2019 ASCCP Risk-Based Management Consensus Guidelines For Abnormal Cervical Cancer Screening Tests

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University of New Mexico

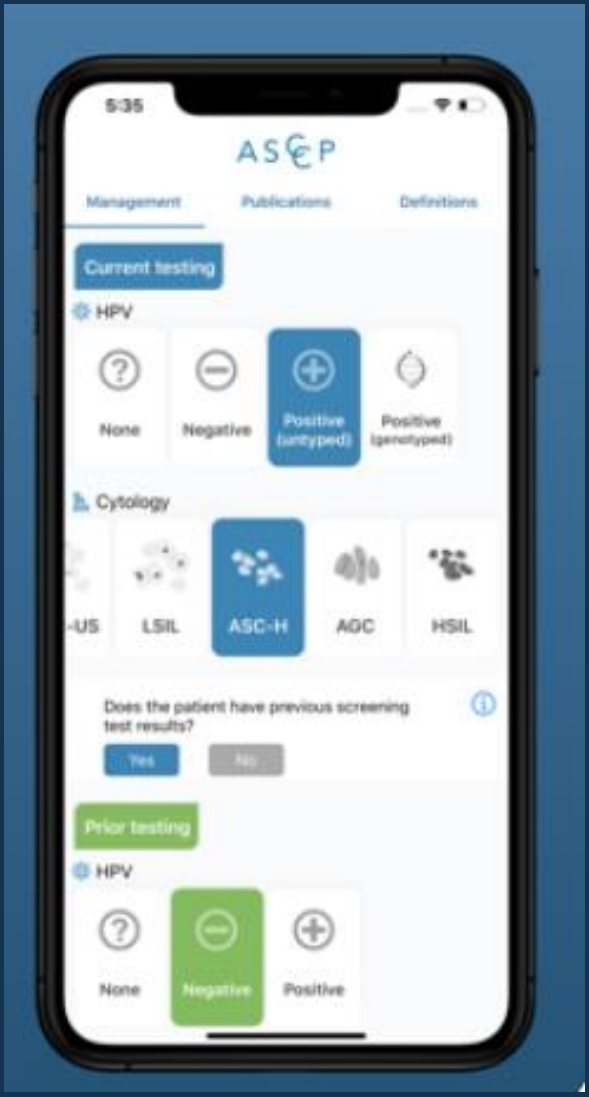
Disclosures

- I have no financial disclosures.

Reference: Perkins RB, Guido RS, Castle PE, et.al. 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. J Lower Genit Tract Dis 2020;24:102-131

Available at ASCCP.org

The ASCCP App



Compatible with:

- **iPhone**
- **iPad**
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Web version available through www.asccp.org

Objectives

1. Discuss how the ASCCP Guidelines were developed.
2. Review how risk-based management was a cornerstone to the guidelines
3. List four changes in these new guidelines from the previous 2012 recommendations
4. Discuss use of the ASCCP web applications in patient care.
5. Review the new American Cancer Society Screening Guidelines.

19 Participating Organizations

Patient Advocacy Organizations

- American Sexual Health Association
- Cervivor
- Latino Cancer Institute
- Team Maureen

Federal Agencies

- Centers for Disease Control & Prevention
- National Cancer Institute

Medical Professional Societies

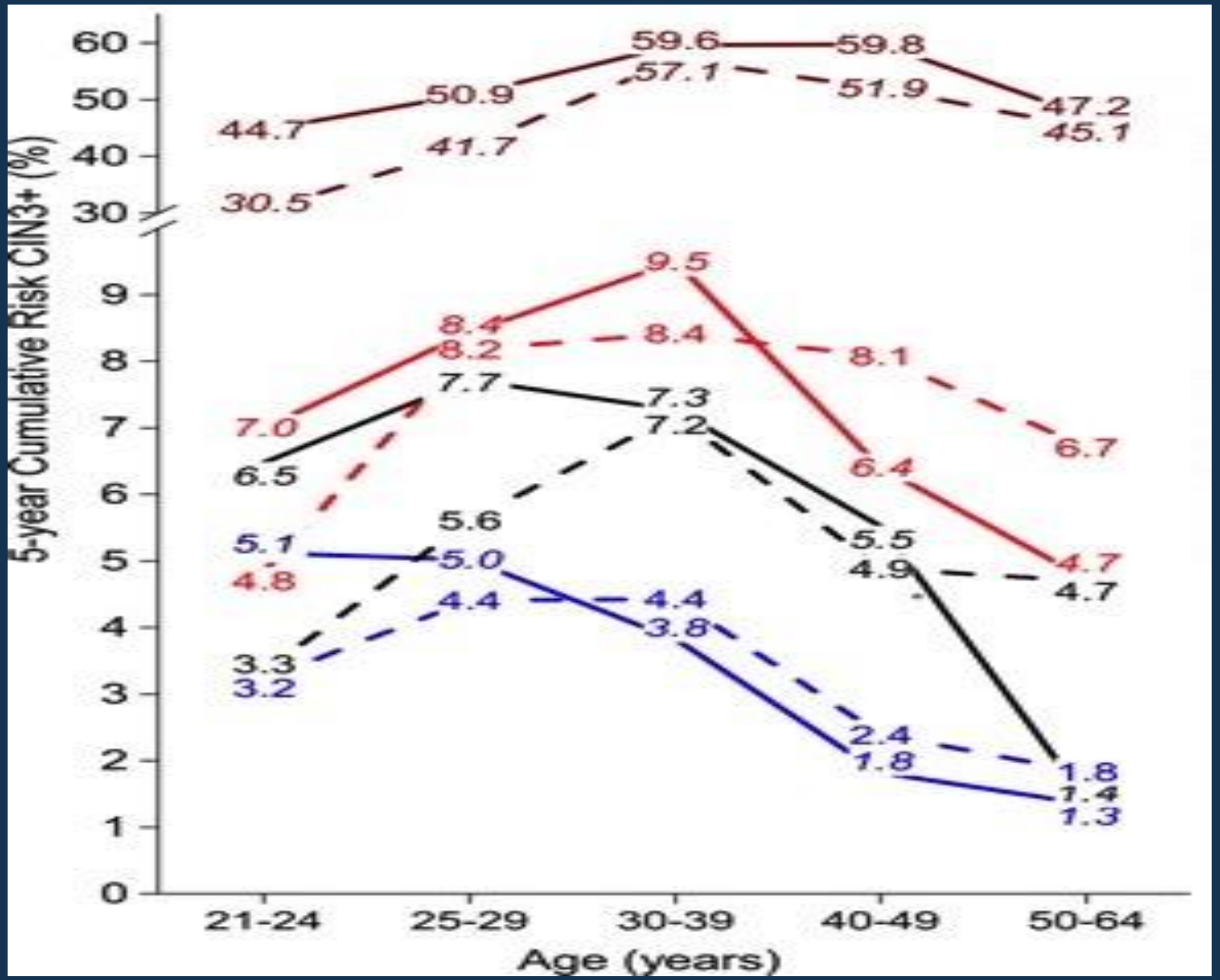
- ASCCP
- American Academy Of Family Physicians
- American Cancer Society
- American College Of Nurse-Midwives
- American College Of Obstetricians and Gynecologists
- American Society For Clinical Pathology
- American Society Of Cytopathology
- College Of American Pathologists
- Nurses For Sexual And Reproductive Health
- Nurse Practitioners In Women's Health
- Papanicolaou Society Of Cytopathology
- Society Of Gynecologic Oncology
- Women Veterans Health Strategic Healthcare Group

Data sources: data sets from different populations

- Kaiser Permanente Northern California Data (KPNC)
  - Principal source of data
  - Over 1.5 million women with routine cotesting from 2003-2017
  - HPV genotyping for ~19,000 patients

- New Mexico HPV Pap Registry (~450k)
- CDC NBCCEDP - well-screened (~200k)
- CDC NBCCEDP - rarely/never/unknown screened (~150k)
- BD Onclarity Trial (~30k with genotyping)

KPNC and New Mexico Similar risk profile



Baseline Screen:

HSIL

LSIL

HPV-positive/ASC-US

ASC-US

HPV-negative/ASC-US

Pap-negative

---- KPNC

NMHPVPR

Gage…Wheeler, Obstet Gynecol 2016

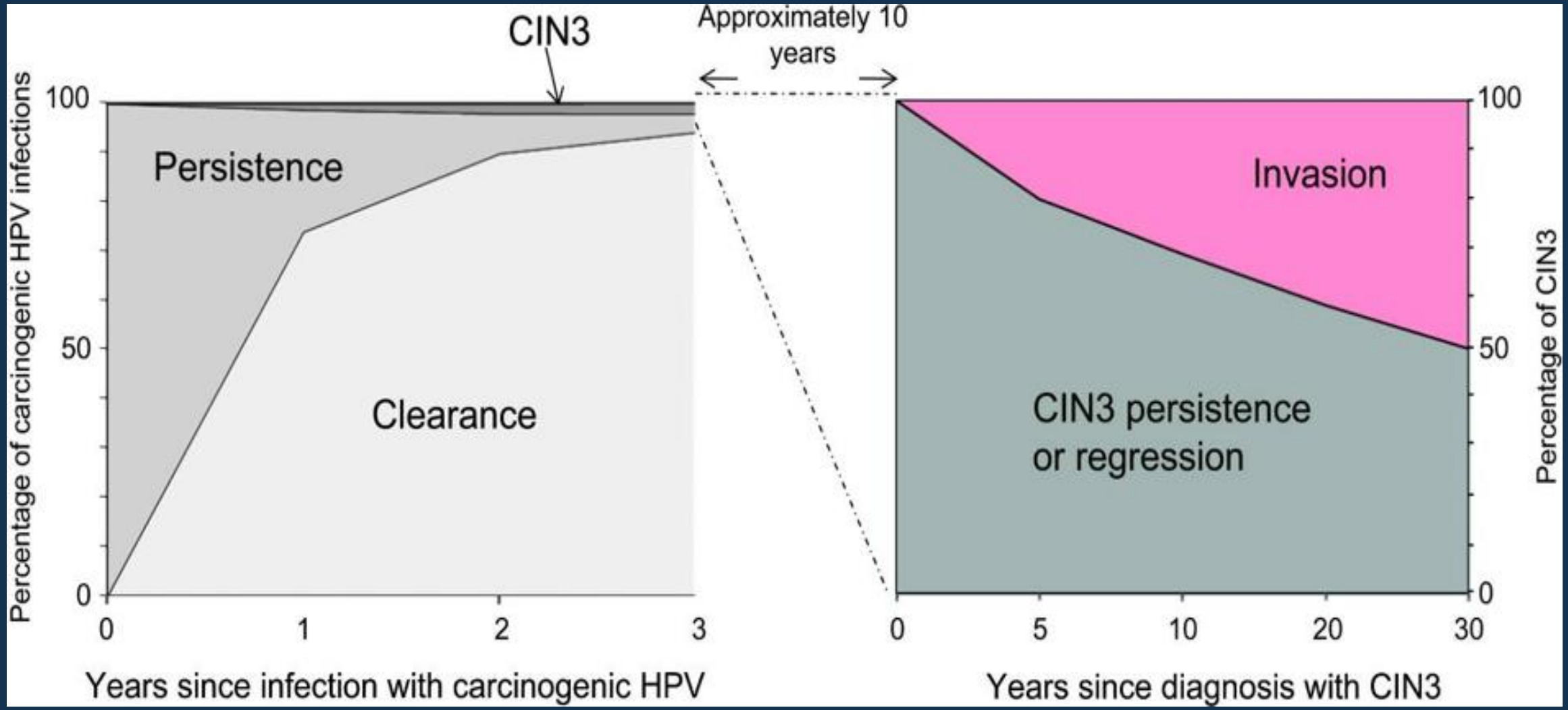
Fundamental Concept #1:
Equal Management for Equal Risk

- Risk of precancer (CIN 3+) is benchmark for clinical action.
  - Depending on level of risk, either immediate risk of CIN 3+ or 5 year cumulative risk of CIN 3+ is used.
    - Established from multiple data bases
    - Data includes results of cytology, HPV tests and biopsy results
- Action thresholds established for different management options
  - Management differs at different levels of risk of CIN 3+

Fundamental Concept #2

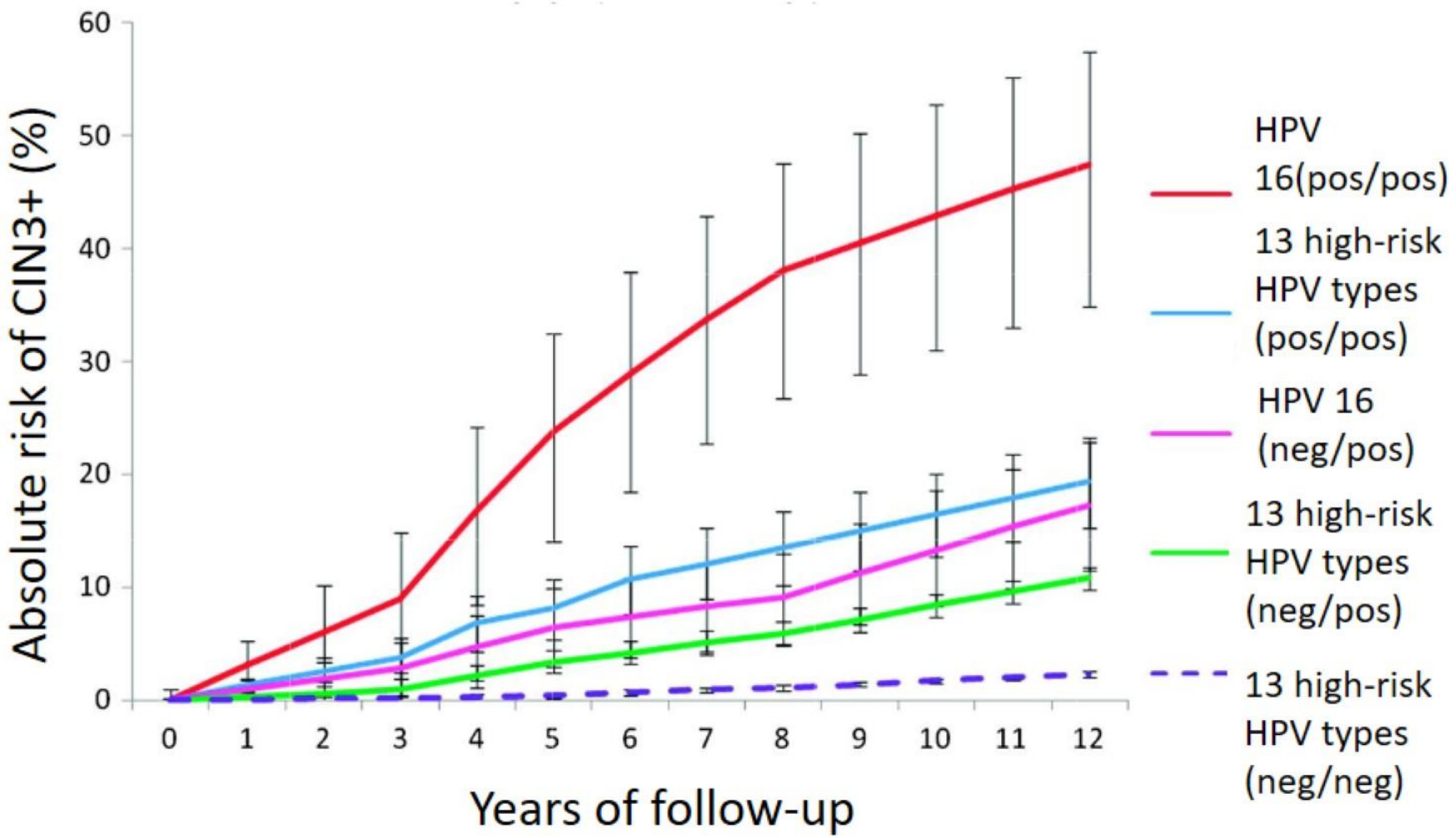
- The longer an HPV infection has been present, the higher the risk of pre-cancer and cancer
  - *Time matters (persistent infections much higher risk than new or transient infections)*
  - *Type matters (HPV 16 most dangerous)*
  - *Other patient factors don't matter if you know about HPV*
    - *Age, income, race/ethnicity, smoking, BMI, OCP, DMPA*
    - *Vaccination status will factor in future with more data and as vaccinated cohort ages into screening*

