Updates in Primary Care

KAREN STENEHJEM, MD

Disclosures

- N/A

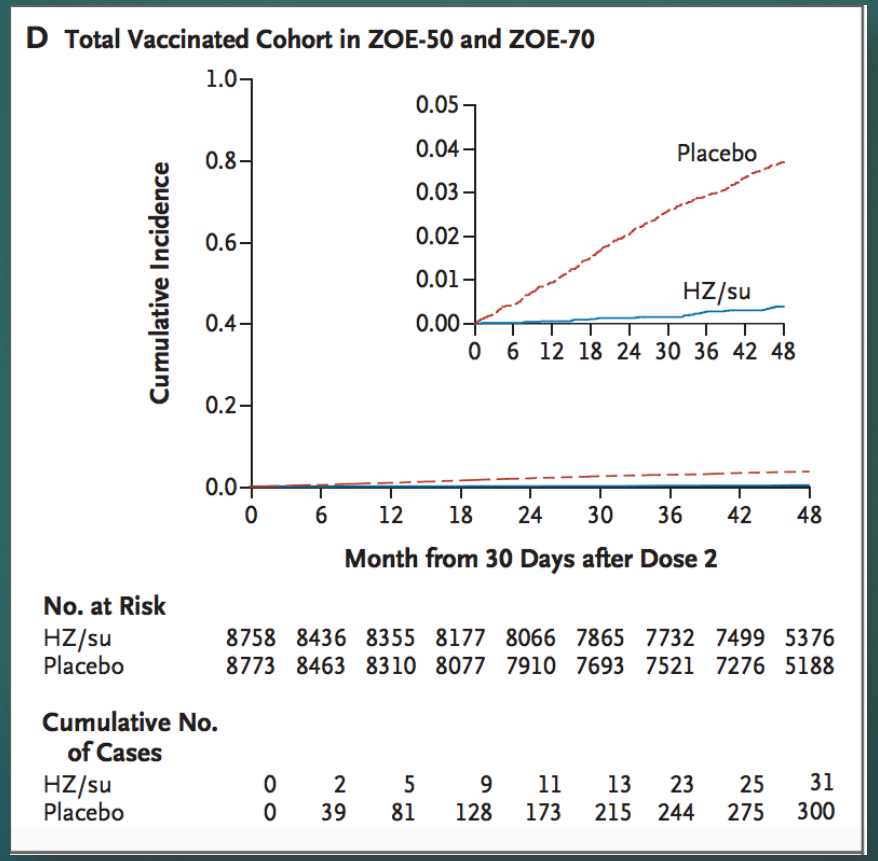
Objectives

- Vaccination Updates:
  - Recombinant Herpes Zoster (SHINGRIX)
  - Recombinant HPV Vaccine (GARDASIL-9)
  - Hepatitis A Vaccine
- Colon Cancer Screening Guidelines
- Aspirin for Primary Prevention of CV Disease
- Omega-3 Fatty Acids for Prevention of CV Disease

Vaccination Updates

Recombinant Herpes Zoster Vaccine (SHINGRIX)

Recombinant Herpes Zoster Vaccine (SHINGRIX)



Cunningham AL, Lal H, Kovac M, et al. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. N Enlg J Med. 2016;375(11):1019-32.

Zoster Vaccines

SHINGRIX

- Recombinant Vaccine
- Efficacy
  - AGE 60-69: 97.4%
  - AGE >70: 89.8%
- Durability: Approx. 19 yrs.

ZOSTAVAX

- Live Attenuated Virus
- Efficacy
  - AGE 60-69: 63.9%
  - AGE >70: 37.6%
- Durability: Approx. 5 yrs.

Zoster Vaccines

CDC recommendations:

- Shingrix preferred over Zostavax for the prevention of herpes zoster
  - All immunocompetent adults age 50 years and older

SHINGRIX - Practical Considerations

- **Immunocompromised Patients**
  - Not contraindicated; Not studied
- **Prior Zoster Vaccination**
  - Revaccination studied at 5 years; per CDC only need to wait 8 weeks
- **Prior Zoster Infection**
  - Vaccinate as soon as no signs of active infection
- **No History of Varicella**
  - No need to screen (>99% Seropositive)
- **Multiple Vaccinations**
  - OK with Influenza, Pneumonia, Tetanus

