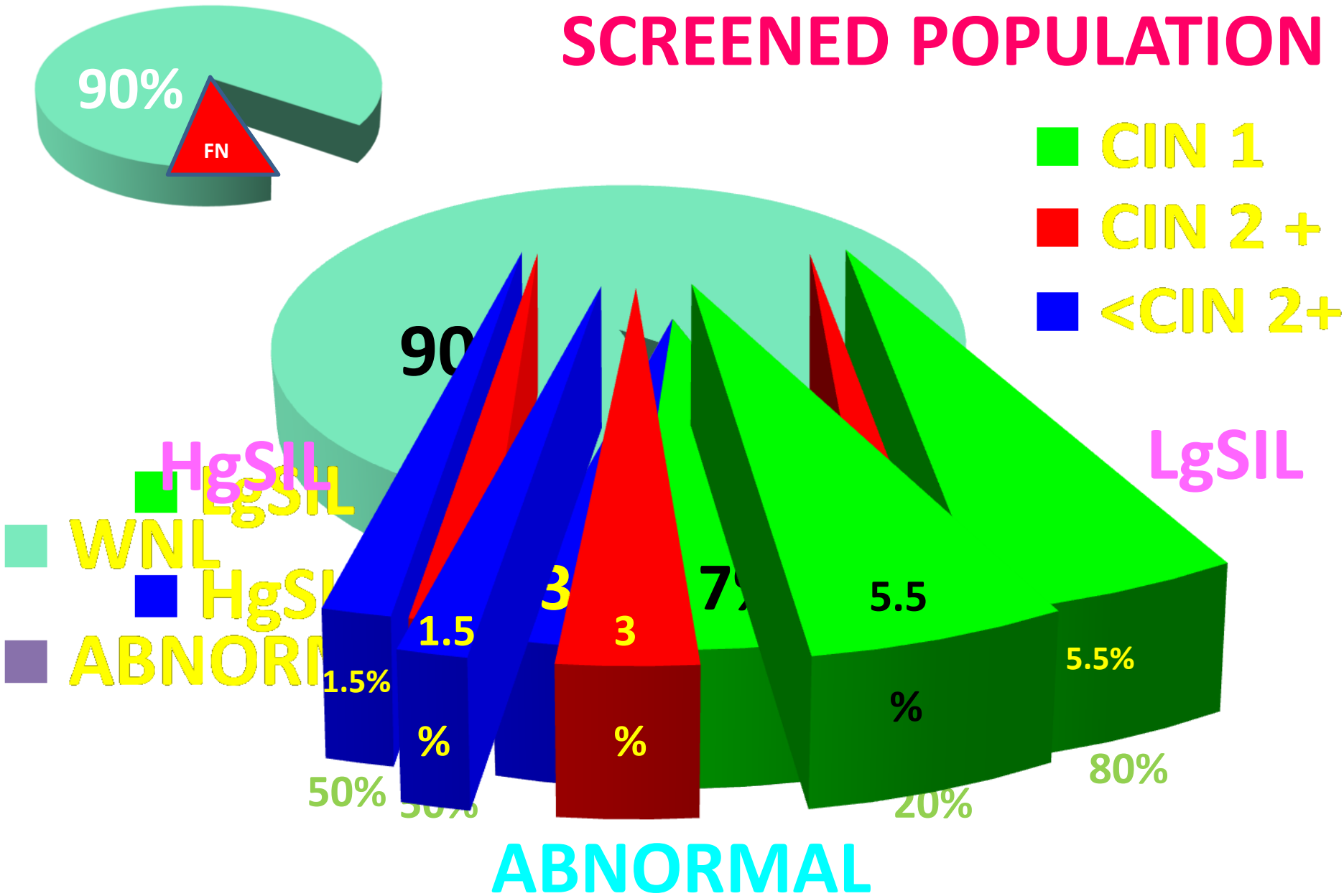
ΡΟΔΟΣ , 3 ΙΟΥΝΙΟΥ 2017

Professor Evangelos Paraskevaïdis
Ioannina Medical School
Greece

President of the

- ***Hellenic Society for Colposcopy & Cervical Pathology (HSCCP)***
- ***Hellenic Cervical Pathology Academic study Group (HeCPA Group)***

SCREENED POPULATION



- CIN 1
- CIN 2 +
- <CIN 2+

- WNL
- LgSIL
- HgSIL
- ABNORMAL

ABNORMAL

WE SHOULD be aware...

Background(1)

- HG SIL: 33-40% regress

Östör Int J Gyn Pathol 1993

- CIN2: 54% spontaneously regress 12m

- CIN

Severity of the lesion	Regression	Persistence	Progression to CIN3	Progression to invasive cancer
CIN1	60%	30%	10%	1%
CIN2	40%	40%	20%	5%
CIN3	33%	<55%	-	>12%

Diati 2011

- Exp

- No immediate Tx in young women with CIN2

Am Guidelines 2007,2012



British Society for Colposcopy and Cervical Pathology

BSCCP Certificate – First Prize

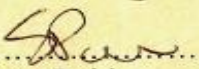
is hereby awarded to

Dr Maria Kyrgiou

For the best Oral Presentation at the BSCCP Annual Scientific Meeting held in Gateshead 2012

'Follow-up of untreated high-grade lesions – is there a role for surveillance with HPV-related biomarkers?'

"Authors: M Kyrgiou, K Papkonstantinou, G Valasoulis, M Cowen, S M Stasinou, P Karakitsos, D Lyons, E Paraskevaidis"


.....
Sharon Parisi
Society Co-ordinator

Date: 20th April 2012
Registered Charity no: 296198

Ioannina Univ Hsptl (GR) + St.Mary's + Queen Charlotte , London, (UK)

1st Prize_s BSCCP 2012 & ΒΟΛΟΣ 2015 (Μ+Γ)

WE SHOULD be aware...

Cervical PBs....

Considered as: *(mainly by epidemiologists, but not only...)*

the GOLD-DIAGNOSTIC-STANDARD

(they can very well be : silver or bronze... > need for multiple PBs...)