Most HPV infections become undetectable in 1-3 years
Precancer and cancer increase when infections persist



McCredie et al. Lancet Oncol. 2008 May;9(5):425-34.
Rodriguez ac. Et al J Natl Cancer Inst. 2008 2;100(7):513-7

Persistent HPV, especially HPV 16, is High Risk



Kjaer et al, *J Natl Cancer Inst*, 2010

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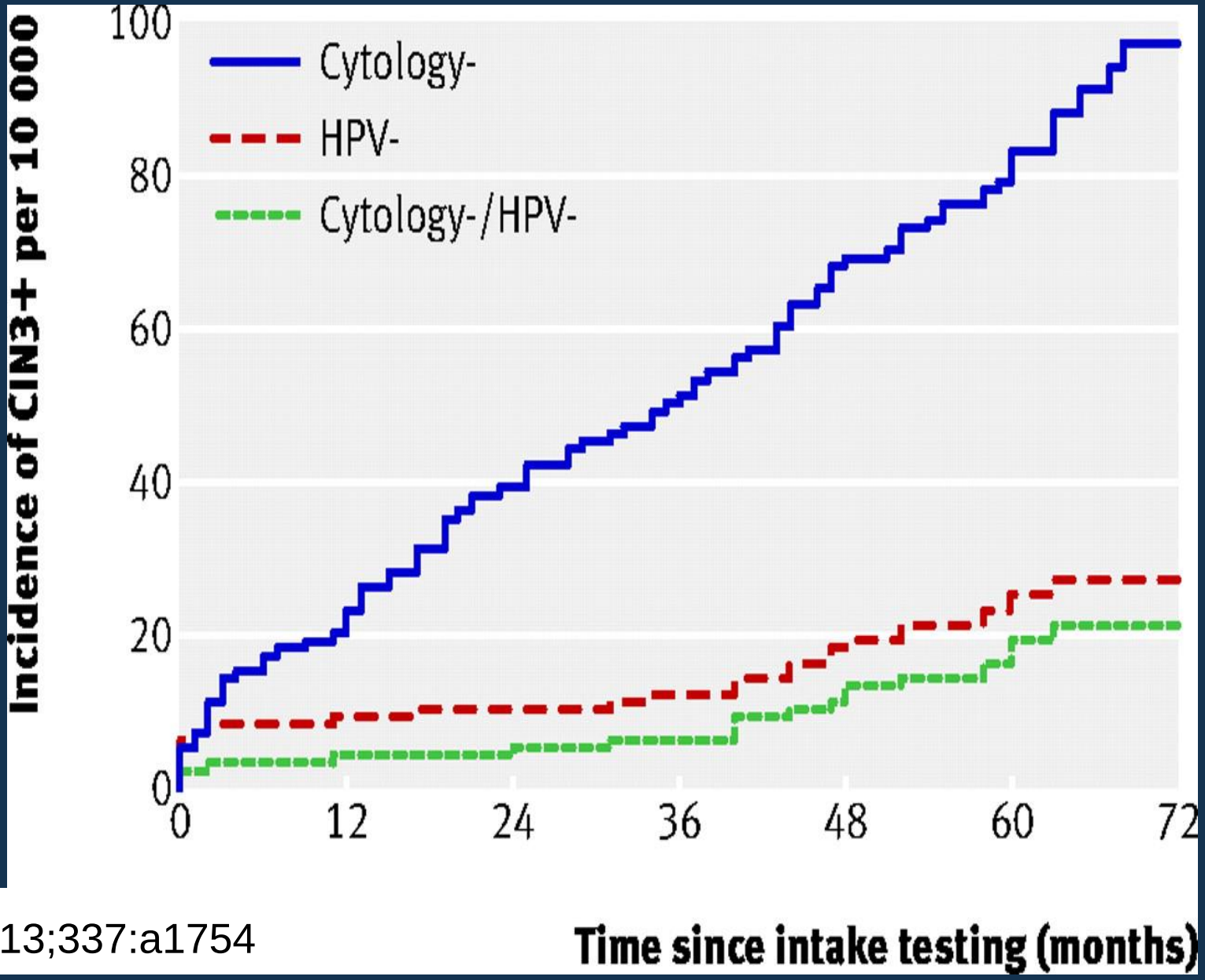
HPV-based screening is better than cytology alone

- Cytology is less sensitive than HPV testing.
- When cytology is used, it should be repeated more often.
  - When HPV testing or cotesting is recommended annually, if cytology is used instead, repeat it every 6 months..
  - When 3-year intervals are recommended for HPV or cotesting, repeat cytology annually.



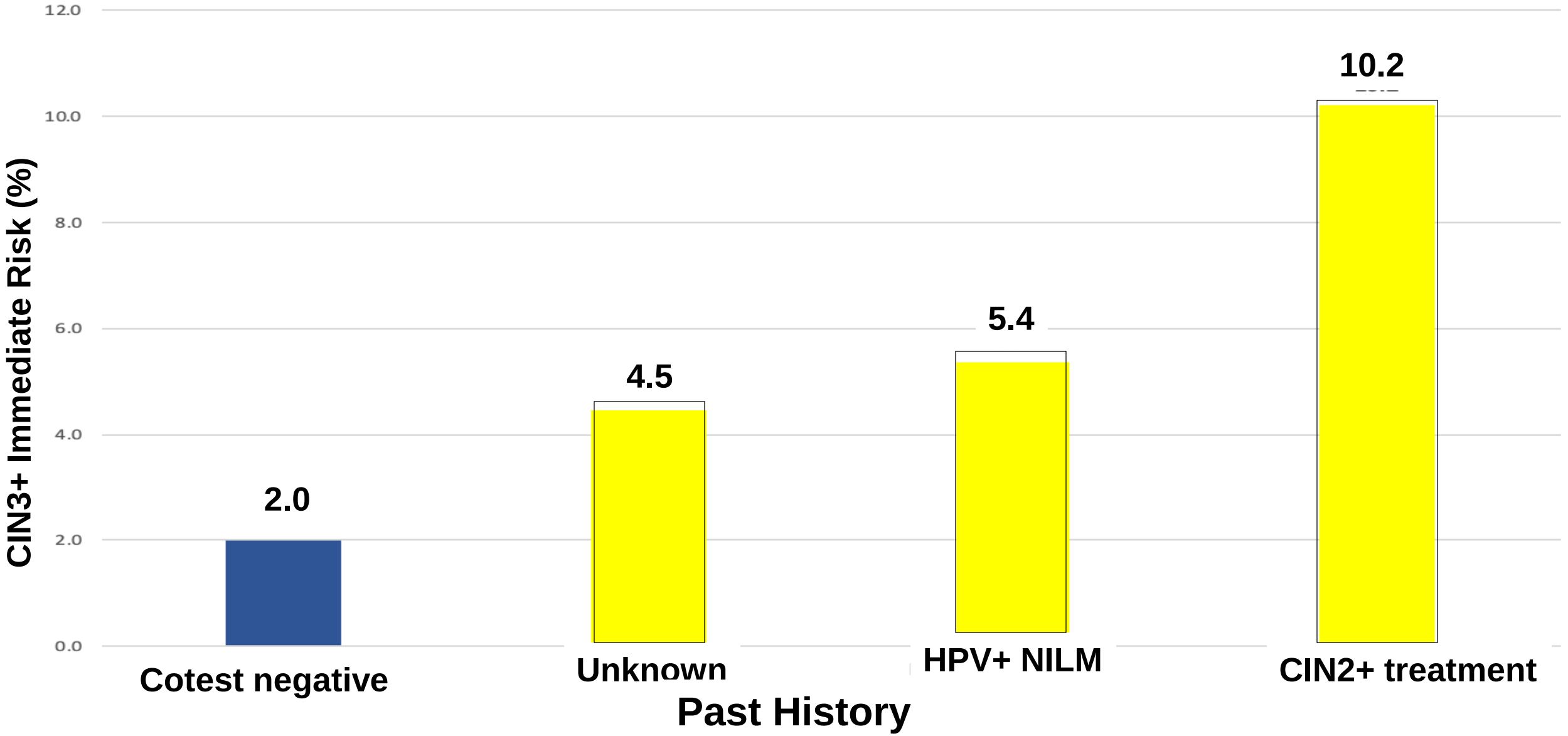
Dillner, BMJ 2008 Oct 13;337:a1754

Fundamental concept #3:
Management is based on risk, not results

- Risk of CIN3+ is determined by **current results** and **past history** *(including unknown history)*.
  - Same test results may yield different risk and recommendations depending on prior test results.

Past history influences current risk

Risk of CIN 3+ for HPV positive ASC-US based on prior testing

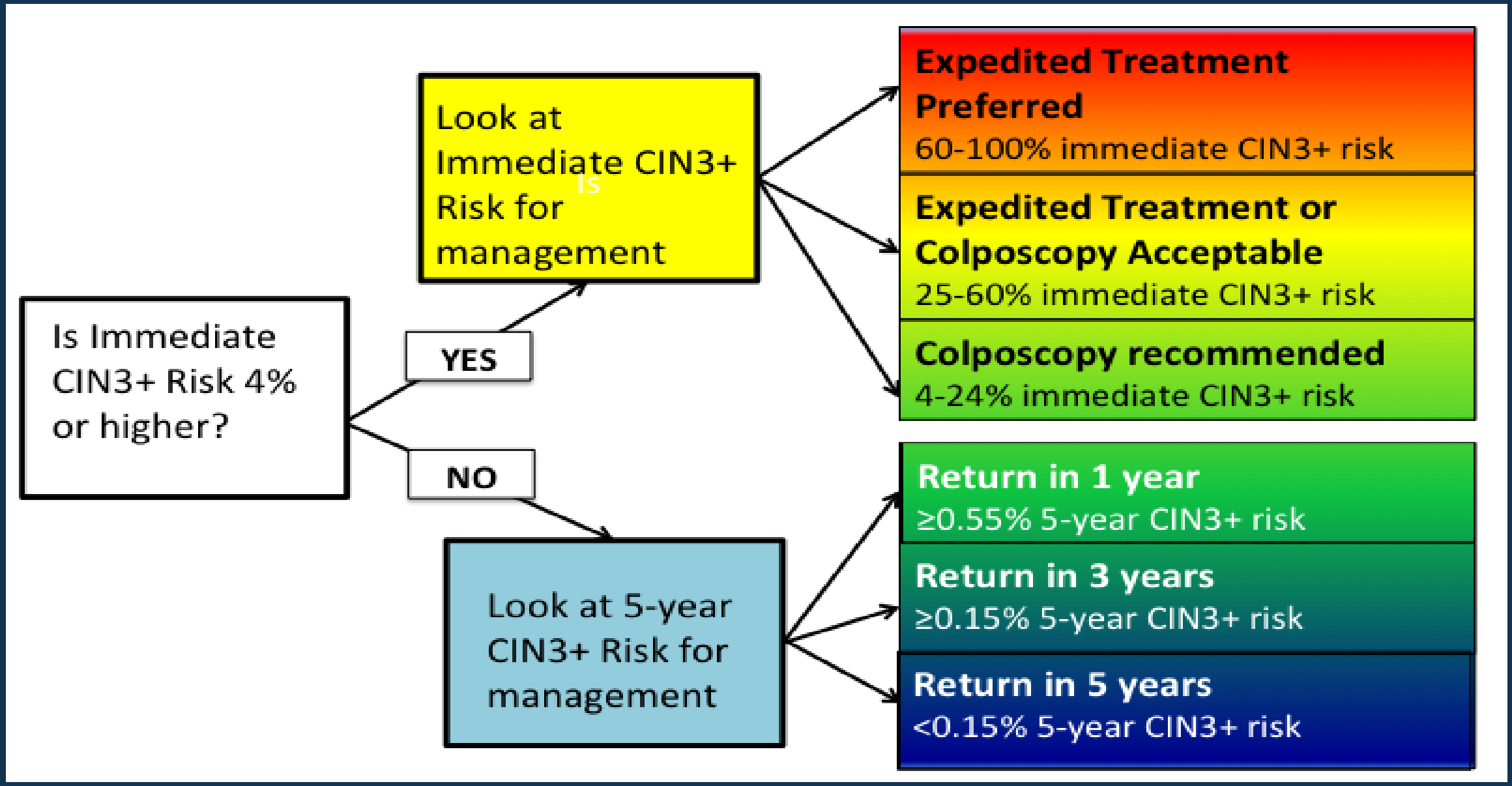


Management is stratified by risk levels

- ***Manage high-risk patients more aggressively***
- ***Manage moderate-risk patients the same***
- ***Manage low-risk patients less aggressively***

R. Perkins

Patients stratified into risk levels



Perkins RB et al. J Low Genit Tract Dis. 2020;24(2):102-131.

Case 1a

- Age: 39
- Pap: HSIL
- HPV-positive (no genotyping)
- History: Patient had cotesting within approximately the last 5 years) but she doesn’t remember the result.

3:02 40%

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Clinical Situation — Testing — Recommendation

Age

Under 25 YEARS | 25 to 29 YEARS | **30 to 65 YEARS** | Over 65 YEARS

Clinical Situation

- **Management of routine screening results**
- Return visit during pre-colposcopy surveillance
- Evaluation of a colposcopic biopsy
- Management of results during post-colposcopy surveillance
- Follow-up after treatment
- Special situation: Rarely screened patients
- Special situation: Symptomatic patients
- Special situation: Immunosuppressed patients

NEXT →

3:02 40%

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Clinical Situation — Testing — Recommendation

Current testing

HPV

None | Negative | **Positive (untyped)** | Positive (genotyped)

Cytology

rmal | ASC-US | LSIL | ASC-H | AGC | **HSIL**

Does the patient have previous screening test results?

