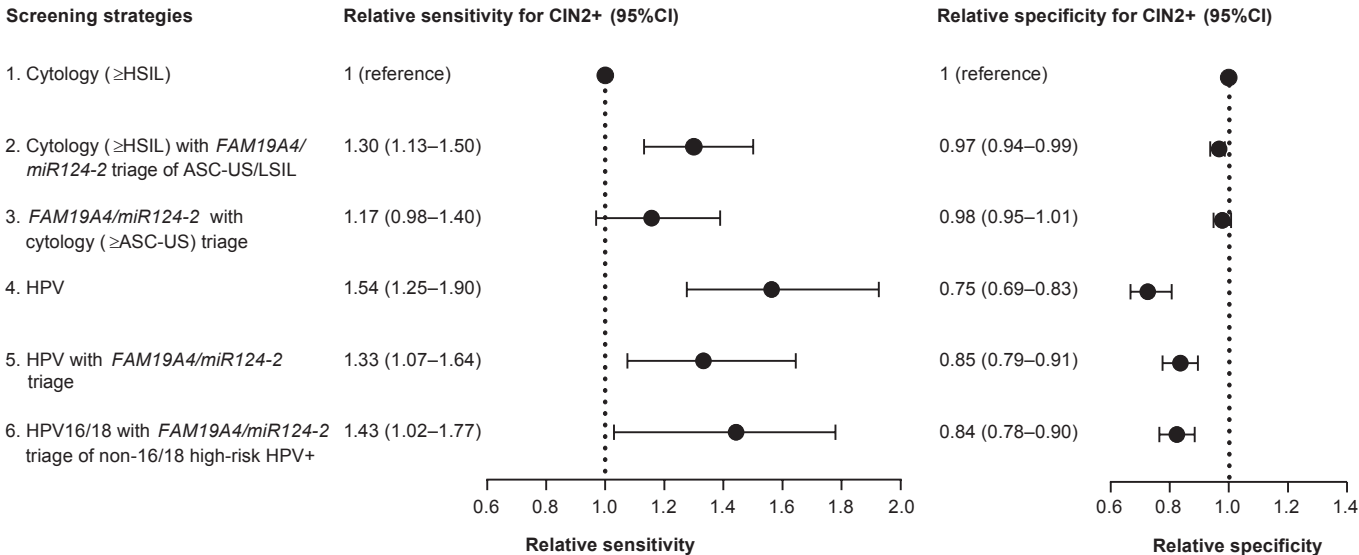**SUPPLEMENTAL DIGITAL CONTENT 1**

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Supplemental Table. Accuracy and diagnostic efficiency of screening strategies to detect CIN2 or worse (CIN2+)
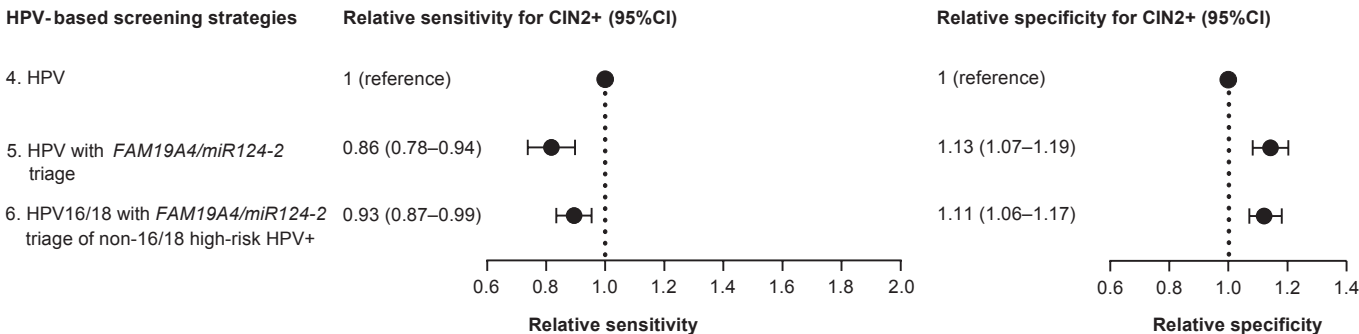
No.	Strategy	Sensitivity (95% CI)		$n1/N1$	Specificity (95% CI)		$n2/N2$	PPV	NPV	Referral rate	Referrals needed to detect one CIN3+	Number of tests/1,000 women screened
Cytology-based screening												
1	Cytology (≥HSIL)	50.5%	(40.3-60.8)	46/91	95.9%	(93.1-98.7)	186/194	85.2%	80.5%	18.9%	1.2	1000
2	Cytology (≥HSIL) with *FAM19A4/miR124-2* triage of ASC-US/LSIL	65.9%	(56.2-75.7)	60/91	92.8%	(89.1-96.4)	180/194	81.1%	85.3%	26.0%	1.2	1095
3	*FAM19A4/miR124-2* with cytology (≥ASC-US) triage	59.3%	(49.2-69.4)	54/91	93.8%	(90.4-97.2)	182/194	93.8%	83.1%	23.2%	1.2	1674
HPV-based screening												
4	HPV	78.0%	(69.5-86.5)	71/91	72.2%	(65.9-78.5)	140/194	56.8%	87.5%	43.9%	1.8	1000
5	HPV with *FAM19A4/miR124-2* triage	67.0%	(57.4-76.7)	61/91	81.4%	(76.0-86.9)	158/194	62.9%	84.0%	34.0%	1.6	1440
6	HPV16/18 with *FAM19A4/miR124-2* triage of non-16/18HPV+	72.5%	(63.4-81.7)	66/91	80.4%	(74.8-86.0)	156/194	63.5%	86.2%	36.5%	1.6	1315

