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HPV and Cytology Co-Testing vs. HPV Testing for Secondary Cervical Cancer Prevention: Is the Juice Worth the Squeeze?

Dr. Philip Castle has disclosed that he has received HPV tests and assays for research at a reduced or no cost from Roche, Cepheid, and Becton Dickson.

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Science at the heart of medicine

HPV and Cytology Cotesting vs. HPV Testing for Secondary Cervical Cancer Prevention: Is the Juice Worth the Squeeze?

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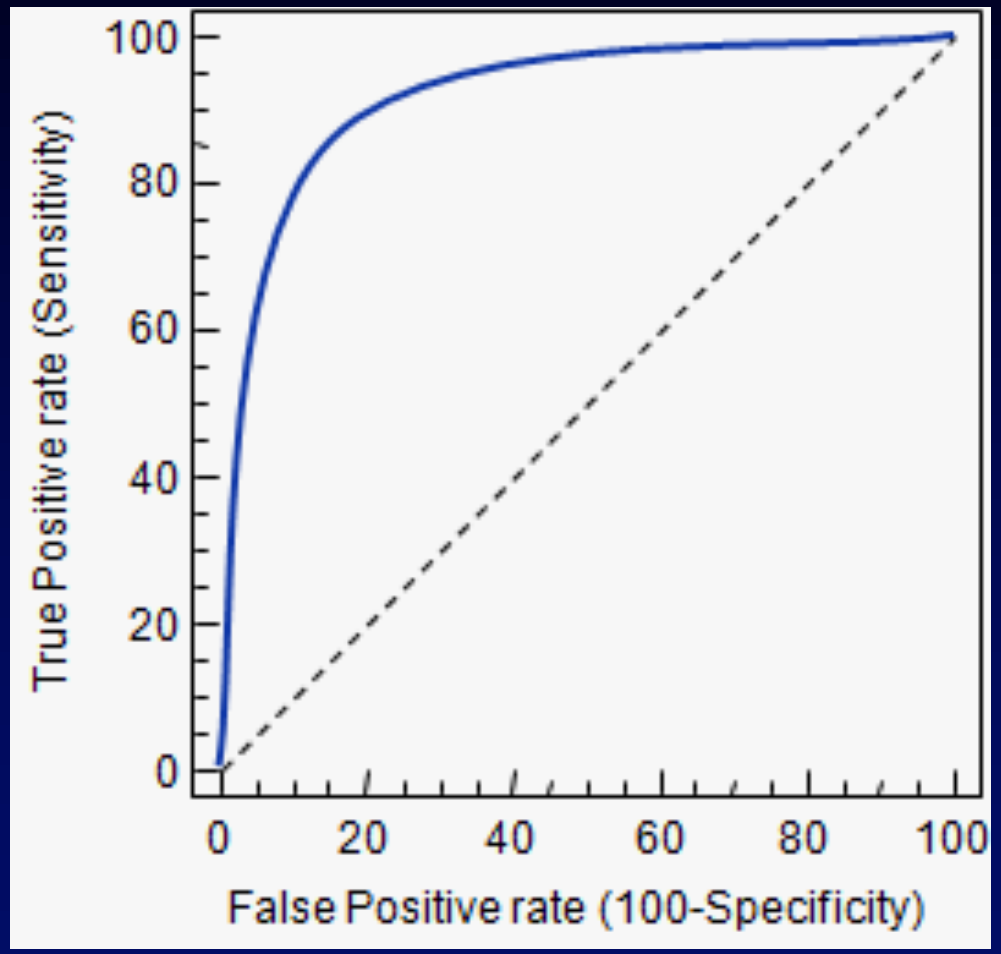
April 26, 2019

Disclosures:

- I have received HPV tests and assays for research at a reduced or no cost from Roche, Becton Dickinson, Cepheid, and Arbor Vita Corporation.
- I am a member of the Board of Directors of the American Society for Colposcopy and Cervical Pathology (ASCCP) (until May 4, 2019)
- I am a member of the Medical Advisory Board of the Prevent Cancer Foundation

The ROC Curve: "Curve of Diminishing Returns"

