Primary HPV Screening for Cervical Cancer

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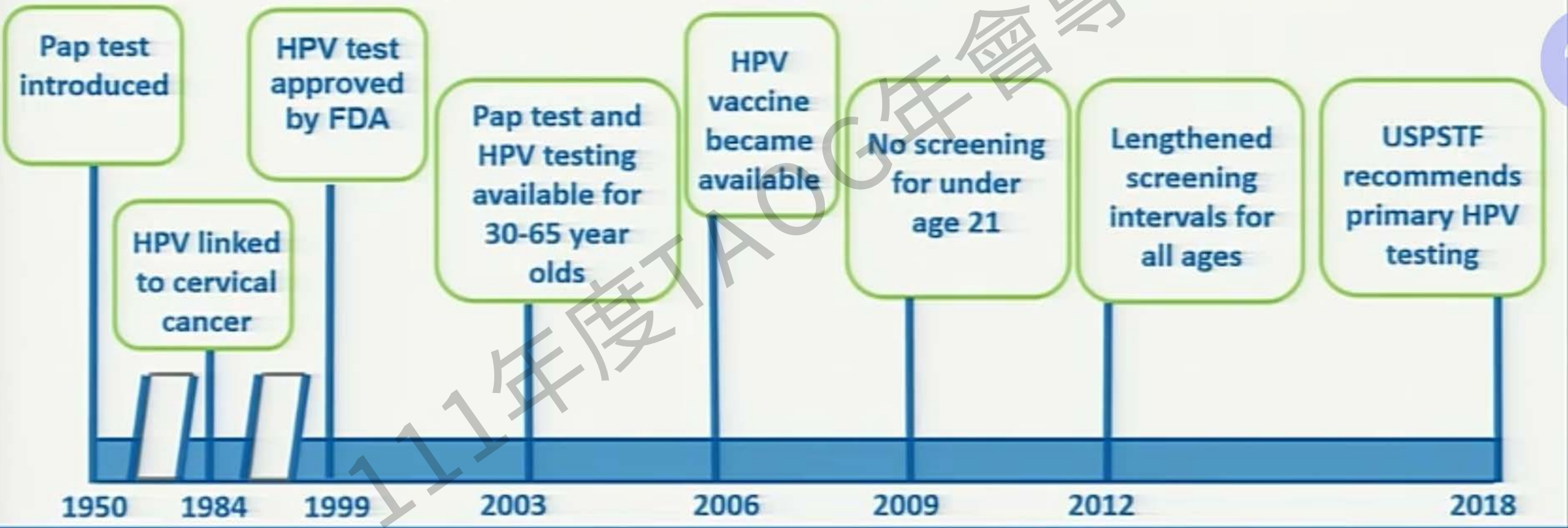
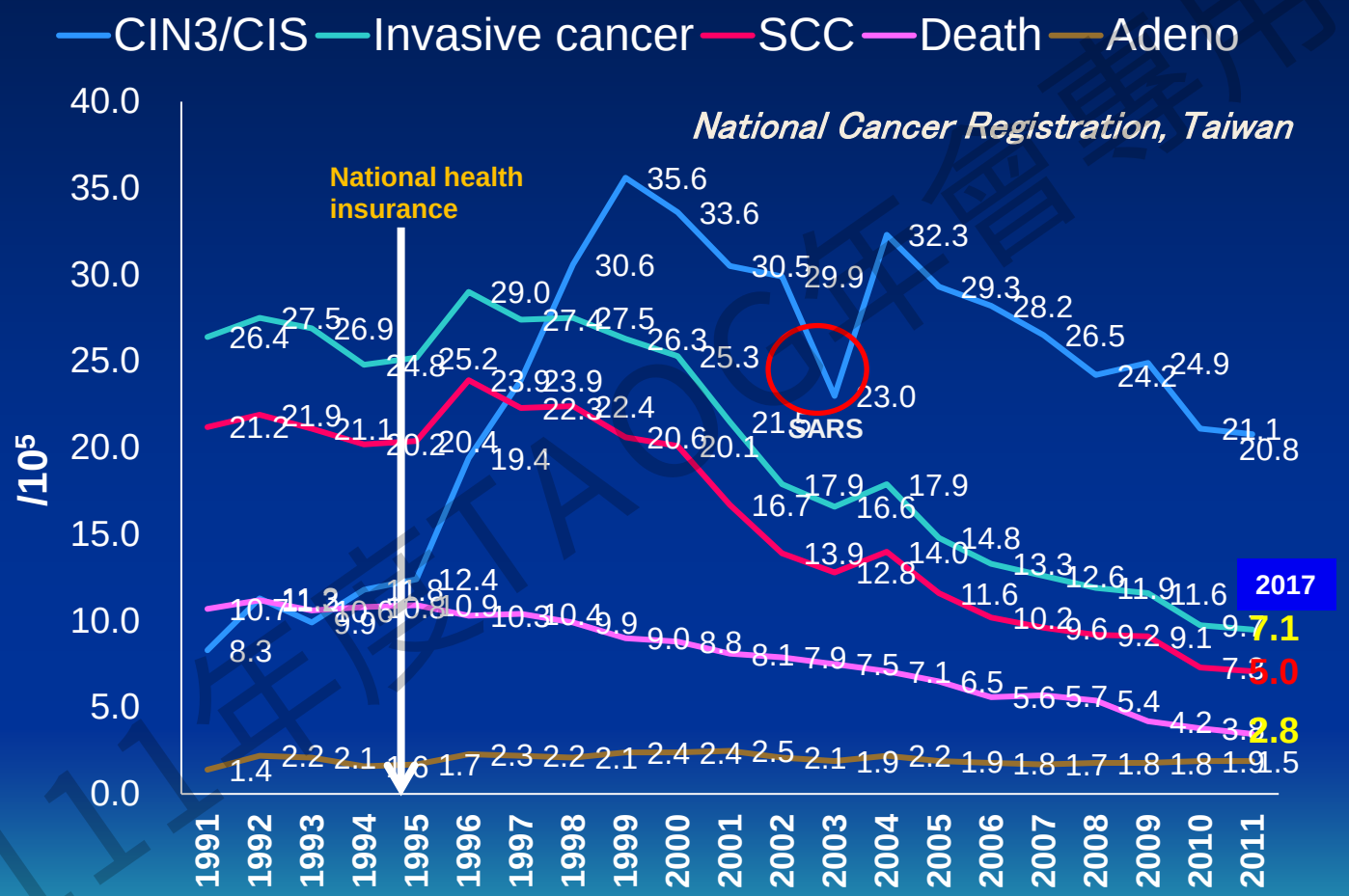
(2022-08-13 台灣婦產科醫學會)

Our Understanding and Interventions Have Progressed

Major Events for Cervical Cancer Prevention in the United States




CIN3/CIS
Invasive cancer
SCC
Death
Adeno
National Cancer Registration, Taiwan
National health insurance
SARS
/10⁵
2017
7.1
3.0
2.8
40.0
35.0
30.0
25.0
20.0
15.0
10.0
5.0
0.0
1991
1992
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2006
2007
2008
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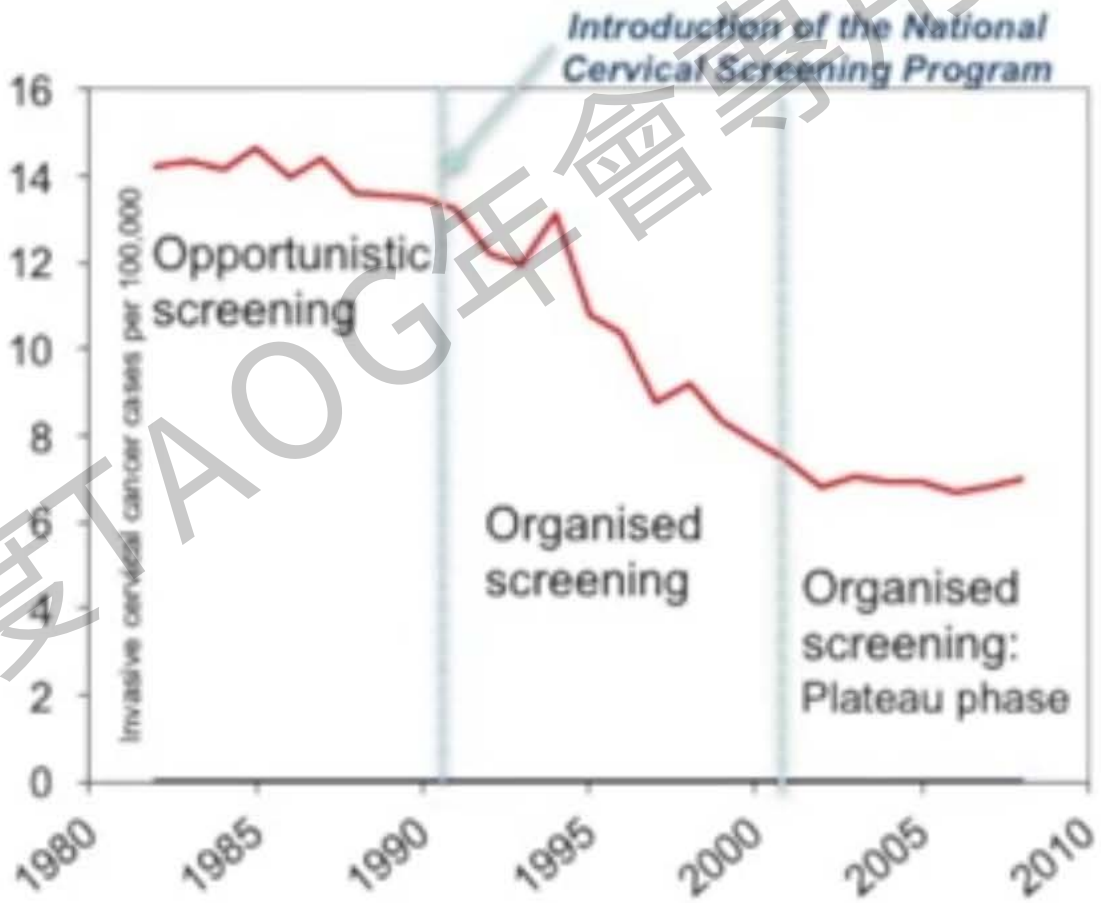
2010
2011

Australian Government
Department of Health

Cervical screening in Australia

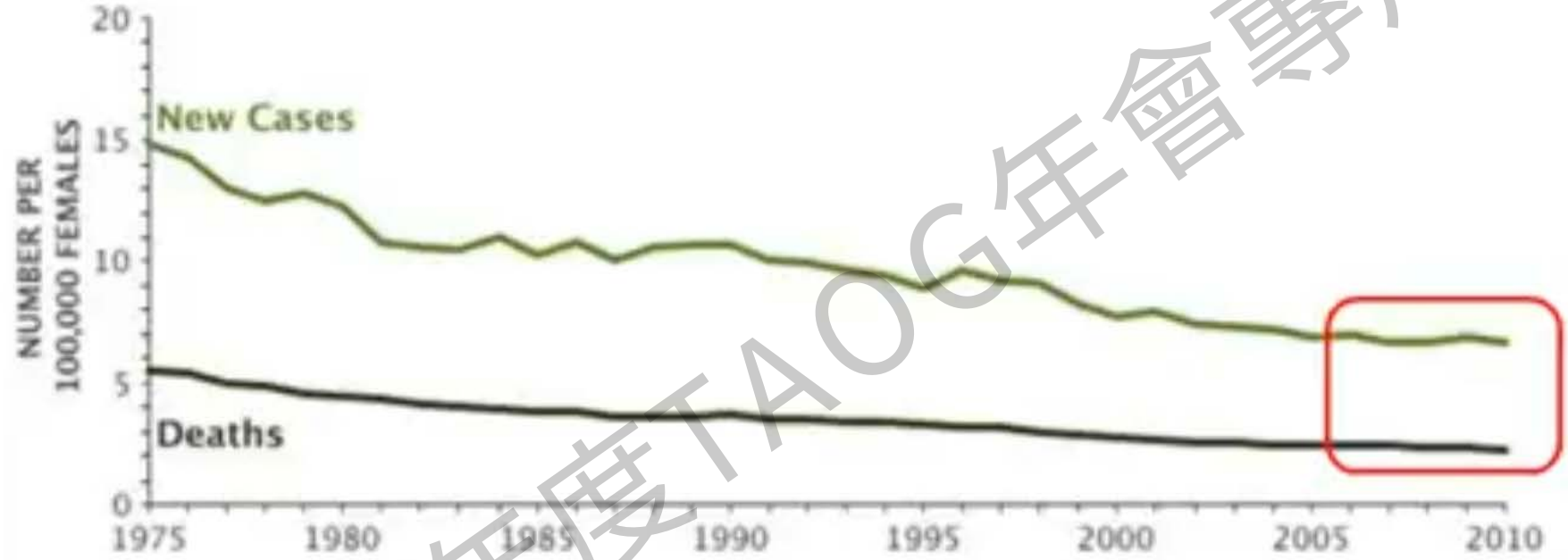
- 1991 NCSP Policy:
  - 2-yearly (Pap test)
  - 18 to 69 years[1]
  - Registry reminder
- Participation:[2]
  - 2-yearly 58%
  - 5-yearly 83%[2]
- 50% reduction in incidence & deaths



[1]NHMRC Australia, Guidelines for Cervical Screening 2005. [2]Australian Institute of Health and Welfare 2014, 2011-2012.

PAP Testing Has Reduced Cervical Cancer Incidence

But has it reached the limitations of effectiveness?

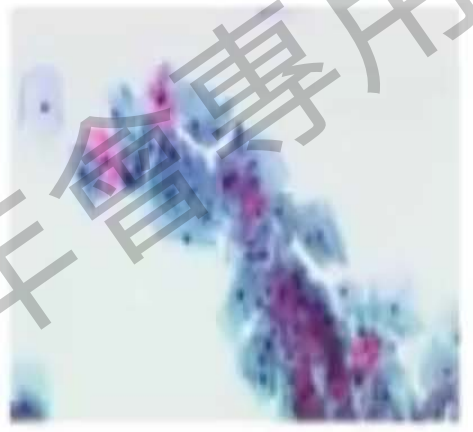


Year	1975	1980	1985	1989	1993	1997	2001	2005	2010
5-Year Survival	68.1%	67.9%	66.4%	71.0%	70.9%	71.6%	70.4%	68.0%	67.9%

http://seer.cancer.gov/statfacts/html/cervix.html SEER 9 Incidence & U.S. Mortality 1975-2010, All Races, Females. Rates are Age-Adjusted.

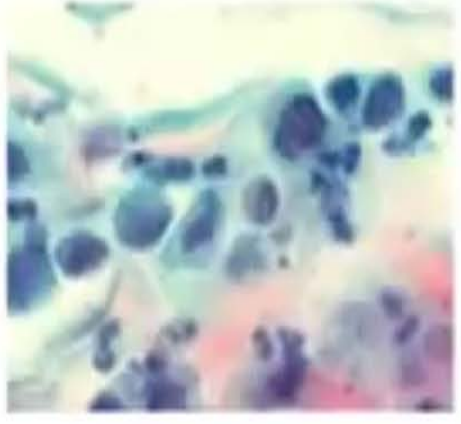
Challenges with Cytology Based Screening

Subjective – leading to intra- and inter-laboratory variability[1]



Limited sensitivity for >= CIN 2

Does not establish risk



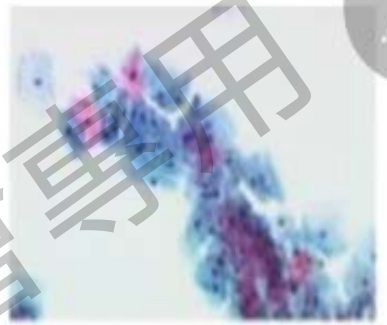
Highly complex

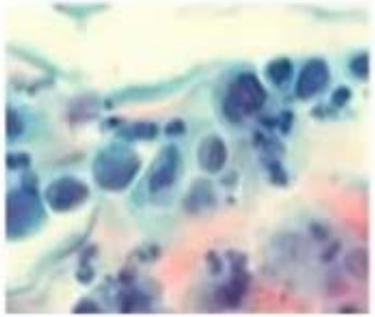
1. Castle PE, et al. Lancet Oncol 2011; 12:880–890 plus supplementary tables.
2. Wright TC et al. Int J Cancer. 2013 Oct 7. doi: 10.1002/ijc.28514. [Epub ahead of print]

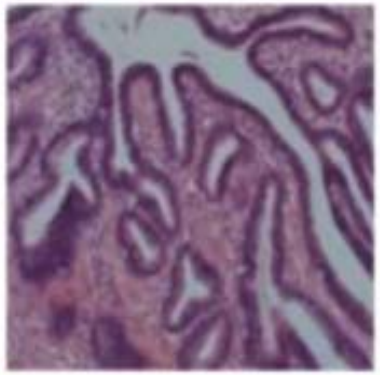
Cytology-based screening

Significant limitations exist that reduce the overall effectiveness

- Cytology has low sensitivity for detecting CIN2 or worse[1]
  - Multiple attempts have been made to improve it's sensitivity
    - Work load limits: CLIA 1988
    - Liquid-based cytology: late 1990's
    - Computer-assisted screening: late 1990's
- Cytology is less effective in detecting AIS and adenocarcinoma[2]
- Subjectivity of cytology leads to low reproducibility[3]
- Identifies individuals with cancer *precursors* but not women *at risk* of developing these



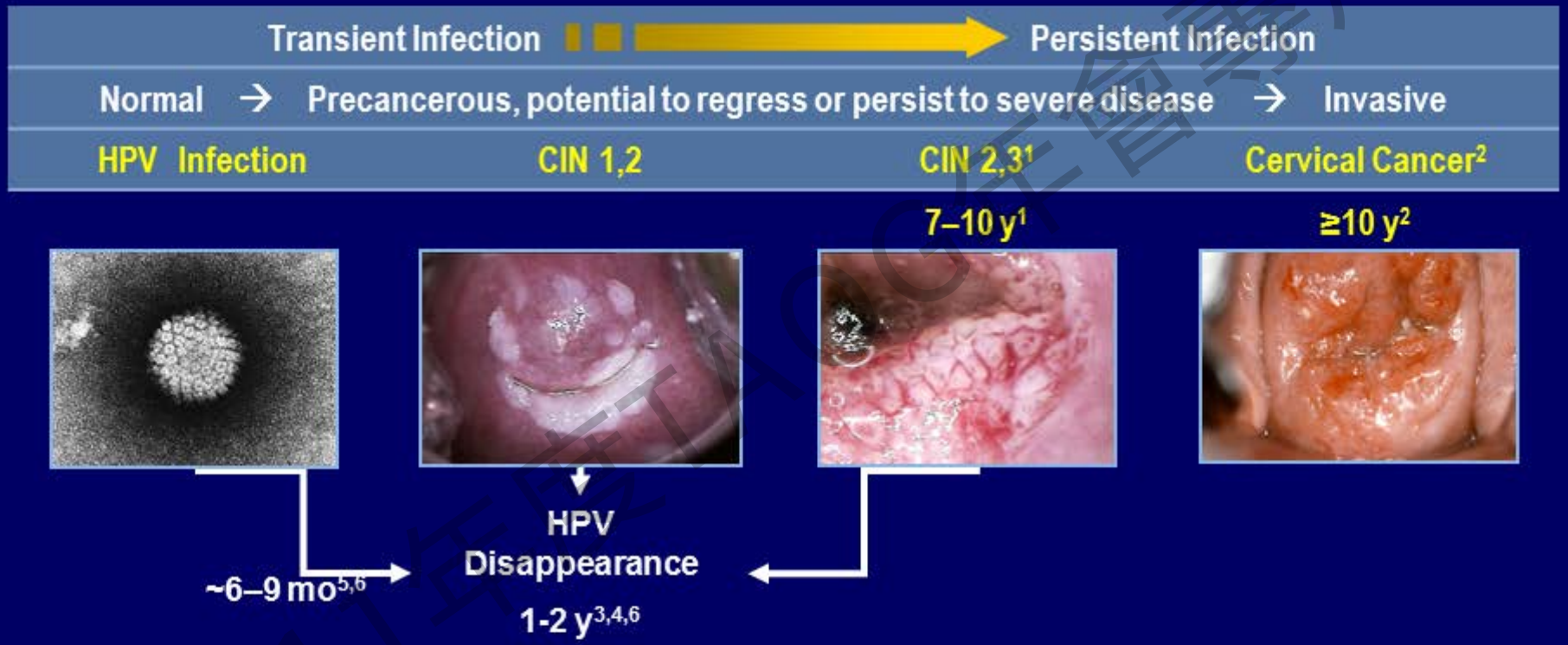




1. Castle et al. (2011). Lancet Oncol
2. Kinney et al. (2011). Gynecol Oncol
3. Stoler and Schiffman. (2001). JAMA

Evolution of an HPV infection

Most HPV infections resolve; progression to cancer takes time



The <10% of HPV infections that persist for 2 years are highly linked to precancer.[3]

The primary risk factor for cervical cancer is persistent infection with specific HR HPV strains.[4,6]

CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; HR, high risk.