YES | **NO**

← BACK | → NEXT

3:00 41%

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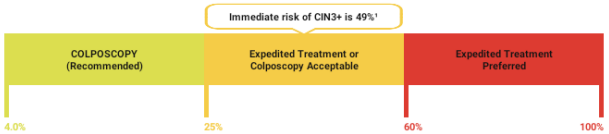
Clinical Situation — Testing — Recommendation

Recommendation

Colposcopy/Treatment[1]

After treatment, HPV-based testing at 6 months is preferred at follow-up visit[2]

Risk



Immediate risk of CIN3+ is 49%[1]

Special Populations

Pregnancy

← BACK | → START OVER

References

1. Egemen D, Cheung LC, Chen X, et al. Risk estimates supporting the 2019 ASCCP Risk-Based Management Consensus Guidelines. J Low Genit Tract Dis 2020;24:132–43.
2. Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis 2020;24:102–31.

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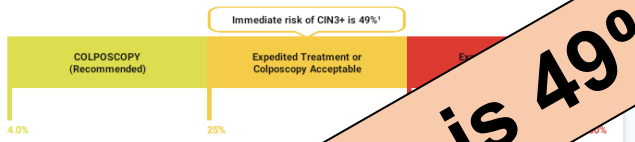
Colposcopy/Treatment[1]

After treatment, HPV-based testing at 6 months is preferred at follow-up visit[2]

Risk



Immediate ris

Special Pop

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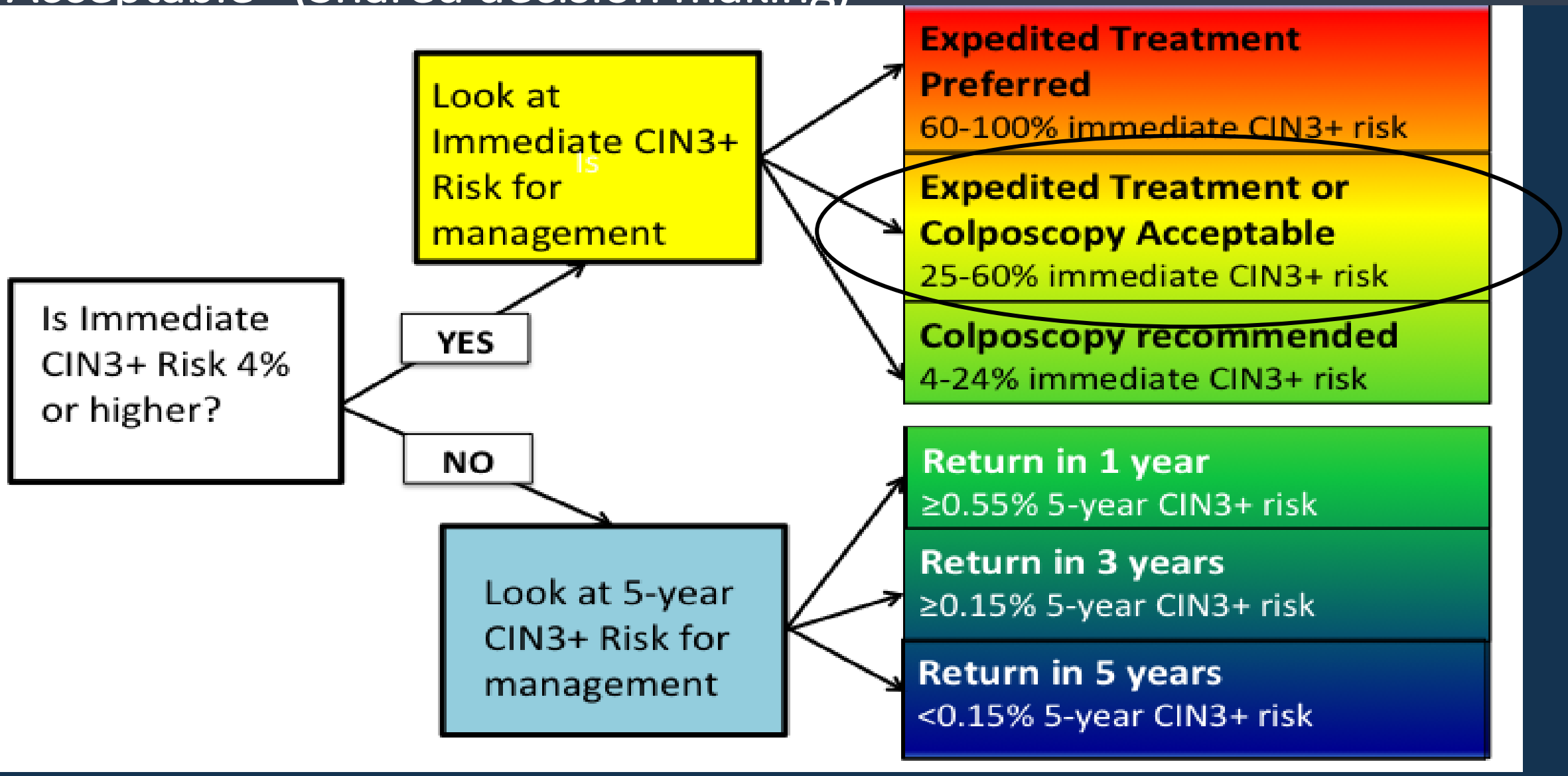
Immediate risk of CIN 3+ is 49%

Risk between 25 and 60%, Either Expedited Treatment or Colposcopy Acceptable (Shared decision making)



Perkins RB et al. J Low Genit Tract Dis. 2020;24(2):102-131.

Case 1b

- Age: 39
- Pap: HSIL
- HPV-positive (no genotyping)
- History: Pt has not had regular screening (last time >5 years ago) *i.e. She's rarely screened*

3:07 40%

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- Special situation: Symptomatic patients
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NEXT →

3:07 40%

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Clinical Situation — Testing — Recommendation

Current testing

HPV

None | Negative | **Positive (untyped)** | Positive (genotyped)

Cytology

rmal | ASC-US | LSIL | ASC-H | AGC | **HSIL**

← BACK → NEXT

3:07 40%

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Clinical Situation — Testing — Recommendation

Recommendation

Treatment[1]

After treatment, HPV-based testing at 6 months is preferred at follow-up visit[1]

Risk

Immediate risk of CIN3+ is 64%[1]

Special Populations

Pregnancy

← BACK → START OVER

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3:07 40%

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NEXT →

3:07 40%

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None | Negative | **Positive (untyped)** | Positive (genotyped)

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← BACK → NEXT

3:07 40%

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Clinical Situation — Testing — Recommendation

Recommendation

Treatment[1]

After treatment, HPV-based testing at 6 months is preferred at follow-up visit[1]

Risk

Immediate risk of CIN3+ is 64%[1]

Special Populations

Pregna…

← BACK → START OVER

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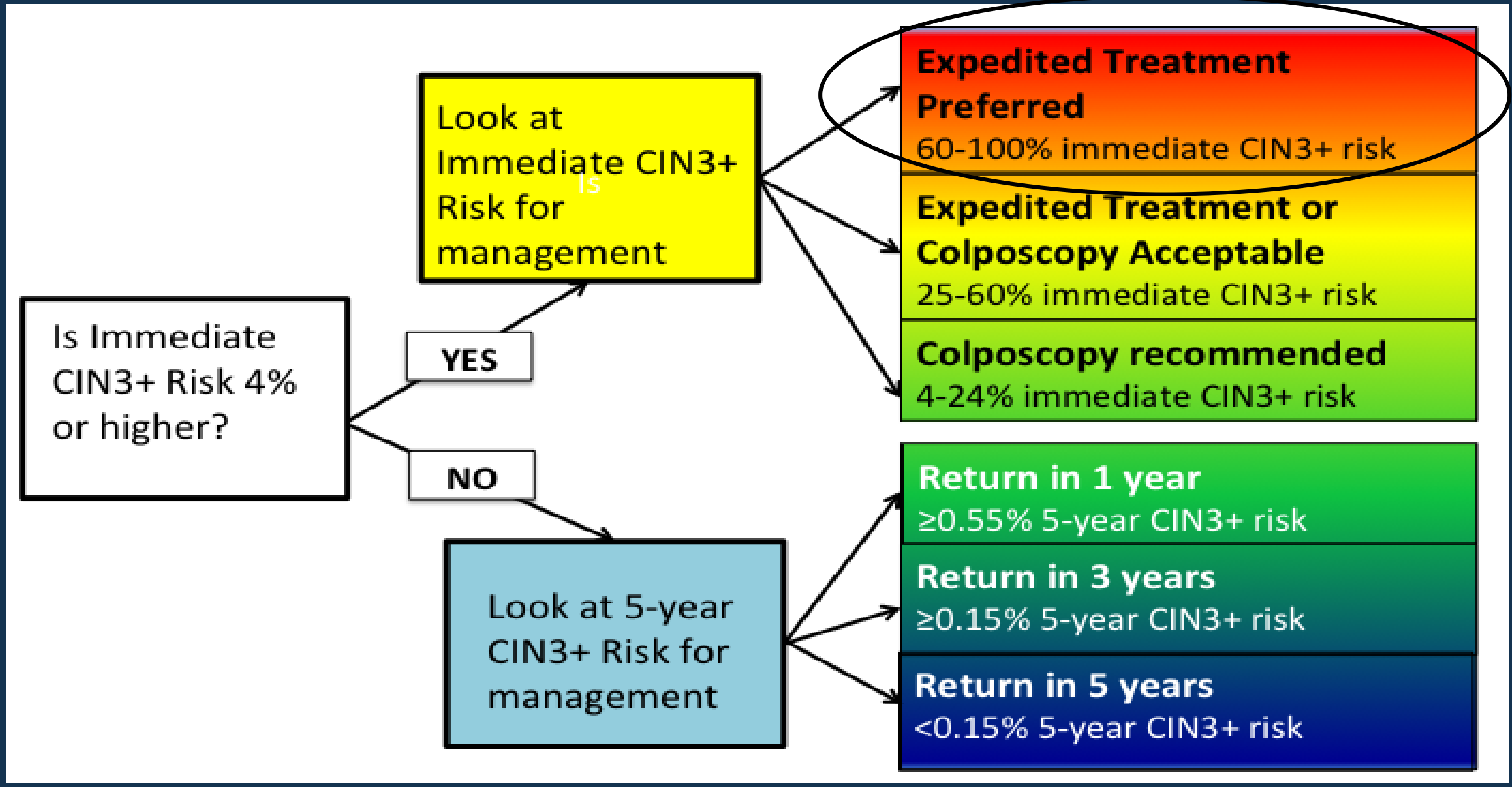
Immediate risk of CIN 3+ is 64%

Immediate treatment is preferred for highest risk.



Perkins RB et al. J Low Genit Tract Dis. 2020;24(2):102-131.

Case 1c

- 39 y.o. G2P2 presents for cervical screening.
  - Pap: HSIL
  - HPV: positive with genotyping - Type 16+
  - Has had regular screening, but doesn’t remember last results
- Next step?

11:10

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Clinical Situation — Testing — Recommendation

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- Over 65 YEARS

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- Special situation: Symptomatic patients
- Special situation: Immunosuppressed patients

Next →

11:12

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Clinical Situation — Testing — Recommendation

Current testing

HPV

- None
- Negative
- Positive (untyped)
- **Positive (genotyped)**

HPV DNA

- **HPV 16**
- HPV 18
- HPV Other

Cytology

-US | LSIL | ASC-H | AGC | **HSIL**

Does the patient have previous screening test results?

Yes | No

11:13

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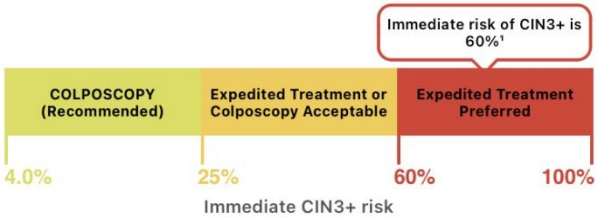
Clinical Situation — Testing — Recommendation

Recommendation

Treatment[1]

After treatment, HPV-based testing at 6 months is preferred at follow-up visit[2]

Risk



Immediate risk of CIN3+ is **60%[1]**

Special populations

Pregnancy

← Back | **Start Over**

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Next →

11:12

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HPV

- None
- Negative
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- **Positive (genotyped)**

HPV DNA

- **HPV 16**
- HPV 18
- HPV Other

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-US | LSIL | ASC-H | **HSIL**

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11:13

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Treatment[1]

After treatment, HPV-based testing at 6 months is preferred at follow-up visit[2]

Risk

mediate risk of CIN3+ is **60%**[1]

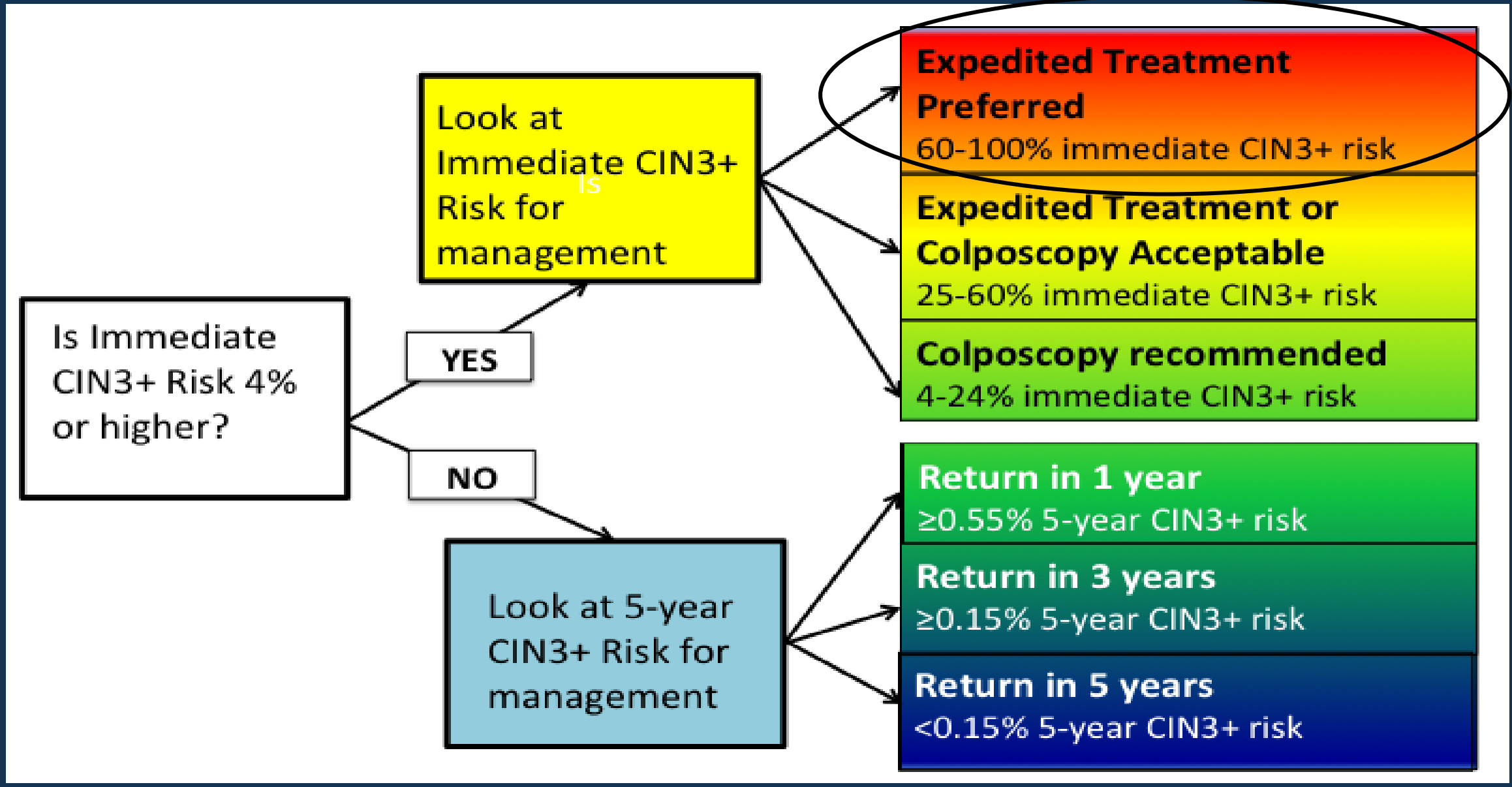
Special populations

Pregnancy

← Back | **Start Over**

Immediate risk of CIN 3+ is 60%

Immediate treatment is preferred for highest risk.