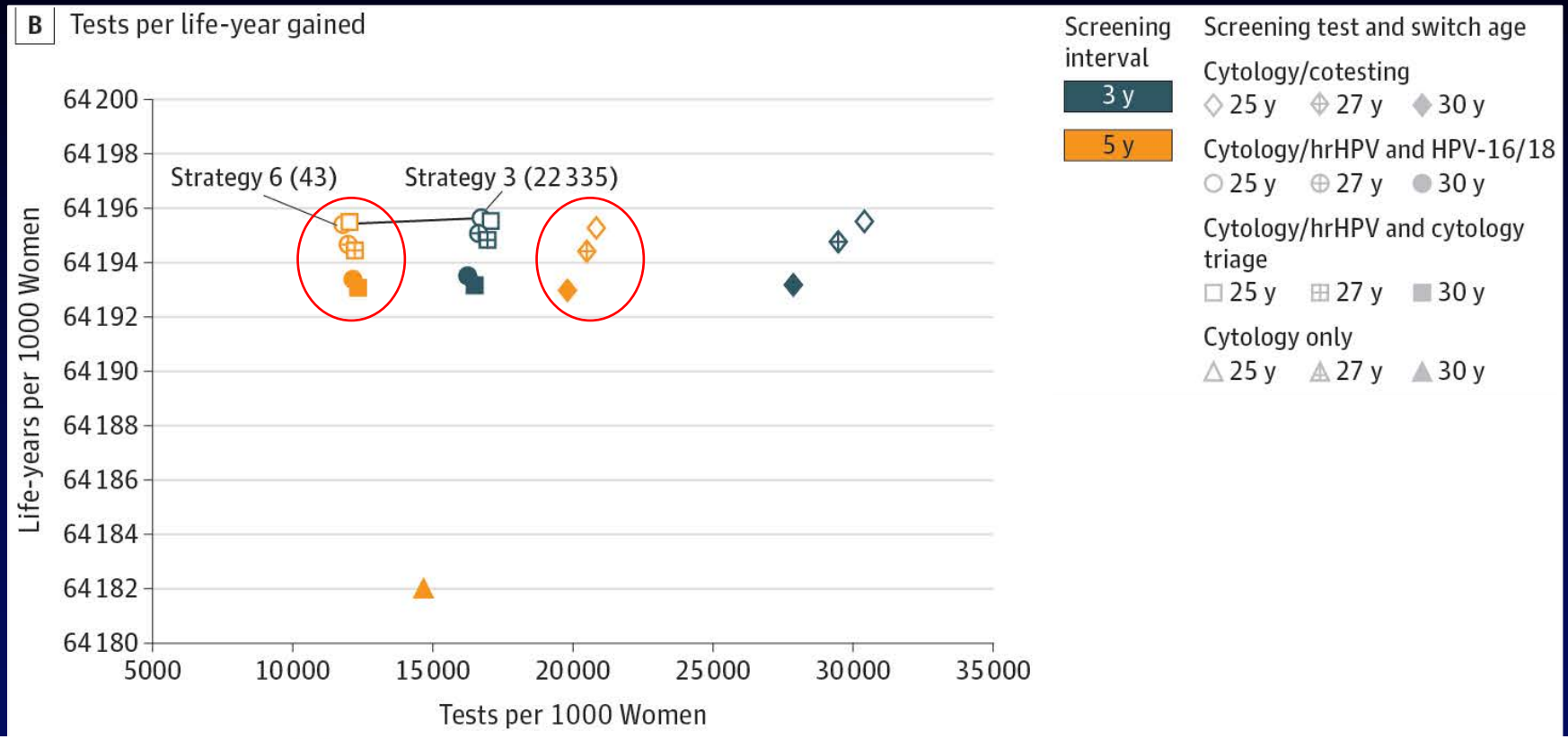


Question: Is Cotesting Life-Saving and If So, A Good Value (Good Bang for the Healthcare Buck)?

Caveats:

1. 100% cervical cancer prevention practically and financially is NOT achievable; and
2. More can always be done at a diminishing return….

Modeling Approach (Kim et al., JAMA 2018)



Strategy		Per 1000 Women									
No.	Name[b]	Cytology Tests	HPV Tests	Total Tests[c]	No. of Colposcopies	CIN 2 or 3 Detected	CIN 3+ Detected[d]	False-Positives[e]	Cervical Cancer Cases	Cervical Cancer Deaths	Life-Years
0	No screening	0	0	0	0	0	0	0	18.86	8.34	63 921.34
1	CYTO-3Y, 21	13 877	786	14 662	645	160	46	484	2.34	0.76	64 181.89
2	CYTO-3Y, 21 /COTEST-5Y, 30	11 425	8380	19 806	1630	201	54	1429	1.08	0.30	64 192.97
14	CYTO-3Y, 21 /HPV-5Y (cyto), 30	3888	8459	12 348	1452	198	53	1254	1.08	0.29	64 193.07

Costs of Services (Medicaid)

Cost (2017)	
HPV Testing	$46
Cytology	$26
Cotesting	$72
HPV Testing with Cytology Triage*	$49