SHINGRIX – Vaccine Shortage

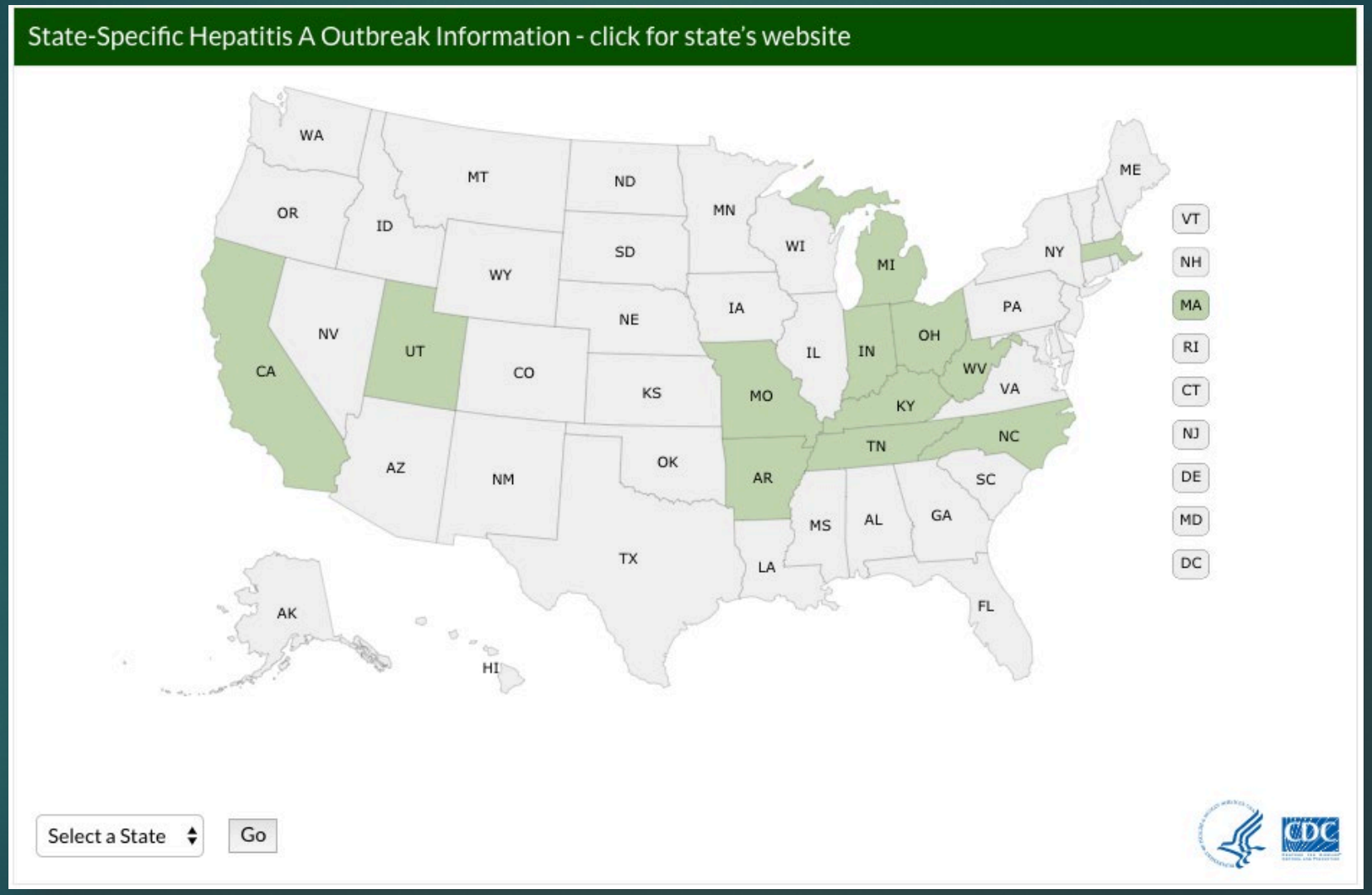
- **Where to Find the Vaccine:**
  - Vaccinefinder.org
  - Shingrix.com/shingles-vaccine-locator.html
- **Missed or Delayed Second Dose**
  - Give second Shingrix ASAP
  - Do Not Repeat Series
  - Do Not Replace with Zostavax

HPV Vaccine – GARDASIL 9

HPV Vaccine – GARDASIL 9

- FDA Expanded approval to Men and Women aged 27-45
  - All men and women ages 9 – 45
- Based on Unpublished Data from Gardasil-4 Approval
  - In Women Aged 27-45, vaccination was 88% effective at preventing persistent infection and HPV-associated vaginal/cervical disease
  - Durable at up to 10 years
  - Extrapolated to Include Gardasil-9
  - Extrapolated to Include Men
- No updated CDC vaccination guidelines

Hepatitis A Outbreak



"Viral Hepatitis." *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, 3 Dec. 2018, www.cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm.

Hepatitis A Outbreak 2017- 2018

- 281 Cases (9.2/100,000 Person Years)
- 69.4% in Salt Lake County
- 55.9% Hospitalizations

Risk Factors		
Homelessness and Drug Use	101	35.9%
Drug Use	78	27.8%
Homelessness	21	7.5%
Epi-Linked	40	14.2%
Travel	4	1.4%
Unknown	37	13.2%
Incarcerated	40	14.2%
Co-infection		
Hepatitis B (HBV)	3	1.1%
Hepatitis C (HCV)	43	15.3%
HBV & HCV	12	4.3%

"Bureau of Epidemiology." *Hepatitis A Outbreak*, health.utah.gov/epi/diseases/hepatitisA/HAVoutbreak_2017.

Hepatitis A Vaccination

- **Current Vaccination Recommendations:**
  - Children > Age 1
  - Adults At Risk
    - Travelers
    - MSM
    - Chronic Liver Disease
    - Food Handlers
    - **IV and non-IV Drug Users**
    - **Homeless Persons***
- **Post-Exposure Prophylaxis**
  - Single dose Hep A Vaccine within 2 weeks or Immune Globulin