[M.Arbyn,C.Redman,E.Moss et.al,BJOG 2012,Meta-,high (S):verification bias ??]

QUESTION 1:

Even if histology of PBs = TZ (for any grade of SIL)

does it really tell us the truth ???

(or it is just a photograph of the tissue,at the particular moment) ???

[combined with adequate knowledge of Cx Ca natural history(Ostor,etc,etc)]

QUESTION 2:

Do we need a photograph of the tissue, or a true indicator of malignant potential ?

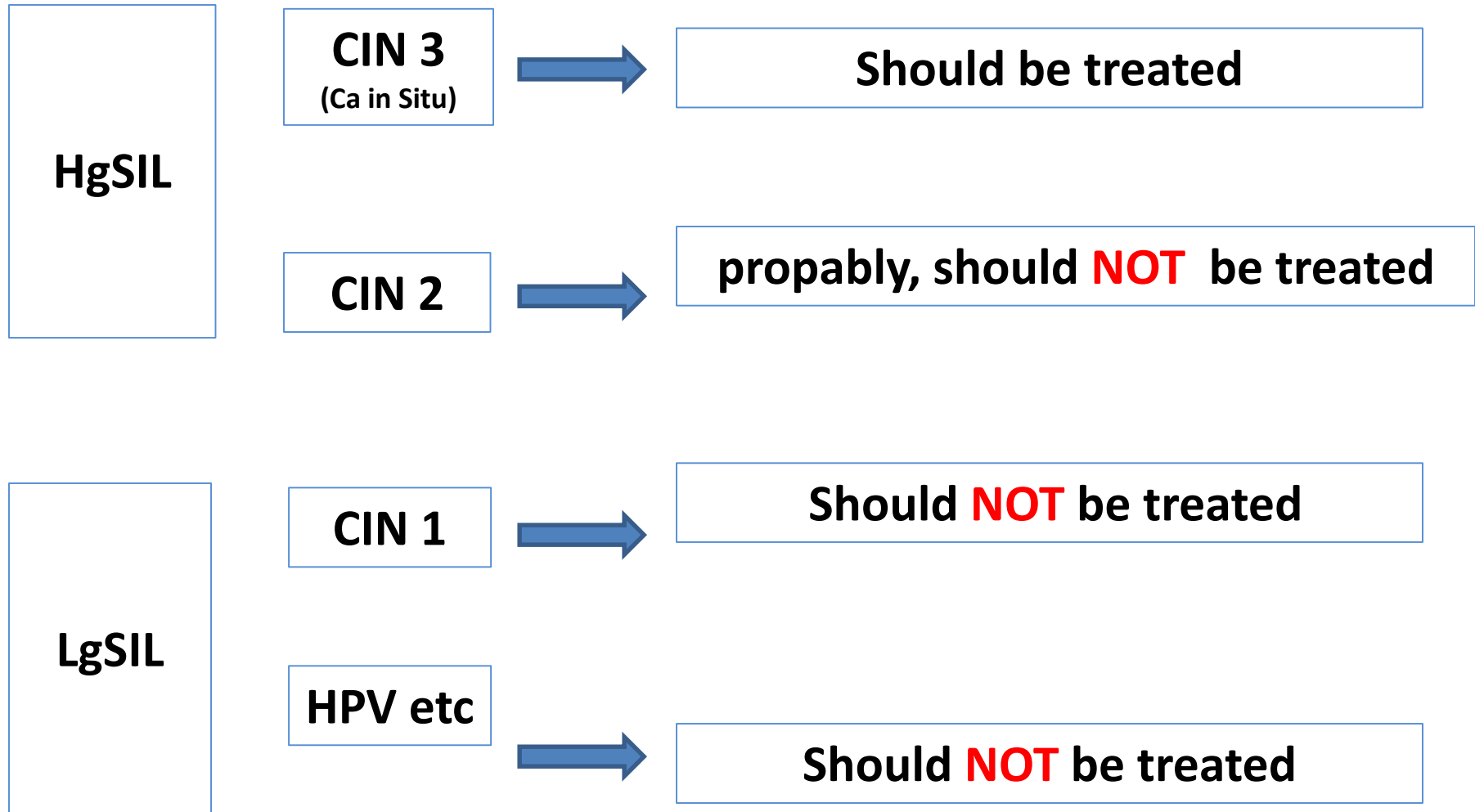
(marker(s) or a combination=risk algorithm,ideally individualized..)

Or justtime , even without biopsies ???

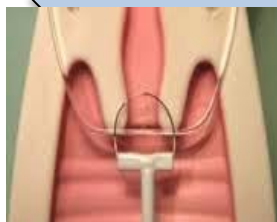
important issues in young patients...

- Who really needs to be treated ??
- How cautious - "*fine art*" - treatment should be...??

Young Women
(Nulliparous , Further Fertility)



Gestation (Weeks)



12

24

28

32

37

Dose Effect

2006 Kyrgiou

THE LANCET

Overall prematurity

2008 Arbyn



Severe & extreme PD

Perinatal mortality

2014 Kyrgiou **BMJ**

2nd trimester miscarriages=early pregnancy losses

The treatment effect increased with increasing Tx cone length/volume...