*Assumes 10% of women are HPV Positive

Courtesy of Professor Jane Kim

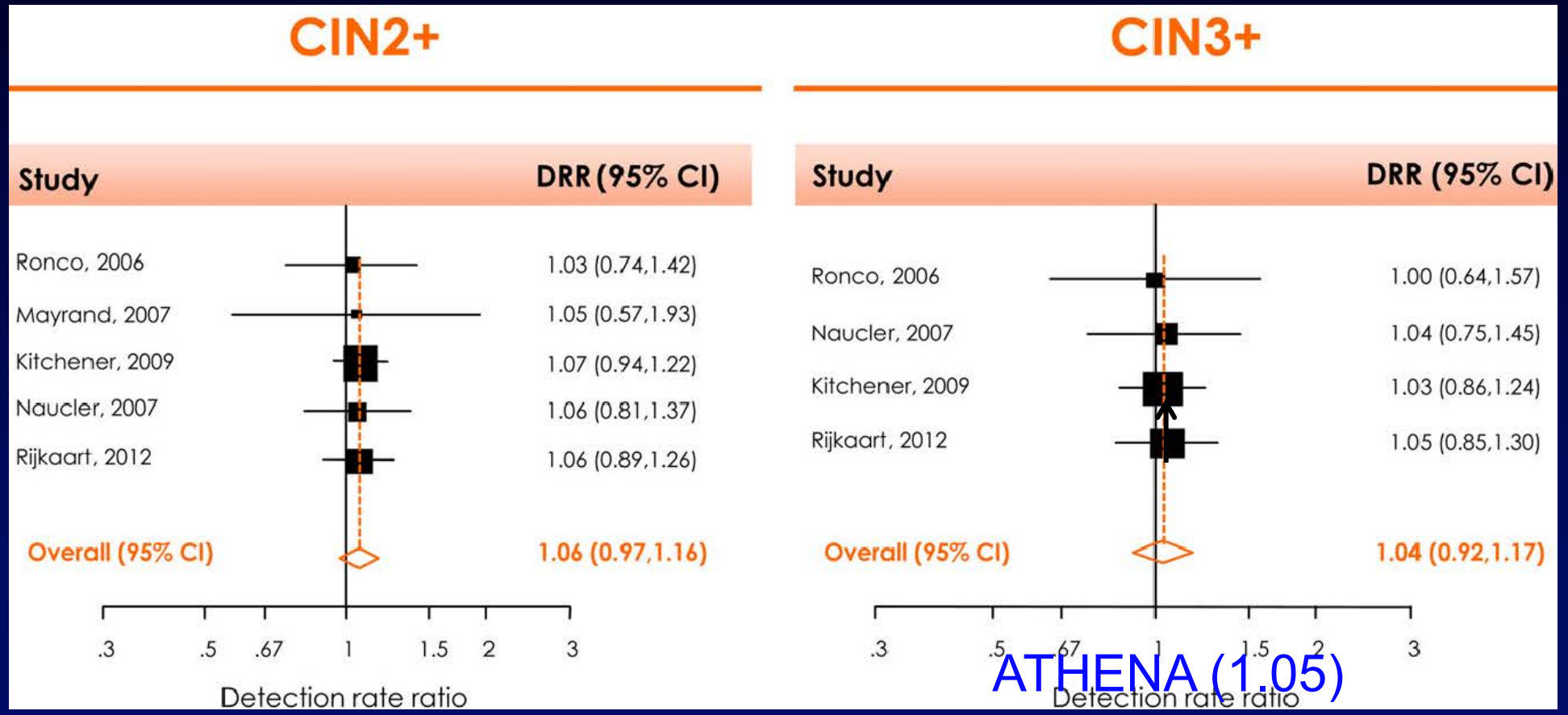
A Simplified View

- 75 Million Women Between Ages 30-64 Years (86 Million Ages 25-64 Years)
- Assume that 1/5 need screening every year
- Cost of Cotesting = $1.08 Billion ($1.24 Billion) per year
- Cost of HPV Testing = $0.74 Billion ($0.84 Billion) per year

- Difference = $350 Million ($400 Million) per year

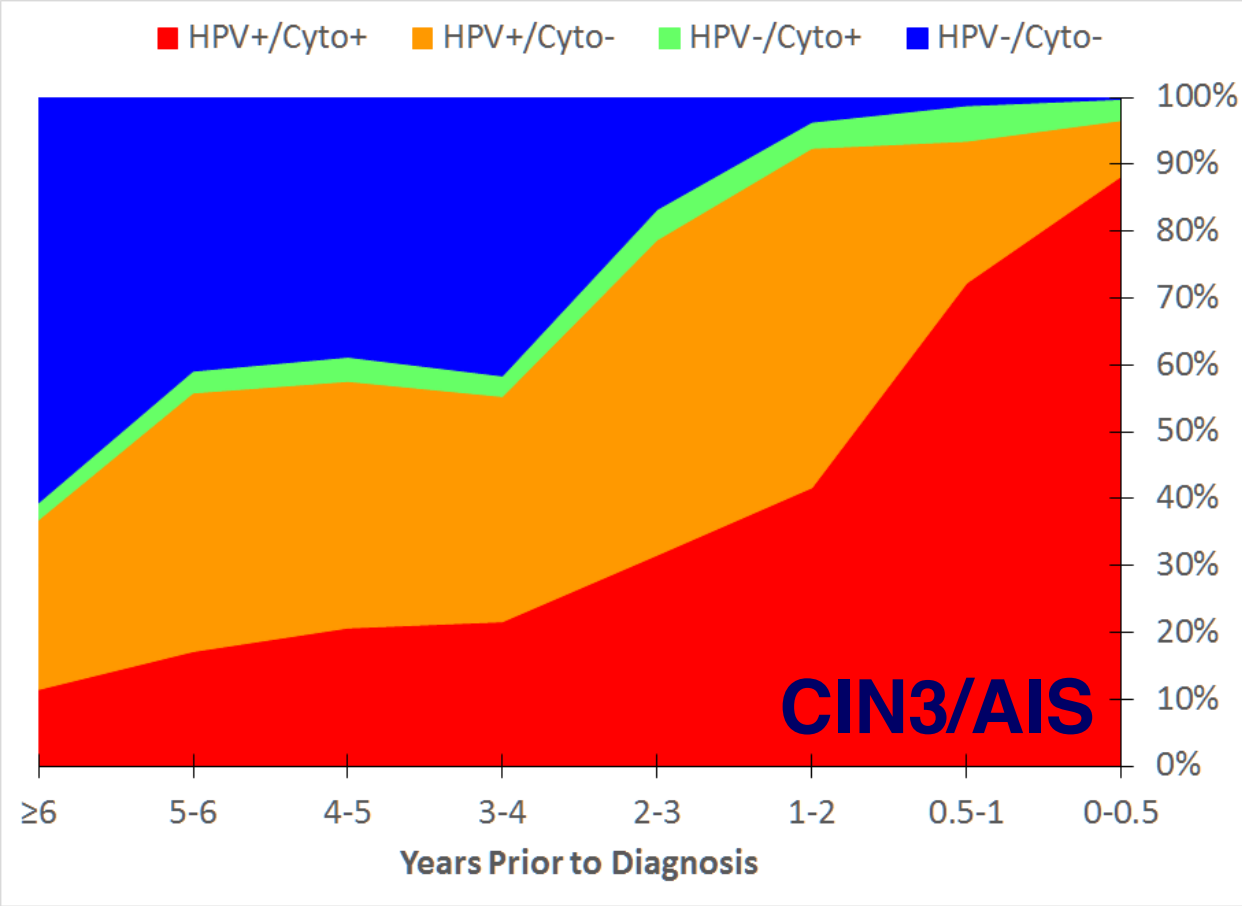
What are you getting for your money?

