EUROGIN 2022

SELF- versus CLINICIAN collected samples for the detection of HPV by 14-type DNA and 7-type mRNA tests a Mexican trial

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Disclosures

- Dr. Aranda Flores has nothing to disclose
- Financial support was provided by the General Hospital of Mexico
- Mel-Mont Medical provided self-sampling devices FOC
- Abbott provided reagents at research cost
- PreTect provided reagents at research cost

Background

- Cervical cancer remains a major public health problem in Mexico
- Self-sampling is a powerful tool to reach under-screened women, improving prevention of CC
- Self-sampling is proven suitable for HPV-testing, not for Cytology
- Most HPV-screening programs rely on cytology as reflex triage of screen positives
- Cytology triage requires a new sample - increased risk of loss to follow-up
- Biomarkers E6/E7 mRNA in triage is a risk-based approach compatible on self-sampled material
- Not all HPV types carry equal risk: 7 HPV-types (16, 18, 31, 33, 45, 52, and 58) cause 90% of all cervical cancer incidents worldwide

Objectives

- Evaluate the performance of a novel self-sampling device (XytoTest, Mel-Mont Medical)
- Compare self-sampling versus clinician-sampling with respect to:
  - sample quality
  - HPV prevalence
- Calculate the concordance and kappa statistic for self- and clinician-collected samples
- Assess the self-reported acceptability of the self-collection procedure

Study design

1. Sample collection was done the same day, in altering order
    - Self-sampling (XytoTest, Mel-Mont Medical LLC. US)
    - Clinician-sampling (Cervex-Brush, Rovers Medical Devices)

2. Molecular HPV-tests was performed on split samples, preserved in PreservCyt (Hologic)
    - 14-type DNA: Abbott RealTi*m*e HR HPV test (Abbott, Germany)
    - 7-type mRNA: PreTect HPV-Proofer`7 (PreTect AS, Norway)

3. Cellularity was calculated on a subset of paired samples
    - Bürker chamber manual cell count

4. Questionnaire
    - Reported experience of the self-collection procedure scored on an 8-point Likert scale

Selection of study population - Mexico

Invited were:

- women attending cervical cancer screening at Mexico General Hospital (MGH)
- health professionals working at the Mexico General Hospital

Inclusion criteria:

- sexually active women, 30-65 years of age, no history of treatment for CC

Exclusion criteria:

- pregnant and breastfeeding women
- had sexual activity within 24 hours prior to collecting samples

Ethics:

- the study was approved by the institutional ethics review board (CI/243/18), MGH
  - signed informed consent
  - All women were invited to a revisit to decide on further follow-up

Study population characteristics

Eduardo Liceaga, Mexico General Hospital

n= 505 women - 1,010 samples collected - 2,020 HPV-tests performed

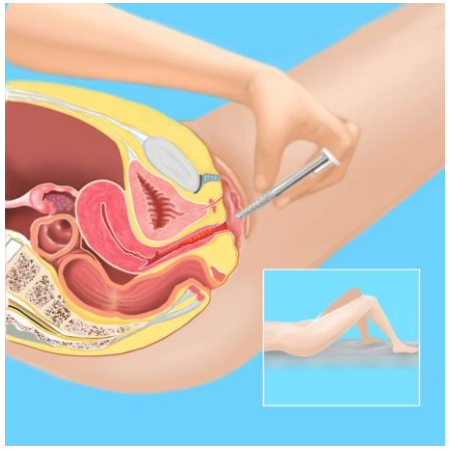
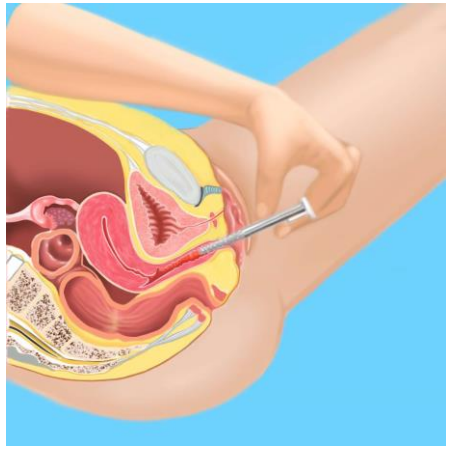
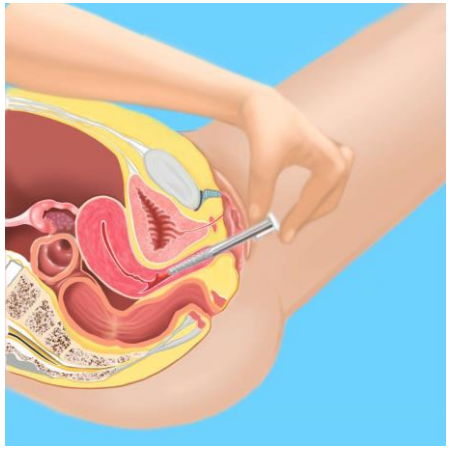
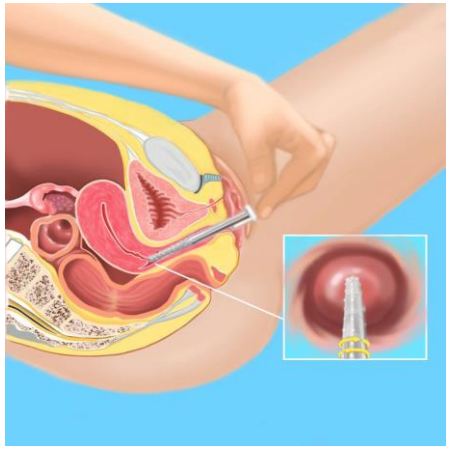
Age		
Mean ± SD	43.8	±8.1
Recruitment source	**n**	**(%)**
Health professionals	169	(33.5)
Women attending screening	336	(66.5)
Age at first sexual intercourse		
<18	153	(30.3)
>18	352	(69.7)

