

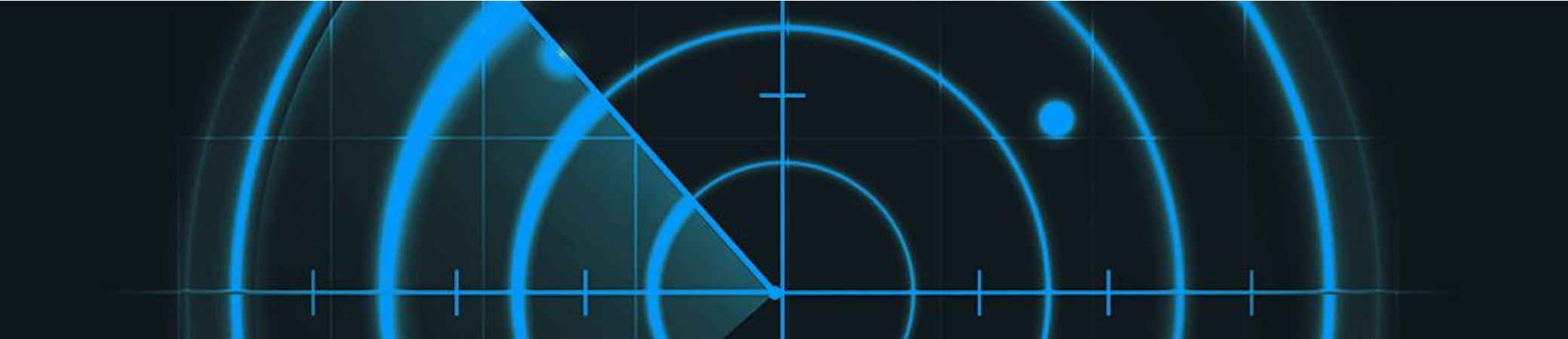
# Innovating to Help End Cervical Cancer

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*EMEA-LATAM TPM Network Member*

*SAS-RMS*

*DME-FZCO, MC, Dubai, UAE*



# The goal of cervical cancer screening is to identify disease early, with certainty

## Keep in Routine Screening



- Negative Predictive Value: rule out
- High sensitivity
- Drives the screening interval

**RISK STRATIFICATION**

## Treat Disease



- Positive Predictive Value: rule in
- High specificity
- Drives the intervention protocol

**DISEASE STRATIFICATION**

# Pap cytology lacks accuracy & misses disease

## Concordance with QC Reviewers Diagnosis

Re-read of 4,948 liquid-based cytology slides

	NILM	ASC-US	LSIL	≥HSIL
Original Diagnosis NILM	76%	19%	3%	< 1%
ASC-US	<b>57%</b> misdiagnosed	<b>43%</b>	17%	2%
LSIL		22%	6%	6%
≥HSIL	3%	23%	<b>53%</b> misdiagnosed	<b>47%</b>

# Portfolio: built on science that creates certainty

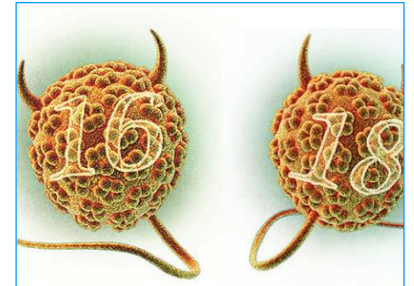
## WE ARE CERTAIN...

cobas<sup>®</sup> HPV 16/18

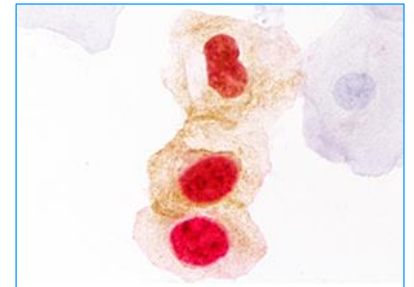
CINtec *PLUS* Cytology

CINtec Histology

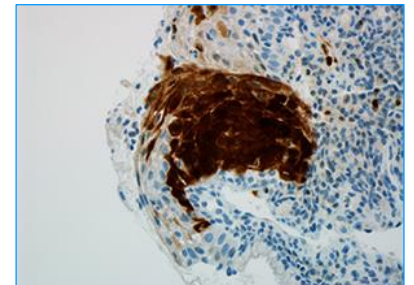
...that HPV is the primary cause of cervical cancer and that HPV genotypes 16 and 18 are the 2 highest risk types



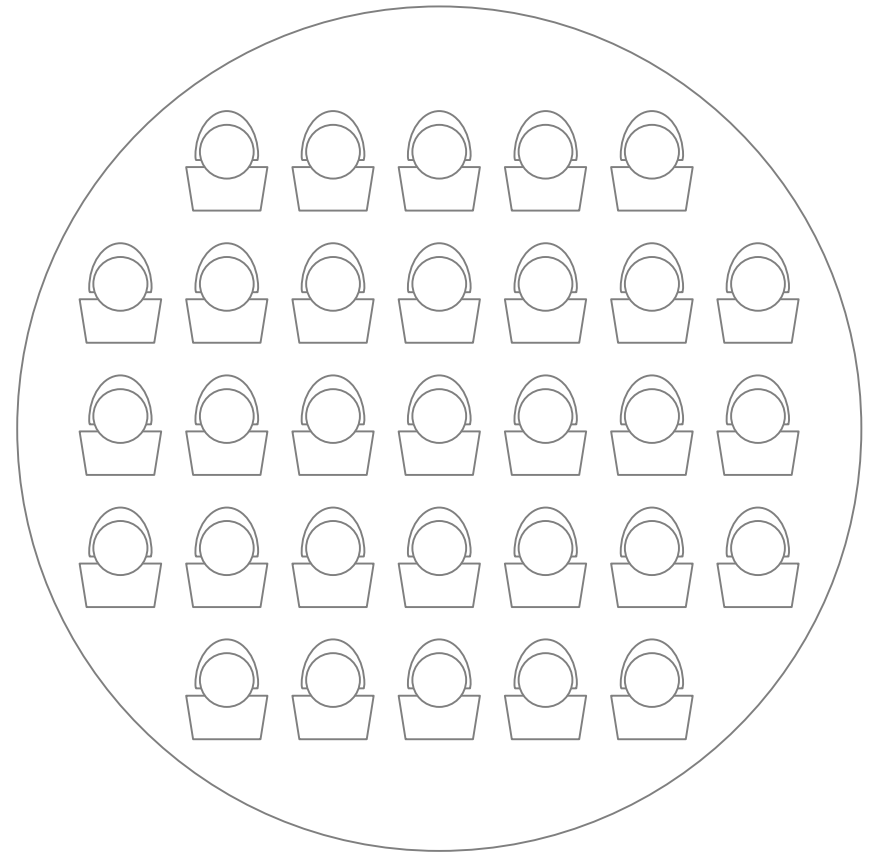
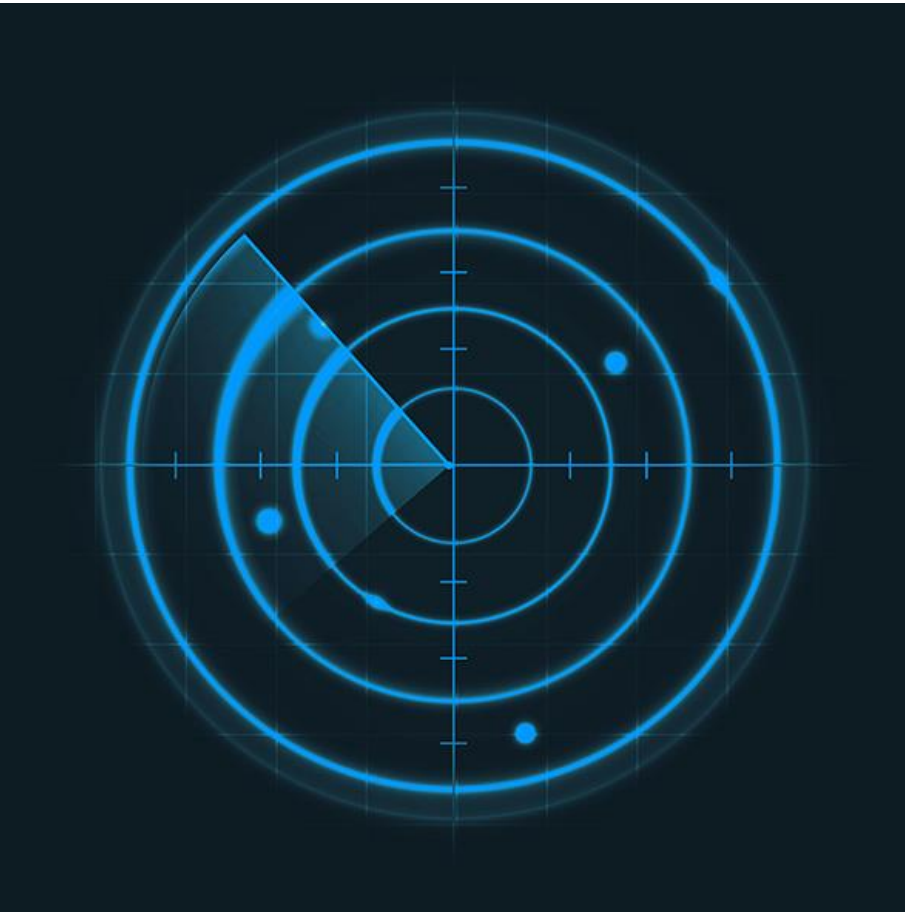
...that the co-expression of p16 & Ki-67 in the same cell indicates cell cycle deregulation