Colon Cancer

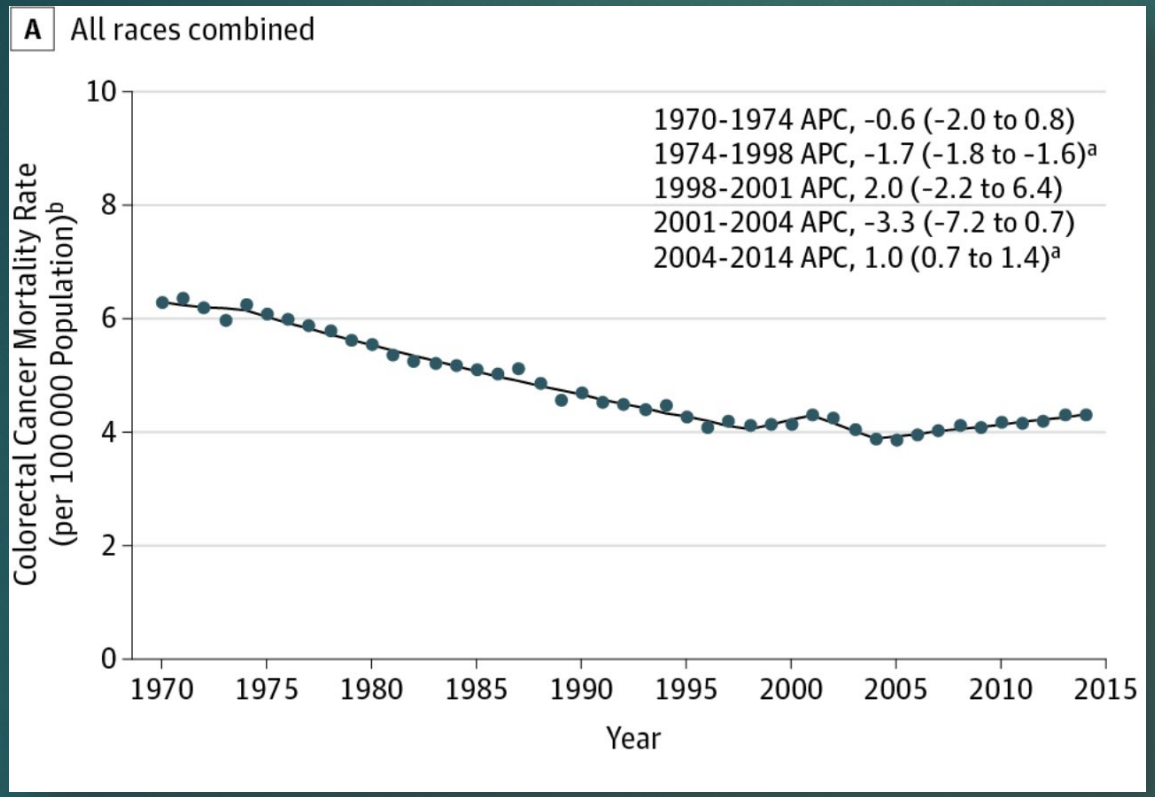
GUIDELINES FOR SCREENING

Colon Cancer Screening: ACS

"Adults aged 45 years and older with an average risk of colorectal cancer undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) examination…"

- Qualified Recommendation

Colon Cancer Screening: ACS



Annual Percent Change (APC) in Colorectal Cancer Mortality Rates Among Adults Aged 20 to 54 Years in the United States by Race, 1970-2014

Colorectal Cancer Mortality Rates in Adults Aged 20 to 54 Years in the United States, 1970-2014

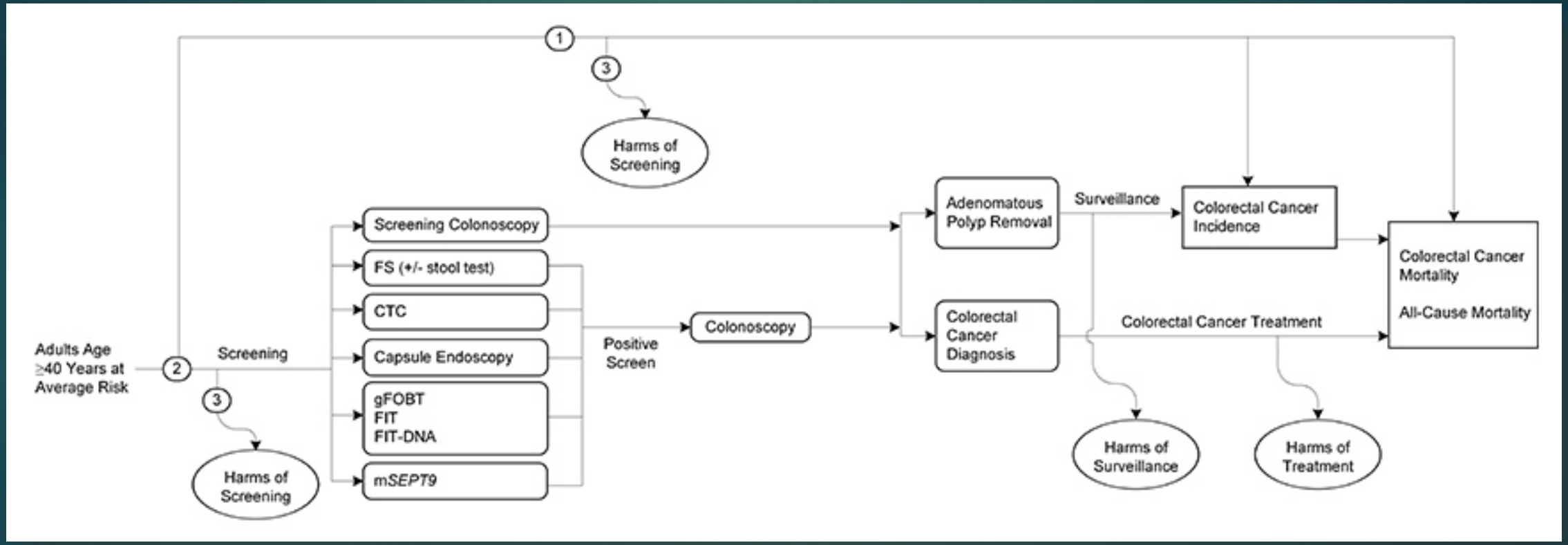
JAMA. 2017;318(6):572-574. doi:10.1001/jama.2017.7630

Colon Cancer Screening: USPSTF

Recommends screening for colorectal cancer starting at age 50 years and continuing until age 75 years.

– GRADE A Recommendation

Colon Cancer Screening: USPSTF

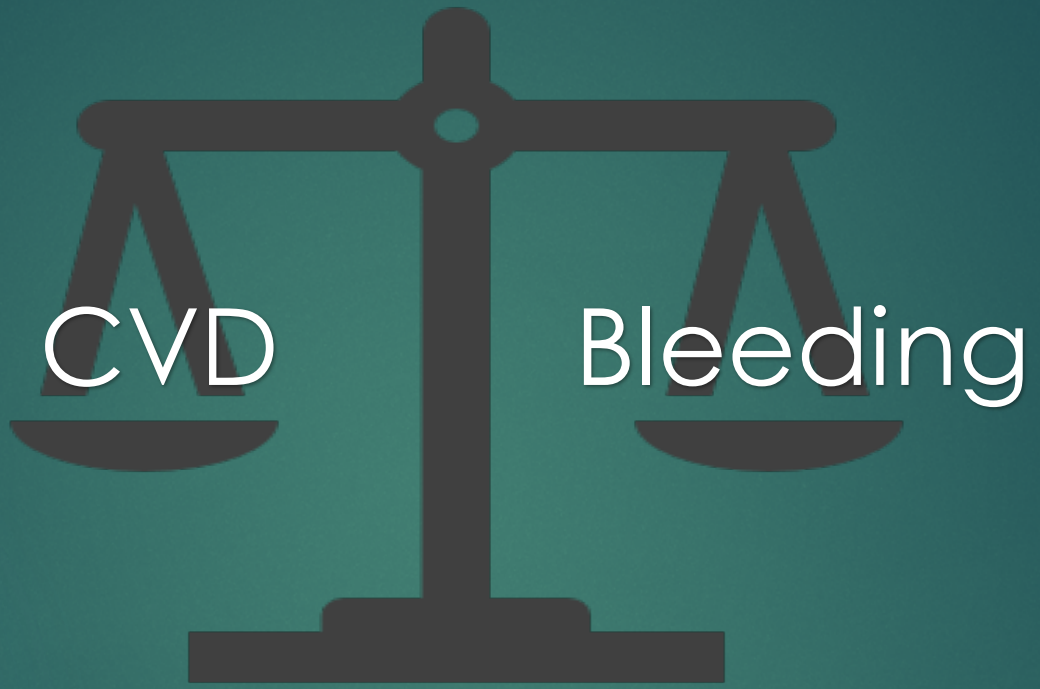


Draft Research Plan: Colorectal Cancer: Screening. U.S. Preventive Services Task Force. January 2019. https://www.uspreventiveservicestaskforce.org/Page/Document/draft-research-plan/colorectal-cancer-screening3/

