

## Supplementary Online Content

Melnikow J, Henderson JT, Burda BU, Senger CA, Durbin S, Weyrich MS. Screening for cervical cancer with high-risk human papillomavirus testing: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. doi:10.1001/jama.2018.10400

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**eReferences**

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Quality Assessment Criteria

Study Design	Adapted Quality Criteria
Randomized and non-randomized controlled trials, adapted from the U.S. Preventive Services Task Force methods	<ul style="list-style-type: none"> <li>• Was there adequate participation in the study by eligible/invited persons?</li> <li>• Valid random assignment?</li> <li>• Was allocation concealed?</li> <li>• Was eligibility criteria specified?</li> <li>• Were groups similar at baseline?</li> <li>• Was there a difference in attrition between groups after randomization?</li> <li>• Was the reading (interpretation) of the pathology results adequate?</li> <li>• Were outcome assessors blinded?</li> <li>• Were measurements equal, valid and reliable?</li> <li>• Was there risk of contamination?</li> <li>• Was there adequate adherence to the intervention?</li> <li>• Were the statistical methods acceptable?</li> <li>• Was the handling of missing data appropriate?</li> <li>• Was there acceptable follow-up?</li> <li>• Was there evidence of selective reporting of outcomes?</li> </ul>
Cohort studies, adapted from the Newcastle-Ottawa Scale	<ul style="list-style-type: none"> <li>• Was there representativeness of the exposed cohort?</li> <li>• Was the non-exposed systematic selected?</li> <li>• Was the ascertainment of exposure reported?</li> <li>• Were eligibility criteria specified?</li> <li>• Were groups similar at baseline?</li> <li>• Was the reading (interpretation) of the pathology results adequate?</li> <li>• Were outcome assessors blinded?</li> <li>• Were measurements equal, valid and reliable?</li> <li>• Was follow-up long enough for outcomes to occur?</li> <li>• Were the statistical methods acceptable?</li> <li>• Was the handling of missing data appropriate?</li> <li>• Was there adjustment for confounders?</li> <li>• Was there acceptable follow-up?</li> </ul>

Good quality studies generally meet all quality criteria. Fair quality studies do not meet all the criteria but do not have critical limitations that could invalidate study findings. Poor quality studies have a single fatal flaw or multiple important limitations that could invalidate study findings. Critical appraisal of studies using a priori quality criteria are conducted independently by at least two reviewers. Disagreements in final quality assessment are resolved by consensus, and, if needed, consultation with a third independent reviewer.

eTable 2. Effectiveness of hrHPV Screening for CIN 3+ and Invasive Cervical Cancer Incidence, Based on Cohort and Cross-sectional Studies

Source	Quality <sup>a</sup>	N Randomized (Ages Recruited)	Screening Round (Follow- Up Period, y)	Screening Approach	CIN3+	ICC
					Absolute Detection (%)	Absolute Detection (%)
<b>hrHPV Primary Screening</b>						
Zorzi, 2017 <sup>1</sup>	Fair	48,736 (25-64)	1 (3)	hrHPV w/CC triage	95/48,736 (0.2)	NR
			2 (3)	hrHPV w/CC triage	6/21,827 (0.03)	NR
			Cumulative (6)	hrHPV w/CC triage	101/48,736 (0.2)	NR
<b>hrHPV Co-testing with Cytology</b>						
Katki, 2011 <sup>2-7</sup> KPNC	Fair	331,818 (≥30)	1 (3)	hrHPV w/CC	NR	NR
			2 (2.9)	hrHPV w/CC	102/195,975 (0.05)	13/195,975 (0.01)
			Cumulative (6)	hrHPV w/CC	834/331,818 (0.3)	87/331,818 (0.03)
Ibanez, 2014 <sup>8</sup>	Fair	1,832 (40-88)	1 (4-5)	hrHPV w/CC	9/767 (1.2)	2/767 (0.3)
Luyten, 2014 <sup>9,10</sup> WOLPHSCREEN	Fair	19,795 (≥30)	1 (5)	hrHPV w/CC	172/19,795 (0.87)	20/19,795 (0.1)
			2 (5)	hrHPV w/CC	2/4,067 (0.05)	NR

<sup>a</sup>Assessed using criteria from the US Preventive Services Task Force<sup>11</sup>