...that p16 is over-expressed as a result of transforming HPV infection

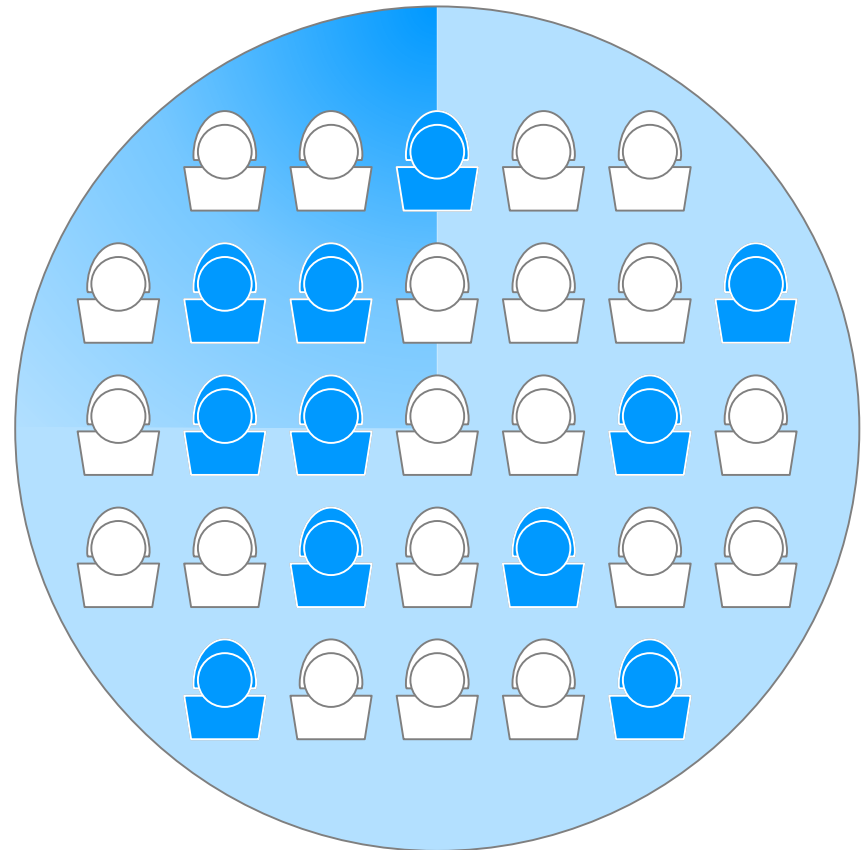


# Helping protect women from cervical cancer



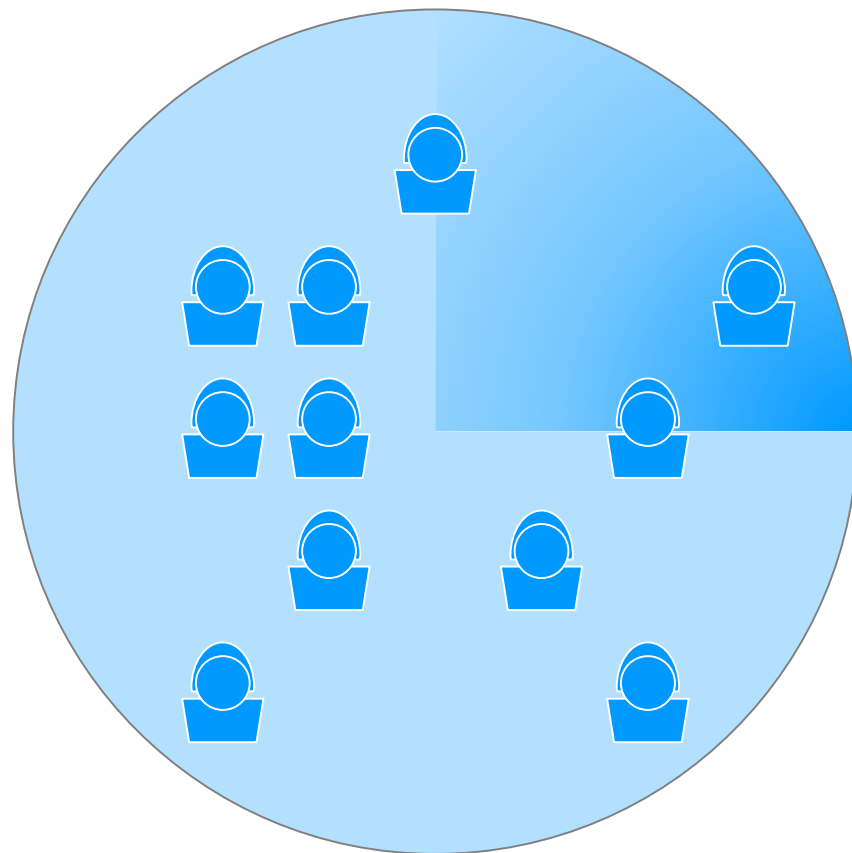
# Three tests answer key questions with more certainty

<b>cobas<sup>®</sup> HPV</b>	Is the cause of cervical cancer present?
<b>CINtec PLUS</b>	
<b>CINtec Histology</b>	



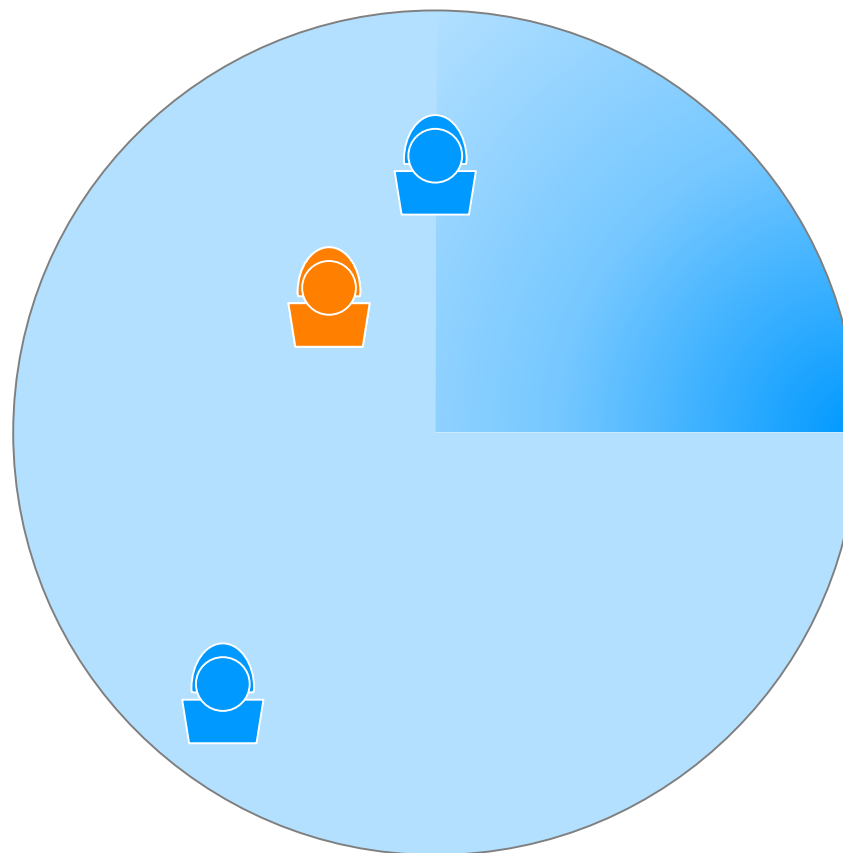
# Three tests answer key questions with more certainty

<b>cobas<sup>®</sup></b> <b>HPV</b>	Is the cause of cervical cancer present?
<b>CINtec</b> <b>PLUS</b>	Are there oncogenically transformed cells?
<b>CINtec</b> <b>Histology</b>	

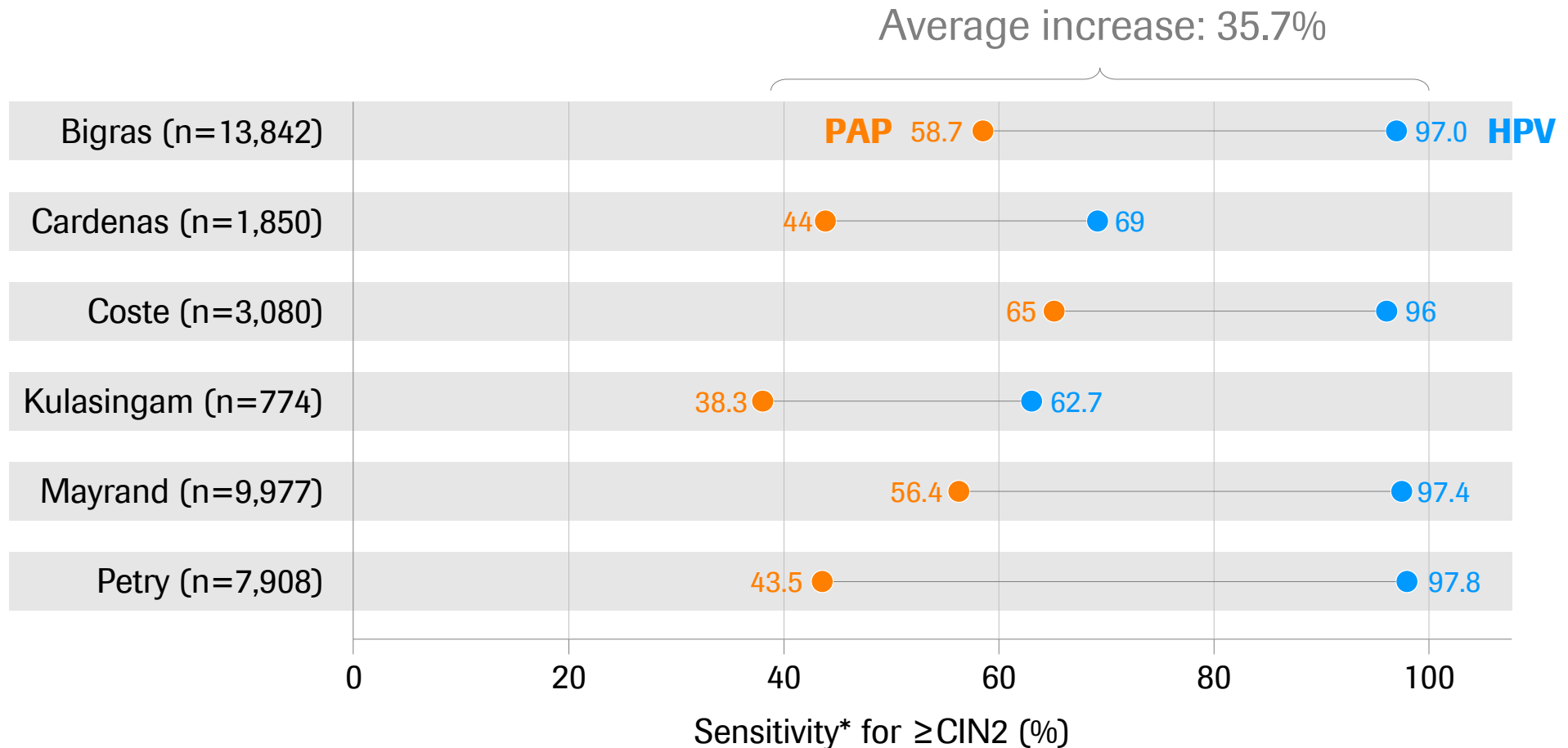


# Three tests answer key questions with more certainty

<b>cobas<sup>®</sup> HPV</b>	Is the cause of cervical cancer present?
<b>CINtec PLUS</b>	Are there oncogenically transformed cells?
<b>CINtec Histology</b>	Is cervical disease present?

