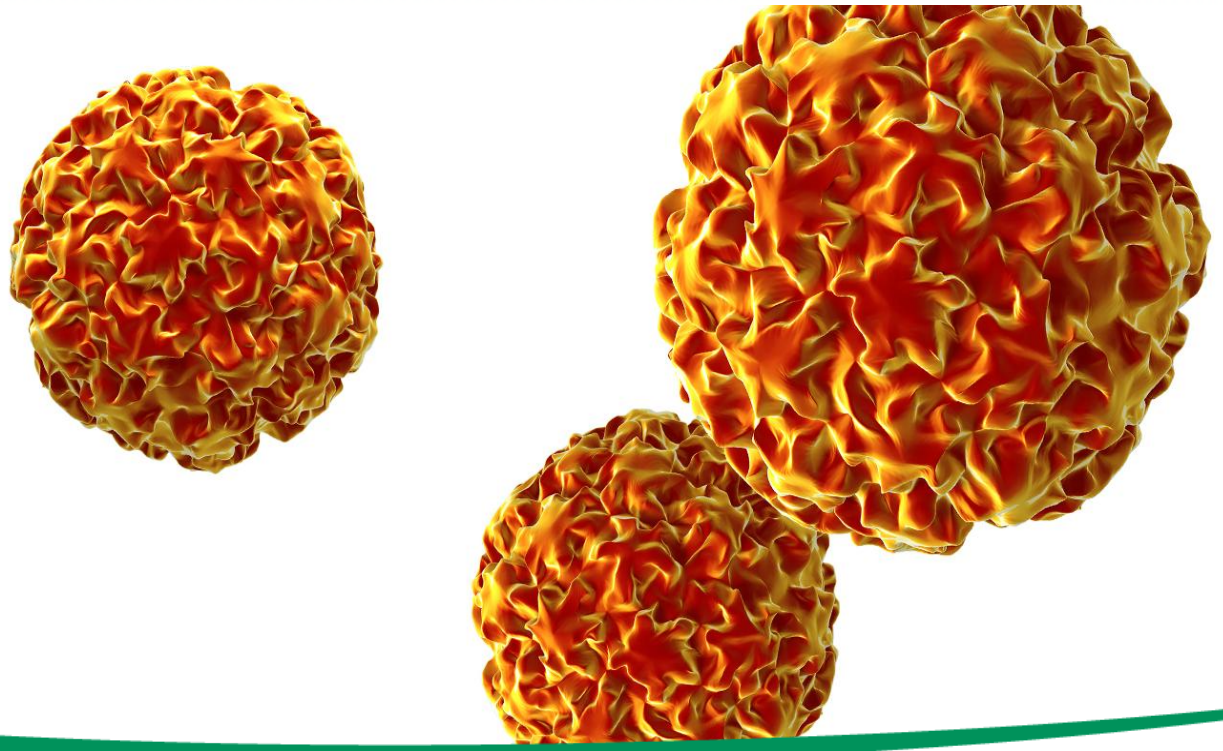
BỆNH VIỆN PHỤ SẢN TRUNG ƯƠNG
National Hospital of Obstetrics and Gynecology



HPV DNA primary in cervical cancer screening
What benefits for patients?

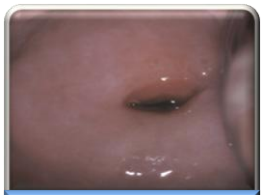
Prof. Vu Ba Quyet

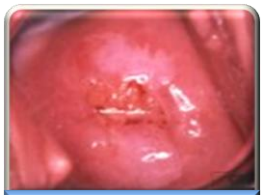
Director of National O&G hospital

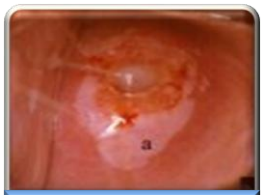
Vice President of Vietnam Association of Gynecology & Obstetrics

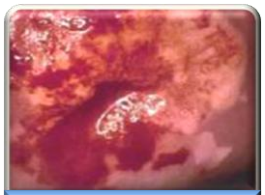
Cervical cancer screening
Patient expectation?

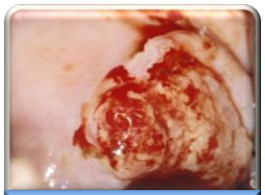
Cervical Cancer progression


Cervix nomal/


CIN 1


CIN 2


CIN 3


Cancer

Primary prevention

Vaccine HPV

Secondary prevention: Screening with VIA, cytology, HPV test

Early treatment of cacner

Treatment

Cryotherapy, laser

LEEP,...

Model of screening
Patient benefit centric

Preventive & safe

Convenient

Patient centric

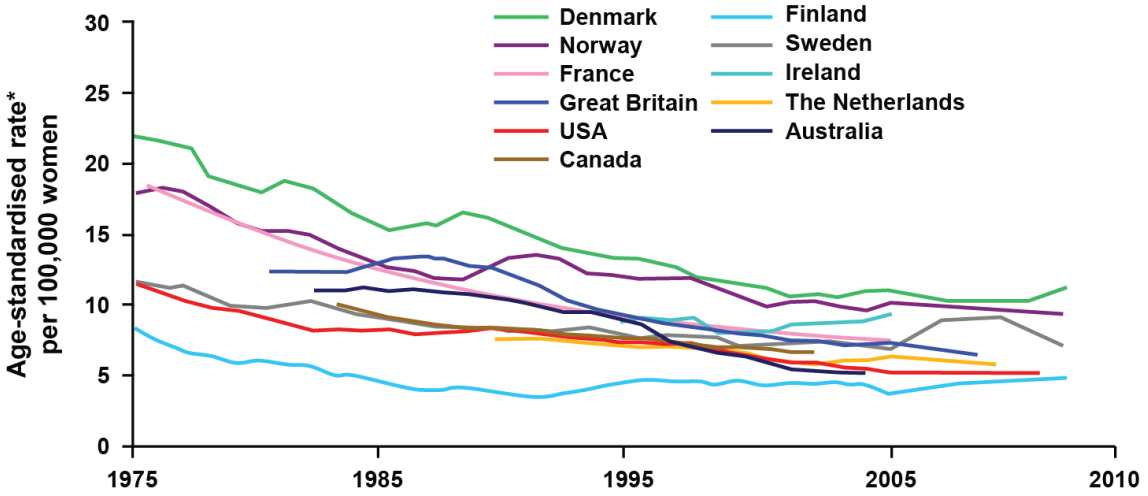
Cost effectiveness

Cervical cancer screening: Cytology based

Introduced in 1940s

Progression from CIN3 to cervical cancer takes approximately 10 years.