**Abbreviations:** CC = conventional cytology; CIN = cervical intraepithelial neoplasia; CG = control group; hrHPV = high risk human papillomavirus; ICC=invasive cervical cancer; IG = intervention group; NR = not reported

eTable 3. Effectiveness of hrHPV Screening for CIN 3+ and Invasive Cervical Cancer Incidence, Based on Randomized Clinical Trials, Among Women Aged ≥ 30-35 Years

Source	Quality <sup>a</sup>	N Randomized (Ages Recruited, y)	Screening Round (Planned Follow-Up Period, y)	Screening Approach	CIN 3+		ICC	
					Absolute Detection (%)	Relative Risk (95% CI)	Absolute Detection (%)	
<b>hrHPV Primary Screening</b>								
Ronco, 2010 <sup>12,13</sup>	Good	35,471 (35-60)	1 (3.5)	hrHPV vs. CC	IG: 52/17,724 (0.3) <sup>b</sup> CG: 22/17,747 (0.1) <sup>b</sup>	2.37 (1.44 to 3.89) <sup>b</sup>	NR	
NTCC Phase II			2 (3.5)	CC vs. CC	IG: 3/17,401 (0.02) <sup>b</sup> CG: 13/17,658 (0.07) <sup>b</sup>		0.23 (0.07 to 0.82) <sup>b</sup>	NR
			Cumulative (7)	-	IG: 55/17,724 (0.3) <sup>b</sup> CG: 35/17,747 (0.2) <sup>b</sup>		1.57 (1.03 to 2.40) <sup>b</sup>	NR
Ogilvie, 2018 <sup>14-18</sup>	Fair	17,294 (≥30)	1 (1) <sup>c</sup>	hrHPV w/LBC triage vs. LBC	IG: 47/8,714 (0.5) CG: 27/8,580 (0.3)	1.71 (1.07 to 2.74)	NR	
HPV FOCAL			2 (4) <sup>c,d</sup>	Co-testing vs. co-testing	IG: 16/8,714 (0.2) CG: 37/8,580 (0.4)		0.43 (0.24 to 0.76)	NR
			Cumulative (4) <sup>c,d</sup>	-	IG: 63/8,714 (0.7) CG: 64/8,580 (0.7)		0.97 (0.69 to 1.37) <sup>de</sup>	NR
Leinonen, 2012 <sup>19</sup>	Fair	109,932 (35-65)	1 (5)	hrHPV w/CC triage vs. CC	IG: 132/55,219 (0.2) CG: 84/54,713 (0.2)	1.56 (1.18 to 2.04) <sup>e</sup>	IG: 16/55,219 (0.03) CG: 7/54,713 (0.01)	
Canfell, 2017 <sup>20</sup>	Fair	3,917 (34-64)	1 (5)	hrHPV w/LBC triage vs. LBC <sup>e</sup>	IG: 12/3133 (0.4) CG: 0/784 (0)	6.26 (0.37 to 105.6)	IG: 0/3133 (0%) CG: 0/784 (0%)	
<b>hrHPV Co-testing with Cytology</b>								
Ronco, 2010 <sup>12,21,22</sup>	Good	33,364 (35-60)	1 (3.5)	Co-testing vs. CC	IG: 52/16,706 (0.3) <sup>b</sup> CG: 33/16,658 (0.2) <sup>b</sup>	1.57 (1.02 to 2.43) <sup>b</sup>	NR	
NTCC Phase I			2 (3.5)	CC vs. CC	IG: 5/16,332 (0.03) <sup>b</sup> CG: 11/16,561 (0.07) <sup>b</sup>		0.46 (0.16 to 1.33) <sup>b</sup>	NR
			Cumulative (7)	-	IG: 57/16,706 (0.3) <sup>b</sup> CG: 44/16,658 (0.3) <sup>b</sup>		1.30 (0.87 to 1.91) <sup>b</sup>	NR
Rijkaart, 2012 <sup>23-25</sup>	Good	33,838 (35-61)	1 (4)	Co-testing vs. CC	IG: 102/16,860 (0.6) <sup>b</sup> CG: 90/16,978 (0.5) <sup>b</sup>	1.14 (.86 to 1.51) <sup>e</sup>	IG: 10/16,860 (0.06) <sup>b</sup> CG: 4/16,978 (0.02) <sup>b</sup>	
POBASCAM			2 (5)	Co-testing vs. co-testing	IG: 55/16,545 (0.3) <sup>b</sup> CG: 77/16,699 (0.5) <sup>b</sup>		0.72 (0.51 to 1.02) <sup>e</sup>	IG: 4/16,545 (0.02) <sup>b</sup> CG: 9/16,699 (0.05) <sup>b</sup>
			Cumulative (9)	-	IG: 157/16,860 (0.9) CG: 167/16,978 (1.0)		0.95 (0.76 to 1.18)	IG: 14/16,860 (0.08) <sup>b</sup> CG: 13/16,978 (0.08) <sup>g</sup>
Naucler, 2007 <sup>26,27</sup>	Fair	12,527 (32-38)	1 (3)	Co-testing vs. CC	IG: 72/6,257 (1.2) CG: 55/6,270 (0.9)	1.31 (0.92 to 1.87)	NR	
SWEDESCREEN			2 (NR)	CC vs. CC	IG: 16/6,257 (0.3) CG: 30/6,270 (0.5)		0.53 (0.29 to 0.98)	NR
			Cumulative (4)	-	IG: 88/6,257 (1.4) CG: 85/6,270 (1.4)		1.04 (0.77 to 1.39) <sup>e</sup>	IG: 1/6,257 (0.02) CG: 5/6,270 (0.08)
Kitchener, 2009 <sup>28-31</sup>	Fair	19,344 (30-64)	1 (2)	Co-testing vs. LBC	IG: 116/14,507 (0.8) CG: 38/4,837 (0.8)	1.12 (0.71 to 1.47) <sup>e</sup>	IG: 5/14,507 (0.03) CG: 3/4,837 (0.06)	
			2 (2)	Co-testing vs.	NR		NR	IG: 2/9,037 (0.02) <sup>h</sup>

