

Importance of triage for HPV DNA positive women by a 7`HPV genotype mRNA E6/E7 test

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Prevention of cervical cancer

- Cervical cancer can be prevented by early detection and treatment of precancerous lesions (attending screening)
- 99.7% of all cases of cervical cancer are caused by HPV
- HPV DNA testing is more sensitive, but less specific than cervical cytology
- Prevalence of HPV is high, ranging from 20-30% in women with normal cytology
- Most women with a positive HPV DNA test do not have clinically significant disease

Screening



KEY STATS.

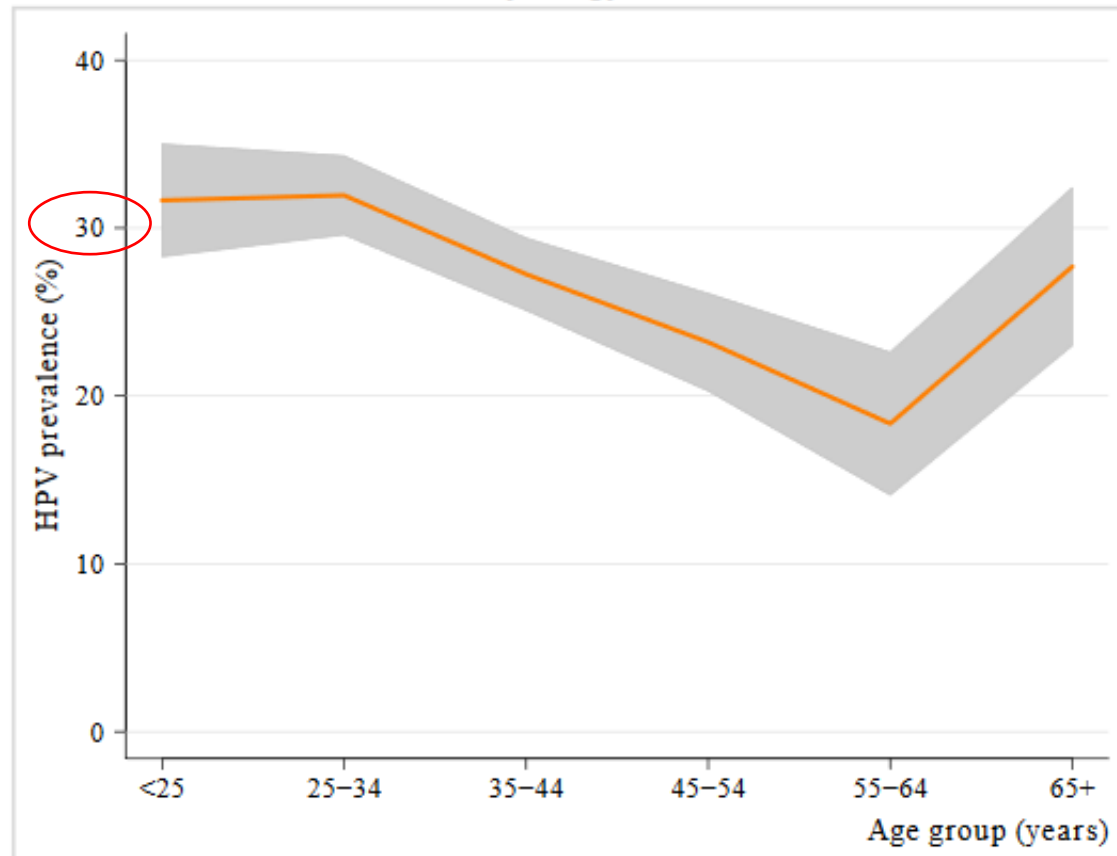
About **7,869 new cervical cancer cases** are diagnosed **annually** in **Mexico** (estimates for 2018).

Cervical cancer **ranks* as the 3rd leading cause** of female cancer in **Mexico**.

Cervical cancer is the **3th most common** female cancer in **women aged 15 to 44 years in Mexico**.