Cytology was successful even with low sensitivity by testing often.

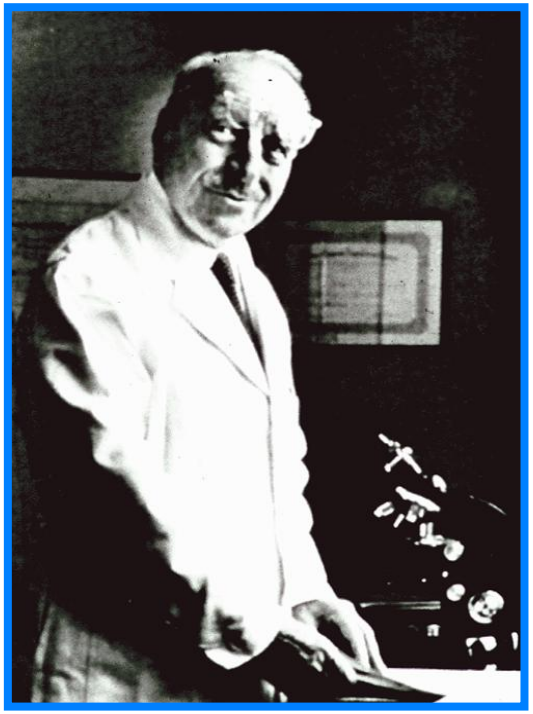


1927 | 1940 | 1950s | 1960s | 1970s | 1980s | 1990 | 2000s | 2010

Fist introduced in 1927 by Babes

Become widely adopted over the world and considered as a effectiveness method, reduced cervical cancer rate

Cytology



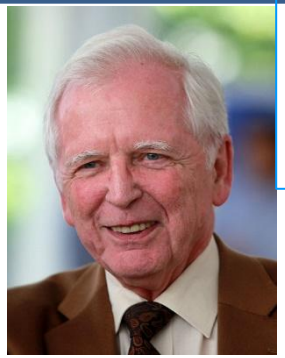
Dr. George M. Papanicolaou
1883-1962

- Low sensitivity # 40-75%
- Results depend on cytologist expertise
- Big investment because of high cost for training and educating specialists

Cervical Cancer screening

Identify root cause: HPV is the main cause

Introduced in 1940s



In 1976, Harald Zur Hausen published the hypothesis that Human papilloma virus plays as an important role in the cause of Cervical Cancers

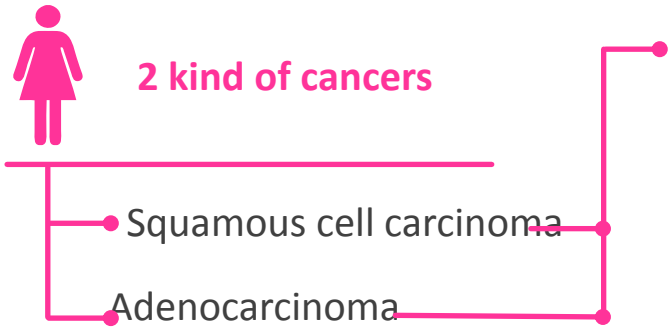
In 1983, HPV 16 & HPV 18 were identified in cervical cancers

1927 1940 1950s 1960s 1970s 1980s 1990 2000s 2010

Fist introduced in 1927 by Babes

Pap become widely adopted over the world and considered as a effectiveness method, reduced cervical cancer rate

Cervical Cancer is caused by hrHPV persistent infection



HPV16 & HPV18 are the most prevalence oncogenic genotypes

- HPV infection is present in almost cases of cervical, pre-cancer, CIN and high grade of lesion
- Persistent infection 1 of 14 of high-risk HPV genotypes causes greater than 99% of all cervical cancer cases

1. Herzog *et al*. 2007 **2**. Saslow D *et al*. 2012 **3**. Schiffman *et al*. 2007

Cervical cancer screening HPV based

Introduced in 1940s

In1999, HPV was indicated for ASCUS triage

In 2006, HPV was indicated for co-testing with pap for women >30 yo.

In 2014 HPV DNA was approved as primary screening test for women from 25 years old.