Abbreviations: cytology with threshold high-grade squamous intraepithelial lesion or worse (≥HSIL, includes atypical squamous cells - cannot exclude HSIL); cytology with threshold atypical squamous cells of unknown significance or worse (≥ASC-US); LSIL, low-grade squamous intraepithelial lesion; 95% CI, 95% confidence interval; n1, number of screen-positive disease cases; N1, total number of disease cases; n2, number of screen-negative non-disease cases; N2, total number of non-disease cases; PPV, positive predictive value; NPV, negative predictive value.

Figure. Forest plots showing the relative sensitivities and specificities for the detection of CIN2 or worse (CIN2+) of different screening strategies compared with (A) cytology (threshold ≥HSIL); and (B) HPV-based strategies

Abbreviations: HSIL, high-grade squamous intraepithelial lesion; ASC-US, atypical squamous cells of unknown significance; LSIL, low-grade squamous intraepithelial lesion; 95%CI, 95% confidence interval

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Supplemental Table. Complementarity of *FAM19A4/miR124-2* methylation analysis to cytology-based (A) and HPV-based (B) screening strategies.

A.	≤CIN2 n	≤CIN2 %	CIN3+ n	CIN3+ %	B.	≤CIN2 n	≤CIN2 %	CIN3+ n	CIN3+ %
NILM	**186**	**82.3%**	**18**	**30.5%**	**High-risk HPV positive**	**76**	**33.6%**	**49**	**83.1%**
methylation negative	74	39.8%	4	22.2%	methylation negative	22	28.9%	6	12.2%
methylation positive	112	60.2%	14	77.8%	methylation positive	54	71.1%	43	87.8%
ASC-US/LSIL	**21**	**9.3%**	**6**	**10.2%**	**HPV16/18 positive**	**14**	**6.2%**	**21**	**35.6%**
methylation negative	6	28.6%	1	16.7%	methylation negative	3	21.4%	4	19.0%
methylation positive	15	71.4%	5	83.3%	methylation positive	11	78.6%	17	81.0%
≥HSIL	**19**	**8.4%**	**35**	**59.3%**	**Non16/18 high-risk HPV positive**	**62**	**27.4%**	**28**	**47.5%**
methylation negative	5	26.3%	3	8.6%	methylation negative	19	30.6%	2	7.1%
methylation positive	14	73.7%	32	91.4%	methylation positive	43	69.4%	26	92.9%

Abbreviations: ≤CIN2, CIN2 or less; CIN3+, CIN3 or worse; ≥HSIL, cytology with threshold high-grade squamous intraepithelial lesion or worse (includes atypical squamous cells - cannot exclude HSIL); ASC-US, atypical squamous cells of unknown significance; LSIL, low-grade squamous intraepithelial lesion.