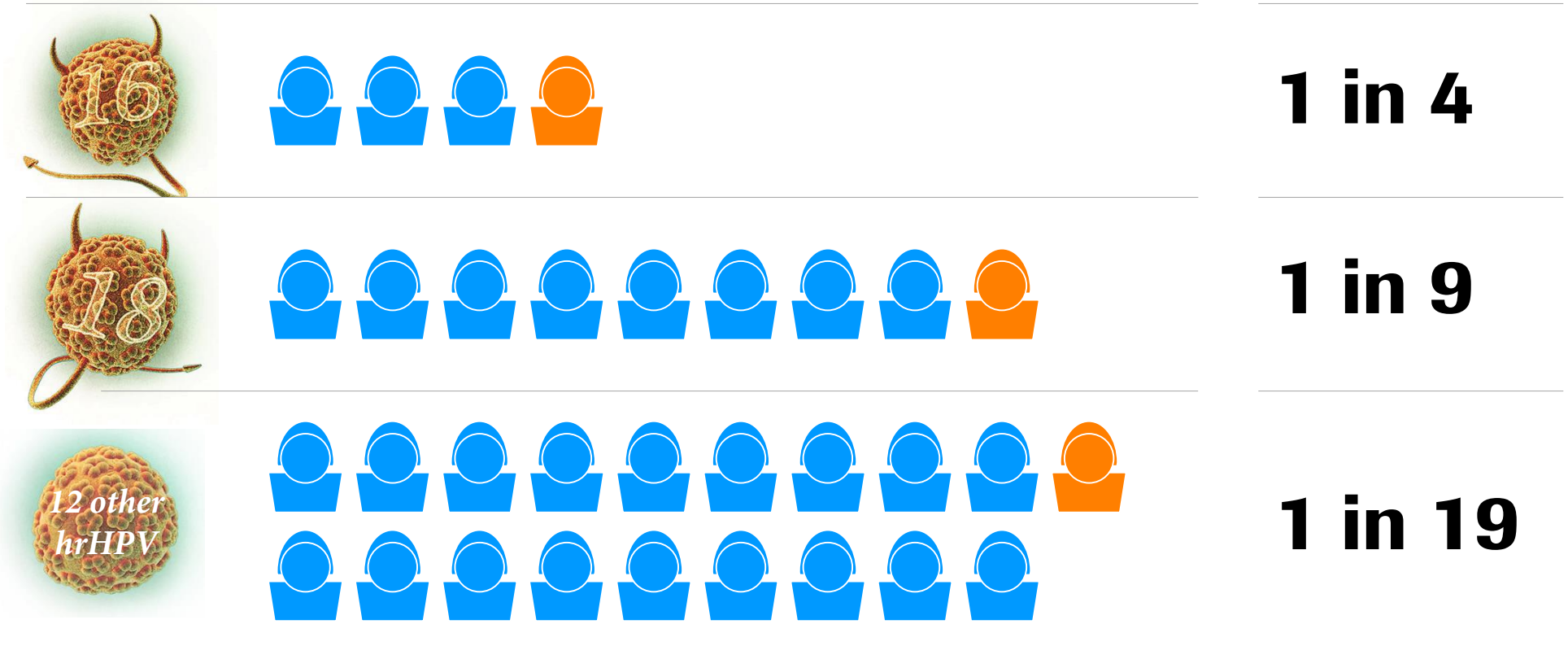


# HPV screening superior to Pap cytology across multiple studies



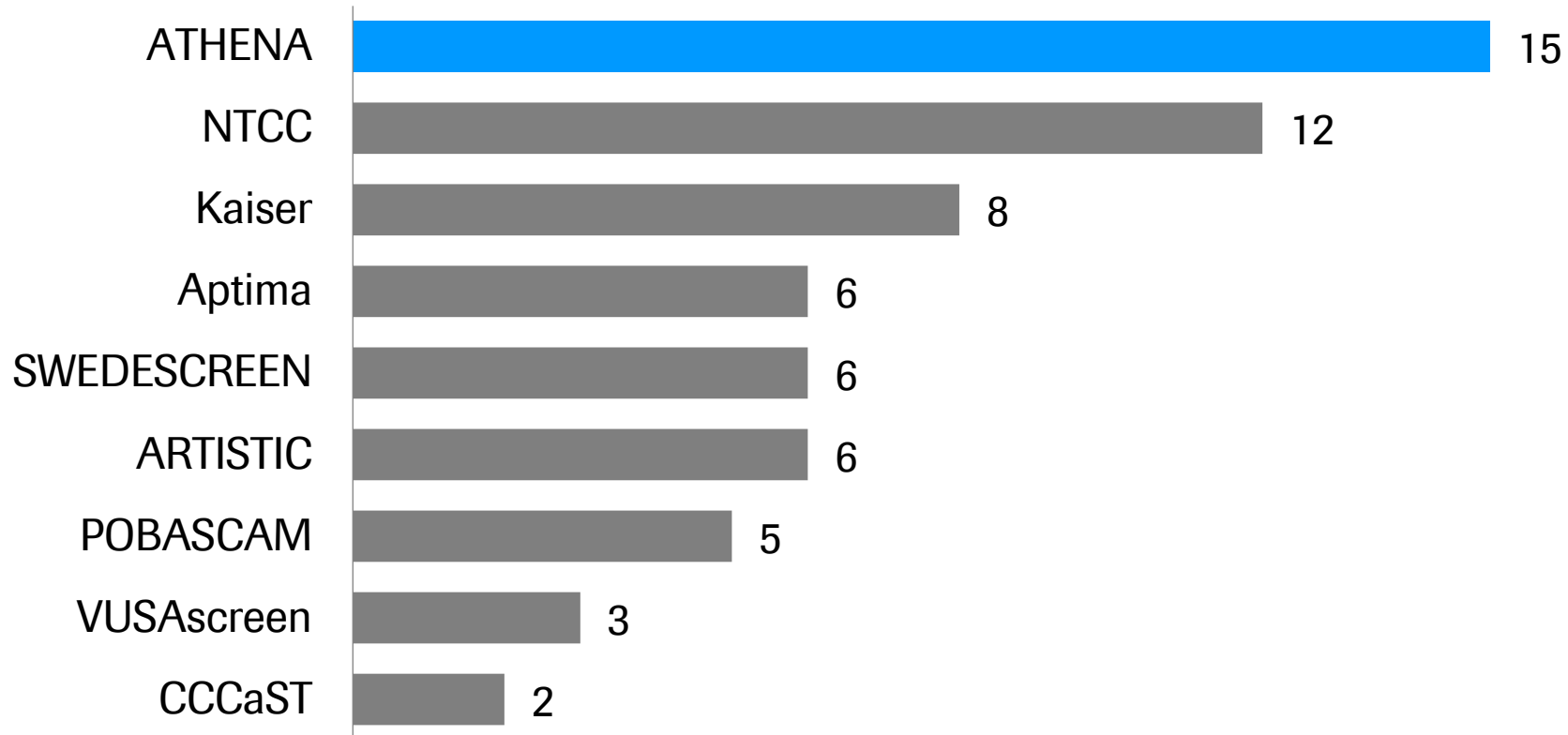
# Genotyping identifies women at highest risk

Risk of developing CIN3+ within 3 years



# Roche's trial is a major contributor to scientific body of evidence

## Comparison of Peer-Reviewed Publications from HPV Screening Studies\*



\* As of July 1<sup>st</sup>, 2015

# Roche has led innovation in HPV genotyping

## Channel 1

Detects 12  
hrHPV Genotypes

## Channel 2

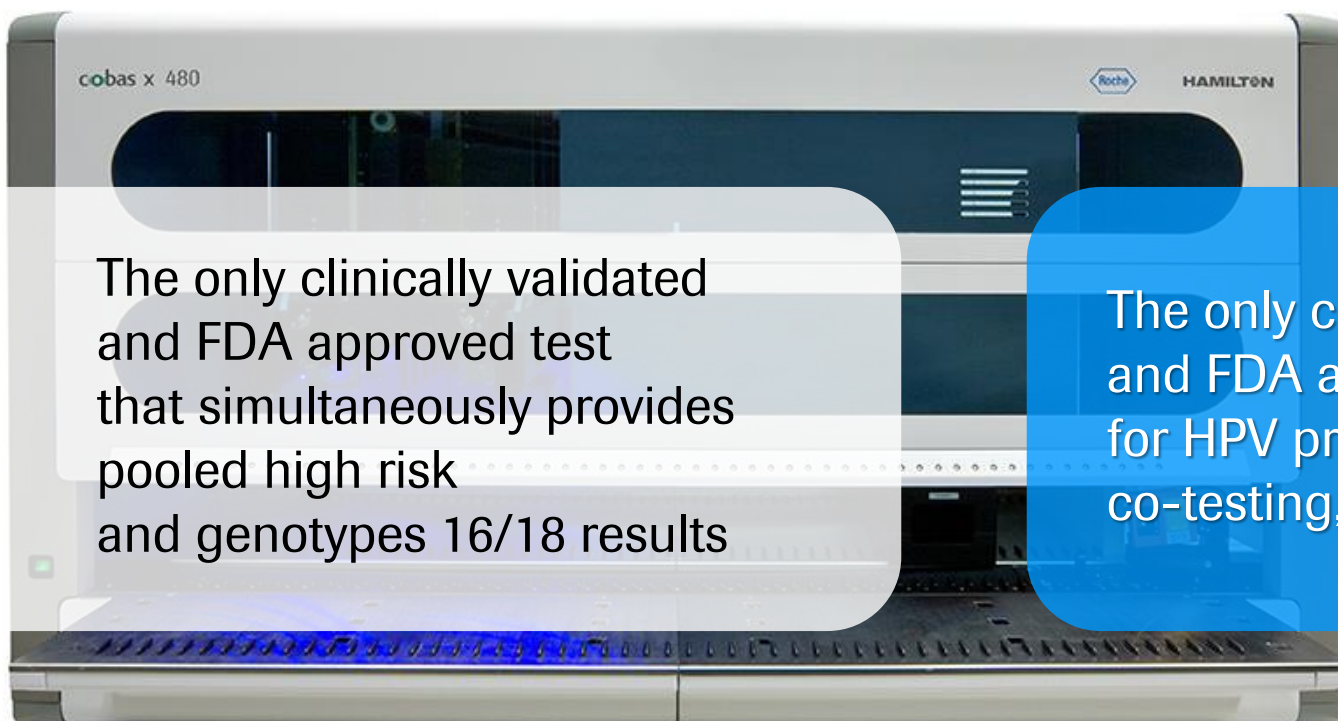
Detects  
HPV16

## Channel 3

Detects  
HPV18

## Channel 4

Internal cellular  
control



The only clinically validated and FDA approved test that simultaneously provides pooled high risk and genotypes 16/18 results

The only clinically validated and FDA approved test for HPV primary screening, co-testing, and ASC-US triage

# Where are we innovating now?

## Wait and Worry...

### 2015

JANUARY	FEBRUARY	MARCH
S M T W T F S 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31	S M T W T F S 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31	S M T W T F S 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
APRIL	MAY	JUNE
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JULY	AUGUST	SEPTEMBER
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OCTOBER	NOVEMBER	DECEMBER
S M T W T F S 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31	S M T W T F S 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30	S M T W T F S 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31

### 2016

JANUARY	FEBRUARY	MARCH
S M T W T F S 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31	S M T W T F S 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29	S M T W T F S 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31
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## Definitive Answers



# CINtec *PLUS* Cytology: objective aid in triage

CINtec *PLUS*

**Negative**

Expression of p16 (brown) signals halting of cell division

CINtec *PLUS*

**Negative**

Expression of Ki-67 (red) signals progression of cell division

CINtec *PLUS*

**Disease**

Co-expression of p16 & Ki-67 (brown & red) indicates abnormality

Pap Cytology

**Subjective**

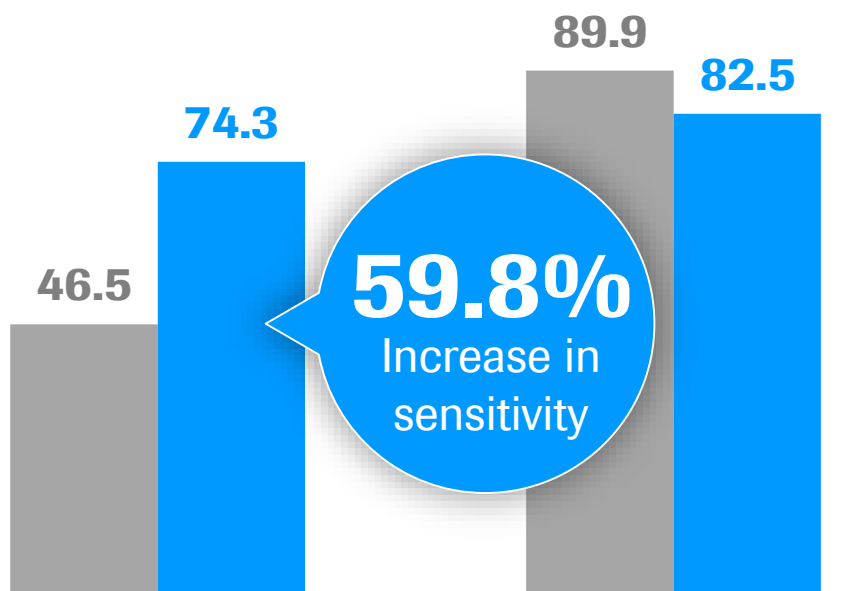
Reliant on interpretation of morphology only

# The Roche portfolio delivers the optimal screening strategy

## cobas® HPV & CINtec PLUS

Sensitivity

Specificity



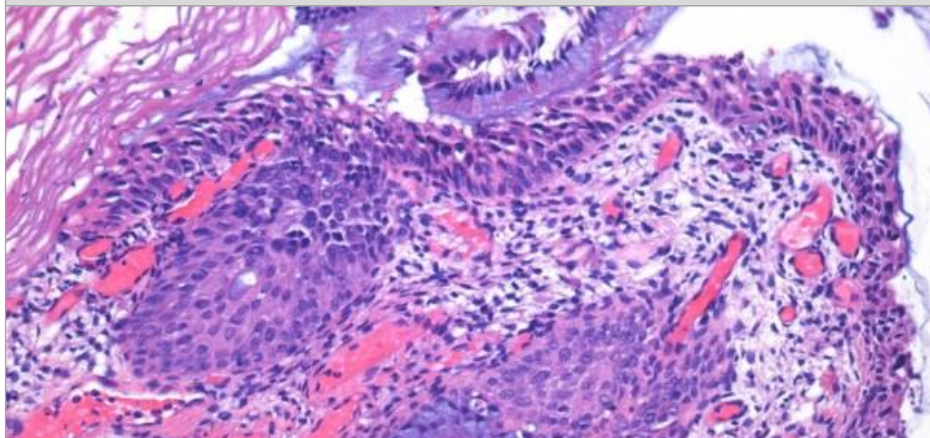
HR Pool + Roche  
Pap triage

## Study Design

- Retrospective study; end-point biopsy CIN2+
- ATHENA study sub-population of women 25 or older with cobas HPV positive result
- Comparison of HPV primary screening with LBC triage vs HPV primary screening with 16/18 genotyping and CINtec PLUS triage for 12 other hrHPV
- Testing performed on residual ATHENA samples in PreservCyt vials