1. Schiffman M, Kjaer SK. *J Int Cancer Natl Monogr.* 2003;31:14-19; 2. Ostör AG. *Int J Gynecol Pathol.* 1993;12:186-192; 3. Schiffman M et al. *Lancet.* 2007;370:890-907; 4. Bory JP et al. *Int J Cancer.* 2002;102:519-525; 5. Ho GY et al. *N Engl J Med.* 1998;338:423-428; 6. Nobbenhuis MA et al. *Lancet.* 1999;354:20-25.

Australian Government
Department of Health

Cervical Cancer: the HPV connection

Papillomaviruses

4 main groups in man:

-skin warts (HPV1,2)
-EV associated (HPV 5,8)

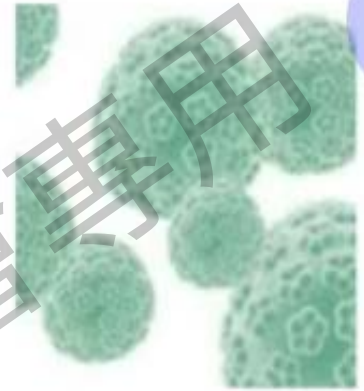
genital warts (HPV6,11)
genital cancers (HPV16,18)

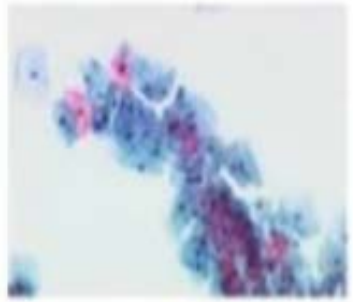
Courtesy Prof Ian Frazer

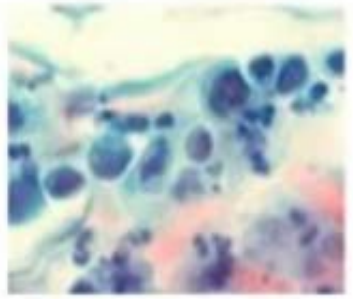
HPV DNA testing

Addresses limitations associated with cytology-based screening

- HPV DNA testing increases sensitivity of CIN2+ and CIN3+ detection compared to cytology[1,2] and leads to a reduction in incidence of cervical cancer[3]
- HPV DNA testing provides a higher negative predictive value than cytology and longer safety interval[1-7]
- HPV DNA testing is more effective in detecting AIS and adenocarcinoma[4]
- HPV DNA testing is able to predict short- and long-term risk of developing high-grade lesions and HPV16/18 genotyping is able to further stratify this risk[2,6,7]







1. Whitlock et al. (2011). Ann Intern Med.
2. Wright et al. (2015) Gynecologic Oncology
3. Ronco et al. (2013). Lancet
4. Katki et al. (2011). Lancet Oncol
5. Dillner et al. (2008). BMJ
6. Khan et al. (2005). JNCI
7. Kjaer et al. (2010). JNCI

Cervical Cancer Screening Recommendations and Guidelines Are Based on Age

Cervical Cancer Screening Recommendations and Guidelines	ACS and ACOG, 2012	USPSTF, 2018
Screening Methods for Women Based on Age		
Ages 21-29 years	Pap every 3 years	Pap every 3 years
Ages 30-65 years	1) Co-testing (HPV and Pap) every 5 years (preferred) 2) Pap alone every 3 years	1) Co-testing every 5 years 2) Pap alone every 3 years **3) HPV alone every 5 years**
Age to start	Age 21 years	Age 21 years
Screening among fully vaccinated	Same as for non-vaccinated	Same as for non-vaccinated

*All guidelines recommend that women who have been adequately screened can discontinue Pap at age 65.

ACS: American Cancer Society

USPSTF: US Preventive Services Task Force

ACOG: American College of Obstetricians and Gynecologists

Difference between recommendations of 2020 ACS, 2012 ACS and 2018 USPSTF

	2020 ACS	2012 ACS	2018 USPSTF
Age 21–24	No screening	Pap test every 3 years	Pap test every 3 years
Age 25–29	HPV test every 5 years (preferred) HPV/Pap cotest every 5 years (acceptable) Pap test every 3 years (acceptable)	Pap test every 3 years	Pap test every 3 years
Age 30–65	HPV test every 5 years (preferred) HPV/Pap cotest every 5 years (acceptable) Pap test every 3 years (acceptable)	HPV/Pap cotest every 3 years (preferred) Pap test every 3 years (acceptable)	Pap test every 3 years, HPV test every 5 years, or HPV/Pap cotest every 5 years
Age 65 and older	No screening if a series of prior tests were normal	No screening if a series of prior tests were normal	No screening if a series of prior tests were normal and not at high risk for cervical cancer

WHO CALLS FOR "A WORLD FREE OF CERVICAL CANCER" --

EACH COUNTRY SHOULD MEET THE 90-70-90 TARGETS BY 2030 TO GET ON THE PATH TO ELIMINATE CERVICAL CANCER WITHIN THE NEXT CENTURY

90%

of girls fully **vaccinated** with HPV vaccine by 15 years of age

70%

of women HPV **screened** at 35 and 45 years of age and all managed appropriately

90%

of women identified with cervical disease receive **treatment** for precancerous lesions or invasive cancer

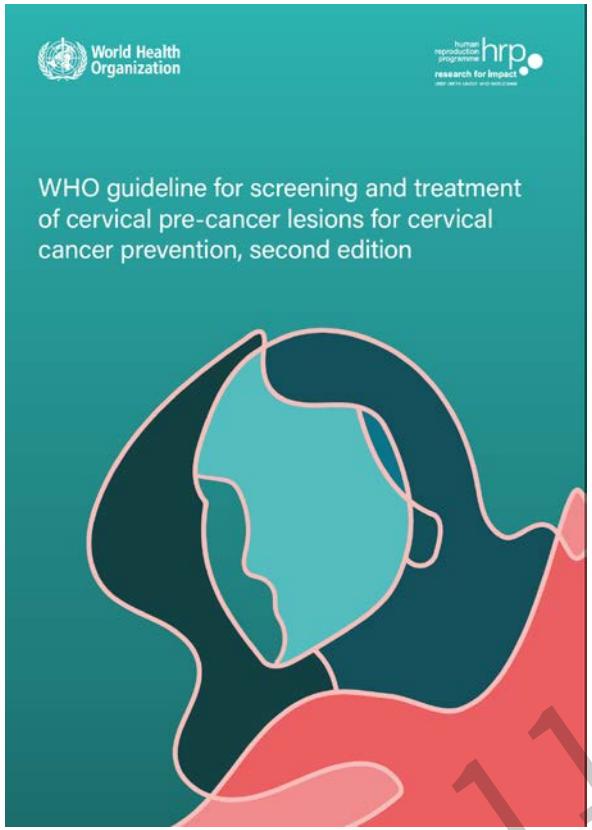
Every country must introduce and scale-up HPV screening for women between 30 and 49 years old, and ensure appropriate treatment and follow-up.

– Dr Tedros Adhanom Ghebreyesus, WHO Director-General, 24 September 2018

https://www.who.int/initiatives/cervical-cancer-elimination-initiative
http://www.who.int/dg/speeches/2018/UNGA-cervical-cancer/en/ ; IPV 2018 (R. Herrero, IARC)

2021 WHO GUIDELINE RECOMMENDATION

HPV DNA TEST SCREENING IS RECOMMENDED



For the general population of women	For women living with HIV
Screen and Treat **OR** Screen, Triage and Treat	Screen, Triage and Treat - **ONLY**
• HPV DNA as primary screening test • Starting at age 30 • Every 5 to 10 years screening interval	• HPV DNA as primary screening test • Starting at age 25 • Every 3 to 5 years screening interval

https://www.who.int/news/item/06-07-2021-new-recommendations-for-screening-and-treatment-to-prevent-cervical-cancer

Primary HPV Screening

SGO and ASCCP guidance recommendations

Representatives from professional societies convened to provide interim guidance:

- Primary HPV screening is an alternative to current cervical cancer screening methods due to equivalent or superior effectiveness
- A negative hrHPV test provides greater reassurance of low CIN3+ risk than a negative cytology result
- Women 25 and older
  - About 1/3 of all CIN3+ cases found in ATHENA were in women 25-29
  - More than half of CIN3+ cases in women 25-29 were negative by cytology
- Only FDA-approved assay with specific primary HPV screening indication
  - Performance characteristics vary between HPV tests so assumptions around test comparability should not be made
  - At this time, only the cobas® HPV Test is FDA-approved for this indication

Huh et al. (2015). Gynecologic Oncology
Huh et al. (2015). Obstet Gynecol

Primary HPV Screening: Recommendations and Benefits:

1. A negative hrHPV test provides greater reassurance of low CIN3+ risk than a negative pap (cytology) result.
2. Because of equivalent or superior effectiveness, primary hrHPV screening can be considered as an alternative to cytology based cervical cancer screening.
3. More reproducible than Pap cytology.
4. Negative test (and most women will test negative) associated with very low risk of developing precancer / invasive cancer (also, a much better predictor).
5. More sensitive than cytology (lower FN rates): pick up most women with precancers.

Collecting a ThinPrep Sample

Broom-Like Device Protocol

3 to 5 rotations of broom

Cap vial

Crush 10 times on base of vial and swirl

Record patient details

HOLOGIC

BD SurePath™ Sample Collection Method for Rover's® Cervex-Brush® With Detachable Head

1. Collect

1. Insert into endocervical canal. Rotate broom **five times** in a clockwise direction.

2. Drop

2. Drop detachable head of device into BD SurePath™ vial.

3. Send

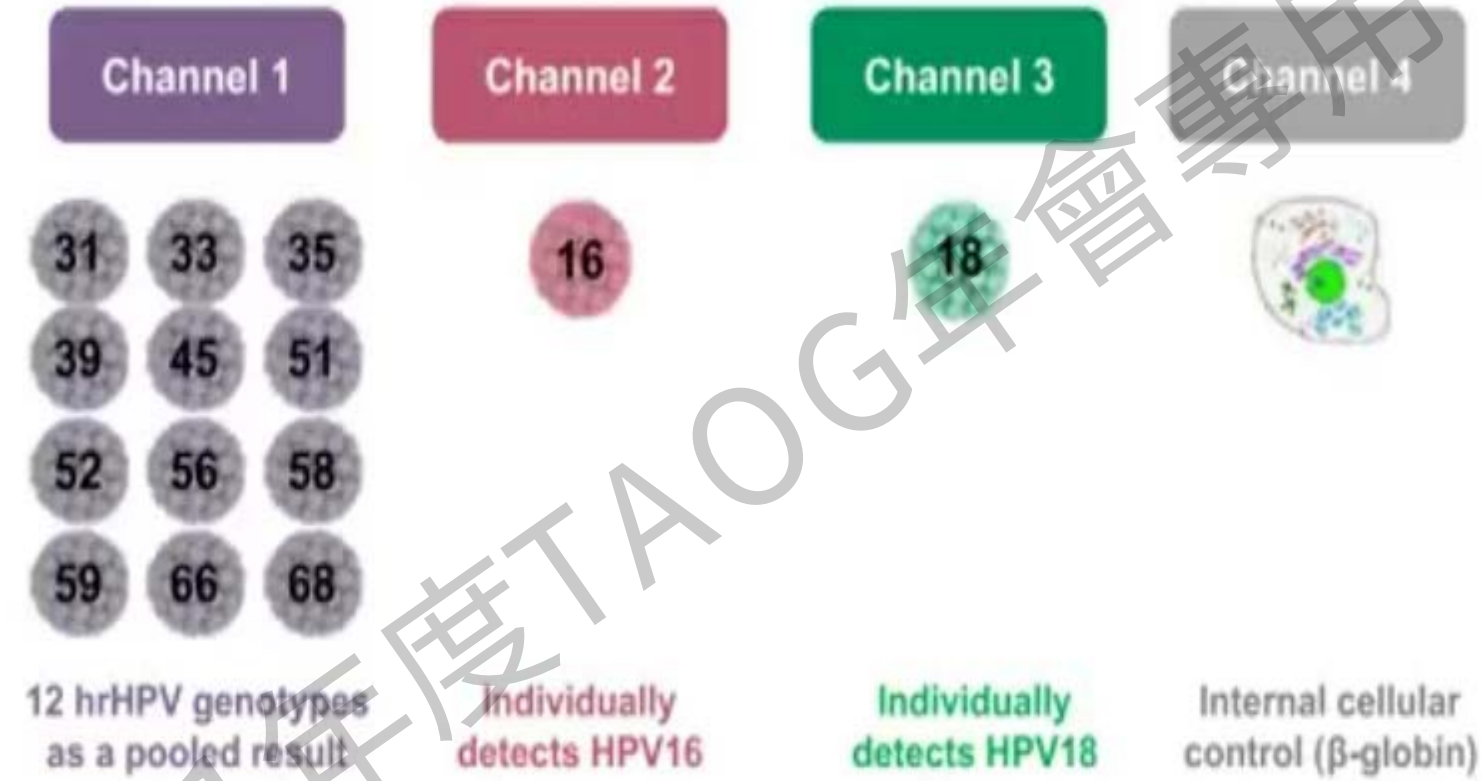
3. Place cap on vial and tighten. Send BD SurePath™ vial to lab for processing.

BD

Helping all people live healthy lives

cobas® HPV Test

Integrated genotyping assay design



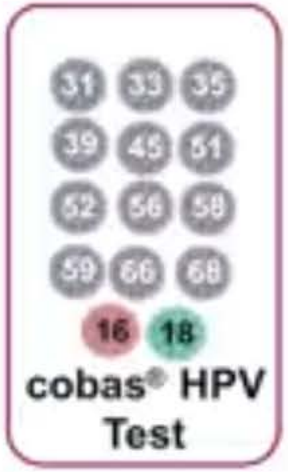
4 channel design allows reporting of pooled hrHPV result and simultaneous HPV16/18 specific genotyping from a single test tube

Roche

Wright TC Jr, et al. *Am J Obstet Gynecol* 2012; 206:46.e1-.e11

HPV Primary Screening Algorithm: women ≥25 years

FDA-approved 2014, SGO/ASCCP[1] & ACOG[2] supported



cobas® HPV Test with HPV 16/18 genotyping and reflex cytology

[1]Huh et al., *Gynecol Oncol* 2014 124:670
[2]ACOG Practice Bulletin No.157, 2016

HPV Primary Screening Algorithm: women ≥25 years

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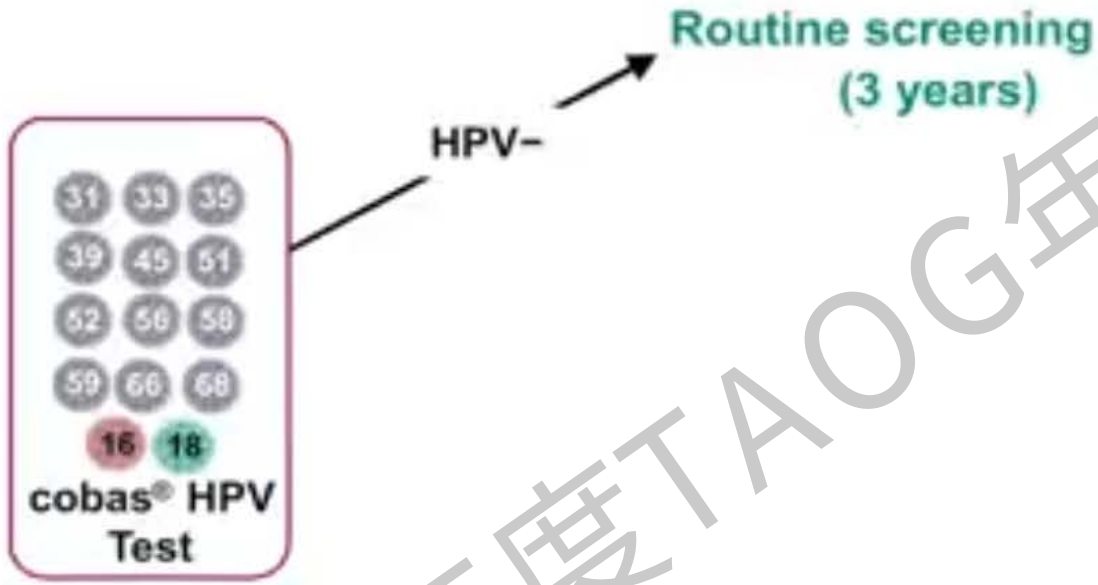

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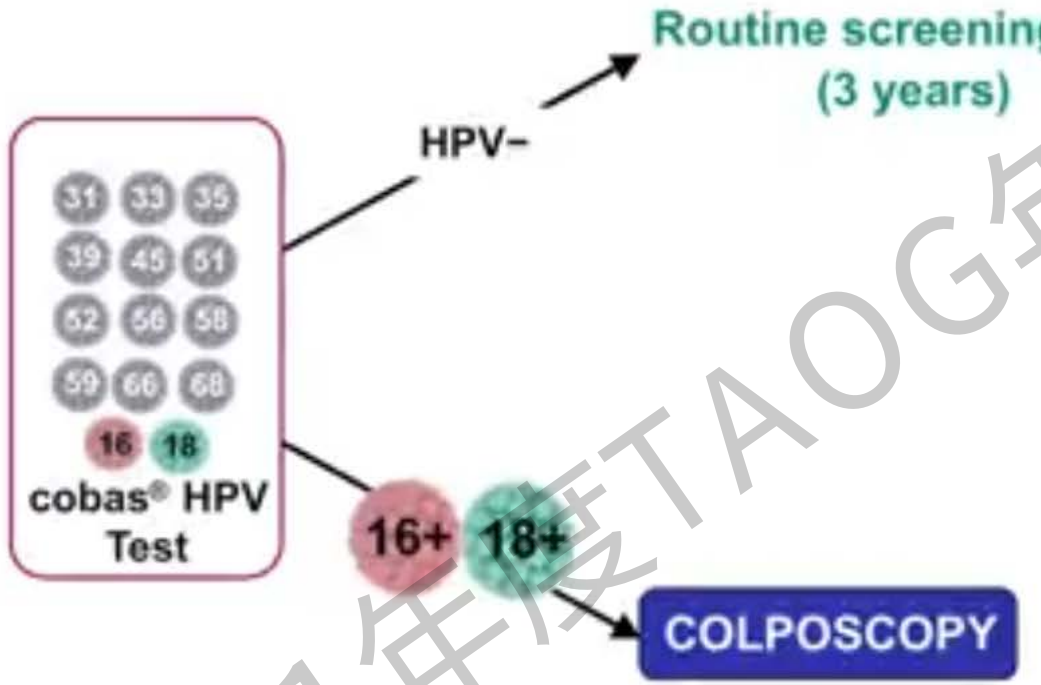