Aspirin

PRIMARY PREVENTION FOR CARDIOVASCULAR DISEASE

Aspirin: Background



"Low Dose aspirin use for the primary prevention of cardiovascular disease (CVD) and colorectal cancer (CRC) in adults aged 50 to 59 years who have a ≥ 10% CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years." – USPSTF; GRADE B

Aspirin: 2018

Use of aspirin to reduce risk of i
patients at moderate risk of ca
a random

J Michael Gaziano, Ca
Peter M Rothwell, Lui

The NEW

Effects of As
in Persons with Diabetes Mellitus

The ASCEND Study Collaborative Group*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly

J.J. McNeil, R. Wolfe, R.L. Woods, A.M. Tonkin, G.A. Donnan, M.R. Nelson, C.M. Reid, J.E. Lockery, B. Kirpach, E. Storey, R.C. Shah, J.D. Williamson, K.L. Margolis, M.E. Ernst, W.P. Abhayaratna, N. Stocks, S.M. Fitzgerald, S.G. Orchard, R.E. Trevaks, L.J. Beilin, C.I. Johnston, J. Ryan, B. Radziszewska, M. Jelinek, M. Malik, C.B. Eaton, D. Brauer, G. Cloud, E.M. Wood, S.E. Mahady, S. Satterfield,* R. Grimm, and A.M. Murray, for the ASPREE Investigator Group†

Aspirin 2018: Cardiovascular Events

- ARRIVE (ALL COMERS): **No difference** in rate of composite CV events
  - Aspirin 4.29% vs Placebo 4.48%
    - Hazard ratio 0.96; 95% CI: 0.81–1.13
- ASCEND (DIABETICS): **Lower** rates of composite CV events
  - Aspirin 8.5% vs Placebo 9.6%
    - Rate ratio 0.88; 95% CI: 0.79 to 0.97
- ASPREE (ELDERLY): **No difference** in rate of composite CV events
  - Aspirin10.7 / 1000 person-years vs Placebo11.3 / 1000 person-years
    - Hazard Ratio 0.95; 95% CI: 0.83 to 1.08

Aspirin 2018: Myocardial Infarction

- ARRIVE (ALL COMERS): **No difference** in rate of fatal or non-fatal MI
  - Aspirin 1.52% vs Placebo 1.78%
    - Hazard Ratio 0.85; 95% CI 0.64–1.11
- ASCEND (DIABETICS): **No difference** in rate of non-fatal MI
  - Aspirin 2.5% vs Placebo 2.5%
    - Rate ratio 0.98; 95% CI 0.80-1.19
- ASPREE (ELDERLY): **No difference** in rate of fatal or non-fatal MI
  - Aspirin 4.0 /1000 person years vs 4.3 / 1000 person-years
    - Hazard Ratio 0.93; 95% CI 0.76-1.15

Aspirin 2018: Stroke

- ARRIVE (ALL COMERS): **No difference** in rate of Stroke
  - Aspirin 1.20% vs Placebo 1.07%
    - Hazard Ratio 1.12; 95% CI 0.80–1.55
- ASCEND (DIABETICS): **No difference** in rate of non-fatal (ischemic) Stroke
  - Aspirin 2.6% vs Placebo 3.0%
    - Rate ratio 0.88; 95% CI 0.73-1.06
- ASPREE (ELDERLY): **No difference** in rate of non-fatal ischemic stroke
    - Aspirin 3.5 / 1000 person-years vs Placebo 3.9 / 1000 person years
      - Hazard Ratio 0.89; 95% CI 0.71-1.11

Aspirin 2018: Bleeding

- ARRIVE (ALL COMERS): **Higher** Rates of GI Bleeding with Aspirin
  - Aspirin 0.97% vs Placebo 0.47%
    - Hazard Ratio 2.11; 95% CI 1.36-3.28
- ASCEND (DIABETICS): **Higher** Rates of Major Bleeding with Aspirin
  - Aspirin 4.1% vs Placebo 3.2%
    - Rate ratio 1.29; 95% CI 1.09-1.52
- ASPREE (ELDERLY): **Higher** Rates of Major Hemorrhage
  - Aspirin 8.6 per 1000 person years vs Placebo 6.2 per 1000 person years
    - Hazard Ratio 1.38; 95% CI 1.18-1.62

Aspirin 2018: All Cause Mortality

- ARRIVE (ALL COMERS): **NO DIFFERENCE**
  - Aspirin 160 (2.55%) vs Placebo 161 (2.57%)
  - Hazard Ratio 0.99; 95% CI 0.80-1.24
- ASCEND (DIABETICS): **NO DIFFERENCE**
  - Aspirin 748 (9.7%) vs Placebo 792 (10.2%)
  - Hazard Ratio 0.94; 95% CI 0.85-1.04
- ASPREE (ELDERLY): **NO DIFFERENCE**
  - Aspirin 12.7 per 1000 person years vs 11.1 per 1000 person years
  - Hazard Ratio1.14; 95% CI 1.01-1.29

Aspirin 2018: Controversy

"Moderate Risk"?

