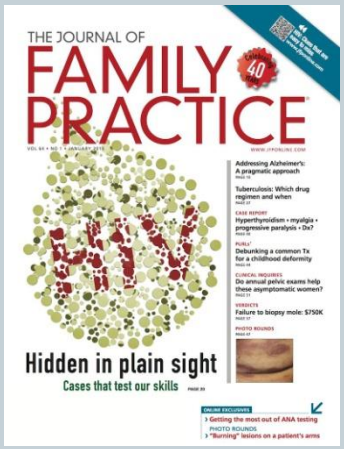
Key Articles & Clinical Developments of 2018 in Family Medicine

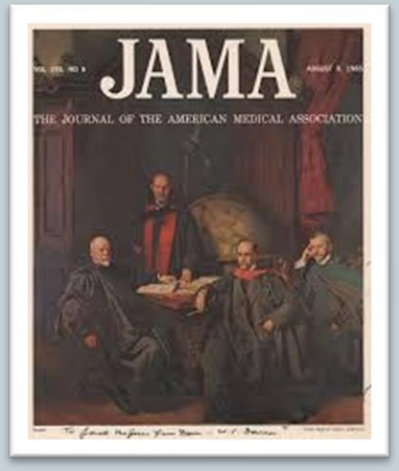
WHAT WAS IMPORTANT…

…AT LEAST TO SOME OF US

DAN WALDMAN, MD
UNM FAMILY AND COMMUNITY MEDICINE

A Survey of The Year's Stories





How Did I Choose Things?

- Essential Evidence
- Journal Watch
- Practice Update
- Our Faculty
- “Top of 2018” Lists
- Dr. Frank Domino’s “Frankly Speaking” Podcast

- Prioritized:
  - key areas of FM practice
  - might directly change clinical practice
  - might be leading to paradigm changes

Aspirin for Primary Prevention

ASA: No to Limited Benefit in Primary Prevention

- Clarification: Primary vs Secondary prevention!
- All ASA 100mg vs placebo
- **ASPREE**: RCT 19,000 pts. All cause mortality higher in aspirin group. Mostly Age>70. (increased CA deaths? increased hemorrhage seen)
- **ARRIVE**: 12.5k adults >55 (men), >60 women, all with 10 year CAD risk 10-20%. No difference in CV outcomes, increased in GI bleeds
- **ASCEND**: pts with DM >40, no known CAD: ~15k pts Slight benefit of aspirin, but driven by TIA outcomes. Increase in major bleeding.

But Wait…There's More

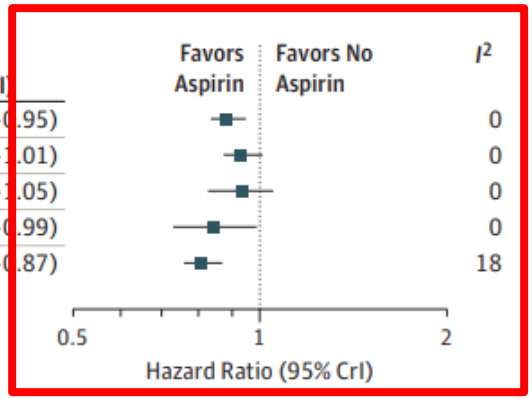
- 13 trials: 164,225 participants
- Mean age 62, 47% men, 19% with diabetes. Median baseline 10 year risk: 9.2%.
- reductions in composite CV outcome compared with no aspirin (HR 0.89) absolute risk reduction, 0.38%, number (NNT 265)
- increased risk of major bleeding events compared with no aspirin (HR 1.43) absolute risk increase, 0.47% number (NNH 210)

JAMA®

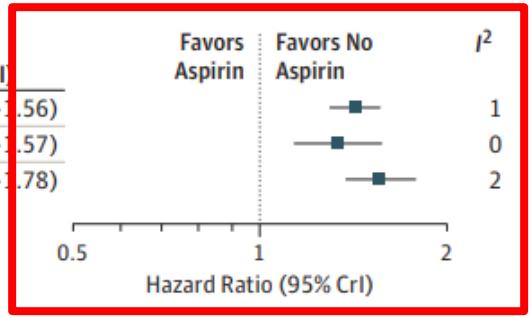
JAMA. 2019;321(3):277-287.
doi:10.1001/jama.2018.20578

Figure 1. Cardiovascular and Bleeding Outcomes in all Participants

Cardiovascular Outcomes	No. of Studies	Aspirin		No Aspirin		Absolute Risk Reduction, % (95% CI)	HR (95% CrI
		No. of Events	No. of Participants	No. of Events	No. of Participants		
Composite CV outcome	11	2911	79 717	3072	78 147	0.38 (0.20 to 0.55)	0.89 (0.84-0.95)
All-cause mortality	13	3622	81 623	3588	80 057	0.13 (-0.07 to 0.32)	0.94 (0.88-1.01)
CV mortality	13	995	81 623	997	80 057	0.07 (-0.04 to 0.17)	0.94 (0.83-1.05)
Myocardial infarction	13	1469	81 623	1599	80 057	0.28 (0.05 to 0.47)	0.85 (0.73-0.99)
Ischemic stroke	10	831	65 316	942	63 752	0.16 (0.06 to 0.30)	0.81 (0.76-0.87)



Bleeding Outcomes	No. of Studies	Aspirin		No Aspirin		Absolute Risk Increase, % (95% CI)	HR (95% CrI
		No. of Events	No. of Participants	No. of Events	No. of Participants		
Major bleeding	11	1195	74 715	834	73 143	0.47 (0.34 to 0.62)	1.43 (1.30-1.56)
Intracranial bleeding	12	349	80 985	257	79 419	0.11 (0.04 to 0.18)	1.34 (1.14-1.57)
Major GI bleeding	10	593	70 336	380	70 465	0.30 (0.20 to 0.41)	1.56 (1.38-1.78)



The composite cardiovascular (CV) outcome consisted of cardiovascular mortality, nonfatal myocardial infarction, and nonfatal stroke. Hazard ratios (HRs) and 95% credible interval variables (CrIs) were calculated using Bayesian meta-analysis of trial-level event counts. The absolute risk reductions and increases were calculated by multiplying the control event risk by the relative risk and 95% CIs derived by frequentist meta-analysis (eFigure 4 in Supplement 2). GI indicates gastrointestinal.

European Heart Journal

Efficacy and safety of aspirin for primary prevention of cardiovascular events: a meta-analysis and trial sequential analysis of randomized controlled trials

Ahmed N Mahmoud, Mohamed M Gad, Akram Y Elgendy, Islam Y Elgendy, Anthony A Bavry ✉ Author Notes

- 11 trials: 157,248 subjects, mean follow-up 6.6 years
- Focus on mortality
- aspirin ***not*** associated with lower incidence of all-cause mortality
- increased incidence of major bleeding RR 1.47 (NNH 250) + intracranial hemorrhage RR 1.33 (NNH 1000)

European Heart Journal

Efficacy and safety of aspirin for primary prevention of cardiovascular events: a meta-analysis and trial sequential analysis of randomized controlled trials

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- Similar effects demonstrated in diabetic and high cardiovascular risk patients (10-year risk >7.5%)
- lower incidence of MI, RR 0.82 (NNT 333), however… effect no longer evident when limiting the analysis to more recent trials