# CINtec Histology: improved tissue diagnosis

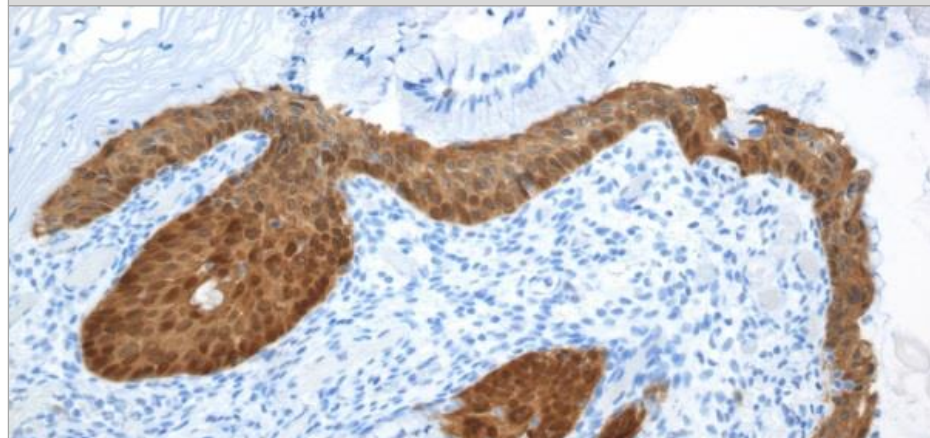
H&E Only



**Subjective**

Relies on interpretation of morphology only

H&E and CINtec Histology

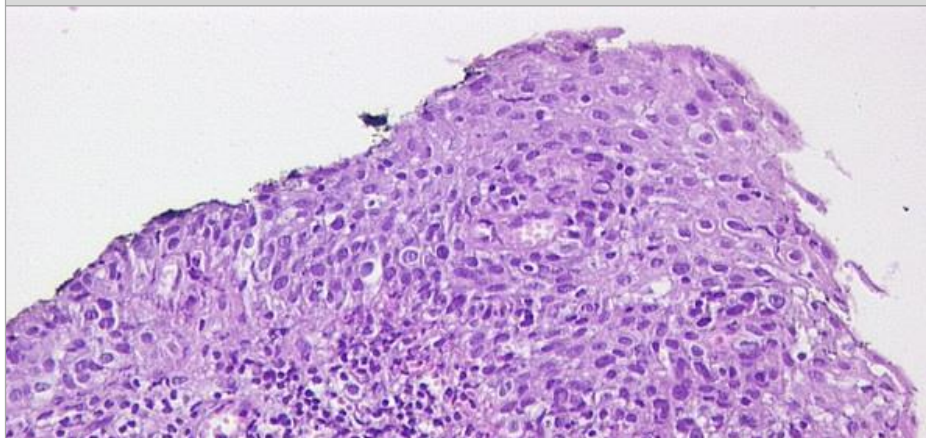


**Objective Biomarker: Disease**

Expression of p16 in tissue sections (brown) indicates abnormality

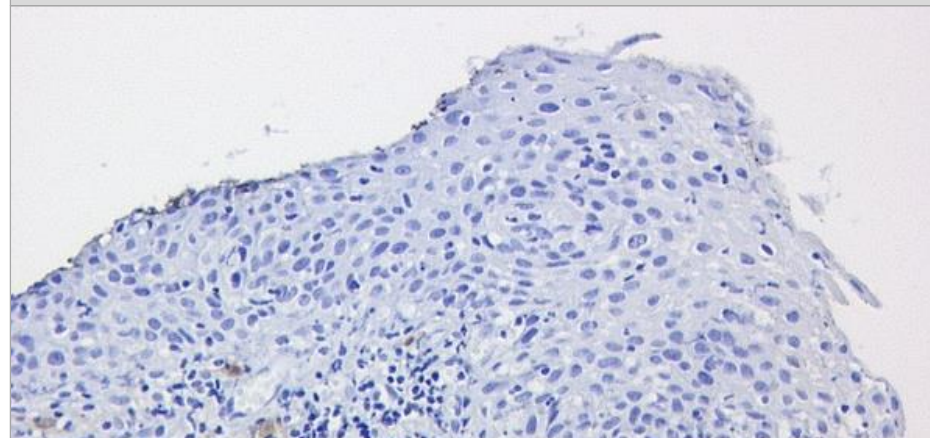
# CINtec Histology: improved tissue diagnosis

H&E Only



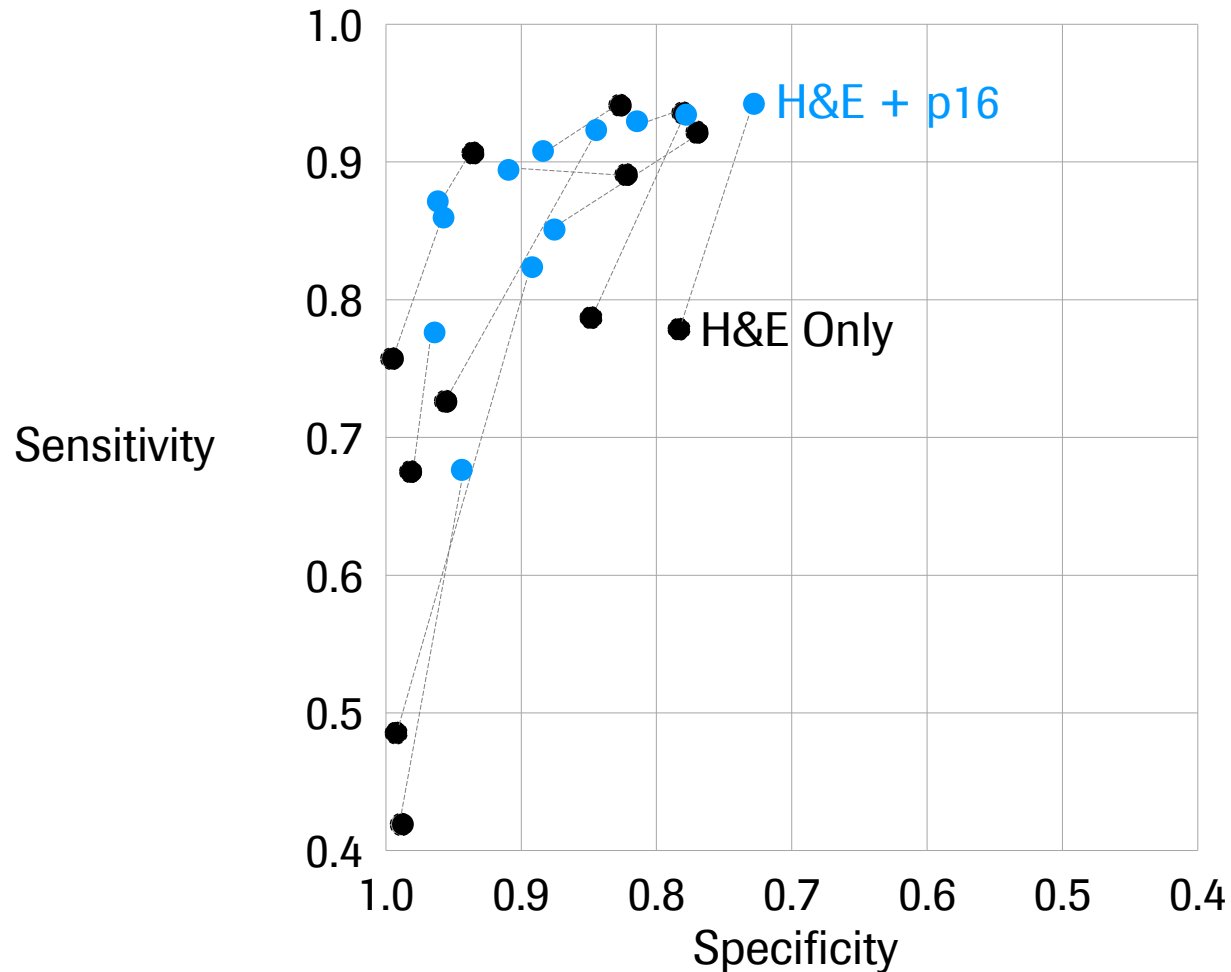
**Subjective Diagnosis: CIN2**

H&E and CINtec Histology



**Objective Biomarker: No Disease**

# CINtec Histology improves H&E diagnosis



- One pathologist

12 community-based pathologists assessed:

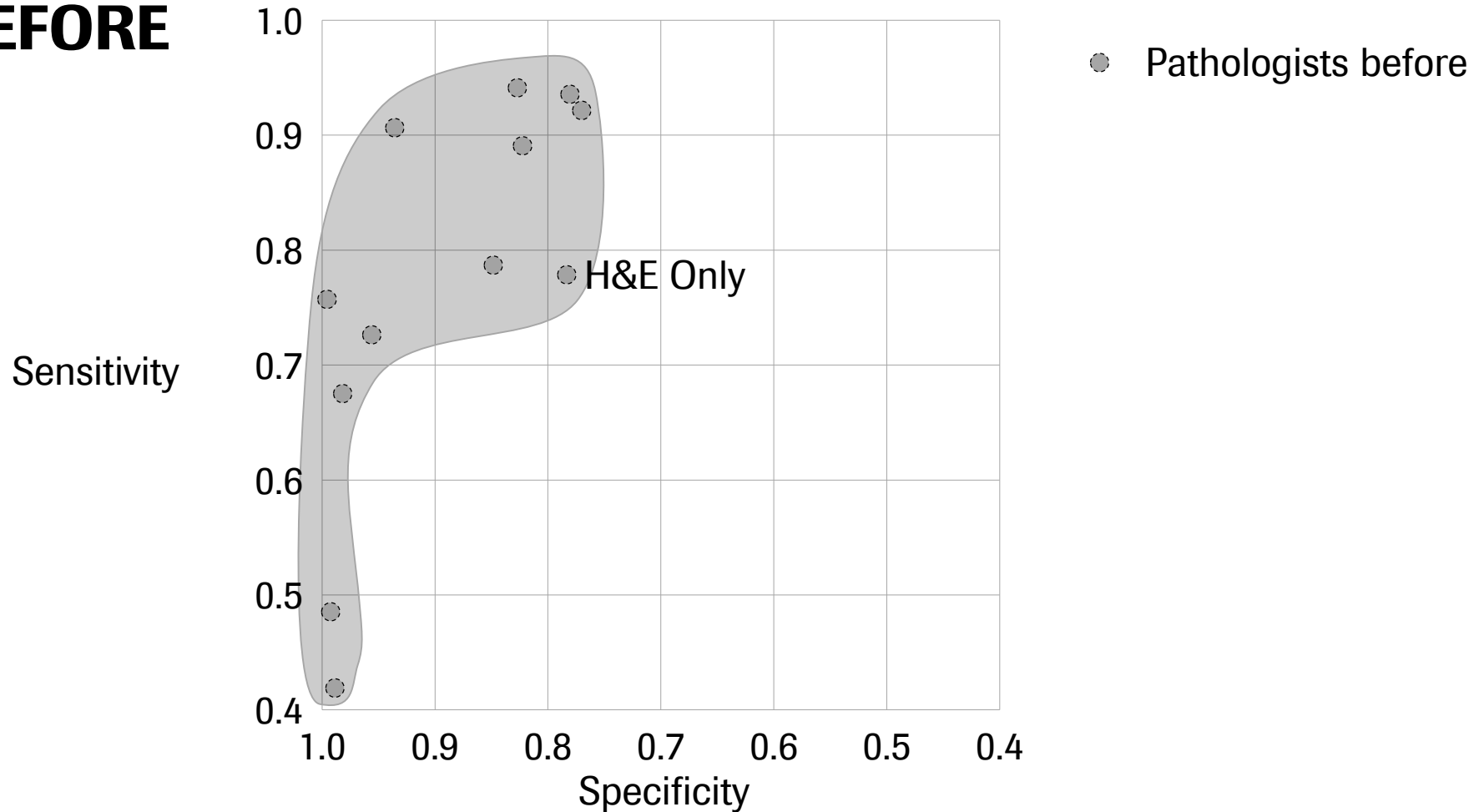
- 500 tissue specimens
- H&E vs H&E + p16
- Total of 12,000 readings