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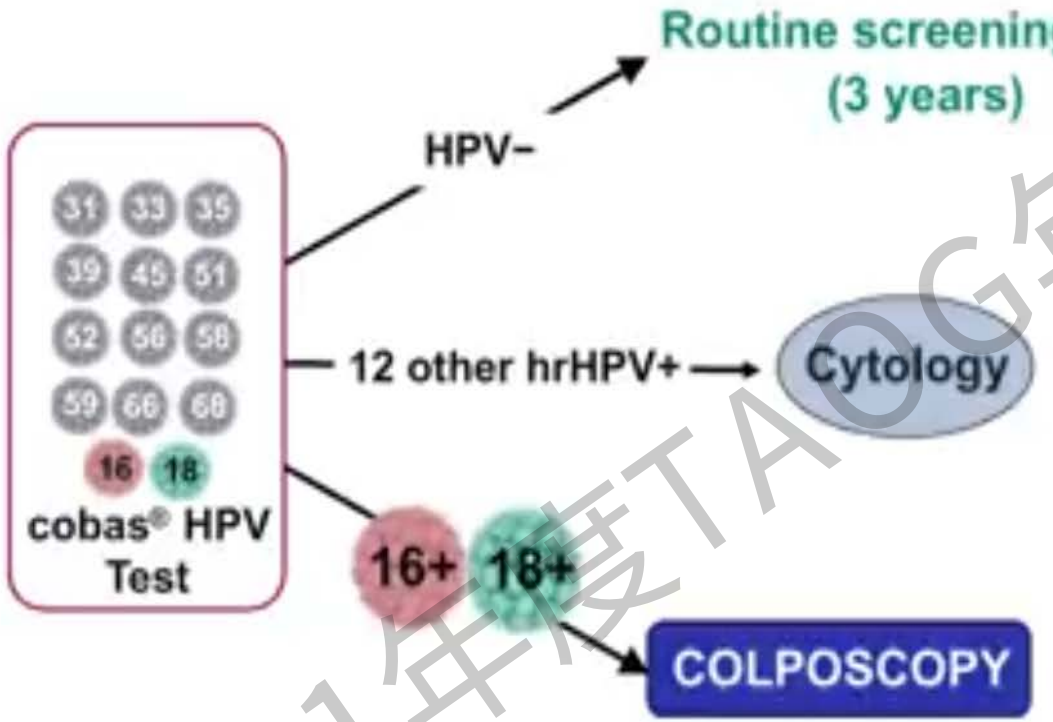

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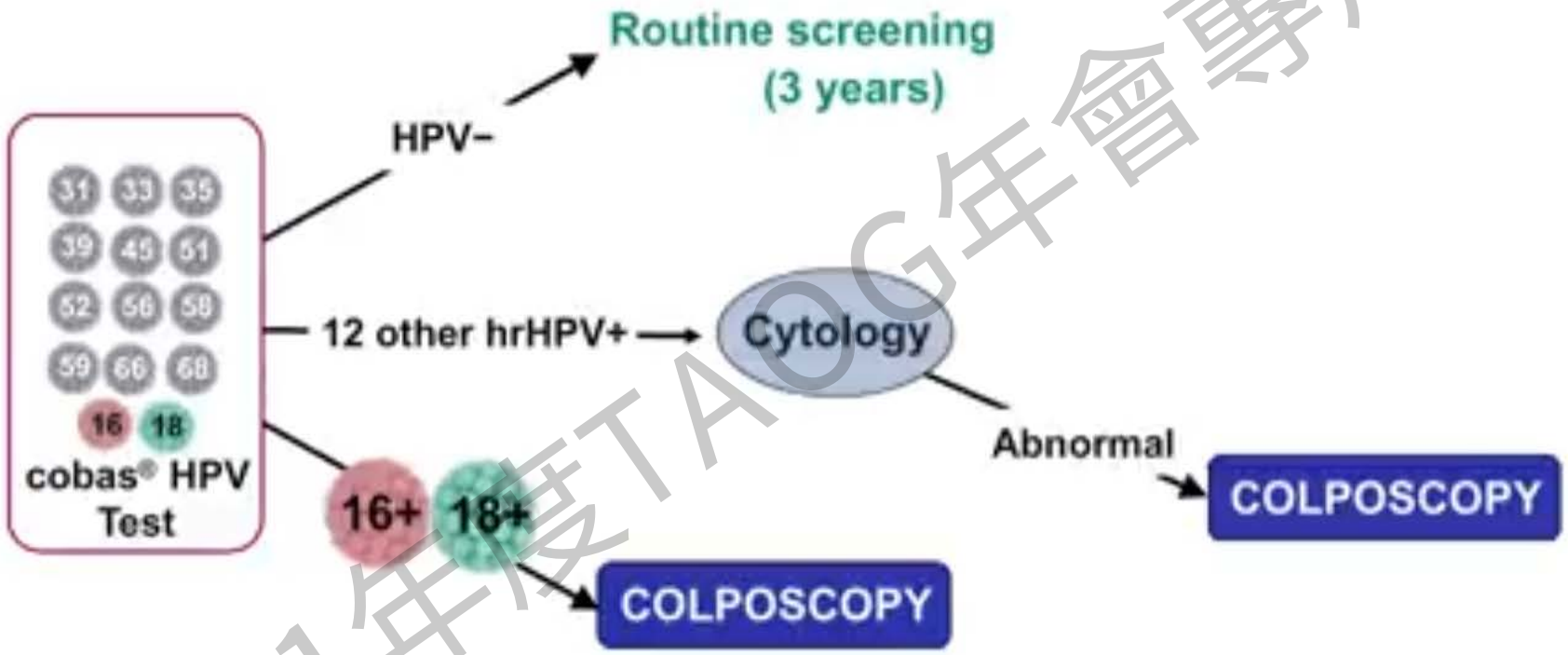

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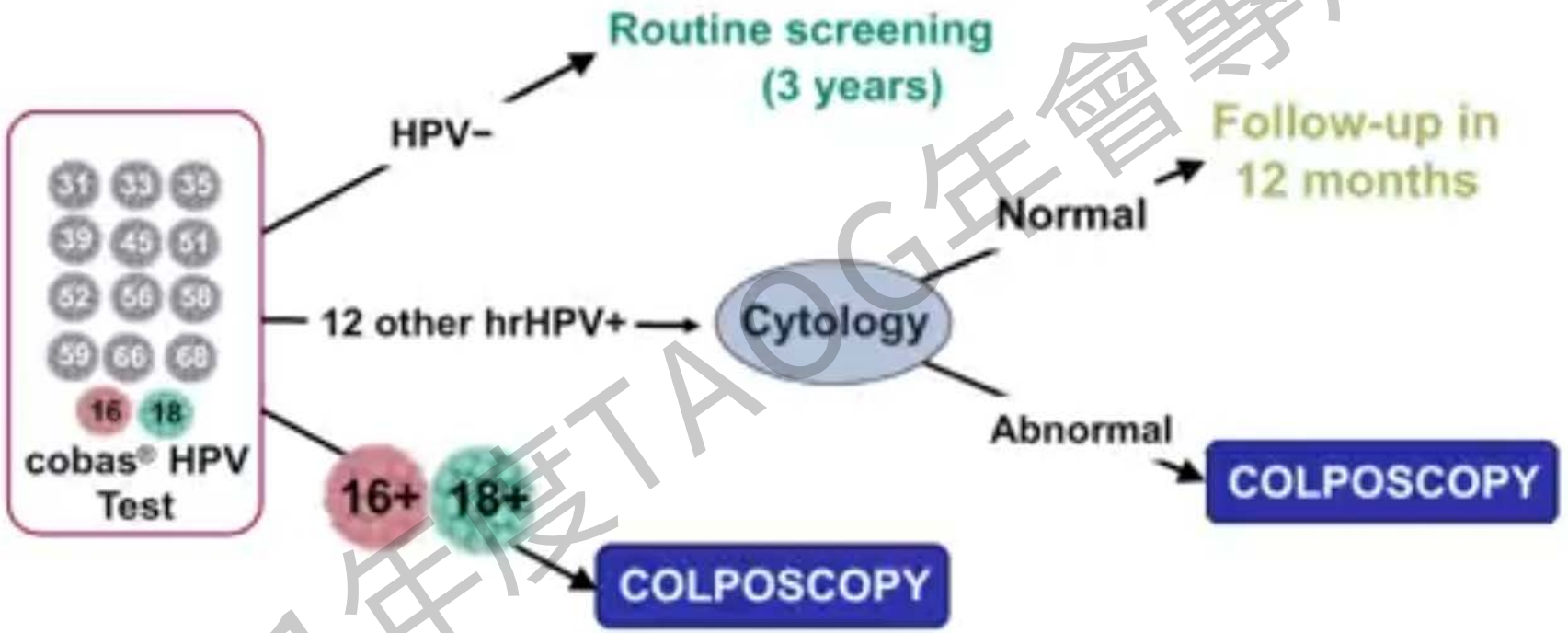

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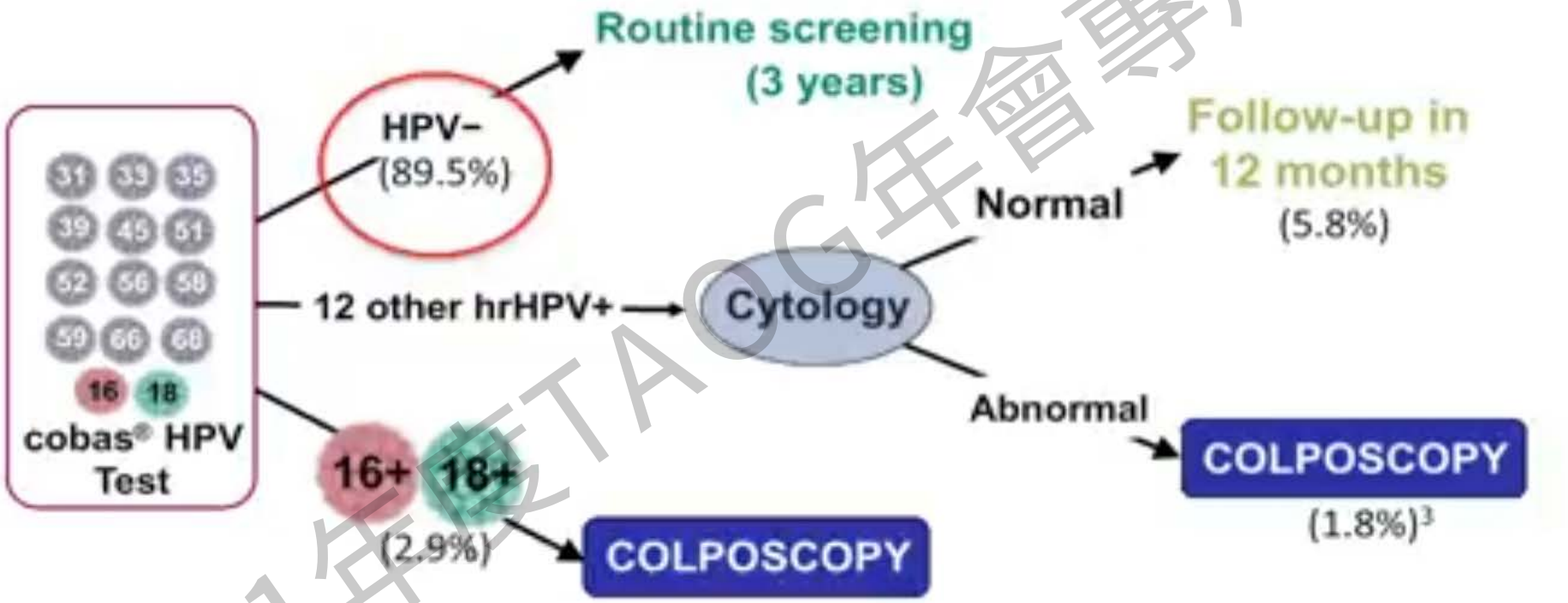

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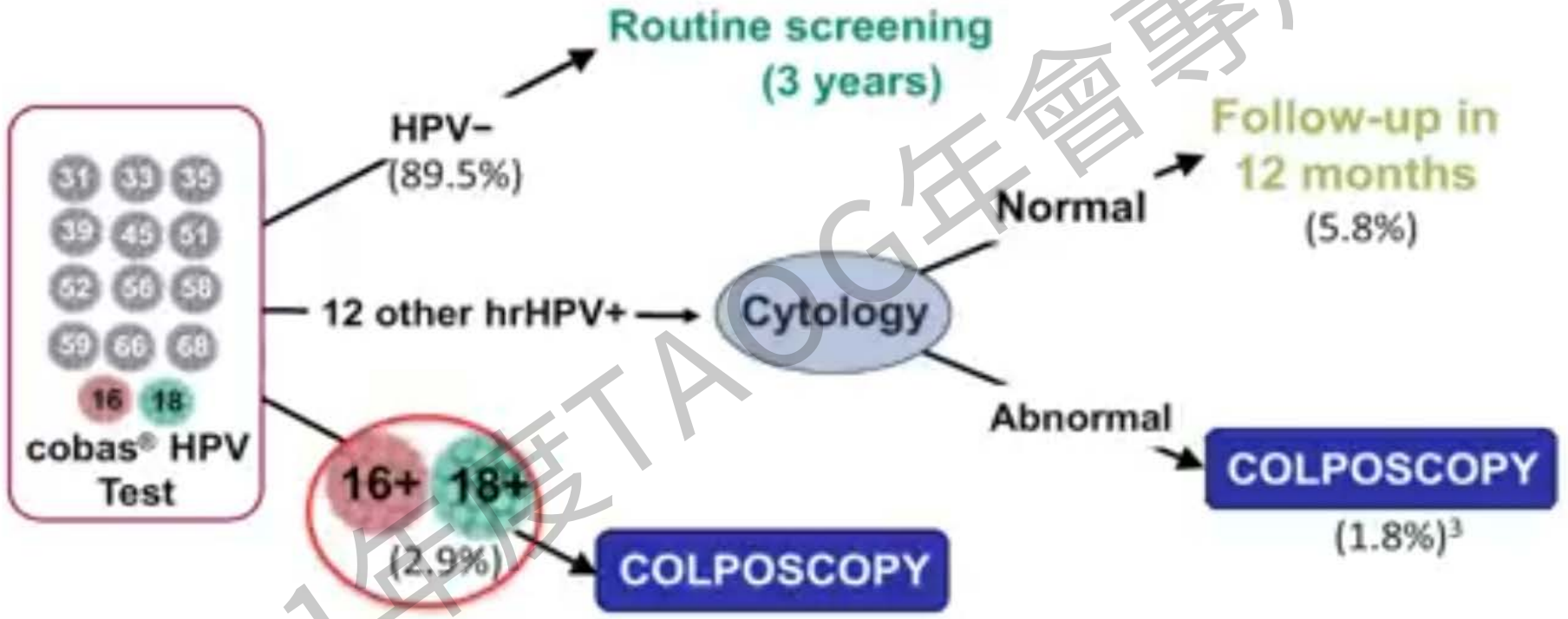

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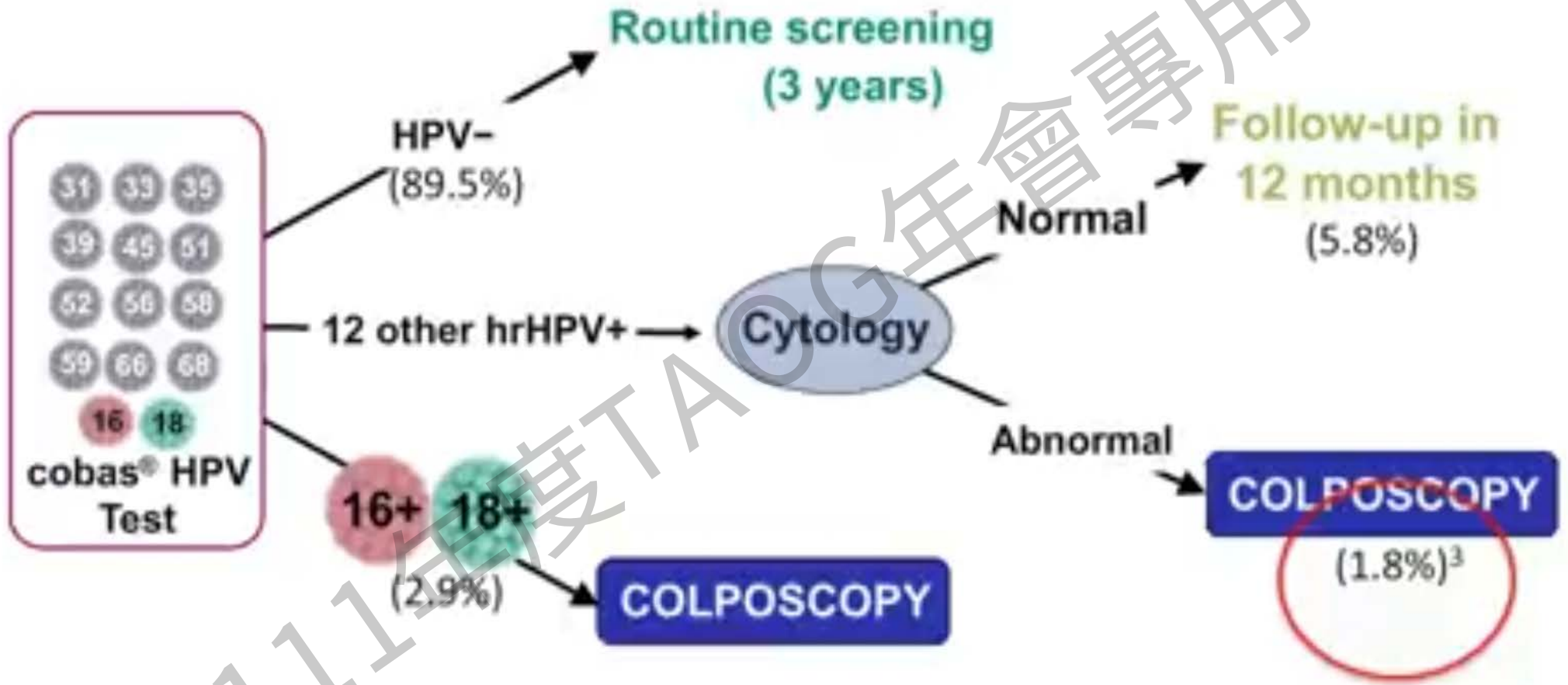


cobas® HPV Test with HPV 16/18 genotyping and reflex cytology

[1]Huh et al., *Gynecol Oncol* 2014 124:670

Reproducibility of Cervical Cytology

Re-read of 4948 Liquid-based Cytology Slides

Original Diagnosis	QC Reviewer's Diagnosis: NILM	ASC-US	LSIL	≥HSIL
NILM	78%	19%	3%	<1%
ASC-US	39%	43%	17%	2%
LSIL	4%	22%	68%	6%
≥HSIL	3%	23%	27%	47%

Roche

Stoler and Schiffman *JAMA*, 2001.