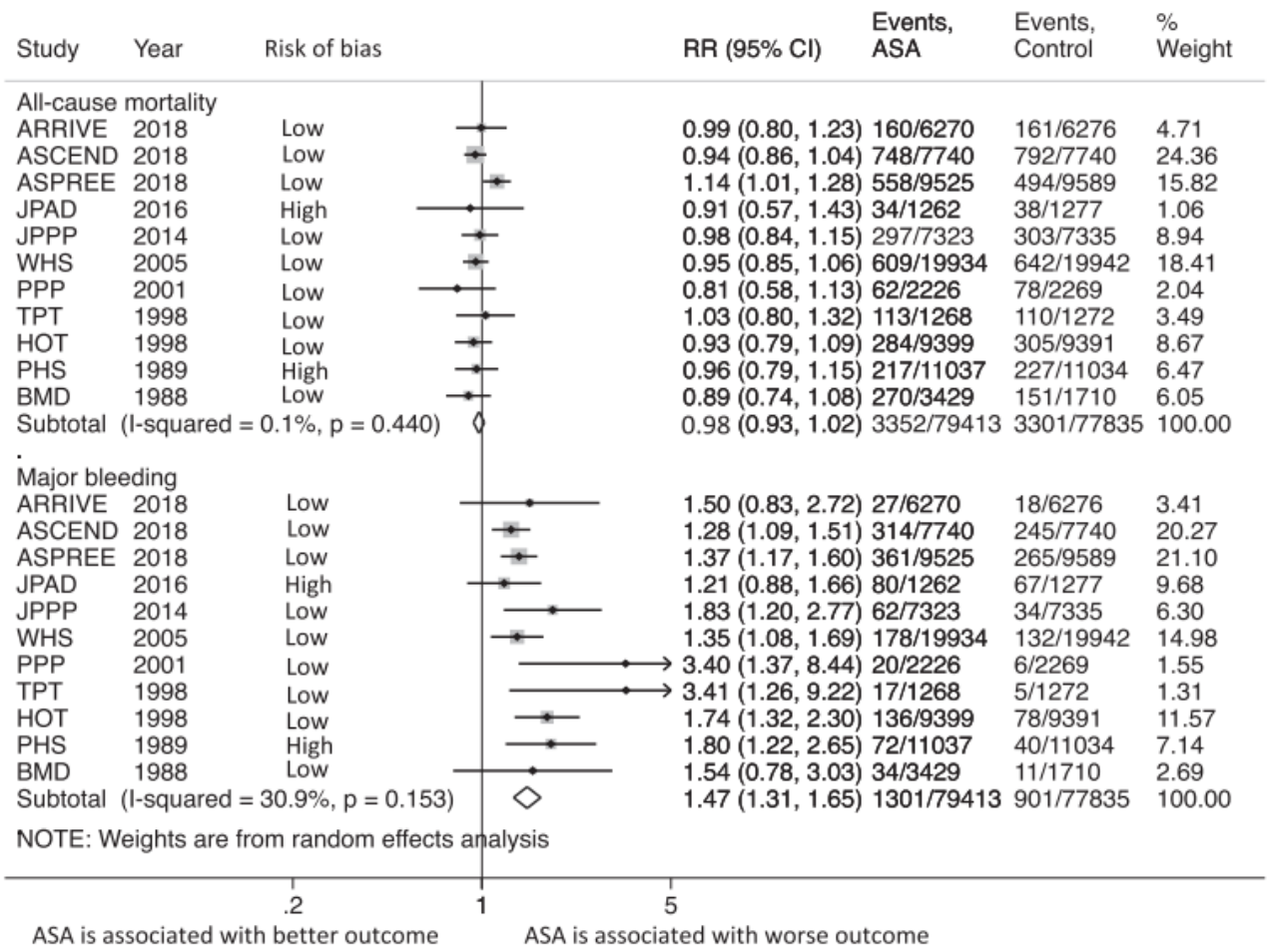
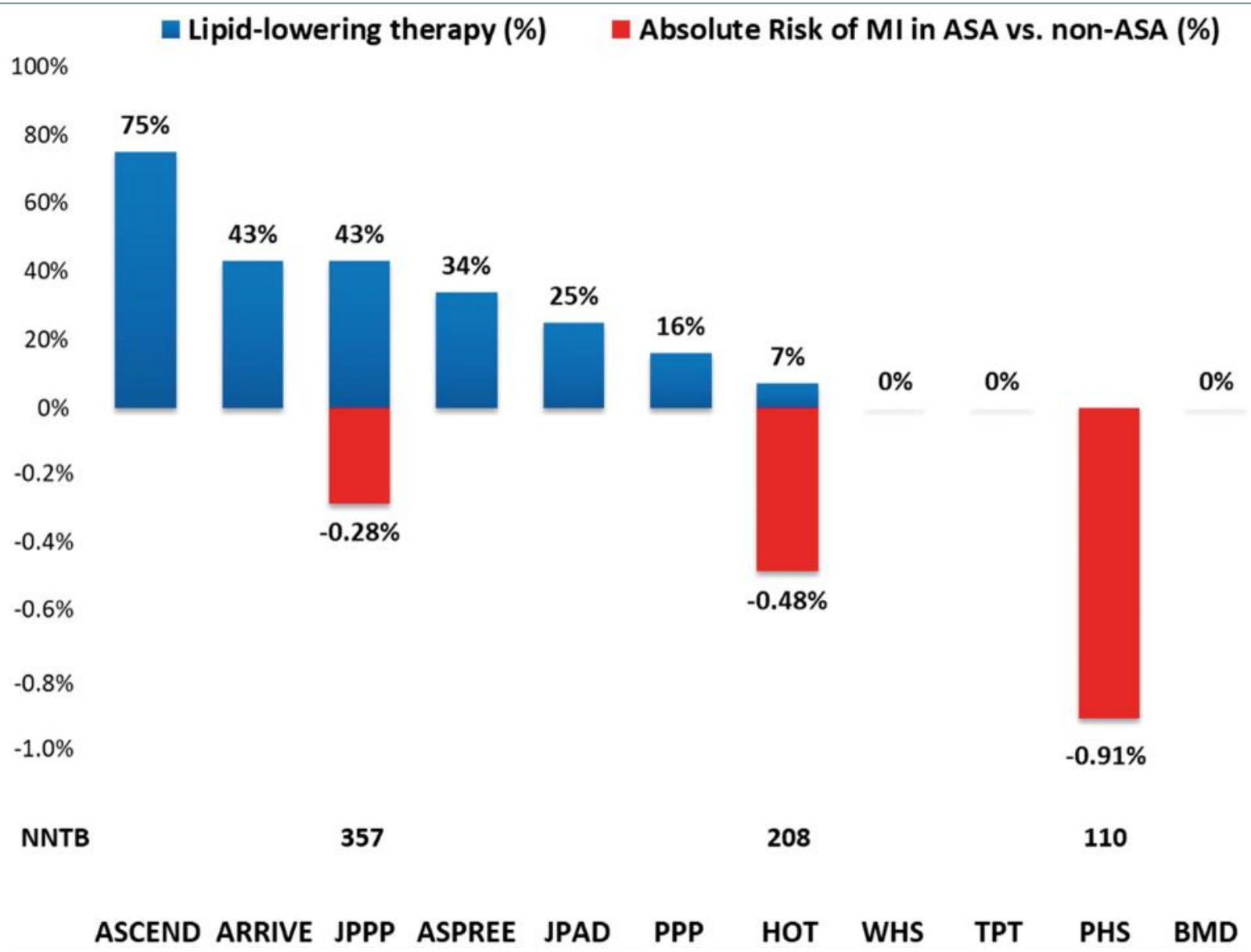


Figure 2 Summary plot for primary efficacy (all-cause mortality) and safety (major bleeding) outcomes. The relative size of the data markers indicates the weight of the sample size from each study. ASA, aspirin; CI, confidence interval; RR, risk ratio.



European Heart Journal, ehy872, https://doi.org/10.1093/eurheartj/ehy872
Published: 27 December 2018

Guidance for pts?

Hormonal Contraceptives and Cancer Risk

#1: Modern hormonal contraceptives: increased risk of breast cancer?

- Prospective cohort, 1.8 million women, Denmark
- longer exposure to HC's associated with increased incidence of breast cancer.
- ~13 additional breast cancers per 100,000 person-years (NNH for 1 year= 7690)
- Reminder: maternal mortality rate of 26 per 100,000 pregnancies in the United States

Mørch LS, Skovlund CW, Hannaford PC, Iversen L, Fielding S, Lidegaard Ø. Contemporary hormonal contraception and the risk of breast cancer. N Engl J Med 2017;377(23):2228-2239.

The NEW ENGLAND JOURNAL of MEDICINE

Table 1. Characteristics of the Study Population.*

Variable
Never used hormonal contraception
Used hormonal contraception >6 mo previously
Current or recent use of hormonal contraception
Current or recent use of combined hormonal contraception
Oral ethinyl estradiol, 50 μg
Norethisterone
Levonorgestrel
Oral ethinyl estradiol, 20–40 μg
Norethisterone
Levonorgestrel
Norgestimate
Desogestrel
Gestodene
Drospirenone
Cyproterone
Estradiol valerate and dienogest
Nonoral contraceptive
Patch (norgestimate)
Vaginal ring (etonogestrel)
Current or recent use of progestin-only products
Oral contraceptive
Norethisterone
Levonorgestrel
Desogestrel
Nonoral contraceptive
Implant
Levonorgestrel-releasing intrauterine system
Depot medroxyprogesterone acetate

#2: OCP's..Protect Against Cancer?

- Prospective NIH-AARP Diet and Health Study (enrolled 1995-6)
- Identified 1241 ovarian, 2337 endometrial, 11,114 breast, and 3507 colorectal cancer cases during follow-up
- Population: white (91%), postmenopausal (96%)
- OC use in the contexts of modifiable risk factors: obesity and smoking

JAMA®

Michels KA et al. JAMA Oncol 2018 Jan 18

#2: OCP's..Protect Against Cancer?

Risk reductions seen:

- **ovarian cancer**: consistent across health behaviors
- **endometrial cancer**: strongest among current smokers, obese women, and those who exercised rarely
- **breast and colorectal cancer**: no significant change seen, consistent across health behaviors
- More on Breast CA: trend of slight increase in risk, especially among current smokers

JAMA®

Michels KA et al. JAMA Oncol 2018 Jan 18

Figure 1. Oral Contraceptive Use and Time to Ovarian Cancer Diagnosis Across Baseline Smoking Status and BMI

Modifiable Factors	HR (95% CI)	P Value for Trend
OC use		
Smoking status		
Nonsmokers		<.001
Never or <1 y	1 [Reference]	
1-4 y	0.85 (0.67-1.08)	
5-9 y	0.77 (0.57-1.03)	
≥10 y	0.55 (0.38-0.79)	
Former smokers		.003
Never or <1 y	1 [Reference]	
1-4 y	0.78 (0.60-1.03)	
5-9 y	0.65 (0.47-0.90)	
≥10 y	0.70 (0.49-1.00)	
Current smokers		.03
Never or <1 y	1 [Reference]	
1-4 y	0.82 (0.51-1.31)	
5-9 y	0.78 (0.45-1.35)	
≥10 y	0.44 (0.20-0.97)	
Current BMI		
<25		<.001
Never or <1 y	1 [Reference]	
1-4 y	0.83 (0.65-1.07)	
5-9 y	0.67 (0.49-0.90)	
≥10 y	0.55 (0.38-0.78)	
25-29		.006
Never or <1 y	1 [Reference]	
1-4 y	0.77 (0.56-1.06)	
5-9 y	0.64 (0.43-0.95)	
≥10 y	0.66 (0.42-1.01)	
≥30		.12
Never or <1 y	1 [Reference]	
1-4 y	0.85 (0.61-1.18)	
5-9 y	0.94 (0.64-1.37)	
≥10 y	0.64 (0.38-1.08)	