Self sampling device

XytoTest® is designed to collect cells from the whole of the lower female genital tract for molecular diagnostics of HPV

A chemical release of cells occurs when resuspending the device in a methanol-based preservative

Self-sampling step by step

A written and illustrated instructions for use in Spanish were provided to all participants:

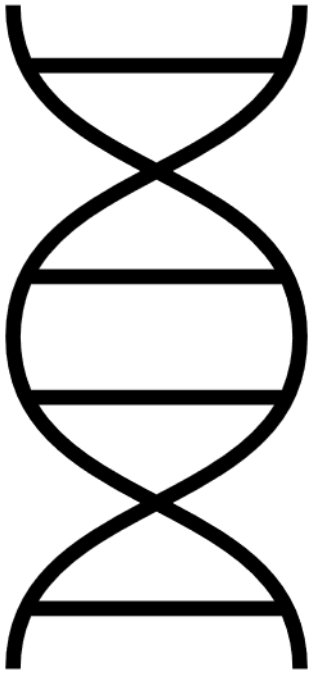
1. insert the device as far as possible into the vagina
2. slowly rotate it 3x360° in the same direction
3. retract the device and place it in a container
4. the clinician immersed the device in 5 ml PreservCyt

HPV DNA 14-type

Abbott Real-Time HR HPV test

- Real-time PCR
- Partial genotyping (HPV 16/18)
- Pooled result (31,33,35,39,45,51,52,56,58,59,66,68)
- Internal Control: Human Beta-globin

- All samples were tested and interpreted according to the manufacturer’s standard procedure and threshold for positivity CT<32.0



7-type HPV E6/E7 mRNA

PreTect®
HPV-Proofer `7

- Tests for oncogenic activity of 7 high risk HPV-types
- Individual typing for HPV 16, 18, 31, 33, 45, 52 and 58
- Includes intrinsic sample control
- NASBA (nucleic acid sequence-based amplification) method

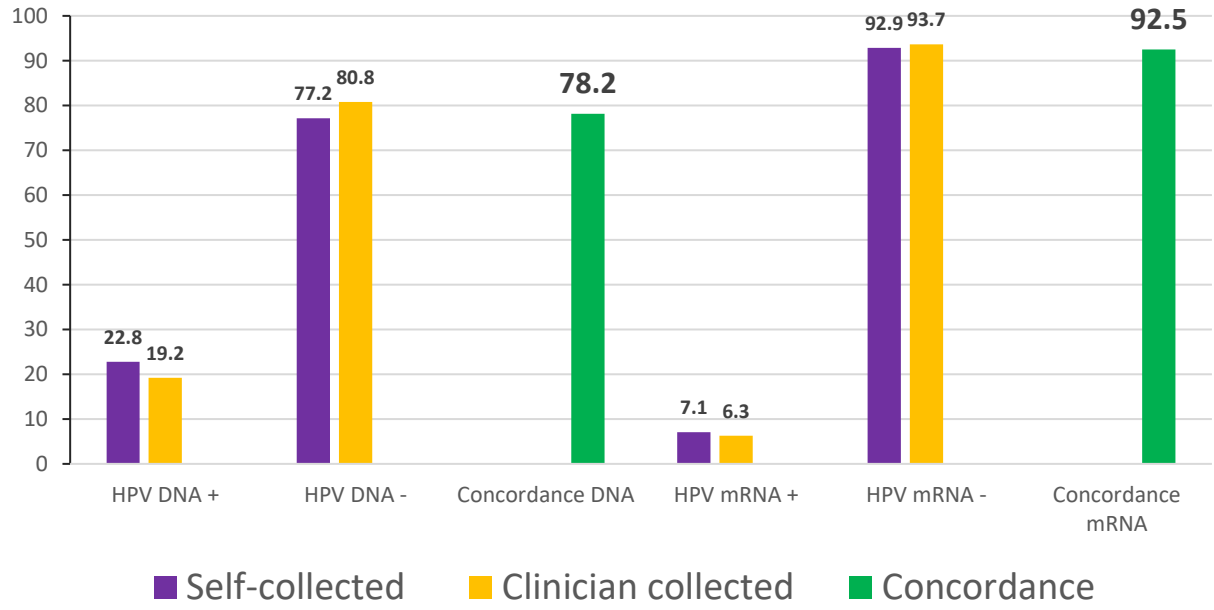
- All samples were tested and interpreted according to the manufacturer’s standard procedure