<https://www.hpvcentre.net/statistics/reports/MEX.pdf>

Figure 23: Crude age-specific HPV prevalence (%) and 95% confidence interval in women with normal cervical cytology in Mexico



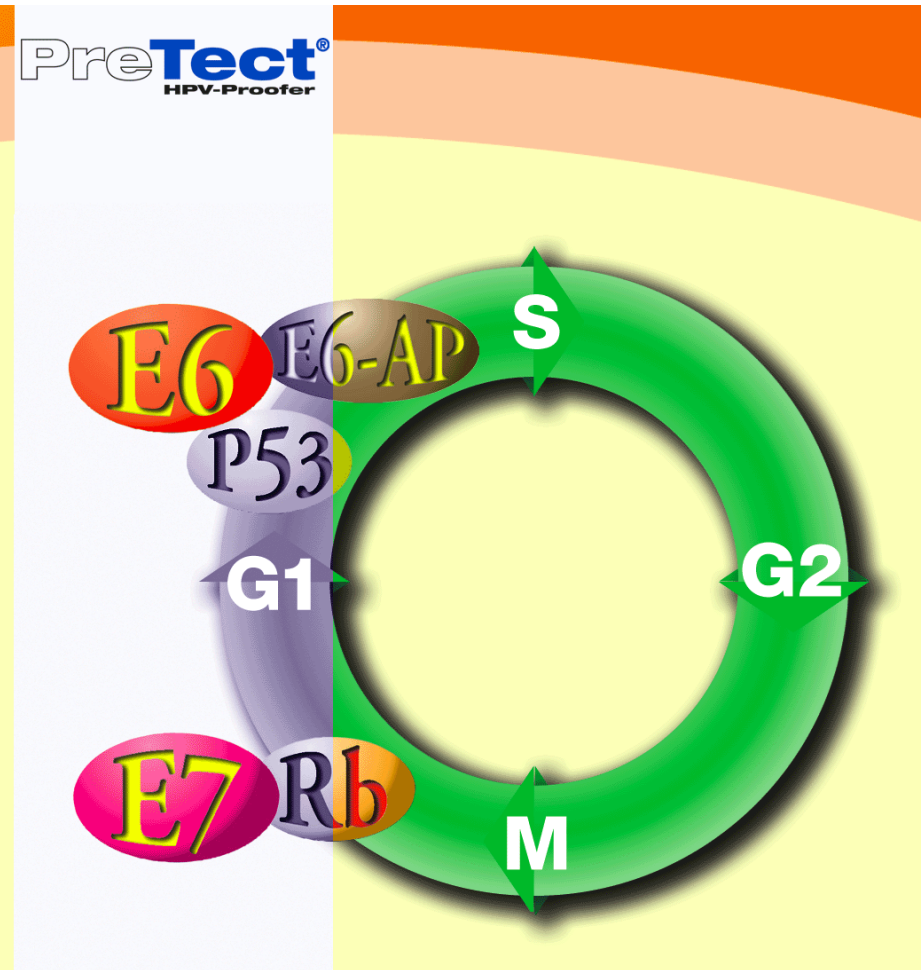
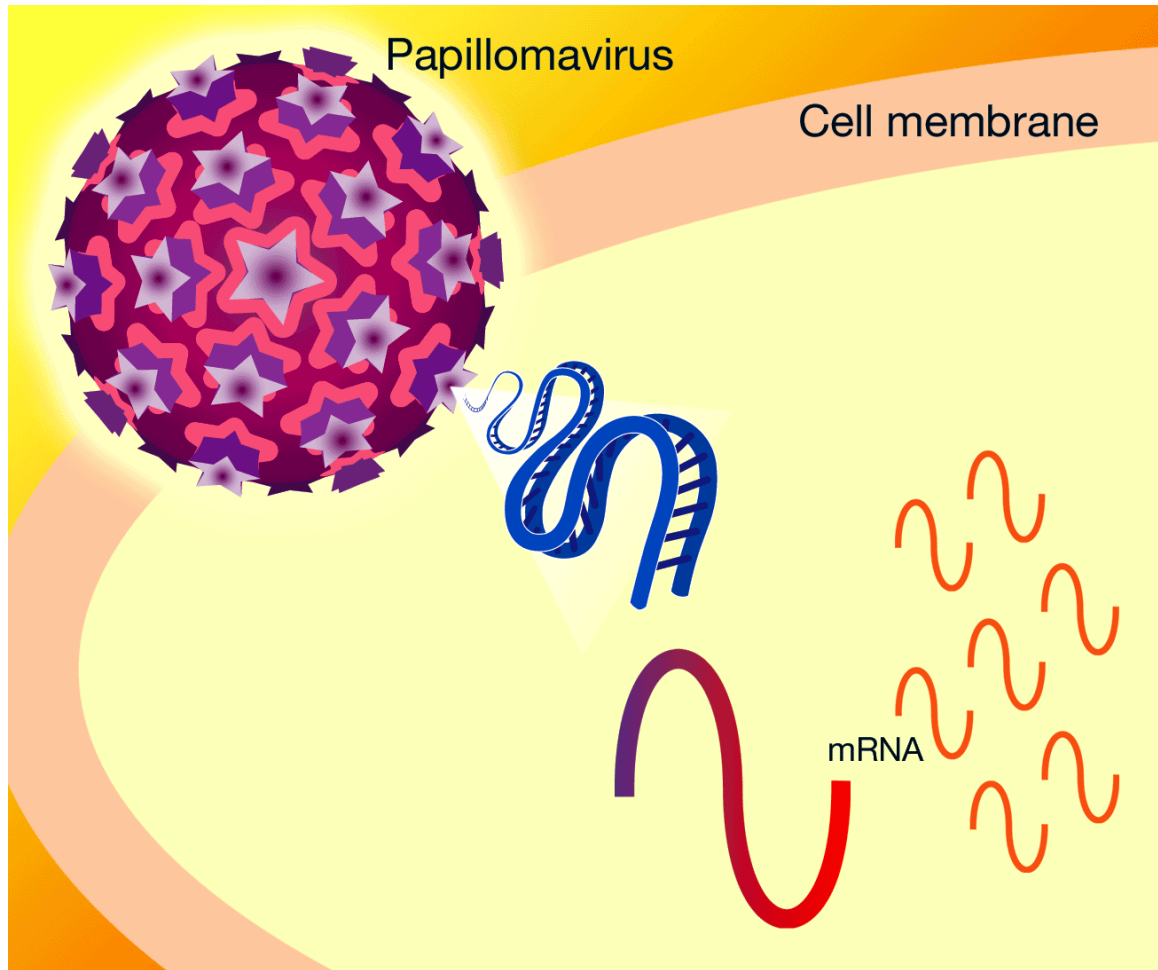
<https://www.hpvcentre.net/statistics/reports/MEX.pdf>