JAMA Oncol & BMJ, August 2016

<10/12mm

>10/12mm

>15/17mm

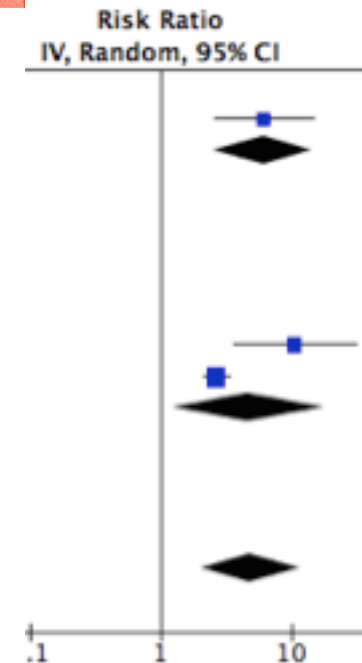
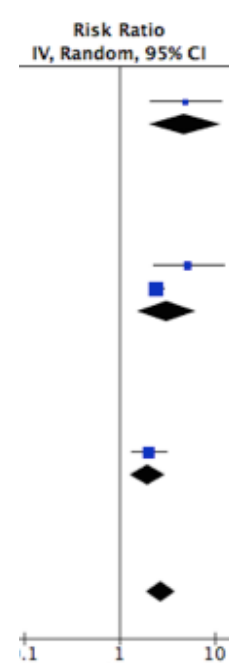
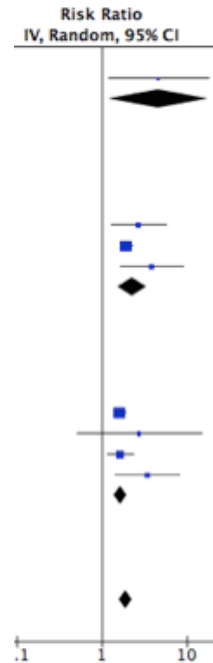
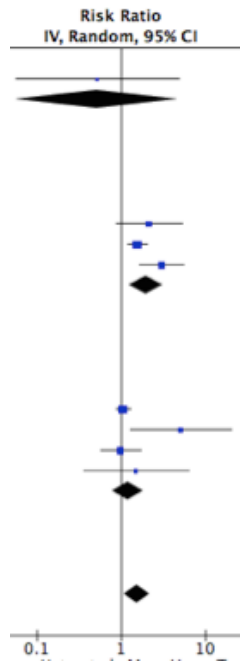
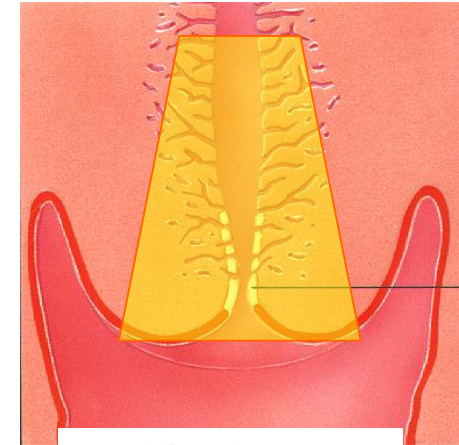
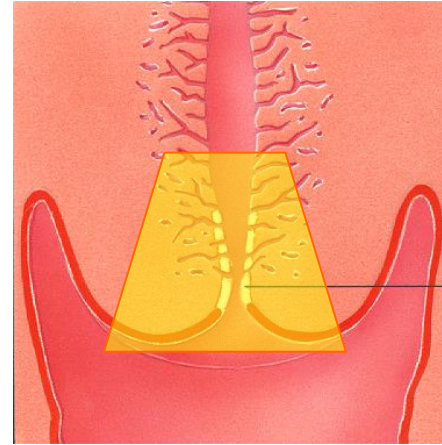
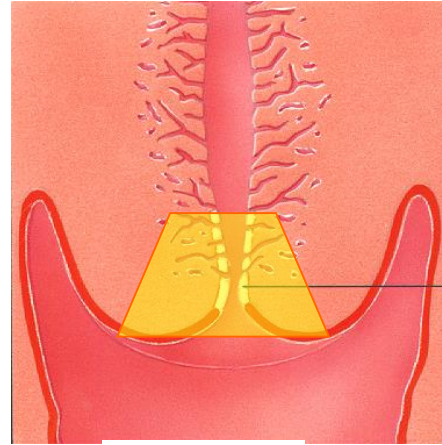
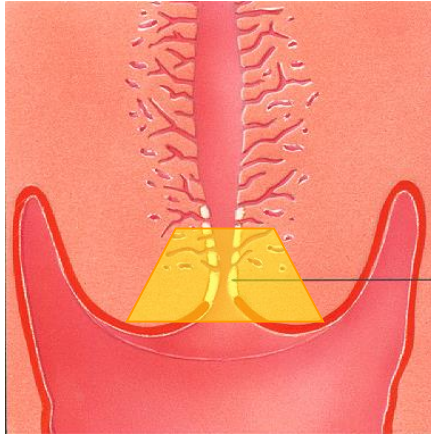
>20mm

1.54 [1.09, 2.18]

1.93 [1.62, 2.31]

2.77 [1.95, 3.93]

4.91 [2.06, 11.68]



Pregnancy Outcomes after Treatment for Cervical Cancer Precursor Lesions: An Observational Study

Sheila Weinmann^{1*}, Allison Naleway¹, Geeta Swamy², Girishanthi Krishnarajah^{3^{oa}}, Bhakti Arondekar^{3^{ob}}, Jovelle Fernandez^{4^{oc}}, Evan Myers²

1 The Center for Health Research, Kaiser Permanente Northwest, Portland, Oregon, United States of America, **2** Department of Obstetrics & Gynecology, Duke University Medical Center, Durham, North Carolina, United States of America, **3** US Health Outcomes and Medical Policy, GlaxoSmithKline, Philadelphia, Pennsylvania, United States of America, **4** North American Vaccine Development, GlaxoSmithKline Biologicals, Philadelphia and King of Prussia, Pennsylvania, United States of America

Conclusion

Women with ≥ 1.0 cm excisional treatment had elevated risk of preterm birth and low birth weight when compared to unexposed women and women with cervical diagnostic procedures. This suggests that increased risk derives from the treatment itself, not from other characteristics. The observed association between pregnancy loss and ablative surgical treatment requires further investigation.



BJOG 2017 May 8

Can we prevent preterm birth after radical trachelectomy?

Kyrgiou M, Bennett P.

EDITORIAL

cervical cancer remains the **fourth** CA in women / > **30.000** new cases annually in Europe

..HPV vaccination will reduce incidence,
but full impact will require decades. ...

...The peak age of CIN matches the mean age of first pregnancy in the Western World.

„Most cervical cancers are diagnosed at an early stage through screening allowing fertility-sparing procedures such as radical trachelectomy, performed vaginally or abdominally or even simple conisation.

Lancet 1997

Invasive cervical cancer after conservative therapy for cervical intraepithelial neoplasia.

