USPSTF Recommendation for 5-year HPV Testing Alone (vs. 5-year Cotesting): What is the Evidence?

Against- Not yet ready for prime time.

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Disclosures

- No financial relationships or conflict of interest to disclose

On April 24, 2014, the FDA approved use of the Cobas HPV test for primary screening for cervical cancer.

The New York Times

BUSINESS DAY

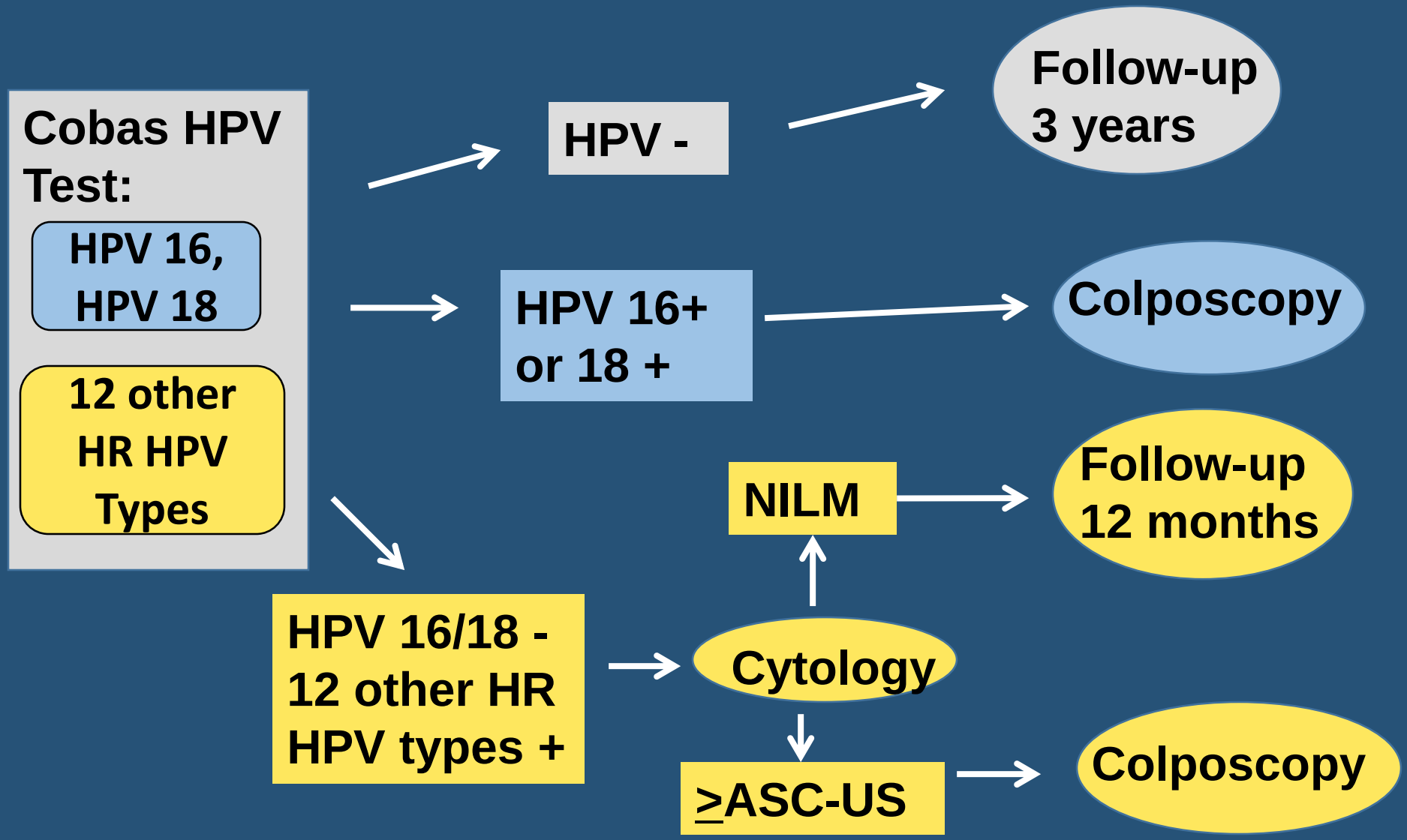
Alternative to Pap Test Is Approved by F.D.A.