Variability of Cervical Cytology

ATHENA Results

	Lab A	Lab B	Lab C	Lab D
Number	12,294	4218	16,979	12,442
Median Age	40.9	37.9	39.3	40.1
≥ASC-US	3.8%	5.2%	8.1%	9.9%
Sensitivity of Cytology*	42.0	51.0	60.5	73.0
Sensitivity of cobas®*	90.1	88.2	88.4	88.9

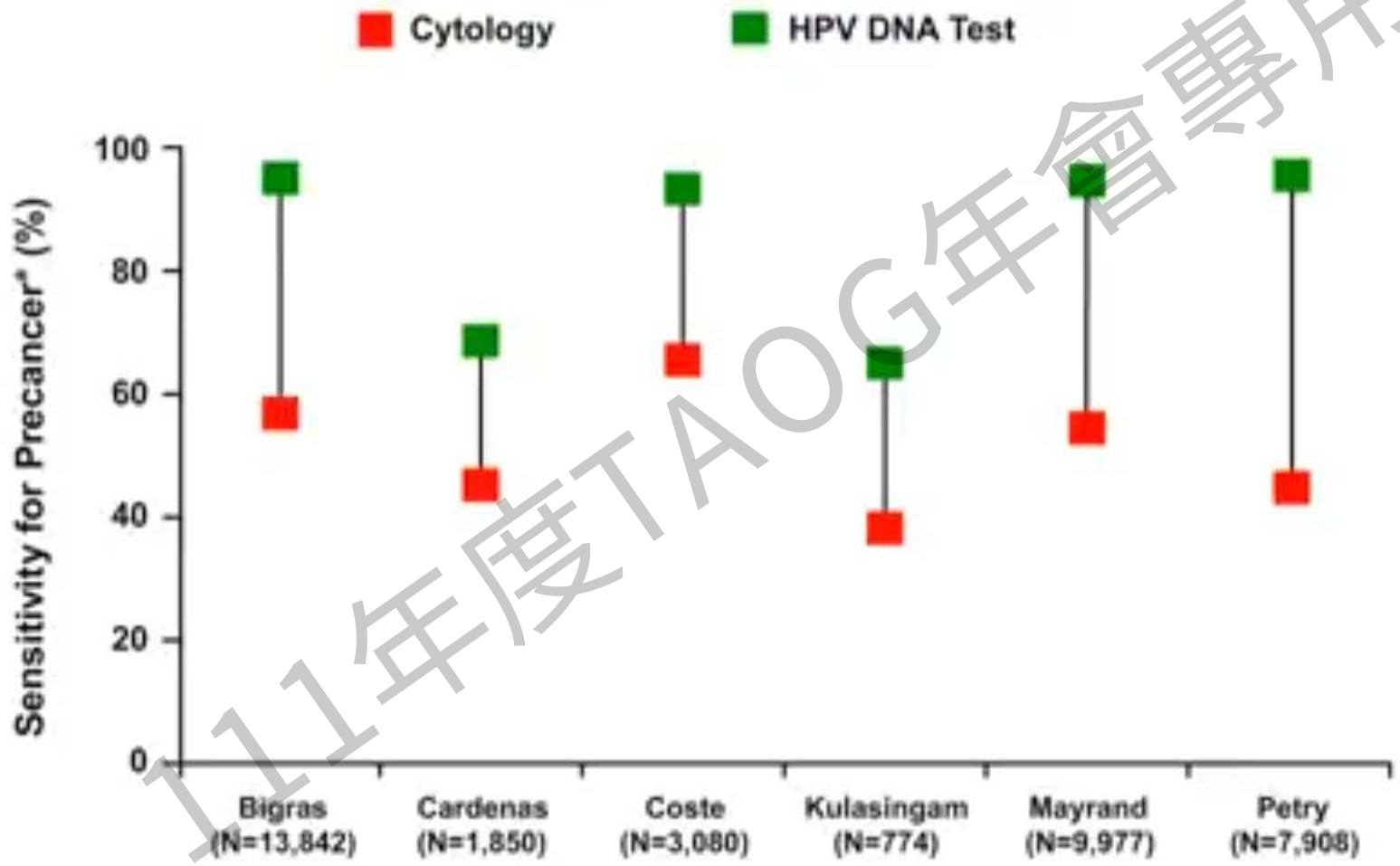
Roche

*Note: for ≥CIN2

Wright et al. *Int. J. Cancer*, 2013. Oct 7 epub

HPV Consistently Has a Higher Clinical Sensitivity than Cytology

Can HPV be an effective tool for screening?



*CIN2+

Whitlock EP, *et al. Ann Intern Med.* 2011;155:687

Studies performed in developed countries in women 30 years and older.

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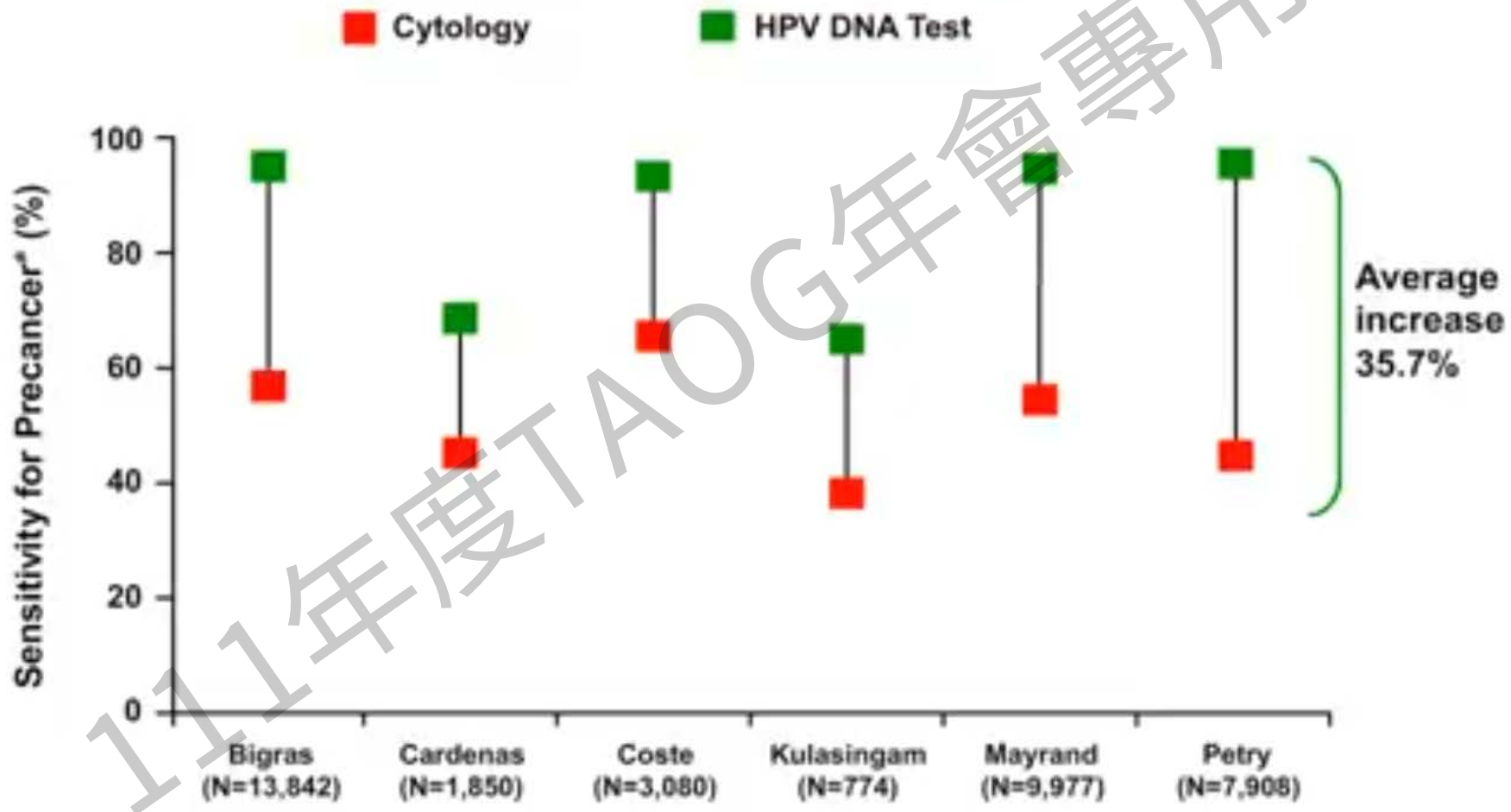


*CIN2+

Whitlock EP, *et al. Ann Intern Med.* 2011;155:687

Studies performed in developed countries in women 30 years and older.

HPV test is more sensitive and detects more high grade precursor lesions compared to pap smear

Evidence from cross-sectional studies

	Year	No.	End point	Pap	HPV
Petry[1]	2003	8,466	CIN2+	44%	98%
Ronco[2]	2006	16,706	CIN2+	74%	97%
Bigras[3]	2005	13,842	CIN2+	59%	97%
Mayrand[4]	2007	10,154	CIN2+	58%	83%
Ikenberg[5]	2013	19,205	CIN2+	66%	93%
ATHENA[6]	2014	40,901	CIN3+	43%	92%
Onclarity trial[7]	2017	33,858	CIN3+	59%	93%

1. Br J Cancer . 2003 May 19;88(10):1570-7. doi: 10.1038/sj.bjc.6600918.
2. J Natl Cancer Inst . 2006 Jun 7;98(11):765-74. doi: 10.1093/jnci/djj209.
3. British Journal of Cancer volume 93, pages575–581 (2005)
4. N Engl J Med . 2007 Oct 18;357(16):1579-88. (https://www.nejm.org/doi/full/10.1056/NEJMoa071430)
5. J Natl Cancer Inst . 2013 Oct 16;105(20):1550-7. doi: 10.1093/jnci/djt235.
6. Wright, T. C., et al. Gynecol Oncol 2015; 136(2):189-197
7. Gynecol Oncol 2018 Jun;149(3):498-505. doi: 10.1016/j.ygyno.2018.04.007

CCCaST Study: First Screening Round Results*

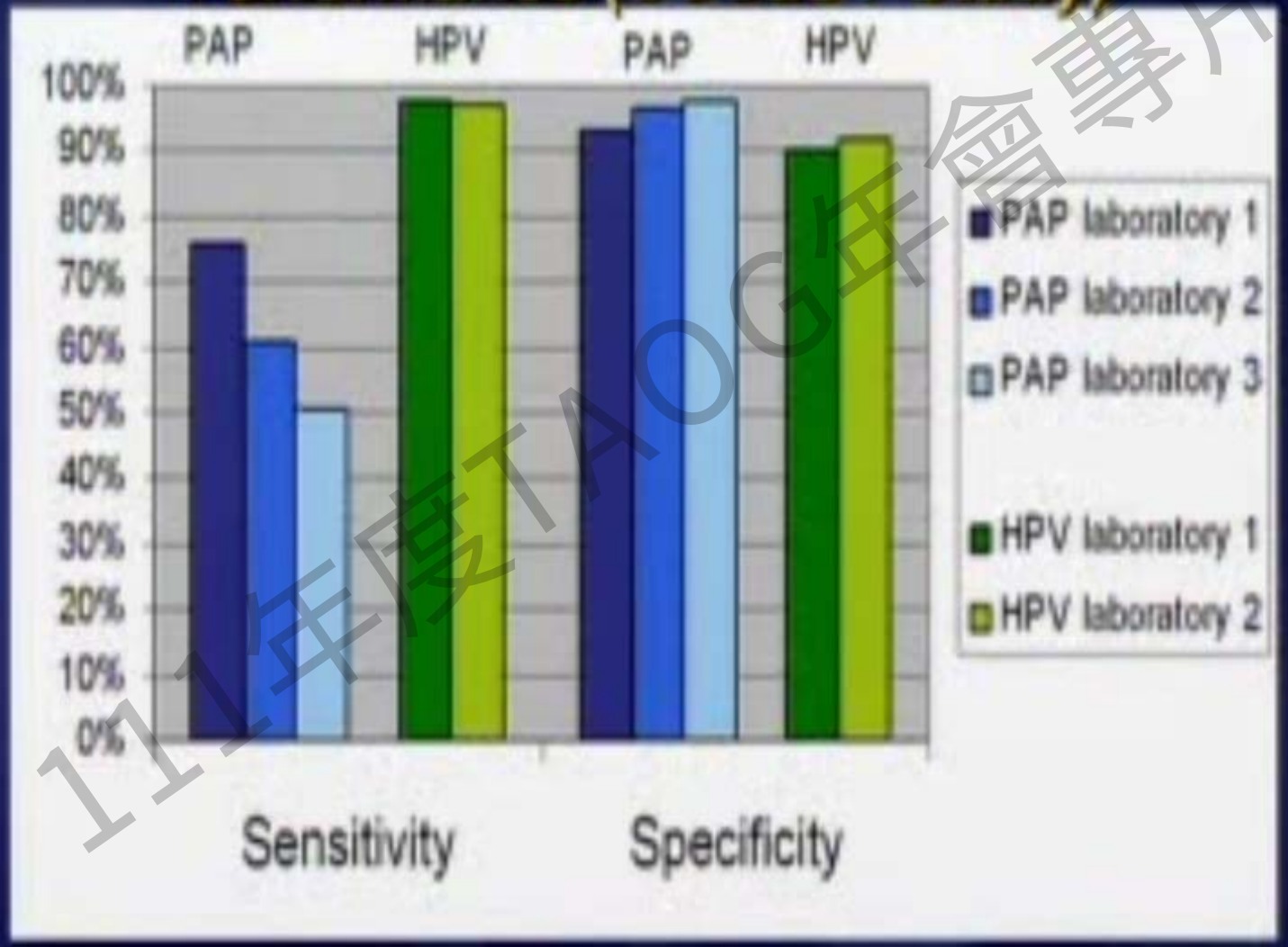
Indices	Screening test	Estimate (95%CI)
Sensitivity	Pap	55.4 (33.6-77.2)
	HPV	94.6 (84.2-100)
Specificity	Pap	96.8 (96.3-97.3)
	HPV	94.1 (93.4-94.8)
PPV	Pap	7.1 (4.8-10.3)
	HPV	6.4 (5.0-8.0)
NPV	Pap	99.8 (99.7-99.9)
	HPV	100 (98.6-100)

CCCaST: Canadian Cervical Cancer Screening Trial

* 10,171 women in Montreal and St. John's, aged 30-69 years, randomized to Pap or HPV as primary screening method; detection of CIN2+; estimates corrected for verification bias

(Mayrand et al., NEJM 2007 357: 1,579-88)

Influence of Laboratory Performing the Test on Pap and HPV Testing Performance (CCCaST Study)



Comparison of Strategies in Women Age ≥ 25 Years

Traditional Performance Metrics for CIN3+

Strategy	Relative Sensitivity	Relative Specificity	Positive Predictive Value (%)	Negative Predictive Value (%)
Cytology (ASC-US triage)	1.00	1.00	11.58	99.41
Hybrid Cotesting strategy[1]	1.28*	0.99	11.04	99.52*
HPV primary	1.40*^	0.99	12.25*^	99.58*^

HPV Primary Screening with 16/18 GTing increases the sensitivity of screening by 40% over cytology and raises the specificity to be approximately equal to cytology

* Significantly higher than ASC-US triage
^Significantly higher than the Hybrid

Wright TC et al, *Gyneco/ Oncol* 2015;146:391

Projected Measures of Clinical Management for Disease (≥CIN3)

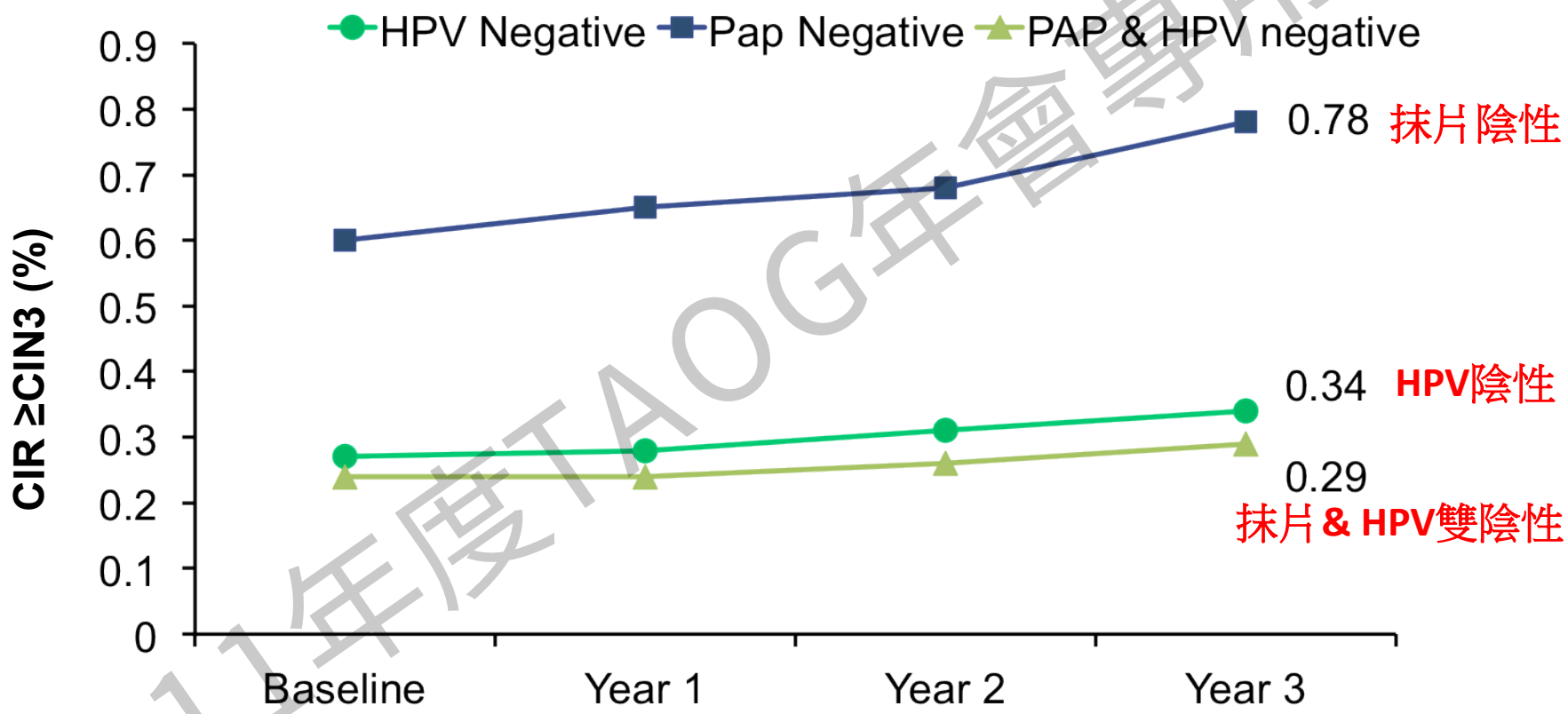
Primary HPV screening 或 co-testing 較 Cytology 能找出更多 HSIL，但須要做陰道鏡檢查的次數僅微幅增加

Algorithm	Screening Tests	≥CIN3 Cases	No. missed cases	Colpos	Colpos per ≥CIN3
Cytology alone	45,166	179 0.3 %	168 0.3%	1,934	10.8
HPV Primary Screening	52,651	294 0.5 %	53 0.1%	3,769	12.8
Co-Testing*	82,994	240 0.3 %	107 0.1%	3,097	12.9

*Co-testing for women 30+, Cytology with ASC-US triage for women 25-29
Co-testing is not supported by US Guidelines for women <30 years

Presented to FDA panel, 124
Wright TC Jr, Stoler MH, Behrens CM, Sharma A, Zhang G, Wright TL. *Gynecol Oncol*. 136 (2015) 189-197.