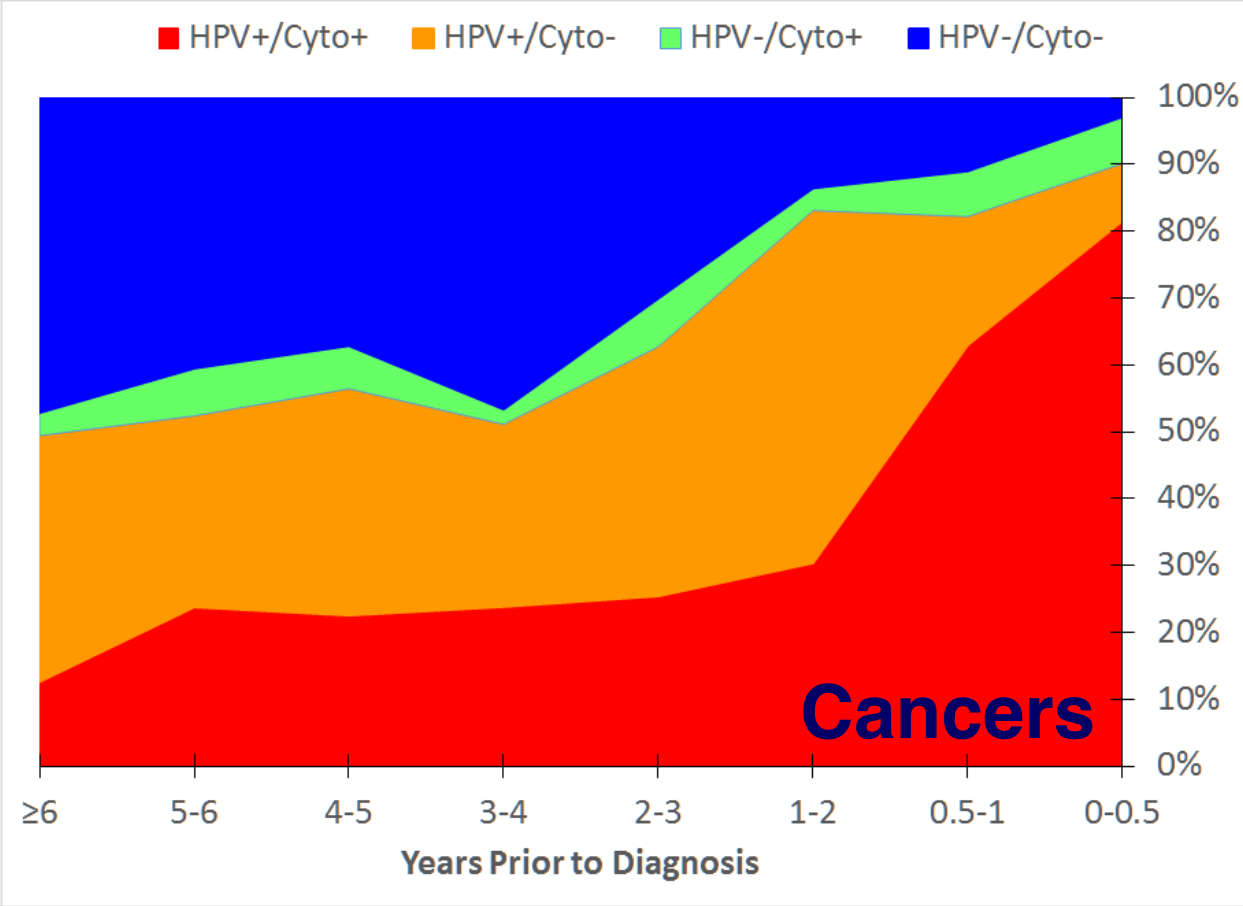
Cross-Sectional Detection of CIN2+ and CIN3+ by Cotesting vs. HPV