Perkins RB et al. J Low Genit Tract Dis. 2020;24(2):102-131.

Case 2a

- 35 y.o. P1 has cotesting at the time of insertion of her IUD
  - Pap: LSIL
  - HPV: Positive
  - Has had regular screening, but results unknown

- Next step?

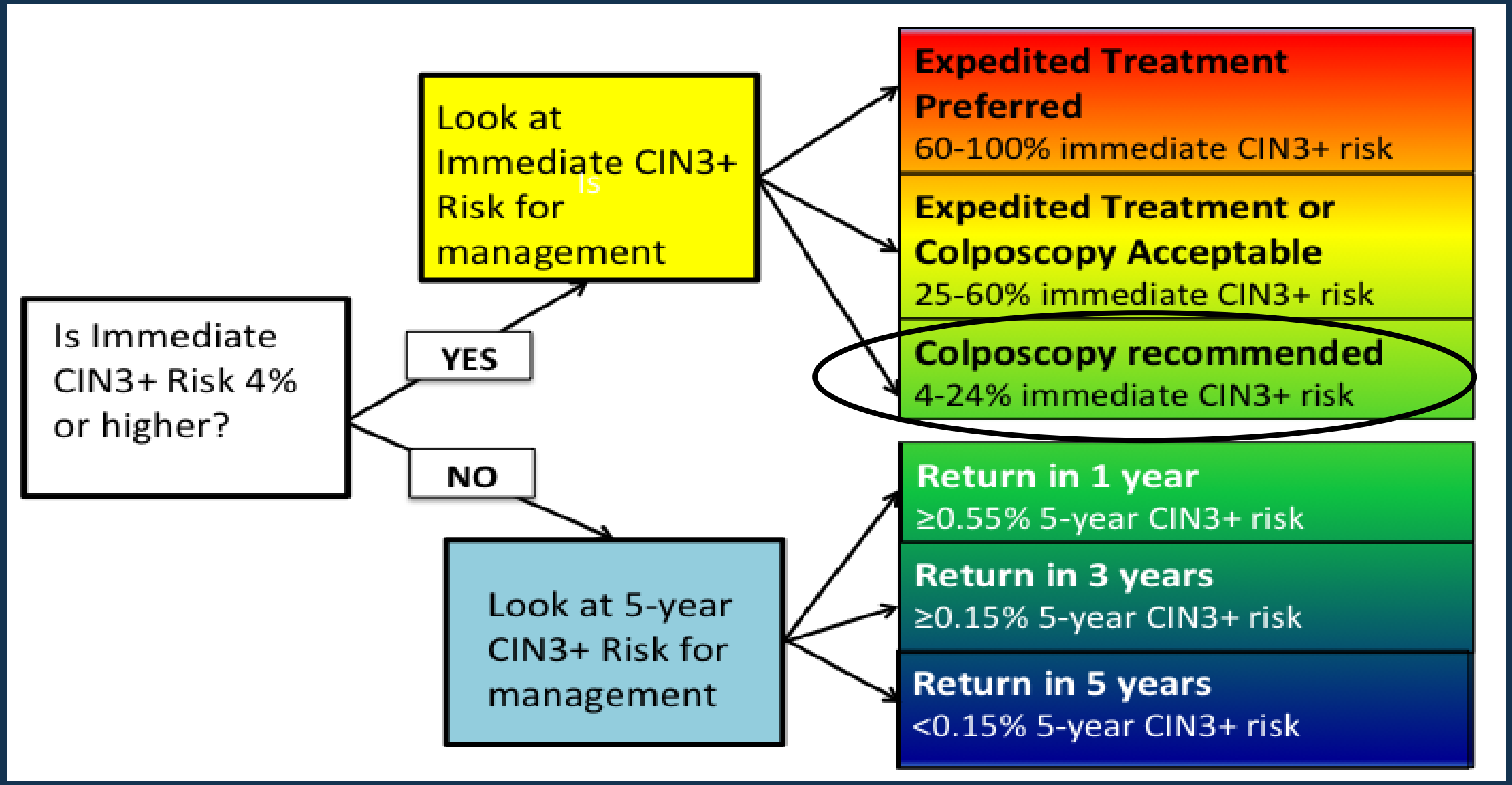
Case 2a

- 35 y.o. P1 has cotesting at the time of insertion of her IUD
  - Pap: LSIL
  - HPV: Positive
  - Has had regular screening, but results unknown

- Next step?

Immediate risk of CIN 3+ is 4.3%
Recommended management: Colposcopy

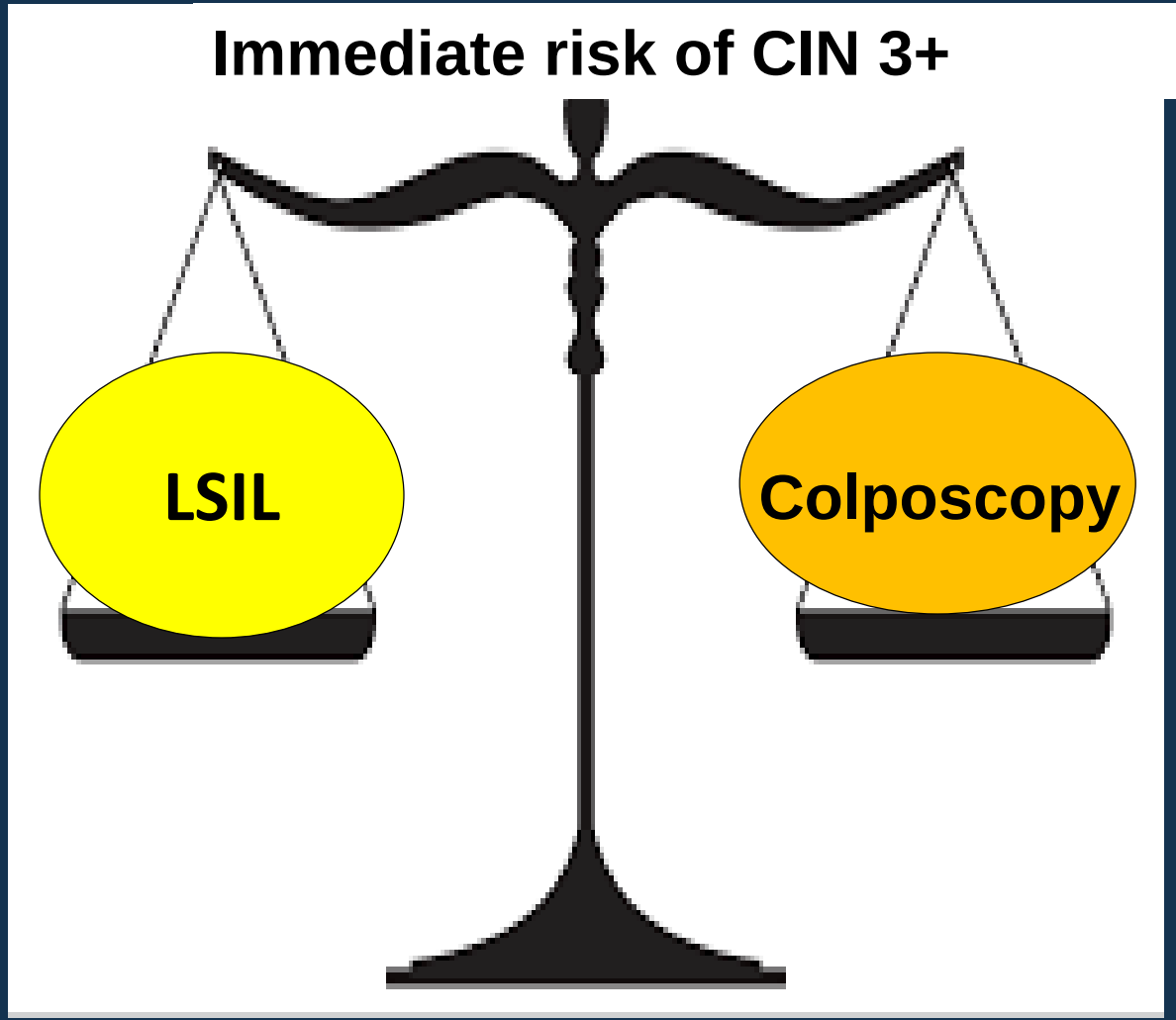
Colposcopy recommended when immediate risk is between 4 and 25%.



Perkins RB et al. J Low Genit Tract Dis. 2020;24(2):102-131

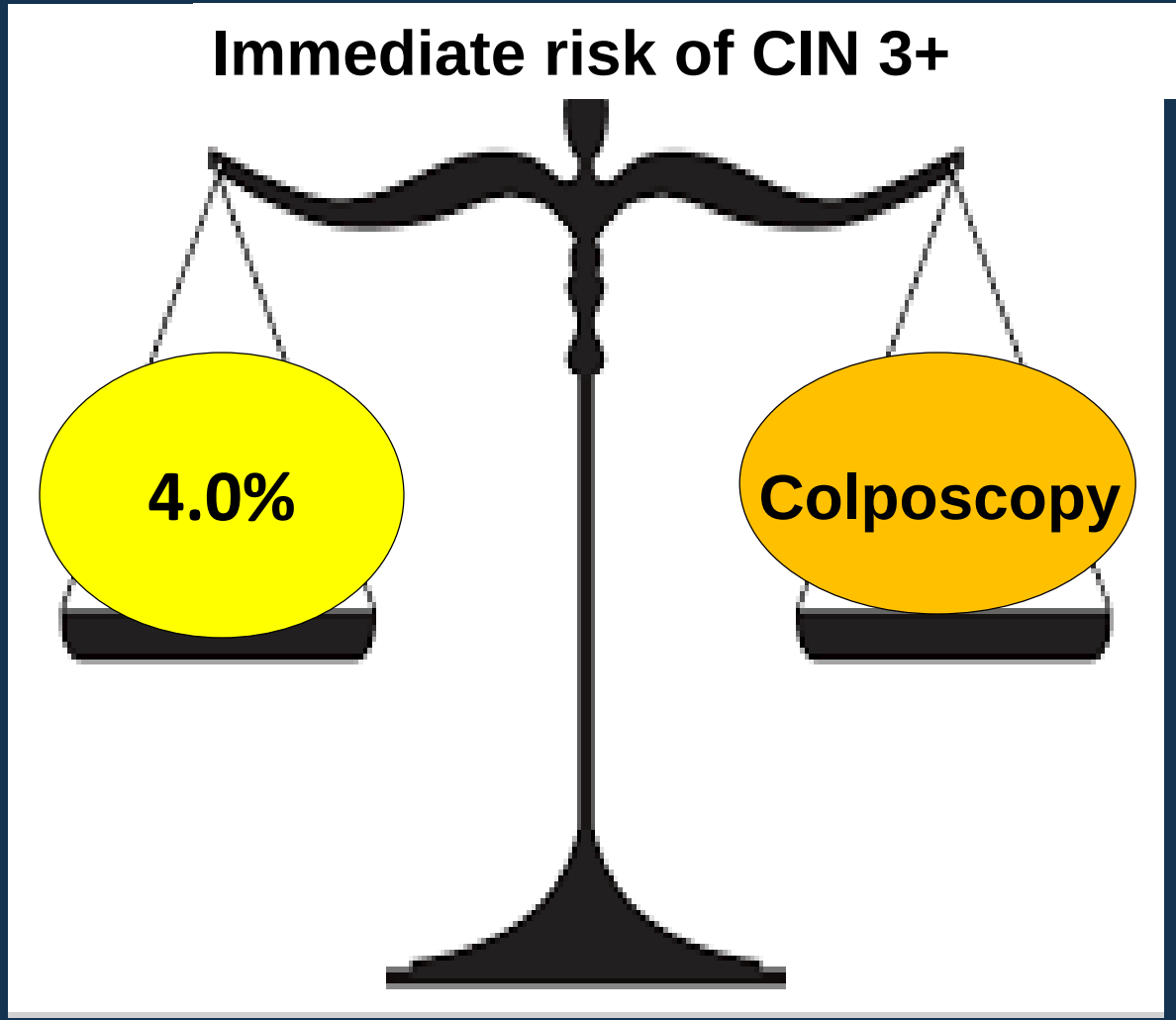
Colposcopy Threshold: 4%

- When estimated immediate risk of CIN3+ is ≥ 4.0% based on prior history and current results, referral to colposcopy is recommended.