Soutter WP, de Barros Lopes A, Fletcher A, Monaghan JM, Duncan ID,
Paraskevaidis E, Kitchener HC

- 44 699 woman-years FU, 2116 women, 8 yrs post tx
- Tx reduces the risk of invasive cancer by 95%
- *However, it still remains:*
5 times **greater** than that among the general population

“Why & How that happens ? How could it be prevented ?”

2017, in preparation

Invasive cervical cancer after conservative treatment of CIN

A. REVIEW of the LITERATURE

B. 21 CASES REPORT

Nikos Raftis – Ikka Kalliala

Kyrgiou M, Lever S, Mitra A, Tsagkas N, Anaforidou M-E, Karamanis G, Karakitsos P, Loufopoulos A, Nasioutziki M, Martin-Hirsch P, Nieminen P, Arbyn M, Paraskevaidis E.

and the HeCPa study group

EUROGIN, AMSTERDAM, OCTOBER 2017





Ghaem-Maghani S et al.

Lancet Oncology 2007

Tx failure / margins

PD/2nd Tx

1-2 % vs **20-30 %**

x 5-10

CHALLENGES TO ACHIEVE ...

Treating & eradicating cervical precancer efficiently
(single treatment)

Post-op Life-time Risk

Cervical cancer :

NOT 5 times greater.....***BUT***

Obstetrical complications :

NOT 2,3,4,5 times greater.....***BUT***

Equal to the***general population***

EDITORIALS

Long term outcomes for women treated for cervical precancer
Cervical cancer risk increases with age and looks worse for women treated
more recently
We need to find out why

Feb 2014

M Arbyn , M Kyrgiou , J Gondry , K U Petry , E Paraskevaidis

*... better standardisation and quality assurance in colposcopy
to achieve the*

***Fine Art of..... optimal balance on future :
risk of cancer & obstetric safety...***

Hellenic Cervical Pathology Academic Group (HeCPA Group)

Design Prospective **pragmatic** diagnostic studies

Setting Academic Depts. OB-GYN, Greece
Coordinating centers: Ioannina
Attikon
Thes/niki

Population Women referred with any SIL

Period 10/2008-**ongoing**

Intervention HPV typing, NASBA, flow cytometry, p16, etc.

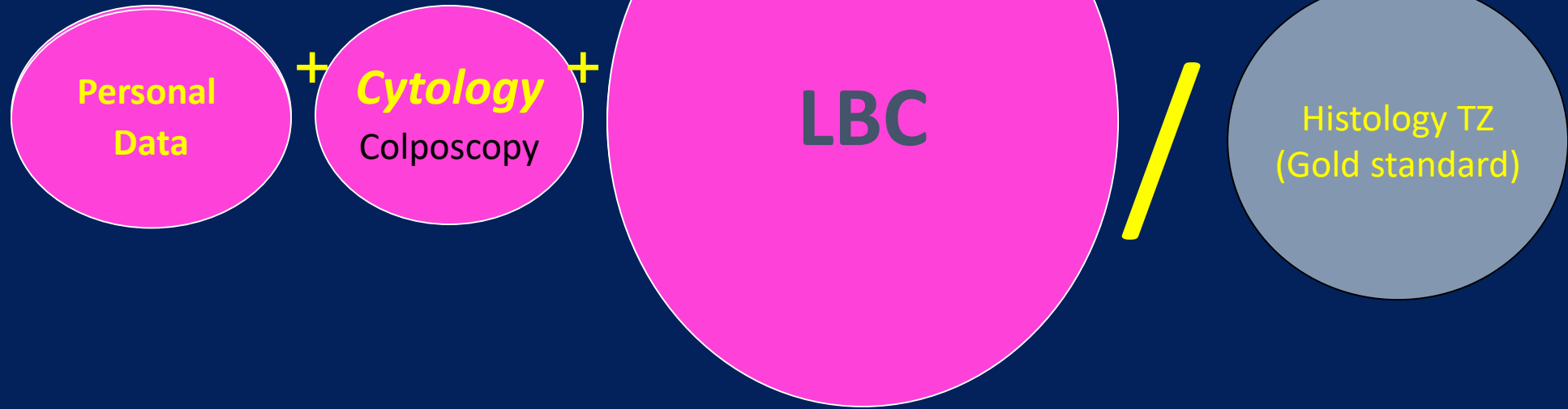
Outcomes S, SP, PPV, NPV for each marker and combinations

End point CIN2+



Scoring System

12 +, parameters





















Life Style - Cervical Pathology Risk

LS-CPR

BSCCP Apr 2016

'in press'

1. -smoking	No 	socially 	>20cg 
2. -menarche/onset sex	>10 	>5 	<3 
3. -sexual partners	<5 	5-10 	>10 
4. condom use	100% 	50% 	0% 
5. -vaccine(bs,as,no)	Before sex 	After sex 	No 
6. -post-tx:grade,margins	free 	involved 	inv+G3 

Scoring System

Starting Line:

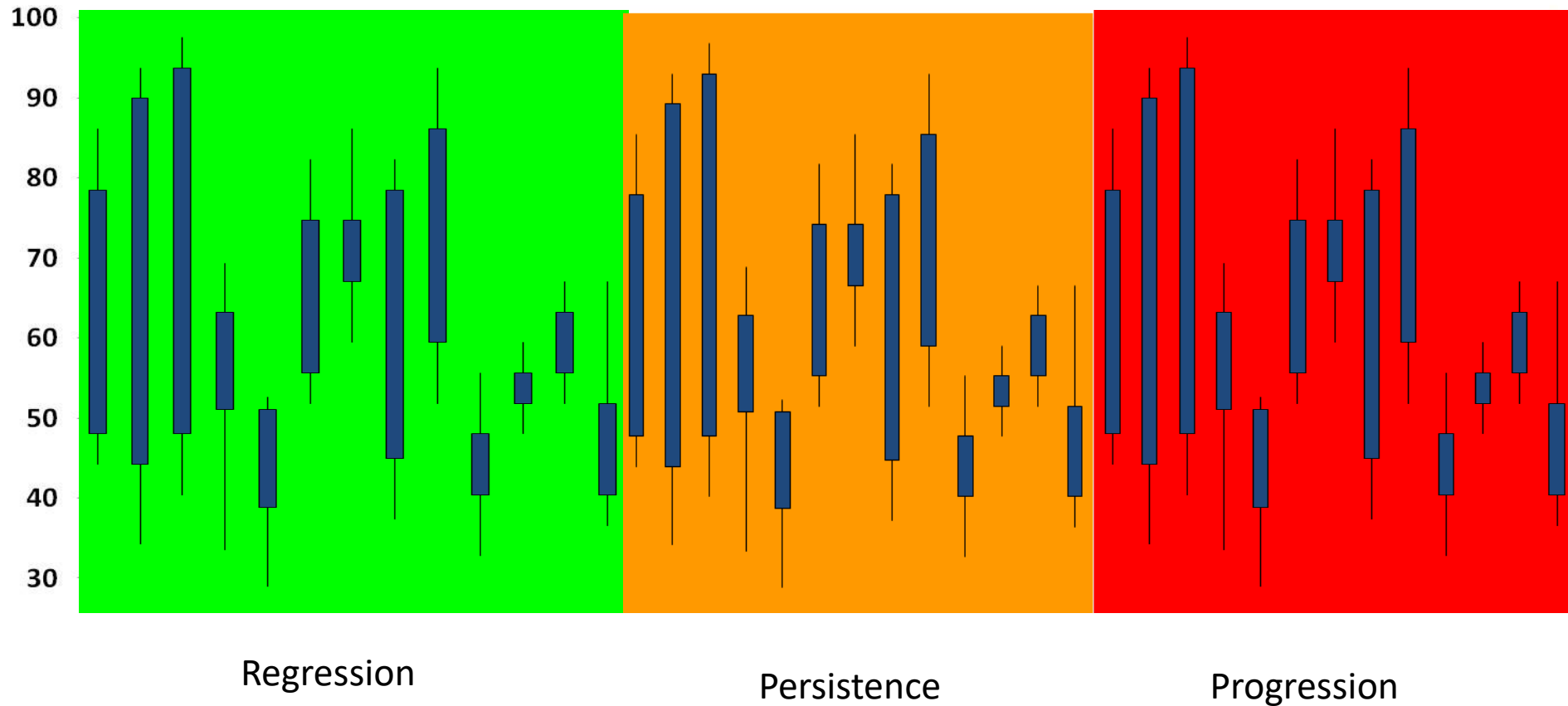
Cytology OR
HPV DNA test



Patient
characteristics
Colposcopy

+

Best combination
of biomarkers...
+ APTIMA....



Optimal individualisation...

Best combination

HPV biomarkers risk +Life Style Risk

Hellenic Cervical Pathology Academic Group

- ~ 12 years,prospective data (*pragmatic design*)
- > 20,000 women
- > 50 publications (*pubmed*)
- > 20 awards

American Guidelines ? (JLGTD April 2017)

Australian Guidelines ?

Personalized management of women with cervical abnormalities using Clinical Decision Support Scoring System

M Kyrgiou, A Pouliakis, JG Panayotides, N. Margari, P Bountris, G Valasoulis, M Paraskevaidi, E Bilirakis, M Nasioutziki, A Loufopoulos, M Haritou, DD Koutsouris, P Karakitsos, E Paraskevaidis