Arbyn *et al*., Vaccine, 2012; Castle *et al*., Lancet Onc, 2011

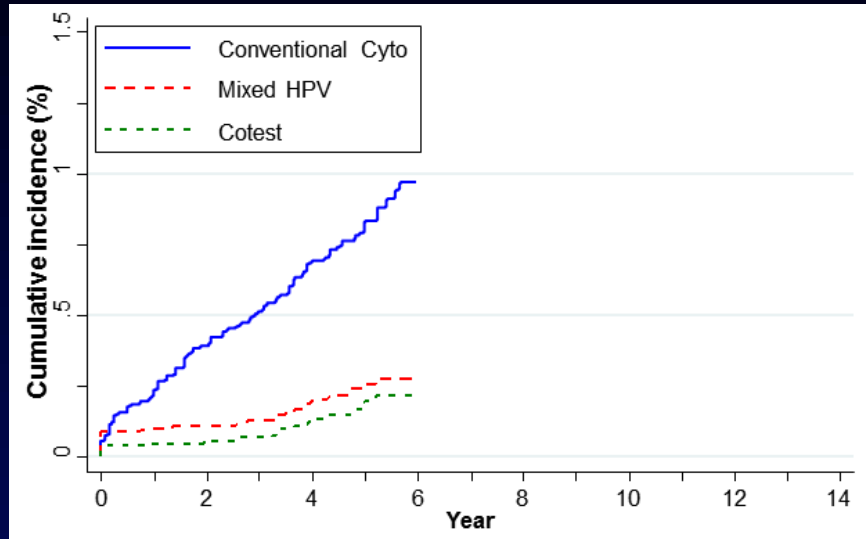
Cotesting Results Prior to Cervical Precancer and Cancer Diagnoses



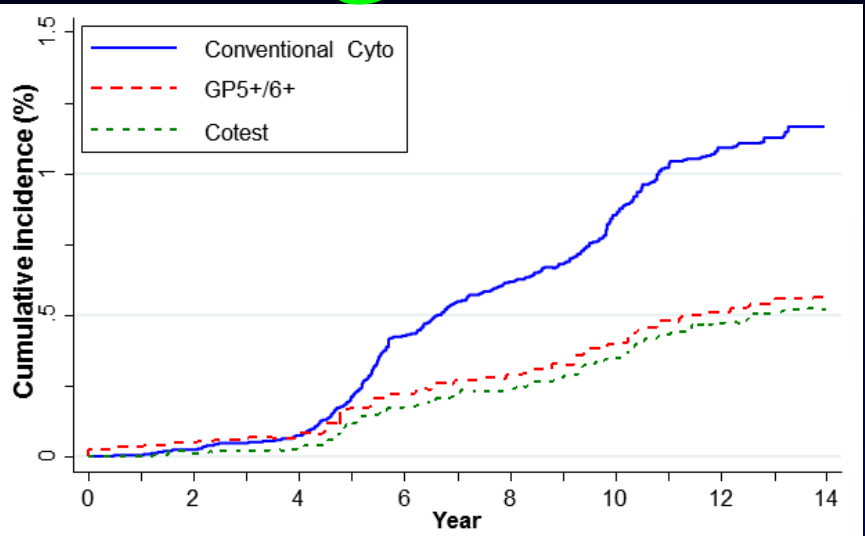


Schiffman…Castle, JNCI, 2018

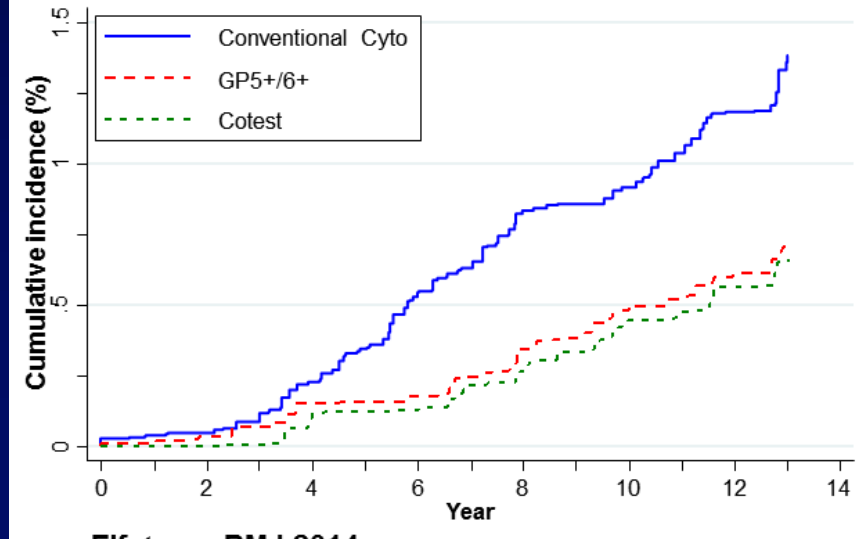
Reassurance vs. CIN3+ following a negative cervical screening test