By ANDREW POLLACK APRIL 24, 2014

The Food and Drug Administration on Thursday approved the first alternative to the long-used Pap test as a primary screening method for cervical cancer, in the face of opposition from some women's groups and health organizations.

Algorithm for Primary HPV Screening

Modified from SGO ASCCP Interim Guidance Huh et al Gynecol Oncol 2015



In October 2017, The U.S.P.S.T.F. distributed a draft recommendation for comment

Draft: Recommendation Summary

Population	Recommendation	Grade (What's This?)
Women ages 21 to 65 years	The USPSTF recommends screening for cervical cancer every 3 years with cervical cytology alone in women ages 21 to 29 years. The USPSTF recommends either screening every 3 years with cervical cytology alone or every 5 years with high-risk human papillomavirus (hrHPV) testing alone in women ages 30 to 65 years. See the Clinical Considerations section for the relative benefits and harms of alternative screening strategies for women age 30 years or older.	A
Women older than age 65 years	The USPSTF recommends against screening for cervical cancer in women older than age 65 years who have had adequate prior screening and are not otherwise at high risk for cervical cancer. See the Clinical Considerations section for a discussion of adequate prior screening and risk factors that support screening after age 65 years.	D
Women younger than age 21 years	The USPSTF recommends against screening for cervical cancer in women younger than age 21 years.	D
Women who have had a hysterectomy	The USPSTF recommends against screening for cervical cancer in women who have had a hysterectomy with removal of the cervix and do not have a history of a high-grade precancerous lesion (i.e., cervical intraepithelial neoplasia [CIN] grade 2 or 3) or cervical cancer.	D

Note: The first three recommendations apply to women who have a cervix, regardless of their sexual history or HPV vaccination status. None of these recommendations apply to women who have been diagnosed with a high-grade precancerous cervical lesion or cervical cancer. These recommendations also do not apply to women with in utero exposure to diethylstilbestrol or women who have a compromised immune system (e.g., women living with HIV).

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"…The USPSTF recommends either screening with cervical cytology alone or every 5 years with high risk human papillomavirus (hrHPV) testing alone in women ages 30 – 65."