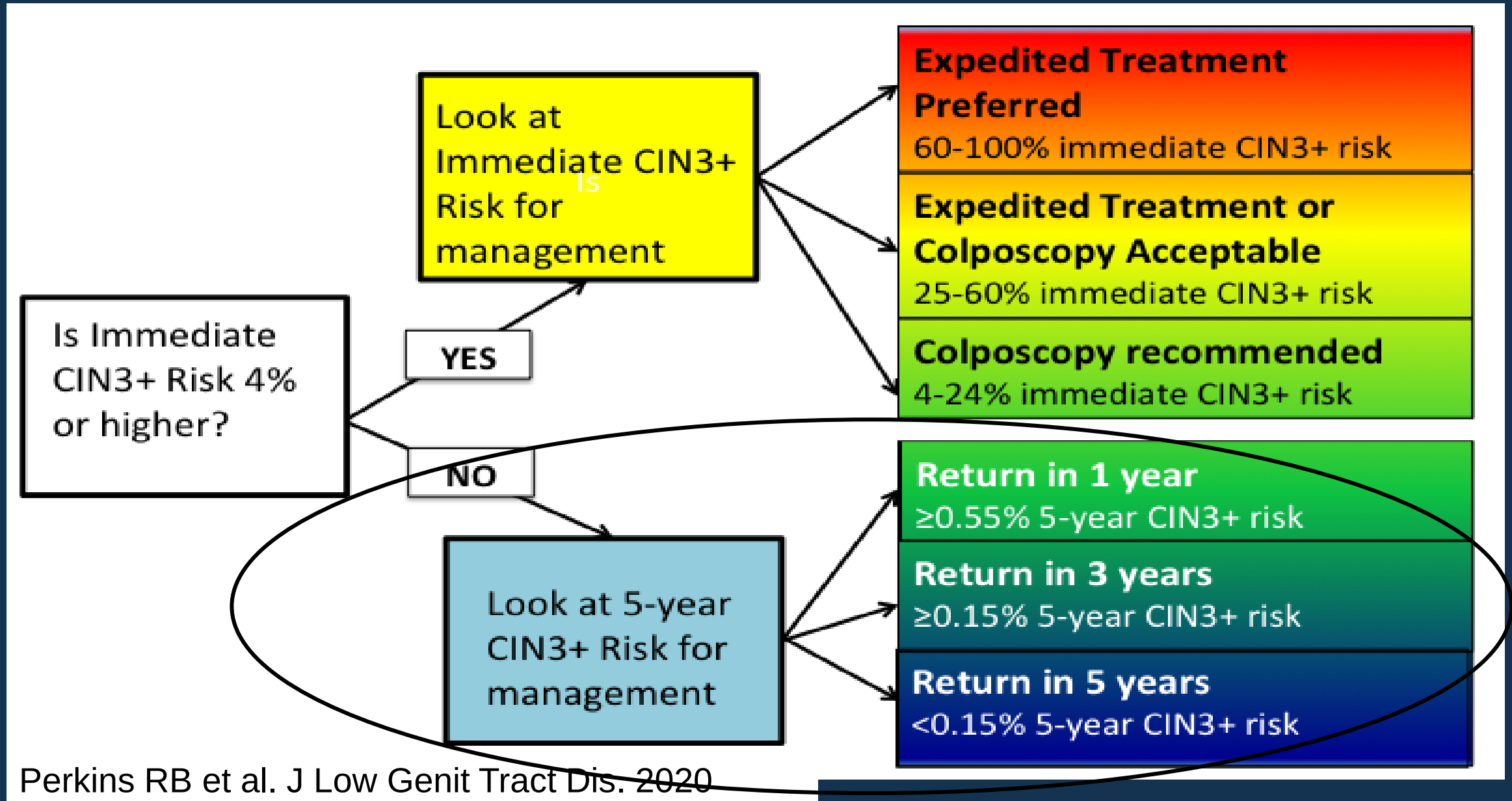


Colposcopy Threshold: 4%

- When estimated immediate risk of CIN3+ is ≥ 4.0% based on prior history and current results, referral to colposcopy is recommended.
- The equivalent risk of LSIL is 4%



If the *immediate* risk of CIN 3+ is <4%, management is based on *5 year* risk for CIN 3+



Perkins RB et al. J Low Genit Tract Dis. 2020

If the *immediate* risk of CIN 3+ is <4%, management is based on *5 year* risk for CIN 3+

1 year return
Risk falls below the risk for immediate colposcopy and the level for 3 year return. (≥0.55%)

3 year return
5 year CIN 3+ risk similar to that of a negative Pap test in a screening population (≥0.15%)

5 year return
5 year CIN3+ risk is similar to the risk of a negative HPV test or cotest in the screening population (<0.15%)

Case 2b

Same patient as case 2a, except now we know her last HPV test was at age 30 and was negative.

- 35 y.o. P1 has cotesting at the time of insertion of her IUD
  - Pap: LSIL
  - HPV: Positive
  - *Prior screening HPV negative*
- Next step?

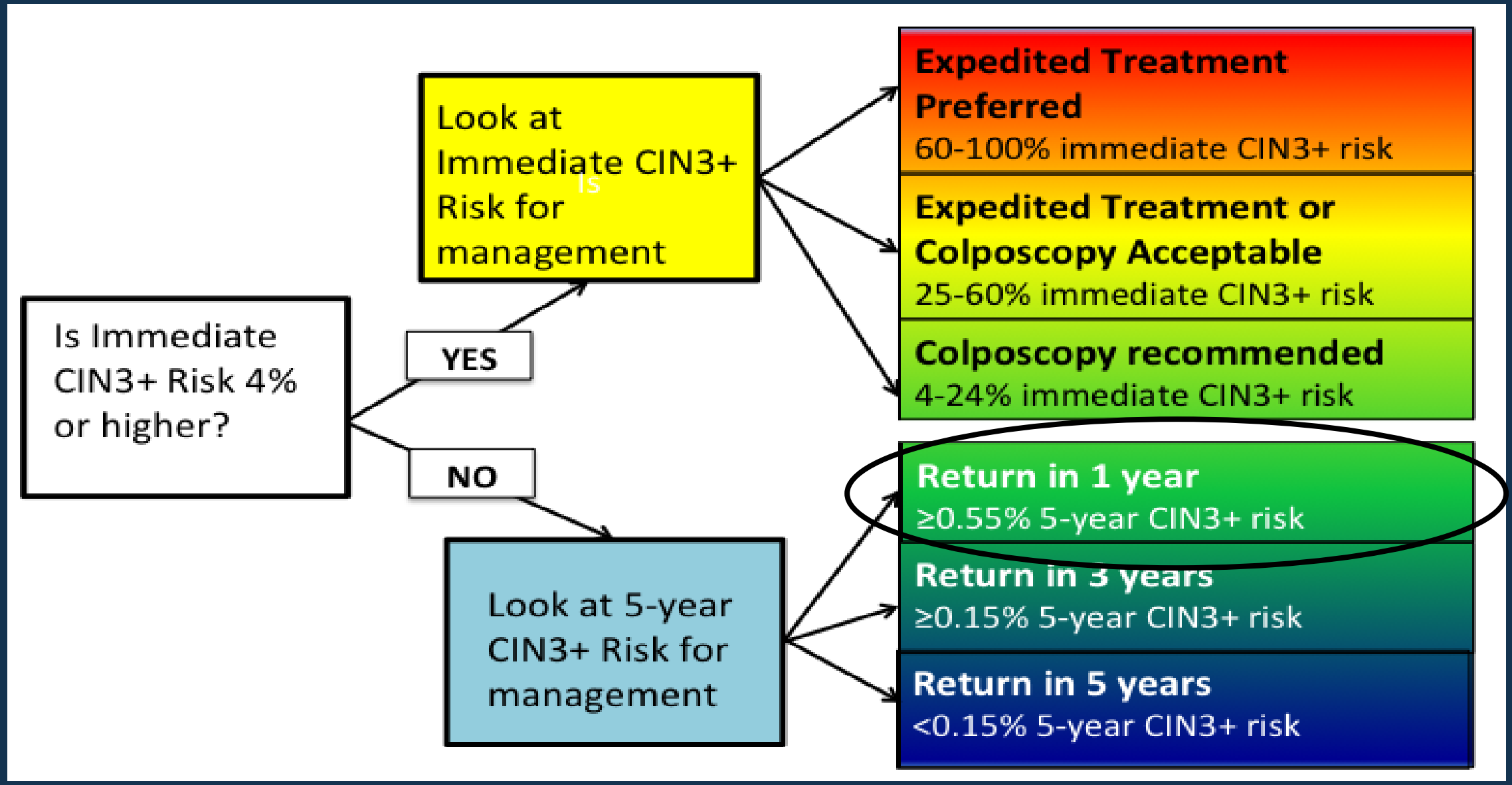
Case 2b

Same patient as case 2a, except now we know her last HPV test was at age 30 and was negative.

- 35 y.o. P1 has cotesting at the time of insertion of her IUD
  - Pap: LSIL
  - HPV: Positive
  - *Prior screening HPV negative*
- Next step?

Immediate risk of CIN 3+ is 2.1%
5 year risk of CIN 3+ is 3.8%
Recommended management: 1 year follow-up

Her immediate risk is 2.1% (<4%) and her 5 year risk is 3.8% (<0.55%)



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Documented prior negative HPV (KPNC)

HPV	Pap	Immediate risk (%) after prior HPV neg	Immediate risk (%) no prior HPV test
Pos	HSIL+	32.28	48.86
Pos	ASC-H	13.56	25.73
Neg	HSIL+	13.80	25.21
Pos	LSIL	2.10	4.27
Pos	ASC-US	2.03	4.45
Pos	NILM	0.74	2.13
Neg	LSIL	0.44	1.05
Neg	ASC-US	0.014	0.04
Neg	NILM	0.001	0.002

LSIL/ASCUS no longer meets colposcopy threshold

Egemen D et al. J Low Genit Tract Dis 2020;24(2):132-143.

Case 2c

What if this same patient with LSIL and prior HPV negative, now is positive for HPV 16?

- 35 y.o. P1 has cotesting at the time of insertion of her IUD
  - Pap: LSIL
  - HPV: Positive with genotyping - HPV 16+
  - *Prior screening HPV negative*

Case 2c

What if this same patient with LSIL and prior HPV negative, now is positive for HPV 16?

35 y.o. P1 has cotesting at the time of insertion of her IUD

Pap: LSIL

HPV: Positive with genotyping - HPV 16+

Prior screening HPV negative

Immediate risk of CIN 3+ is 6.7%
Recommended management: colposcopy

- **Knowing the HPV type and duration of HPV positivity affects risk and management.**

Impact of HPV type with prior negative HPV test (KPNC)

HPV Type	PAP Category	CIN3+ Immediate risk (%)	Cancer Immediate risk (%)
HPV16+	ASC-US	5.34	0.33
HPV 16+	LSIL	6.70	0.89

**HPV16 positive ASC-US and LSIL still exceed 4% threshold*

https://CervixCa.nlm.nih.gov/RiskTables

Clinical examples of 3-year return

Result	CIN3+ risk at 5 years
HPV-negative ASC-US screening result	0.40%
HPV-negative LSIL → HPV-negative NILM cotest	0.40%
Low-grade cotest → colposcopy CIN1 → HPV-negative NILM follow-up	0.42%
CIN2/3 treated with LEEP → 3 negative cotests	0.35%

Screening results leading to *1-year Return*

Result	CIN3+ immediate risk %
HPV-positive NILM	2.1%
HPV-negative LSIL	1.0%

Egemen D et al. J Low Genit Tract Dis. 2020;24(2):132-143

Case 3 Post colposcopy follow-up

- 32 y.o. P3
- Nov. 2019 Cotesting: ASC-US / HPV +
- Dec. 2019 Colposcopy: CIN 1
- Dec. 2020 Cotesting: ASC-US / HPV +

- Next step? (By the 2012 Guidelines, she'd need colposcopy.)

4:09 33%

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MANAGEMENT PUBLICATIONS DEFINITIONS

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- Management of routine screening results
- Return visit during pre-colposcopy surveillance
- Evaluation of a colposcopic biopsy
- **Management of results during post-colposcopy surveillance**
- Follow-up after treatment
- Special situation: Rarely screened patients
- Special situation: Symptomatic patients
- Special situation: Immunosuppressed patients

NEXT →

4:10 33%

ASCCP

MANAGEMENT PUBLICATIONS DEFINITIONS

Clinical Situation — Testing — Recommendation

Current testing

HPV

None | Negative | **Positive (untyped)** | Positive (genotyped)

Cytology

None | Normal | **ASC-US** | LSIL | ASC-H | AG

Does the patient have previous results since colposcopy? (?)

YES | **NO**

Colposcopy

NO CIN | **Histologic LSIL (CIN 1)** | Histologic HSIL (CIN 2)

Cytology prior to colposcopy

Normal | **ASC-US** | LSIL | ASC-H | AGC | HSI

← BACK → NEXT

4:10 33%

ASCCP

MANAGEMENT PUBLICATIONS DEFINITIONS

Clinical Situation — Testing — Recommendation

Recommendation

1-year follow-up[1]

HPV-based screening at follow-up visit[2]

Risk

5 year risk of CIN3+ is 6.0%[1]

← BACK → START OVER

References

1. Egemen D, Cheung LC, Chen X, et al. Risk estimates supporting the 2019 ASCCP Risk-Based Management Consensus Guidelines. J Low Genit Tract Dis 2020;24:132–43.
2. Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. J Low Genit Tract Dis 2020;24:102–31.

Case 3 Post colposcopy follow-up

- 32 y.o. P3
- Nov. 2019 Cotesting: ASC-US / HPV +
- Dec. 2019 Colposcopy: CIN 1
- Dec. 2020 Cotesting: ASC-US / HPV +

- Next step? (By the 2012 Guidelines, she'd need colposcopy.)

5 year risk: 6.0%
Recommended management: 1 year follow-up

Post-colposcopy results leading to 1-year return

Pre-colposcopy test result	Colposcopy result	Post-colposcopy test result	Immediate CIN3+ risk
Low-grade*	<CIN2	HPV-positive NILM	2.0%
Low-grade*	<CIN2	HPV-positive ASCUS/LSIL	3.1%

**Low-grade defined as HPV+/NILM, ASC-US, or LSIL cytology*

Egemen D et al. J Low Genit Tract Dis. 2020;24(2):132-143

What if her cotest at one year follow-up is still ASC-US, HPV+

- She now has a positive HPV that has persisted over two years, and the next step is again colposcopy.

- If CIN 1 persists, observation is still preferred over treatment.
  - Even persistent CIN 1 is low risk. The risk of hiding an occult precancer is low.
  - Treatment is an option after shared decision making.

Case 4a Post LEEP follow-up

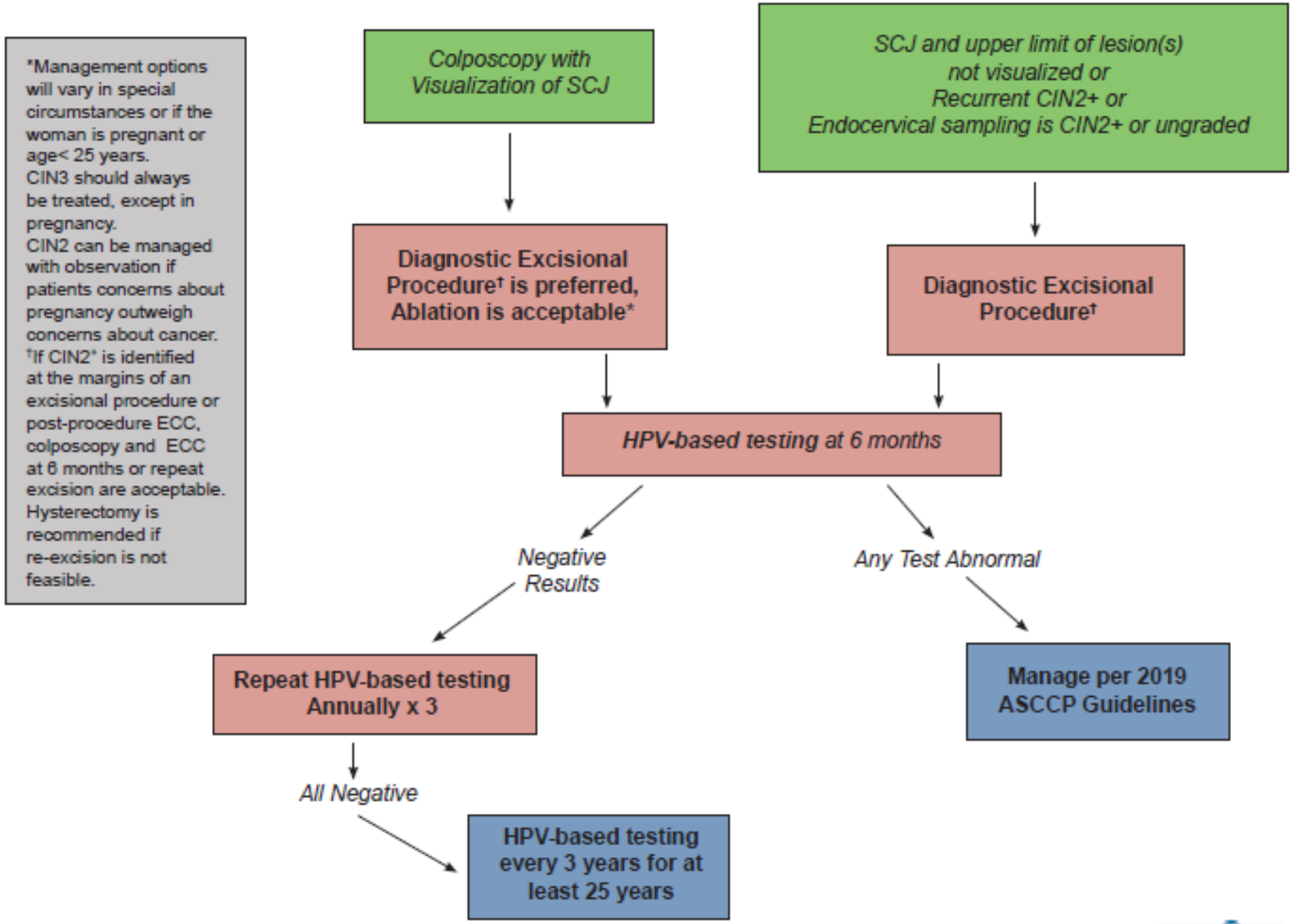
- 36 y.o. P2
- Oct. 2020 Cotesting: ASC-H / HPV + (hr Other)
- Nov. 2020 Colposcopy: CIN 3
- Nov. 2020 LEEP: CIN 3 (excisional margins free of dysplasia)
- How should we follow her post LEEP?