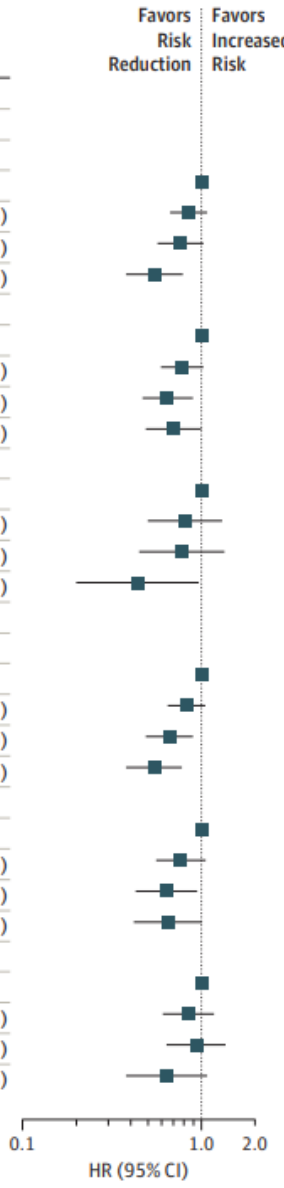
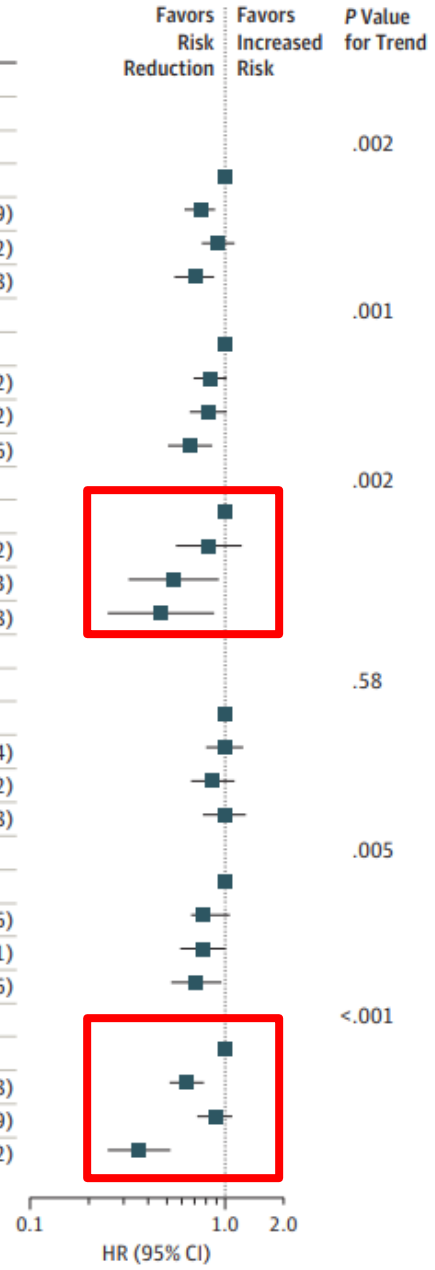
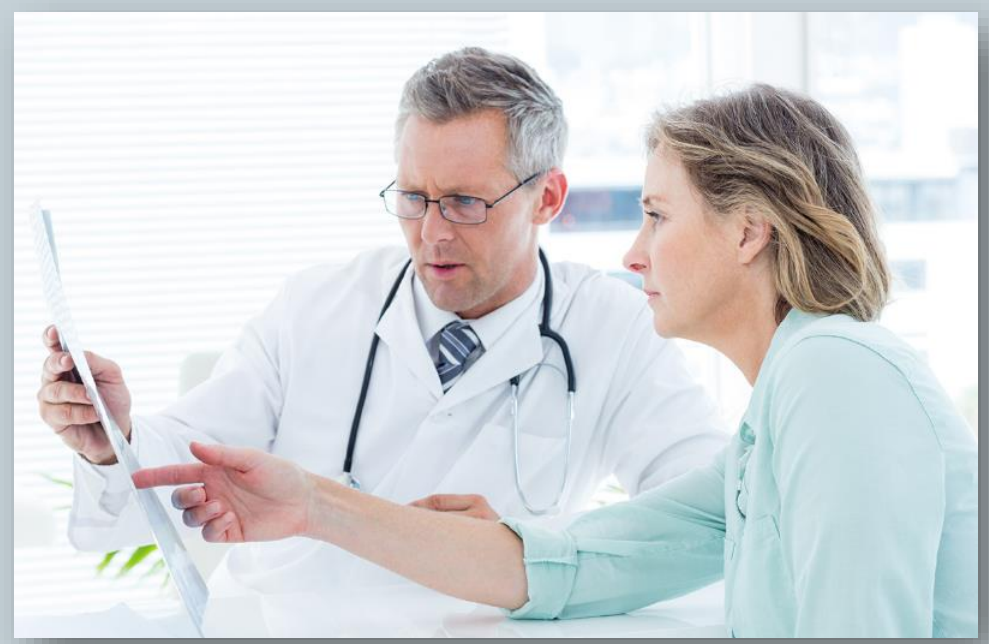


Figure 2. Oral Contraceptive Use and Time to Endometrial Cancer Diagnosis Across Baseline Smoking Status and BMI

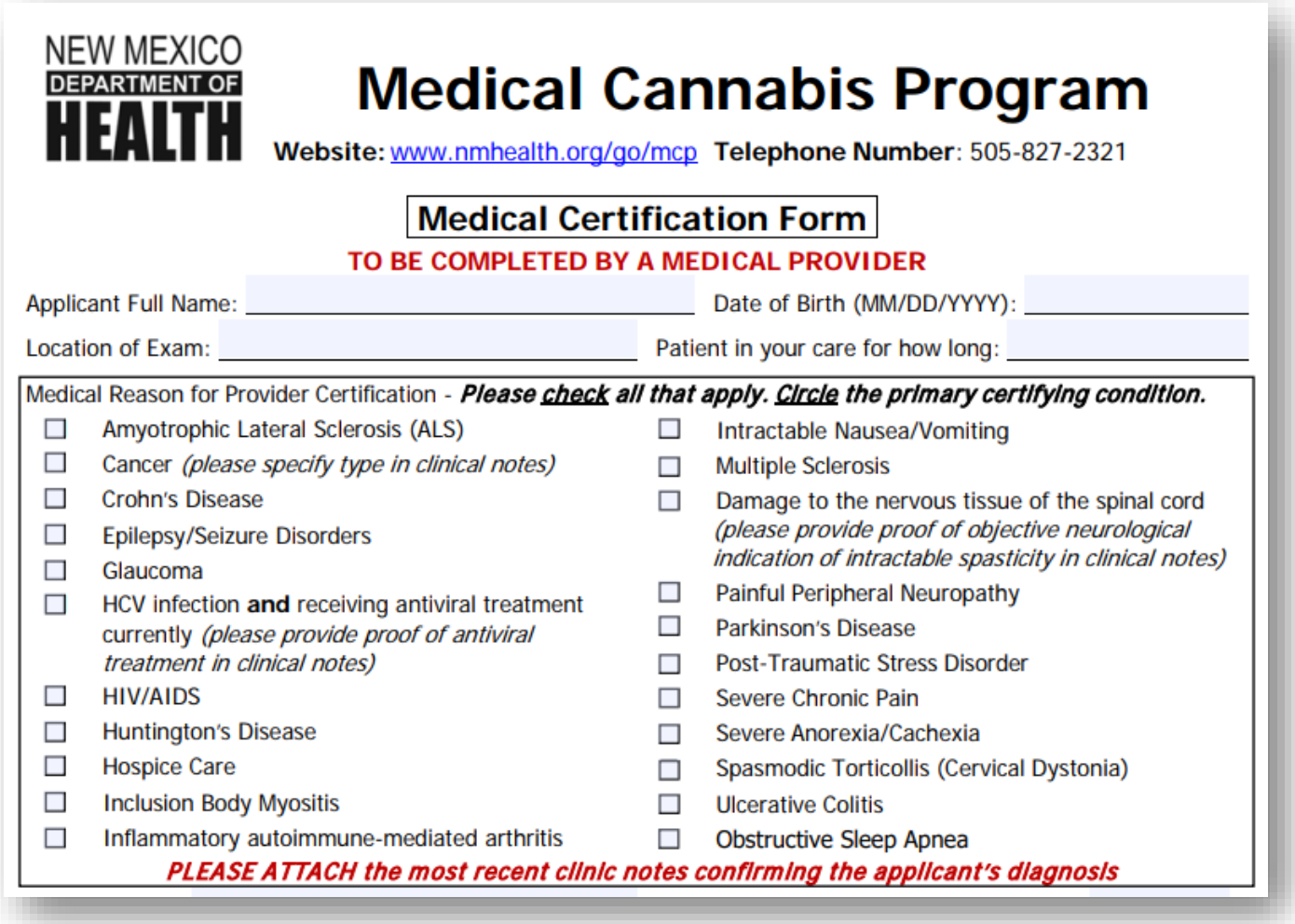
Modifiable Factors	HR (95% CI)	P Value for Trend
OC use		
Smoking status		
Nonsmokers		.002
Never or <1 y	1 [Reference]	
1-4 y	0.75 (0.62-0.89)	
5-9 y	0.92 (0.76-1.12)	
≥10 y	0.70 (0.55-0.88)	
Former smokers		.001
Never or <1 y	1 [Reference]	
1-4 y	0.84 (0.69-1.02)	
5-9 y	0.82 (0.66-1.02)	
≥10 y	0.66 (0.51-0.86)	
Current smokers		.002
Never or <1 y	1 [Reference]	
1-4 y	0.83 (0.56-1.22)	
5-9 y	0.54 (0.32-0.93)	
≥10 y	0.47 (0.25-0.88)	
Current BMI		
<25		.58
Never or <1 y	1 [Reference]	
1-4 y	0.99 (0.80-1.24)	
5-9 y	0.86 (0.67-1.12)	
≥10 y	0.99 (0.77-1.28)	
25-29		.005
Never or <1 y	1 [Reference]	
1-4 y	0.84 (0.67-1.06)	
5-9 y	0.77 (0.59-1.01)	
≥10 y	0.71 (0.53-0.96)	
≥30		<.001
Never or <1 y	1 [Reference]	
1-4 y	0.64 (0.52-0.78)	
5-9 y	0.89 (0.72-1.09)	
≥10 y	0.36 (0.25-0.52)	



Guidance for pts?