Professional organizations responded to the USPSTF's request for comment

ASCCP The society for lower genital tract disorders since 1964

ACOG The American College of Obstetricians and Gynecologists

SGO Society of Gynecologic Oncology

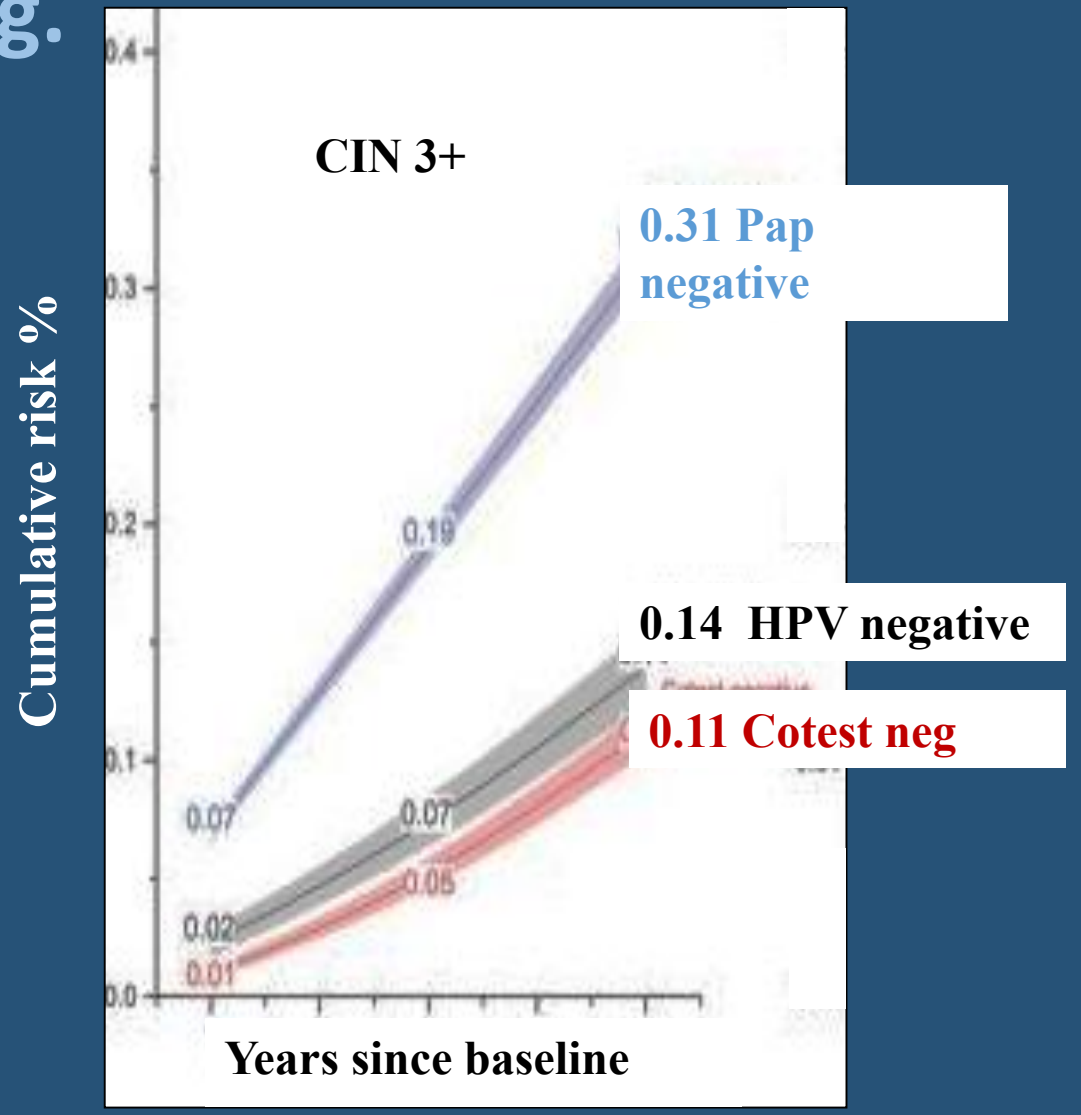
"…we urge the USPSTF to retain 5 year co-testing as a screening option for women aged 30-65 and to strongly consider a shorter interval for primary hrHPV screening."

What were their concerns? 1) Availability of FDA-Approved hrHPV Test for Primary Screening

- There are four FDA approved HPV tests available in the U.S.
  - All have different test characteristics
  - Only one, Roche's Cobas 4800 HPV test has been clinically validated for primary screening and is FDA approved for primary screening.
- The FDA approved algorithm relies on HPV 16/18 genotyping
  - HPV 16/18 genotyping can be reflexed on Cervista
  - HPV 16/18 genotyping is not available on HC2
  - Aptima E6/E7 mRNA test can be reflexed to HPV 16 and HPV 18/45.
    - How does HPV 45 fit in the FDA approved algorithm?
    - How does mRNA fit in the FDA approved algorithm?

What were their concerns? 2) Decreased detection by hrHPV compared with co-testing.

Cotesting provides a small but significantly greater protection from CIN 3+ than HPV alone. The cumulative risk 4 years after negative HPV test is about equivalent to that of a negative cotest at 5 years.