HPV genotypes presented hierarchically by oncogenicity for Clinician-collected and Self-collected samples

	14-type DNA test		7-type mRNA test	
	Clin-C	Self-C	Clin-C	Self-C
N= 505	n (%)	n (%)	n (%)	n (%)
HPV 16	15 (3.0)	16 (3.2)	7 (1.4)	9 (1.8)
HPV 18 (non 16)	6 (1.2)	8 (1.6)	4 (0.8)	5 (1.0)
HPV other (non16/18)	76 (15.0)	91 (18.0)	21 (4.2)	22 (4.4)
HPV prevalence	**97 (19.2)**	**115 (22.8)**	**32 (6.3)**	**36 (7.1)**

- HPV-DNA prevalence was **22.8%** in self-collected versus **19.2%** in clinician-collected samples (P=0.19)
- Overexpression of mRNA E6/E7 from 7 HPV types was **7.1%** in SC and **6.3%** in CC (P=0.71)
- Mostly non-HPV16/18 genotypes were detected
- All 1,010 samples had valid results for both HPV tests, no exclusions were made due to low cellularity

Agreement between Self-collected and Clinician-collected samples



- **Overall agreement between the two collection methods by Cohen's Kappa coefficients was fair (0.21-0.40) with a concordance rate 78.2% / 92.5%**
  - *(390/505), **k=0.34** (95% CI: 0.25-0.44), P<0.001 HPV-DNA test*
  - *92. 78.2%5% (467/505), **k=0.40** (95% CI: 0.25-0.56), P<0.001 HPV mRNA test*

- **No statistically significant differences between the two sample-collection methods (P > 0.05) was observed** (Wilcoxon signed–rank test)

# Descriptive statistics for cellularity
n= 20% of study population

- The self-sampled aliquot contained about 3 times more cells compared to clinician collected aliquot

1.8 million cells/ml versus 0.6 million cells/ml

(P < 0.001 Wilcoxon signed rank test)

Sample	N	Min.	Max.	Mean	Median	SD	95 % CI
Clinician-collected	97	13,300	6,880,000	630,700	353,300	1,031,059	280,000 – 446,700
Self-collected	97	13,300	10,866,700	1,866,800	1,746,700	1,538,900	1,480,000 – 2,006,700

Questionnaire Responses "Acceptability of self-collection"

1 (no discomfort)
8 (unbearable discomfort)

Q1: 88.8% reported no discomfort at all

Q2: 94.0% found no difficulty performing procedure

Q3: 96.6% agreed to perform self-sampling again

Q4: 96.8% felt confident carrying out the procedure

Table 2. Questionnaire Responses (acceptability of self-collection, n=505)

Level of discomfort	**(n)***	**(%)**
1	445	88.8
2	32	6.4
3	10	2.0
4	7	1.4
5	1	0.2
6	3	0.6
7	2	0.4
8	1	0.2
(Total responses)	501	99.2
Level of difficulty		
1	471	94.0
2	21	4.2
3	4	0.8
4	1	0.2
5	1	0.2
6	1	0.2
7	1	0.2
8	1	0.2
(Total responses)	501	99.2
Would you perform self-sampling again?		
Yes	483	96.6
No	17	3.4
(Total responses)	500	99.0
Do you feel confident taking the sample?		
Yes	484	96.8
No	16	3.2
(Total responses)	500	99.0

Conclusions

- Self-sampling (XytoTest by Mel-Mont Medical) is as reliable as clinician-sampling for HPV-testing and allows reflex triage by HPV mRNA genotyping
- The high prevalence of HPV DNA (20%) is comparable to the prevalence reported in other studies from Mexico – and reflects the need for effective triage
- Only 1/3 of HPV DNA positive women had overexpression of mRNA E6/E7 an appealing situation for effective triage
- A combination of self-sampling and molecular diagnostics may significantly aid prevention of cervical cancer, by simplicity, increased accessibility to screening and accurate diagnostics for improved patient management


Thank you!
Muchas gracias!