Cannabinoids and Chronic Non-Cancer Pain



NEW MEXICO DEPARTMENT OF HEALTH

Medical Cannabis Program

Website: www.nmhealth.org/go/mcp **Telephone Number**: 505-827-2321

Medical Certification Form

TO BE COMPLETED BY A MEDICAL PROVIDER

Applicant Full Name: _____ Date of Birth (MM/DD/YYYY): _____

Location of Exam: _____ Patient in your care for how long: _____

Medical Reason for Provider Certification - ***Please check all that apply. Circle the primary certifying condition.***

- ☐ Amyotrophic Lateral Sclerosis (ALS)
- ☐ Cancer *(please specify type in clinical notes)*
- ☐ Crohn's Disease
- ☐ Epilepsy/Seizure Disorders
- ☐ Glaucoma
- ☐ HCV infection **and** receiving antiviral treatment currently *(please provide proof of antiviral treatment in clinical notes)*
- ☐ HIV/AIDS
- ☐ Huntington's Disease
- ☐ Hospice Care
- ☐ Inclusion Body Myositis
- ☐ Inflammatory autoimmune-mediated arthritis
- ☐ Intractable Nausea/Vomiting
- ☐ Multiple Sclerosis
- ☐ Damage to the nervous tissue of the spinal cord *(please provide proof of objective neurological indication of intractable spasticity in clinical notes)*
- ☐ Painful Peripheral Neuropathy
- ☐ Parkinson's Disease
- ☐ Post-Traumatic Stress Disorder
- ☐ Severe Chronic Pain
- ☐ Severe Anorexia/Cachexia
- ☐ Spasmodic Torticollis (Cervical Dystonia)
- ☐ Ulcerative Colitis
- ☐ Obstructive Sleep Apnea

PLEASE ATTACH the most recent clinic notes confirming the applicant's diagnosis

Stockings E et al. Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. Pain. 2018 Oct;159(10):1932-1954

Cannabinoids and Chronic Non-Cancer Pain

- RCT and observational data, >100 studies, ~10k pts
- Variability in pain reduction measures
- cannabinoids (any form): higher rates of achieving 30% reduction in their pain (29% vs 25.9%)
- For 50% reduction in pain: wider confidence interval, not statistically significant

PAIN®
The Journal of the International Association for the Study of Pain

Stockings E et al. Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. Pain. 2018 Oct;159(10):1932-1954

Table 6

Summary of key statistics on the effectiveness of cannabinoids for chronic noncancer pain in randomised controlled trials.

Outcome	Pooled odds ratio (95% CI)	Pooled event rate (%), cannabinoid vs placebo	Number needed to treat to benefit (NNTB) (95% CI)
Pain outcomes			
30% reduction in pain	**1.46 (1.16-1.84)**	**29.0% vs 25.9%**	**24 (15-61)**
50% reduction in pain	1.43 (0.97-2.11)	18.2% vs 14.4%	*
Patient global impression of change			
Perceived "much" to "very much" improved	**1.62 (1.34-1.96)**	**18.9% vs 11.8%**	**38 (27-62)**
	Pooled odds ratio (95% CI)	**Pooled event rate (%), cannabinoid vs placebo**	**Number needed to treat to harm (NNTH) (95% CI)**
Adverse events			
All-cause adverse events	**2.33 (1.88-2.89)**	**81.2% vs 66.2%**	**6 (5-8)**
Study withdrawals—adverse events	**3.47 (2.64-4.56)**	**15.8% vs 4.6%**	**40 (35-49)**

Bold font indicates a statistically significant result. Only categorical outcomes with a moderate or higher GRADE rating are reported here.

* Number needed to treat to benefit unable to be calculated as the pooled odds ratio crossed the line of no effect.

CI, confidence interval.

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Stockings E et al. Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. Pain. 2018 Oct;159(10):1932-1954

Cannabis "Umbrella Review"

<u>31 systematic reviews, each with at least 2 RCTs</u>

- Looked at:
  - pain
  - nausea and vomiting
  - spasticity
  - adverse events
- Variation: populations, interventions, doses, masking
- Adverse events such as feeling high, disorientation, confusion were common (NNTH= 2 - 15), psychosis relatively rare
- The NNTH to discontinue the medication was between 8 and 22

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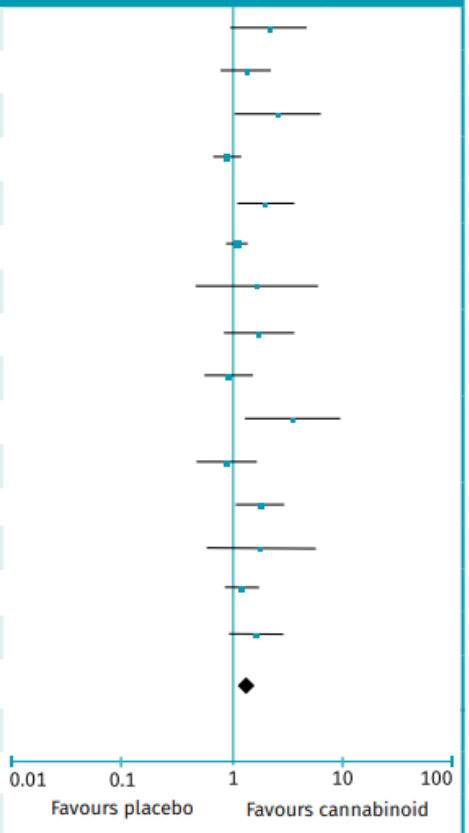
Allan GM, Finley CR, Ton J, et al. Systematic review of systematic reviews for medical cannabinoids: Pain, nausea and vomiting, spasticity, and harms. Can Fam Physician 2018;64: e78-e94.

Figure 1. Responder meta-analysis of patients attaining ≥ 30% reduction in pain with medical cannabinoids compared with placebo

	EXPERIMENTAL		CONTROL				
STUDY OR SUBGROUP	EVENTS	TOTAL	EVENTS	TOTAL	WEIGHT, %	RISK RATIO* (95% CI)	RISK RATIO* (95% CI)
Abrams, 2007	13	25	6	25	4.2	2.17 (0.98 to 4.79)	
Berman, 2004	34	93	13	48	7.2	1.35 (0.79 to 2.31)	
Ellis, 2009	13	28	5	28	3.5	2.60 (1.07 to 6.32)	
GW Pharmaceuticals, 2005	54	149	59	148	12.7	0.91 (0.68 to 1.22)	
Johnson, 2010	23	53	12	56	6.4	2.03 (1.12 to 3.65)	
Langford, 2013	83	167	77	172	14.5	1.11 (0.89 to 1.39)	
Lynch, 2014	5	18	3	18	1.9	1.67 (0.47 to 5.96)	
Nurmikko, 2007	16	63	9	62	4.7	1.75 (0.84 to 3.66)	
Portenoy, 2012	22	90	24	91	7.9	0.93 (0.56 to 1.53)	
Rog, 2005	15	34	4	32	2.9	3.53 (1.31 to 9.51)	
Selvarajah, 2010	8	15	9	15	5.9	0.89 (0.47 to 1.67)	
Serpell, 2014	34	128	19	128	7.8	1.79 (1.08 to 2.97)	
Ware, 2010	16	64	3	22	2.3	1.83 (0.59 to 5.70)	
Wilsey, 2008	46	69	18	33	11.1	1.22 (0.86 to 1.74)	
Wilsey, 2013	35	73	11	38	7.0	1.66 (0.95 to 2.88)	
Total (95% CI)		**1069**		**916**	**100.0**	**1.37 (1.14 to 1.64)**	
Total events	417		272				
Heterogeneity: $\tau^2 = 0.05$; $\chi^2_{14} = 24.42$ ($P = .04$); $I^2 = 43\%$							
Test for overall effect: $Z = 3.32$ ($P = .0009$)							



*Mantel-Haenszel method, random-effects meta-analysis.
Meta-analysis of studies from Whiting et al[2] (GW Pharmaceuticals, 2005, Johnson, 2010, Portenoy, 2012), Andreae et al[15] (Abrams, 2007, Ellis, 2009, Ware, 2010, Wilsey, 2008, Wilsey, 2013), and Petzke et al[16] (Berman, 2004, Langford, 2013, Lynch, 2014, Nurmikko, 2007, Rog, 2005, Selvarajah, 2010, Serpell, 2014).