Source	Quality <sup>a</sup>	N Randomized (Ages Recruited, y)	Screening Round (Planned Follow- Up Period, y)	Screening Approach	CIN 3+		ICC
					Absolute Detection (%)	Relative Risk (95% CI)	Absolute Detection (%)
ARTISTIC				LBC			CG: 0/2,965 (0.0) <sup>h</sup>
			Cumulative (4.5)	-	NR	NR	IG: 7/14,507 (0.05) <sup>h</sup> CG: 3/4,837 (0.06) <sup>h</sup>

<sup>a</sup>Assessed using criteria from the US Preventive Services Task Force<sup>11</sup>

<sup>b</sup>From author inquiry

<sup>c</sup>The full HPV FOCAL trial included two randomized hrHPV intervention groups; a safety group (2 year screening interval) and a main study group (4 year screening interval); only the main study results are included in this table.

<sup>d</sup>The 4 year results compare one round of HPV screening in the IG with two rounds of cytology screening in the CG.

<sup>e</sup>Calculated (unadjusted)

<sup>f</sup>Triage could be done via LBC or dual-stained cytology

<sup>g</sup>Estimated data from figure

<sup>h</sup>Preliminary or incomplete results

**Abbreviations:** ARTISTIC, A Randomised Trial in Screening to Improve Cytology; CC, conventional cytology; CIN, cervical intraepithelial neoplasia;; HPV FOCAL = Human Papillomavirus For CervicAL cancer screening trial; hrHPV, high risk human papillomavirus; ICC, invasive cervical cancer;; LBC, liquid-based cytology; NR, not reported; NTCC, New Technologies for Cervical Cancer Screening; POBASCAM, Population Based Screening Study Amsterdam Program

eTable 4. Effectiveness of hrHPV Screening to for CIN 3+ and Invasive Cervical Cancer Incidence, Based on Randomized Clinical Trials, Among Women Aged < 30-35 Years