Athena trial
抹片, HPV 或 co-testing單次檢測為陰性，三年內發生CIN3以上的機率



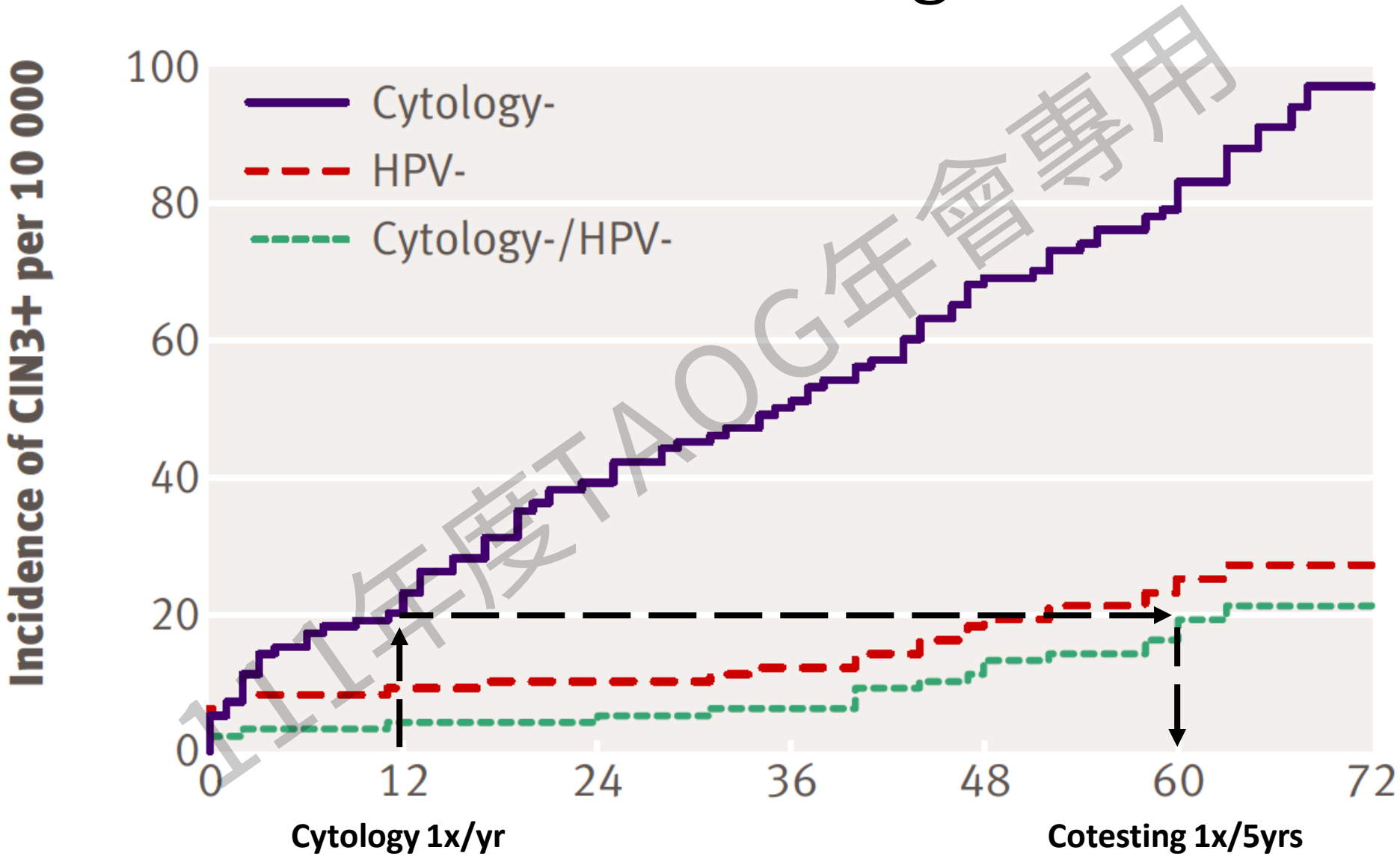
The lower risk of disease of a negative hrHPV at Baseline confirms the safety of a negative hrHPV result over 3 years

應選擇具有臨床數據佐證，三年後罹癌率低的HPV檢測

Presented to FDA panel, 12 March 2014

Wright TC, et al, Gynecol Oncol (2014), http://dx.doi.org/10.1016/j.ygyno.2014.11.076

Rationale For Screening Interval



BMJ 2008;377:a1754

Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials

*Guglielmo Ronco, Joakim Dillner, K Miriam Elfström, Sara Tunesi, Peter J F Snijders, Marc Arbyn, Henry Kitchener, Nereo Segnan, Clare Gilham, Paolo Giorgi-Rossi, Johannes Berkhof, Julian Peto, Chris J L M Meijer, and the International HPV screening working group**

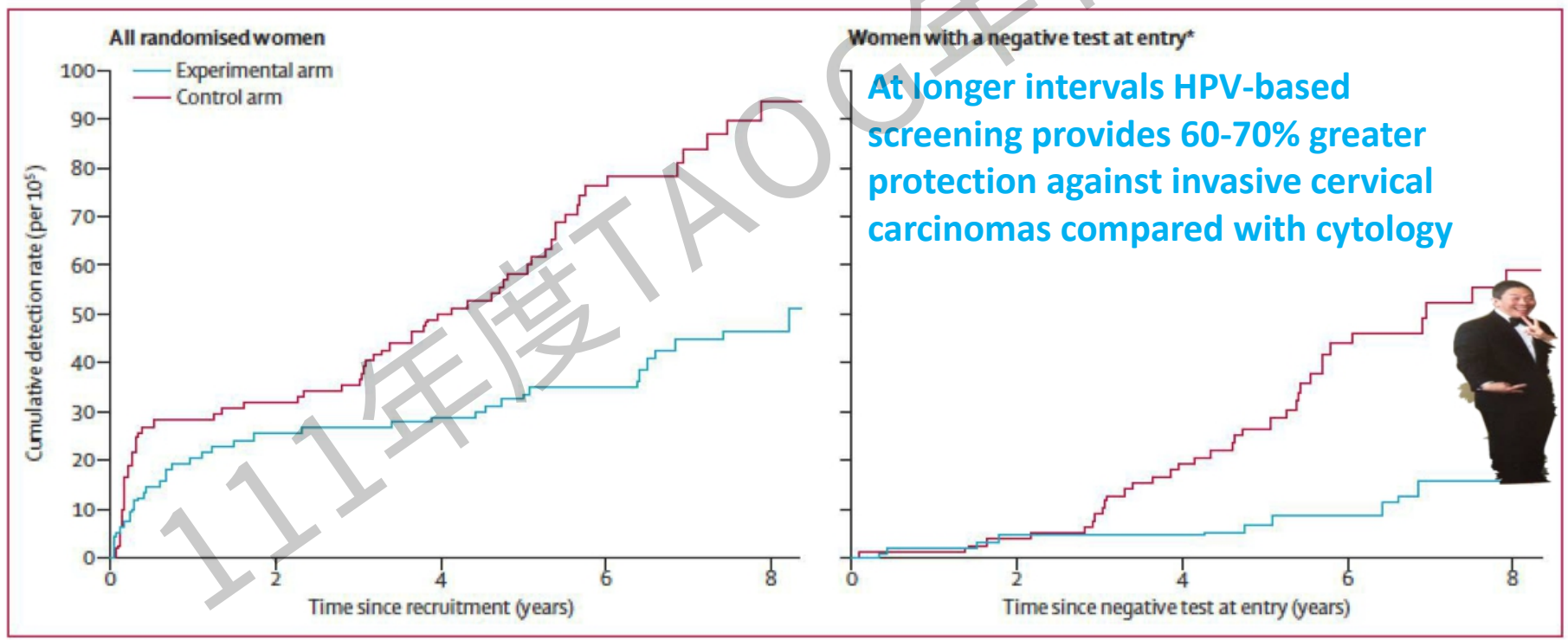
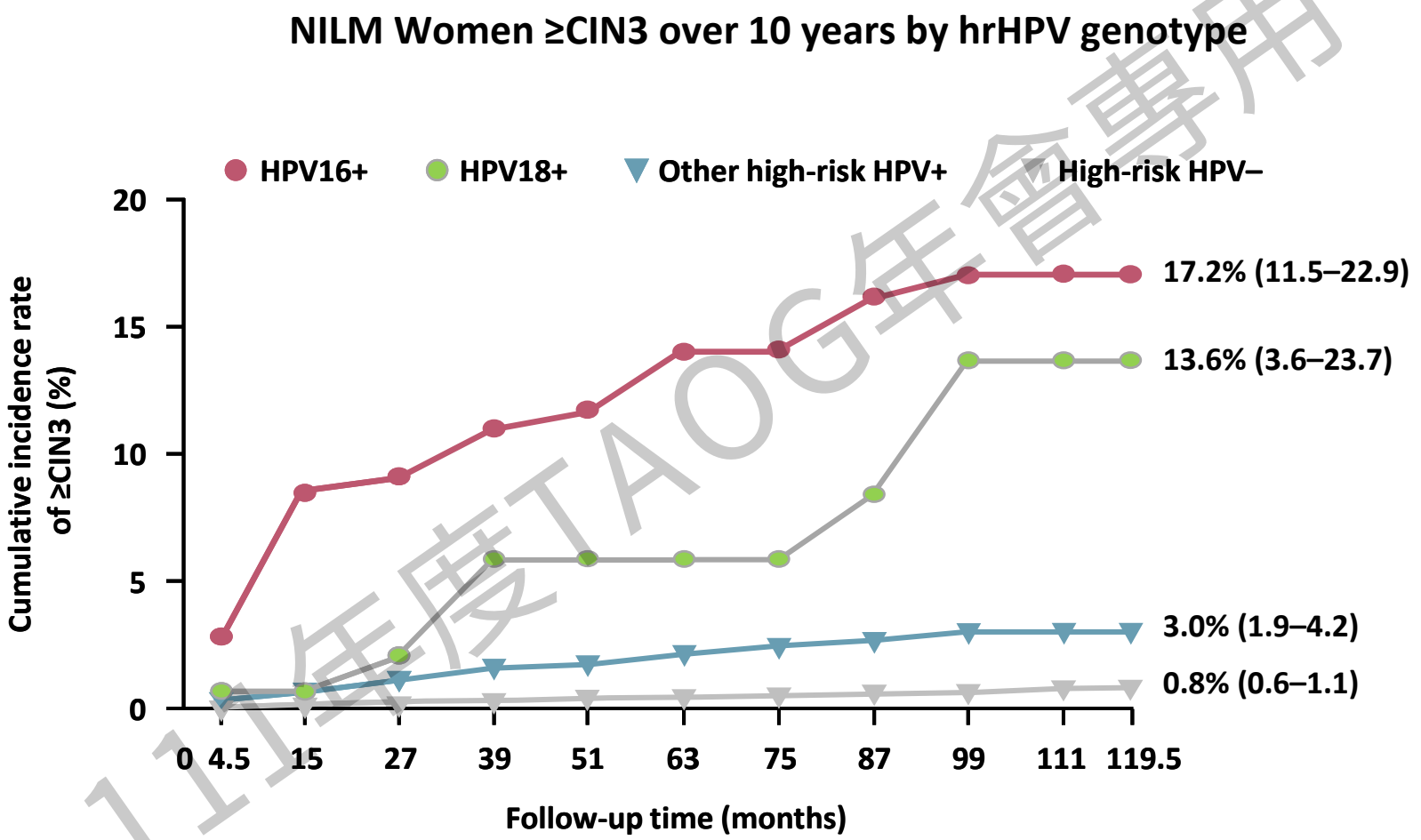


Figure 2: **Cumulative detection of invasive cervical carcinoma**

*Observations are censored 2·5 years after CIN2 or CIN3 detection, if any.

Study Length Effect on ≥CIN3

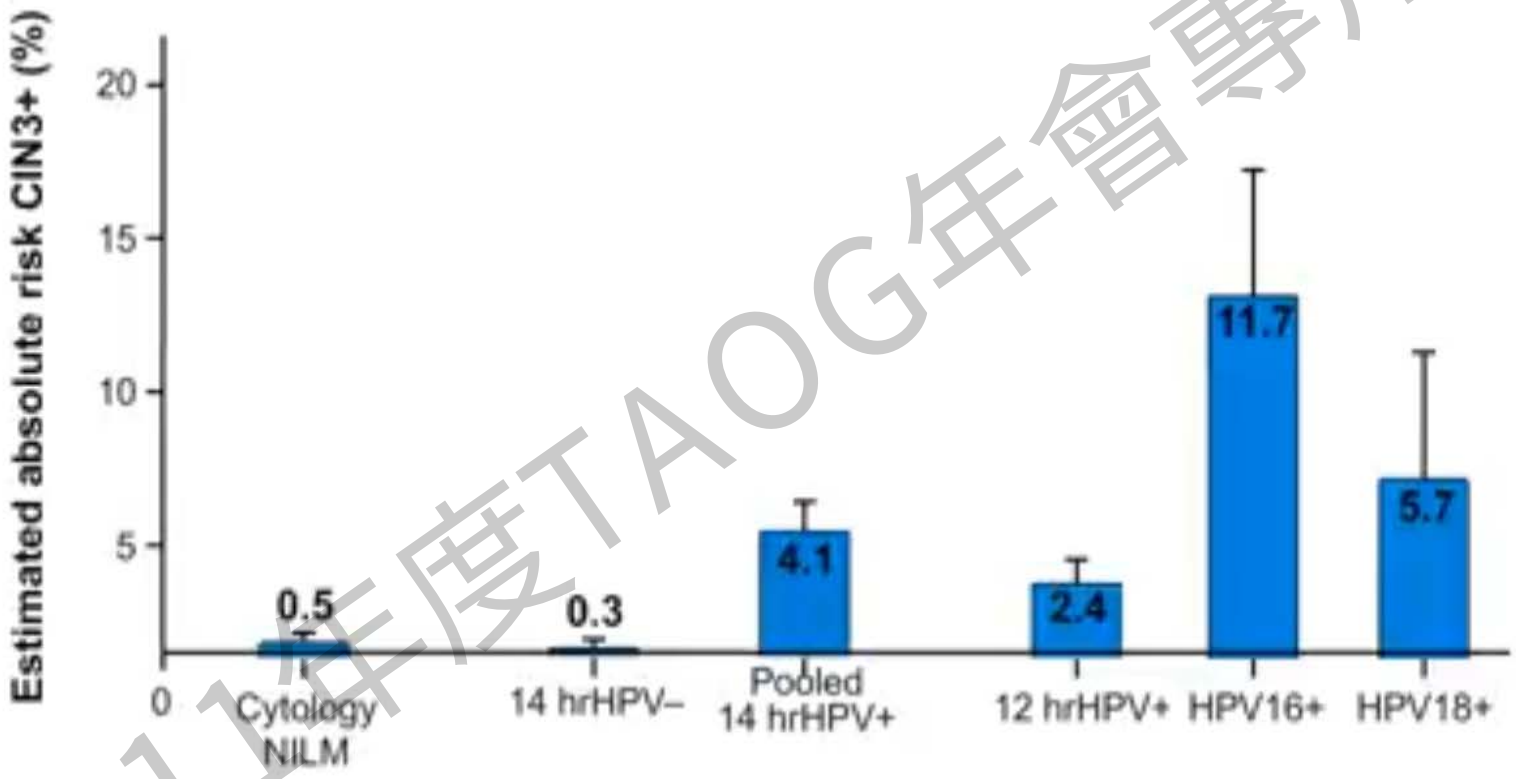


Disease Course: HPV16 and HPV18 distinguish themselves from the other pooled hrHPV, providing a better representation of genotype oncogenicity

Khan MJ, *et al. J Natl Cancer Inst* 2005

ATHENA NILM population ≥30 years: Absolute risk of ≥CIN3 at Baseline

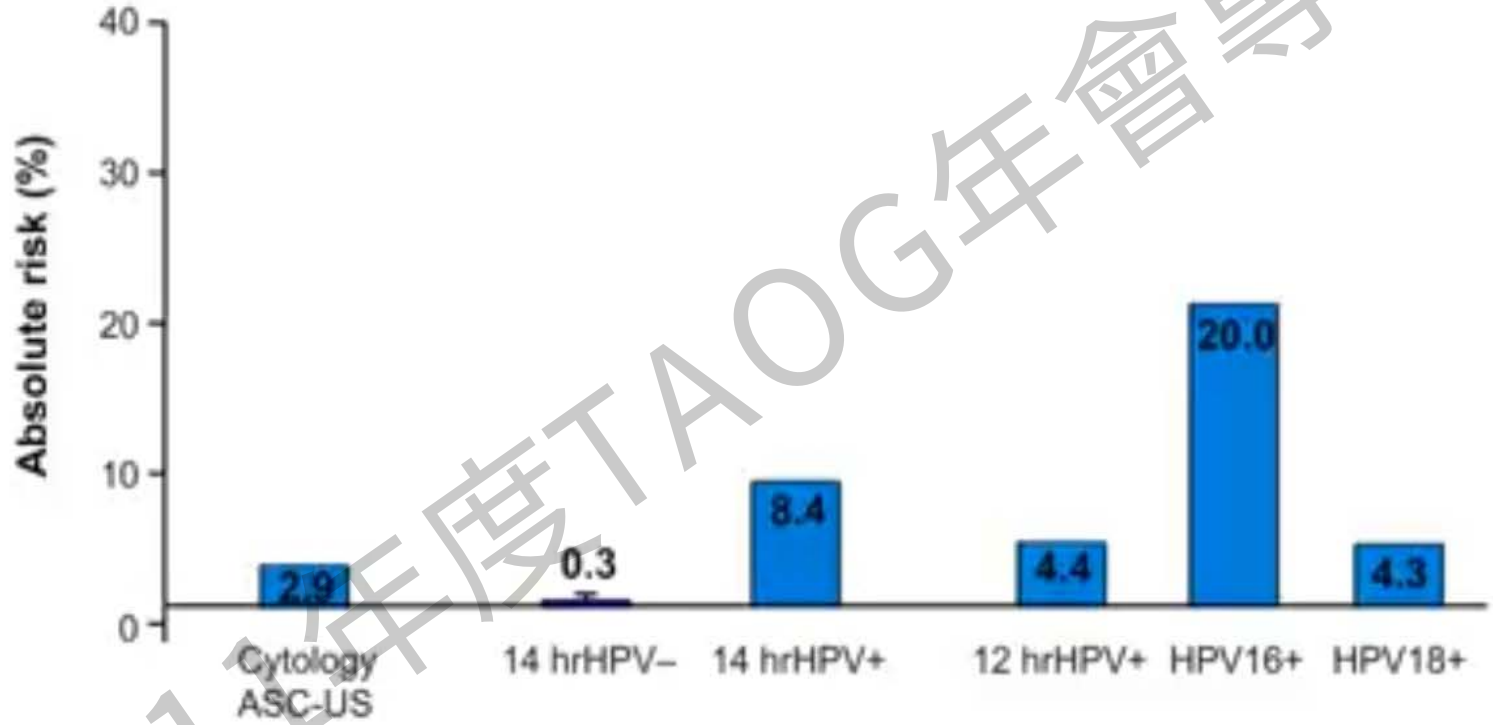
16/18 Genotyping Stratifies Risk in Cotesting



cobas® HPV16/18 genotyping results identify a sub-population of women with negative cytology who are at the highest risk of CIN3+

Wright TC Jr, *et al. Am J Clin Pathol*, 2011;136:578.