- ARRIVE (ALL COMERS): Calculated ASCVD Risk 17.3%; Actual Event Rate: ~5% over 5 years of the study
- ASCEND (DIABETICS): Only 17.2% of study population had 5 year event risk of >10%

Omega-3 Fatty Acids

CARDIOVASCULAR OUTCOMES

Omega-3 Fatty Acids: BACKGROUND

Short Chain Ω-3

Alpha-linolenic acid

10%

Long Chain Ω-3

Eicosapentaenoic acid
Docosahexaenoic acid

Omega-3 Fatty Acids: BACKGROUND

- **Known:**
  - **Lower risk of death from Coronary Heart Disease in populations with high fish consumption**
  - **Improvements in Interim Cardiac Measures:↓ TG (30%) / ↓ Systolic BP(1-2 mmHg) /↓ HR (1-2 bpm)**

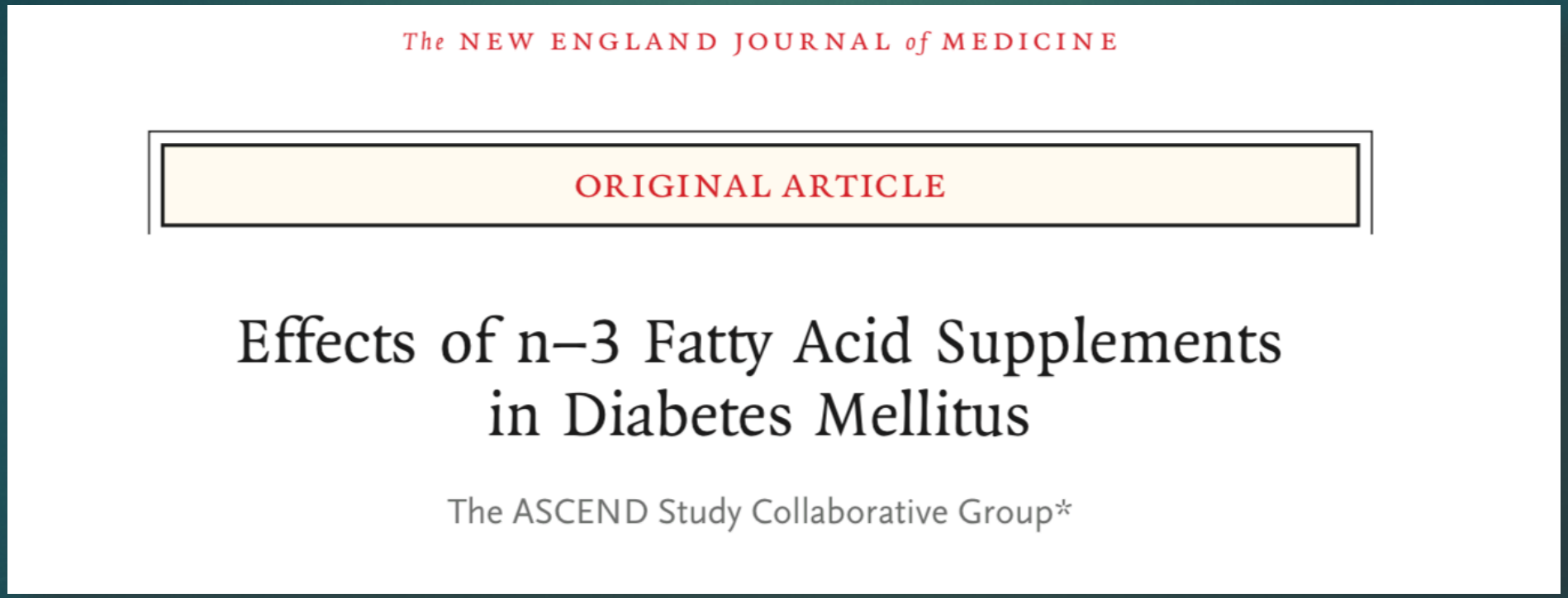
- **Unknown:**
  - **Benefits from Supplementation of Omega-3**
  - **Cardiac Outcomes (Death, Vascular Events, Etc.)**

Omega-3 Fatty Acids: ACC/AHA

"The American Heart Association recommends eating fish (particularly fatty fish) at least two times (two servings) a week…Increasing omega-3 fatty acid consumption through foods is preferable. However, those with coronary artery disease, may not get enough omega-3 by diet alone. These people may want to talk to their doctor about supplements."

"Fish and Omega-3 Fatty Acids." *Fish and Omega 3 Fatty Acids*, American Heart Association, 23 Mar. 2017, www.heart.org/en/healthy-living/healthy-eating/eat-smart/fats/fish-and-omega-3-fatty-acids.