What were their concerns? 3) Lack of U.S. Validation Studies

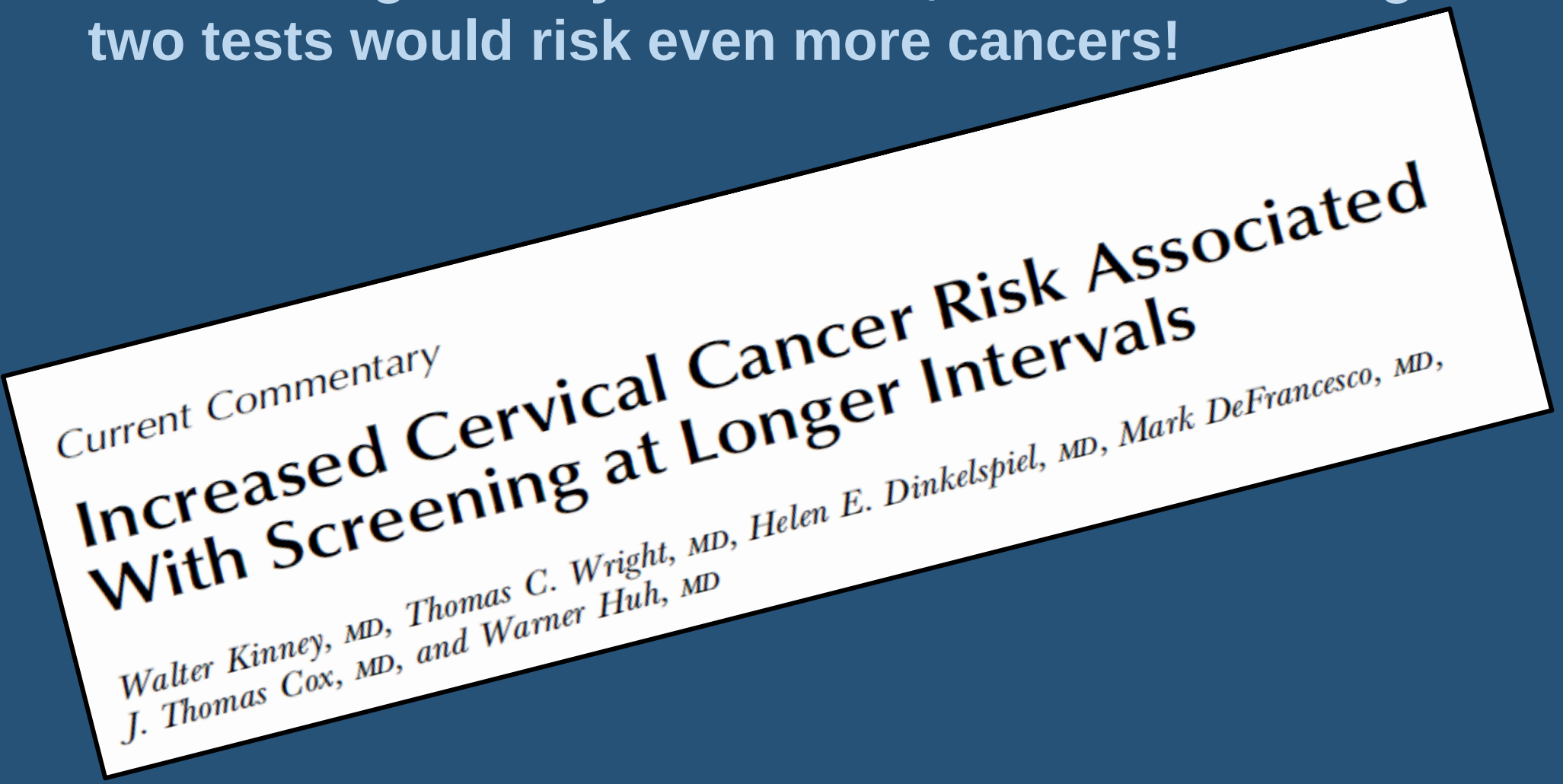
- There is no primary HPV screening trial with a second round of testing at 5 years.
  - The ATHENA Trial, on which Roche's FDA approval is based, stopped at 3 years.
  - POBSCAM from Holland used a 5 year interval, but it was a test of cotesting vs cytology, not primary HPV testing, and it was done in a country with a formal screening program, unlike opportunistic screening in the U.S.

ASCCP, ACOG, and SGO concluded their comments to USPSTF:

"… without prospective U.S.-based validation, available data are insufficient to justify extending the interval for primary hrHPV screening to 5 years."

Haywood L Brown, MD President ACOG
Anna Barbara Moscicki, MD, President ASCCP
Laurel W. Rice, MD, President SGO
Letter to U.S. Preventive Services Task Force Oct 9, 2017

Concern was raised a few years ago over the risk that cancer rates in the U.S. would increase by change from q 3 year cotesting to the current q 5 year cotesting interval. Surely maintaining that 5 year interval, while eliminating one of the two tests would risk even more cancers!