1927 | 1940 | 1960s | 1990s | 2000s | 2010s | 2010

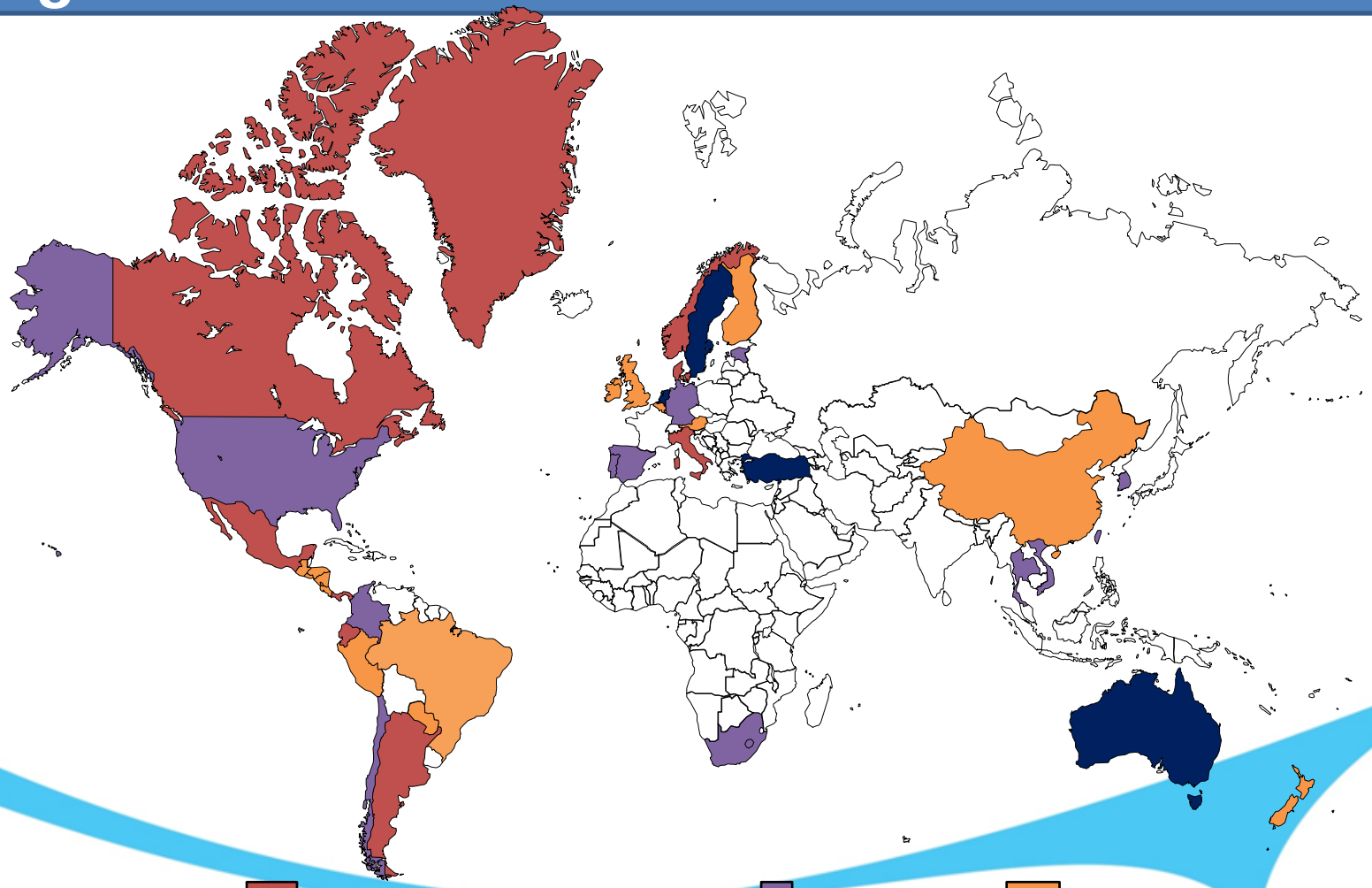
Fist introduced in 1927 by Babes

Pap become widely adopted over the world and considered as a effectiveness method, reduced cervical cancer rate

HPV primary screening

A few years ago

HPV primary screening
Progression over the world



Current to the best of our knowledge on 27APR17; South Korea, Taiwan – co-testing but not stand-alone primary screening

HPV DNA based screening

ATHENA trial

4/2014

US FDA approved for cobas HPV as primary screening test

ACOS issued algorithm using HPV as primary test

1/2015

10/2015

Netherland issued national guideline using HPV DNA as primary screening

VN MOH approved for cobas HPV as primary test

7/2016

ASCO issued guideline using HPV DNA as primary test for women from 25yo & elder

10/2016

10/2016

VN MOH issued national action plan for cervical cancer prevention period 2016 – 2025, In which HPV DNA recommended as primary test for women 25yo and above

Australia issued national program using HPV DNA as primary test for women from 25yo above

12/2017

Thái Lan, HongKong, Italia.. Đưa vào hướng dẫn quốc gia

HPV DNA as the primary screening test

All clinical trials find the similar results

- Several randomized clinical trials in Europe– NTCC, POBOSCAM, VUSA, ARTISTIC,
  SWEDESCREEN, Finnish Screening Trial
- One observational clinical from the US – *ATHENA*
- Kaiser. clinical – *NCI's Kaiser N. California study*
- *All demonstrated that HPV primary screening is safe and effectiveness*

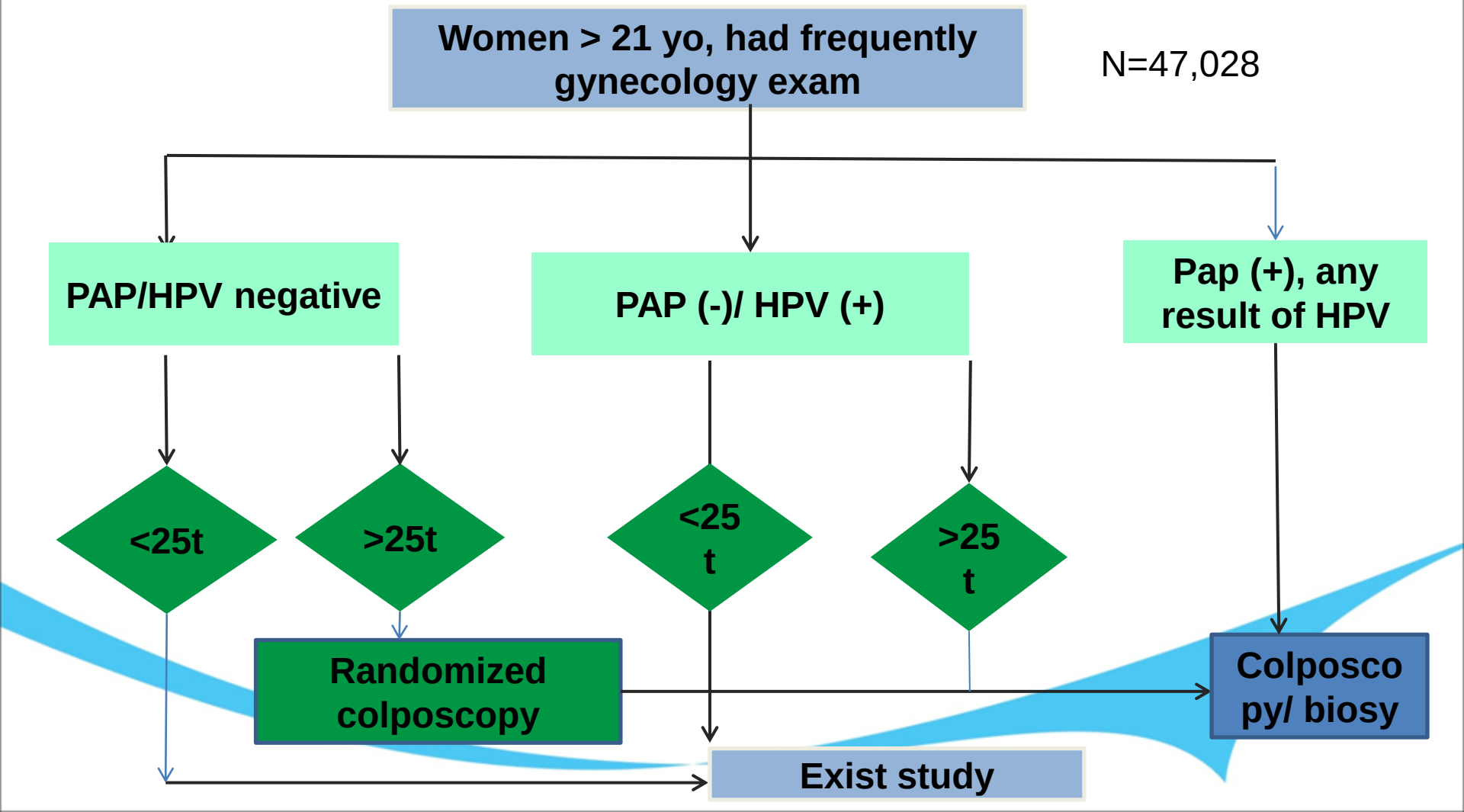
HPV as the primary screening test in the US