Gold standard assessment: performance compared to consensus diagnosis of 3 expert gynecopathologists\*

\*Christine Bergeron, Jaume Ordi, Dietmar Schmidt

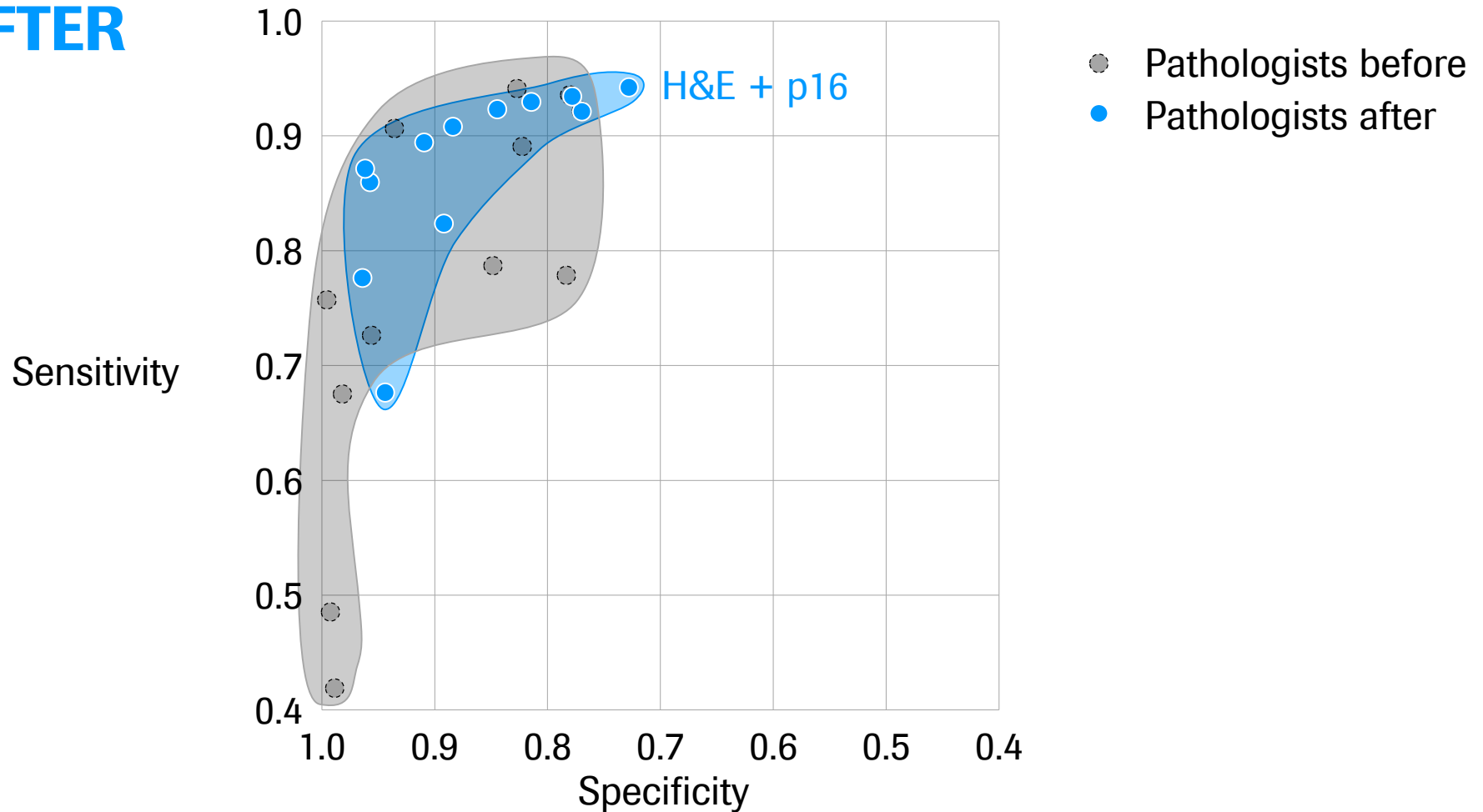
# CINtec Histology improves H&E diagnosis

**BEFORE**





# CINtec Histology improves H&E diagnosis

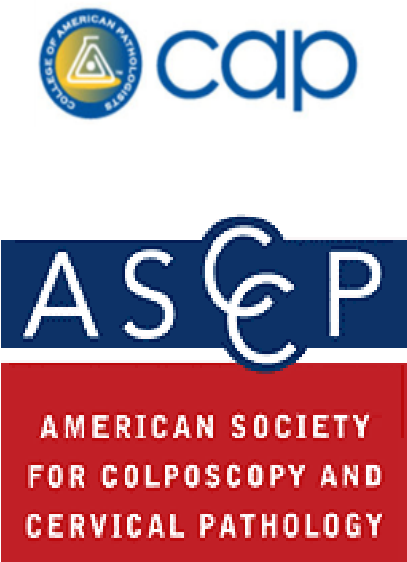
**AFTER**






# LAST assessment and recommendation

WORKING GROUP	ASSESSED	SELECTION CRITERIA
 	<p>p16</p> <p>Ki-67 (Mib1)</p> <p>ProEx C</p> <p>L1</p> <p>HPV 16/18</p> <p>mRNA</p> <p>Telomerase/TERC</p> <p>HPV genotyping</p>	<div style="border: 1px solid gray; border-radius: 10px; padding: 10px; background-color: #f9f9f9;"> <p><b>2,291:</b> papers identified</p> <p><b>72:</b> met inclusion criteria</p> <p><b>53:</b> papers on p16</p> </div> <p>Size of study: &gt;100 subjects</p> <p>Clinical validation studies (e.g. established sensitivity/specificity, performance against histological standard)</p> <p>Cytology studies including histologic standards/true (3-way) adjudication may be included</p>

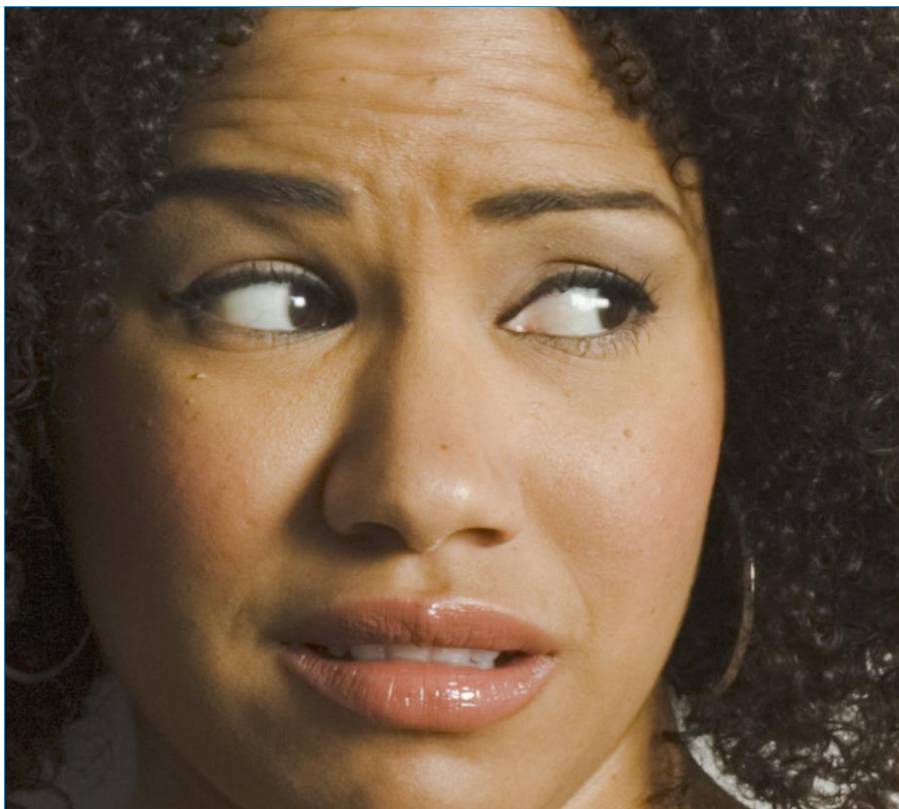
# LAST assessment and recommendation

WORKING GROUP	ASSESSED	RECOMMENDATION
	<p><b>p16</b></p> <p>Ki-67 (Mib1)</p> <p>ProEx C</p> <p>L1</p> <p>HPV 16/18 mRNA</p> <p>Telomerase/TERC</p> <p>HPV genotyping</p>	<p>“We concluded that <b>only p16</b>, a biomarker that is recognized in the context of HPV biology to reflect the activation of E6/E7 driven cell proliferation, <b>had sufficient evidence</b> on which to make recommendations regarding use in lower anogenital tract lesions.”</p>

# LAST assessment and recommendation

WORKING GROUP	ASSESSED	RECOMMENDATION	GL
 	<p><b>p16</b></p> <p>Ki-67 (Mib1)</p> <p>ProEx C</p> <p>L1</p> <p>HPV 16/18</p> <p>mRNA</p> <p>Telomerase/TERC</p> <p>HPV genotyping</p>	<p>“We concluded that <b>only p16</b>, a biomarker that is recognized in the context of HPV biology to reflect the activation of E6/E7 driven cell proliferation, <b>had sufficient evidence</b> on which to make recommendations regarding use in lower anogenital tract lesions.”</p>	

# Inconclusive Pap results raise many questions



**WAIT AND WORRY**

Was my screening test accurate?

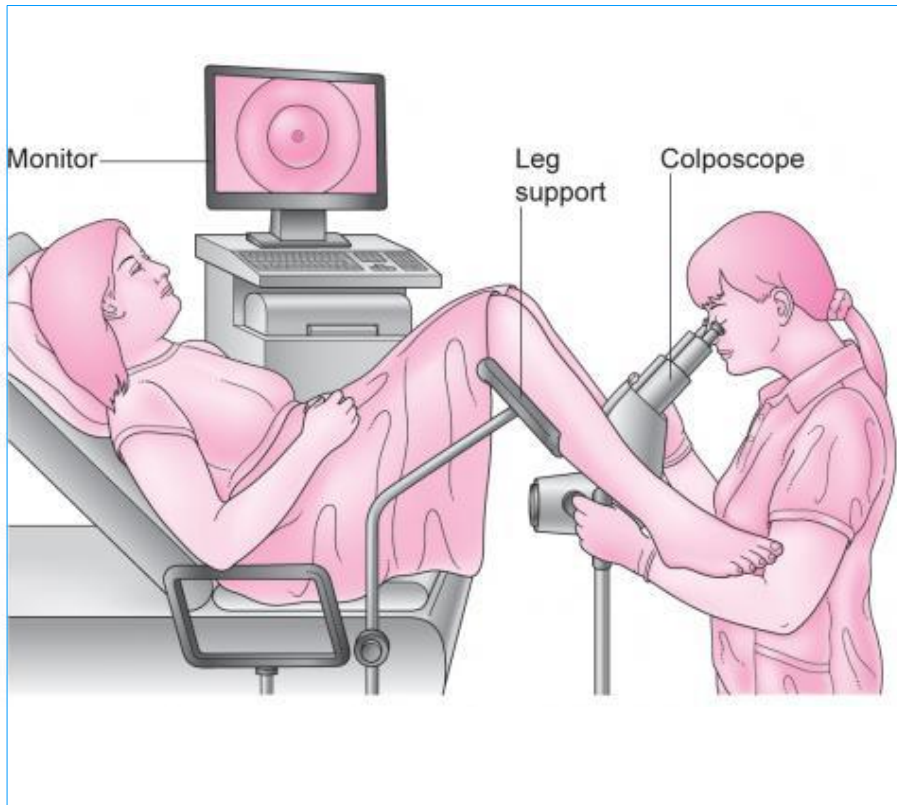
What does it mean that I'm at risk?