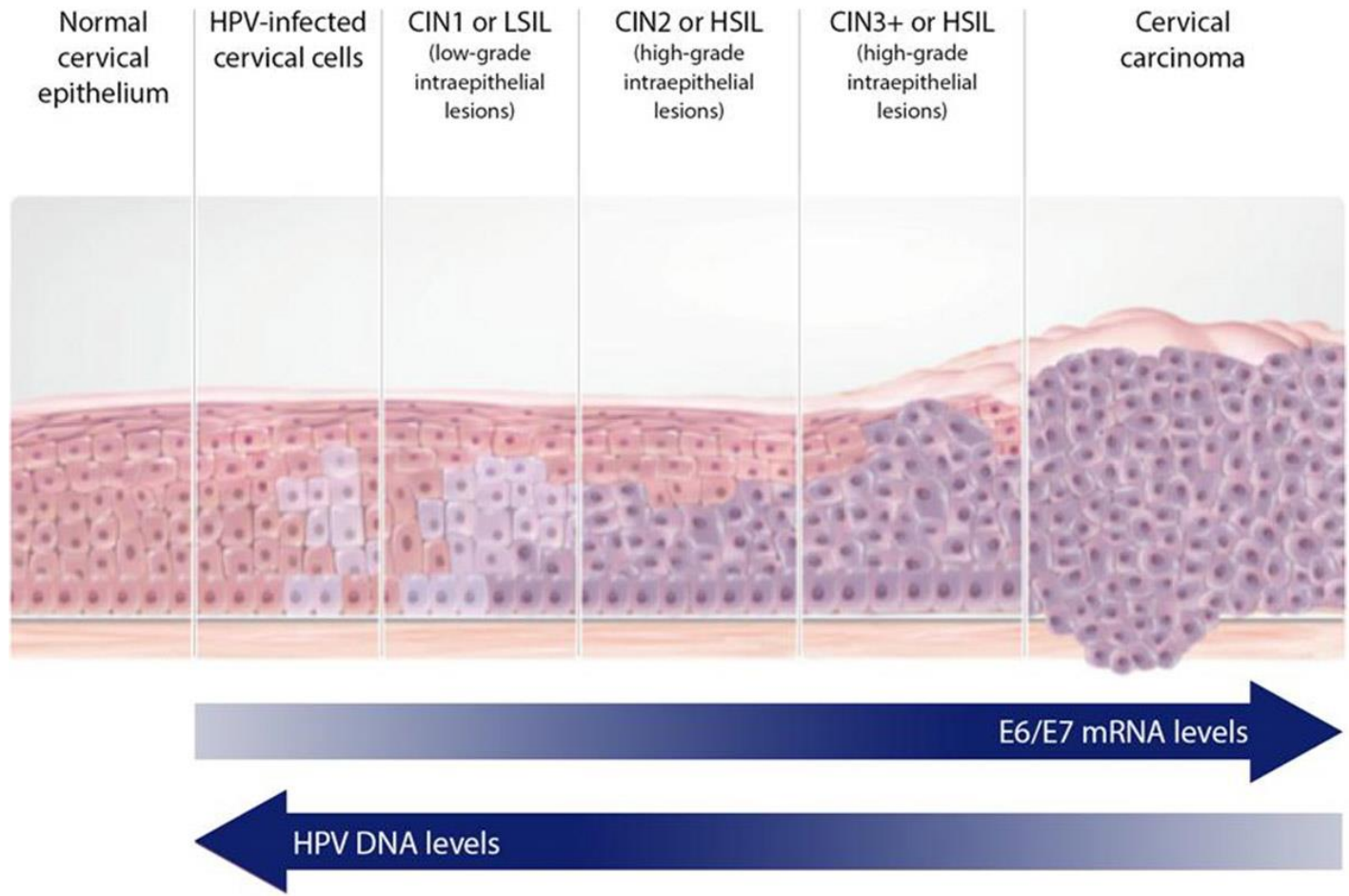
Why Triage? A risk-based approach

- Most HPV infections are transient; 90% regress spontaneously within two years
- To more accurately identify the women who are warranted for colposcopy by discriminating among the transient HPV infections
- To reduce unnecessary interventions and overtreatment
- Requires a highly specific test, detecting as few false positives as possible

Triage options

- Most countries using HPV DNA test in primary screening, utilities cervical cytology in triage of test-positive women
- Cytology is subjective, poorly reproducible and has a low sensitivity
- Cytology can not be used in self-collected material
- HPV mRNA testing is more specific, targeting the E6/E7 genes from the 7 most prevalent HPV-types in cervical cancer (PreTect HPV-Proofer⁷)





HPV genotypes

- Only a few HPV genotypes are highly associated with cervical cancer and require the most aggressive management, whereas others carry a lower risk of disease
- HPV 16 and 18 cause 70% of all cases of cervical cancer
- 7 HPV-types (16, 18, 31, 33, 45, 52 and 58) cause 90% of all cases of cervical cancer
- The same 7 genotypes are covered by the 9-valent HPV vaccine; documented to enable the highest level of protection possible

“The 9vHPV vaccine could potentially provide broader coverage and prevent 90% of cervical cancer cases worldwide”

HPV vaccines

Bivalent	Cervarix ®	16	18							
Quadrivalent	Qardasil ®	16	18	6	11					
9-valent	Qardasil ® 9	16	18	6	11	31	33	45	52	58

Numerous studies show a large reduction on genital warts and vaccine-related HPVs in females¹⁻⁴

¹ Chow EP et al. *Lancet Inf Dis.* 2015; 15: 1314-1323

² Chow EP et al. *Sex Trans Inf.* 2015; 91: 214-219

³ Ali H et al. *BMJ.* 2013; 346: f2032.