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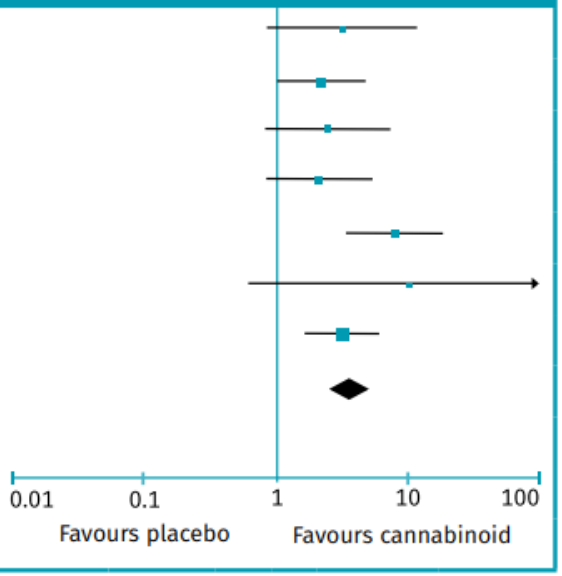
Nausea/Vomiting vs Placebo

Figure 2. Responder meta-analysis of patients having control of their nausea and vomiting resulting from chemotherapy: *A) Medical cannabinoid compared with placebo; B) medical cannabinoid compared with another antiemetic (neuroleptics).*

A)

	EXPERIMENTAL		CONTROL			
STUDY OR SUBGROUP	**EVENTS**	**TOTAL**	**EVENTS**	**TOTAL**	**WEIGHT, %**	**RISK RATIO* (95% CI)**
Duran, 2010	5	7	2	9	5.4	3.21 (0.87 to 11.90)
Frytak, 1979	16	38	7	37	21.8	2.23 (1.04 to 4.78)
Meiri, 2007	8	14	3	13	9.6	2.48 (0.83 to 7.37)
Melhem-Bertrandt, 2014	11	30	5	29	15.6	2.13 (0.84 to 5.37)
Orr, 1980	40	55	5	55	15.4	8.00 (3.42 to 18.74)
Sallan, 1975	5	15	0	14	1.6	10.31 (0.62 to 170.96)
Wada, 1982	32	92	10	92	30.7	3.20 (1.67 to 6.12)
Total (95% CI)		**251**		**249**	**100.0**	**3.60 (2.55 to 5.09)**
Total events	117		32			
Heterogeneity: $\chi^2_6 = 7.29$ ($P = .29$); $I^2 = 18\%$						
Test for overall effect: $Z = 7.24$ ($P < .00001$)						



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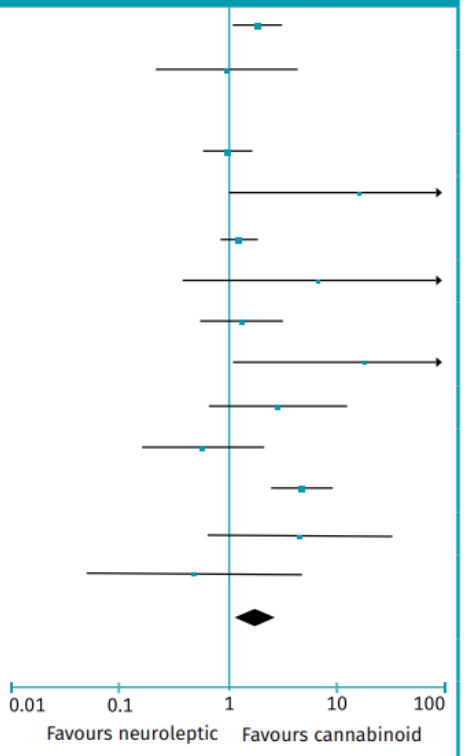
Nausea/Vomiting vs Antiemetic

Figure 2. Responder meta-analysis of patients having control of their nausea and vomiting resulting from chemotherapy: *A) Medical cannabinoid compared with placebo; B) medical cannabinoid compared with another antiemetic (neuroleptics).*

B)

	EXPERIMENTAL		CONTROL			
STUDY OR SUBGROUP	EVENTS	TOTAL	EVENTS	TOTAL	WEIGHT, %	RISK RATIO† (95% CI)
Ahmedzai, 1983	19	27	11	30	14.1	1.92 (1.13 to 3.26)
Chan, 1987	3	30	3	30	5.9	1.00 (0.22 to 4.56)
Dalzell, 1986	0	18	0	18		Cannot be estimated
Frytak, 1979	16	38	17	41	14.2	1.02 (0.60 to 1.71)
Herman, 1979	8	113	0	113	2.2	17.00 (0.99 to 291.06)
Hutcheon, 1983	35	81	27	81	15.5	1.30 (0.87 to 1.93)
Johansson, 1982	3	18	0	18	2.1	7.00 (0.39 to 126.48)
Lane, 1991	7	17	6	20	10.6	1.37 (0.57 to 3.30)
McCabe, 1988	9	36	0	36	2.3	19.00 (1.15 to 314.66)
Niederle, 1986	6	20	2	20	6.1	3.00 (0.69 to 13.12)
Niiranen, 1985	3	24	5	24	7.1	0.60 (0.16 to 2.23)
Orr, 1980	40	55	8	55	12.8	5.00 (2.58 to 9.68)
Sallan, 1980	6	15	1	12	4.0	4.80 (0.67 to 34.63)
Sheidler, 1984	1	16	2	16	3.2	0.50 (0.05 to 4.98)
Total (95% CI)		**508**		**514**	**100.0**	**1.85 (1.18 to 2.91)**
Total events	156		82			
Heterogeneity: $\tau^2 = 0.30$; $\chi^2_{12} = 30.22$ ($P = .003$); $I^2 = 60\%$						
Test for overall effect: $Z = 2.67$ ($P = .008$)						



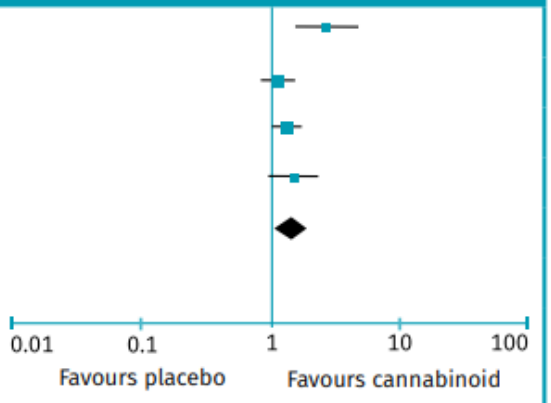
CFP·MFC
CANADIAN FAMILY PHYSICIAN • LE MÉDECIN DE FAMILLE CANADIEN
The official journal of the College of Family Physicians of Canada

Allan GM, Finley CR, Ton J, et al. Systematic review of systematic reviews for medical cannabinoids: Pain, nausea and vomiting, spasticity, and harms. Can Fam Physician 2018;64: e78-e94.

Spasticity

Figure 3. Responder meta-analysis of patients with a positive global impression of change for spasticity with medical cannabinoids compared with placebo

	EXPERIMENTAL		CONTROL			
STUDY OR SUBGROUP	EVENTS	TOTAL	EVENTS	TOTAL	WEIGHT, %	RISK RATIO* (95% CI)
Berman, 2007	30	56	12	60	16.8	2.68 (1.53 to 4.70)
Collin, 2007	66	124	31	65	29.6	1.12 (0.82 to 1.51)
Collin, 2010	72	141	56	144	32.2	1.31 (1.01 to 1.70)
Wade, 2004	32	79	21	77	21.4	1.49 (0.94 to 2.33)
Total (95% CI)		**400**		**346**	**100.0**	**1.45 (1.08 to 1.95)**
Total events	200		120			
Heterogeneity: $\tau^2 = 0.05$; $\chi^2_3 = 7.58$ ($P = .06$); $I^2 = 60\%$						
Test for overall effect: $Z = 2.46$ ($P = .01$)						



*Mantel-Haenszel method, random-effects meta-analysis.
Meta-analysis of studies from Whiting et al[2] (Berman, 2007, Collin, 2007, Wade, 2004) and Wade et al[28] (Collin, 2010).

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Where are We?