What do I do while I wait to be retested?

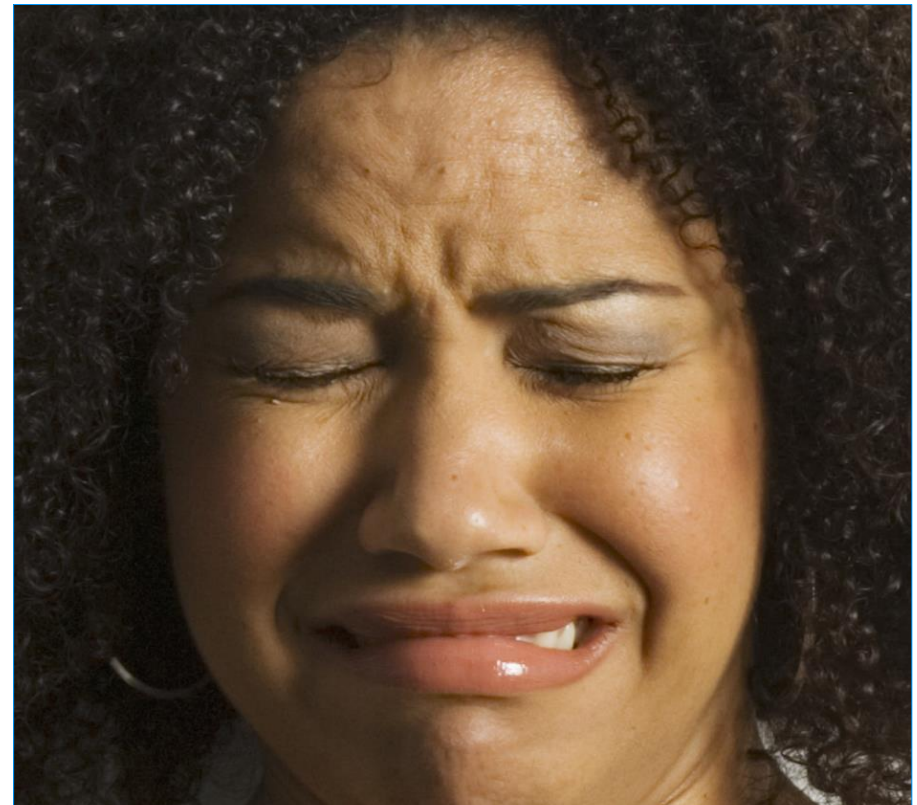
Do I need to be treated?

**WITH UNANSWERED QUESTIONS**

# We want to avoid over- or under-treatment



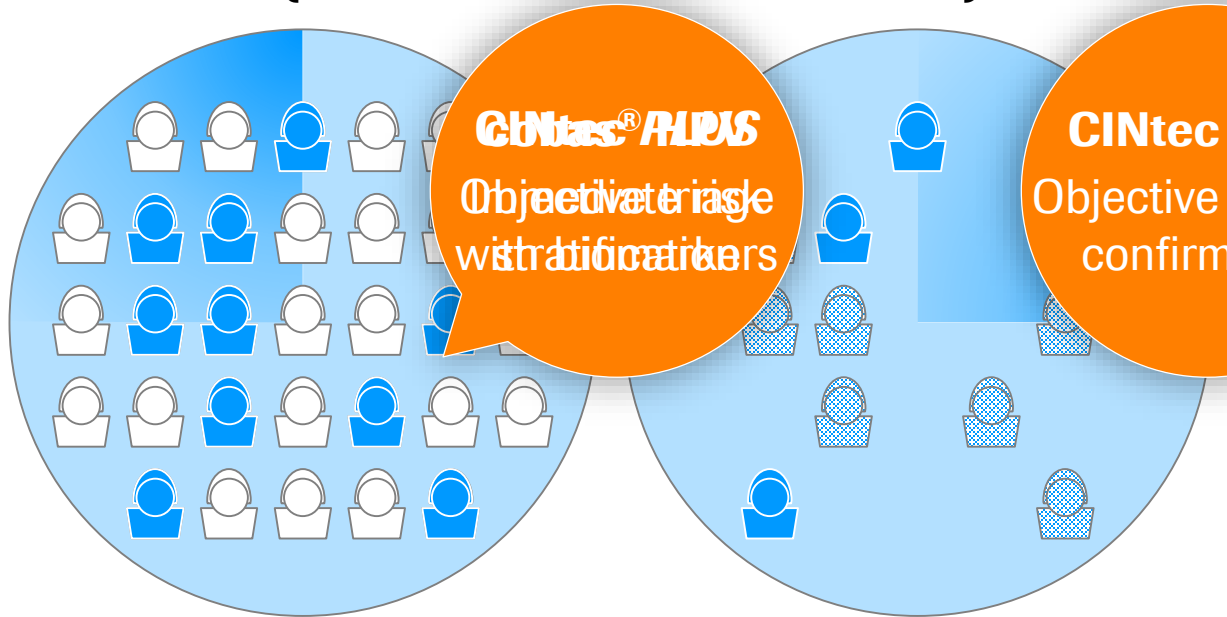
**COLPOSCOPY: HOW IT'S DONE**



**MIS-DIAGNOSIS: HOW IT FEELS**

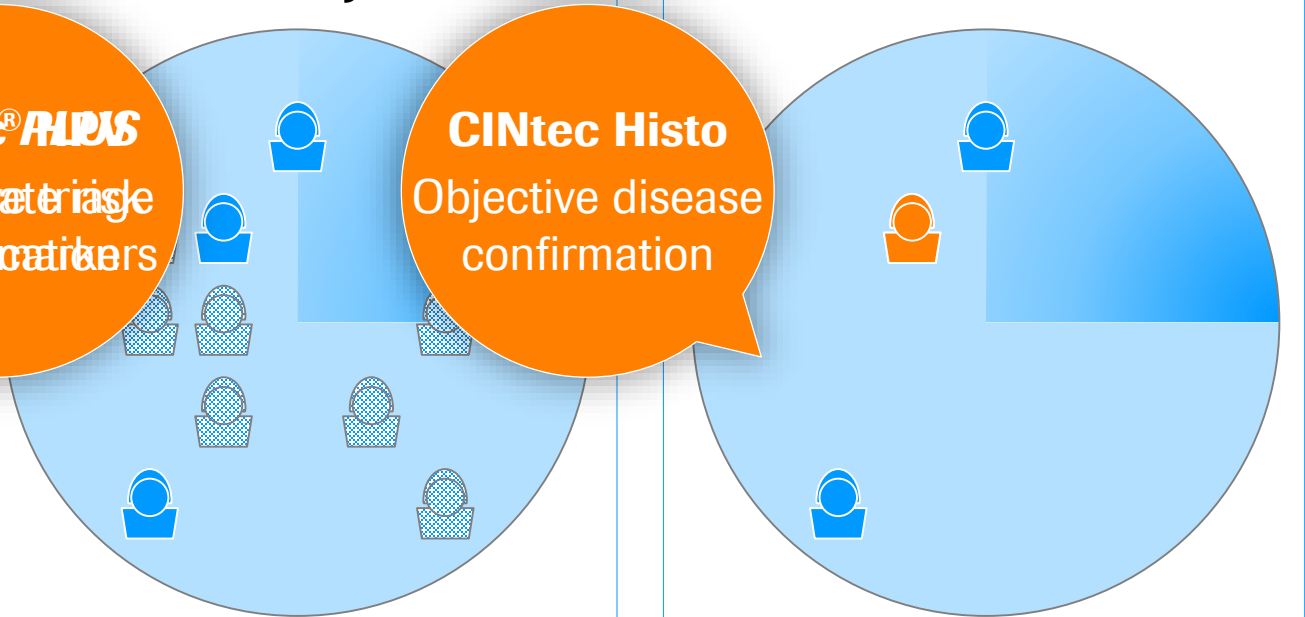
# We believe the combination is powerful