Omega-3 Fatty Acids: ASCEND



The NEW ENGLAND JOURNAL of MEDICINE

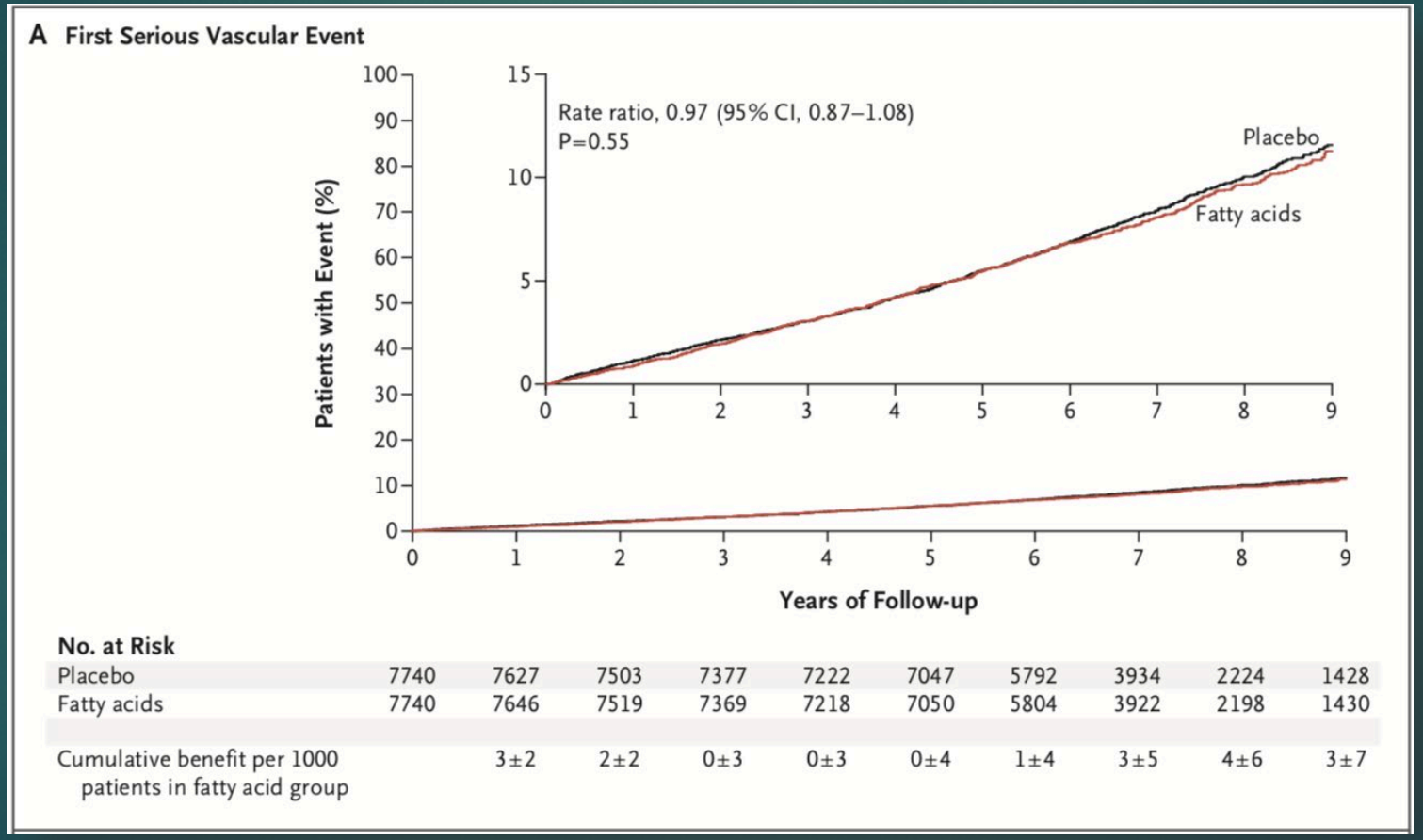
ORIGINAL ARTICLE

Effects of n–3 Fatty Acid Supplements in Diabetes Mellitus

The ASCEND Study Collaborative Group*

Bowman L, Mafham M, Wallendszus, et al. Effects of n-3 Fatty Acid Supplements in Diabetes. N Engl J Med. 2018; 379:1540-1550

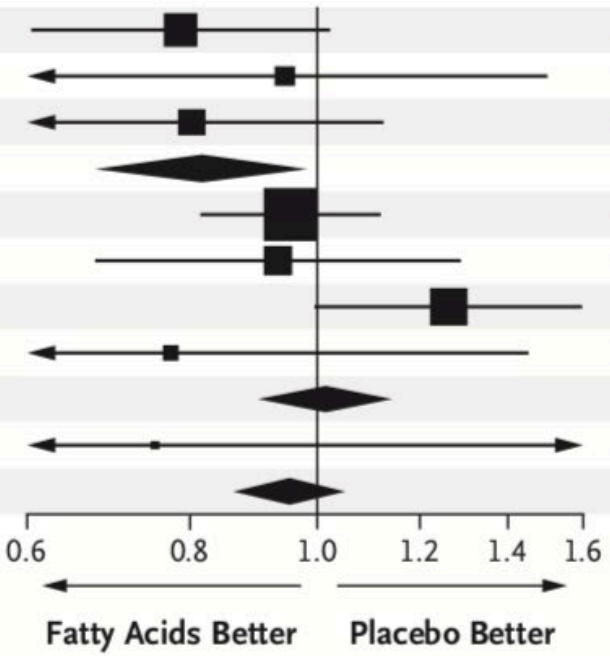
Omega-3 Fatty Acids: ASCEND



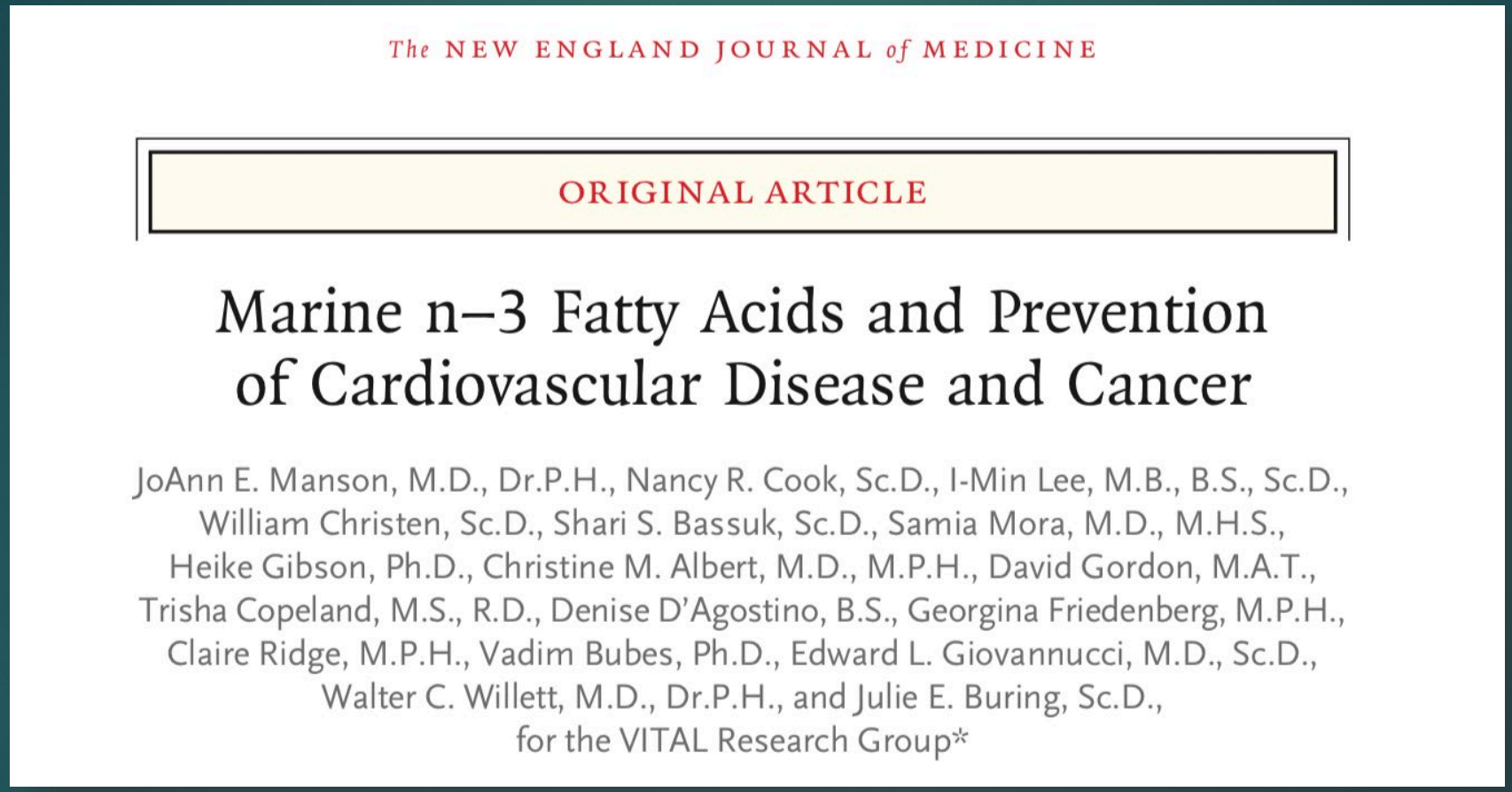
No. at Risk										
Placebo	7740	7627	7503	7377	7222	7047	5792	3934	2224	1428
Fatty acids	7740	7646	7519	7369	7218	7050	5804	3922	2198	1430
Cumulative benefit per 1000 patients in fatty acid group		3±2	2±2	0±3	0±3	0±4	1±4	3±5	4±6	3±7

