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COMPARISON OF CLINICAL EFFICACY OF HUMAN PAPILLOMAVIRUS (HPV) TESTING WITH PARTIAL GENOTYPING TO LIQUID-BASED CYTOLOGY AS PRIMARY TEST IN CERVICAL SCREENING FOR WOMEN BETWEEN 25 AND 29 YEARS OLD IN SINGAPORE

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INTRODUCTION

- 2003: National Cervical Cancer Screening launched
  - Cytology-based (LBC)
  - Women 25 to 65 years old
- 2019: Primary hr-HPV DNA introduced
  - Women aged 25-29 years old: 3 yearly LBC
  - Women >30 years old: 5 yearly HPV
- Difference in screening due to the argument that predictive value of HPV was lower than LBC
  - High prevalence of HPV in younger women
  - High regression rate of low-grade lesions

However, these arguments lack convincing evidence

AIMS

- Compare clinical efficacy of primary HPV testing and LBC in cervical cancer screening for women < 30 years old in Singapore
- Test performance compared to women at older 5-year groupings up to 44 years old

METHODS

- Retrospective cohort study from 2013 to 2019
- Inclusion:
  - Women attending cervical cancer screening using co-testing
  - Age 25 and above
- Exclusion
  - History of CIN
  - Attendance for management of abnormal screening
- Criteria for referral to colposcopy
  - Positive hrHPV with ASCUS on LBC
  - HPV16+ or HPV18+ regardless of LBC result
  - LBC showing LSIL, HSIL or ASCH

CONCLUSION

- Clinical efficacy of primary HPV testing was comparable to cytology in cervical cancer screening in women between 25 and 29 years old.
- More importantly, the efficacy was comparable to older women between 30 and 44 years old who are recommended primary HPV-based screening.
- These data give strong support for incorporating women aged 25 to 29 years old into HPV-based primary screening program in Singapore.

RESULTS

- n=6,398 women
- Mean age: 44.2 years old (95%CI 22.1-66.3)
- 5,733 (89.6%) were aged 30 years and older
- Overall, 503 women were positive for hrHPV (7.9%) (95%CI 7.2-8.6)
- Declining trend of prevalence of hrHPV DNA with age from 25 to 69 years old
- Age-related difference was mainly the effect of a markedly lower prevalence of HPV in women > 45 years
- hrHPV positivity in age-groupings 30-34, 35-39, 40-44 years old not significantly different (p=0.764)