Absolute risk of ≥CIN3 stratified by hrHPV status in the *ATHENA* ASC-US population



cobas® HPV16 genotyping results identifies a sub-population of women with ASC-US cytology that is at the highest risk of ≥CIN3

•ASC-US, atypical squamous cells of undetermined significance

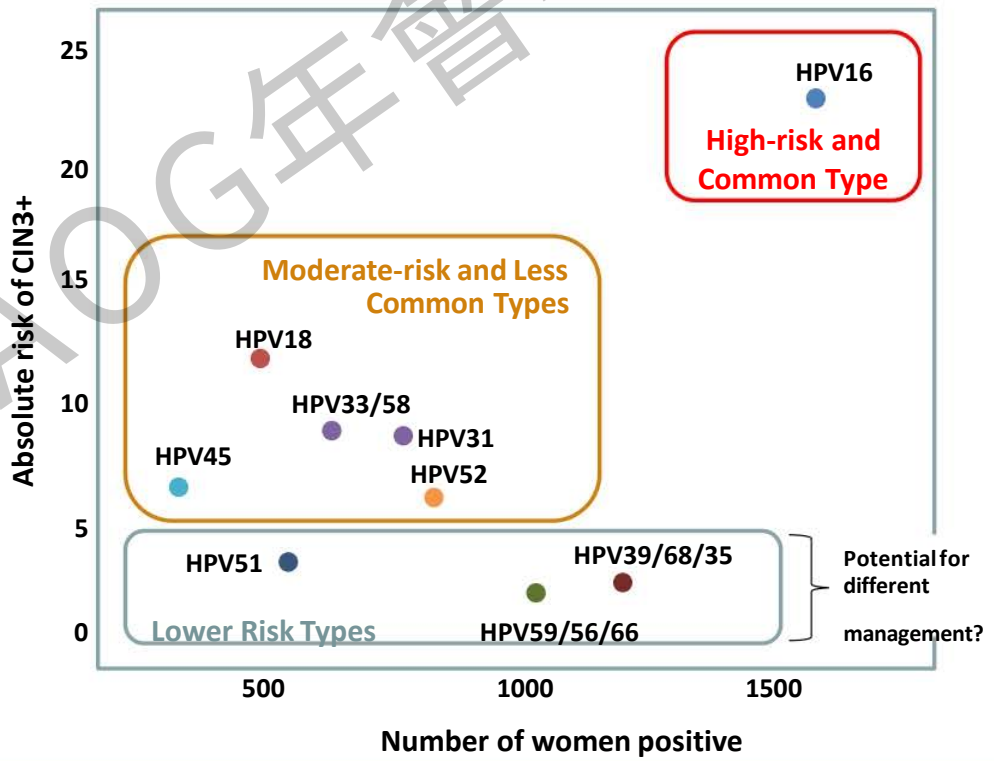
Stoler MH, *et al. Am J Clin Pathol* 2011; 135:468.

HPV Genotype
Implications for Screening and Management

- **Extended HPV genotyping gives information about:**
  - Individual risk
  - Insight into how common is each type of virus
- **HPV16 was both high-risk and common**
- **Other types with lower risk**
  - Consider different management?

Type restriction in low-resource settings

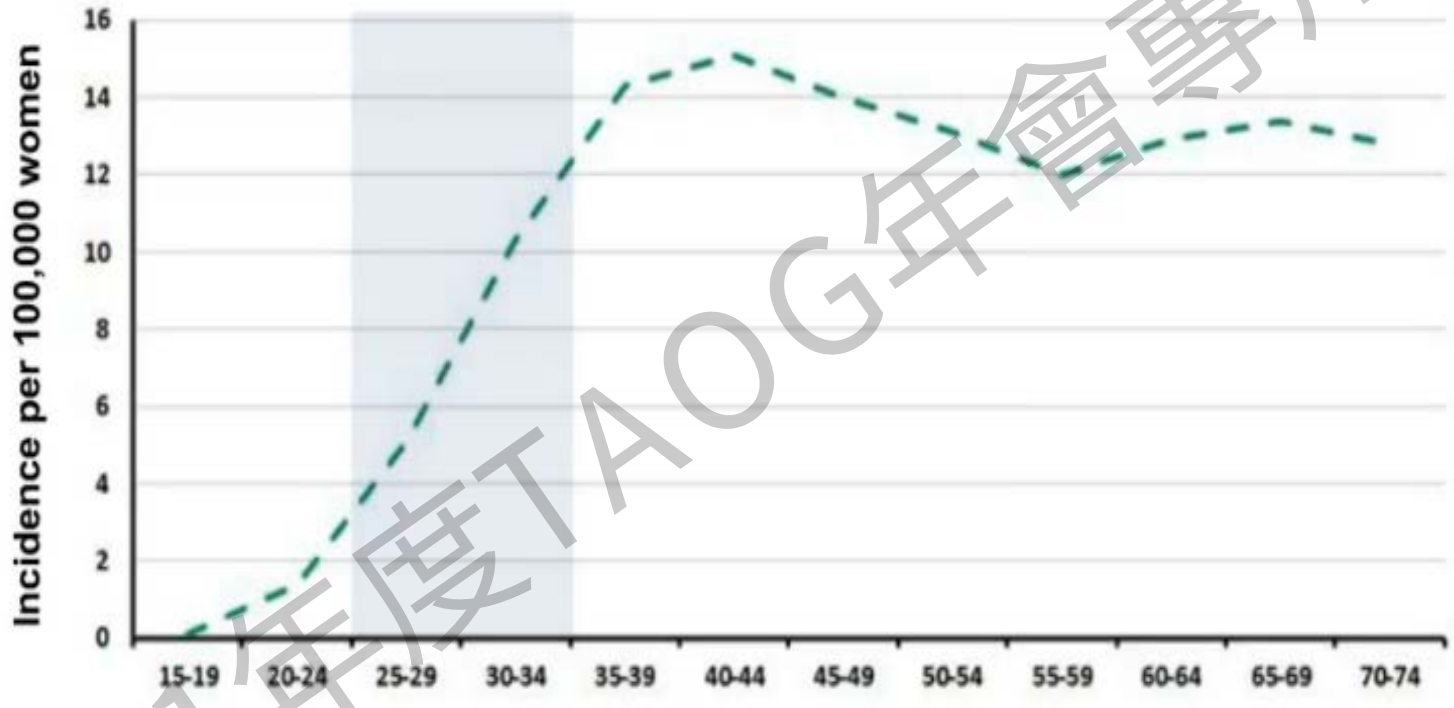
Risks of CIN3 by HPV Type Groups and Cytology, NCI/KPNC PaP cohort



Adapted from Schiffman M, Hyun N, Raine-Bennett TR, et al. *Int J Cancer* 2016 Dec 1;139(11):2606–15

Incidence of Invasive Cervical Cancer

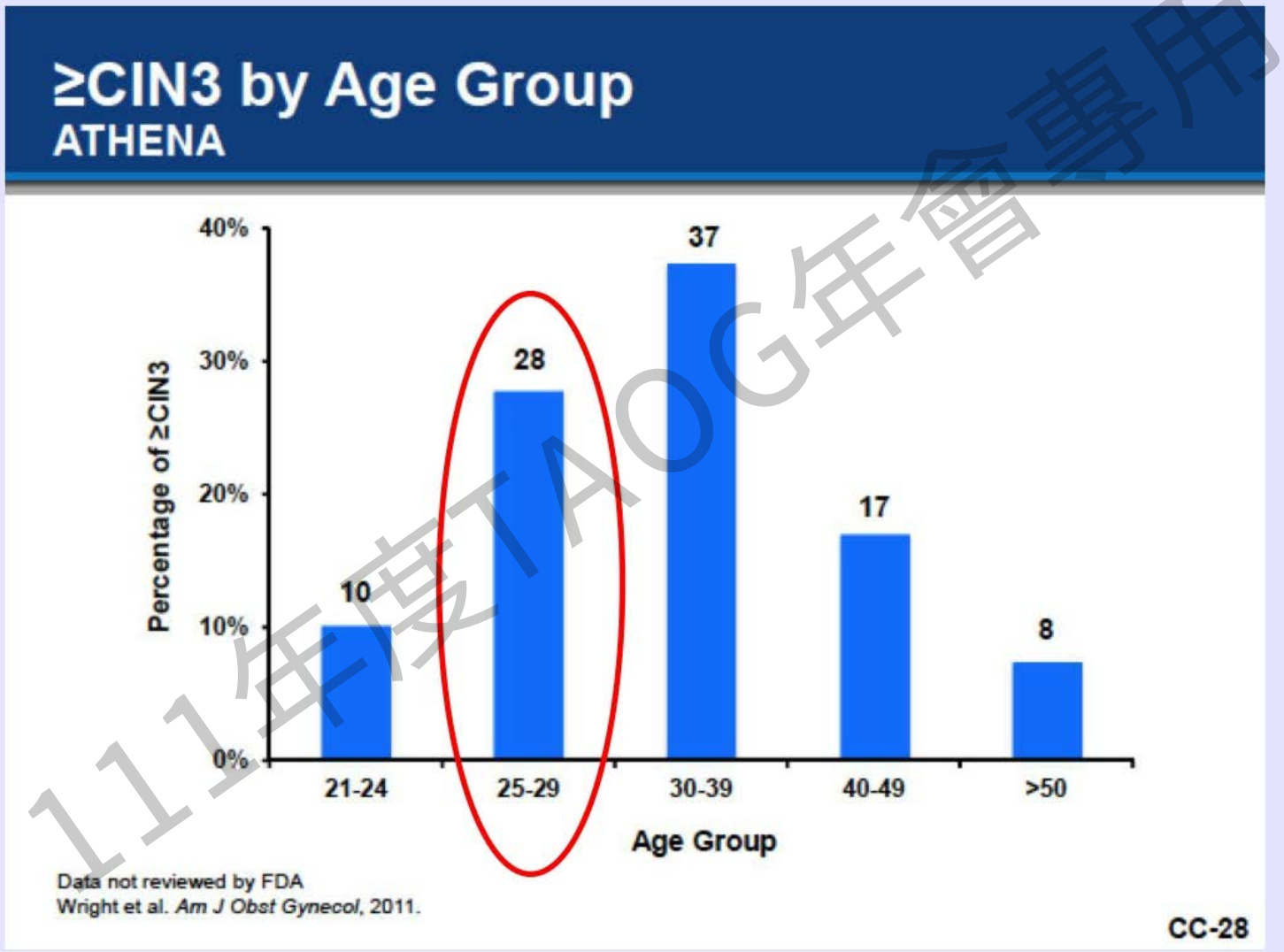
SEER Tumor Registry data (1975-2010)



Proper identification and treatment of precancerous lesions helps *prevent* cervical cancer from developing

Cancer of the Cervix Uteri (Invasive). SEER incidence and US death rates, age-adjusted and age-specific rates, by race. Table 5.7. http://seer.cancer.gov/archive/csr/1975_2010/results_merged/sect_05_cervix_uteri.pdf Accessed May 15, 2014.

Why Start at 25 years of age?



From 3/12/2014 FDA Panel Materials

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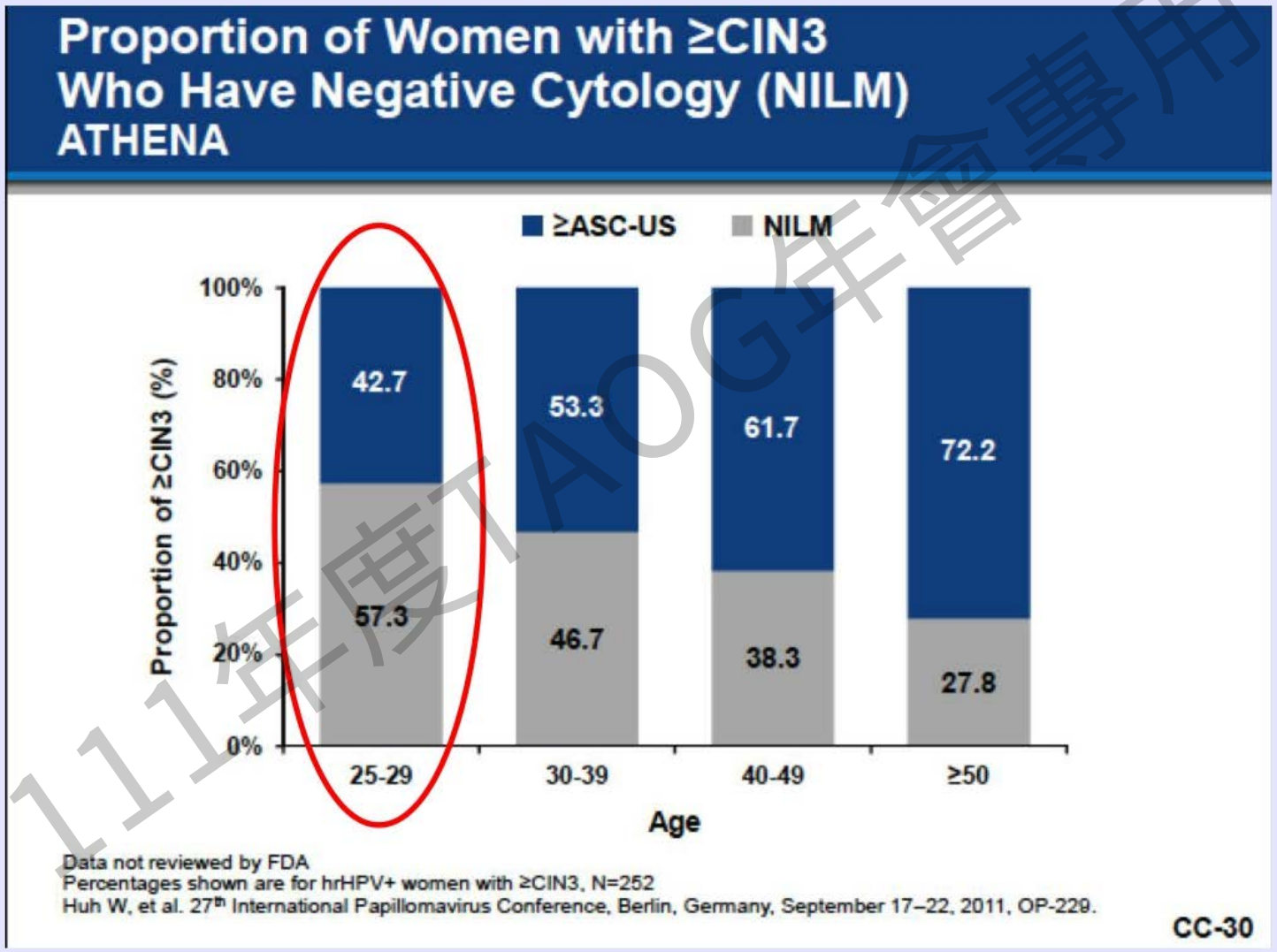
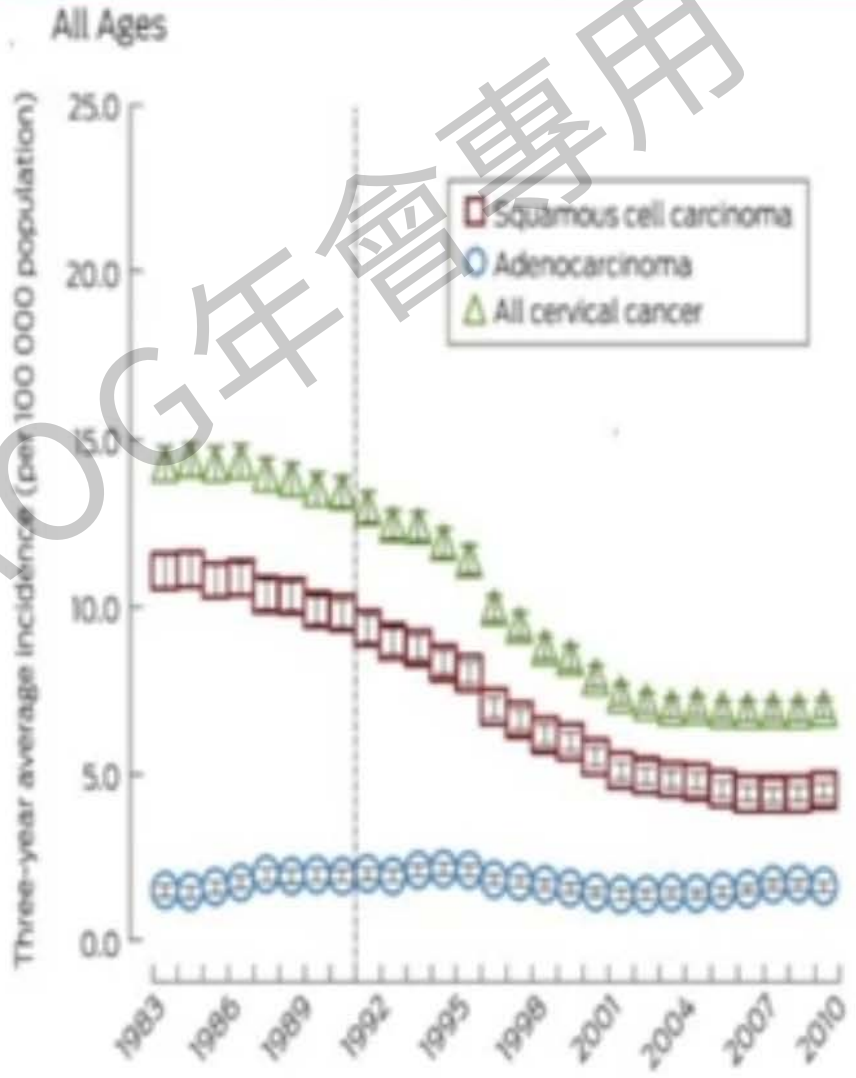


From 3/12/2014 FDA Panel Materials

Australian Government
Department of Health

Three-year average cervical cancer incidence (with 95% CIs), by all ages and histological type, 1982-2010



M.Smith, K. Canfell: Med J Aust 2016; 205(8): 359-64

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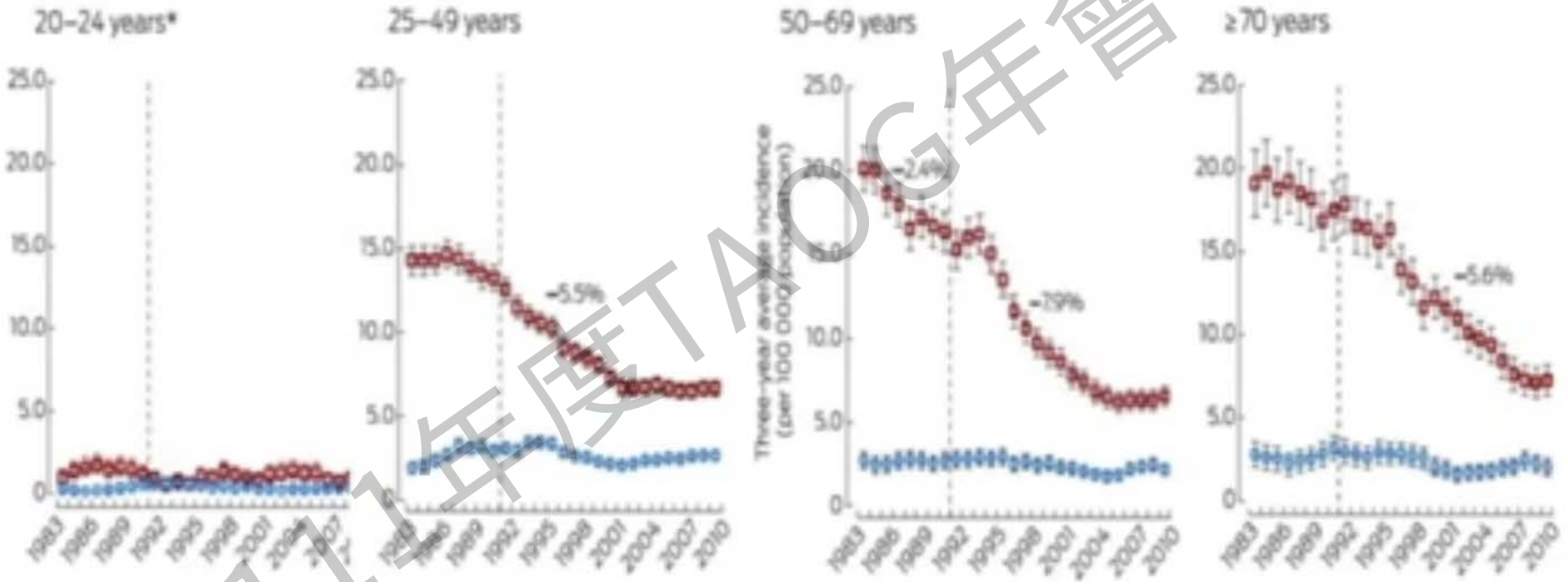


M.Smith, K. Canfell: Med J Aust 2016; 205(8): 359-64

Australian Government
Department of Health

Renewal: the bottom line

Primary HPV screening program will lead to:

Up to 30% ↓

Fewer cases of cervical cancer

Fewer deaths from cervical cancer

Australian Government
Department of Health

Main changes from Dec 2017

Now	Dec 2017
• Pap smear	• **Cervical Screening Test (oncogenic HPV test)**
• 2 yearly	• **5 yearly**
• Start 18 years	• **Start 25 years**
• End 69 years	• **End 70-74 years**
• Reminders	• **Invitations/Reminders**
	• **Self-collection**

Cytology vs HPV to Screen for Cervical Cancer

Cytology

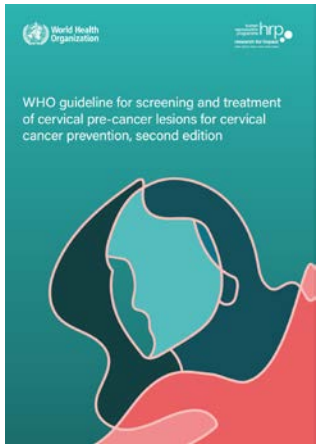
- Requires screening Infrastructure (CT, schools)
- Cost …depends, but generally lower
- Issues with false negatives and positives
- Colposcopy rates…depends on triage
- Self collected specimens, inferior
- Screening for pre cancer and cancer

HPV

- None required
- Depends on vendor and price, generally more
- Same! (people are just not aware)
- Increased. Can be high depending upon prevalence
- Self collected specimens can be equivocal (if highly sensitive test used)
- Screening for infection that causes most cervical cancers

There is no perfect test!