*Gynecologic Oncology, April 2016
'Precision in Medicine'*

<http://cxcadss.biomed.ntua.gr/> Select Demo

Pap Test Result

Completed

CA

HPV DNA Test Result

Completed

06	11	16	18	26	31	33	35	39	40	42	43	44	45	51	52	53	54	56	58	59	61	
62	66	68	70	71	72	73	81	82	83	84	85	89	N/A									

NASBA Result

Completed

16	18	31	33	45	N/A
----	----	----	----	----	-----

Flow Cytometry Result

Completed

POSITIVE

p16 Result

Completed

NEGATIVE

Histology

Colposcopy

Results

Prediction Results

The case is classified by the system as Ca

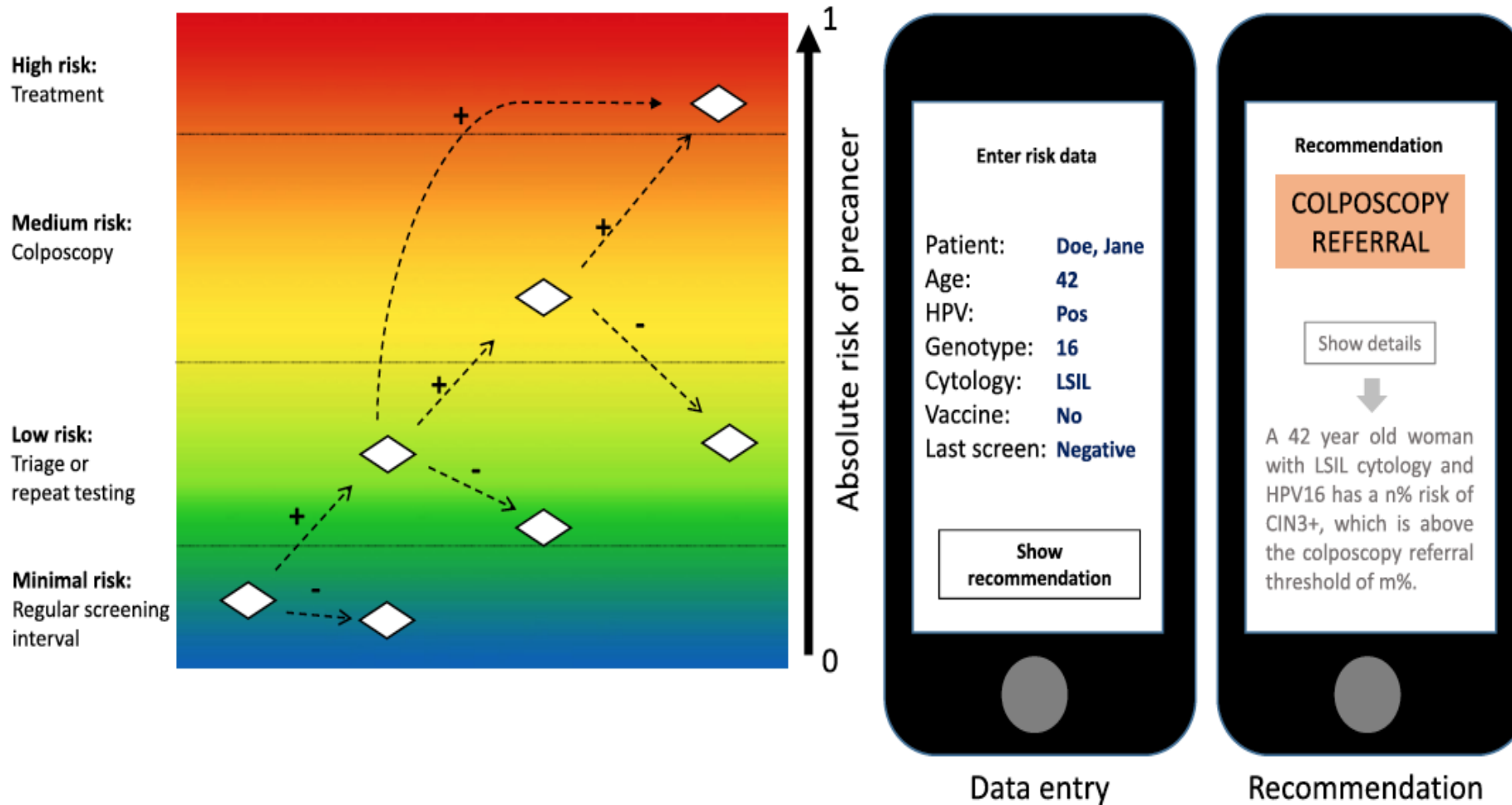
Probability of Negative Histology
0%

Probability of CIN 1
0%

Probability of CIN 2/3
0%

Probability of Ca
100%

Preparing for the Next Round of ASCCP-Sponsored Cervical Screening & Management Guidelines



Preparing for the Next Round of ASCCP-Sponsored Cervical Screening & Management Guidelines

Mark Schiffman, MD, MPH

National Cancer Institute Rockville, MD

Nicolas Wentzensen, MD

Division of Cancer Epidemiology and Genetics National Cancer Institute
Rockville, MD

Michelle J. Khan, MD

Kaiser Permanente Northern California San Leandro, CA

Philip E. Castle, PhD David Chelmow, MD Warner K. Huh, MD

Anna Barbara Moscicki, MD Colleen K. Stockdale, MD Teresa M.

Darragh, MD Michelle Silver, PhD

Richard S. Guido, MD

National Cancer Institute Rockville, MD

Infect Dis. 2017 Feb 7

Quantitative measurement of L1 HPV16 methylation for the prediction of pre-invasive and invasive cervical disease.

Kottaridi C1, Kyrgiou M, Pouliakis A1, Magkana M1, Aga E1, Spathis A1, Mitra A, Makris G2, Chrelias C2, Mpakou V3, Paraskevaidis E4, Panayiotides JG5, Karakitsos P1

Cochrane Database Syst Rev. 2017 Jan 26

Immediate referral to colposcopy versus cytological surveillance for minor cervical cytological abnormalities in the absence of HPV test.

Kyrgiou M1,2, Kalliala IE1,2, Mitra A2, Fotopoulou C1,2, Ghaem-Maghani S1,2, Martin-Hirsch PP3, Cruickshank M4, Arbyn M5, Paraskevaidis E6

Sci Rep. 2016 Dec 15

Tracking the Impact of Excisional Cervical Treatment on the Cervix using Biospectroscopy.

Halliwell DE1, Kyrgiou M2,3, Mitra A2,3, Kalliala I2,3, Paraskevaidis E4, Theophilou G5, Martin-Hirsch PL6, Martin FL1,7.

Int J Cancer. 2017 Jan 1

Immediate referral to colposcopy versus cytological surveillance for low-grade cervical cytological abnormalities in the absence of HPV test: A systematic review and a meta-analysis of the literature.

Kyrgiou M1,2, Kalliala I1, Mitra A1, Ng KY3, Raglan O1, Fotopoulou C1,2, Martin-Hirsch P4,5, Paraskevaidis E6, Arbyn M7

BMJ. 2017 Feb 28.

Adiposity and cancer at major anatomical sites: umbrella review of the literature.

Kyrgiou M1,2, Kalliala I3, Markozannes G4, Gunter MJ5, Paraskevaidis E6, Gabra H3,2, Martin-Hirsch P7,8, Tsilidis KK4,9

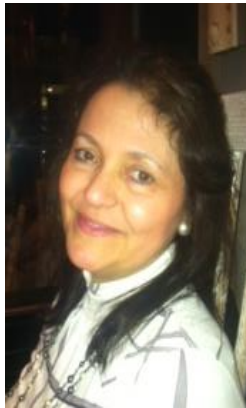
Why Most Published Research Findings Are False

John P. A. Ioannidis



Ioannidis has devoted much of his career to empirically examining the biases and the reproducibility of published science. (Reproducibility, meaning that an experiment can be reproduced with the same results, is key to validating and building on scientific findings.) Ioannidis is one of the most highly cited scientists of his generation in the scientific literature, according to Microsoft Academic rankings. He is best known for his 2005 *PLoS Medicine* paper “Why most published research findings are false,” which is the most accessed and downloaded article in the history of *Public Library of Science*, with more than 1 million views to date.