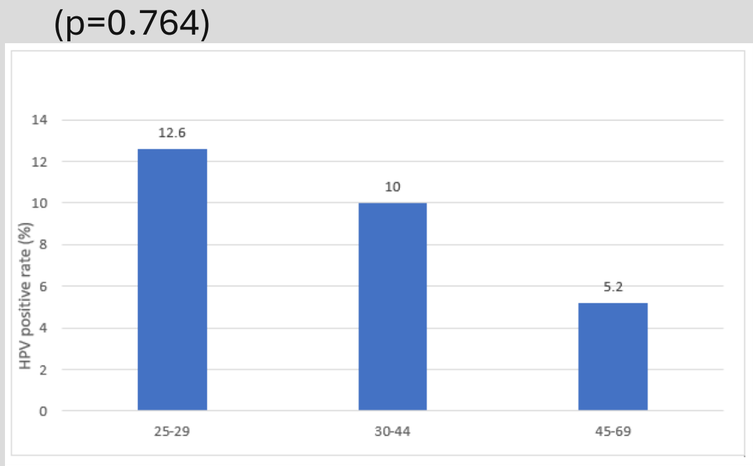

Fig 1 Comparison of HPV positivity between three groups of women

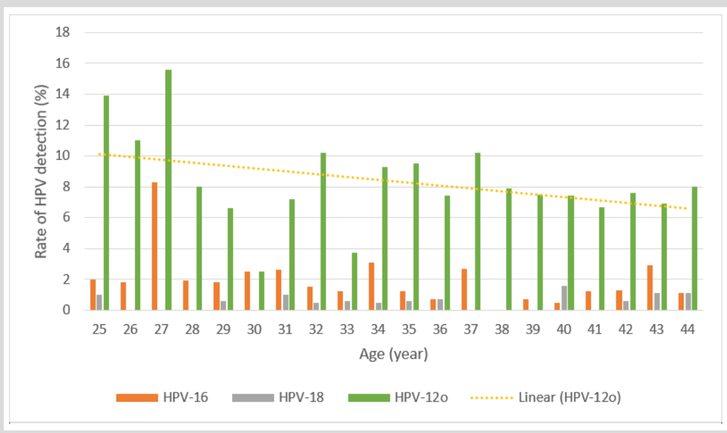

Fig 2 Rate of HPV detection in women aged 25 – 44 years old

- In women aged 25-29 years old, the rate of discharge to routine screening was not statistically different at 87.4% with hrHPV screening and 89.5% with LBC (p=0.2302) and was similar for the three age-cohorts of women

Table 1: Comparison of HPV Comparison of cytology and primary HPV screening on first testing

Age	Total	Cytology Negative		HPV Negative		p-value
		n	%	n	%	
25 – 29	665	595	89.5	581	87.4	0.2302
30 – 44	2577	2348	91.1	2320	90.0	0.1828
45 – 69	3156	2972	94.0	2999	94.8	0.1402
Total	6398	5915	92.4	5900	92.1	0.6208

- Immediate colposcopy referral rates was not statistically different at 6.6% for LBC and 7.8% for hrHPV screening in women aged 25-29 years old (p=0.3966). There was no statistical difference comparing LBC to hrHPV screening through the age groups. The colposcopy referral rate from both LBC and hrHPV screening was higher compared to women aged 30-44 years old (p<0.001).

Table 2: Comparison of rate of immediate colposcopy referral between cytology and HPV screening

Age	Total	Cytology Screening			HPV Screening			p-value
		n	%	95% CI	n	%	95% CI	
25 – 29	665	44	6.6	4.81 – 8.88	52	7.8	5.84 – 10.25	0.3966
30 – 44	2578	143	5.5	4.68 – 6.53	127	4.92	4.11 – 5.86	0.3172
45 – 69	3163	93	2.9	2.37 – 3.60	74	2.3	1.84 – 2.94	0.1362
Total	6406	280	4.6	4.05 – 5.14	253	3.7	3.54 – 3.85	0.2322

- Overall, 27 cases of CIN2+ were detected on LBC screening and 30 cases on HPV screening. More high-grade lesions were detected among younger women aged 25-29 and 30-44 years old compared to women ≥ 44 years old.

Table 3: Detection rate of high-grade lesions of the cervix compared by screening methods

Age	Total	Cytology screening					HPV screening				
		CIN2	CIN3+	Total CIN2+			CIN2	CIN3+	Total CIN2+		
				n	%	95% CI			n	%	95% CI
25 – 29	665	3	2	5	0.76	0.25 – 1.78	3	2	5	0.76	0.25 – 1.78
30 – 44	2577	4	14	18	0.70	0.41 – 1.10	4	15	19	0.74	0.44 – 1.15
45 – 69	3156	0	4	4	0.13	0.03 – 0.32	0	6	6	0.13	0.07 – 0.41
Total	6398	7	20	27	0.42	0.28 – 0.61	7	23	30	0.47	0.32 – 0.67

- Among women aged 25-29 years old, the number of colposcopies per case of CIN2+ was 5 for LBC screening and 7 for HPV-based screening (p=0.5582). This trend was similarly observed for women aged 30-44 years old.
- In comparison, the number of colposcopies needed for detection of a case of CIN2+ was more than 2-fold higher for women above 45 years old, owing to a higher detection rate of CIN2+ among the younger women

Table 4: Comparison of number of colposcopies per case of CIN2+ detected by method of screening

Age	Total Colposcopies Performed		Number of Colposcopies Per Case of CIN2+		
	LBC	HPV	Cytology screening	HPV screening	p-value
25 – 29	25	35	5.0	7.0	0.5582
30 – 44	86	106	4.8	5.6	0.5995
45 – 69	52	69	13.0	11.5	0.8427
Total	163	210	6.03	7.0	0.5441

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