2021 WHO guideline recommendation



4.1 Recommendations and good practice statements: general population of women[6]

4. When providing HPV DNA testing, WHO suggests using either **samples taken by a health-care provider or self-collected samples** among both the general population of women and women living with HIV.*
[Conditional recommendation, low-certainty evidence]

How do we know self-sampling is efficacious?

Overall, our study shows over 90% correlation between clinician collected endocervical and self-collected vaginal specimens

Self-Collected Vaginal Sample using FLOQSwabs 552C.80 (14 hrHPV Result)	Clinician-Collected Cervical Sample (14 hrHPV Result) Positive	Negative	Total
Positive	165	43	208
Negative	26	472	498
Total	191	515	706

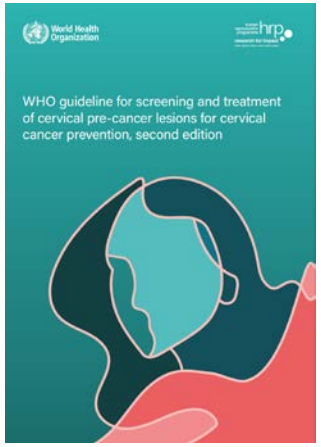
	Result %	95% Confidence Interval
Positive Percent Agreement	86.4%	80.8% - 90.5%
Negative Percent Agreement	91.7%	88.9% - 93.7%
Overall Percent Agreement	90.2%	87.8% - 92.2%

*https://www.who.int/news/item/06-07-2021-new-recommendations-for-screening-and-treatment-to-prevent-cervical-cancer
*Correlation study data from Roche

2021 WHO guideline recommendation

Note
WHO考量不同國家因民情或醫療資源不同，接受將自採樣本納入HPV DNA testing可用檢體中

亦有多個研究指出自採與醫師採檢的一致性高



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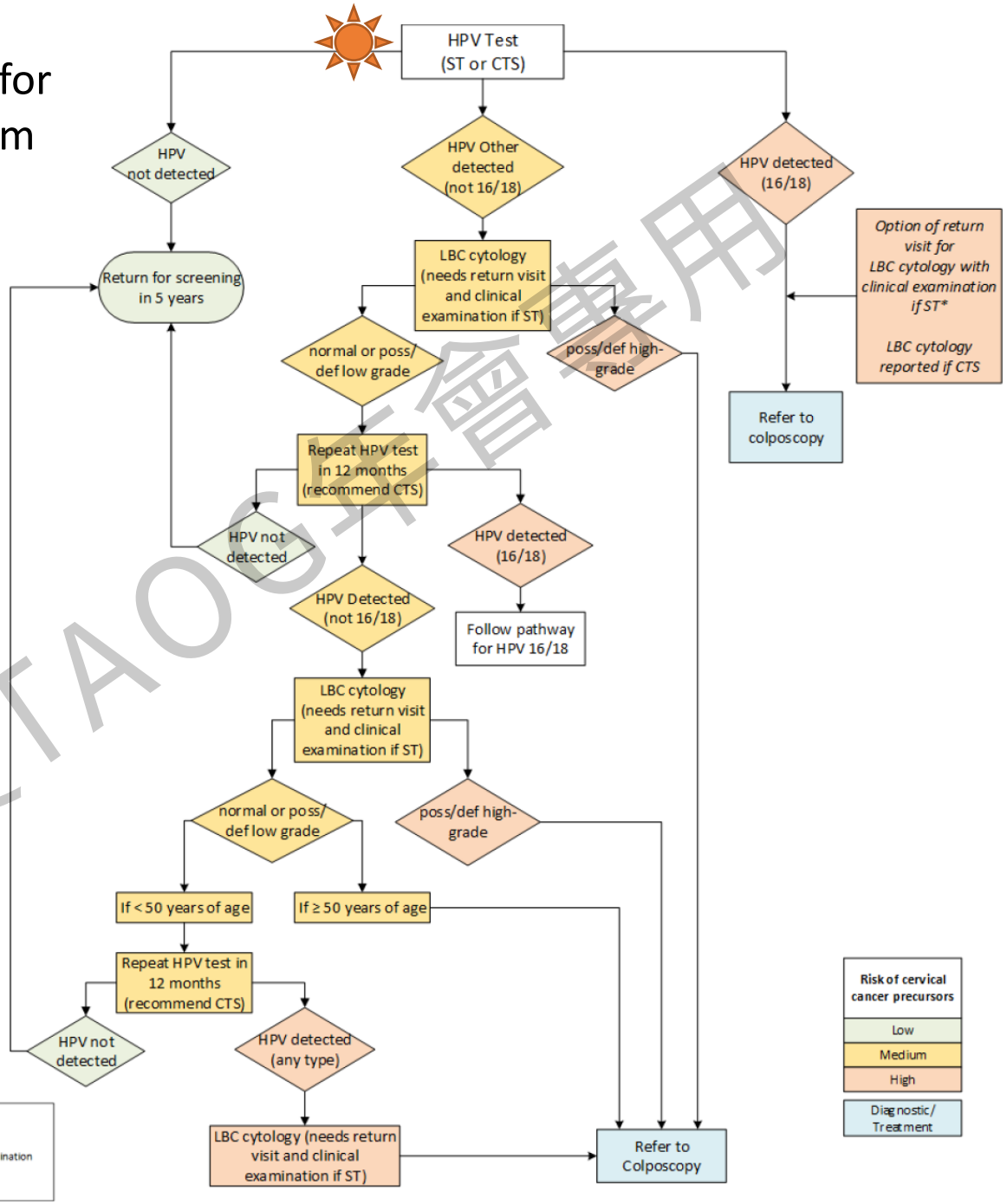
From July 2023, the primary test for cervical screening will change from cytology to HPV testing,
with the option of self-testing.

MINISTRY OF HEALTH
MANATŪ HAUORA

New Zealand Government

Revised HPV screening clinical pathway for asymptomatic participants

Over May and June 2021, the NCSP undertook a public consultation on the HPV primary screening clinical pathway to introduce self-testing. The following diagram is the revised HPV primary screening clinical pathway for asymptomatic participants, updated to include screening sector feedback and recommendations.



ST = self-test
CTS = clinician-taken sample, including speculum examination
LBC Cytology: reflex cytology or clinically taken cytology sample
*Participants with *HPV 16/18: Detected* on a self-test sample (ST) have the option of adding LBC cytology with clinical (speculum) examination prior to colposcopy.

https://www.nsu.govt.nz/health-professionals/national-cervical-screening-programme

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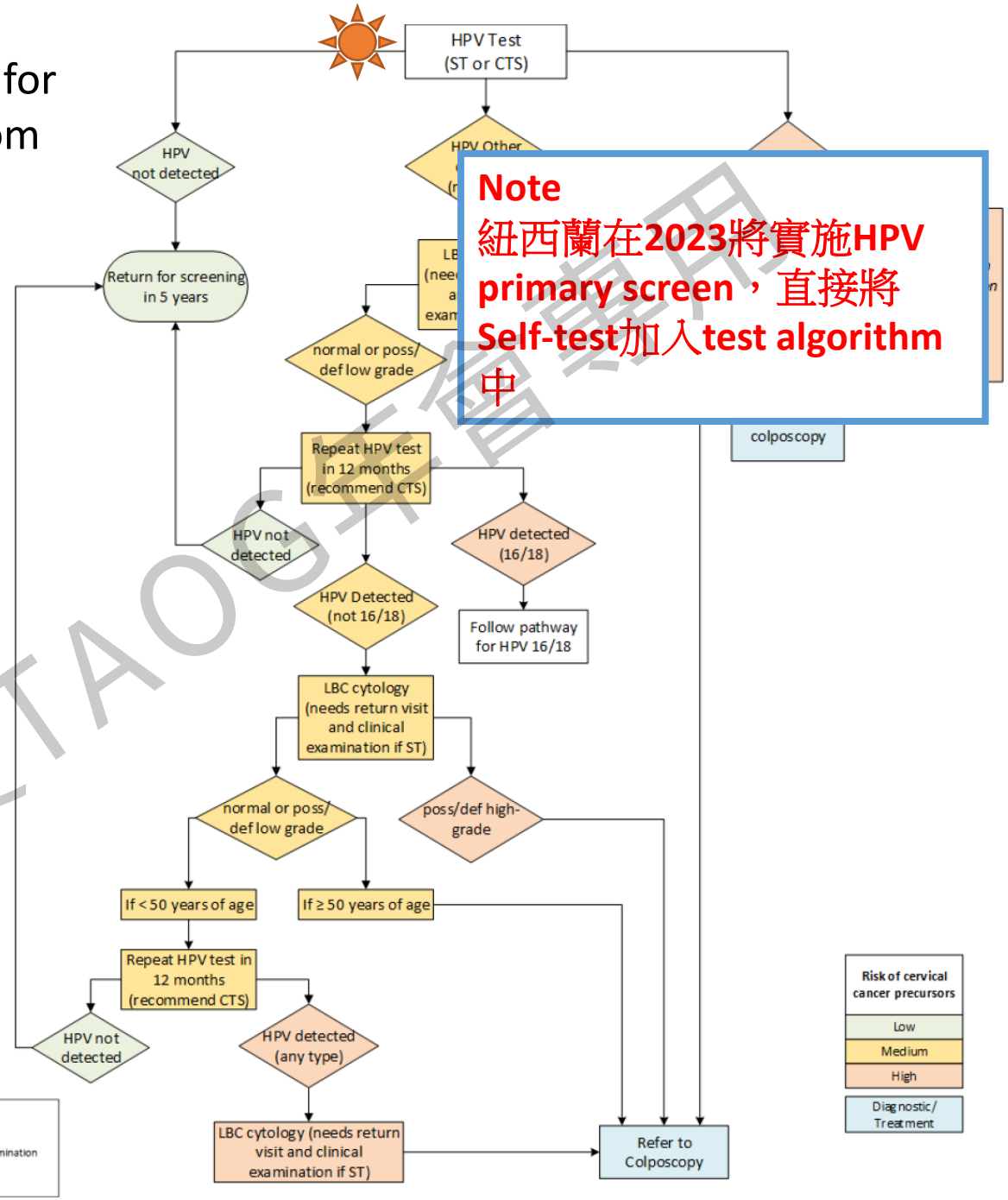

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Note
紐西蘭在2023將實施HPV primary screen，直接將Self-test加入test algorithm中

Why is HPV Testing an Attractive Option for Cervical Cancer Screening?

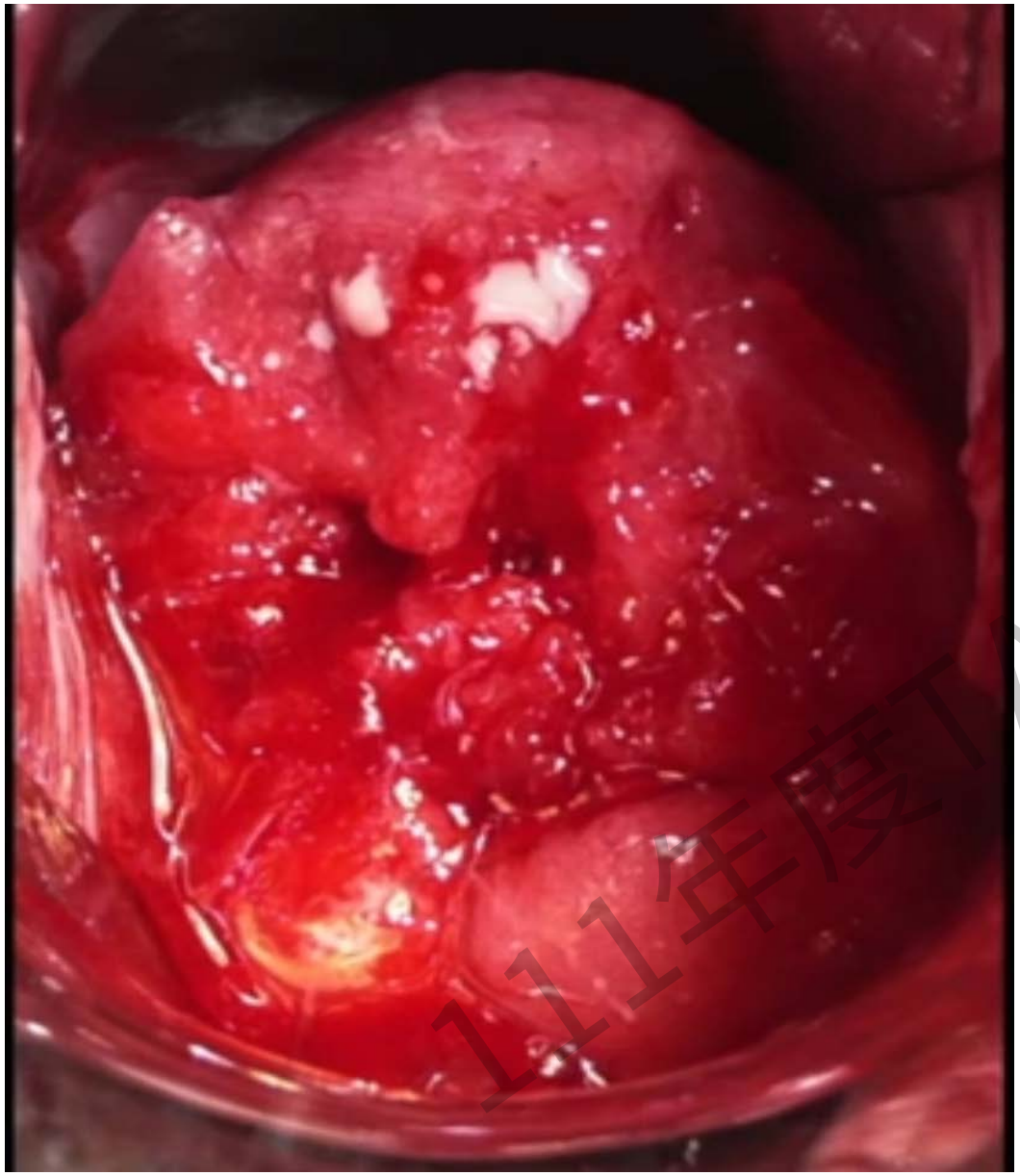
1. More sensitive and reproducible than the Pap test.
2. More “upstream” in the carcinogenic process, thus enabling a longer safety margin for screening intervals.
3. Assesses future risk (and not just the presence of current disease).
4. Can be automated, centralized , and be quality-checked for large specimen throughput.
5. May be more cost-effective than cytology if deployed for high volume testing, such as in primary screening.
6. A more logical choice for screening women vaccinated against HPV infection.