Cervical CA screening

Figure 2. Clinical Summary: Screening for Cervical Cancer

Population	Women aged 21 to 29 years	Women aged 30 to 65 years	Women younger than 21 years, women older than 65 years with adequate prior screening, and women who have had a hysterectomy
Recommendation	Screen for cervical cancer every 3 years with cytology alone. Grade: A	Screen for cervical cancer every 3 years with cytology alone, every 5 years with hrHPV testing alone, or every 5 years with cotesting. Grade: A	Do not screen for cervical cancer. Grade: D

U.S. Preventive Services TASK FORCE

Considerations

- New Partners
- Immuno-suppressed
- Abnormal screenings in the past
- DES exposure in utero

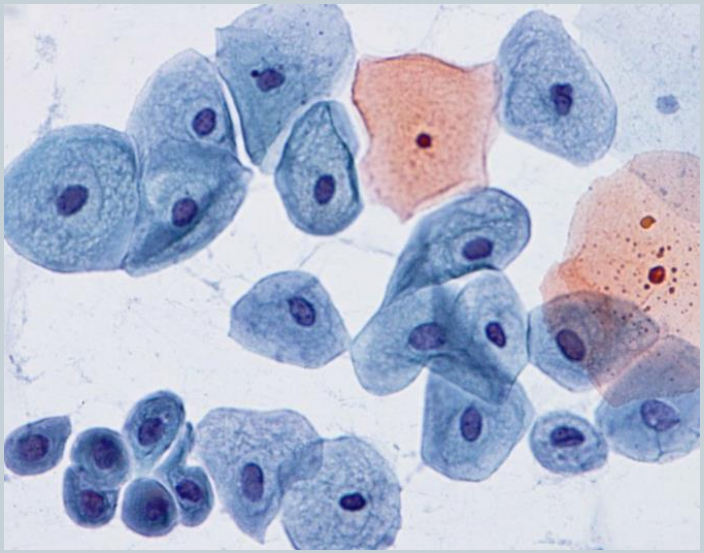


Table. Characteristics of Cervical Cancer Screening Tests

Method	Frequency	Evidence of Efficacy	Other Considerations
Women Aged 21-29 y			
Cytology	Every 3 y	Observational data[23] Modeling study[27]	Screening with cytology is recommended in this age group Screening with hrHPV testing is not recommended because of the transient nature of infection and natural clearance of HPV
Women Aged 30-65 y			
Cytology	Every 3 y	Observational data[23] Modeling study[3,27]	Cytology has lower sensitivity than primary hrHPV testing or cotesting and a lower false-positive rate and rate of additional testing The modeling study suggests that, compared with no screening, screening with cytology every 3 y can reduce the number of cervical cancer deaths from 8.34 to 0.76 deaths per 1000 women[a]
Primary hrHPV testing	Every 5 y	4 RCTs of hrHPV testing vs cytology (screening intervals of 3.5 y,[28,34] 4 y,[29,56-58] and 5 y[30,31]) 2 RCTs[37,54] of cotesting, with 13-14 y of follow-up of HPV-negative component 1 US prospective cohort study[53] of cotesting, with analysis of 5-y risk of death from HPV component Modeling study[3]	Primary hrHPV testing has adequate sensitivity; see the Clinical Considerations section for triage protocols following a positive hrHPV test result The modeling study suggests that, compared with no screening, switching from cytology to primary hrHPV testing every 5 y at age 30 y can reduce the number of cervical cancer deaths from 8.34 to 0.29 deaths per 1000 women[a]
Cotesting	Every 5 y	4 RCTs of cotesting vs cytology (screening intervals of 3 y[28,32,33,36-40,42] and 5 y[41,54,59]) 3 prospective cohort studies (United States,[46-51] Spain,[52] and Germany[60,61]) Modeling study[3]	Cotesting may detect slightly more cases of CIN than screening with hrHPV testing alone but with a significant increase in the number of tests and procedures The modeling study suggests that, compared with no screening, switching from cytology to cotesting every 5 y at age 30 y can reduce the number of cervical cancer deaths from 8.34 to 0.30 deaths per 1000 women[a]

Abbreviations: CIN, cervical intraepithelial neoplasia; HPV, human papillomavirus; hrHPV, high-risk humanpapillomavirus; RCT, randomized clinical trial.

[a] Outcomes calculated from models of cohorts of women aged 20 to 100 years; screening is assumed to end at age 65 years.

Curry, J. (2018). Screening for cervical cancer: US Preventive Services Task Force Recommendation Statement. JAMA.320(7):674-686. doi:10.1001/jama.2018.10897

WHAT IS HPV SELF-SAMPLING?

HPV self-sampling is an alternative screening tool for cervical cancer. It enables women to take a self-collected cervico-vaginal sample at home for HPV testing.

Early Solids and Infant Sleep

Earlier Solid Foods Introduction

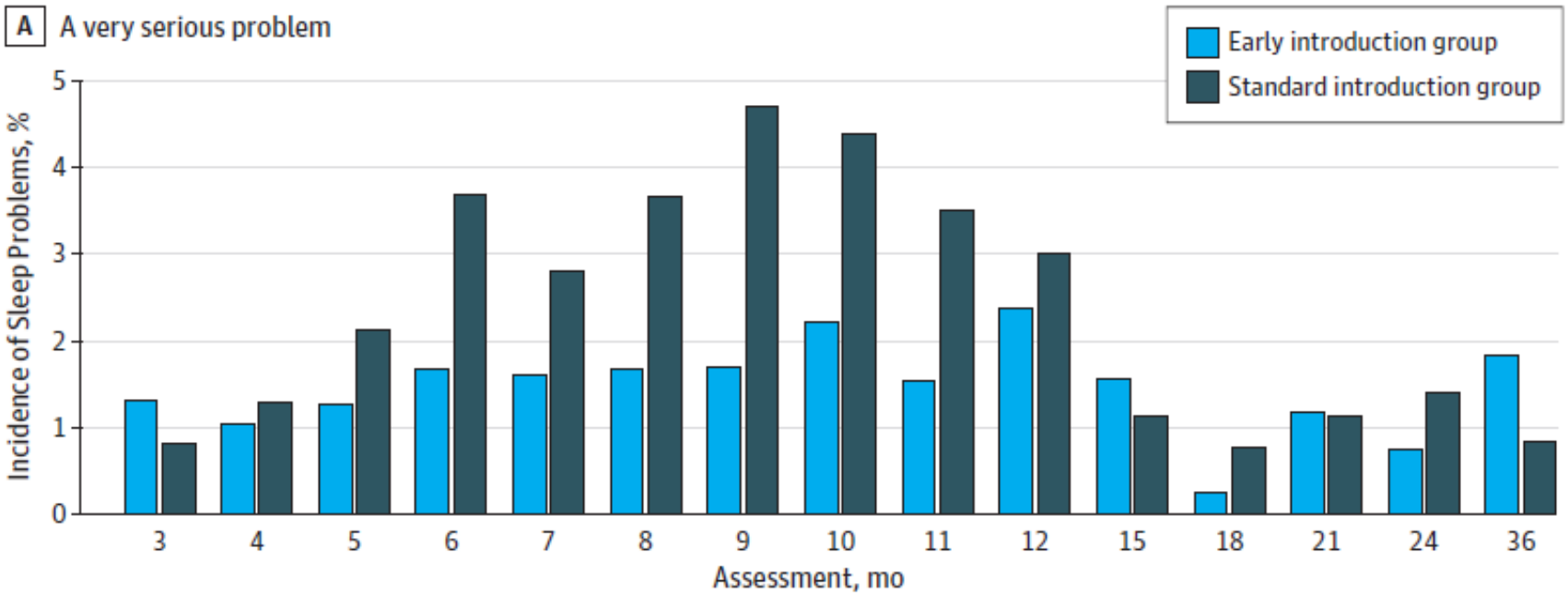
WHO/AAP Recommendation: Breast feed exclusively for first 6 months "The Perfect Food"

- RCT: 1200 babies, 6 months exclusive breastfeeding vs introducing solids at 3-5 months
- Infants in the EIG slept significantly longer (16.6 mins) and woke significantly less frequently than infants in the SIG (1.74 wakings vs 2.01)

JAMA Pediatrics

Perkin MR, Bahnson HT, Logan K, et al. Association of Early Introduction of Solids With Infant Sleep: A Secondary Analysis of a Randomized Clinical Trial. JAMA Pediatr. 2018;172(8):e180739. doi:10.1001/jamapediatrics.2018.0739

Figure 4. Parent Reporting of a Sleep Problem in Their Child by Study Group (Intention-to-Treat Analysis)



AAP Website

American Academy of Pediatrics

Breastfeeding:

- *Exclusive breastfeeding for approximately 6 months.*
- *Continue breastfeeding until the baby's first birthday or longer while mutually desired by mother and baby.*

Recommendations

- Start discussions with parents at around 2 mo: expectations about sleep and diet
- If there are sleep problems at ~4 mo, perhaps allow introduction of foods
- May cause decrease of breast milk, but rec's are still for continuing breast feeding

UK: "The proportion of mothers who achieve 6 months of exclusive breastfeeding is low, at around 1% in the last Infant Feeding Survey undertaken in 2010, and 75% of mothers had chosen to introduce solids by the time their baby was 5 months old."

NPH


U-100
NDC 59060-1834
Novolin® N
NPH, Human Insulin
Isophane Suspension
(recombinant
DNA origin)
100 units/mL 10 mL
ReliOn

NPH vs Long-Acting Analogs

Question: do long-acting insulin analogs like glargine (Lantus) or detemir (Levemir), reduce hypoglycemia, vs NPH insulin?

- NPH (Humulin N, Novolin N): much less $$

<u>Study: 2006-2015, Kaiser Permanente</u>

- 25k adults starting a basal insulin, not on insulin in last 12 months
- Risk of severe hypoglycemia: trend for lower in NPH starters (8.8 vs 11.9/1000 person-years)
- Glycemic control improved: .22% better **A1C** (significant)

JAMA

JAMA 2018;320(1):53-62.

Elective Induction of Labor at 39 weeks

Elective Induction of Labor at 39 weeks

- multicenter RCT
- routine labor induction of low-risk nulliparous women at 39 weeks (n = 3062) vs expectant management until at least 40 weeks 5 days (n = 3044)
- Rates of C sections: 19% (induction) versus 22% (expectant management) $P<0.001$
- 22,000 invited, 71% declined

The NEW ENGLAND JOURNAL of MEDICINE

Grobman WA, Rice MM, Reddy UM, et al, for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Maternal–Fetal Medicine Units Network. Labor induction versus expectant management in low-risk nulliparous women. N Engl J Med 2018;379(6):513-523.