> 1.3 million views, 2017





**HSCCP -Ελληνική Εταιρεία
Παθολογίας Τραχήλου
και Κολποσκόπησης**

Μέλος των:
EFC - The European Federation For Colposcopy
IFCPC - The International Federation for Cervical Pathology and Colposcopy

Παθολογία Τραχήλου & Κολποσκόπηση:

Κυτταρολογία - Βιοδείκτες - Κολποσκόπηση
Ιστολογία & περαιτέρω διαχείριση

Παρουσίαση Περιστατικών

Σε συνεργασία με:

HeCPA Group

Hellenic Cervical Pathology Academic Group

Ελληνική Ακαδημαϊκή Ομάδα Μελετών Παθολογίας Τραχήλου

Ελληνική Εταιρεία Κλινικής Κυτταρολογίας

**Problem
Based
Learning**

16-19 Νοεμβρίου 2017

16-19 Νοεμβρίου
Ξενοδοχείο Du Lac
Ιωάννινα 2016

www.hsccp-ioannina.gr

To be submitted for recertification by the
British Society for Colposcopy and Cervical Pathology - BSCCP

Συνδιοργάνωση με EFC

ΠΕΜΠΤΗ 16 Νοεμβρίου 2017

09.00-14.00

Εκπαιδευτικό σεμινάριο :

ΕΞΑΤΟΜΙΚΕΥΜΕΝΗ ΑΝΤΙΜΕΤΩΠΙΣΗ ΓΥΝΑΙΚΩΝ ΜΕΤΑ ΠΑΘΟΛΟΓΙΚΟ SCREENING ΤΡΑΧΗΛΟΥ

Εισαγωγή -Overview : *E.Παρασκευαΐδης*

Screening τραχηλου σήμερα : *M.Νασιουτζίκη*

Screening τραχήλου αύριο: *Π.Καρακίτσος*

Φυσική ιστορία τραχ καρκινογένεσης : *Γ.Βαλασούλης*

Παθολογικο screening (ψευδώς παθολογικό) & πραγματικότητα τραχήλου : *A.Μπατιστατου*

Διερεύνηση παθολογικού screening test: *E.Μπιλιράκης*

Ο ρολος των Punch Biopsies : *I.Παναγιωτίδης*

Ο ρολος των βιοδεικτων : *Χ.Κοτταρίδη*

Molecular Cytopathology : *Christine Bergeron*

Αλγοριθμοι triage/ Scoring Systems: *Π.Μπουντρής*

Ο ρολος του life-style : *N.Τσάγκας*

New Technologies : *John Tidy*

Γιατι η εξατομίκευση είναι ζωτικη ? *M.Κύργιου*

Είναι εφικτη ? *A.Λουφόπουλος*

Can individualization work within NHS frame? *P.M.Hirsch*

Θεματα cost-effectiveness : *Peter Sasieni*

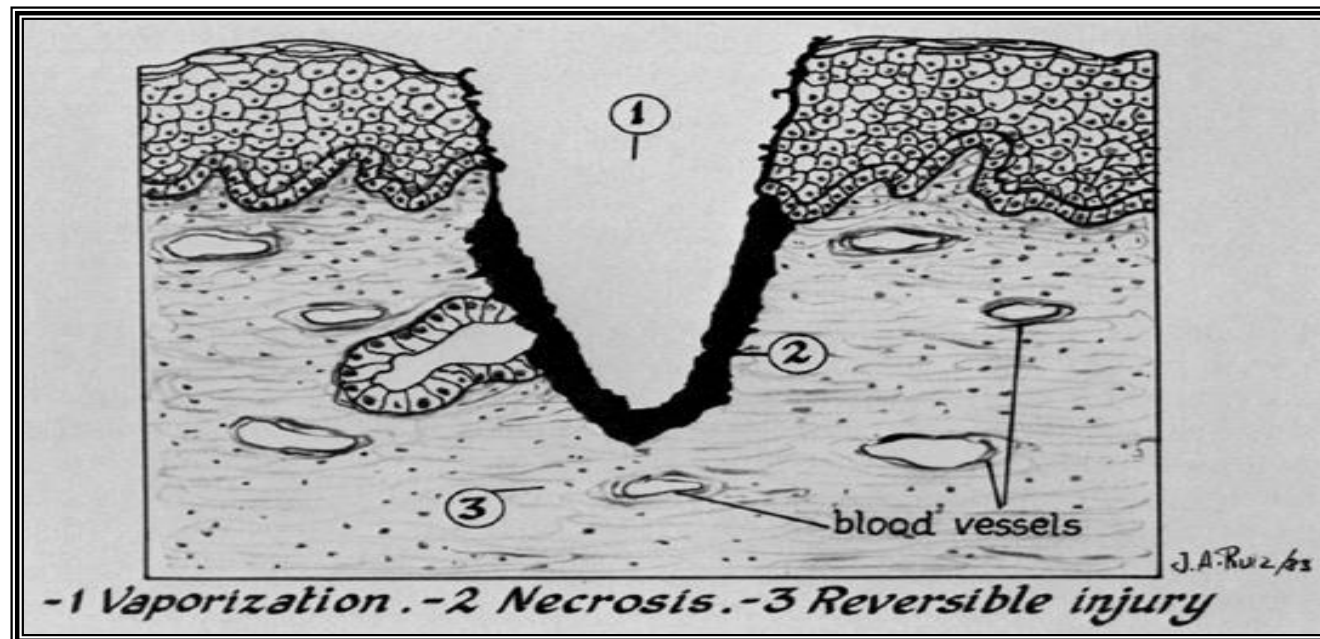
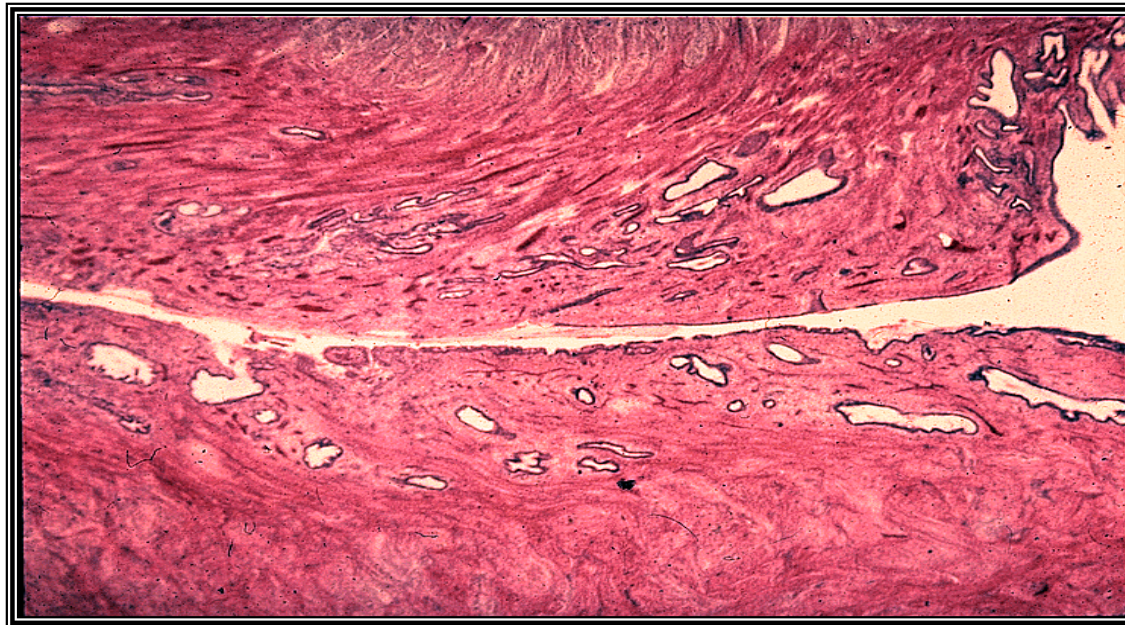
Ioannina, Greece