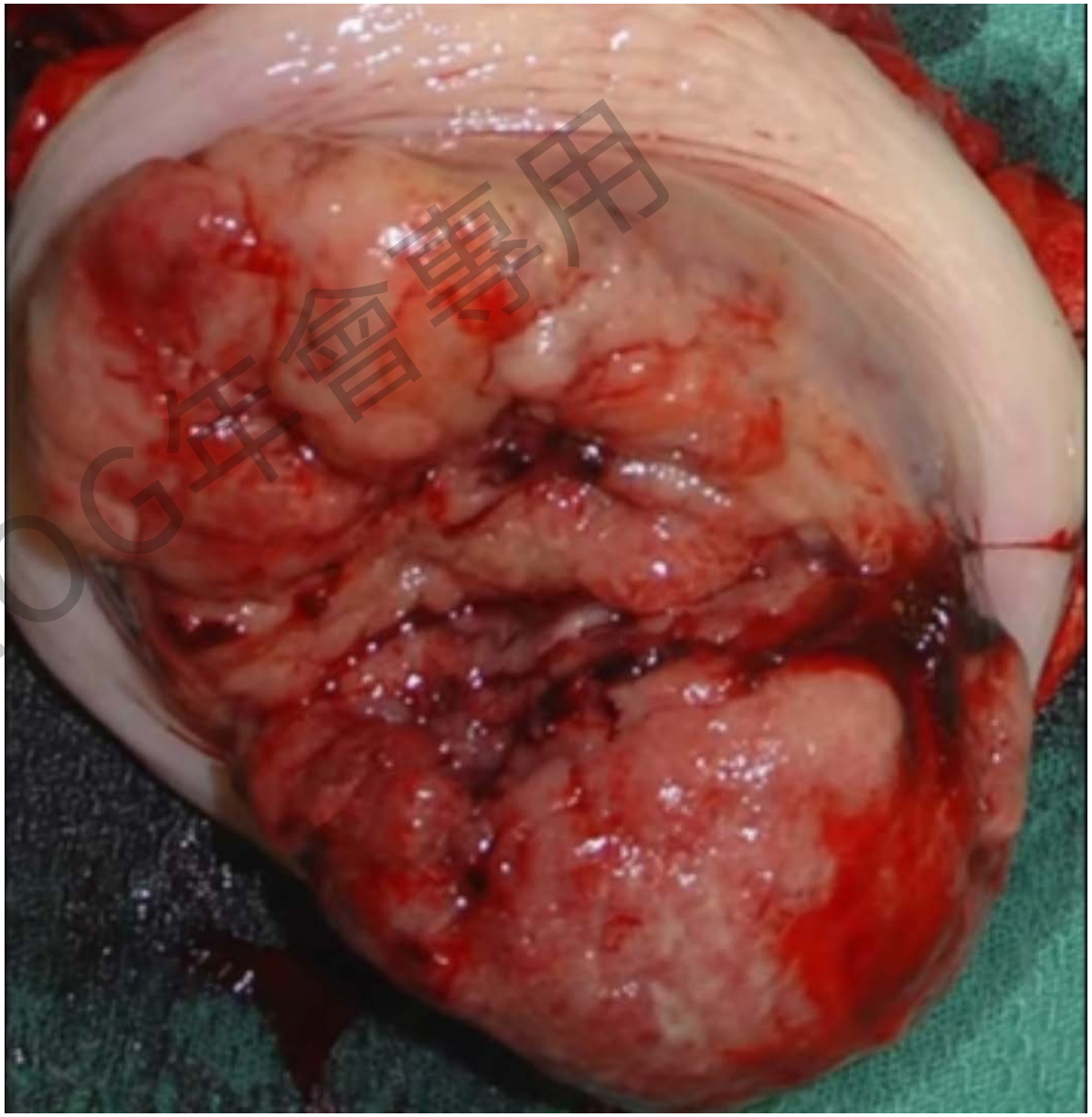
Psychosocial Impact of HPV + test results

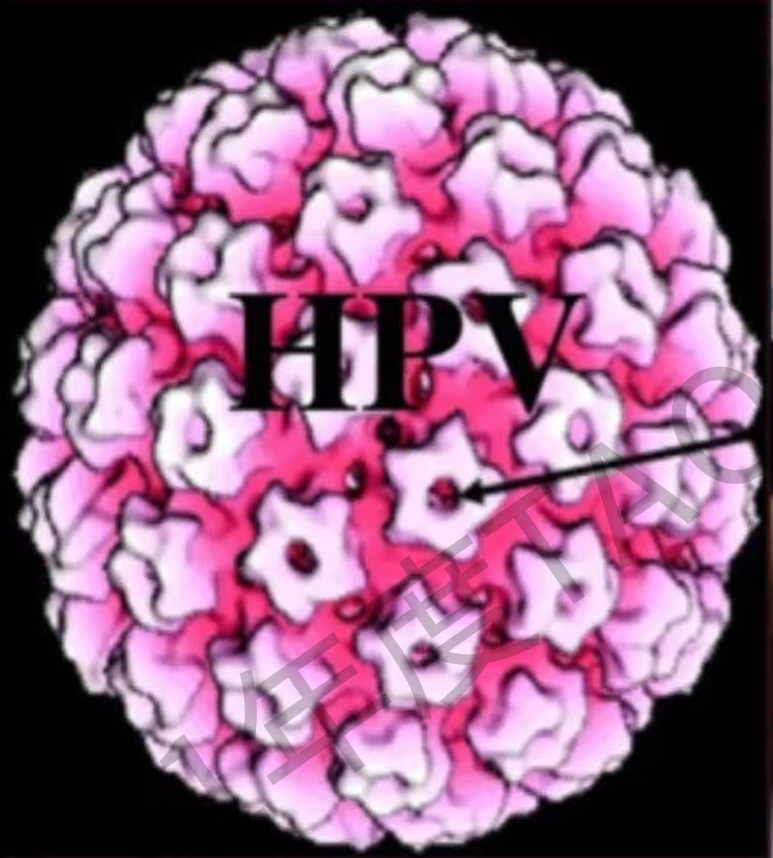
Summary

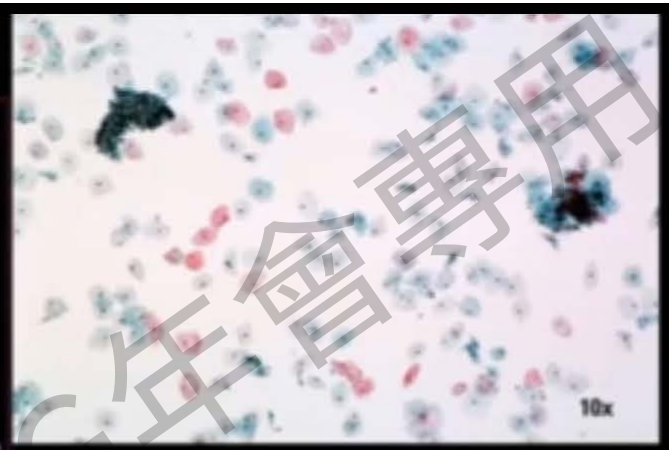
Testing positive for HPV may have an adverse psychosocial impact:

- Surprise and increased anxiety
- Distress
- Cervical cancer worry
- Feeling stigmatised
- Feeling ashamed
- Concern about sexual relationships
- Worry about disclosing results to others
- Risk of colposcopy and surgery





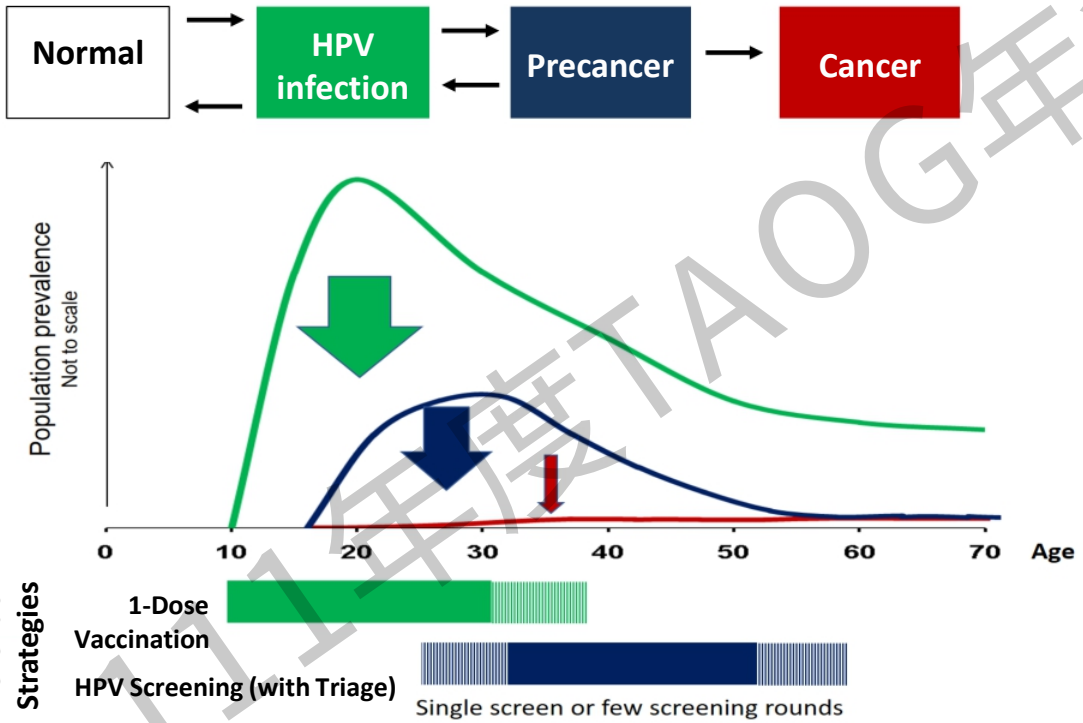

HPV


10x


GARDASIL™
GARDASIL™
[Quadrivalent Human Papillomavirus
(Types 6, 11, 16, 18) Recombinant Vaccine]
MSD

Combined Vaccination and Screening Program for Low-resource Settings

Progression of HPV Infection to Cervical Cancer Over Woman's Lifetime

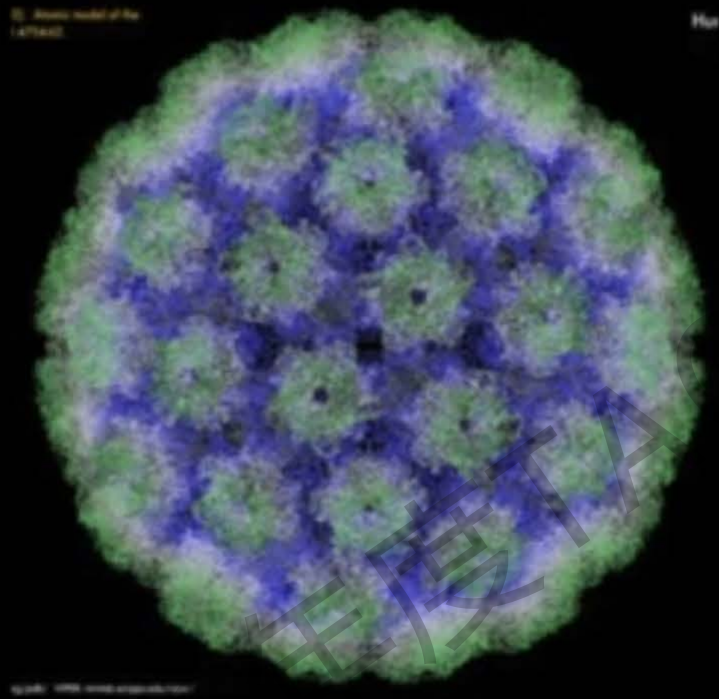


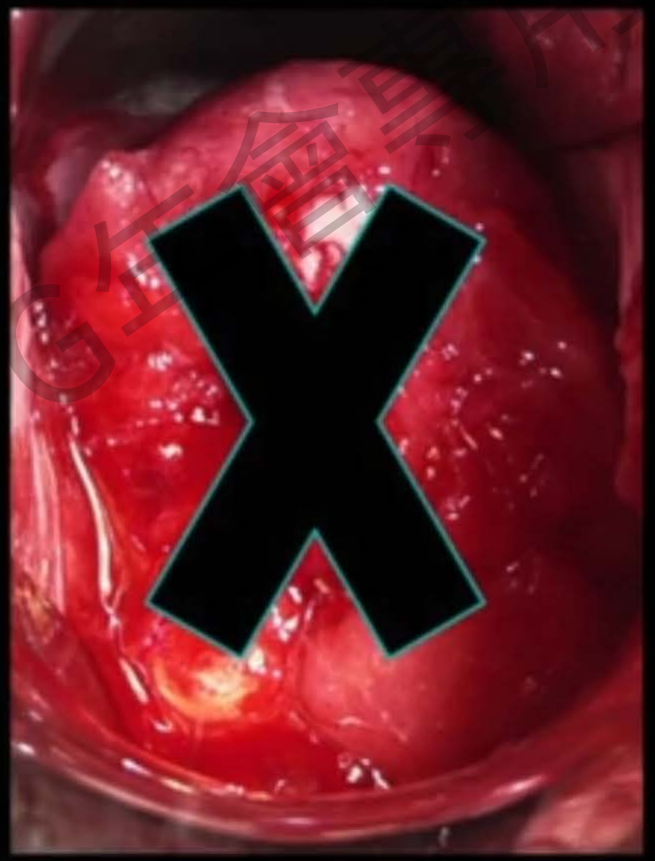
Extended age range of vaccination reduces HPV population prevalence faster

HPV screen and treat reduces cancer prevalence faster

Wentzensen N & Schiffman M *Lancet Public Health* 2018 Jan;3(1):e6–e7

HPV Vaccine





Cervical Screening Test

Conclusions

Clinical implications of HPV primary screening

- Cytology based screening has been successful, but has limitations
- HPV Primary Screening allows for improved clinical sensitivity over cytology while maintaining high efficiency
- HPV primary screening utilizing integrated HPV16/18 genotyping and cytology reflex of the 12 other hrHPV genotypes, demonstrates a good balance of clinical resources
  - Provides improvements in clinical sensitivity while maintaining high efficiency (colposcopies per disease case detected)
  - In younger women, the primary screening algorithm finds more disease while addressing concerns about unnecessary follow-ups
- Primary HPV testing is now an alternative option to current cytology-based screening methods due to equivalent or superior effectiveness

國健署為提升癌症防治成效，
111年延續“子宮頸抹片+HPV Test試辦計畫”

補助HPV檢測

- **針對45歲以上**
- **六年未篩者**

(四) 我國 45 歲以上 6 年以上未做子宮頸癌篩檢者提供 HPV 檢測服務(分項 1-6 擇優選辦)

執行內容				
111 年補助對象	補助項目	預定補助家數	每家補助經費上限	總經費 單位：元
45 歲以上 6 年以上未做子宮頸癌篩檢之婦女	HPV 檢測補助上限 570 案	35	798,000	27,930,000

Primary HPV screening in Singapore

HPV DNA test is recommended

SINGAPORE CANCER SOCIETY

The Society for Colposcopy & Cervical Pathology of Singapore

National screening from pap smear (2004) to primary HPV screening (2016)

Position statement[1]: Format of Primary HPV Screening

Primary HPV screening should employ the use of a **PCR based assay to detect HPV DNA**.

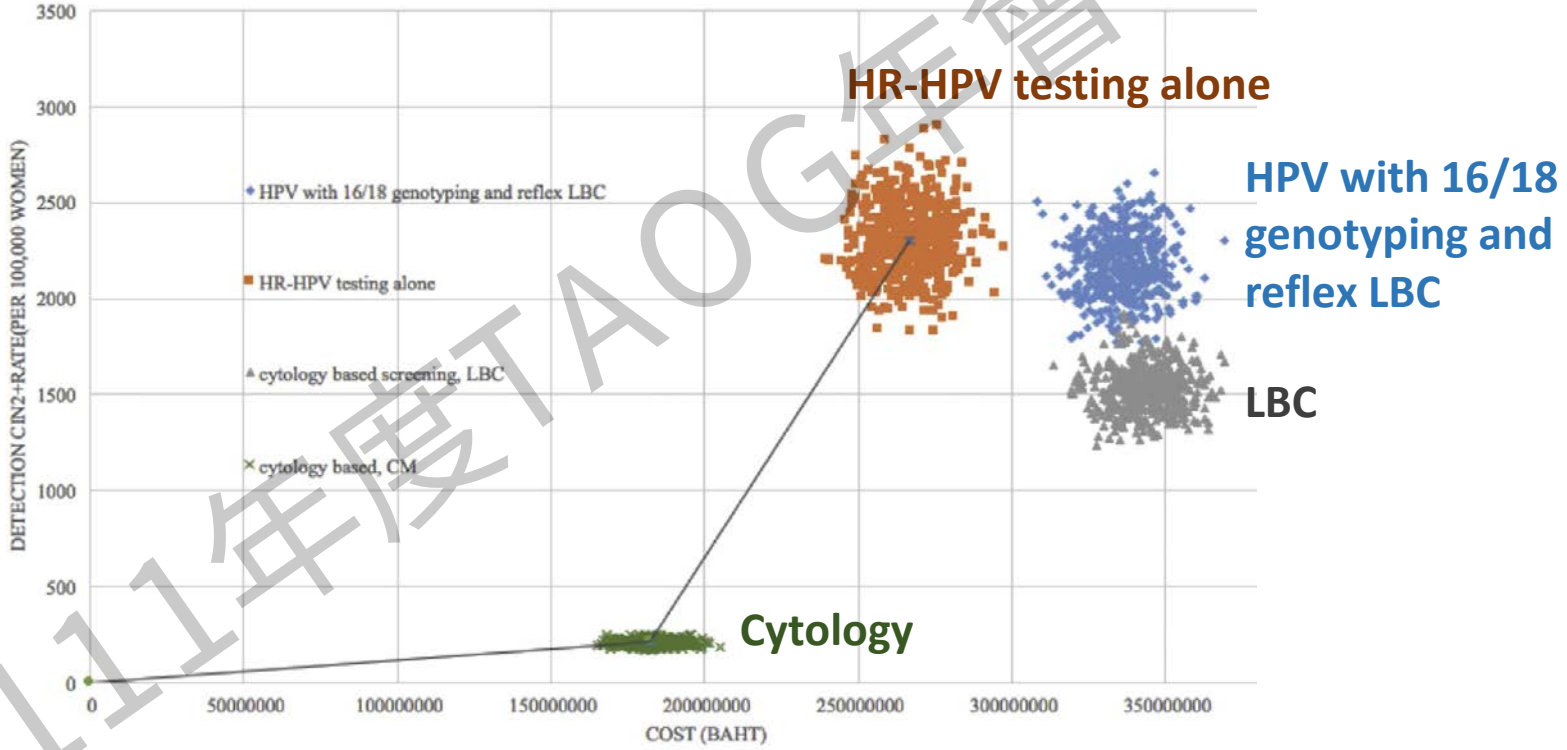
The test should provide the following information to be clinically useful:

1. **HPV 16** subtype identification
2. **HPV 18** subtype identification
3. **High-risk group** identification which should include subtypes 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, 68.

1. https://www.sccps.org/wp-content/uploads/2018/03/SCCPS-Scientific-Committee-Position-Paper-on-HPV-Screening.pdf

Cost-effectiveness study to support primary HPV screening (in Thailand)

High risk HPV testing alone was most effective and less expensive



Wichai et al. Gynecologic Oncology Reports 22 (2017) 58–63

Primary HPV testing versus cytology-based cervical screening in women in Australia vaccinated for HPV and unvaccinated: effectiveness and economic assessment for the National Cervical Screening Program

Jie-Bin Lew, Kate T Simms*, Megan A Smith, Michaela Hall, Yoon-Jung Kang, Xiang Ming Xu, Michael Caruana, Louiza Sofia Velentzis, Tracey Bessell, Marion Saville, Ian Hammond, Karen Canfell*

Summary

Background Australia's National Cervical Screening Program currently recommends cytological screening every 2 years for women aged 18–69 years. Human papillomavirus (HPV) vaccination was implemented in 2007 with high population coverage, and falls in high-grade lesions in young women have been reported extensively. This decline prompted a major review of the National Cervical Screening Program and new clinical management guidelines, for which we undertook this analysis.

Methods We did effectiveness modelling and an economic assessment of potential new screening strategies, using a model of HPV transmission, vaccination, natural history, and cervical screening. First, we evaluated 132 screening strategies, including those based on cytology and primary HPV testing. Second, after a recommendation was made to adopt primary HPV screening with partial genotyping and direct referral to colposcopy of women positive for HPV16/18, we evaluated the final effect of HPV screening after incorporating new clinical guidelines for women positive for HPV. Both evaluations considered both unvaccinated and vaccinated cohorts.

Findings Strategies entailing HPV testing every 5 years and either partial genotyping for HPV16/18 or cytological co-testing were the most effective. One of the most effective and cost-effective strategies comprised primary HPV screening with referral of women positive for oncogenic HPV16/18 direct to colposcopy, with reflex cytological triage for women with other oncogenic types and direct referral for those in this group with high-grade cytological findings. After incorporating detailed clinical guidelines recommendations, this strategy is predicted to reduce cervical cancer incidence and mortality by 31% and 36%, respectively, in unvaccinated cohorts, and by 24% and 29%, respectively, in cohorts offered vaccination. Furthermore, this strategy is predicted to reduce costs by up to 19% for unvaccinated cohorts and 26% for cohorts offered vaccination, compared with the current programme.

Interpretation Primary HPV screening every 5 years with partial genotyping is predicted to be substantially more effective and potentially cost-saving compared with the current cytology-based screening programme undertaken every 2 years. These findings underpin the decision to transition to primary HPV screening with partial genotyping in the Australian National Cervical Screening Program, which will occur in May, 2017.

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