Omega-3 Fatty Acids: ASCEND

Cause of Death	Fatty Acids (N=7740)	Placebo (N=7740)	Rate Ratio (95% CI)
	no. of patients with event (%)		
Coronary	100 (1.3)	127 (1.6)	0.79 (0.61–1.02)
All stroke	35 (0.5)	37 (0.5)	0.94 (0.59–1.50)
Other vascular	61 (0.8)	76 (1.0)	0.80 (0.57–1.12)
Vascular	**196 (2.5)**	**240 (3.1)**	**0.82 (0.68–0.98)**
Cancer	305 (3.9)	319 (4.1)	0.95 (0.82–1.12)
Respiratory	73 (0.9)	78 (1.0)	0.93 (0.68–1.28)
Other medical	158 (2.0)	125 (1.6)	1.26 (1.00–1.59)
External causes	17 (0.2)	22 (0.3)	0.77 (0.41–1.45)
Nonvascular	**553 (7.1)**	**544 (7.0)**	**1.01 (0.90–1.14)**
Unknown cause	3 (0.0)	4 (0.1)	0.75 (0.17–3.31)
All causes	**752 (9.7)**	**788 (10.2)**	**0.95 (0.86–1.05)**



Omega-3 Fatty Acids: VITAL



The NEW ENGLAND JOURNAL of MEDICINE

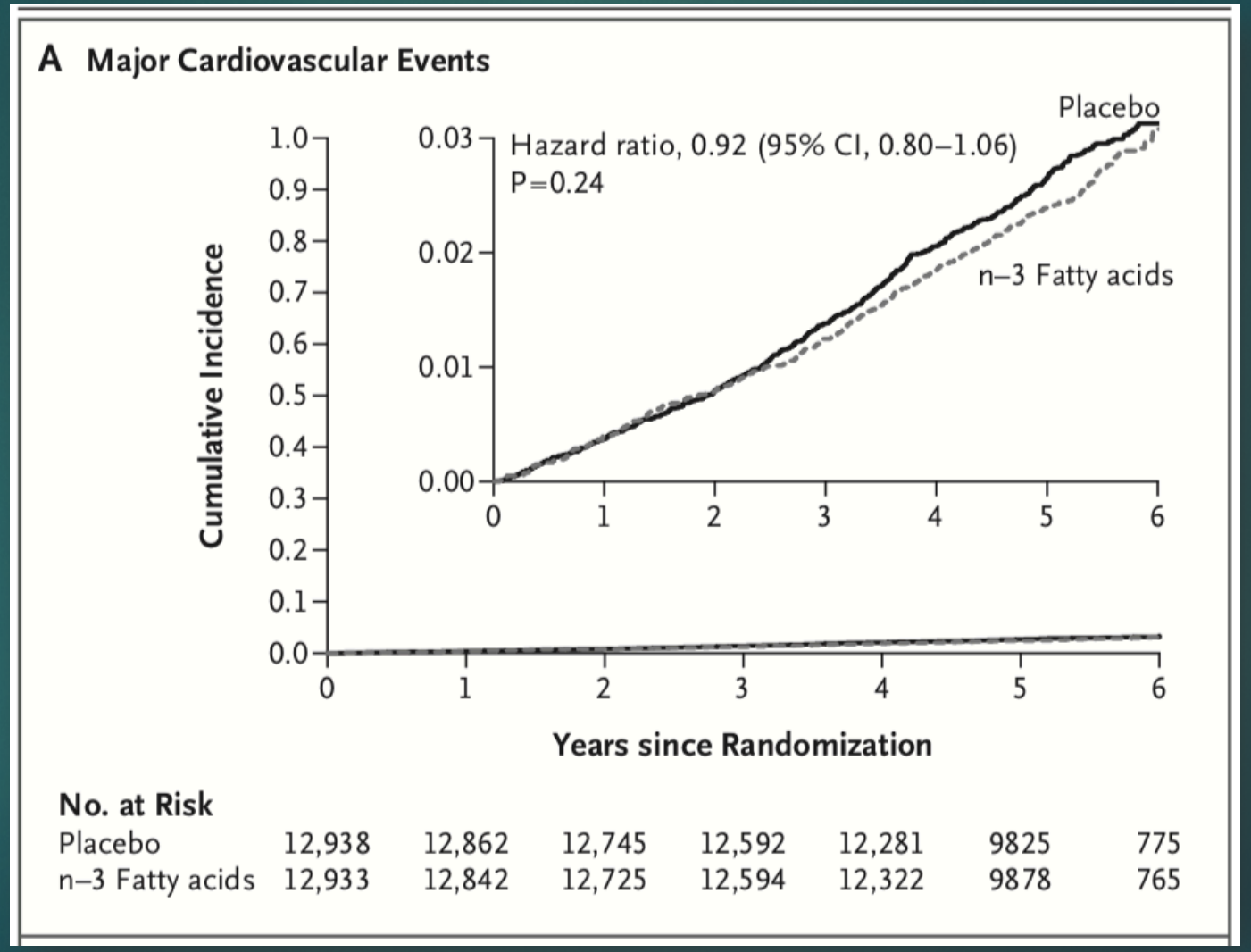
ORIGINAL ARTICLE

Marine n–3 Fatty Acids and Prevention of Cardiovascular Disease and Cancer

JoAnn E. Manson, M.D., Dr.P.H., Nancy R. Cook, Sc.D., I-Min Lee, M.B., B.S., Sc.D., William Christen, Sc.D., Shari S. Bassuk, Sc.D., Samia Mora, M.D., M.H.S., Heike Gibson, Ph.D., Christine M. Albert, M.D., M.P.H., David Gordon, M.A.T., Trisha Copeland, M.S., R.D., Denise D'Agostino, B.S., Georgina Friedenberg, M.P.H., Claire Ridge, M.P.H., Vadim Bubes, Ph.D., Edward L. Giovannucci, M.D., Sc.D., Walter C. Willett, M.D., Dr.P.H., and Julie E. Buring, Sc.D., for the VITAL Research Group*

Manson JE, Cook NR, Lee I, et al. Marine n-3 Fatty Acid and the Prevention of Cardiovascular Disease and Cancer. N Enlg J Med. 2018 doi: 10.1056/NEJMoa1811403. [Epub ahead of print]

Omega-3 Fatty Acids: VITAL



Omega-3 Fatty Acids: VITAL

Table 2. Hazard Ratios and 95% Confidence Intervals for the Primary, Secondary, and Other End Points, According to Randomized Assignment to n–3 Fatty Acids or Placebo, in Intention-to-Treat Analyses.*

End Point	n–3 Group (N=12,933)	Placebo Group (N=12,938)	Hazard Ratio (95% CI)
	no. of participants with event		
Cardiovascular disease			
Death from any cause	493	485	1.02 (0.90–1.15)
event†			
Cardiovascular event in expanded composite end point‡	527	567	0.93 (0.82–1.04)
Total myocardial infarction	145	200	0.72 (0.59–0.90)
Total stroke	148	142	1.04 (0.83–1.31)
Death from cardiovascular causes	142	148	0.96 (0.76–1.21)

Omega-3 Fatty Acids: Meta-Analysis

Cochrane Library

Cochrane Database of S

Omega-3 fatty acids for the primary and secondary prevention of cardiovascular disease (Review)

Abdelhamid AS, Brown TJ, Brainard JS, Biswas P, Thorpe GC, Moore HJ, Deane KHO, AlAbdulghafoor FK, Summerbell CD, Worthington HV, Song F, Hooper L