**REDUCE WAIT AND WORRY**  
(without over- or under-treatment)



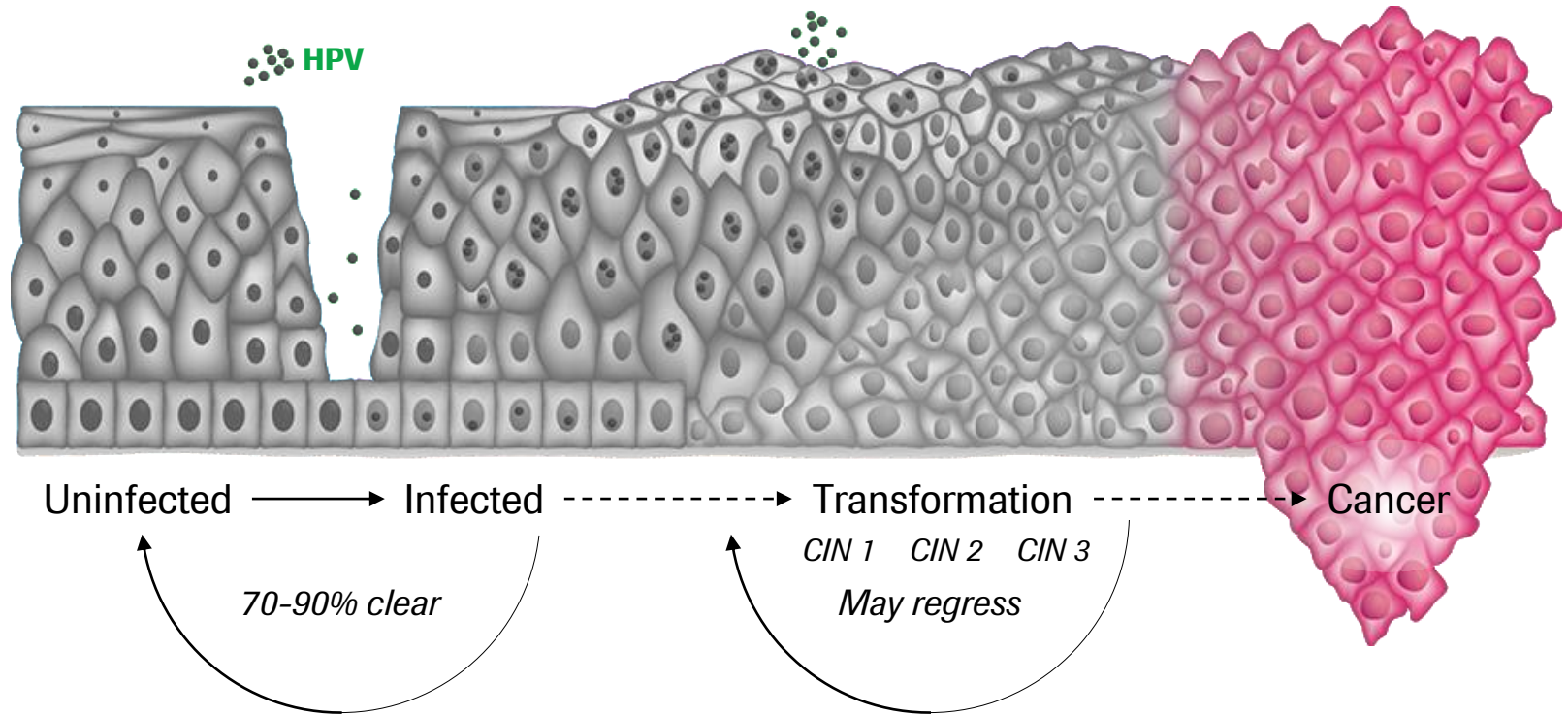
**cobas® HPV + CINtec PLUS Cytology**

**ID & TREAT HIGHEST RISK**

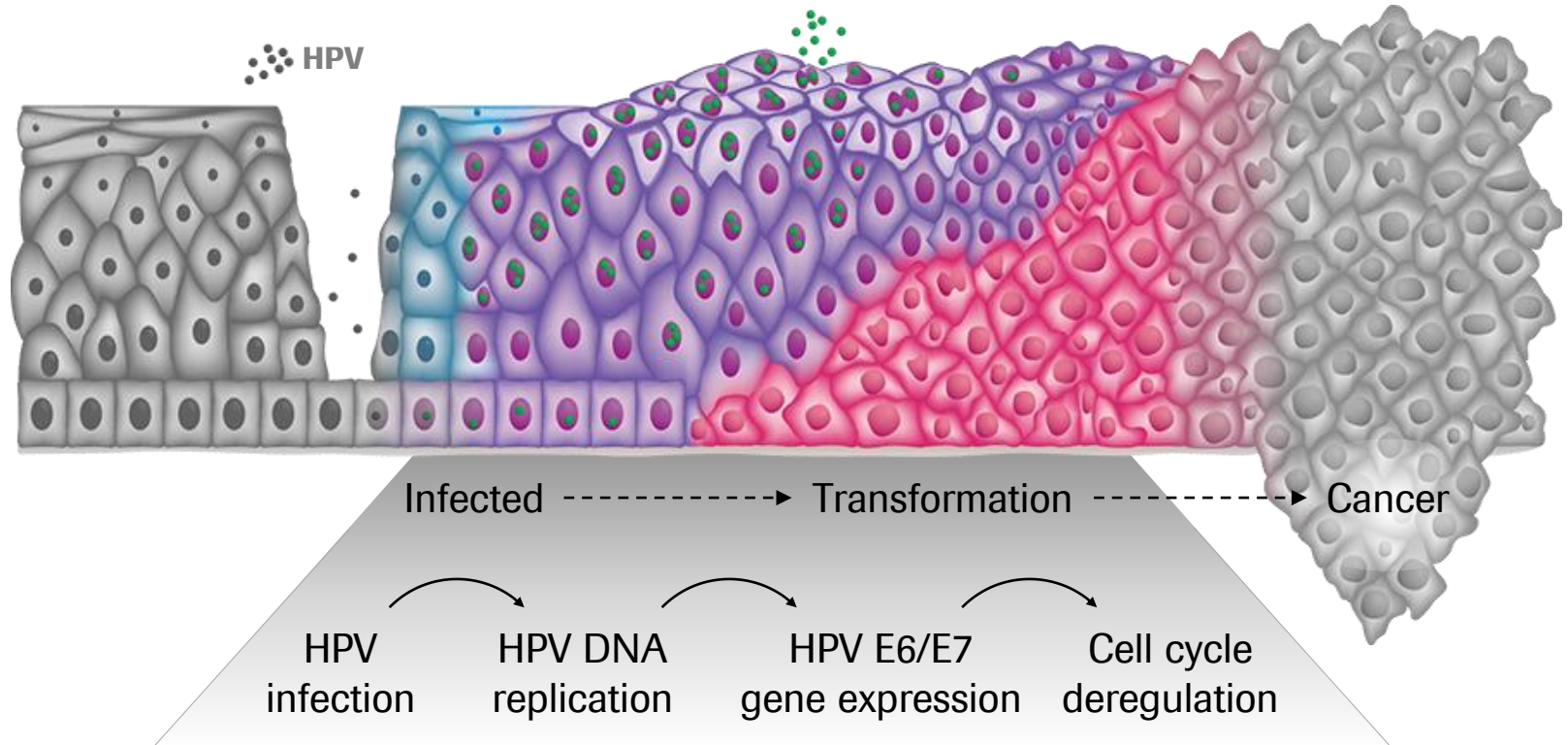


**CINtec Histology**

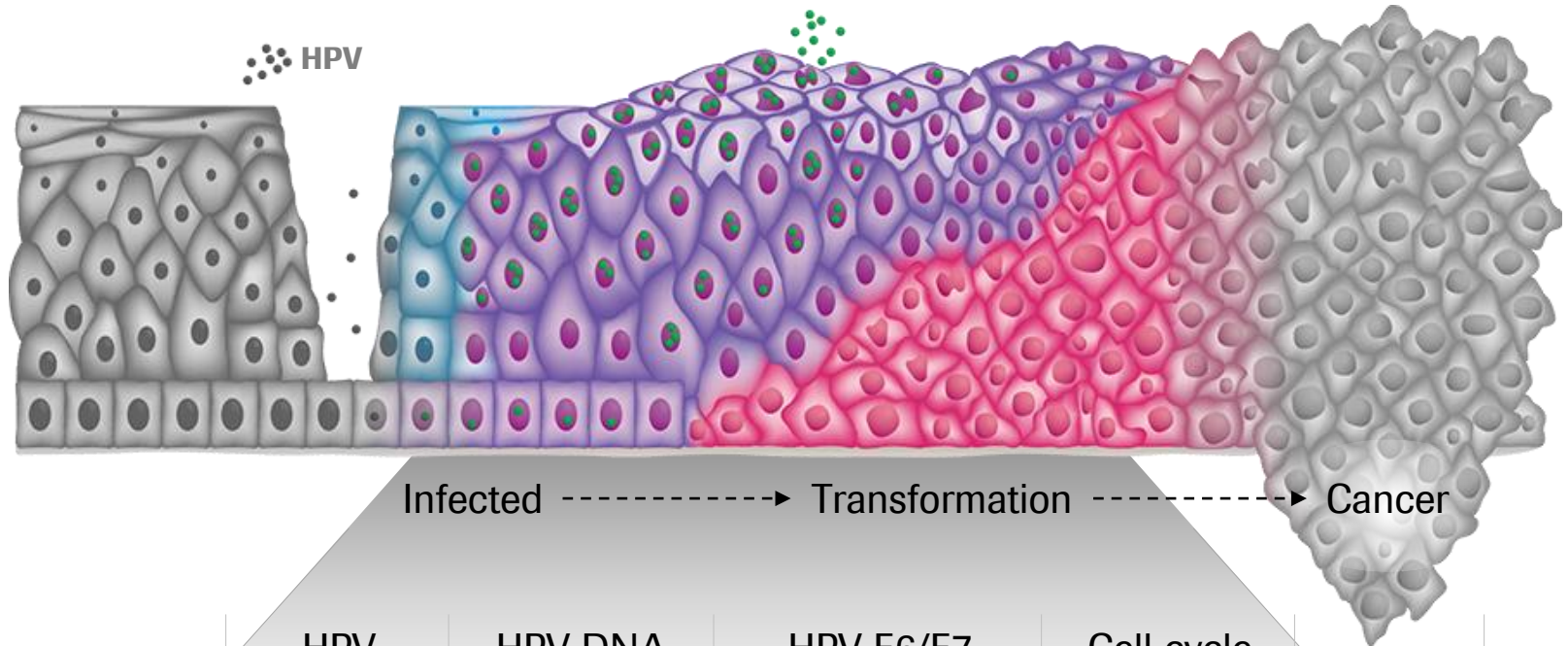
# We span the spectrum of disease progression