ATHENA trial, women >25 years old

- Studied 42,208 women≥25 in the US
- Had gynaecology exam, LBC , HPV (with genotyping)
- Colposcopy for all women with HPV (+), and/or LBC (+) and a randomized subgroup of hrHPV (-)
- First large US study of HPV based screening

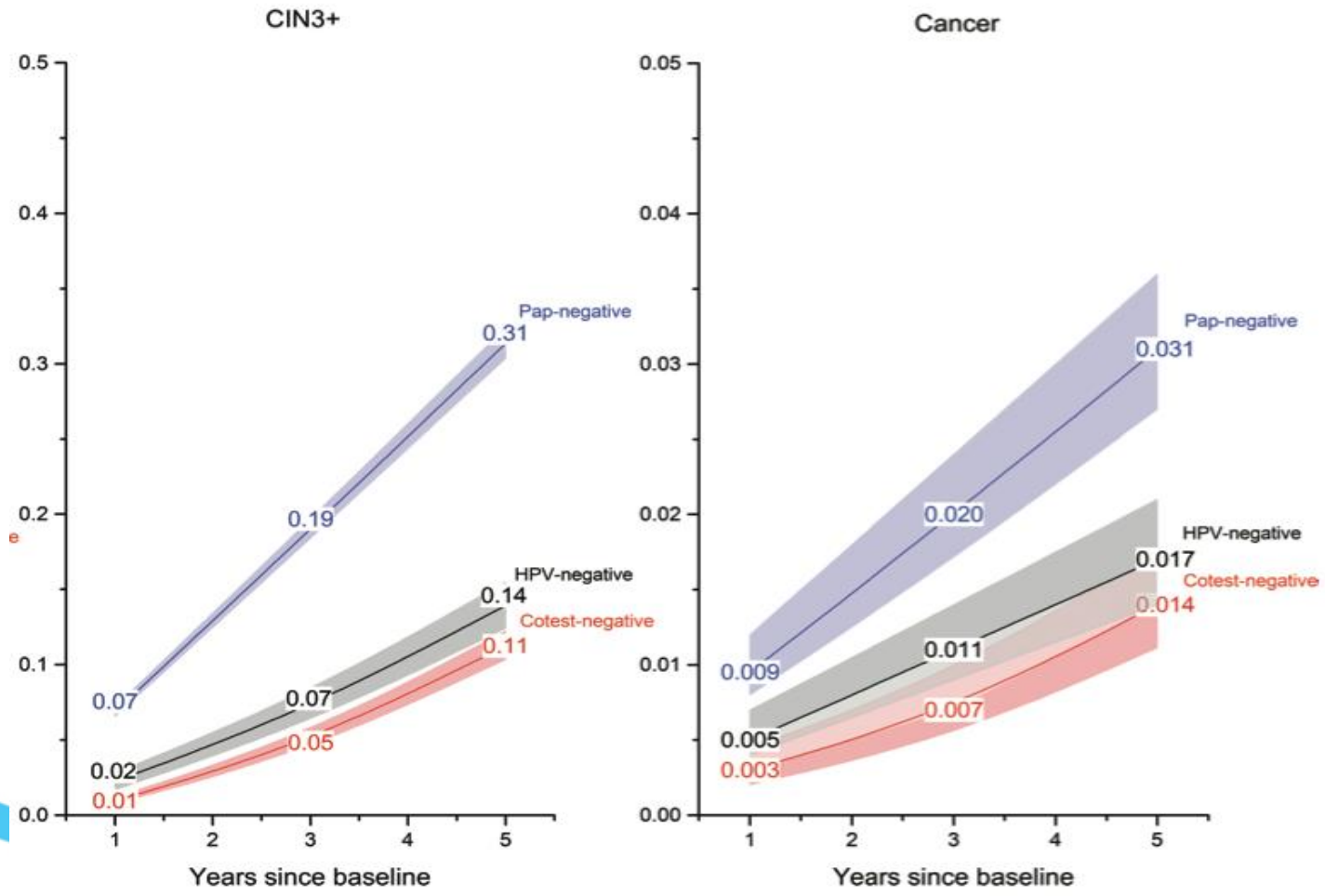
Wright et al. (2011) Am J Clin Path

ATHENA trial: Study design



Risk of CIN 3/ Cancer of group with PAP (-),HPV(-)

Kaiser N. California; 1,011,092 women ≥30 yrs



Gage *et al.* JNCI 2014; 106

Comparison of test's sensitivity

- Systematic review of cohort studies
- Calculation of sensitivity and specificity

	HPV	Cytology
Sensitivity	95% (95% CI:84 -98)	70% (95% CI: 54 – 81)
Specificity	84% (95% CI: 72-91)	95% (95% CI 92 – 97)

IFCPC2017 World Congress presentation

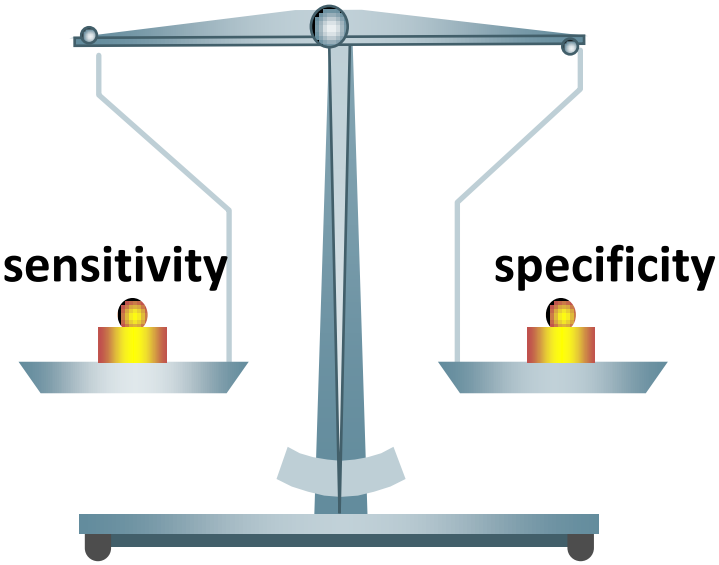
Cervical cancer screening guidelines: Balancing between benefits versus harm