Case 4a Post LEEP follow-up

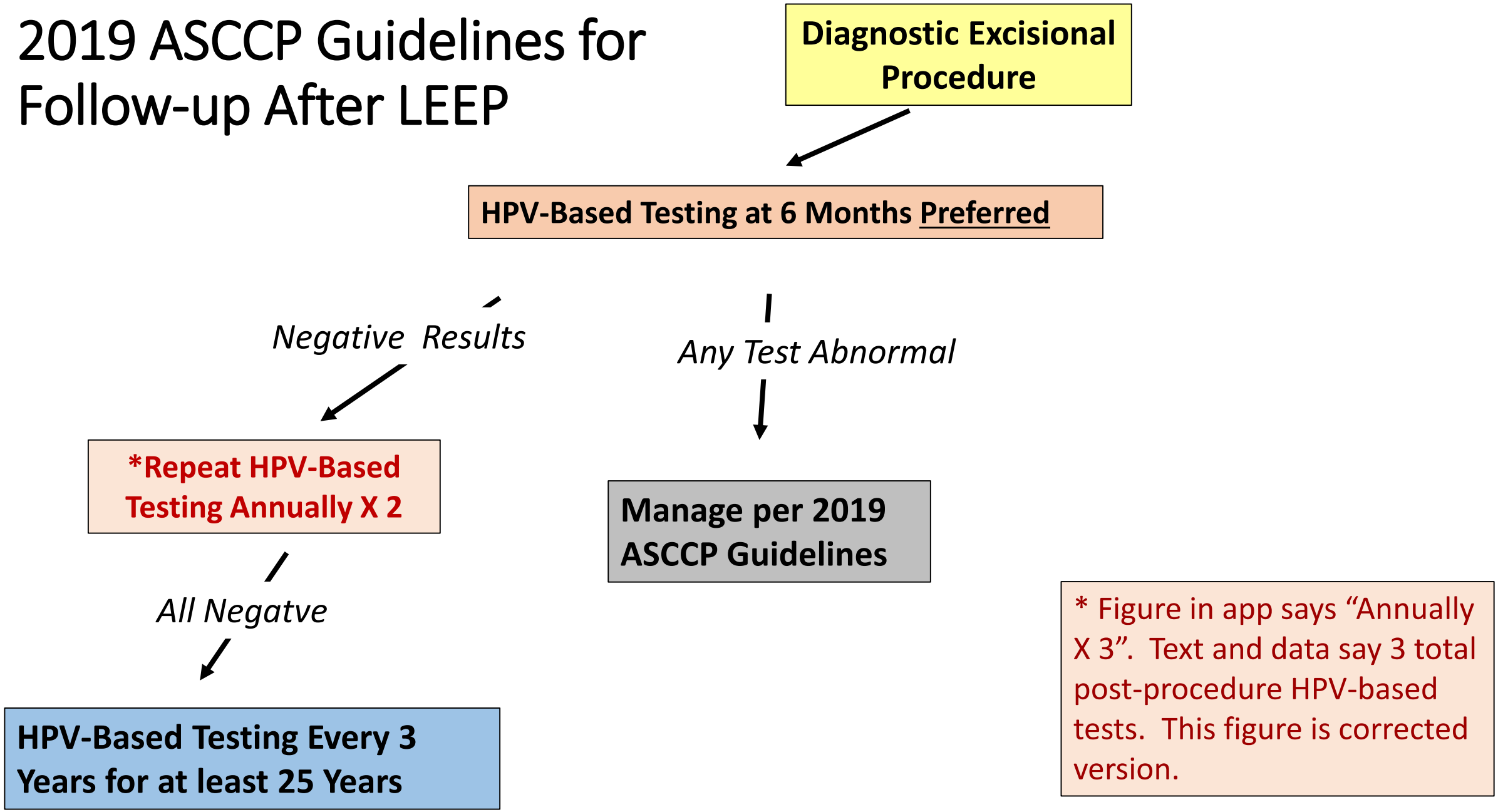
- 36 y.o. P2
- Oct. 2020 Cotesting: ASC-H / HPV + (hr Other)
- Nov. 2020 Colposcopy: CIN 3
- Nov. 2020 LEEP: CIN 3 (lesion extends to endocervical margin)
- How should we follow her post LEEP?

F/u visit	5 year risk CIN 3+ after negative HPV / Cotest	Recommended next visit
#1 six months post LEEP	1.7 /2.0	Return 1 year
#2 one year later	0.68 / 0.91	Return 1 year
#3 one year later	0.35 / 0.44	Return 3 years

Figure 7: Management of Histologic HSIL (CIN2 or CIN3 or Not Further Specified)*



2019 ASCCP Guidelines for Follow-up After LEEP



* Figure in app says “Annually X 3”. Text and data say 3 total post-procedure HPV-based tests. This figure is corrected version.

Perkins RB, Guido RS, Castle PD et al J Lower Genital Tract Dis. 2020;24(2):120-131

Case 4b Post LEEP follow-up (positive margins)

- 36 y.o. P2
- Oct. 2020 Cotesting: ASC-H / HPV + (hr Other)
- Nov. 2020 Colposcopy: CIN 3
- Nov. 2020 LEEP: CIN 3 (HSIL present at endocervical margin)
- How should we follow her post LEEP?

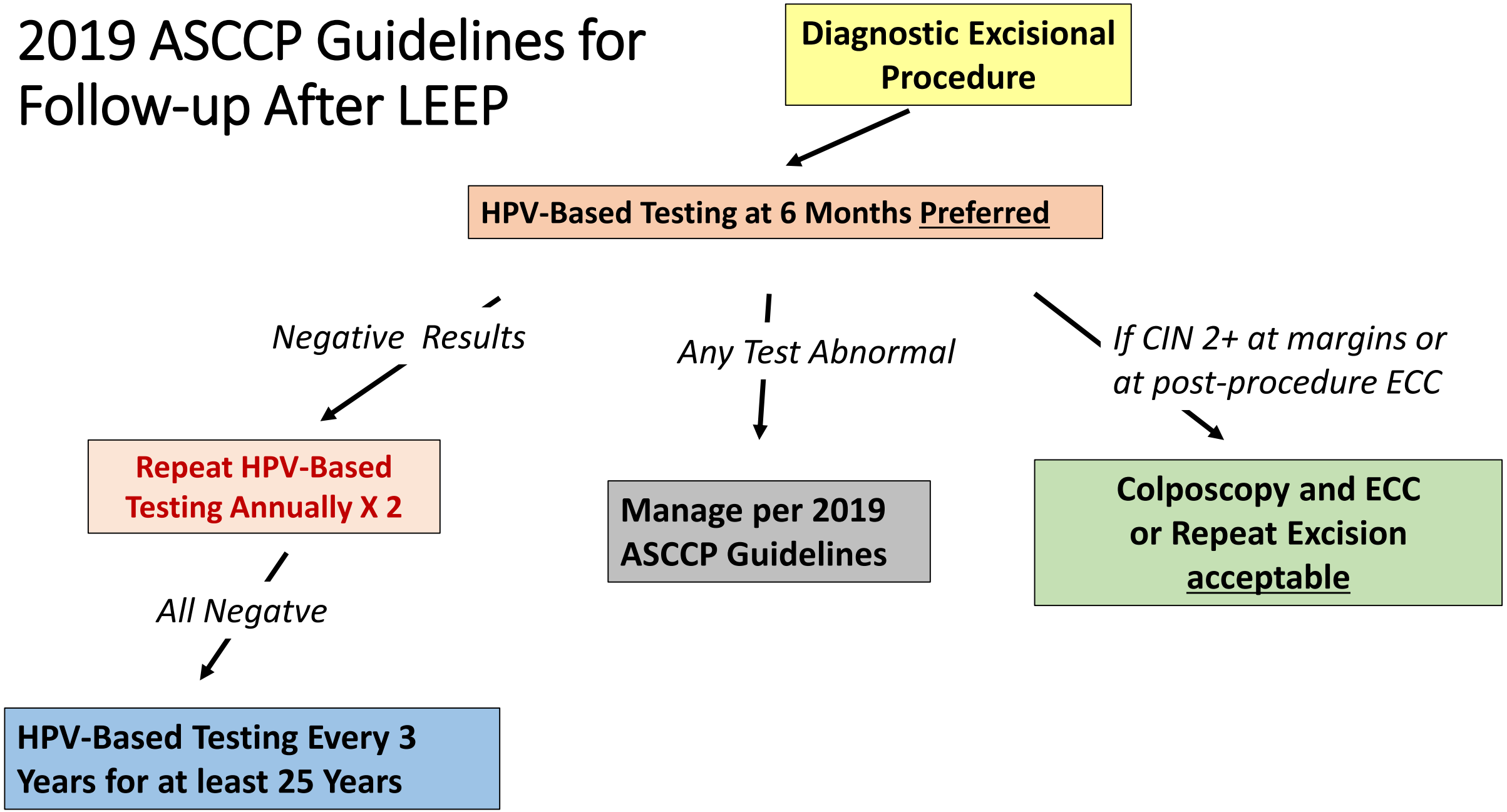
Risk of Recurrence Post LEEP / Cone if Margins Involved

- Meta analysis of 97studies (44,446 women)
  - Frequency of incomplete excision: LLETZ/ LEEP 25.9%
- Frequency of persistent / recurrent CIN 2+ after excision
  - Clear margins - 6.6%
  - Margins involved - 17.1%
  - RR 4.8

- HPV testing finds recurrence better than margin status
  - Sensitivity of positive margin to detect recurrent CIN 2+: 55.8%
    - Sensitivity of positive HPV test : 91.0%
  - Neg HPV test associated with 0.8% risk of recurrent CIN 2+
    - Recurrence risk with negative margins: 3.7%

Arbyn M et al Lancet Oncol 2017; 18:1665-79

2019 ASCCP Guidelines for Follow-up After LEEP



Perkins RB, Guido RS, Castle PD et al J Lower Genital Tract Dis. 2020;24(2):120-131

Summary: What's New in the 2019 Guidelines?

- Colposcopy can now be deferred in certain patients with HPV infection but low risk of CIN 3+
  - LSIL, ASC-US, NILM/HPV+ (HRO) ***after a documented negative screening HPV test or cotest.***
  - Repeat HPV test or cotest in 1 year recommended.

Summary: What's New in the 2019 Guidelines?

- New Guidance for Expedited Treatment Without Colposcopic Biopsy, e.g. "see and treat" - For non-pregnant patients ≥ 25 years of age
  - *Preferred* if immediate risk of CIN 3+ ≥60%
    - HSIL Cytology plus HPV 16+: 60%
    - HSIL Cytology plus HPV + regardless of HPV genotype in rarely or never screened patients (no screening in > 5 years): 64%
  - *Acceptable* if immediate risk of CIN 3+ ≥25% and <60%
    - HPV negative HSIL: 25%
    - HPV + ASC-H: 26%
    - HPV + AGC: 26%
    - HPV + HSIL: 49%
  - Shared decision making recommended with expedited treatment especially if future fertility is a consideration

Summary: What's New in the 2019 Guidelines?

Recommendations for treatment

- Excision is recommended over ablation in the U.S. for CIN 2, CIN 3, AIS.
- Observation rather than treatment is recommended for CIN 1.

Immediate surveillance after treatment of CIN 2/3

- HPV-based testing at 6 months, then annually for a total of 3 consecutive negative tests
  - Preferred even if margins positive.
- Surveillance with HPV testing or co-testing should continue at 3-year intervals for at least 25 years
- Continued surveillance at 3-year intervals beyond 25 years is acceptable for as long as the patient's life expectancy and ability to be screened are not significantly compromised by serious health issues.

Summary: What's New in the 2019 Guidelines?