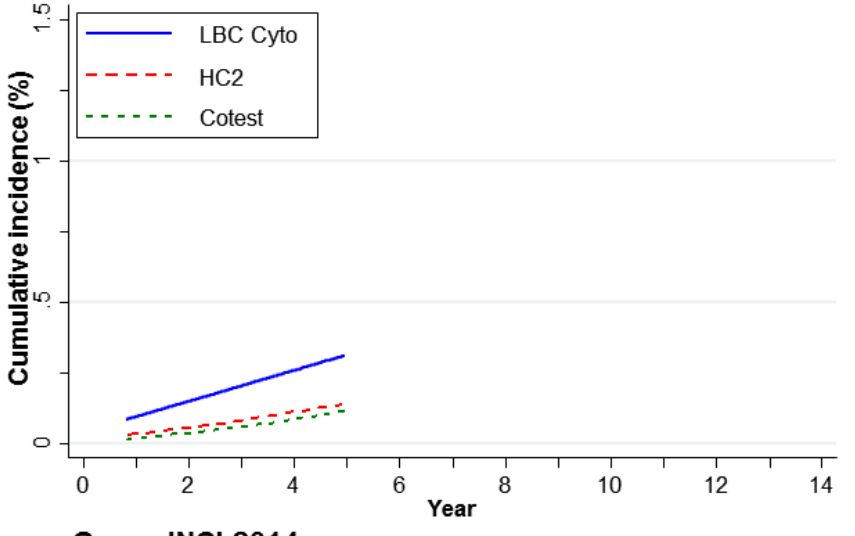
Dillner, BMJ 2008



Dijkstra, BMJ 2016



Elfstrom, BMJ 2014

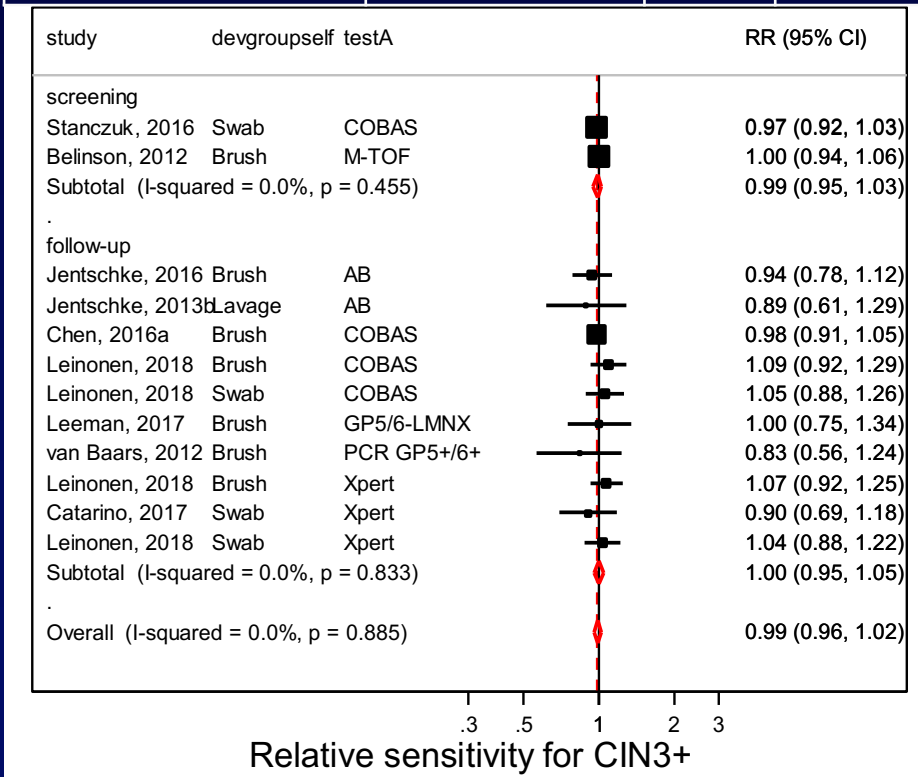


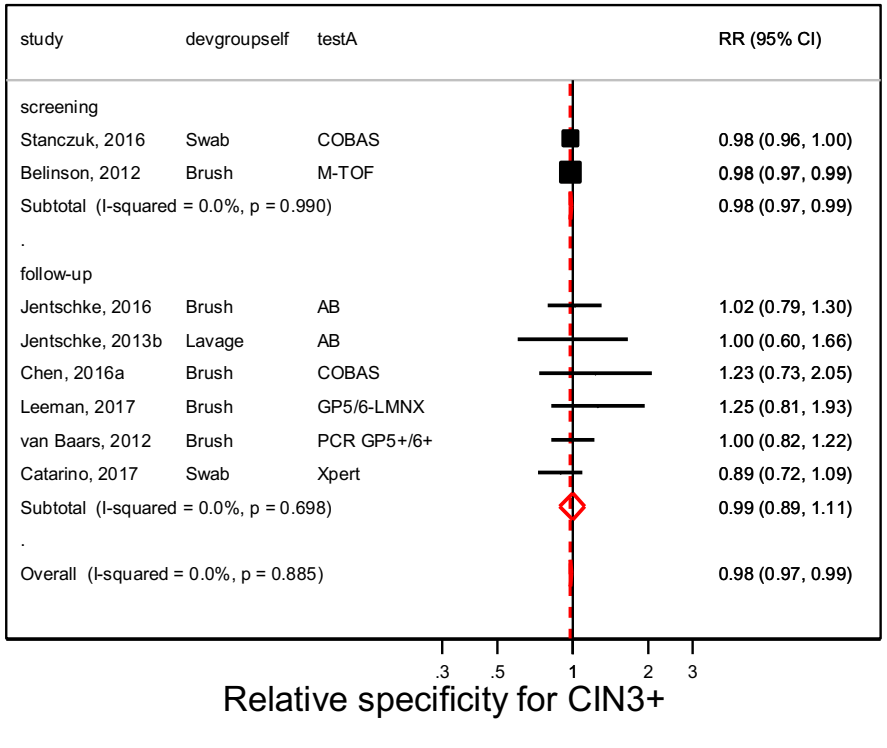
Gage, JNCI 2014

Courtesy of Dr. Marc Arbyn

Self-Collection & HPV Testing Meta-Analysis

Method	Endpoint	N	Relative Sensitivity	Relative Specificity
Signal Amp.	CIN2+	23	0.85 (0.80-0.89)*	0.96 (0.93-0.98)*
	CIN3+	9	0.86 (0.76-0.98)*	0.97 (0.95-0.99)*
PCR	CIN2+	17	0.99 (0.97-1.02)	0.98 (0.97-0.99)*
	CIN3+	8	0.99 (0.96-1.02)	0.98 (0.97-0.99)*