Goal:

- Minimal mortality and morbidity

Optimal strategy should:

- Identify precursors that likely progress to cervical cancer
- Avoid to detection and unnecessary treatment of infections & lesions that are not tendency become cancerous



Saslow, et al. Am J Clin Pathol. 2012 Apr;137(4):516-42

How to balance benefits & harm

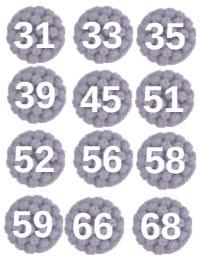
- Be confident in a negative result
  - Use clinical validated HPV DNA test with internal cellularity control.
- Managing positive result
  - Use proven screening strategies

Clinical validation of HPV DNA test

- HPV infections are very common, about 80% of sexually active women become infected:
  - Almost of infections do not cause a problem
  - The goal is not identify all of cases of HPV infection
  - The goal is identify infected women who currently have CIN2 of wha are at increased risk of developing of CIN 2 in the future.
- Clinical validation helps to maximizes HPV detections that have clinical relevant and minimize unnecessary intervention

Stoler MH, et al. *Am J Clin Pathol.* 2007;127:335-337

Internal Cellularity control



Ø

Positive ß-globin

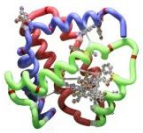
Valid result

True negative

negative ß-globin

Invalid result

Avoid false negative result

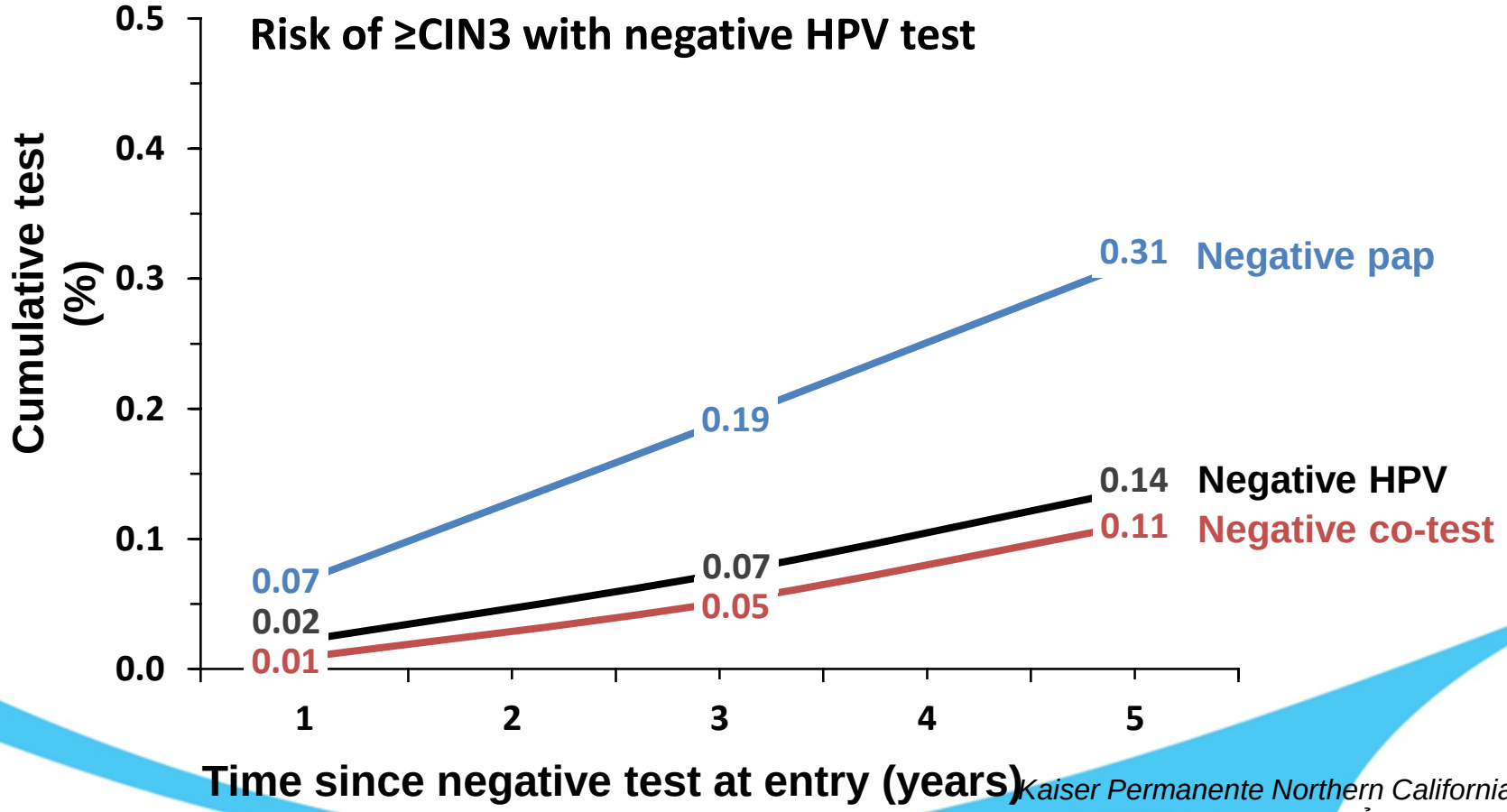


Internal control (ß-globin)

Internal cellularity control based human ß-globin in cobas® HPV increases the creditability and reduces false negative results.

Risk of CIN 3 with negative test

1,011,092 women aged 30-64 years



Kaiser Permanente Northern California
1,011,092 phụ nữ 30-64 tuổi

Gage JC, et al. *J Natl Cancer Inst*. 2014;106(8):dju153.