# We span the spectrum of disease progression

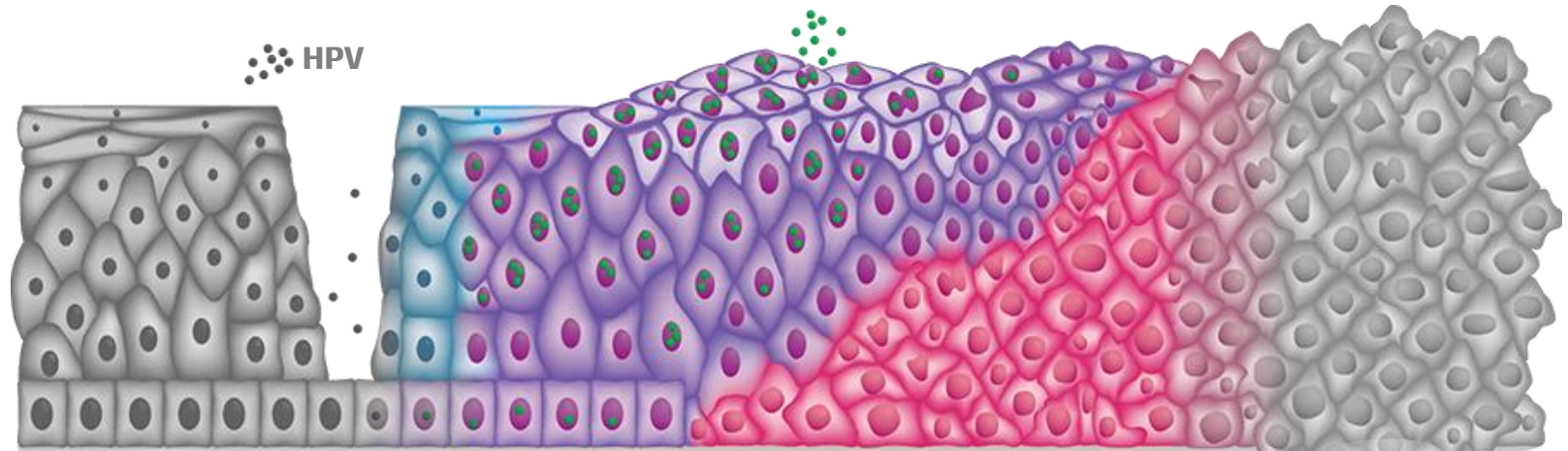


# We span the spectrum of disease progression



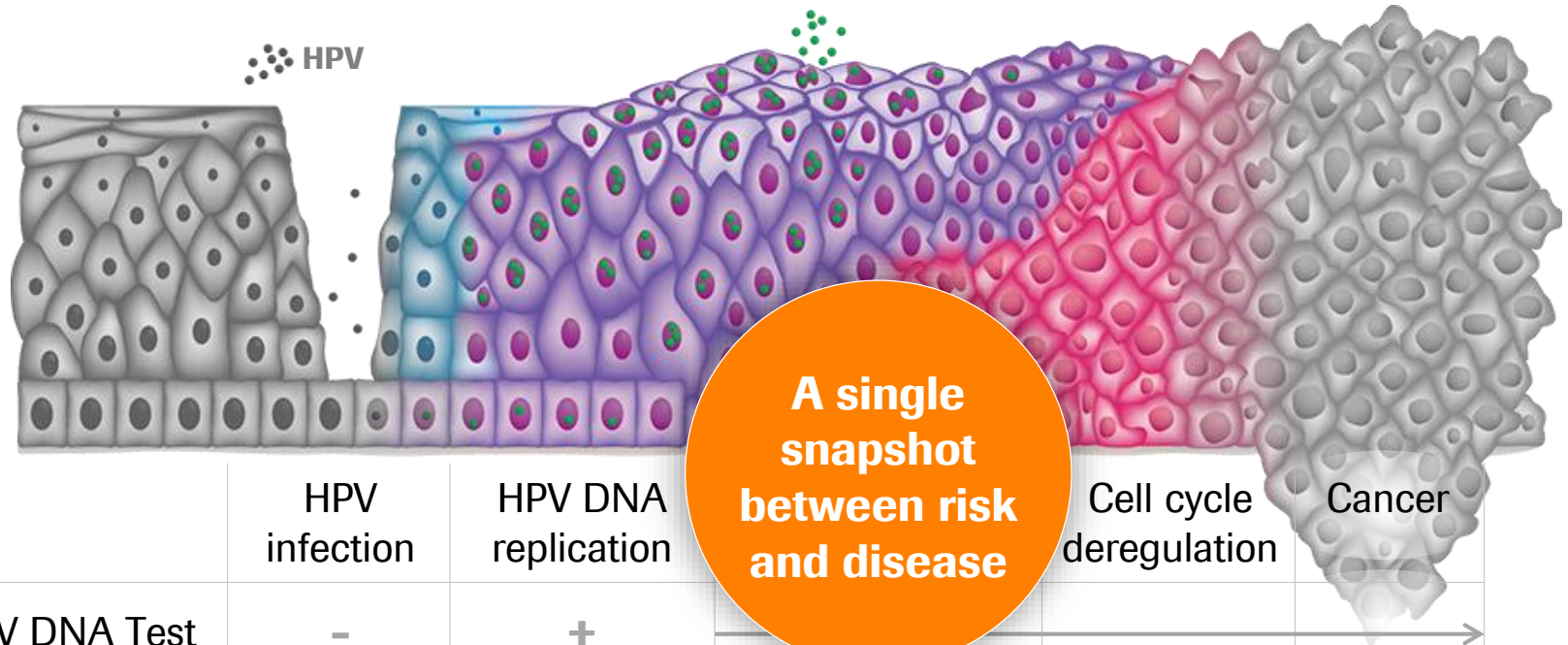
	HPV infection	HPV DNA replication	HPV E6/E7 gene expression	Cell cycle deregulation
HPV DNA Test				
HPV E6/E7 mRNA Test				

# We span the spectrum of disease progression



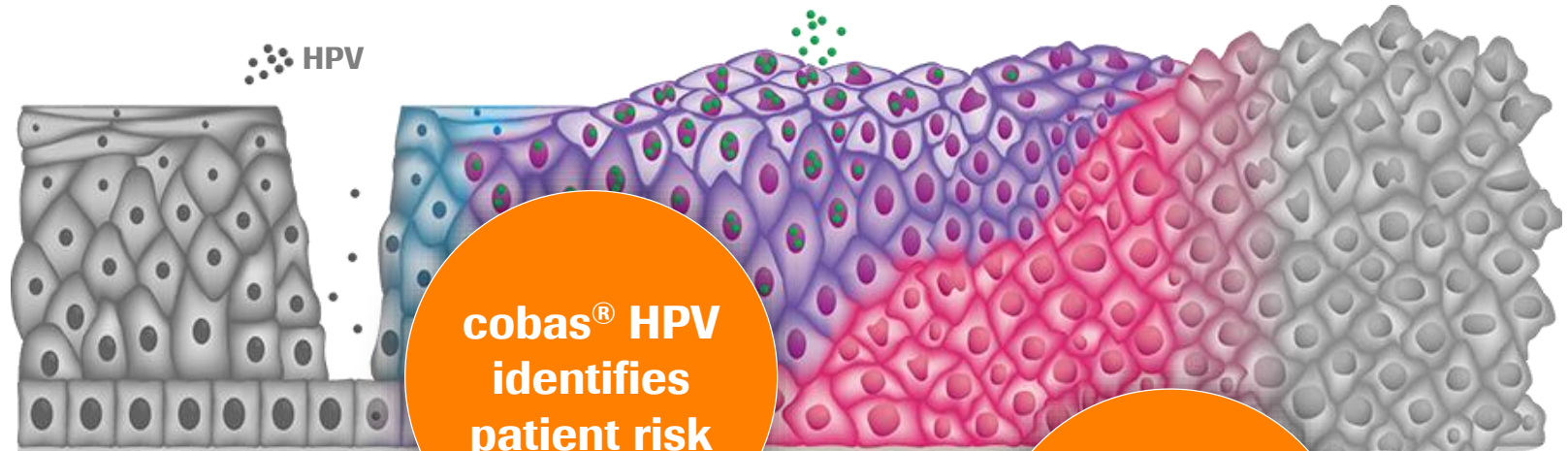
	HPV infection	HPV DNA replication	HPV E6/E7 gene expression	Cell cycle deregulation	Cancer
HPV DNA Test	-	+	→		
HPV E6/E7 mRNA Test	-	-	+	→	
p16/Ki-67 Test	-	-	-	+	→

# Our tests identify both risk & progression



	HPV infection	HPV DNA replication	A single snapshot between risk and disease	Cell cycle deregulation	Cancer
HPV DNA Test	-	+		→	→
<b>HPV E6/E7 mRNA Test</b>	-	-	<b>+</b>	→	→
p16/Ki-67 Test	-	-	-	+	→

# Our tests identify both risk & progression

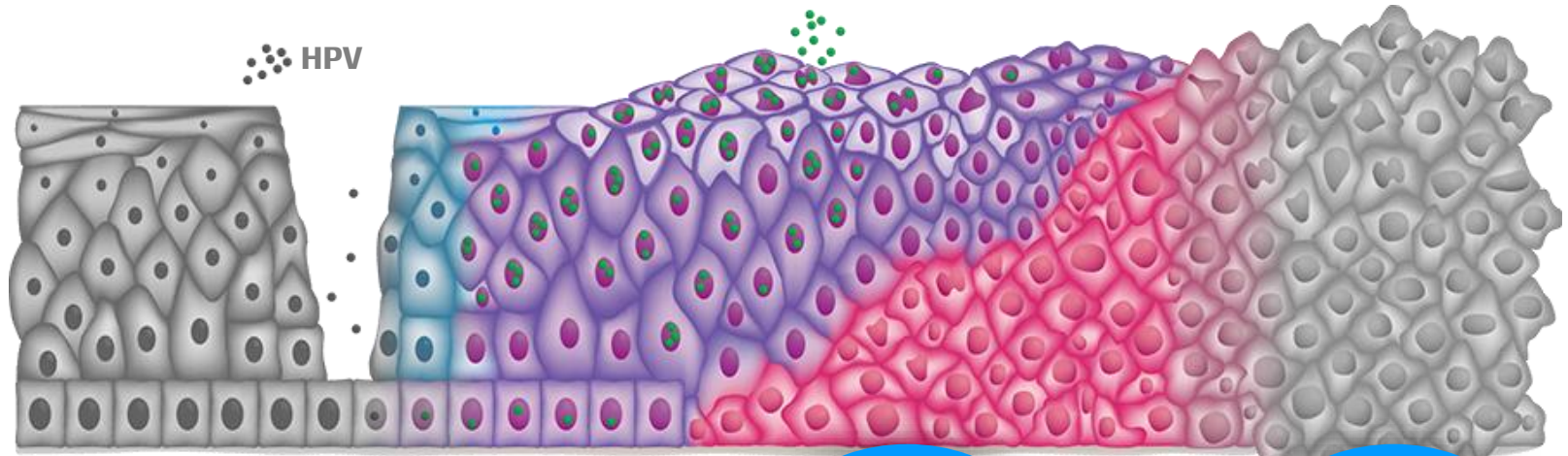




**cobas<sup>®</sup> HPV identifies patient risk**

**Only biomarkers detect cell transformation**

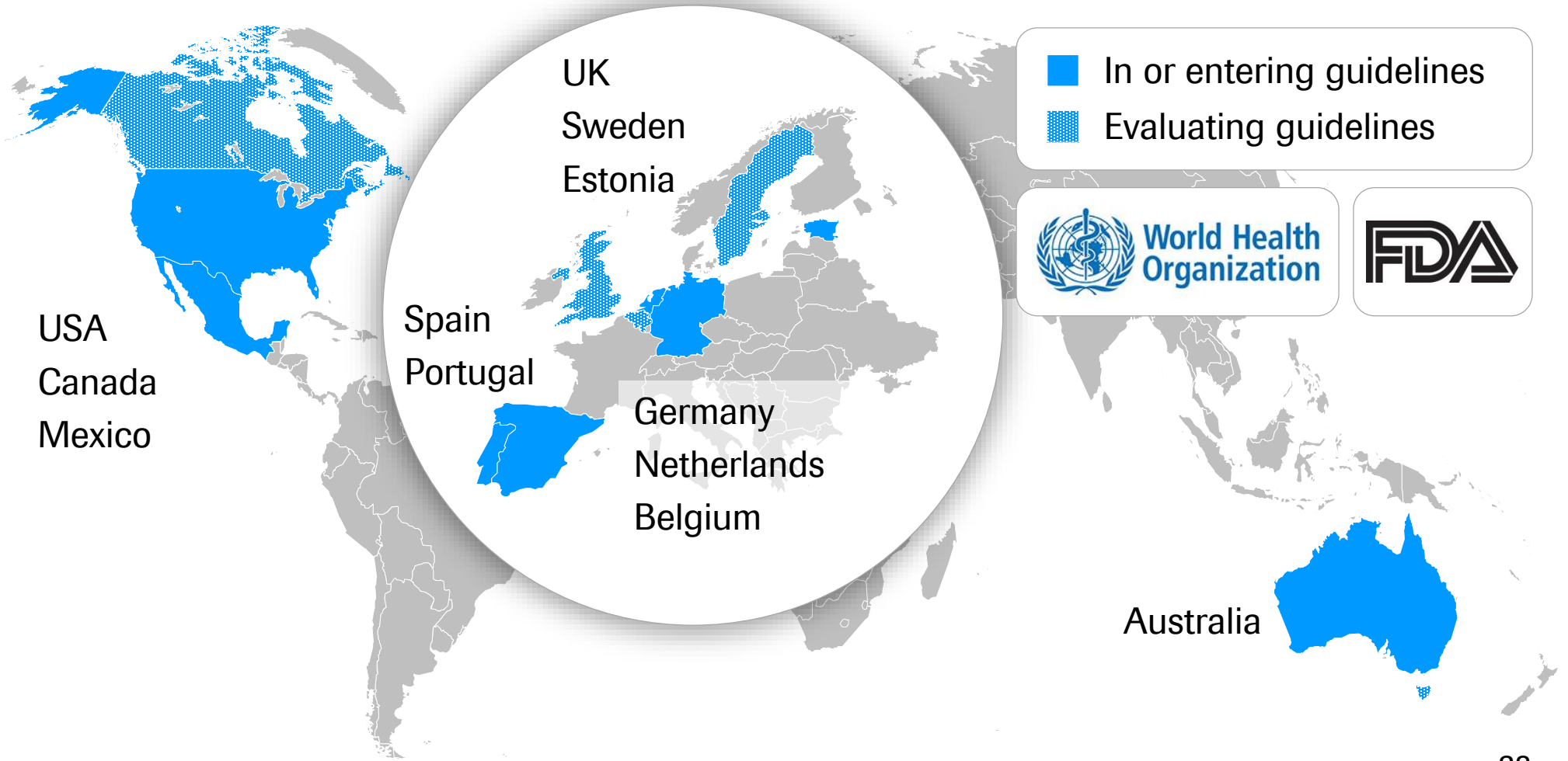
	HPV infection	HPV E6/E7 gene expression	p16/Ki-67	Cancer
<b>HPV DNA Test</b>	-	<b>+</b>	-	→
HPV E6/E7 mRNA Test	-	-	+	→
<b>p16/Ki-67 Test</b>	-	-	-	<b>+</b>

# Our tests identify both risk & progression



	HPV infection	HPV DNA replication	CINtec PLUS	Cell cycle deregulation	CINtec Histo
<b>HPV DNA Test</b>	-	<b>+</b>		-	-
HPV E6/E7 mRNA Test	-	-	-	-	-
<b>p16/Ki-67 Test</b>	-	-	-	<b>+</b>	

# Our innovation is leading to worldwide change



# Our goal is to help end Cervical Cancer



*Doing now what patients need next*