- All positive primary HPV screening tests, regardless of genotype, should have reflex cytology testing from the same specimen.
  - Cytology may inform colposcopy practice, e.g. expedited treatment for HPV-16 positive HSIL cytology.
- If HPV based testing is not available, surveillance with cytology alone may be used
  - Because cytology is less sensitive than HPV testing, when 1 year intervals are recommended for HPV or cotesting, every 6 months testing with cytology may be used. When every 3 year testing is recommended for HPV or cotesting, annual testing with cytology may be substituted.
- Only two HPV tests are currently FDA approved for primary HPV screening. Other FDA approved tests should only be used as part of cotesting in the context of management.
  - Unless sufficient, rigorous data are available to support use in management

2019 Consensus Guidelines can Accommodate Future Technologies Currently Under Development *plus* Vaccination Status.

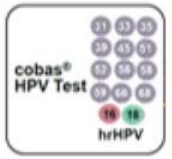
Cytology-based

Cytology / Automation

p16/Ki-67 / Automation

Molecular

HPV genotyping

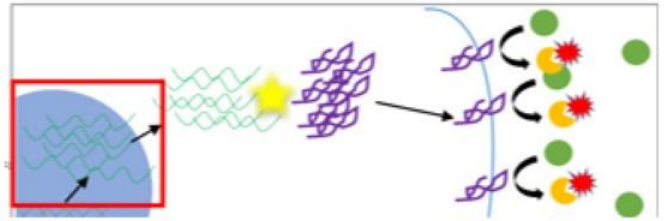


Methylation

Visual

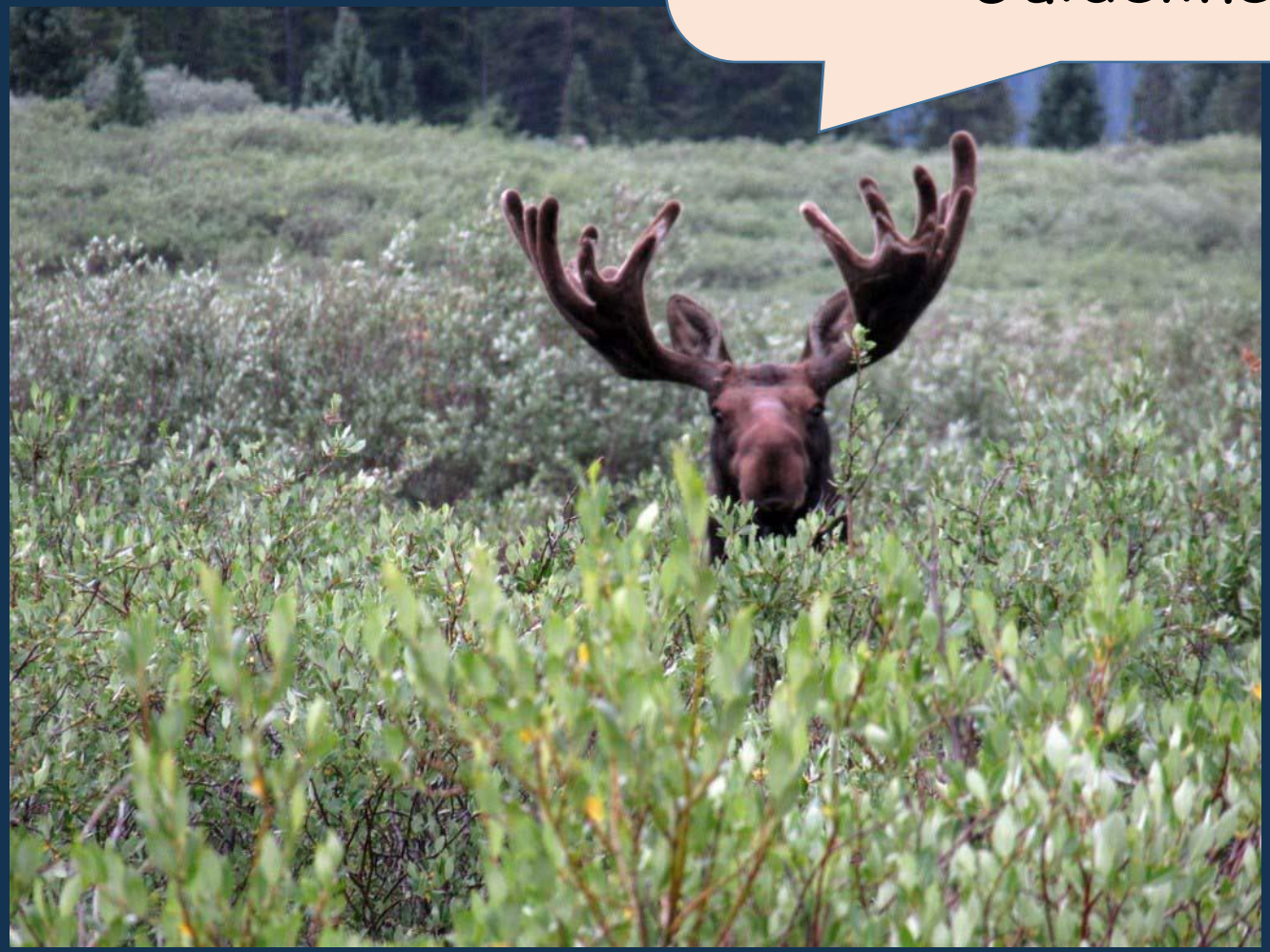
VIA / Automation

In-vivo imaging



ASCCP

Finally, a brief discussion of the new American Cancer Society screening Guidelines



U.S. Preventive Services Task Force 2018 Cervical Cancer Screening Guidelines

Population	Recommendation	Grade (What's This?)
Women aged 21 to 65 years	The USPSTF recommends screening for cervical cancer every 3 years with cervical cytology alone in women aged 21 to 29 years. For women aged 30 to 65 years, the USPSTF recommends screening every 3 years with cervical cytology alone, every 5 years with high-risk human papillomavirus (hrHPV) testing alone, or every 5 years with hrHPV testing in combination with cytology (cotesting). See the Clinical Considerations section for the relative benefits and harms of alternative screening strategies for women 21 years or older.	A
Women older than 65 years	The USPSTF recommends against screening for cervical cancer in women older than 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer. See the Clinical Considerations section for discussion of adequate prior screening and risk factors that support screening after age 65 years.	D
Women younger than 21 years	The USPSTF recommends against screening for cervical cancer in women younger than 21 years.	D
Women who have had a hysterectomy	The USPSTF recommends against screening for cervical cancer in women who have had a hysterectomy with removal of the cervix and do not have a history of a high-grade precancerous lesion (ie, cervical intraepithelial neoplasia [CIN] grade 2 or 3) or cervical cancer.	D

U.S. Preventive Services Task Force
2018 Cervical Cancer Screening Guidelines
for women aged 21 – 65.
Level A recommendation

The USPSTF recommends screening for cervical cancer every 3 years with cervical cytology alone in women aged 21 to 29 years.

For women aged 30 to 65 years, the USPSTF recommends screening

- **every 3 years with cervical cytology alone,**
- **every 5 years with cotesting (hrHPV testing in combination with cytology) OR**
- **every 5 years with high-risk human papillomavirus (hrHPV) testing alone.**

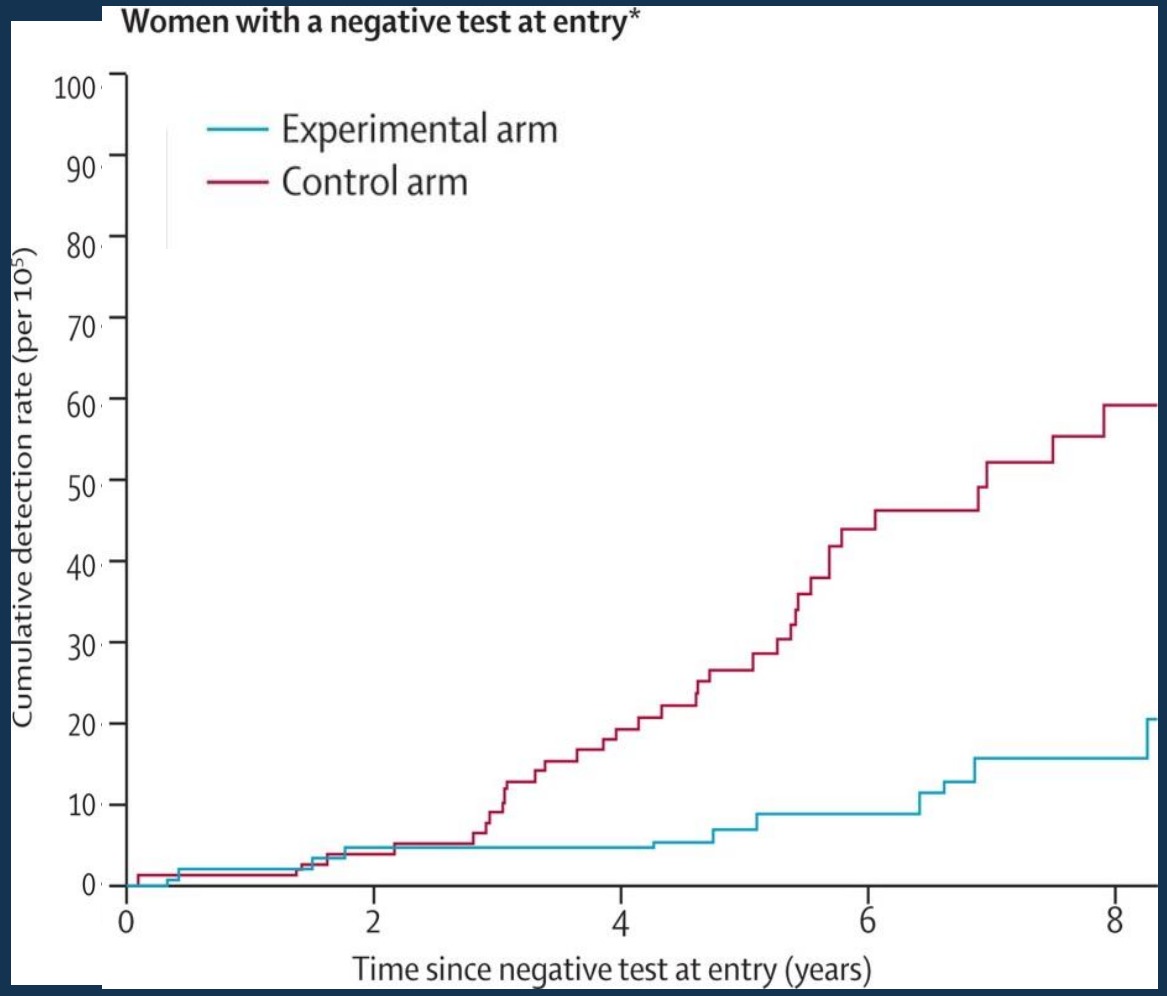
Some terminology:
Primary HPV Testing, Reflex HPV testing, Cotesting

- "*Reflex HPV*" uses HPV status to triage minimally abnormal Pap results
  - ASC-US or LSIL
- "*Cotesting*" is the combined use of cytology plus HPV for cervical screening
  - In wide use for screening women ≥ age 30 with introduction of 2012 guidelines
- "*Primary HPV Testing*" is screening with HPV alone.

Benefits of screening with HPV: Studies from U.S. and Europe

- HPV based screening has higher sensitivity and NPV than Pap alone. Sensitivity of cotesting is highest
  - Increased sensitivity = lower specificity
- HPV based screening leads to earlier diagnosis of CIN 3+ and Cancer
- Incorporating HPV finds more AIS than cytology alone

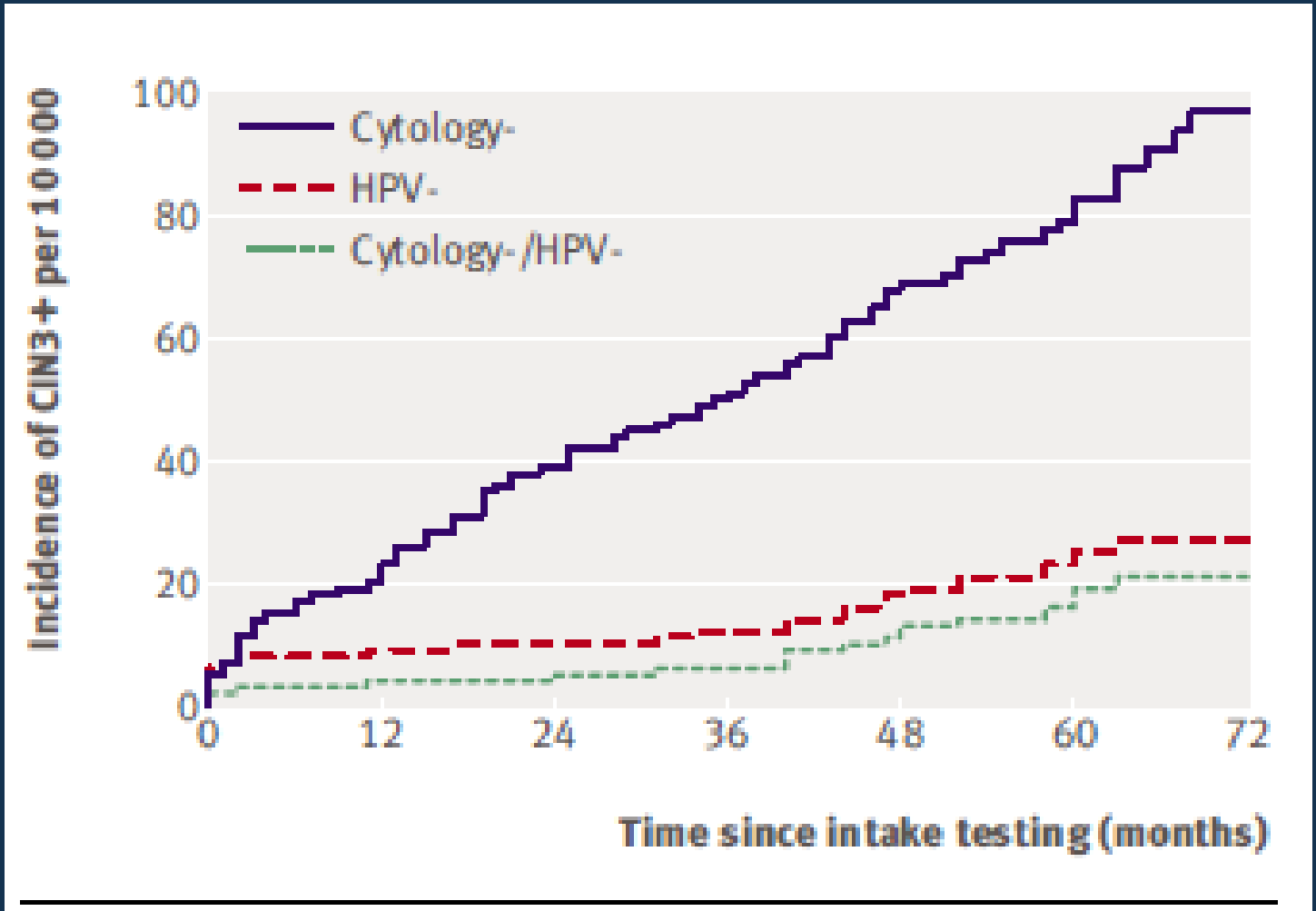
Pooled Analysis of 4 European RCTs of HPV-based Screening vs Cytology



Ronco G, Dillner J, Elfstrom KM et al. Lancet Nov 3, 2013


Won't our patients lose a lot of protection if we stop cotesting and screen with HPV alone?
agw