Table 2. Primary Perinatal Outcome and Components.*

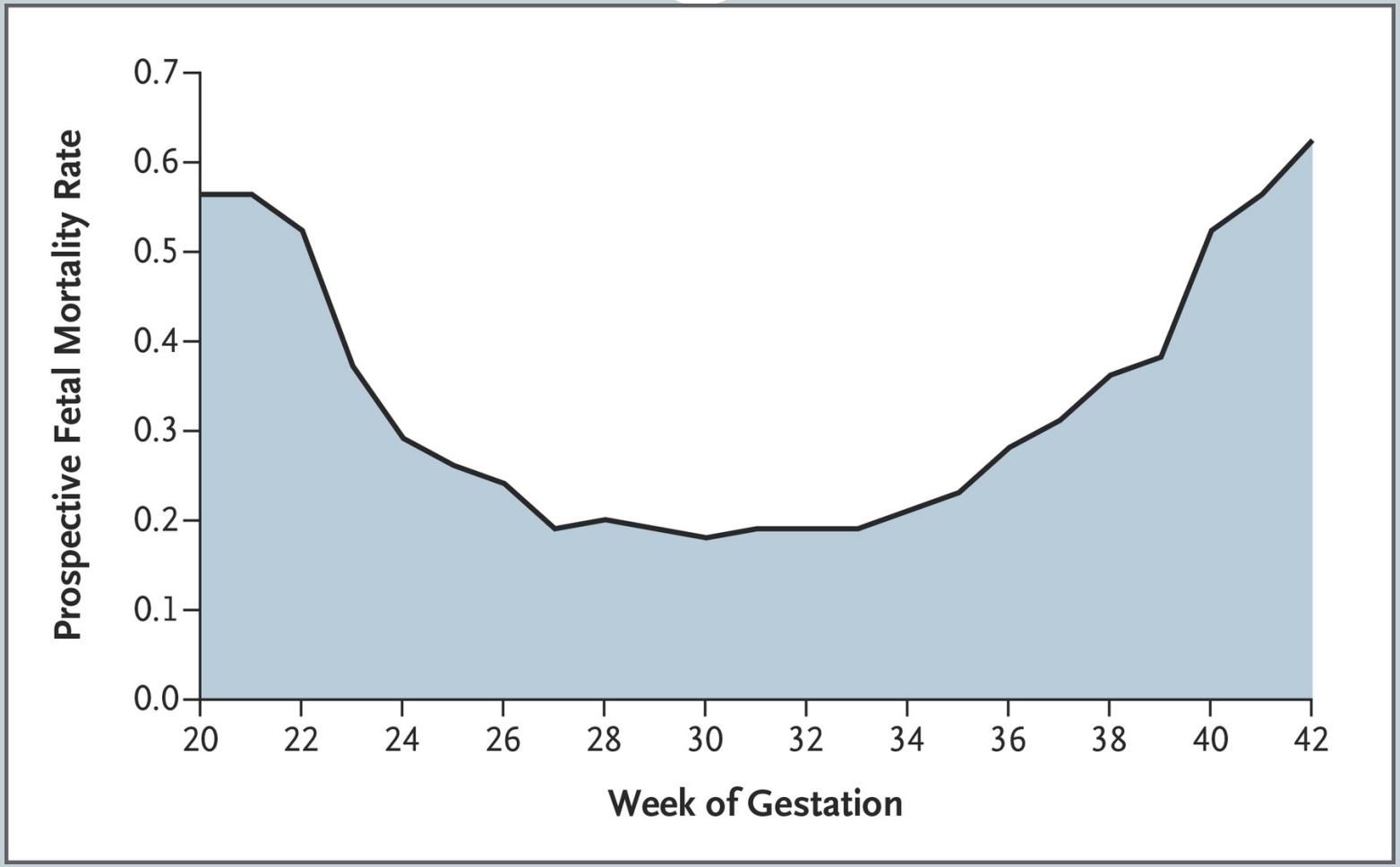
Outcome	Induction Group (N=3059)	Expectant-Management Group (N=3037)	Relative Risk (95% CI)†	P Value‡
	no. (%)			
Primary composite outcome	132 (4.3)	164 (5.4)	0.80 (0.64–1.00)	0.049
Perinatal death	2 (0.1)	3 (0.1)	0.66 (0.12–3.33)	
Respiratory support	91 (3.0)	127 (4.2)	0.71 (0.55–0.93)	
Apgar score ≤3 at 5 min	12 (0.4)	18 (0.6)	0.66 (0.32–1.37)	
Hypoxic–ischemic encephalopathy	14 (0.5)	20 (0.7)	0.70 (0.35–1.37)	
Seizure	11 (0.4)	4 (0.1)	2.74 (0.91–8.12)	
Infection	9 (0.3)	12 (0.4)	0.74 (0.31–1.76)	
Meconium aspiration syndrome	17 (0.6)	26 (0.9)	0.65 (0.35–1.19)	
Birth trauma	14 (0.5)	18 (0.6)	0.77 (0.38–1.55)	
Intracranial or subgaleal hemorrhage	9 (0.3)	7 (0.2)	1.28 (0.48–3.42)	
Hypotension requiring vasopressor support	2 (0.1)	5 (0.2)	0.40 (0.06–1.79)	

Cochrane Review

"A policy of labor induction at or beyond term compared with expectant management is associated with fewer perinatal deaths and fewer caesarean sections; but more operative vaginal births"

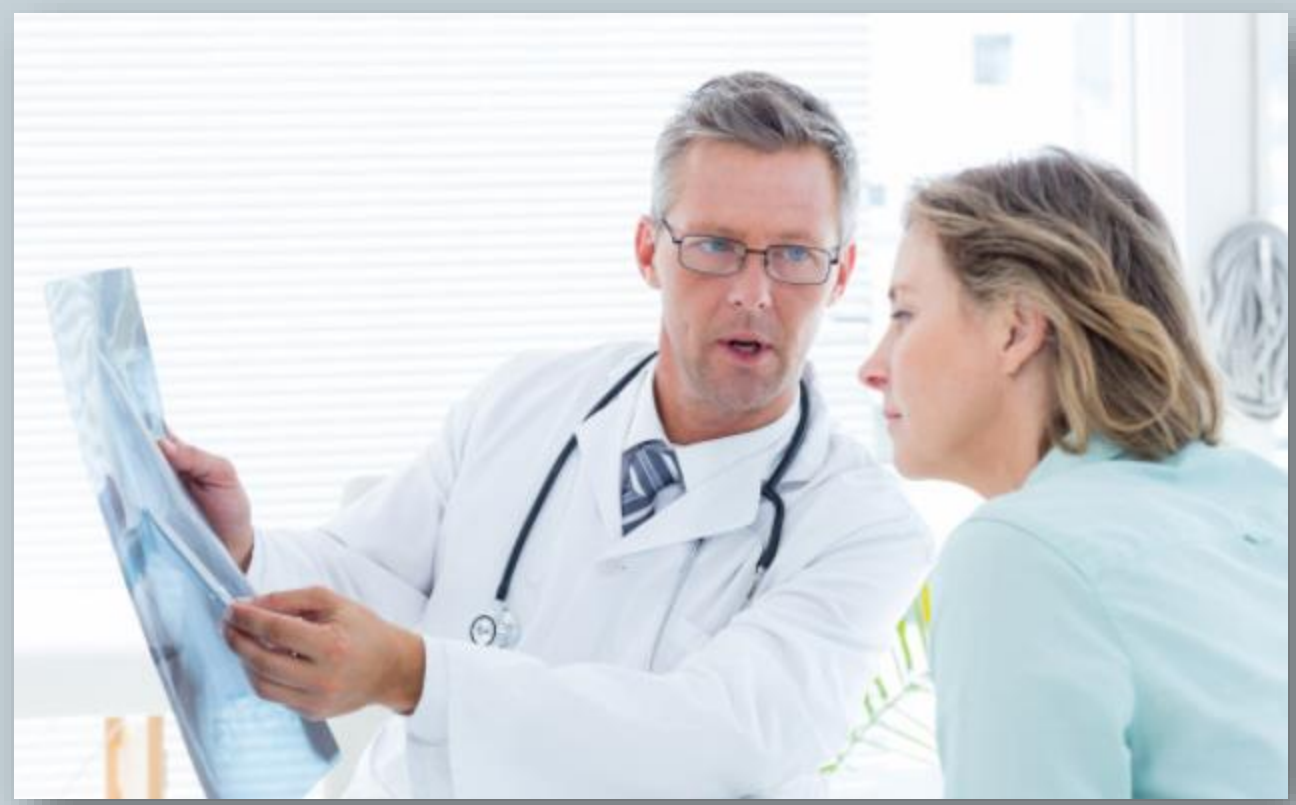
Cochrane Library

Cochrane Database Syst Rev. 2018 May 9;5:CD004945. doi: 10.1002/14651858.CD004945.pub4.



N Engl J Med 2018; 379:580-581
DOI: 10.1056/NEJMe1807747

Advice?



BP Readings

Are Office or Ambulatory BP Measures better Correlated with Mortality?

- large Spanish hypertension registry
- Looked at association between clinic BPs, ambulatory blood BPs, and mortality
- Looked at adults with a specific indication for ambulatory BP monitoring
- Included data on clinic BPs (automated devices after 5 minutes of seated rest) and 24-hour ambulatory BP measurements.

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2018;378:1509-1520.

Are Office or Ambulatory BP Measures better Correlated with Mortality?

Results

- mean ambulatory BP was 129/76, vs 148/87 in clinic
- all-cause mortality association seen with ambulatory BP but NOT clinic BP

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2018;378:1509-1520.

Is your office checking BP correctly?