Conclusion 1

HPV DNA as primary screening offers strong prevention and safety for patients/women

Patient benefit centric

Preventive & safe

Convenient

Cost effectiveness

Patient centric

Comparing different strategies

- Based on the complete 3 year follow-up data, we evaluated the performance of 3 different screening algorithms in women ≥25 years
- Evaluated Strategies were:
  - Cytology
  - HPV primary screening with HPV 16/18 genotyping
  - Co-testing*

Wright, et al. *Gynecol Oncol.* 2015 doi:10.1016/j.ygyno.2014.11.076

Comparison of strategies for women ≥25 years olds

CIN3+ were identified and colposcopy

Strategy	Screening tests	CIN3+ at baseline	CIN 3+ Year 1-3	Colposcopy	Colposcopy per CIN3
cytology	45,166	143	36	1,934	10.8
Co-testing	82,994	143	97	3,097	12.9
HPV primary	52,651	197	97	3,769	12.8

Wright et al. Gynecol Oncol 2015

Total women ≥CIN3 =347

Comparision of screening strategies

Value for patients

Attribute	PAP	Co-testing	HPV Primary
Level of protection	Low	High	High
Cost	1x test	2x tests	1x test
Complexity	High	High	Low
Number of colposcopy	Low	High	High
Interval	Short	Long	Long

Conclusion 2

HPV DNA primary screening offers cost effectiveness with high protection and long interval for patients/women

Patient benefit centric

Prevention & safety

Convenience

Cost effectiveness

Patient centric

VIỆN PHỤ SẢN TRUNG ƯƠNG
Hospital of Obstetrics and Gynecology

Coverage of HPV DNA

- Almost O&G hospitals have HPV DNA test
- Effective sample collection system covering nationwide

Conclusion 3

HPV DNA with high coverage and effective sample collection process that facilitates the accessibility and comfort for patients/women

HPV DNA highly and widely recommended

special article

Primary Prevention of Cervical Cancer:
American Soci
Resource-Stra

Phòng ngừa thứ pl
Khuyến cáo thực hành lâm
ASCO

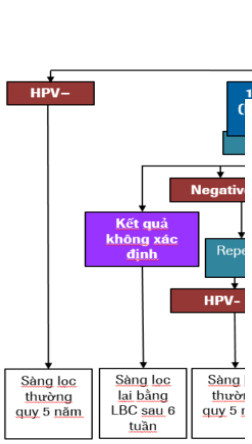
Tầm soát đầu tay:

- XN HPV DNA được khu
- Quan sát CTC với acid a
- Khuyến cáo tuổi và tần sau:
  - Điều kiện rất tốt: 25
  - Điều kiện tốt: 30 – 6 thời gian 5 năm, lần
  - Điều kiện giới hạn:
  - Điều kiện cơ bản: 3

Jeronimo J et al. J Oncol Pract. 2016 Nov 15

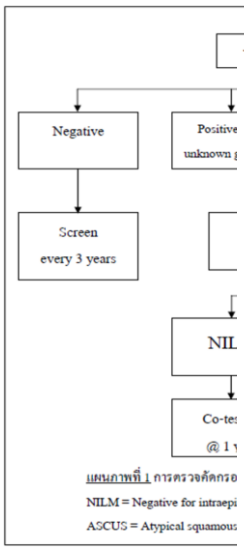
Hướng dẫn sàng lọc UTCTC của Úc
Chương trình Quốc Gia 1/12/2017

Roche

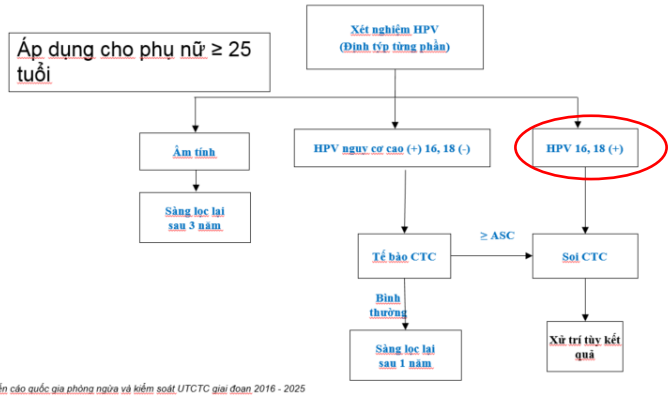


http://www.cancer.org.au/health-professionals/clinical-gui

Hướng dẫn sàng lọc của Thái Lan



Phác đồ 2B: HPV đầu tay (định týp từng phần)



Khuyến cáo quốc gia phòng ngừa và kiểm soát UTCTC giai đoạn 2016 - 2025

ASCO Resource Stratified Guidelines for Cervical Cancer Secondary Prevention

	Basic	Limited	Enhanced	Maximal
Screen	HPV DNA test; if not available VIA	HPV DNA test	HPV DNA test	HPV DNA test (Co-testing an option)
Age Range	30-49	30-49	30-65	25-65
Frequency	1-3 screenings per lifetime	Every 10 years	5 years; if negative x2 then 10 years	5 years
Triage	VAT	HPV 16/18 GT or cytology or VAT	HPV 16/18 GT or cytology	HPV 16/18 GT or cytology
Triage (-)	f/u 12 months	f/u 12 months	f/u 12 months	f/u 12 months
Triage (+)	Treat	Colpo or VAT (if Colpo not available)	Colpo	Colpo

VIA – visual inspection with acetic acid; VAT – visual assessment and treatment
https://pilotguidelines.atlassian.net/wiki– accessed 06JUN2017