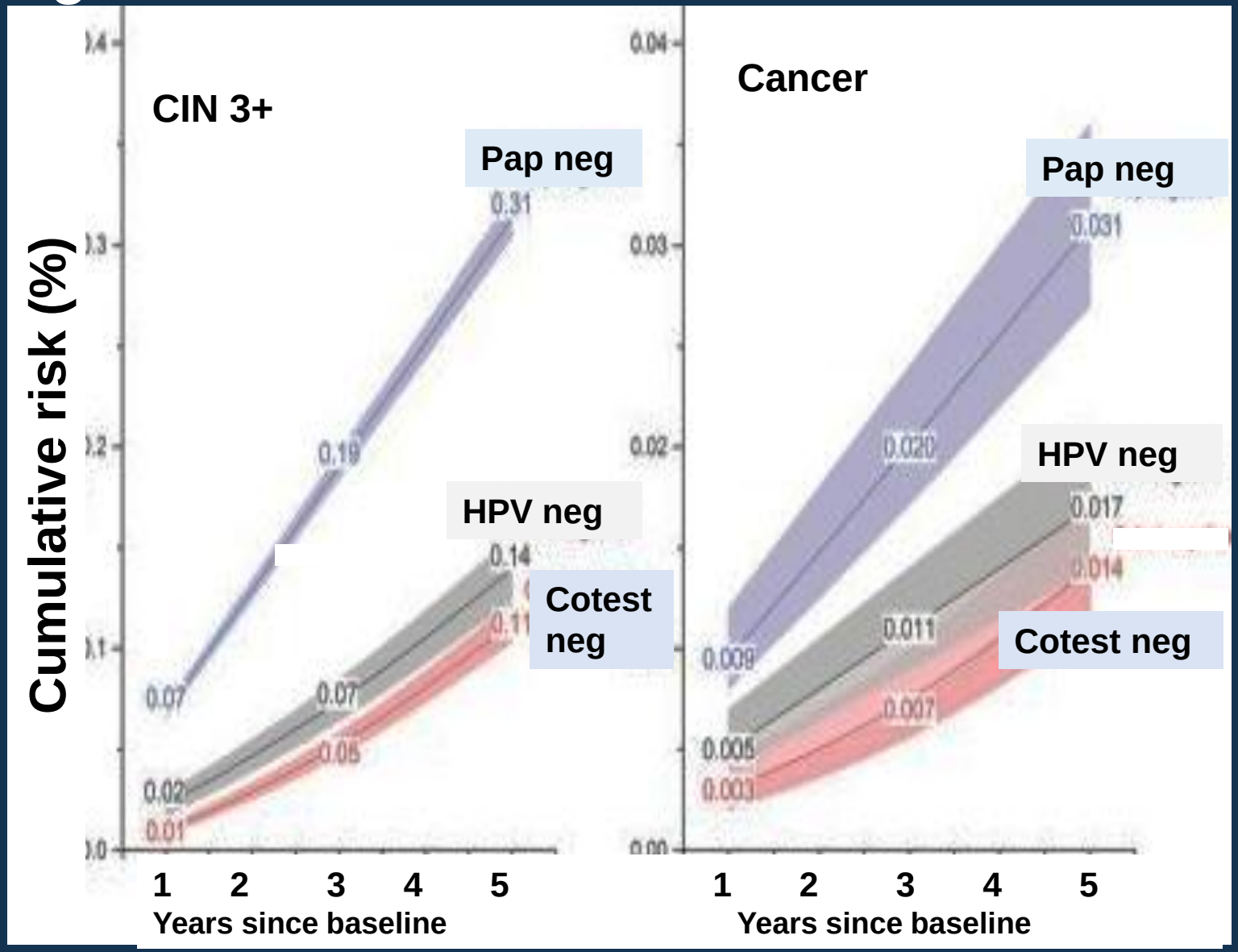
Development of Precancer Over 6 Years in Women Screened with Cytology, HPV, and Cotesting



Dillner, J. et al. BMJ 2008;337:a1754

The contribution cytology makes to cotesting is minimal compared to HPV testing.

Risk of CIN 3+ and Invasive cancer in KPNC cohort of women age 30-64 following an initial negative screening test



Gage JC JNCI. 2014 2014;106

Cervical Cancer Screening: 2020 Guideline Update

Fontham ETH et al CA Cancer J Clin 2020;0:1-26.

The ACS recommends that individuals with a cervix

- **Initiate cervical cancer screening at age 25 yrs.**
- **Undergo primary HPV testing every 5 yrs through age 65 (preferred).**
  - **If primary HPV testing is not available, individuals aged 25-65 yrs should be screened with cotesting (HPV testing in combination with cytology) every 5 yrs or**
  - **cytology alone every 3 yrs (acceptable)**

Why start screening at age 25?

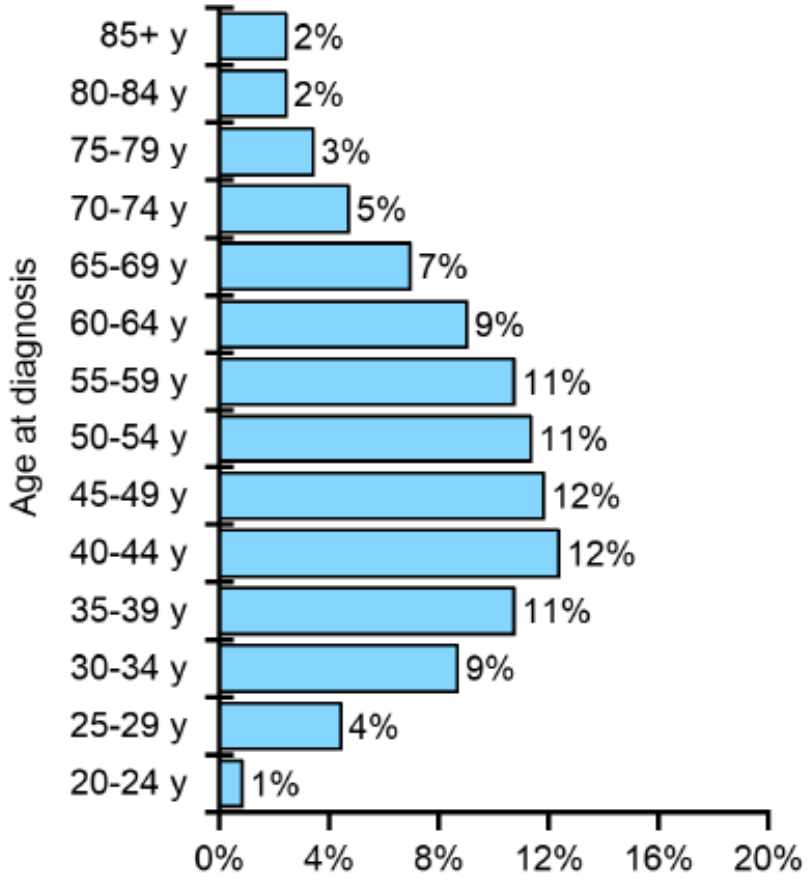


FIGURE 1. Distribution of Cervical Cancer Cases by Age at Diagnosis, United States, 2012 to 2016. Data Source: North American Association of Central Cancer Registries Incidence Data-Cancer in North America Analytic File.[46]

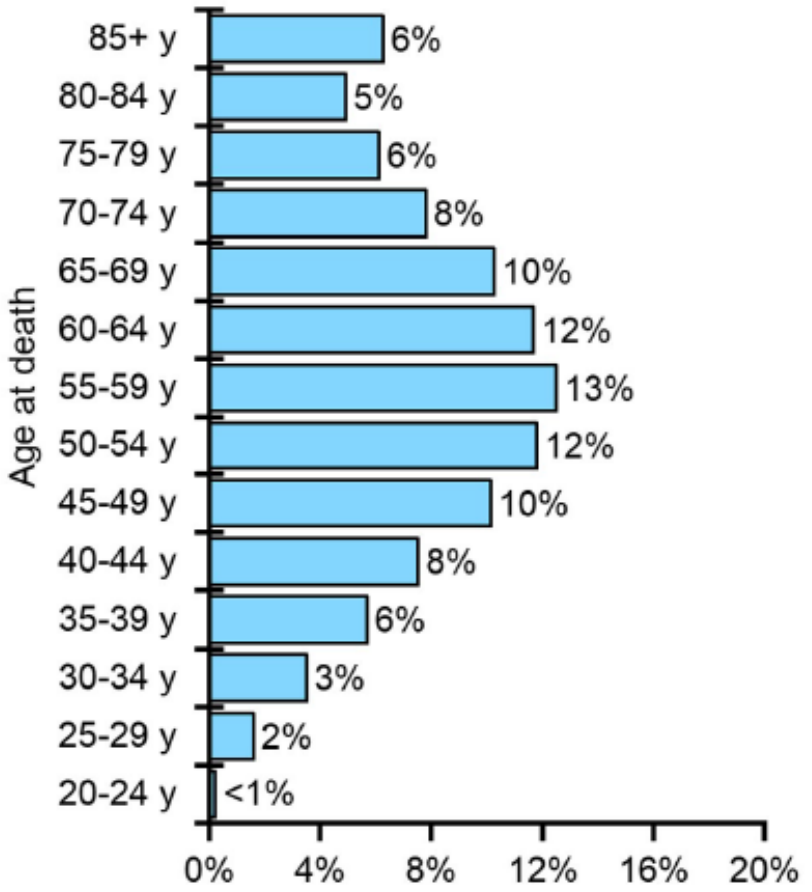


FIGURE 2. Distribution of Cervical Cancer Deaths by Age at Death, United States, 2013 to 2017. Data Source: National Center for Health Statistics.[47]

Fontham ETH et al. CA Cancer J Clin 2020;0:1-26.

Benefits and Burdens of Cervical Cancer Screening Strategies- Estimates from Modeling

Strategy	Total tests	Colpos	CIN 2,3	Cancer cases	Cancer deaths	Life Yrs Gained
No screening	0	0	0	18.86	8.34	63,921
Cyto q 3 y from age 21/ Cotest q 5 y age 30-65	19,806	1,630	201	1.08	0.30	64,193
HPV q5 y age 25-65	10,954	1,775	195	0.94	0.28	64,194

Estimates are per 1000 persons with a cervix screened over a lifetime.

Fontham ETH et al. CA Cancer J Clin 2020;0:1-26.

Cervical Cancer Screening: 2020 Guideline Update

Fontham ETH et al CA Cancer J Clin 2020;0:1-26.

- **Cotesting or cytology testing alone are included as acceptable options for cervical cancer screening because access to primary HPV testing with a *test approved by the FDA for primary screening* may be limited in some settings. As the United States makes the transition to primary HPV testing, the use of cotesting or cytology alone for cervical cancer screening will be eliminated from future guidelines.**

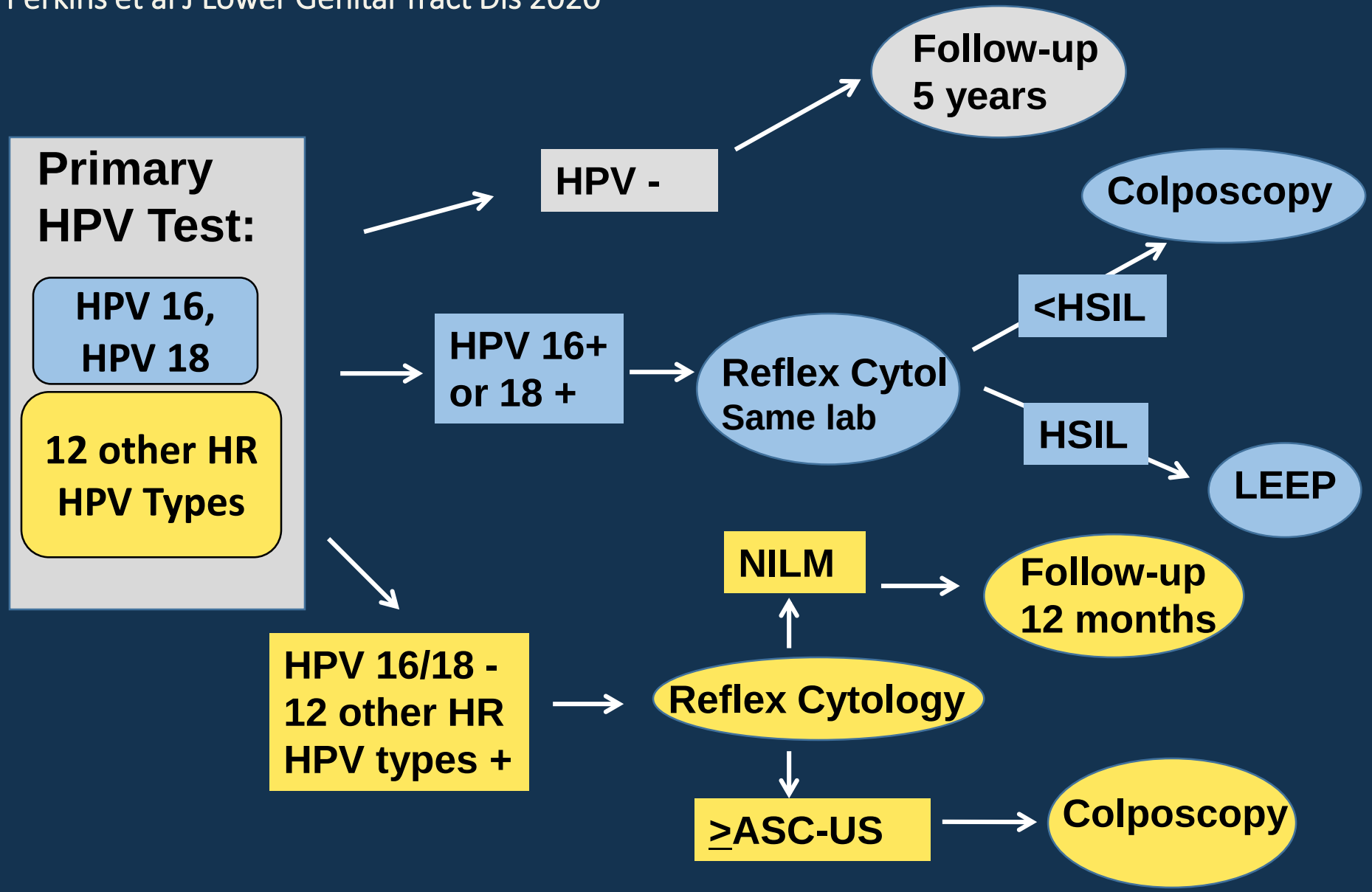
FDA-approved high-risk HPV tests

Only 2 are approved for primary HPV testing

Assay	HC2	Cervista	Cobas	Aptima	Onclarity
Detection of…	HPV DNA	HPV DNA	HPV DNA	HPV E6/E7 mRNA	HPV DNA
# of HPV types	13	14	14	14	14
Approved for primary screening	No	No	Yes	No	Yes
Assay type	RNA-DNA hybrids	Invader technology	PCR	E6, E7 mRNA	E6, E7 PCR
Internal control for specimen adequacy	No	Yes	Yes	No	Yes
HPV 16/18 genotyping available	No	Yes 16, 18, 12 other	Yes 16, 18, 12 other	Yes 16, 18/45 11 other	Yes 16, 18, 45, 31, 51, 52, [33,58], [56,69,66], [35,39,68]

Algorithm for Primary HPV Screening

Huh et al Gynecol Oncol 2015
Perkins et al J Lower Genital Tract Dis 2020



- **The ACS recommends that individuals with a cervix who are older than age 65 yrs, who have no history of CIN 2 or worse within the past 25 yrs, and who have *documented* adequate negative prior screening in the 10-y period before age 65 discontinue cervical cancer screening with any modality.**

- **Individuals older than age 65 yrs without conditions limiting life expectancy for whom sufficient documentation of prior screening is not available should be screened until criteria for screening cessation are met.**

- **Cervical cancer screening may be discontinued in individuals of any age with limited life expectancy**

Fontham ETH et al. CA Cancer J Clin 2020;0:1-26.

So there are two sets of national guidelines. Which should we use?


It’s very confusing!!!
agw

My suggestions (for what it's worth…)

- In the next few months, I suspect that the U.S.P.S.T.F. and national professional organizations, e.g. ACOG, AAFP, will weigh in on the ACS Guidelines and either endorse or reject them.
- In the meantime, as long as you have one of the FDA approved HPV tests, you can use either set of guidelines.
  - This is a good time for shared decision making with the patient.
- Do I start screening at age 21 or 25?
  - Again, the risk of cancer is low in this age group.
  - Many young women under age 25 find a Pap test somewhere on the spectrum from embarrassing to traumatic.
  - Again, I'd recommend offering a Pap at 21 coupled with shared decision making acknowledging permission from ACS to defer screening until age 25.

Questions?