⁴ Tabrizi SN et al. *Lancet Inf Dis.* 2014; 14: 958-66

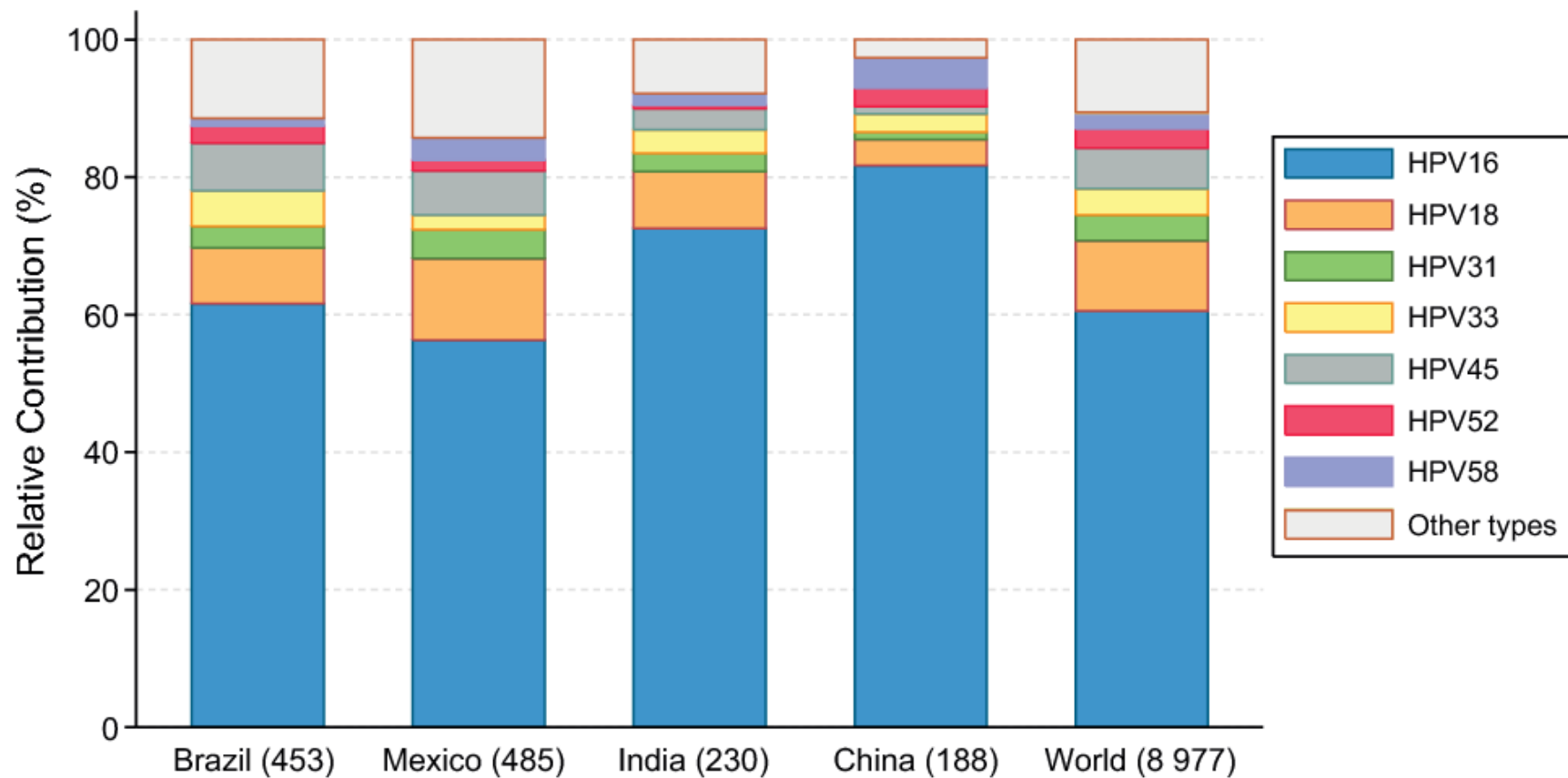
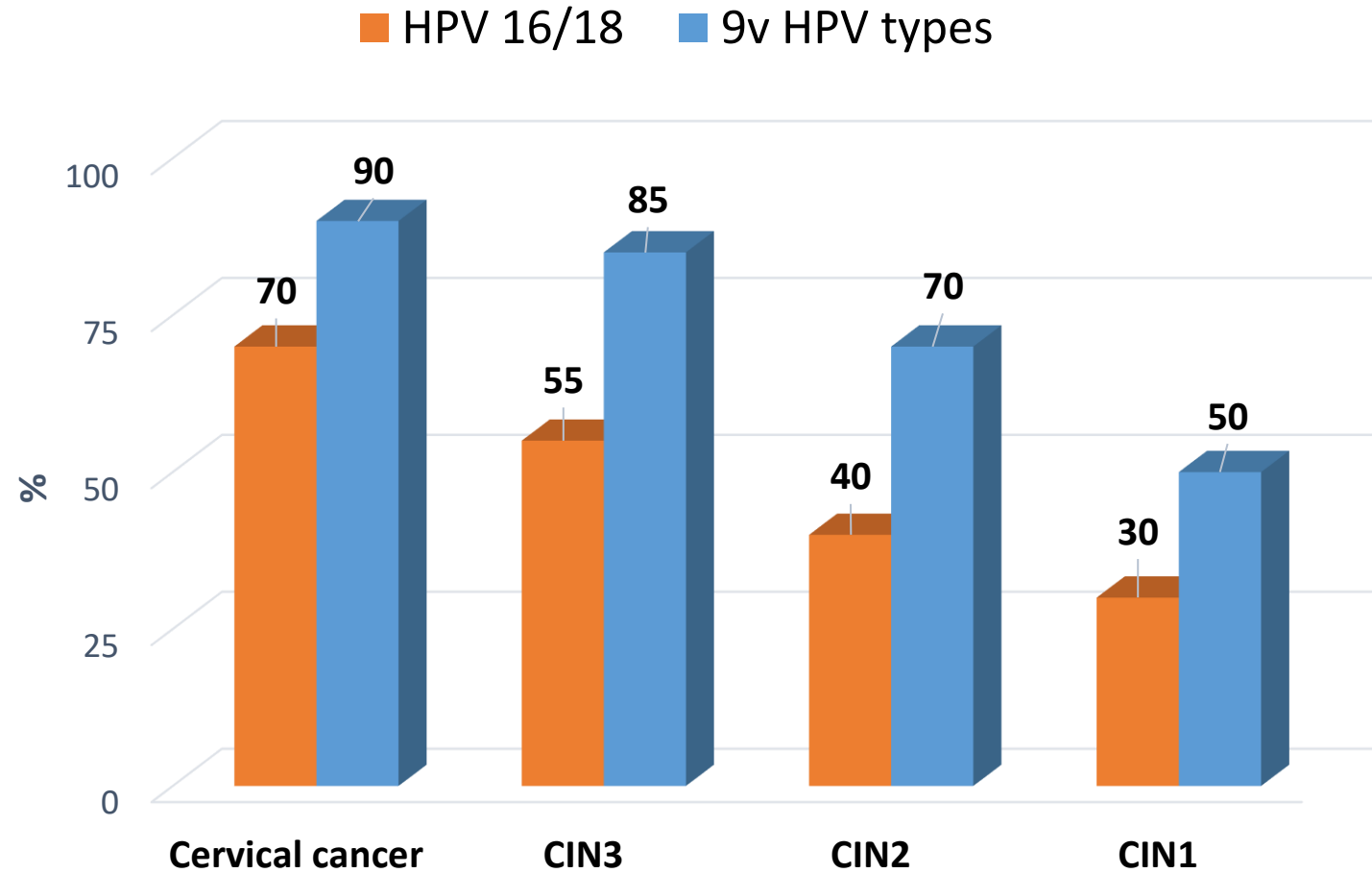