Source	Quality <sup>a</sup>	N Randomized (Ages Recruited, y)	Screening Round (Planned Follow- Up Period, y)	Screening Approach	CIN 3+		ICC
					Absolute Detection (%)	Relative Risk (95% CI)	Absolute Detection (%)
<b>hrHPV Primary Screening</b>							
Ronco, 2010 <sup>12,13</sup> NTCC Phase II	Good	13,725 (25-34)	1 (3.5)	hrHPV vs. CC	IG: 45/6,937 (0.6) <sup>b</sup> CG: 11/6,788 (0.2) <sup>b</sup>	4.00 (2.07 to 7.73) <sup>b</sup>	NR
			2 (3.5)	CC vs. CC	IG: 2/6,577 (0.03) <sup>b</sup> CG: 10/6,714 (0.15) <sup>b</sup>	0.20 (0.05 to 0.93) <sup>b</sup>	NR
			Cumulative (7)	-	IG: 47/6,937 (0.7) <sup>b</sup> CG: 21/6,788 (0.3) <sup>b</sup>	2.19 (1.31 to 3.66) <sup>b</sup>	NR
Ogilvie, 2018 <sup>14-17 18</sup> HPV FOCAL	Fair	1,654 (25-29)	1 (1) <sup>c</sup>	hrHPV vs. w/LBC triage vs. LBC	IG: 20/826 (2.4) CG: 14/828 (1.7)	1.43 (0.73 to 2.82)	NR
			2 (4) <sup>c,d</sup>	Co-testing vs. co- testing	IG: 6/826 (0.7) CG: 15/828 (1.8)	0.40 (0.16 to 1.02)	NR
			Cumulative (4) <sup>c,d</sup>	-	IG: 26/826 (3.1) CG: 29/828 (3.5)	0.90 (0.53 to 1.51)	NR
Leinonen, 2012 <sup>19</sup> FINNISH	Fair	22,262 (25-34)	1 (5)	hrHPV w/CC triage vs. CC	IG: 63/11,191 (0.6) CG: 34/11,071 (0.3)	1.83 (1.21 to 2.78) <sup>e</sup>	IG: 1/11,191 (0.01%) CG: 2/11,071 (0.02%)
Canfell, 2017 <sup>20</sup> Compass	Fair	1,078 (25-33)	1 (5)	hrHPV w/LBC triage vs. LBC <sup>e</sup>	IG: 18/867 (2.1) CG: 1/211 (0.5)	4.38 (0.59 to 32.6)	IG: 0/867 (0%) CG: 0/211 (0%)
<b>hrHPV Co-testing with Cytology</b>							
Ronco, 2010 <sup>12,21,22</sup> NTCC Phase I	Good	11,810 (25-34)	1 (3.5)	Co-testing vs. CC	IG: 23/6,002 (0.4) <sup>b</sup> CG: 25/5,808 (0.4) <sup>b</sup>	0.89 (0.51 to 1.57) <sup>b</sup>	NR
			2 (3.5)	CC vs. CC	IG: 8/5,761 (0.1) <sup>b</sup> CG: 8/5,769 (0.1) <sup>b</sup>	1.00 (0.38 to 2.67) <sup>b</sup>	NR
			Cumulative (7)	-	IG: 31/6,002 (0.5) <sup>b</sup> CG: 33/5,808 (0.6) <sup>b</sup>	0.91 (0.56 to 1.48) <sup>b</sup>	NR
Rijkaart, 2012 <sup>23-25</sup> POBASCAM	Good	6,267 (29-33)	1 (4)	Co-testing vs. CC	IG: 69/3,139 (2.2) <sup>b</sup> CG: 60/3,128 (1.9) <sup>b</sup>	1.15 (0.81 to 1.61) <sup>e</sup>	IG: 2/3,139 (0.06) <sup>b</sup> CG: 2/3,128 (0.06) <sup>b</sup>
			2 (5)	Co-testing vs. co- testing	IG: 33/3,034 (1.1) <sup>b</sup> CG: 45/3,032 (1.3) <sup>b</sup>	0.73 (0.47 to 1.15) <sup>e</sup>	IG: 0/3,034 (0.0) <sup>b</sup> CG: 5/3,032 (0.16) <sup>b</sup>
			Cumulative (9)	-	IG: 102/3,139 (3.3) CG: 105/3,128 (3.4)	0.97 (0.74 to 1.27)	IG: 2/3,139 (0.06) <sup>b</sup> CG: 7/3,128 (0.22) <sup>g</sup>
Kitchener, 2009 <sup>28-31</sup>	Fair	5,166 (20-29)	1 (2)	Co-testing vs. LBC	IG: 117/3,879 (3.0) CG: 42/1,287 (3.3)	0.92 (0.65 to 1.31) <sup>e</sup>	IG: 0/3,879 (0.0) CG: 1/1,287 (0.08)

ARTISTIC		2 (2)	Co-testing vs. LBC	NR	NR	IG: 1/1,679 (0.06) <sup>h</sup> CG: 0/549 (0.0) <sup>h</sup>
		Cumulative (4.5)	-	NR	NR	IG: 1/3,879 (0.03) <sup>h</sup> CG: 1/1,287 (0.08) <sup>h</sup>

<sup>a</sup>Assessed using criteria from the US Preventive Services Task Force<sup>11</sup>

<sup>b</sup>From author inquiry

<sup>c</sup>The full HPV FOCAL trial included two randomized hrHPV intervention groups; a safety group (2 year screening interval) and a main study group (4 year screening interval); only the main study results are included in this table.