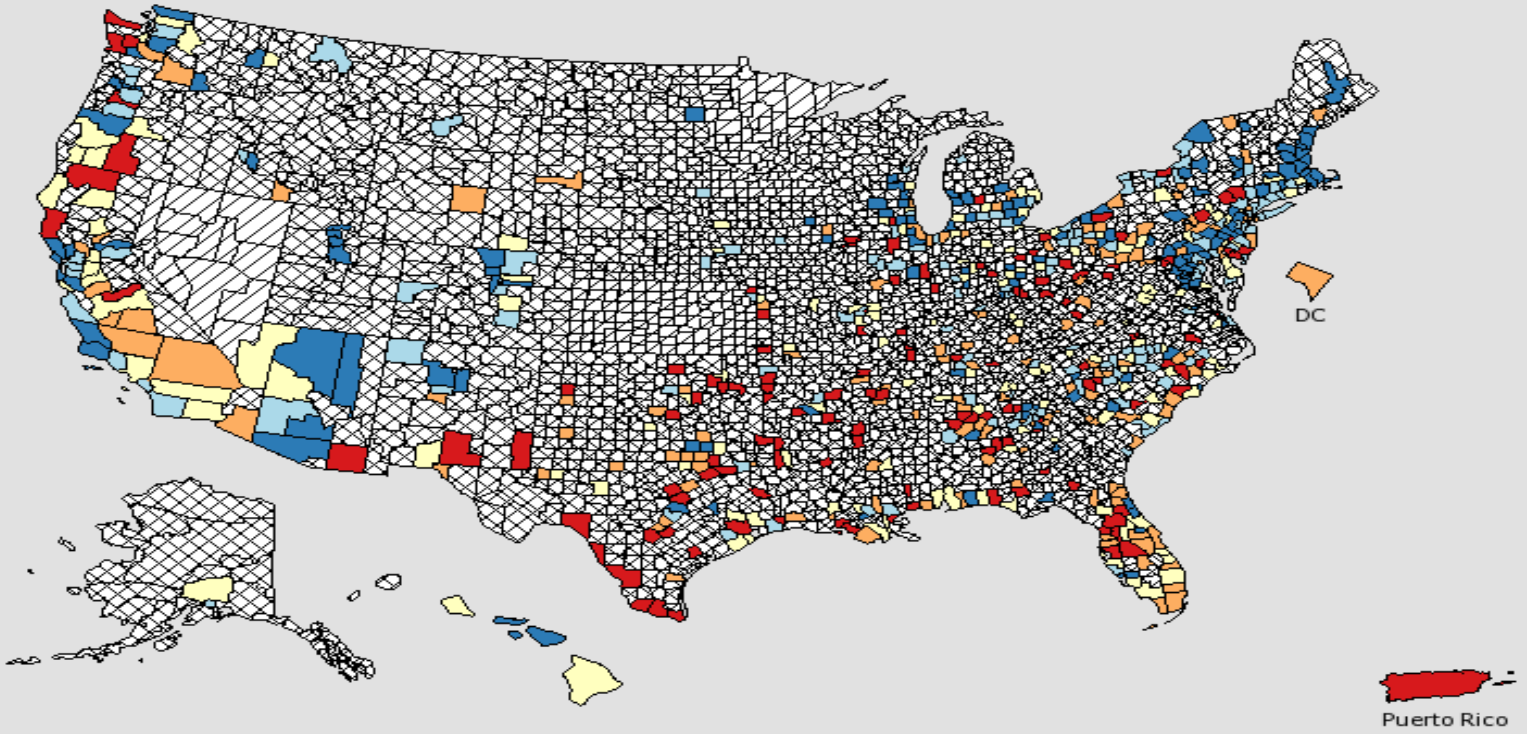
Arbyn…Castle, BMJ, 2018

Self-Collection is Preferred across Countries and Cultures

Scenario of invitation	# of Studies	Absolute participation		Relative participation (95% CI)	Participation difference % (95% CI)
		Self-Collection % (95% CI)	Control % (95% CI)		
Per-protocol					
Mail-to-all	17	19.2 (15.3-23.5)	11.1 (7.5-15.5)	1.78 (1.29-2.45)	7.8 (3.9-11.7)
Opt-in	4	7.0 (2.4-13.6)	13.1 (11.1-15.2)	0.51 (0.31-0.85)	-5.3 -(-11.6 to -1.0)
Campaign	1	15.6 (12.4-19.5)	6.0 (4.2-8.7)	2.58 (1.67-3.99)	9.5 (5.4-13.7)
Door-to-door	4	94.2 (80.2-100)	53.3 (10.5-93.2)	1.99 (0.68-5.85)	39.7 (4.0-75.4)
Intention-to-treat					
Mail-to-all	17	24.0 (20.6-27.5)	11.1 (7.5-15.5)	2.25 (1.73-2.94)	**12.1 (9.3-14.8)**
Opt-in	4	14.5 (10.1-19.6)	13.1 (11.1-15.2)	0.98 (0.71-1.35)	**0.2 (-3.6 to 4.0)**
Campaign	1	15.6 (12.4-19.5)	6.0 (4.2-8.7)	2.58 (1.67-3.99)	**9.5 (5.4-13.7)**
Door-to-door	4	94.6 (83.0-99.9)	53.3 (10.5-93.2)	2.01 (0.66-6.15)	**40.5 (3.0-78.0)**

Arbyn…Castle, BMJ, 2018

Incidence Rates† for United States by County
Cervix, 2010 - 2014
All Races (includes Hispanic), Female, All Ages



Age-Adjusted
Annual Incidence Rate
(Cases per 100,000)
Quantile Interval

- 3.3 to 6.1
- > 6.1 to 7.2
- > 7.2 to 8.4
- > 8.4 to 10.2
- > 10.2 to 21.1
- Suppressed * /**
- Data Not Available ◇

US (SEER + NPCR)
Rate (95% C.I.)
7.5 (7.5 - 7.6)

Notes:
Note: Alaska, DC, Hawaii and Puerto Rico are not drawn to scale.
¶¶ - Data for the United States does not include data from Nevada.
¶ - Data for the Minnesota and Kansas is not availible at the county level.
State Cancer Registries may provide more current or more local data.
Data presented on the State Cancer Profiles Web Site may differ from statistics reported by the State Cancer Registries (for more information).