Automated Cuff Preferred

- Seated for five minutes
- No caffeine/cigarettes for 30 minutes prior
- don’t talk to them, and they're not supposed to talk to you
- seated in a chair with their feet flat and their back supported
- make sure that your equipment has been calibrated, cuff is the right size
- arm should be positioned at heart level and pt should be relaxed
- A minimum of two pressures taken to count as elevated. If 1st elevated then you take a 2nd within one to two minutes

N Engl J Med 2018;378:1509-1520.

Quicker Summaries

Imaging for Breast Pain

- 799 Patients referred for breast pain
- Median age 43 (many young patients)
- Excluded: breast cancer history, nipple or skin findings of concern, lactating women
- 95% evaluated had negative findings (~5% benign findings)
- 1 cancer found: in opposite breast in a 70 y.o.
- If clinic exam normal and screening mammography negative (in age appropriate women) opt for reassurance

AJR American Journal of Roentgenology Diagnostic Imaging and Related Sciences

American Journal of Roentgenology 2018 211:1, 217-223

LR in Non-Critically Ill Adults?

- ED study
- 13,347 patients enrolled
- median crystalloid volume administered: 1079 ml
- **Balanced crystalloids**: lower incidence of major adverse kidney events within 30 days than saline (4.7% vs. 5.6%; adjusted odds ratio, 0.82)
- No difference in "hospital-free days"

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2018; 378:819-828
DOI: 10.1056/NEJMoa1711586

LR in Critically Ill Adults?

- 15,802 adult patients in 5 ICU's
- ICU's assigned balanced crystalloids or NS for a month and then alternated
- 14.3% "adverse kidney events" in crystalloid group vs 15.4% in NS
- Trend towards decreased 30d in hospital mortality (10.3% vs 11.1%, p = 0.06), **significant in subset of septic patients** (25.2% vs 29.4%)

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2018;378(9):829-839.

Steroids and Alcoholic Hepatitis

Severe alcoholic hepatitis (DF>32), carries very high 1 month mortality risk, guidelines recommend corticosteroids:

- meta-analysis of 16 RCTs
  - systemic corticosteroids (median duration, 1 month) vs placebo or no intervention
- no benefit on 3-month mortality other serious adverse events or QOL

Cochrane Library

Cochrane Database Syst Rev 2017 Nov 2

Vitamin D Plus Calcium Supplementation

- Guidelines: supplementation with ≥ 1,000 units/day vitamin D + calcium (commonly given at 1,000-1,200 mg/day) to community dwellers age >65
- Meta-analysis of 33 RCTs: no significant difference in risk of fractures- hip or otherwise
- Results similar for subgroups with 25-hydroxyvitamin D levels <20 ng/mL or with previous fractures

JAMA The Journal of the American Medical Association

Zhao JG, Zeng XT, Wang J, Liu L. Association between calcium and vitamin D supplementation and fracture incidence in community-dwelling older adults. A systematic review and meta-analysis. JAMA 2017;318(24):2466-2482.

Omega 3 FA supplements

- ASCEND Trial: Fish oil supplements in Diabetics don't reduce CV outcomes over 7.4 years

N Engl J Med 2018; 379:1540

Statins in Age >75

- Statins in patients >75 without CVD did not change the likelihood of developing CVD or reduce any-cause mortality.

- However, patients aged 75 -84 years **with diabetes** had less CVD development and mortality benefit (NNT 15.63)

BMJ

Ramos R, Comas-Cufi M, Marti-Lluch R, et al. Statins for primary prevention of cardiovascular events and mortality in old and very old adults with and without type 2 diabetes: retrospective cohort study. BMJ 2018;362:k3359.

And finally…

Stigmatizing Language vs Neutral Language

Curricula: *intended* vs *delivered* vs *hidden*

- Stigmatizing language : “refuses to wear his mask”… “narcotic dependent”… “hung out at McDonald’s”
- Neutral language: “not tolerating his mask”…“8-10 pain crises a year”…”spent afternoon with friends”

JGIM
Journal of General Internal Medicine

Goddu AP, O'Conor KJ, Lanzkron S, et al. Do words matter? Stigmatizing language and the transmission of bias in the medical record. J Gen Intern Med 2018;33(5):685–691.

Stigmatizing Language vs Neutral Language

- Simulation of practice, with students (233) and IM residents (180)
- Read one of 2 notes, then completed “Positive Attitudes toward Sickle Cell Patients Scale” then selected 1 of 4 treatments

JGIM
Journal of General Internal Medicine

Goddu AP, O'Conor KJ, Lanzkron S, et al. Do words matter? Stigmatizing language and the transmission of bias in the medical record. J Gen Intern Med 2018;33(5):685–691.

Stigmatizing Language vs Neutral Language

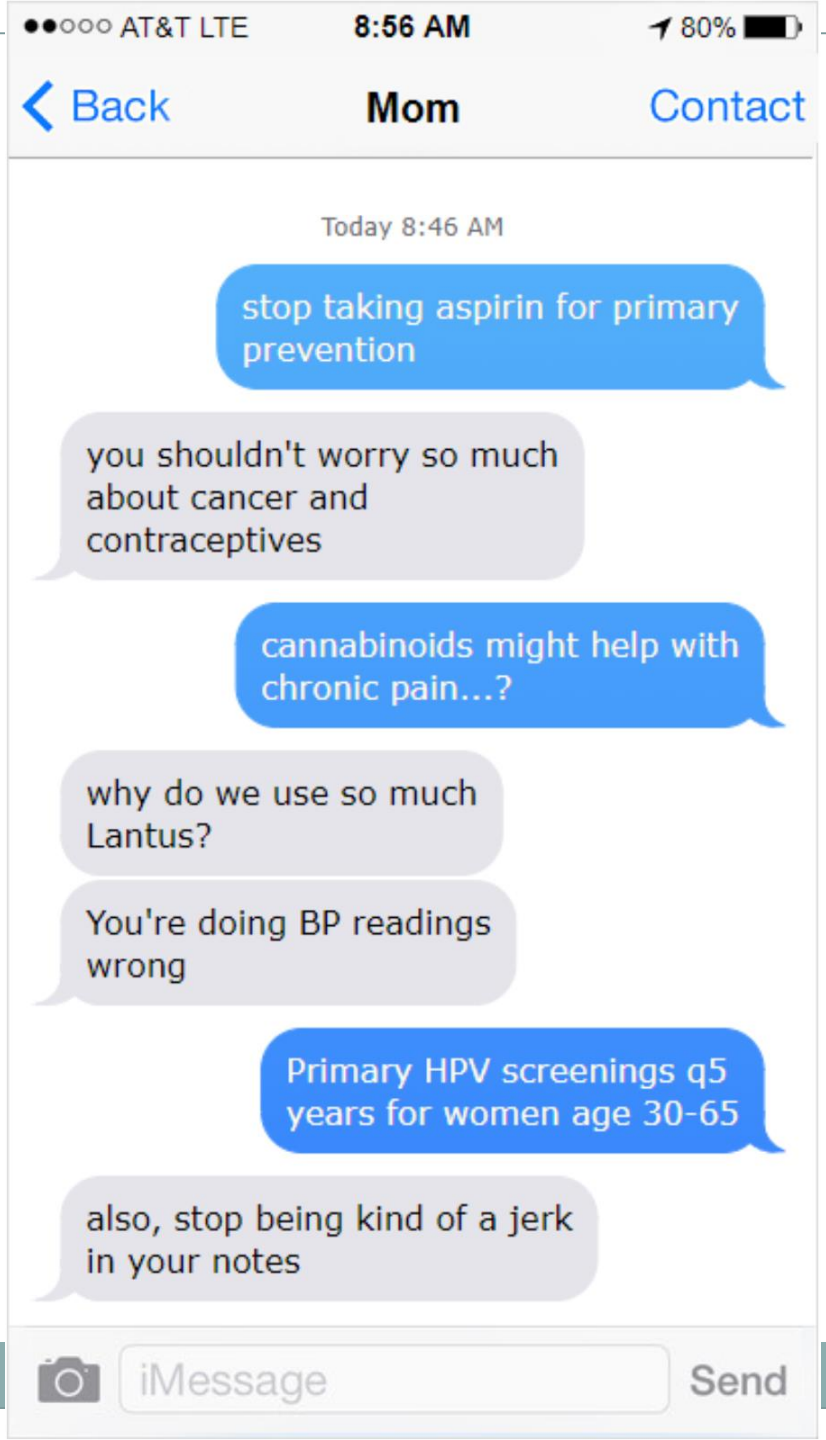
- Attitudes (on scale) were significantly lower for participants presented stigmatizing language
- Residents were more likely to select less aggressive treatment if exposed to stigmatizing language
- Attitudes worse with more years of training

JGIM
Journal of General Internal Medicine

Goddu AP, O'Conor KJ, Lanzkron S, et al. Do words matter? Stigmatizing language and the transmission of bias in the medical record. J Gen Intern Med 2018;33(5):685–691.

Interested in precepting medical students?
Email: SOM-Preceptorship@salud.unm.edu

Summary: What Do We Think We Know?


●●○○○ AT&T LTE
8:56 AM
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Back
Mom
Contact
Today 8:46 AM
stop taking aspirin for primary prevention
you shouldn't worry so much about cancer and contraceptives
cannabinoids might help with chronic pain...?
why do we use so much Lantus?
You're doing BP readings wrong
Primary HPV screenings q5 years for women age 30-65
also, stop being kind of a jerk in your notes
iMessage
Send

THANKS!