<sup>d</sup>The 4 year results compare one round of HPV screening in the IG with two rounds of cytology screening in the CG.

<sup>e</sup>Calculated (unadjusted)

<sup>f</sup>Triage could be done via LBC or dual-stained cytology

<sup>g</sup>Estimated data from figure

<sup>h</sup>Preliminary or incomplete results

**Abbreviations:** ARTISTIC, A Randomised Trial in Screening to Improve Cytology; CC, conventional cytology; CIN, cervical intraepithelial neoplasia;; HPV FOCAL = Human Papillomavirus For Cervical cancer screening trial; hrHPV, high risk human papillomavirus; ICC, invasive cervical cancer; LBC, liquid-based cytology; NR, not reported; NTCC, New Technologies for Cervical Cancer Screening; POBASCAM, Population Based Screening Study Amsterdam Program

eTable 5. Colposcopy Referrals and False-Positive Rates as Harms of hrHPV Screening, Based on Cohort Studies

Source	Quality <sup>a</sup>	N Randomized (ages recruited)	Screening Round (Follow-Up Period, y)	Screening Approach	Test Positivity <sup>b</sup> (%)	Colposcopy Referrals (%)	False Positive Rate % (n screened positive without CIN2+ / N total screened without CIN2+) <sup>d</sup>
<b>hrHPV Primary Screening</b>							
Zorzi, 2017 <sup>1</sup>	Fair	48,736 (25-64)	1 (3)	hrHPV w/CC triage <sup>c</sup>	3,133/48,736 (6.4)	2,136/48,736 (4.4)	2973/48576 (6.1%)
			2 (3)	hrHPV w/CC triage <sup>c</sup>	777/21,827 (3.5)	472/21,827 (2.2)	760/21,827 (3.5%)
			Cumulative (6)	hrHPV w/CC triage <sup>c</sup>	3,910/48,736 (8.0)	2,608/48,736 (5.4)	3733/70403 (5.3%)
<b>hrHPV Co-testing with Cytology</b>							
Katki, 2011 <sup>2,7</sup>	Fair	331,818 (≥30)	1 (NR)	hrHPV w/CC	hrHPV+ or ASC-US+: 24,849/331,818 (7.5%)	NR	22539/329508 (9.4%)
KPNC							
Ibanez, 2014 <sup>8</sup>	Fair	1,832 (>39)	1(4-5)	hrHPV w/CC	139/1,832 (7.6%)	NR	121/1814 (6.7%)
Luyten, 2014 <sup>9,10</sup>	Fair	19,795 (≥30)	1 (5)	hrHPV w/CC	201/19,795 (1.0)	765/19,795 (3.9)	1168/19486 (6.0%)
			2 (5)	hrHPV w/CC	7/4,067 (0.2)	41/4067 (1.0)	NR
WOLPHSCREE N							

<sup>a</sup>Assessed using criteria from the US Preventive Services Task Force<sup>11</sup>

<sup>b</sup>Test positivity was defined based on study protocol. Test findings that would lead to a clinical action, based on the study protocol, such as colposcopy or more intensive follow-up were considered test positive. Thus, in some studies, the test positivity rate in the intervention group is simply the rate of hrHPV test positivity, whereas in others it is the rate of hrHPV+ with ASC-US+.

<sup>c</sup>Women with +hrHPV had conventional cytology triage: ASC-US+ were referred to colposcopy; normal cytology were rescreened at 1 year (those who remained hrHPV+ were referred to colposcopy); hrHPV- were rescreened at 3 years

<sup>d</sup>Only calculated for the baseline screen for each study.