† Incidence rates (cases per 100,000 population per year) are age-adjusted to the 2000 US standard population (19 age groups: <1, 1-4, 5-9, ... , 80-84, 85+). Rates are for invasive cancer only (except for bladder which is invasive and in situ) or unless otherwise specified. Rates calculated using SEER*Stat. Population counts for denominators are based on Census populations as modified by NCI. The 1969-2015 US Population Data File is used for SEER and NPCR incidence rates.
* Data have been suppressed to ensure confidentiality and stability of rate estimates. Data is currently being suppressed if there are fewer than 16 counts for the time period.
** Data have been suppressed for states with a population below 50,000 per sex combination for American Indian/Alaska Native or Asian/Pacific Islanders because of concerns regarding the relatively small size of these populations in some states.
◇ Data not available for this combination of geography, statistic, age and race/ethnicity.
Data for the United States does not include data from Puerto Rico

Courtesy of Dr. Mona Saraiya, CDC

Head-To-Head Comparison of Cotesting vs. HPV Testing

	Co-Testing	HPV Primary
Cervical Cancer Prevention	+/-	
Gynecologic Cancer Prevention	+/-	
Lower Cost		+
Self-Collection*		+

*Cytology does not work on a self-collected specimen.

Final Comments

- As long as routine screening includes testing for high-risk HPV (but not too frequently)…for all women, GLOBALLY. We are quibbling over negligible effects when 90% of the women worldwide cannot get one high-quality cervical screen in their lifetime.
- When do we start paying attention to how we spend our money? 17.9% of our GDP is spent on healthcare.
- Are there better ways to spend $350-400 million (est.) per year to save lives?