JAMA Cardiology | Original Investigation

Associations of Omega-3 Fatty Acid Supplement Use With Cardiovascular Disease Risks

Meta-analysis of 10 Trials Involving 77 917 Individuals

Theingi Aung, MBBS, FRCP; Jim Halsey, BSc; Daan Kromhout, PhD; Hertzel C. Gerstein, MD; Roberto Marchioli, MD; Luigi Tavazzi, MD; Johanna M. Geleijnse, PhD; Bernhard Rauch, MD; Andrew Ness, PhD, FFPH; Pilar Galan, MD, PhD; Emily Y. Chew, MD; Jackie Bosch, PhD; Rory Collins, FMedSci, FRCP; Sarah Lewington, DPhil; Jane Armitage, FRCP, FFPH; Robert Clarke, MD, FRCP, FFPH; for the Omega-3 Treatment Trialists' Collaboration

References

- ASCEND Study Collaborative Group, Bowman L, Mafham M, et al. Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus. N Engl J Med 2018; 379:1529.
- Bowman L, Mafham M, Wallendszus, et al. Effects of n-3 Fatty Acid Supplements in Diabetes. N Engl J Med. 2018; 379:1540-1550
- Colorectal Cancer Mortality Rates in Adults Aged 20 to 54 Years in the United States, 1970-2014 JAMA. 2017;318(6):572-574. doi:10.1001/jama.2017.7630
- Cunningham AL, Lal H, Kovac M, et al. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. N Enlg J Med. 2016;375(11):1019-32.
- *Draft Research Plan: Colorectal Cancer: Screening*. U.S. Preventive Services Task Force. January 2019. https://www.uspreventiveservicestaskforce.org/Page/Document/draft-research-plan/colorectal-cancer-screening3/
- "Fish and Omega-3 Fatty Acids." *Fish and Omega 3 Fatty Acids*, American Heart Association, 23 Mar. 2017, www.heart.org/en/healthy-living/healthy-eating/eat-smart/fats/fish-and-omega-3-fatty-acids.

References

- Food and Drug Administration."Summary Basis for Regulatory Action." *Summary Basis for Regulatory Action*, October 5, 2018.
- Gaziano JM, Brotons C, Coppolecchia R, et al. Use of aspirin to reduce risk of initial vascular events in patients at moderate risk of cardiovascular disease (ARRIVE): a randomised, double-blind, placebo-controlled trial. Lancet 2018; 392:1036.
- Lal H, Cunningham AL, Godeaux O, et al. Efficacy of an adjuvanted herpes zoster subunit vaccine in older adults. N Enlg J Med. 2015;372(22):2087-96.
- Manson JE, Cook NR, Lee I, et al. Marine n-3 Fatty Acid and the Prevention of Cardiovascular Disease and Cancer. N Enlg J Med. 2018
- McNeil JJ, Wolfe R, Woods RL, et al. Effect of Aspirin on Cardiovascular Events and Bleeding in the Healthy Elderly. NEJM 2018; 379:1509
- Oxman MN, Levin MJ, Johnson GR, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. N Engl J Med 2005;352:2271-84.