**Abbreviations:** ASC-US, Atypical squamous cells of undetermined significance; CC, conventional cytology; CIN, cervical intraepithelial neoplasia;; hrHPV, high risk human papillomavirus;; LBC, liquid-based cytology; NR, not reported.



eTable 6. Colposcopy Referrals and False-Positive Rates as Harms of hrHPV Screening, Based on Randomized Clinical Trials, Among Women Aged  $\geq 30$ -35 Years

Source	Quality <sup>a</sup>	N Randomized (ages recruited)	Screening Round (Follow-Up Period, y)	Screening Approach	Test Positivity <sup>b</sup> (%)	Colposcopy Referrals (%)	False Positive Rate % (n screened positive without CIN2+ / N total screened without CIN2+)
<b>hrHPV Primary Screening</b>							
Ronco, 2010 <sup>12,13</sup> NTCC Phase II	Good	35,471 (35-60)	1 (3.5)	hrHPV vs. CC	IG (hrHPV+): 1,029/17,724 (5.8) CG (ASC-US+): 555/17,747 (3.1)	IG: 1,029/17,724 (5.8) CG: 435/17,747 (2.5)	IG: 960/17,655 (5.4) CG: 519/17,711 (2.9)
Ogilvie, 2018 <sup>14-18</sup> HPV FOCAL	Fair	17,294 ( $\geq 30$ )	1 (1) <sup>c</sup>	hrHPV w/LBC triage vs. LBC	NR	NR	NR
2 (4) <sup>c</sup>			Co-testing vs. co-testing	NR	NR	NR	
Cumulative (4) <sup>c</sup>			-	NR	NR	NR	
Leinonen, 2012 <sup>19</sup> FINNISH	Fair	109,932 (35-65)	1 (5)	hrHPV w/CC triage vs. CC	NR	IG: 506/55,219 (0.9) CG: 544/54,713 (1.0)	NR
Canfell, 2017 <sup>20</sup> Compass	Fair	3,917 (34-64)	1 (5)	hrHPV w/LBC triage vs. LBC <sup>e</sup>	NR	IG: 80/3,133 (2.6) CG: 17/784 (2.2)	NR
<b>hrHPV Co-testing with Cytology</b>							
Ronco, 2010 <sup>12,21,22</sup> NTCC Phase I	Good	33,364 (35-60)	1 (3.5)	Co-testing vs. CC	IG (hrHPV+ or ASC-US+): 1,783/16,706 (10.7) CG (ASC-US+): 594/16,658 (3.6)	IG: 1,773/16,706 (10.6) <sup>f</sup> CG: 501/16,658 (3.0)	IG: 1,704/16,335 (10.4) CG: 543/16,607 (3.3)
Rijkaart, 2012 <sup>23-25</sup> POBASCAM	Good	33,838 (34-56)	1 (4)	Co-testing vs. CC	IG (hrHPV+): 684/16,860 (4) CG: NR	NR	NR
Naucler, 2007 <sup>26,27</sup> SWEDESCREEN	Fair	12,527 (32-38)	1 (3)	Co-testing vs. CC	IG (hrHPV+ or ASC-US+): NR CG (ASC-US+): 150/6,270 (2.4)	NR	IG: NR CG: 72/6,192 (1.2)
Kitchener, 2009 <sup>28-31</sup> ARTISTIC	Fair	19,344 (30-64)	1 (2.2)	Co-testing vs. LBC	IG (hrHPV+ or ASC-US+): 2,465/14,507 (17.0) CG (ASC-US+): 508/4,837 (10.5)	NR	NR

<sup>a</sup>Assessed using criteria from the US Preventive Services Task Force<sup>11</sup>

<sup>b</sup>Test positivity was defined based on trial protocol. Test findings that would lead to a clinical action, based on the study protocol, such as colposcopy or more intensive follow-up were considered test positive. Thus, in some trials, the test positivity rate in the intervention group is simply the rate of hrHPV test positivity, whereas in others it is the rate of hrHPV+ with ASC-US+.

<sup>c</sup>The full HPV FOCAL trial included two randomized hrHPV intervention groups; a safety group (2 year screening interval) and a main study group (4 year screening interval); only the main study results are included in this table.

<sup>d</sup>Percent of women; converted from rate per 1,000 participants

<sup>e</sup>Triage could be done via LBC or dual-stained cytology

<sup>f</sup>Estimated data from figure

**Abbreviations:** ARTISTIC = A Randomised Trial in Screening to Improve Cytology; ASC-US = Atypical squamous cells of undetermined significance; CC = conventional cytology; CIN = cervical intraepithelial neoplasia;; HPV FOCAL = Human Papillomavirus For CervicAL cancer screening trial; hrHPV = high risk human papillomavirus; LBC = liquid-based cytology; NR = not reported; NTCC = New Technologies for Cervical Cancer Screening; POBASCAM = Population Based Screening Study Amsterdam Program

eTable 7. Colposcopy Referrals and False-Positive Rates as Harms of hrHPV Screening, Based on Randomized Clinical Trials Among Women Aged < 30-35 Years