ASCO Resource Stratified Guidelines for Cervical Cancer Secondary Prevention

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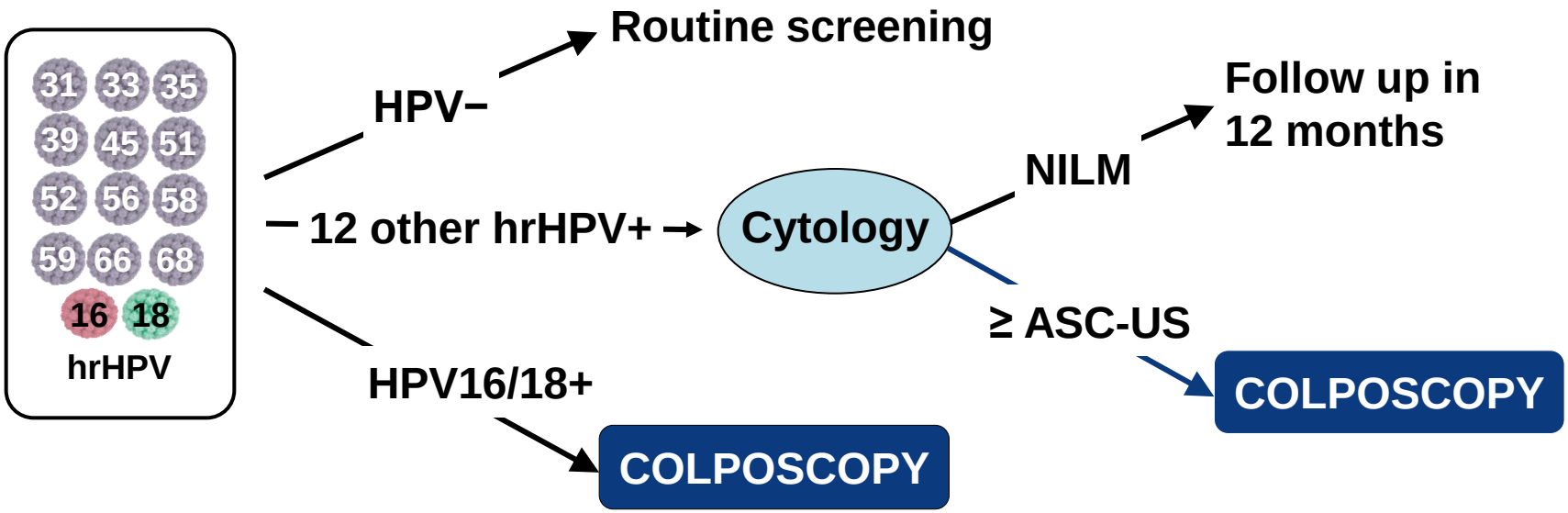
Triage	VAT	HPV 16/18 GT or cytology or VAT	HPV 16/18 GT or cytology	HPV 16/18 GT or cytology
Triage (-)	f/u 12 months	f/u 12 months	f/u 12 months	f/u 12 months
Triage (+)	Treat	Colpo or VAT (if Colpo not available)	Colpo	Colpo

VIA – visual inspection with acetic acid; VAT – visual assessment and treatment

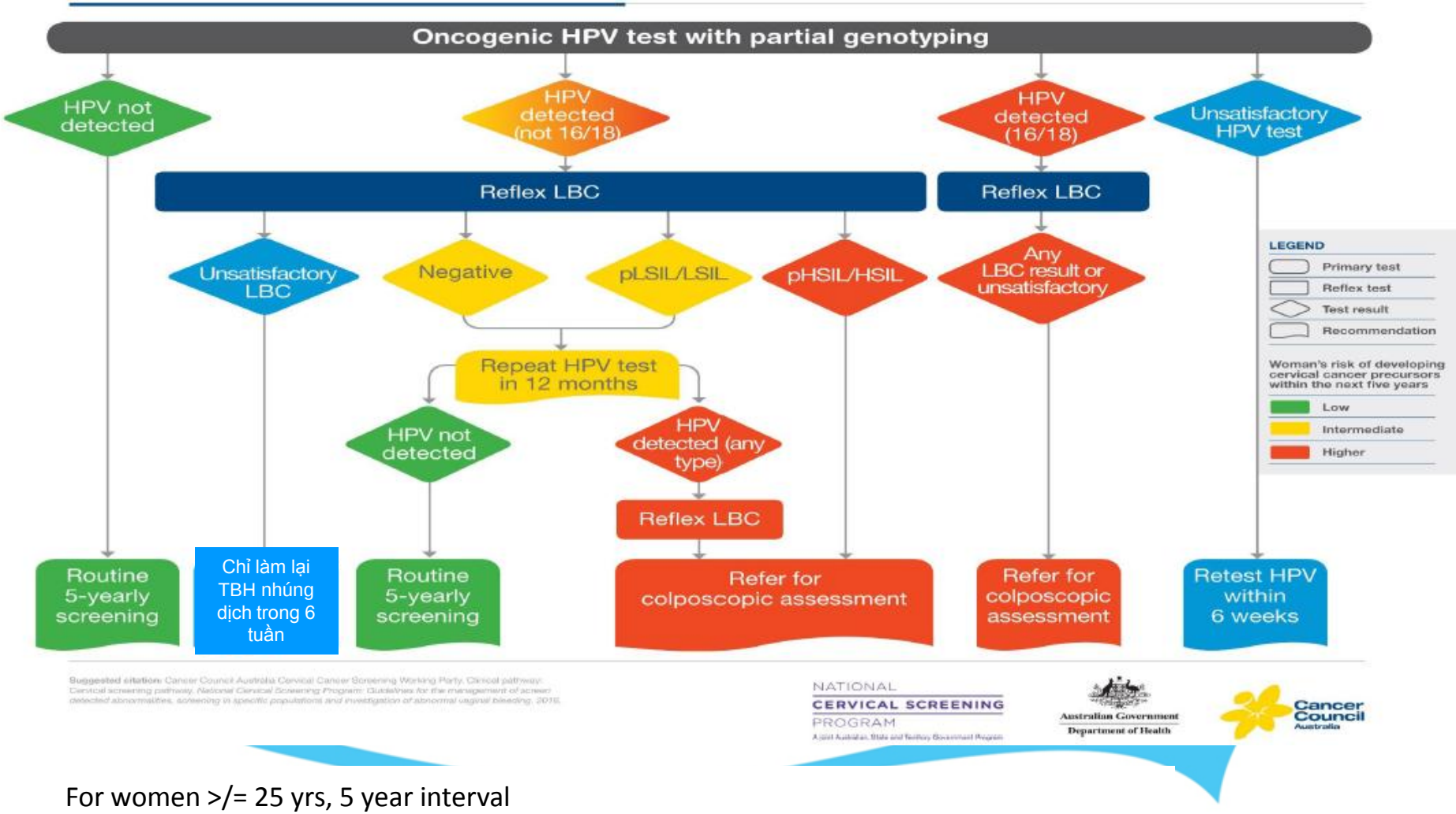
https://pilotguidelines.atlassian.net/wiki– accessed 06JUN2017