Thank you

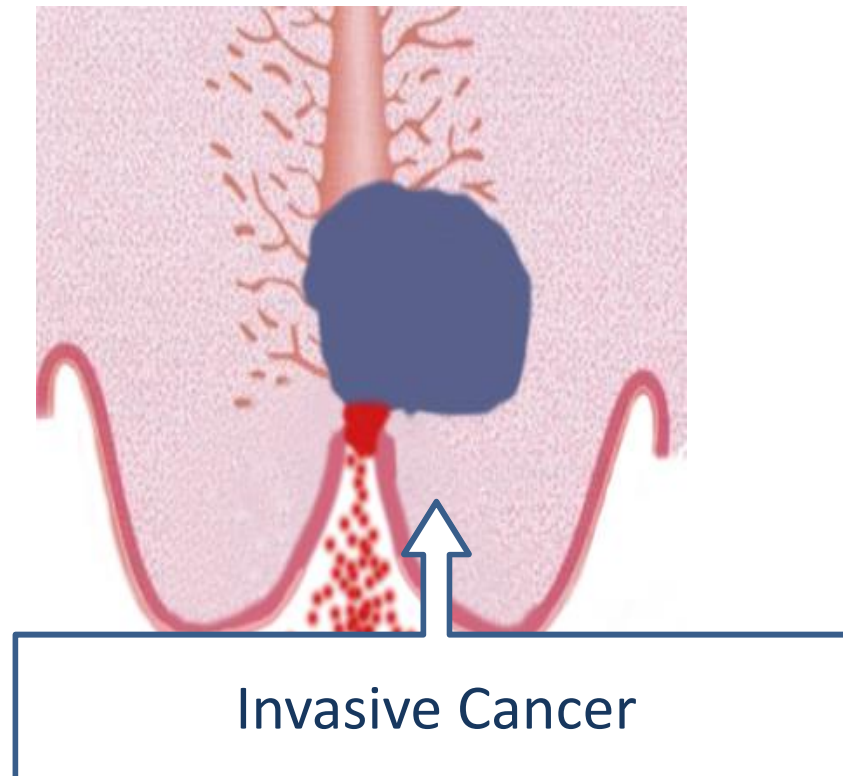
All studies show increased risk...

Study	Relative Risk	Proposed follow-up (years)	Notes
Soutter, (1997)	5	10+	44,699 woman-years of follow-up: 85/100000woman years
Kalliala, (2005)	2.8	20+	Anogenital cancers also
Strander, (2007/2014)	4.52	25+	Increased incidence with age (treatment / follow-up)
Melnikow, (2009)	6.2		Increased >50years
Rebojl, (2012)	6.1		increased for all ages



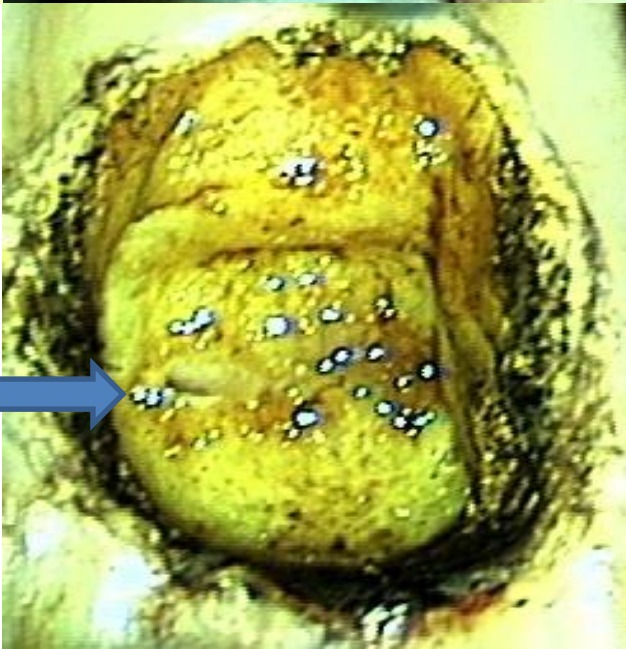
Ball cauterization - "Embankment effect"??

Cervical crypt theory





***Cervical gland/
Cancer crypt?***



**European Registry(Data Base) for CIN3,
untreated(alternatives,refusers,etc) lesions**

E.Paraskevaidis,P.Karakitsos,M.Arbyn,W.Prendiville,C.Redman

open call...

- HeCPA Group
- BSCCP,LONDON hsptls
- EFC
- IFCCP

LBC sample,WHO accredited Lab,free of charge,
very careful documentation & consent