Fig. 2. Contribution of HPVs 16/18/31/33/45/52/58 in cases of **invasive cervical cancer** that tested positive for HPV DNA, in Brazil, **Mexico**, India and China compared to the worldwide HPV type distribution.

HPV 16/18
versus
7 HPV-types



Van Damme P et al. Use of the nonavalent HPV vaccine in individuals previously fully or partially vaccinated with bivalent or quadrivalent HPV vaccines. *Vaccine*. 2016 Feb 3;34(6):757-61.

PreTect HPV-Proofer`7

- Detects **HPV mRNA E6/E7**; precursors of the oncoproteins known to disturb normal cell cycle control (oncogene activity)
- Genotypes the **7 most prevalent HPV-types** causing cervical cancer (HPV 16, 18, 31, 33, 45, 52 and 58)
- Holds a **high clinical specificity** and positive predictive value (PPV) for CIN2+
- Holds **low positivity rate** in general population (only 1/3 of HPV-DNA positives)
- Identifies the women at **increased risk** for future abnormalities; warranted for immediate colposcopy and biopsy

Infection

Cin I, II and III

Cervical-cancer

Persistence

PreTect[®]
HPV-Proof



no risk

moderate risk

high risk

very high risk

Follow-up of triage positives

- Only about 1/3 of the women carrying an HPV-DNA infection express mRNA from the 7 genotypes and should be referred for immediate colposcopy

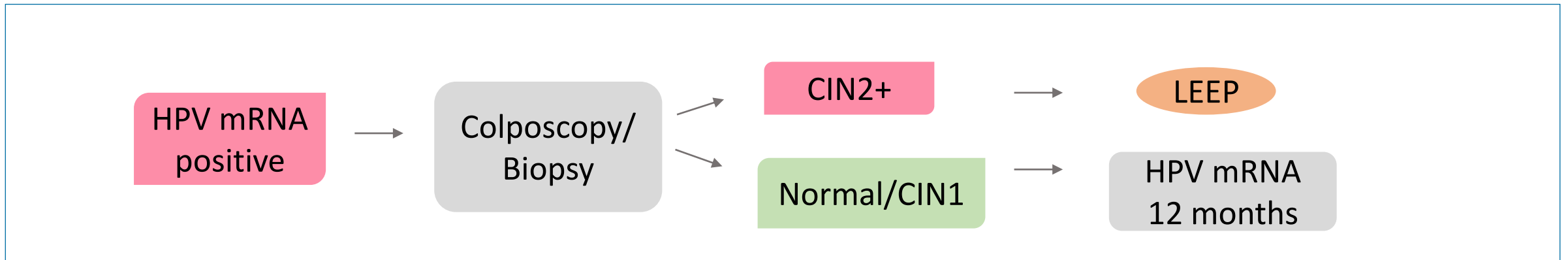
Follow-up of triage negative women

- The remaining 2/3 can be followed up with a new HPV DNA test after 12-24 months where only women with a persistent positive HPV DNA test needs colposcopy and biopsy
- In women with at positive HPV DNA test, 50% have a negative test after 12-24 months

PreTect® HPV-Proofer

HPV mRNA E6/E7 genotyping 16-18-31-33-45-52-58

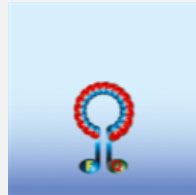
Follow-Up Recommendations



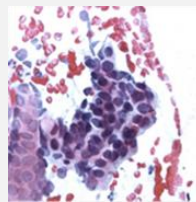
Norway,
women 34-69
years of age



1/10 WOMEN (10%) have a
positive HPV DNA test

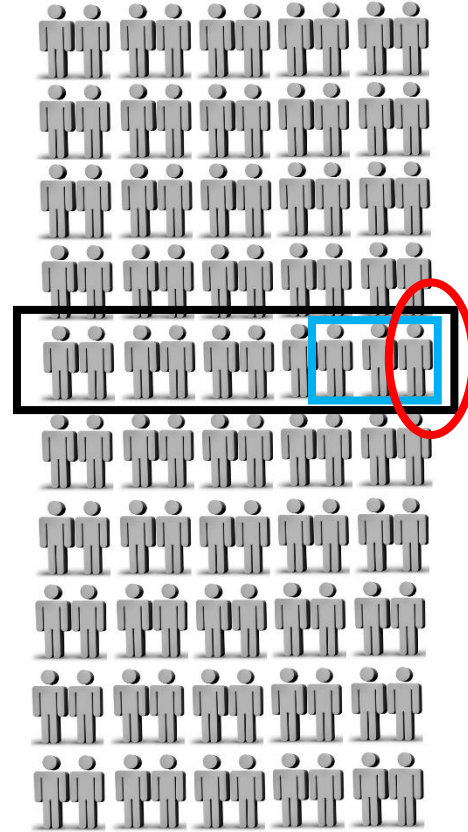


1/30 women (3%) have a
positive HPV mRNA test



1/100 women (1%) have
clinically significant disease
(CIN2+)