Source	Quality <sup>a</sup>	N Randomized (ages recruited)	Screening Round (Follow-Up Period, y)	Screening Approach	Test Positivity <sup>b</sup> (%)	Colposcopy Referrals (%)	False Positive Rate % (n screened positive without CIN2+ / N total screened without CIN2+)
<b>hrHPV Primary Screening</b>							
Ronco, 2010 <sup>12,13</sup> NTCC Phase II	Good	13,725 (25-34)	1 (3.5)	hrHPV vs. CC	IG (hrHPV+): 907/6,937 (13.1) CG (ASC-US+): 270/6,788 (4.0)	IG: 970/6,937 (13.1) CG: 244/6,788 (3.6)	IG: 839/6,869 (12.2) CG: 251/6,769 (3.7)
Ogilvie, 2018 <sup>14-18</sup> HPV FOCAL	Fair	1,654 (25-29)	1 (1) <sup>c</sup>	hrHPV w/LBC triage vs. LBC w/ hrHPV triage	NR	NR	NR
2 (4) <sup>c</sup>			NR		NR	NR	
Cumulative (4) <sup>c</sup>			NR		NR	NR	
Leinonen, 2012 <sup>19</sup> FINNISH	Fair	22,262 (25-34)	1 (5)	hrHPV w/CC triage vs. CC	NR	IG: 290/11,191 (2.3) CG: 211/11,071 (1.9)	NR
Canfell, 2017 <sup>20</sup> Compass	Fair	1,078 (25-33)	1 (5)	hrHPV w/LBC triage vs. LBC <sup>e</sup>	NR	IG: 74/867 (8.5) CG: 10/211 (4.7)	NR
<b>hrHPV Co-testing with Cytology</b>							
Ronco, 2010 <sup>12,21,22</sup> NTCC Phase I	Good	11,810 (25-34)	1 (3.5)	Co-testing vs. CC	IG (hrHPV+ or ASC-US+): 1,047/6,002 (17.4) <sup>f</sup> CG (ASC-US+): 261/5,808 (4.5) <sup>f</sup>	IG: 697/6,002 (11.6) CG: 237/5,808 (4.1)	IG: 998/4,980 (20.0) CG: 228/5,775 (3.9)
Rijkaart, 2012 <sup>23-25</sup> POBASCAM	Good	6,267 (29-33)	1 (4)	Co-testing vs. CC	IG (hrHPV+): 373/3,139 (12.0) CG: NR	NR	NR
Kitchener, 2009 <sup>28-31</sup> ARTISTIC	Fair	5,166 (20-29)	1 (2.2)	Co-testing vs. LBC	IG (hrHPV+ or ASC-US+): 1,554/3,879 (40.1) <sup>g</sup> CG (ASC-US+): 278/1,287 (21.6) <sup>g</sup>	NR	NR

<sup>a</sup>Assessed using criteria from the US Preventive Services Task Force<sup>11</sup>

<sup>b</sup>Test positivity was defined based on trial protocol. Test findings that would lead to a clinical action, based on the study protocol, such as colposcopy or more intensive follow-up were considered test positive. Thus, in some trials, the test positivity rate in the intervention group is simply the rate of hrHPV test positivity, whereas in others it is the rate of hrHPV+ with ASC-US+.

<sup>c</sup>The full HPV FOCAL trial included two randomized hrHPV intervention groups; a safety group (2 year screening interval) and a main study group (4 year screening interval); only the main study results are included in this table.

<sup>d</sup>Percent of women; converted from rate per 1,000 participants

<sup>e</sup>Triage could be done via LBC or dual-stained cytology

<sup>f</sup>Estimated data from figure

<sup>g</sup>Preliminary or incomplete results

**Abbreviations:** ARTISTIC = A Randomised Trial in Screening to Improve Cytology; ASC-US = Atypical squamous cells of undetermined significance; CC = conventional cytology; CIN = cervical intraepithelial neoplasia;; HPV FOCAL = Human Papillomavirus For CervicAL cancer screening trial; hrHPV = high risk human papillomavirus;; LBC = liquid-based cytology; NR = not reported; NTCC = New Technologies for Cervical Cancer Screening; POBASCAM = Population Based Screening Study Amsterdam Program

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