Current Commentary

Increased Cervical Cancer Risk Associated With Screening at Longer Intervals

Walter Kinney, MD, Thomas C. Wright, MD, Helen E. Dinkelspiel, MD, Mark DeFrancesco, MD, J. Thomas Cox, MD, and Warner Huh, MD

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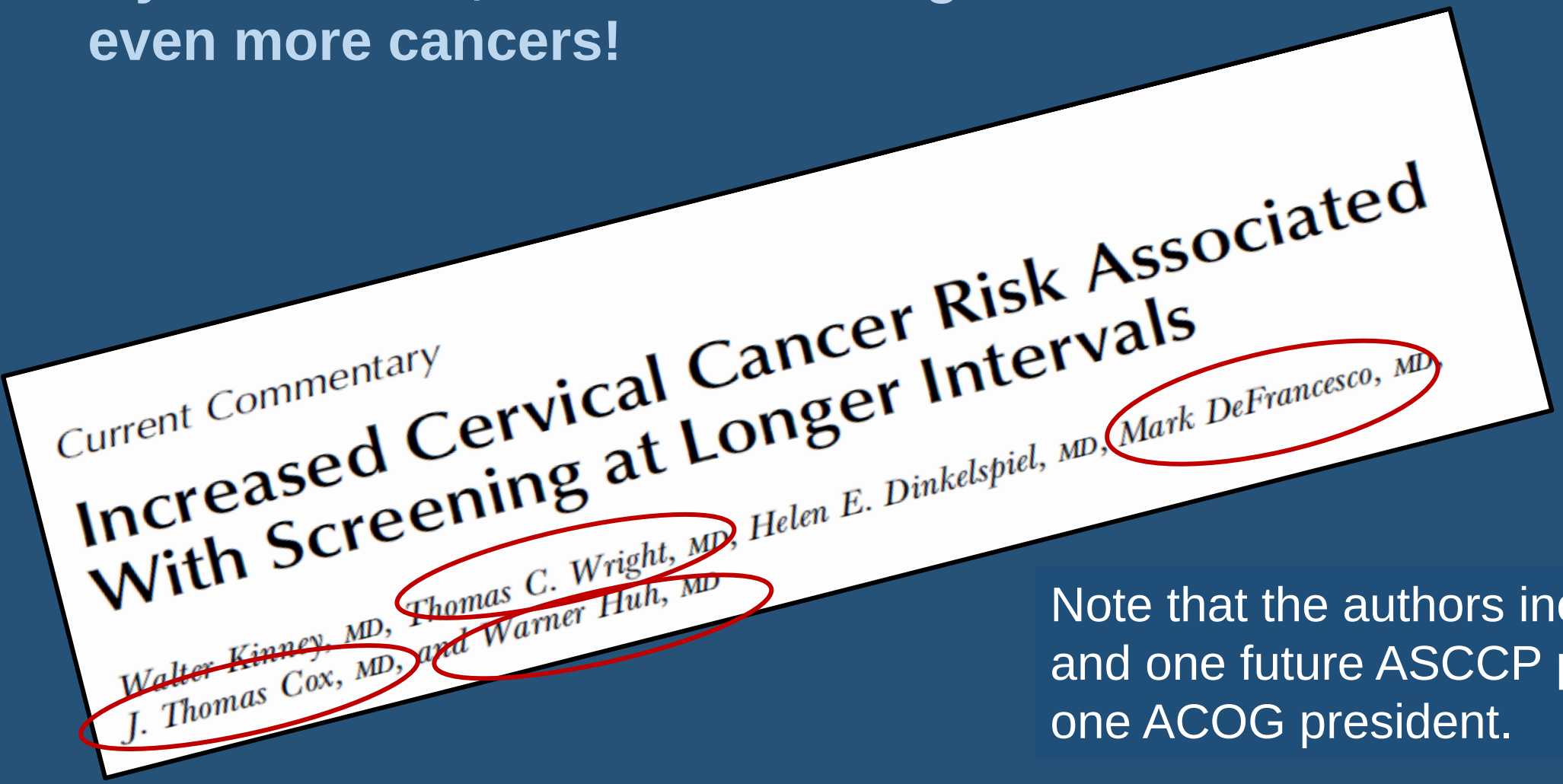

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Note that the authors include two past and one future ASCCP presidents and one ACOG president.