US HPV Primary Screening Algorithm



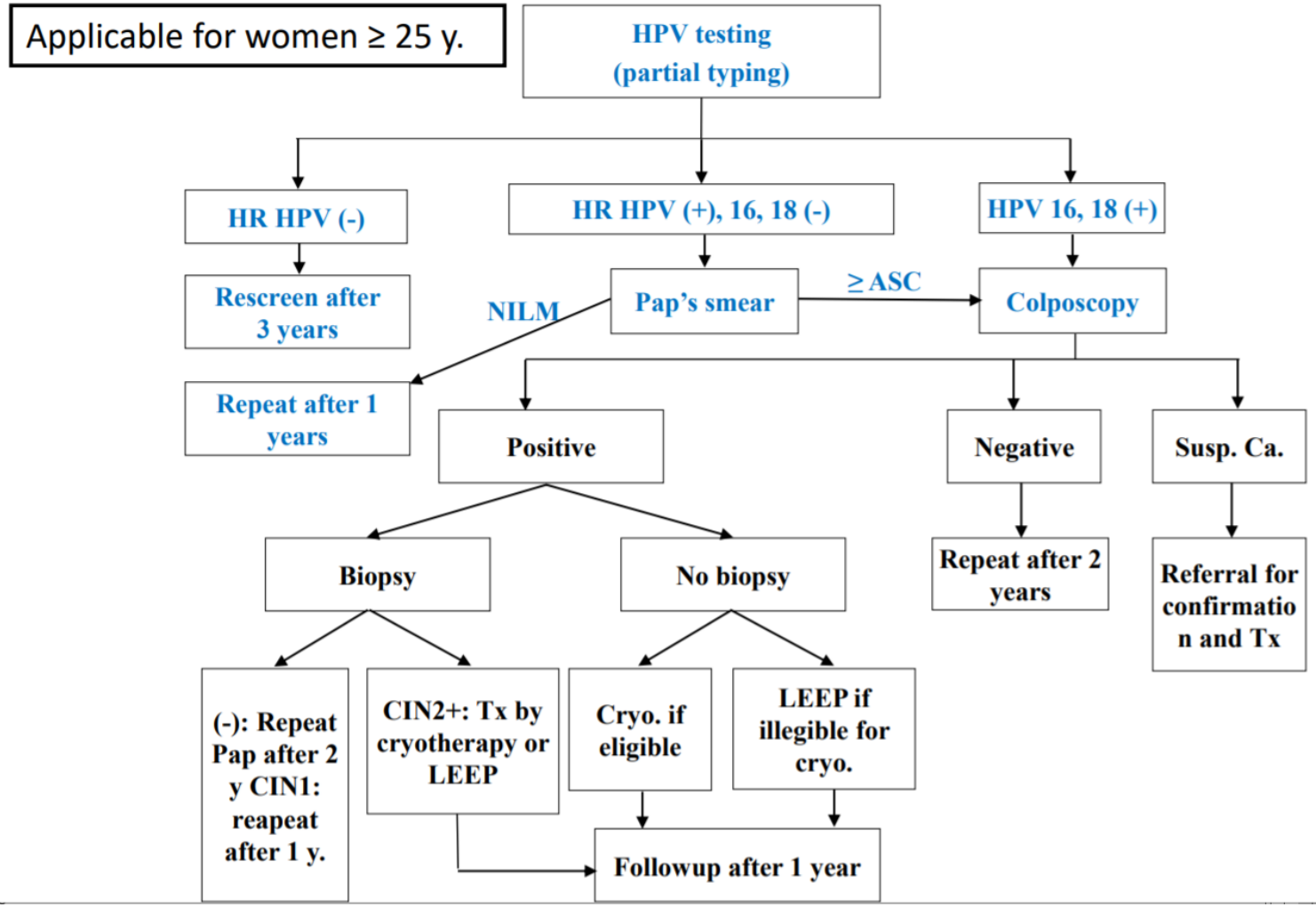
hrHPV, high risk HPV

National program of Australia
Starting by HPV

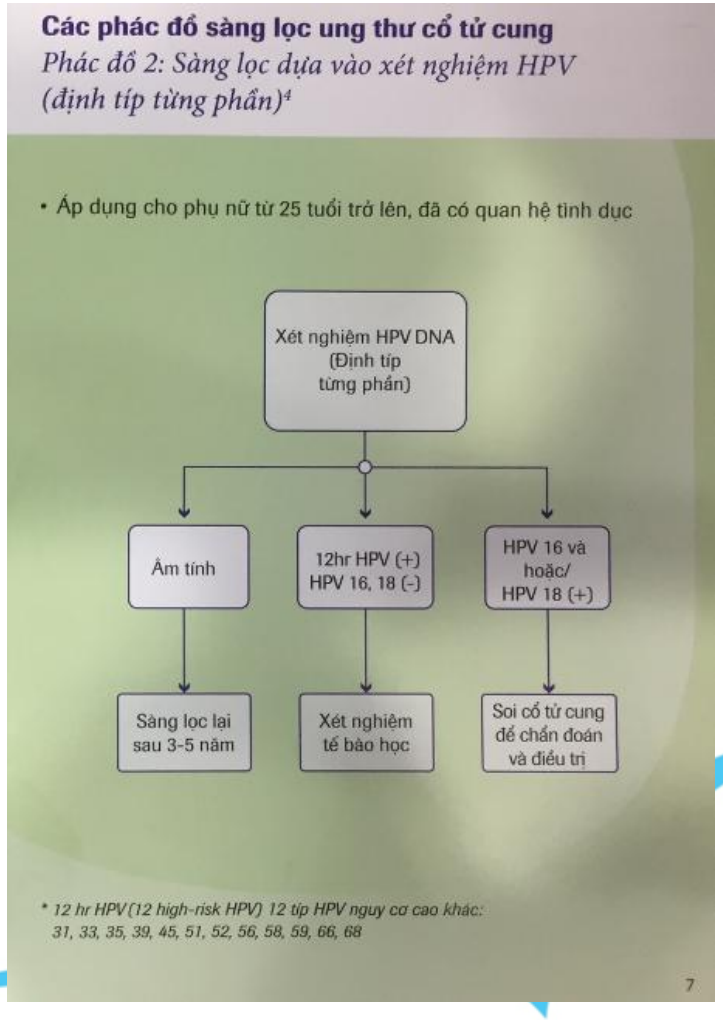


For women >/= 25 yrs, 5 year interval

Vietnam guideline: HPV primary



National O&G guideline



Conclusion

- HPV primary screening in cervical cancer screening offers strong prevention and safety, cost effectiveness and convenience for patients/women
- HPV primary screening startegy based on the balance between risks and harm
  - Clinical validated tests with proven longitudinal safety and internal cellularity control
  - Appropriate interval screening
- HPV DNA is becoming popular and convenient for patients/women to access because of high coverage and effective sample collection process.

Thank you for your attention!

CERVICALCANCER
AWARENESS

NEVER GIVE UP!
JANUARY