Norway, 100 women 34-69 years of age



10 HPV DNA positive

3 HPV mRNA positive

1 CIN2+

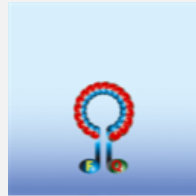
Triage results in Tromsø, Norway

- 2970 women 34-69 years screened with a HPV DNA test
- 176 women (5.9 %) with a positive HPV DNA test
- 69 women (2.3%) with a positive HPV mRNA test (PreTect HPV-Proofer'7)
- 39.2% triage positive (69/176)

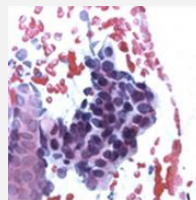
Mexico,
women 30-65
years of age



1 IN 3 WOMEN (~30%) HAVE
AS POSITIVE HPV DNA TEST

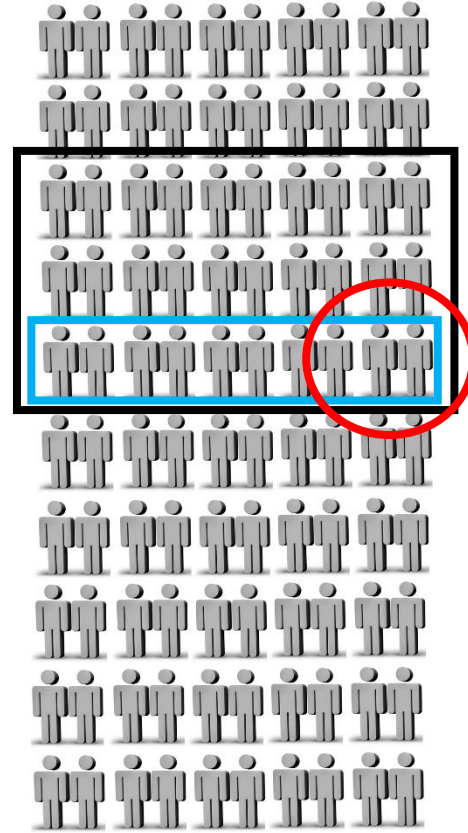


1 IN 10 WOMEN (10%) HAVE
A POSITIVE HPV MRNA
TEST



1 IN 30 WOMEN (3 %) HAVE
CLINICALLY SIGNIFICANT
DISEASE (CIN2+)

Mexico, 100 women 30-65 years of age



30 HPV DNA positive

10 HPV mRNA positive

3 CIN2+

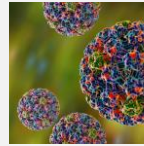
Triage results in Mexico

- 505 women aged 30–65 years at Mexico General Hospital underwent self-sampling (Mia by XytoTest)
- 150 women (29.7%) with a positive HPV DNA test
- 36 women (7.1%) with a positive HPV mRNA test (PreTect HPV-Proofer'7)
- 24.0% triage positive (36/150)

Conclusions



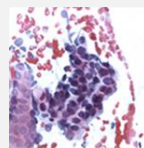
Self-sampling (Mia by XytoTest) using HPV DNA test provides high sensitivity



7 HPV-types are crucial:
HPV 16, 18, 31, 33, 45, 52 and 58 cause 90% of cervical cancer



Triage of HPV DNA positives
PreTect HPV-Proofer'7 enables risk stratification for accurate patient management, holding high specificity



A low positivity rate translates into a low referral rate for colposcopy and **reduces over-treatment**

An aerial night view of Tromsø, Norway, showing the city lights reflecting on the water and the Aurora Borealis in the dark sky. The city is illuminated with warm yellow and orange lights, while the surrounding mountains and water are in deep shadow. The Aurora Borealis appears as vibrant green and blue streaks across the upper half of the frame.

Tromsø

the Gateway to the Arctic

MUCHAS GRACIAS!